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PHYSIOLOGICAL RESPONSES IN MAN DURING COLD WATER IMMERSION

by

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ABSTRACT

The initial changes in ventilation which accompany immersion of men in cold water were determined by the rate of change of deep skin temperature, and under some circumstances also to the temperature gradient but not to the rate of change of the superficial skin temperature. There was no correlation of the ventilatory changes with deep or surface skin temperatures, nor with subcutaneous fat thickness. Two factors which attenuated the initial ventilatory responses and fall in end-tidal PCO_2 during cold water immersion were pre-heating in a sauna and clothing.

There was no evidence that circulating catecholamines were correlated with or that diazepam in the quantity ingested had any significant effect on the ventilatory responses. However a depressant action of alcohol on total expired ventilation as compared with the control was evident during immersions in water at 22° and 30°C.

The evidence of this study does not contradict previous statements that the changes in heart rate and blood pressure seen during immersion were thought to be due to increased sympathetic nervous activity rather than to a large increase in circulating catecholamines even though no significant correlation of these changes with increased dopamine-β-hydroxylase activity was seen. The ingestion of substances such as alcohol or diazepam in the doses given in this study had no effect on heart rate during the cold or warm water immersions.

There were no significant changes in body temperatures measured rectally and aurally during these short-term cold water immersions and neither alcohol (>80 mg $\cdot$ 100 ml^{-1}) nor diazepam in small doses affected

the body heat loss in the cold water.

The initiation of shivering appeared to be related to a specific deep skin, rather than a superficial skin temperature. The latency to shivering was longer during cold water immersions after sauna heating and alcohol consumption. Shivering could be abolished by performance of a mental arithmetic task and sometimes attenuated by a voluntary isometric forearm muscle contraction.

Recognition and recall were employed to test memory processes during acute cold water immersions. The only significant decrement in recognition was seen in the experiment in which subjects were given information while immersed and tested subsequently out of the water. The number of errors was significantly correlated to changes in end-tidal PCO_2, suggesting that a reduction in cerebral blood flow might have some effect on the learning process.

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INTRODUCTION

A. TEMPERATURE REGULATION

The relationships between environmental temperature and living creatures are many and varied. The fact that some organisms achieve a certain freedom and are able to maintain a constant temperature (homeothermy) because of frequently changing external temperature conditions, is a significant achievement. Even more remarkable than the actual maintenance of temperature within a narrow limit, is the regulation of this temperature in the midst of slight or severe fluctuations in the external environment. For homeotherms this regulation is generally accomplished by central integration of afferent information from receptors, central and peripheral, which monitor alterations in the body's temperature and the subsequent execution of appropriate measures, both physiological and behavioral, to ensure maintenance of temperature within the programmed normothermic range.

The elucidation of the actual mechanisms governing temperature regulation has generated much research from the late nineteenth century to date, in the areas of anatomy, physiology and biochemistry. However, the greatest developments have occurred in the last 20 years, in conjunction with recent advances in and sensitivity of the electrophysiological, biochemical, pharmacological and neurochemical techniques used (see reviews by Hammel, 1968; Hellon, 1975; Hensel, 1973; Lomax, 1970 and Satinoff, 1974).

A compilation of evidence to date from a wide assortment of animal studies allows the description of the hypothalamus and part of the brain stem as having neurons sensitive to temperature (Eisenman

and Jackson, 1967; Wit and Wang, 1968) and chemical input (Feldberg and Myers, 1963, 1965). The incoming information would herald some deflection from the "set-point" of about 37°C (an intrinsically established reference temperature around which appropriate adjustments are made) and suitable efferent pathways for heat conservation, production or dissipation would be stimulated, to allow the necessary correction to be made.

One of a number of models of the present concepts with regard to temperature regulation (Myers, 1974) is seen in Fig. 1. The data shown here are derived chiefly from experiments using the cat and monkey. The working of the system is envisioned in the following manner. In the anterior hypothalamic preoptic area arterial blood cooled below the normal set-point or afferent impulses from peripheral receptors stimulate the 5-hydroxytryptamine (5-HT) containing cells and 5-HT is released synaptically to trigger the heat production effector mechanism. Warm blood or agents such as antipyretics or anesthetics impinge on catecholamine containing cells and noradrenaline (NA) is released onto postsynaptic sites, to block the heat production pathway. This area is also sensitive to pyrogens and prostaglandins. Pathways between the anterior and posterior hypothalamus would appear to be cholinergic (Myers and Beleslin, 1971).

The posterior hypothalamus appears to be responsible for the maintenance of a set-point temperature and this is dependent upon the ratio between sodium and calcium ions (Myers and Veale, 1970). Some inhibitory pathways within the system are postulated so that the effector mechanisms of heat gain and heat loss do not cancel each other

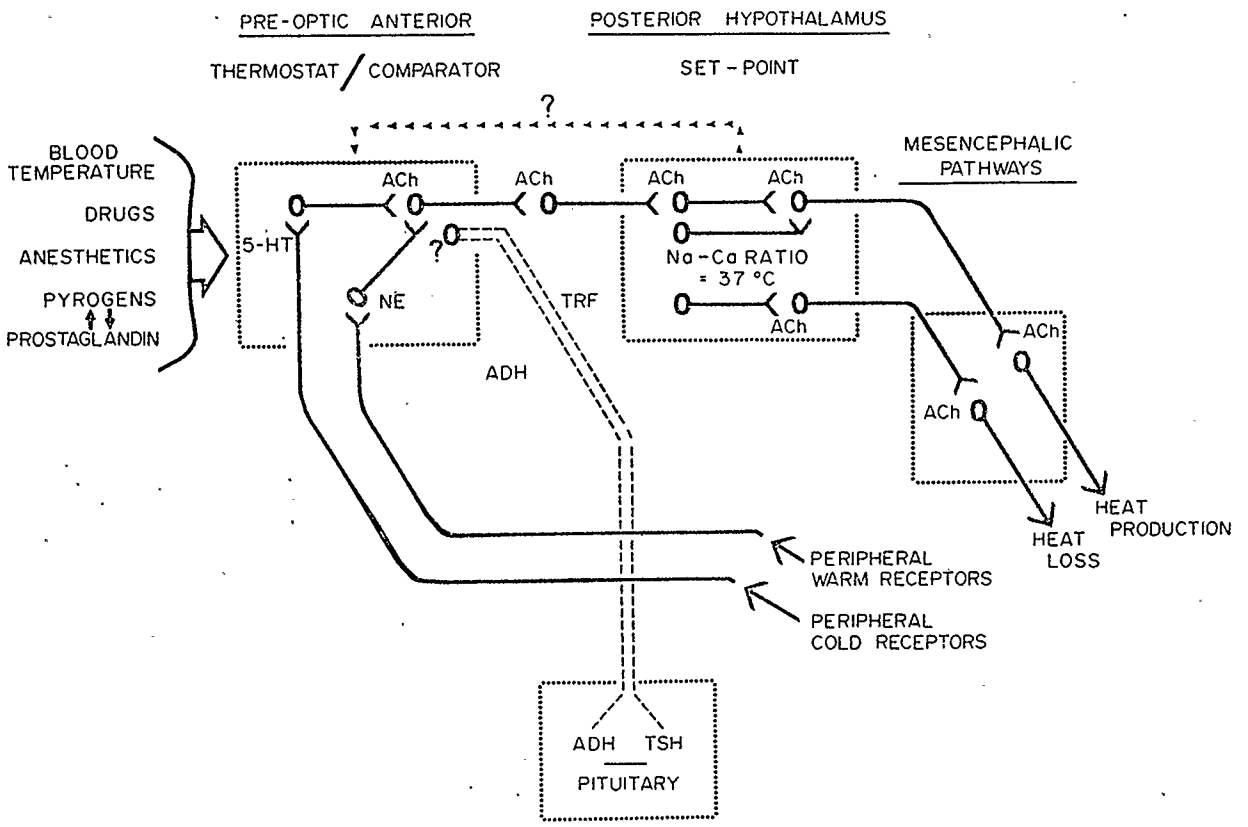

Fig. 1. Temperature regulation model based on data from the cat and monkey. ACH acetylcholine, NE norepinephrine, 5-HT serotonin. Explanation in text (Taken from Myers, 1974).

and thus prevent effective thermoregulation.

This thesis does not deal with the central mechanisms of thermoregulation as such, and this aspect is not reviewed in detail.

B. COLD EXPOSURE

Homeotherms can thermoregulate when exposed to a variety of environments, one of which is cold. When exposed for short periods to a variable range of temperatures below the neutral temperature zones, the organism initiates various actions which help to maintain a thermoregulatory steady state. These include increasing insulation, altering peripheral vasomotor control (vasoconstriction), behavioral responses (clothing and shelter) and shivering and non-shivering thermogenesis. However, if the period of cooling is extensive and body temperature continues to fall, the animal will exercise an all-out metabolic effort to maintain heat production. A further uncompensated decline in body temperature would be indicative of hypothermia, a state in which the body temperature of the homeotherm is of a variable range, lower than its viable temperature zone (Swan, 1974). Further decline in temperature is characterized by cardiovascular and respiratory difficulties and unless some external heat source is available, the animal has entered acute lethal hypothermia.

1. Vasomotor Control and Insulation

In order to decrease body heat loss in a cold environment, initial compensations are made such as hemodynamic changes with concomitant alterations in thermal insulation, as well as behavioral readjustments. The core and shell hypothesis (Aschoff and Wever, 1958) stated that the body has a central core region which consists of intra-

abdominal, intrathoracic, intracranial and variable amounts of deeper tissues of the limbs. The shell, a more peripheral area is composed of those tissues in which there are considerable variations in temperature. The relative importance of various body insulations for a man exposed to cold has been explored by Burton and Edholm (1955).

When exposed to cold there is a degree of vasoconstriction which serves to decrease the core area and allow for a larger shell and provide more resistance to heat loss from the central area. The decrease in blood flow to peripheral areas under these circumstances also serves to mitigate against heat loss. Burton and Bazett (1936) investigated changes in the conductance of tissues for the entire body, excluding the head, for subjects in stirred water baths of varying temperatures. They found the range of tissue insulation expressed as clo units to be 0.15 to 0.9 clo units from full vasoconstriction to vasodilation. They found that maximum insulation was reached in cool baths but that exposure to still colder water decreased the insulative value. The temperature at which this happened corresponded to the initiation of shivering as a means of increasing heat production. Thus, shivering serves to increase heat production in an effort to maintain body temperature but it does so at the expense of decreasing tissue insulation due to increased muscle blood flow.

The thermal insulation provided by various tissues has been the subject of investigation since the 1890's at which time it was suggested that adipose tissue was a better insulator than muscle (Bordin, 1898). The work of Lefèvre (1901) furthered the concepts of thermal insulation in skin and subcutaneous layers of persons immersed in water and found that vasoconstriction was elicited. An investigation

(Hatfield and Pugh, 1951) of the relative insulating power of fat compared to muscle has shown that fat was a better insulator, twice as good as muscle. It was found that changes in insulative value of muscle increased within 1 to 2 days while those for fat did not change. Although fat is an excellent insulator, the actual value might be less if the tissue is vascularized. There is variation in human subcutaneous adipose tissue blood flow, determined by radioactive xenon washout method, but the blood flow from a single depot is constant during a fixed time, 1 h (Bülow, Hansen and Madsen, 1976). LeBlanc (1954) showed that in man exposed to a cold environment of 50°F, the fatter subjects showed a slower onset to shivering, and at temperatures above this the increased fat layer provided sufficient insulation.

2. Shivering Thermogenesis

Shivering thermogenesis consists of synchronous contractions of flexor and extensor muscles (Bligh, 1973) and may be thought of as a coarse method of adjusting body temperature (Cooper, 1972) while fine adjustment is afforded by vasomotor adjustments and possibly non-shivering thermogenesis. The shivering effector response is mediated via motor nerves whose supraspinal (cerebrospinal and reticulospinal) and peripheral portions (alpha and gamma motoneurons) are known (Hensel, 1973) and the central nervous system (Johnston, 1966). Proprioceptive activity controls the rhythm of shivering (Perkins, 1945).

Various investigators have probed the mechanisms governing shivering and have attributed more or less weight to central and peripheral stimuli in the initiation of this process. Early investigators of the nature of the thermal stimulus which activates and controls shivering

(Lefèvre, 1911; Richet, 1893, 1898) concluded that both central and peripheral stimuli could act as a necessary stimulus in different experimental circumstances. The classic work of Sherrington (1924) pointed out that the shivering produced by cooling an animal with a spinal transection was the result of changes in blood temperature acting on a "center" higher than the spinal level. The importance of a central receptor was highlighted by the clinical investigations of Uprus, Gaylor and Carmichael (1935). Investigators have looked at changes in oxygen consumption consequent on cooled blood in various blood vessels, e.g. carotids, renal vessels, aorta and external jugular, and work with spinal lesion patients (C_7 to T_{10}) and have postulated the importance of a central regulation (Downey, Mottram and Pickering, 1964; Johnston and Spalding, 1964, 1966). A study was conducted by Fusco, Hardy and Hammel (1961) on metabolic and thermal responses on unanaesthetized dogs to localized heating of the hypothalamus at various environmental temperatures. They concluded that localized heating of and indirect cooling of the anterior hypothalamic-preoptic area (AHPOA) can initiate thermoregulatory responses and that these responses are modified by the peripheral temperature. There is some evidence of the sensitivity of the spinal cord in relation to a cold stimulus (Thauer, 1970), but its role in the actual control of shivering thermogenesis for most mammals needs to be clarified, although it has an influence in shivering in the guinea pig (Brück and Wunneberg, 1971).

A homeotherm transferring from a warm to a cold environment increases its oxygen consumption, by as much as 5 times the normal value. Studies of quietly seated subjects exposed to drastic temperatures 1°C to -40°C showed that an increased heat production above the basal levels

was evident and that shivering was approximately 11% efficient in protecting against total heat loss (Horvath, Golden and Wager, 1946; Sellers, Scott and Thomas, 1954). At a body temperature below 33°C, shivering is no longer an effective heat production mechanism, and is frequently supplanted by useless intensive muscle rigidity.

During exposure to cold, there is an increased mobilization of substrate, under the control of the sympathetic nervous system, which is available for the working muscle. The principle, but not the only substrate, utilized during cold exposure is lipid from white adipose tissue (Himms-Hagen, 1972). In addition, carbohydrate metabolism in skeletal muscle during shivering is controlled by adrenaline and noradrenaline (Himms-Hagen, 1967).

3. Non-Shivering Thermogenesis

This regulatory mechanism results in increased heat production by means other than shivering muscle movements. Thus, many body tissues could possibly contribute to an increased metabolic rate when exposed to cold, but it seems that some tissues are more particularly involved.

The idea of a non-muscular chemical process involved in heat production was first proposed by Claude Bernard (1876), and was thought to be distinct from physical thermogenesis (Rubner, 1902). However, this idea was not supported by the classic study of Cannon, Querido, Britton and Bright (1927). They showed that there was an increase in adrenaline from the adrenal medulla with a consequent rise in non-shivering as well as shivering thermogenesis, and thus proved that the central nervous system could mediate both physical and chemical thermogenesis.

The sympathicoadrenomedullary system was perhaps the first neuroendocrine system to be described. It is unique in that central

integrative centers in the hypothalamus and brain stem regulate in common a widely distributed network of noradrenergic terminals concerned with metabolic and vascular homeostasis and a motor supply to the adrenal medulla for release of adrenaline into the circulation. The involvement of hormonal influences in non-shivering thermogenesis during acute and chronic cold exposure has been explored by a number of investigators. If rats are exposed to cold ($3^{o}C$ for 1 month) there is an immediate increase in noredrenaline excretion (Leduc, 1961). This increased excretion persisted during the cold exposure but slowly decreased with time. However, Benedict, Fillentz and Stanford (1977) found that when rats were exposed to cold ($4^{o}C$), the plasma noradrenaline levels increased gradually during the first 4 h of exposure and then declined. An increased excretion of noradrenaline is also found in goats (Andersson, Gale, Hokfelt and Okaga, 1964) and this response can be blocked by substances which block ganglionic transmission with a concommitant reduction in shivering (Andersson, Brook, Gale and Hokfelt, 1964). Similar findings are evident when rats (Carlson, 1960) and baboons (Gale and Ruch, 1966) are exposed to cold.

The secretion of thyroid hormone sets an optimal level of metabolism for most tissues (Gale, 1973). Investigations have shown that the presence of thyroid hormone rather than the actual presence of the gland is required for the animal's survival when exposed to cold (Sellers and You, 1950). As a result of a number of animal studies, it would appear that thyroid and adrenal hormones are both required for the survival of animals exposed to cold (Carlson, 1960; Hsieh and Carlson, 1957; Sellers, Smith and Horowitz, 1969; You and Thomas, 1951). The present concept is that there is a synergistic action between thyroid

hormones and the adrenal catecholamines on adrenergic mechanisms in various tissues (Gale, 1973; Himms-Hagen, 1972).

This synergistic action occurs in brown adipose tissue. The tissue, first described by Konrad von Gesner in 1551, has been postulated to fulfill many roles. Extensive investigations beginning with that of Smith (1962) and expanded during the last 15 years have elucidated its proper role as a primary thermogenic source in the newborn and cold-exposed animal. The investigations have covered different species: rabbits (Dawkins and Hull, 1964; Hull and Segall, 1965a) and human neonates (Dawkins and Scopes, 1965) and similar patterns have been noted. During cold exposure, there is an increased blood flow to the brown adipose tissue (Hein and Hull, 1966) and an increased oxygen consumption by the tissue. It would appear that the increased heat production is mediated by sympathetic nerves which end directly on fat cells, since sympathetic denervation decreased the heat production during cold exposure (Hull and Segall, 1965b; Smith and Horowitz, 1969). The actual control of non-shivering thermogenesis is dependent on thermo-sensitive structures at the periphery and in the hypothalamus (Brück and Schwennicke, 1971).

4. Acclimatization

Many animals possess the ability to survive despite widespread and long lasting fluctuations in the environment. A variety of studies have tried to elucidate the neural and hormonal basis which might underlie such an ability. These experiments have been conducted with a variety of animals and under many conditions. In general, the area shall be considered under the aegis of either acclimation indicating alterations due to changes

in a life time, acclimatization, understood as physiological changes induced by a complex of factors such as seasonal and climatic changes (Hart, 1950) or adaptation understood as differences in genotype which favor survival in a particular environment, or on a broader basis, the morphological, anatomical, physiological, biochemical and behavioral characteristics of the animal which promote welfare and favor survival in a specific environment (Webster, 1974).

It does appear that most mammals will choose, behaviorally, to remain within a preferred range of ambient temperatures which can be defined physiologically as the thermoneutral range, within which the organism can maintain its thermal balance and body temperature without increasing heat production or heat loss. This range is not unalterable, and the critical temperature at which an increase in heat production is necessary to maintain the balance between heat loss and heat production can be lowered as a result of prolonged exposure to cold. Two physiological responses might account for the depression of the critical temperature, a reduction in thermal conductivity through peripheral tissues and an increase in metabolic rate.

Studies of arctic and tropical mammals and birds in Alaska and Panama, subjected to various air temperatures in a respiratory chamber were conducted by Scholander, Hock, Walters, Johnston and Irving (1950). They concluded that the wide range of critical temperatures in the different species indicated by the ambient temperature at which the metabolic rate deviated from a basal rate was largely due to genetic differences in thermal conductivity through peripheral tissues. A broad zone of thermoneutrality was evident for large arctic species ($+30^{o}C$ to $-40^{o}C$), and well adjusted arctic animals do not shiver in any

winter weather (Irving, 1951). However, tropical animals and birds exhibit a critical gradient of only 10°C on occasion, which makes them sensitive to small temperature changes. Acclimatization to cold often results in an increase in the overall insulation of many mammals, generally evidenced as an increase in the density and depth of the coat.

Changes in heat production can be considered under many headings. An increase in food consumption is evidenced during cold acclimatization and early investigators concluded that acclimatization was due primarily to an increase in metabolism. However, the actual role of basal metabolic rate in terms of cold acclimation or acclimatization poses some questions and mammalian experiments have resulted in conflicting evidence. Two studies have shown the importance of distinguishing between acclimation and acclimatization effects (Heroux, Depocas and Hart, 1959; Heroux, 1963), since some effects were noted in only one or other groups. The first study compared rats exposed to 6°C laboratory controlled temperature and those exposed to fluctuating environmental conditions. The second studied laboratory rats, acclimated to cold and kept in cages as groups or single animals, and wild rats trapped during midwinter. The duration of the experiment was 3 months. In both studies, an increase in thermoneutral metabolic rate was seen in all groups except the white rats kept outside. This change did not appear to be related to apparent changes in thyroid rate (an increase was noted in acclimated rats). It is also of interest to note that rats were acclimated in groups or as single animals, and this may have had some effect on one observation, i.e. hypertrophied endocrine glands in the single caged rats. A report of an investigation of arctic and tropical mammals and birds noted that cold exposure resulted in a slight increase in basal metabolic rate in

some species, and a decrease in others (Scholander, Hock, Walters and Irving, 1950).

Two very important effector functions which allow for increased heat production are shivering and non-shivering thermogenesis. The immediate response of the non-cold acclimatized animal to cold is by voluntary activity or shivering. In some species there is an increased ability to shiver during cold acclimation. This was illustrated in a study of the miniature pig, an animal lacking non-shivering thermogenesis, conducted by Brück, Wunnenberg and Zeisberger (1969). Other species do not show a similar behavior as illustrated by a study of laboratory rats (cold and warm acclimatized) who did not show an increased shivering during prolonged exposure to cold (Hart and Jansky, 1963). This fact has also been noted by other investigators who have found in the cold acclimated rat that shivering thermogenesis is replaced by non-shivering thermogenesis (Himms-Hagen, 1972).

The possibility that homeotherms could increase heat production by means other than shivering was first proposed by Bernard (1876). Research since that time has elucidated the possible mechanisms of the contribution to total heat production during acute or prolonged cold exposure and the tissues which are responsible for this activity. Studies of cold acclimated laboratory rats have indicated that non-shivering thermogenesis greatly increases while shivering is suppressed (Cottle and Carlson, 1956; Sellers, Scott and Thomas, 1954). It may be considered a facultative process, which does not occur continuously in the cold-acclimated animal or other animal possessing the necessary adaptation, but may be switched on and off in accordance with the need for the heat it produces (Himms-Hagen, 1972). It may not be correct to

say that non-shivering thermogenesis is intimately involved in cold acclimation or acclimatization for all species but its importance has been documented for some animals, e.g. rabbit, cat, rat and man (Davis, 1961; Davis, 1963; Hemingway, 1963; Himms-Hagen, 1972). The primary tissues involved in non-shivering thermogenesis are brown adipose tissue (particularly the neonate) and skeletal muscle (Himms-Hagen, 1972; Smith and Horowitz, 1969).

Various hormones are known to increase heat production, a concept first put forth by Claude Bernard (1876). A study of cold acclimated rats, exposed for 60 days in a cold room at $5^{o}C \pm 1^{o}C$, showed the importance of the sympathetic nervous system in controlling heat production (Hsieh, Carlson and Gray, 1957). Noradrenaline was more effective than adrenaline in preventing a fall in oxygen consumption. A 5-fold increase in urinary catecholamines was seen in the cold acclimated rats in comparison to the control group (LeBlanc and Nadeau, 1961). Similarly, an increased calorigenic response to noradrenaline infusion by lab rats undergoing cold acclimation was observed by Depocas (1960).

Another investigation by Hsieh and Carlson (1957) showed that the cold adapted rats which secreted larger quantities of noradrenaline became more sensitive to the metabolic effect of this catecholamine. This important finding was confirmed in another investigation (Depocas, 1960). These experiments underscored the fact that this increased sensitivity to noradrenaline was responsible for the non-shivering thermogenic pattern which characterized truly cold acclimatized animals. The verity of this assumption was proved by experiments in which animals that received daily noradrenaline injections became more

sensitive to this amine and at the same time showed a greater resistance to cold (LeBlanc and Pouliot, 1964). Thus, this enhanced calorigenesis, which is seen on continuous exposure to cold plus alterations in cardiac function (LeBlanc, 1975) illustrate the importance of the sympathetic nervous system in true cold acclimatization.

Early investigators had thought that the increased metabolic rate accompanying acute or chronic exposure to cold was mediated by increased production and utilization of thyroid hormone. Again, most investigations have centered around the laboratory rat and it has been concluded that some thyroxine is required for maintenance of the animals at low temperatures (Cottle and Carlson, 1960; Héroux, 1963), and that it may play an indirect role in the increased metabolic rates (Hsieh and Carlson, 1957). A recent investigation has found that hypothyroid rats could become cold acclimated and that this ability was related to increased sympathetic nervous system activity (Sellers, Flattery and Steiner, 1974). Earlier investigators had not found evidence for this fact (Chaffe and Roberts, 1971). The current concept is that a cooperative relationship exists between thyroid hormones and catecholamines during acclimatization to cold (Gale, 1973; Himms-Hagen, 1972; Swanson, 1957; Villemarie and LeBlanc, 1968).

Exposure to cold involves mobilization of a variety of physiological sources, e.g. increased shivering, and non-shivering thermogenesis and increased output of hormones such as thyroxine, adrenaline, glucagon (Kuroshima and Doi, 1976) and for a very short time corticosterone (Jenec, 1966). With the passage of time, these immediate responses became less and the animal becomes adjusted to the new environment without all systems operating at maximum or near maximum levels.

It would appear that some reorganization of heat producing and conserving mechanisms has been accomplished to allow for survival.

Not many acclimatization studies have been conducted with man as the experimental subject, but those which have been completed, in addition to investigations of different native groups have yielded interesting results. Studies of primitive peoples such as the Australian aborigine (Hammel, Elsner, Le Messurier, Andersen and Milan, 1959), the Kalahari Bushmen (Wyndham and Morrison, 1958), and the Alaculuf Indians (Hammel, Elsner, Andersen, Scholander, Coon, Medina, Strozzie, Milan and Hock, 1960) show that in these slightly clad groups exposed to cold for long periods of time there appears to be no undue demand on the organism. They apparently do not show increased metabolism in response to cold, but can survive by allowing a body cooling to occur to a level still compatible with life. Alterations in metabolism, i.e. increased response to noradrenaline was found in the Japanese Ainu divers and thus provides an ability to cope with the cold (Itoh, 1974). In groups exposed to moderate cold for long periods of time, there appears to be a true acclimatization.

Men were artificially acclimatized (Davis, 1961) and changes in shivering, oxygen consumption, rectal and skin temperatures in response to a standard cold exposure, were measured. He found that shivering thermogenesis decreased by the fourteenth day, and that the rectal temperature was maintained at a lower level after the exposure period. Whether man is ever exposed to a sufficient cold load in order to ensure true acclimatization has to be considered. Studies of man who spent time in Antarctica (Budd, 1962; Budd and Warhaff, 1967) concluded that acclimatization had occurred in men of European descent.

Increases in thyroid hormones (T_3 and T_4) during 2 to 3 days of exposure as well as fluctuations in cortisol concentrations were found in 4 men exposed to cold (Eastman, Ekins, Leith and Williams, 1974). Changes in noradrenaline levels have been found in man exposed to cold (Chaffe and Roberts, 1971).

Vasomotor responses to cold are designed to serve two conflicting objectives, the need to minimize heat loss and the need to maintain the integrity of the tissues. A number of people in occupations or environments that necessitate long bouts of cold exposure are able to withstand a local cooling which is painful to other persons. This phenomenon has been noted for Eskimos (Brown, Bird, Boag, Boag, Delahaye, Green, Hatche and Page, 1954; Eagan, 1963), Gaspé fishermen (LeBlanc, Hildes and Heroux, 1960) and Norwegian Lapps and fishermen (Krog, Folkow, Fox and Andersen, 1960). It is thought that blood flow to the hands must be more substantial and regular than in the normal population. Thus, these people have become acclimatized to a local cooling of the hands, and maintain a better heat flow in the hands during the immersion.

Thus, it appears that acclimatization in either a local area or for the whole organism involves a variety of neural and hormonal changes which occur in both the laboratory animals and man. The particular situation involving long or short exposure to either moderate or severe cold can elicit the proper response.

C. IMMERSION HYPOTHERMIA

Hypothermia may occur as a result of immersion in cold water or other circumstances which cause a person to be exposed to cold or wet and cold. This exposure may be the cause of collapse or death in

many situations not involving drowning. The physiological changes during hypothermia affect most body systems including the central nervous system, by altering such functions as metabolism, acid-base balance, circulation and respiration.

Immersion hypothermia was first studied by James Currie (1798), an eighteenth century Liverpool physician, who observed a continuing fall in body temperature (the so-called "after-drop") in a subject after removal from cold water and noted a slowing of the pulse rate which accompanied a decrease in body temperature.

For the next century and a half there was little or no research in the area of hypothermia. However, the 1930's saw a resurgence of interest in the mechanisms of hypothermia because of its use as a therapeutic tool for relief of patients suffering from cancer or schizophrenia. One such report (Talbott, Consolazio and Pecora, 1941) showed that the patient was maintained at a rectal temperature below 98^{o}F for 50 h, with a minimum of 80^{o}F attained. However, during the rewarming process, cardiovascular collapse ensued and the patient died. An intensive investigation of respiratory and metabolic effects of hypothermia was done by (Dill and Forbes, 1941) and the therapeutic effects of hypothermia were examined by Talbott (1941).

Although hypothermia in general had been investigated, the many fatalities of World War II, as well as loss of life in twentieth century shipwreck gave added impetus to the investigation of physiological and psychological effects of immersion hypothermia. These investigations studied survival time, cardiovascular and respiratory effects and possible central nervous system alterations following cold water immersion. In addition, the use of clothing and effect of work during immersion; the

the influence of alcohol, drugs and food added to the cold water stimulus, and the possible acclimation which may occur as a result of repeated exposure to cold water, were considered.

The prediction of survival time in cold water has resulted from a variety of investigations both during the war, Dachau experiments conducted by Rascher (Alexander, 1945; 1949) and after compilation of shipwreck survival data (Molnar, 1946), and from animal studies. Generally, it was found that the lethal limit for smaller animals, e.g. rats, was water at 14.8°C (Adolph, 1948) whereas larger animals, e.g. dogs could maintain thermal balance for some time in water at 0°C but were impaired when rectal temperature decreased to 27°C (Spealman, 1946). These differences might be expected because of the smaller surface area/mass ratio.

Compilation of data from various investigations of clothed and unclothed persons of different body sizes (Alexander, 1946; Keatinge and Sloan, 1972; Kreider, 1967; Molnar, 1946; Spealman, 1946; Wayburn, 1947) allowed the prediction of survival times of humans in very cold water and the level to which rectal temperature could decrease before respiratory and cardiovascular irregularities ensued. More persons survived for a specific time when the range of rectal temperature was between 29.4°C to 32.2°C, than when it was lower, although survival was documented at a rectal temperature of 23.8°C. This was considered the lower limit, but there are cases on record of survival when rectal temperature of 18°C (Laufman, 1951) or 9°C (Niazi and Lewis, 1958) had occurred as a result of accidental hypothermia or surgical procedure. As a result of recent work, Hayward, Eckerson and Collis (1975) have devised a prediction equation for the survival time of the average person accidentally immersed in cold water. The results

are in agreement with earlier studies, but do predict a longer survival time in the colder waters than these earlier estimates. However, the equation does not account for survival times in the event of rough seas, or for the person in an exhausted or alcoholic state.

An interesting consideration emerges from Molnar's chart (1946) and the subsequent U.S. Navy table for life expectancies for persons immersed in water, at various temperatures without protective clothing, and supported by life jacket. The chart implies that immersion at 20°C and above is consistent with infinitely long survival. However, experiments in which male, nude subjects were immersed for a 12 h period in water at 20°C to 25°C highlighted some physiological responses which might limit survival (Beckman and Reeves, 1966). The mean tolerance time for the subjects was 8 h. Factors which called for the termination of the experiment and could thus limit man's survival time were: a slow decrease in rectal temperature to below 35°C, extreme discomfort due to muscle cramp following prolonged shivering and a decrease in blood glucose below 60 mg %. Whether or not any water temperature could be considered "neutral" in which no change in body temperature occurred after 1 h immersion was investigated by Craig and Dvorak (1966) who found a narrow range of 35.0°C to 35.5°C fitted the definition. However, this neutral condition applied only to resting subjects.

Men immersed in cold water (5°C or 15°C) manifested the typical pressor response to cold, i.e. an increased heart rate and arterial pressure (Keatinge and Evans, 1961). As a result of various investigations on intact animals and isolated preparations (Bigelow, Lindsay and Greenwood, 1950; Covino and Beaver, 1958; Currie, 1798; Hegnauer, Shriber and Haterius, 1950; Knowlton and Starling, 1912), it would appear that the

major effects of hypothermia on the cardiovascular system are slowing of the pacemaker, decreased heart rate, cardiac output and force of ventricular contraction, an increase in central venous pressure and an increase in systolic duration and isometric relaxation. The end result may be cardiac arrest or ventricular fibrillation, which condition may be apparent at a rectal temperature of 25°C, and is definitely seen at rectal temperatures below 20°C.

Deep hypothermia affects most measureable respiratory phenomena: there is a shifted oxygen dissociation curve; blood-gas relationships are altered by the increased solubility of carbon dioxide at the lower temperature, and there is a possibility of bubble formation on warming. Both central and reflex control of respiration are depressed; and there is usually an increased respiratory dead space and varying degrees of metabolic and respiratory acidosis occur (Severinghaus, 1959).

Hypothermia was thought to affect gaseous differences in the lungs and to decrease carbon dioxide excretion (Dill and Forbes, 1941). However, experiments on dogs and human patients showed that there was no significant alteration in alveolar dead space or a-A PCO_2 difference; thus, no impairment in carbon dioxide excretion existed (Severinghaus, Stupfel and Bradly, 1957).

Some interesting respiratory responses are noted within the first 1 to 2 min of cold water immersion. These include a fall in end-tidal PCO_2 which is usually sustained, associated with a high pulmonary ventilation (Keatinge and Evans, 1961). The response is so rapid that it is thought to be a reflex initiated by cold receptors in the skin and mediated at midbrain level (Keatinge and Nadel, 1965). The exact mechanism is not known and could be related to absolute surface

or deep skin temperatures, rates of changes of these skin temperatures or existing temperature gradients. Adrenaline and noradrenaline appeared to have no effect on the respiratory responses during the initial immersion time (Keatinge, McIlroy and Goldfien, 1964). The rapid decline in ventilation which is apparent after the first minute is thought to be due to adaptation of cutaneous cold receptors to low skin temperature (Keatinge and Evans, 1961).

Renal and metabolic activities are also affected by hypothermia. Perhaps the most serious renal consequence is excessive sodium and water excretion (Keatinge, 1969) which may result from impairment of renal tubular cells by cold, since cooling dogs to $24^{o}C$-$23^{o}C$ by immersion in an ice bath was found to affect minimal tubular excretion of para-aminohippuric acid (Blatteis and Horvath, 1958). This salt and water excretion could lead to a decreased blood volume and result in the serious problem of reduced arterial pressure and consequent cardiovascular collapse when the person is being reheated.

It would appear from the evidence reviewed that the acid-base condition during hypothermia veers towards acidosis. This respiratory acidosis develops quickly as ventilation is decreased at lower temperatures. A great deal of research during this century has attempted to delineate the actual factors responsible for this state in the various stages of hypothermia. Dill and Forbes (1941) described a respiratory acidosis in their patients which was paradoxically and apparently compensated for by hyperventilation. Boère (1957) and Bigelow, Callaghan and Hopps (1950) described an acidosis which ensued during hypothermia utilized

for cardiac surgery. The possible effect of intermediary enzymes in carbohydrate metabolism were considered as a causitive factor, in the latter case.

Other experiments with anesthetized dogs, in which hypothermia was induced by blood stream cooling, have confirmed the respiratory acidotic state during hypothermia (Cranston, Pepper and Ross, 1955). The fall in pH was shown to be due to a retention of carbon dioxide, this being largely due to the increased solubility of the gas at lower temperatures. The importance of the physiochemical factor, which is related to solubility changes, changes in protein buffer systems and the dissociation of carbonic acid, in determining the pH at lowered temperatures was echoed by Axelrod and Bass (1956). The importance of increased solubility as an important determinant of pH is questioned by Severinghaus (1959) since the effect of lowering pH is opposed by increased affinity of hemoglobin and other blood proteins for hydrogen ions at a lowered temperature.

Anesthetized dogs cooled by cold air were investigated by Kao and Schlig (1956) and two types of responses occurred, cooling with and without shivering. During shivering, ventilation increased and a respiratory alkalosis was evident. In the second response there was a diminution of the total ventilation resulting in a respiratory acidosis. Whether a renal loss of bicarbonate might contribute significantly to the acidosis of hypothermia was considered by Kanter (1962). Excretion of bicarbonate during hypothermia was studied in 5 infused (6% creatinine in saline at 0.4 $ml.min^{-1}$) and 5 non-infused dogs. In the latter there was no significantly increased excretion while in the former there was an increased excretion but not a sufficient

amount to account for the decreased arterial pH.

There is some evidence in the literature that a metabolic acidosis may be apparent during hypothermia. There is a two-fold decrease in metabolic rate for a $10^{o}C$ fall in body temperature but if the experimental animal is allowed to shiver, the blood lactic acid rises and since it cannot be rapidly metabolized at a reduced body temperature it could contribute to some degree of metabolic acidosis (Cooper, 1968). However, it is not usually severe enough to cause significant change in pH (Keatinge, 1969). A metabolic acidosis was also reported by Severinghaus (1959). If surface cooling is used to induce hypothermia a degree of metabolic acidosis is evident, but this pattern is not seen if extracorporeal thermoregulation is used. Changes in pH are primarily due to respiratory factors (Trede, Foote and Maloney, 1961).

The physiological responses to cold water immersion may be augmented or decreased by various factors such as exercise, clothing, subcutaneous fat, alcohol and drugs. Exercise during cold water immersion results in a more rapid loss of body heat possibly due to increased muscle blood flow (Cannon and Keatinge, 1960; Keatinge, 1961). This decrease was attenuated by clothing, particularly at cooler water temperatures (Keatinge, 1961). The rate of body heat loss by a resting subject can also be decreased by the adoption of thermally protective behavior, e.g. self-huddle, while immersed in cold water (Hayward, Eckerson and Collis, 1975).

The built-in insulation of the body depends primarily on subcutaneous fat. A number of studies, using male and female subjects, in cold water and cold air have indicated that a greater tolerance to the cold stimulus is shown by subjects with a greater subcutaneous fat

thickness (Bullard and Rapp, 1970; Daniels and Baker, 1961; Kollias, Bartlett, Bergsteinova, Skinner, Buskirk and Nicholas, 1974; Pugh and Edholm, 1955; Sloan and Keatinge, 1973).

One area of study which seems to have received little attention is the effect of alcohol or drugs and cold water immersion. A previous investigation showed that if resting men were exposed to ambient air temperature of 20°C after alcohol ingestion, there appeared to be no deleterious results (Andersen, Hellstrom and Lorentzen, 1963). However, at 15°C, 1 subject showed a difference in body heat loss as a result of alcohol consumption. It subjects exercised severely, then ingested alcohol and were exposed to cold air, a rapid decrease in body temperature resulted (Haight and Keatinge, 1973). This appeared to be due to a profound fall in blood glucose associated with a failure of the metabolic response to cold, rather than changes in skin circulation. Since the thermal conductance of water is greater than air, it might be expected that alcohol ingestion and cold water immersion would produce significant changes in body temperature. However a study showed that neither alcohol nor hyoscine appeared to have any effect on heat loss during the immersion period (Keatinge and Evans, 1960).

Frequent exposure to cold water does result in acclimatization. Investigators have considered both whole body and limb immersion. In the latter category, Gaspé fishermen had a lower pressor response, higher finger temperature and had a greater heat flow from the hand in comparison to the control group (LeBlanc, Hildes and Heroux, 1960). The studies of the Japanese and Korean diving women have shown they have naturally thicker layers of subcutaneous fat than men (Hong, 1963) and show a lower critical water temperature which allows them to have a reduced

core temperature without shivering (Rennie, Corino, Howell, Song, Kang and Hong, 1962). They exhibit an increased maximal time insulation for a given subcutaneous fat thickness, which may be coupled with either more extensive vascular constriction or a more effective countercurrent heat exchange in the limbs (Hanna and Hong, 1972). Studies of divers in Scandinavian waters also indicate that during short term acclimation there was a tendency to favor heat conservation over heat production mechanisms to maintain a constant rectal temperature (Skreslit and Aarefjord, 1968).

D. SUDDEN DEATH IN COLD WATER

There has been some documentation of cases of sudden death during the initial phase of a cold water immersion. Since hypothermia was not responsible it would appear that initial changes in either the cardiovascular or respiratory responses might account for these cases. The possibility that ventricular fibrillation, due to increased venous and arterial pressure, hyperventilation and adrenaline, might be responsible for these deaths was put forth by Keatinge and Evans (1961). A later study indicated that sympathetic reflex pathways were involved in cardiovascular changes (Keatinge, McIlroy and Goldfien, 1964). Thus increases in arterial pressure and cardiac output together with a decreased $PACO_2$ (Brown and Miller, 1952) might favor ventricular fibrillation in susceptible people.

The central depressant effects of cold in the respiratory centers are more evident and disastrous in small non-hibernating animals than in man. Although some respiratory depression occurs in man, it is ordinarily not severe enough to be dangerous at temperatures too high to cause cardiac

failure, but could cause problems in an anesthetized man (Severinghaus, 1959), where an additive effect of cold and a central depressant would be evident. However, for a person swimming in cold water, the intense reflex respiratory responses which are initiated, could be intolerable and might account for sudden death of these persons when immersed (Keatinge, Prys-Roberts, Cooper, Honour and Haight, 1969).

E. COLD WATER AND MEMORY

The accomplishments of human memory range from storage of visual, verbal and auditory information to abilities to do specific tasks in varied areas. The first organized attempts to understand the processes involved in human memory date from the nineteenth century. These studies included a description of pathology associated with memory (Ribot, 1882), who also described aspects of memory such as recollection and registration; description of the amnesia syndrome by Korsakoff in 1889 and a well-organized study by Henry James (1890) in which he refers to primary and secondary memory. The first systematic study of certain effects of memory was done by Ebbinghaus (1885) in which he covered a number of factors affecting memory such as attentiveness, repetition, individual differences in memory and differences in material to be retained.

The development of sophisticated techniques during the last few decades has allowed the research on memory to be covered from biochemical, neurophysiological as well as psychological viewpoints. As man develops his ability to acquire and master various skills, he requires development and integration of sensory and motor correlates and a brain structure capable of handling the complex system. The presently held idea is that the storage of information in the brain is accomplished by

means of a "memory trace" or engram (Altman, 1967). The storage of new information is visualized as a dynamic activity produced by new input patterns in an unchanging control system. The memory trace may occur as a result of "reverberating circuits", first proposed by Hebb (1949). It is feasible that this concept may account for the storing capacity designated as short-term memory. The importance of neuronal local circuits in higher brain functions has been highlighted by Schmitt, Dev and Smith (1976).

Other memory traces, referred to as secondary or long-term cannot be accounted for on an electrical circuit basis. Research in this area has considered the possibility that structural alteration, or biochemical modification might occur as an engram is formed. A variety of studies are available which have considered the changes in brain protein synthesis which occur as a result of training (Hyden and Egyhazi, 1964; Rose, Hambley and Haywood, 1976; Shashoua, 1976) The actual mechanism, if indeed there is one, to account for memory has still to be elucidated..

The information acquired via various sensory modalities can be processed. Some type of change occurs in the originally received material and it is said to have been coded. Each step in the storage system may elicit a change. The three steps most commonly considered arethose involving sensory information storage, short-term memory and long-term memory.

The afterimage can be used as an example of sensory memory. The characteristics of this kind of memory are that it is brief, lasting only tenths of a second; is able to deal with all of the physical

stimulus energy that can be handled physiologically and anatomically by the receptor; and is able to encode information in a direct fashion (Krech, Crutchfield, and Livson, 1974; Sperling, 1960). The length of time the information stays in the sensory memory is important, in view of the fact that it is only glimpsed for a very brief time. This brief visual memory referred to as an icon (Neissen, 1967), is a representation. Sensory memory in fact does perceive and store more than will be utilized by later steps in the storage systems. It thus serves an excellent purpose in that a wealth of information can be stored for a short period and the processes of pattern recognition are then able to pick and choose (Lindsay and Norman, 1972).

A variety of everyday happenings, e.g. looking up a telephone number, provide us with the fact that some information is retained for a longer time interval than that approached by the sensory information storage. A rather simple but classic experiment (Peterson and Peterson, 1959) in which subjects were asked to remember 3 letters and then asked to recall the correct sequence after various time intervals of 3, 6, 9, 12, 15 and 18 sec. In the interval between the task and the test, the subjects had been given a distracting task and thus were prevented from rehearsing the original consonants. After 6 sec, only 40% could correctly recall the original string, while at the end of 18 sec only 10% were able to perform the recall adequately. Rehearsal would thus appear to be requisite to the transferral of information from this level to long-term memory. This short-term memory storage system is characterized by a longer time (up to 20 sec) in comparison to sensory information storage, and has a limited capacity, e.g. 7 numbers (Miller, 1956), and requires rehearsal in order for information to be

further processed (Peterson, 1966; Waugh and Norman, 1965). Information in short-term memory may be forgotten because of the passage of time or because of interference by other material.

Long-term memory, as its name implies, is able to store information over long periods of time, from 1 min to many years, and has an enormous capacity. Thus, it is most necessary that efficient coding occur to allow for such memory store. Although there may be some question about the feasibility of a two memory system, the weight of the evidence to date would support this concept (Wickelgren, 1973). Investigations by Murdock (1962) showed a precise difference in long- and short-term memory in relation to a particular work list table and noted that longer exposure and consequently longer rehearsal time allowed for improvement in this memory store. Evidence to date, culled from various free recall experiments, would indicate that grouping of items, known variously as chunking or clustering, helps in the prodigious accumulation of information by this memory store (Murdock, 1962).

Common experience tells us that there is not the rapid decay of information from this store as seen in the two initial memory stores and experiments would tend to support the fact that interference either by material learned before the original learning task, or acquired between the learning and test situations, does cause loss from the long-term memory store. In addition, there may be active forgetting (Krech, Crutchfield and Livson, 1974).

For the proper storage of information in long-term memory

there must be consolidation. This process is defined as the process whereby a circuit is altered so that a new memory is encoded (Lindsay and Norman, 1972). This process is envisioned as occurring over a period of time, and two possible mechanisms most frequently considered as contributing to this consolidation are chemical encoding or growth of new synaptic junctions.

Chemical encoding visualizes the possibility that if long-term memory resides in the structure of protein molecule at the synapse it could exert its effect on the actual transmission of neural information across the synaptic cleft. The other consideration would imply that long-term memory occurs because of new synaptic growth. If this were true, there would be physical changes, whenever new concepts are learned. In theory these changes might be visible with the aid of a microscope. However the great difficulty attendant on the actual viewing of live neurons while they are responding to neural activity has made definite proof of this theory virtually impossible. Although the actual system utilized for encoding a permanent memory is not known, the above two possibilities indicate that the synapse maybe where the effect occurs.

Once information is stored in either short- or long-term memory, the process of retrieval allows it to be taken out and used. This may be accomplished according to Sternberg (1966) by means of serial processing (one at a time) or all at once, parallel processing (Neisser, 1967).

In order to judge if a specific task has been learned, the measures of recall and recognition can be utilized. These respectively mean the ability to reproduce previously learned material and the ability

to identify previously learned material from a large array of items (Krech, Crutchfield and Livson, 1974). The actual learning process and its retention of verbal and other information will in turn be influenced by a number of factors including amount of material presented, time for repetition, meaningfulness of material, the mental image evoked by material, the relationship of items comprising the total amount to be mastered and whether or not the information to be learned is similar to or different from previously acquired facts, and the degree of attention given to the task.

Memory, the basis of which may be functional and/or structural, can be separated into three different stores, each with its particular characteristics. Various perturbations can affect the storage of information by interfering with acquisition of information, its coding or retrieval.

1. Non-Human Studies

The proper retention and utilization of information is dependent on a number of factors, some of which have been outlined in a former section. How well does an animal learn if the environment is altered and how does its performance compare to that of the normal situation?

Some of the investigations in this area have been based on animals exposed to a hyperbaric environment or made hypothermic, usually by immersion in cold water. Truitt and Gottlieb (1976) have shown that if mice are exposed to increased oxygen tension (6ATA O_2) or to increased air pressure (6ATA) there were no deleterious effects on retention of a learned task. Interference with memory, possibly the consolidation process, occurred only when the animals were subjected to oxygen-induced

convulsions.

The use of hypothermia administered shortly after training has been used fairly extensively in attempting to delineate the existence of an early or short-term memory phase. Whole body hypothermia was thought to delay the process leading to memory consolidation, as well as engender specific deficits (Gerard, 1955). Other studies (Mrosovsky, 1963; Ransmeier, 1953) in which rodents were made hypothermic showed no direct proof for a cold related memory loss in relation to a multiple-trial task. Failure of these results to comply with most others reported in the literature might be due to the fact that the initiation of the hypothermic state was delayed for many minutes following the training session. Two experiments conducted on mice (Bietel and Porter, 1968) illustrated the point that if mice were cooled to $2^{o}C$ at 0.5 or 5 min after the training task, short-term retention deficits occurred at a test trial 24 h later. No such deficit was observed in the group cooled 20 min after the training session. Other groups were cooled at $2^{o}C$ for either 15 or 30 min and then tested on a simple black-white discrimination task. Both acquisition and long-term retention were impaired in the group cooled for 30 min, while only a fleeting effect on acquisition was noted after the 15 min cooling period. Other investigations (Riccio, Hodges and Randall, 1968) have also found a poorer retention for a passive avoidance task in rats when hypothermia was delivered up to 15 min after the training session. In addition, this retrograde amnesia was related to the depth of body temperature reduction, to $22^{o}C$ or below. No decrement in memory occurred at body temperatures above this level. This fact is not supported by the work of Jacobs and Sorenson (1969) who found that slight alterations in body

temperature in mice, produced by a short cold water immersion could interfere with retention of a passive avoidance task. These investigators considered that their findings supported the view that retrograde amnesia reflected impairment of the memory consolidation processes. This may be possible in view of the fact that body cooling is accompanied by diminished cortical and subcortical electrical activity (Lipp, 1964) and these areas probably include neurons involved in "reverberatory circuits", i.e. the repetition of initial electrical activity through closed neuronal loops. The injection of anaesthetic agents, Surital nad Equithesin, into rats caused a reduced retrograde amnesia after hypothermia (Gehres, Randall, Riccio and Vardaris, 1973). Since these anesthetic agents blocked the cold induced paroxymal spike activity in the hippocampus and amygdala, it was proposed that hypothermia produced amnesia by disrupting electrophysiological activity in these areas. Some difficulties with long-term retention and ability to repeat a simple discrimination task after severe and lengthy hypothermia are hinted at in the investigations of Andjus, Knöpfelmacher, Russell and Smith (1956) and Beitel and Porter (1968).

An interesting study conducted by Misanin and Hoover (1971) highlighted the possibility that amnesia-like effect of hypothermia might be due to failure of retrieval processes rather than memory consolidation disruption. Their study involved experiments in which either depth or duration of hypothermia were held constant, while the recovery rate varied. It was found that animals, whose body temperatures were returned quickly to normal, showed the greatest degree of memory disfunction. This was related to the fact that the part of neuroelectrical activity in memory is to serve as a catalyst

and because this activity is decreased during cooling, there is an alteration in the time of memory fixation. They argue that this longer time for storage to occur allows for possible scrambling of the learning task by subsequent inputs. This scrambling could then interfere with memory retrieval. This conclusion appears to be supported by other studies (Lewis, Misanin and Miller, 1968; Quartermain, McEwan and Azmitia, 1970), and would be in disagreement to the postulated hypothermic induced metabolic alteration as an explanation of deficits due to cold water immersion (Bietel and Porter, 1968; Riccio, Hodges and Randall, 1968).

It appears evident that in rodents some decrement in retention is elicited by severe and possibly long immersion in cold water. Whether the more appropriate reason for this failure is due to disruption of retrieval or memory consolidation processes has still to be finalized.

2. Human Studies

As a result of exposure to unusual and/or hostile environments, it might be expected that man's performance in the realm of acquisition and manipulation of information could be seriously impeded. Many studies have considered the ability of experienced divers to perform tasks, e.g. sentence comprehension, arithmetic test, simple associate memory task (verbal) while subjected to hyperbaric environments, or subjected to diving in the open sea. Biersner and Cameron (1970) found that in divers at 600 ft there was some selective impairment of memory, 60 min after the learning task, whereas there was no memory impairment after 5 min. They concluded that the decrement found in some was due to psychological stress, perhaps their inability to cope with a threatening

situation, rather than nitrogen narcosis. A study of divers in the open sea (30 m) showed no significant deterioration in either long- or short-term memory (Davis, Osborne, Baddeley and Graham, 1972). Other investigations have considered the effect of hyperbaric air on short- and long-term memory. Various work lists were learned and tested at different simulated depths (1, 4, 7, 8.6 and 10 ATA). The general conclusions were that short-term memory is not affected at these depths but that input and possibly output functions of long-term memory are altered (Fowler, 1973; Fowler and Ackles, 1975). A consideration of diver performance and possible decrement in mental performance must take into consideration other factors, such as cold and reduced sensory input, in addition to increased pressure and anxiety.

What happens when the unitiated, virtually unprotected individual is immersed in cold water for varying amounts of time? Most of the information about this situation results from an on-the-spot analysis of the victim's condition during the time of rescue or removal from an experimental or accidental situation. The results show that all states, unconsciousness, delirium, temporary bewilderment and retrograde amnesia, are represented (Currie, 1798; Keatinge, 1969) and in all situations there was an inability to take action necessary for survival. Needless to say, there is a paucity of information culled from well designed and executed experiments, regarding the actual deficits and their causes in either memory or cognition which accrue as a result of cold water immersion. One study considered the ability of subjects to perform a mental arithmetic task while totally immersed in water ranging from $22^{o}C$ to $31^{o}C$ (Lapp and Gee, 1967). The investigators found that subjects who had been immersed twice a week, over a period of 8 weeks,

performed better than the control group. However, after the control group had endured repeated immersions, their performance level improved, indicating that some adaptation of mental processes had occurred. No studies to date have reported on the effects of short-term cold water exposures and its effects on mental function.

F. RATIONALE FOR THIS RESEARCH

The literature survey has indicated that when man is exposed to cold, acute and long term effects are seen. In order to maintain homeostasis various thermoregulatory mechanisms are employed. When man is immersed in cold water for short periods of time, powerful ventilatory and cardiovascular responses ensue and may be accompanied by disturbance in body temperature. Various factors may attenuate these responses and alter body heat loss. In addition, man's mental functions are affected by cold exposure. The work reported in this thesis was undertaken to explore factors which attenuate initial respiratory and cardiovascular responses, alter body temperature, or affect recognition and recall.

The investigations were designed to achieve the following objectives during short-term cold water immersions:

1. To determine the effect of clothing, preheating and deep and surface skin temperature on initial ventilatory responses;

2. To determine the effect of alcohol and diazepam on body temperature, skin temperature and respiratory and cardiovascular responses;

3. To determine the relationship of deep and surface skin temperatures to the initiation of shivering, and the factors which might attenuate or abolish this response;

4. To determine any correlation between dopamine-β-hydroxylase and ventilatory and cardiovascular responses;

5. To study any decrement in retention, especially recognition and recall which might follow cold exposure as a result of potential reduction in cerebral blood flow.

MATERIALS AND METHODS

A. PHYSIOLOGICAL PROCEDURES

1. Subjects

Male and female volunteers of varying ages (20's to 50's) participated in the experiments. Each subject was given a physical examination, by an independent practitioner which included chest X-rays and electrocardiograms. Care was taken to elucidate any history of cold allergies, hypertension, headaches (which might have betrayed possible intracranial aneurysms), and any cardiac abnormalities whether murmurs or disorders of rhythm. Subjects were informed of the possible risk of the experiments and each gave informed consent for the experiments (Appendix A). Special consent forms were signed by those subjects participating in the studies involving ingestion of alcohol and diazepam (Appendices B and C). Experimental procedures were examined by the Ethics Committee of the Faculty of Medicine and approval was granted.

2. Immersion Tank

All immersion experiments were carried out in the laboratory in a tank measuring 2.7 x 1.22 x 1.22 m (total capacity = 2,161 l) which could be filled with water at any desired temperature. During each immersion period the water was continuously stirred by means of a Shakespeare Wonder Troll (#606) outboard motor, the propeller of which was separated by a protective perforated steel plate screen from the subjects, and driven by 12 volt battery. During the immersion periods the subjects sat quietly in the tank and the level of water was such that it just covered the shoulders.

3. Respiratory Measurements

Since the methods used to measure respiratory activity are

common to all phases of study, they will be considered here. Subjects breathed through a mouthpiece attached to a low dead space two-way respiratory valve. A continuous stream of gas was taken from the respiratory valve in the region of the mouth, at 500 $ml.min^{-1}$ via a tube matched for length and diameter to the analyzer, and passed through an infrared CO_2 analyzer (Beckman Instruments LB2) and a polarographic O_2 analyzer (Beckman Instruments OMII). Total expired air volume was measured by an integrating pneumotachograph placed on the expiratory side of the valve. This summated expired volume gave the total ventilation over a specific time period. The experimental arrangement is shown in Fig. 2.

4. Calibrations for Respiratory Responses

Calibration for the total expired volume was done before and after each experiment in the following manner. Two or 3 flow rates of air over the range of volumes likely to be measured were passed by a pump through the pneumotachograph and the total volume in liters (l) for 1 min was recorded on a gas meter (American Meter Co.). The number of pen excursions, full scale min^{-1}, was related to the total airflow min^{-1}, and the result recorded as $l.excursion^{-1}.min^{-1}$. A calibration curve indicated that accuracy of measurement at various rates of flow from 8 to 112 $l.min^{-1}$ was better than ± 1.0 $l.min^{-1}$. All gas volumes are given at STPD.

The O_2 and CO_2 analyzers were calibrated using standard respiratory calibrating gases (Fisher Scientific), and the O_2 and CO_2 content of the gas mixture was determined accurately with a Lloyd-Haldane gas analysis apparatus. Errors in the standard gas of up to 0.2% were found. The output from the CO_2 analyzer, as well as that of the

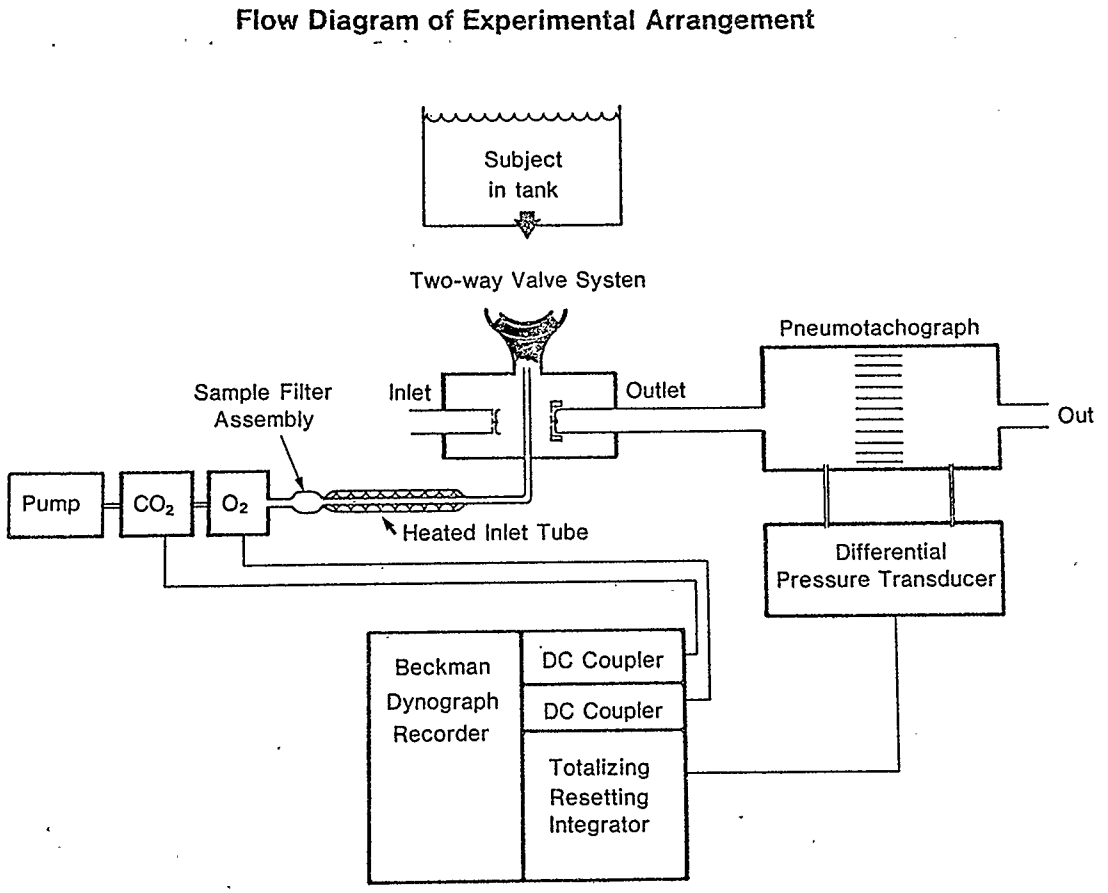

Fig. 2. Experimental arrangement used to measure respiratory activity.

integrating pneumotachograph, were fed directly to a pen recorder (Beckman Dynograph R 411). Tidal volume and respiratory rate were computed from this recording. All experiments were performed at a laboratory altitude of 1,100 m. The gases were not dried before measurement and the calibration was performed with standard gases saturated with water vapour by passing them through a dilute sulphuric acid solution at 37.0°C.

A calibration for end-tidal PCO_2 was achieved by using a three-way stopcock on the calibration gas inflow and adjusting the analyzer to draw gas from the CO_2 source at rates varying from 10 to 100 $ml.min^{-1}$. The stopcock was rotated so that the analyzer sampled calibrating gas and room air alternately. The rate of rotation of the tap was increased gradually to simulate increasing expiratory rate. Thus, approximately square wave samples of gas at known PCO_2 (35 mm Hg) were fed to the analyzer at different flow rates, using rates of tap rotation of up to $50.min^{-1}$. The analyzer was able to follow the changes to within ± 1 to 2 mm Hg. Above this frequency there was a progressive fall off in the amplitude of response.

5. Factors Affecting the Initial Respiratory Responses

a) Sauna Heating and Cold Water Immersion

Twelve volunteers participated in this study. Subjects were immersed up to the neck in water at temperatures ranging from 8.7°C to 21°C. Control experiments were conducted in water at 34.48°C ± 0.09°C. Respiratory responses were recorded as described previously.

Mean unweighted skin temperature ($\bar{T}_{SK}$) was measured with skin thermistors (No. 709, diameter 3/8", Yellow Springs Instruments, Yellow Springs, Ohio), placed in 6 different locations: lower leg, mid thigh,

upper arm, abdomen, back and chest. The various weighting factors utilized in the determination of average skin temperature (Hardy and Du Bois, 1937) were not considered because they might not be applicable to the sensory inputs being studied, since all areas of the body surface may not have the same density of receptors. Body temperature (T_B) was measured beneath the tongue in the closed mouth (sublingually), with a thermistor (No. 701, diameter ¼", length 5/16", Yellow Springs Instruments) or was monitored continuously using the zero gradient aural thermometer (Keatinge and Sloan, 1975). This method measures body temperature by using a battery powered device to measure temperature in the external ear canal by a thermistor, while keeping the temperature of the outer ear, monitored by a second thermistor, at that of the auditory canal using servo-controlled heating.

Electromyograph (EMG) electrodes (Beckman EMG cup electrodes) were attached to the scapular region. Conductivity between skin and electrode was aided by use of Cardiocream (Ingram and Bell Ltd.). Shivering was evidenced by electrical potentials recorded by a Beckman EMG coupler-pre-amplifier system and recorded on the dynograph. The recording included changes in amplitude and frequency of bursts of electrical activity.

Heating of subjects was accomplished by means of a portable sauna (Rick Instruments, British Columbia). The arrangement, with the head outside (Fig. 3), allowed for a suitable, rapid increase in skin temperature without a large rise in deep body temperature. Entry into cold water with or without sauna heating was randomized to offset the possible effects of habituation.

Subcutaneous fat thicknesses of the subjects were estimated using Harpenden calipers (John Bell, British Indicators). One measurement

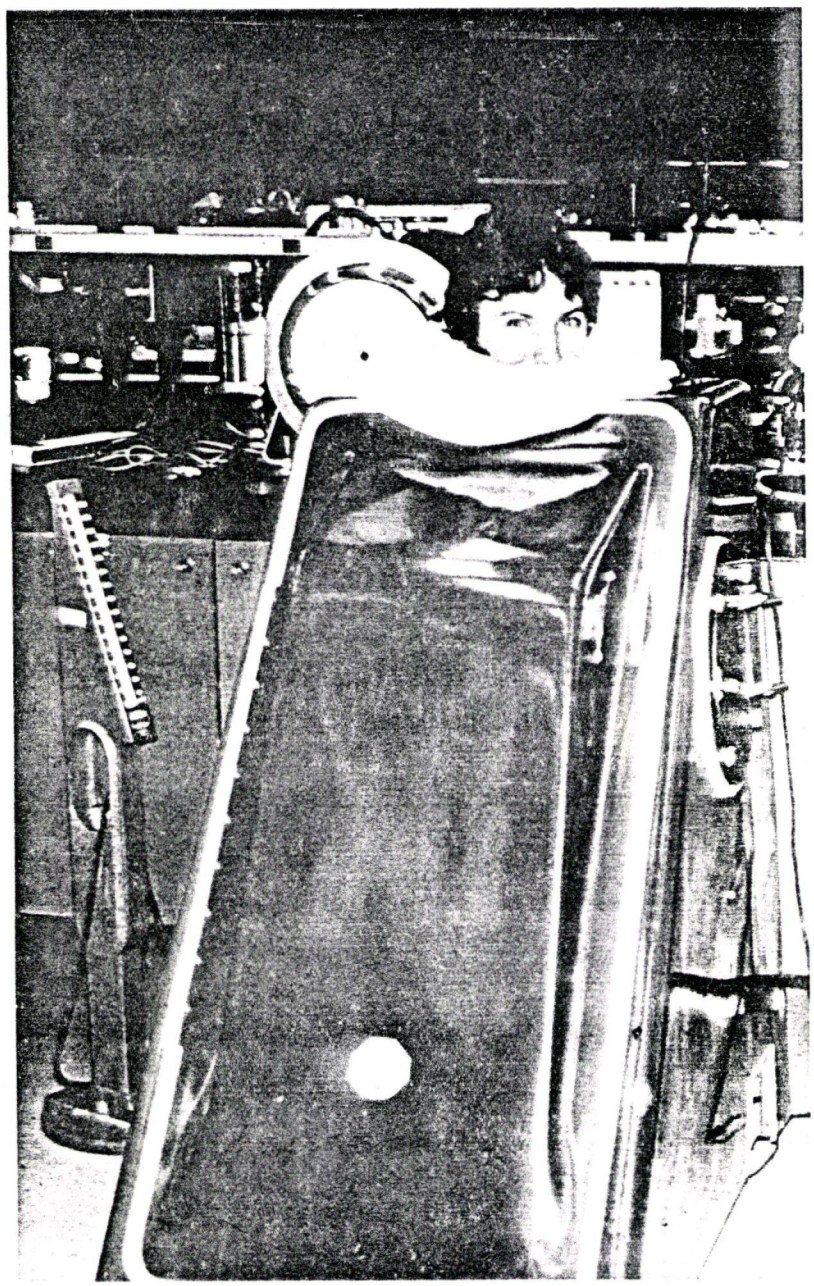

Fig. 3. The arrangement, with use of a portable sauna, for heating subjects before entry into cold water.

on each side of the body was made in the following 4 positions: over the biceps, and in the subscapular, abdominal and subcostal regions (Keatinge, 1961), and the results were averaged.

b) The Use of Clothing During Cold Water Immersion

Fourteen subjects were involved in this study. The subjects were seated in continuously stirred water at a temperature of 13.9°C ± 0.12°C for 20 min on 2 different occasions. During 1 exposure only a bathing suit (either full length or bikini type for the women, and shorts for the men) was worn while for the other immersion period the subjects were clothed. The clothing consisted of cotton trousers and T-shirt, nylon jacket, wool socks and sneakers, with an approximate insulation value of 0.8 clo (Le Blanc, 1975). For the last minute of each immersion period the subjects were asked to perform swimming movements with their hands and feet. Respiratory responses, aural temperature (T_E) and mean skin temperature ($\bar{T}_{SK}$) were recorded as described previously.

6. Alcohol Consumption and Cold Water Immersion

Thirteen subjects participated in this procedure. Subjects were immersed in water for 20 min at 13.59°C ± 0.13°C for the control immersion and 13.58°C ± 0.11°C following alcohol consumption. Respiratory responses, mean skin temperature ($\bar{T}_{SK}$) and the aural temperature (T_E) were measured as previously indicated. Rectal temperature (T_R) was also monitored with an indwelling rectal thermistor probe (Yellow Springs Instruments, Yellow Springs, Ohio) to an accuracy of ± 0.05°C. Oxygen uptake ($\dot{V}O_2$) was measured for 2 subjects. The expired air (3 min samples) was collected in Douglas bags during the pre-immersion control breathing and at 5, 10, 15 min of the immersion period. Heart

rate was monitored from the electrocardiogram using 3 needle electrodes (Grass Instrument Co., Quincy, Mass.), 2 of which were inserted in the pectoral muscle with the ground located over the sternum. The recording was made by means of a Direct-Average EMG coupler (Beckman Instruments). Shivering was also detected by these electrodes.

The volunteers were given varying volumes of pure ethanol (dependent on body weight) mixed with 200 ml of fruit juice. The alcohol was consumed over a 20 min period, and 45 min after beginning ingestion the subjects were immersed in water. Each subject had been fasting for at least 2 h before the experiment. Blood samples (3 ml) were taken from an antecubital vein before immersion and after the subject came out of the tank (about 1 h after drinking the alcohol). The method of analysis of the blood alcohol level is described later.

This experimental procedure was also conducted at 2 higher water temperatures. Ten of the former 13 subjects were immersed for 30 min in water at $22.17^{o}C \pm 0.14^{o}C$ for the control experiment and $21.93^{o}C \pm 0.16^{o}C$ for the immersion after alcohol. All measurements were done as in the earlier procedure. Oxygen uptake ($\dot{V}O_2$) was determined for 2 of the subjects, during the control breathing and at 5, 15 and 25 min of the immersion time.

Five of the original 13 subjects sat for 30 min in water at $30.19^{o}C \pm 0.29^{o}C$ and $29.89^{o}C \pm 0.2^{o}C$ for the control and after alcohol immersions respectively. Oxygen uptake ($\dot{V}O_2$) was calculated for 4 of these subjects at the times quoted for series 2. All other measurements were done as described previously.

7. Diazepam Ingestion and Cold Water Immersion

Six subjects were involved in this study. They sat quietly for

20 min in water at 13.58°C ± 0.08°C for the control immersion and at 13.55°C ± 0.08°C for the immersion following drug ingestion. Measurement of respiratory responses, rectal temperature, mean skin temperature (4 sites) and oxygen uptake were made as reported previously. In the measurement of heart rate for some subjects, the needle electrodes were placed differently than in previous procedures. In these experiments the ground was over the right pectoral muscle and the recording electrodes were placed 1· above the sternum and 1· subcutaneously in the left mid-axillary line at heart level. A clearer recording was obtained during water immersion by this method.

Five of the subjects were given diazepam (Valium, Hoffmann-La Roche Ltd., Quebec) 5 mg orally and one subject was given 15 mg orally. Three blood samples were taken from the subjects who had been given the lower drug dose and 6 samples from the subject given the 15 mg. Normally the 3 samples were taken before drug administration and at 1 h and 1.5 h after drug ingestion. The blood samples from the subject with the larger drug dose were taken before the drug was administered and at 30 min, 1 h, 1.5 h, 2.75 h and 4.3 h after drug ingestion.

The blood samples (10 ml) were taken from an antecubital vein, heparinized, centrifuged, and the plasma pipetted off and placed in test tubes and frozen at -20°C until assayed.

8. Dopamine-β-Hydroxylase Changes During Cold Water Immersion

Thirteen subjects participated in the experiment and were immersed in water at 13.3°C ± 0.20°C for 10 min. Respiratory measurements and electrocardiograph recordings were made during the control and immersion periods. Blood samples (5 ml) were taken by means of an

indwelling venous catheter (Sherwood Medical Industries Inc., St. Louis, Missouri) in an antecubital vein during the control period each minute for the first 5 min of the immersion and at the end of 10 min. Control samples were taken with the arm at rest and while exercising since it was sometimes necessary for some subjects to exercise in the cold water to overcome the peripheral venoconstriction, so that the samples could be taken. Seven subjects were immersed in water at 13.74°C ± 0.06°C for 10 min and blood pressure measurements were taken.

9. Factors Affecting Shivering During Cold Water Immersion

a) Deep and Superficial Skin Temperatures During the Initiation of Shivering

Twelve subjects underwent 2, 10 min water immersions after each was exposed to ambient temperature and sauna heating. Water temperatures were 14.32°C ± 0.16°C and 14.36°C ± 0.17°C respectively. In addition to respiratory responses and subcutaneous fat thickness, the average deep skin temperature (T_{DSK}) was also measured. This was accomplished by using 3, 30-gauge subcutaneous thermocouple probes (Medwire Corp., Mt. Vernon, N.Y.) arranged in a parallel circuit. These were inserted in the back, chest and thigh at a depth of 1 to 2 mm. The average deep skin temperature was recorded on a potentiometric linear recorder (Simpson 2741A-1) which had been previously calibrated within the range of 0° to 40°C. Eight of the subjects also had their superficial skin temperature monitored in the 3 sites. The experimental procedure was repeated for 4 of the subjects.

b) Inhibition of Shivering

Six subjects were immersed for varying lengths of time, 11 to 22 min (average time = 16.5 min) in water at 15.15°C ± 0.42°C. Respiratory

and electromyographic recordings were monitored as previously described. When a suitable degree of shivering had been elicited, the subjects were asked to perform 2 tasks, a 40% and 50% maximum voluntary contraction of 1 forearm and do 2 sets of mental arithmetic tasks. The isometric contraction was accomplished by means of a hand grip dynamometer (Clarke, Hellon and Lind, 1958) which was suspended over the tank within easy reach of the subject's right hand. The mental arithmetic task involved 2 presentations on a screen, easily visible to the subject, of 4 consecutive sets of 7 randomly arranged numbers. Each number was projected on the screen for 1 sec and at a given signal the subject was asked to subtract 2 from each number and give the answer in the correct sequence. The subjects were asked to do the tasks alternately, i.e. number presentation, isometric contraction, number presentation, isometric contraction. A degree of shivering was evident before each task was performed. All subjects were made familiar with both the use of the hand grip dynamometer and the number presentations and were given practice sessions with each procedure some days before the immersions took place.

B. MEMORY TESTING

Experimental procedures were used to determine the effect of cold water immersion on (a) simple recognition and recall of visual information; (b) ability to utilize previously known information and (c) use of information acquired while immersed in cold water. Each procedure will be considered separately.

The hyperventilation and consequent decline in end-tidal PCO_2

which are evident during cold water immersion would be expected to be accompanied by a decrease in cerebral blood flow (Harper and Glass, 1965; Reivich, 1964). Thus, respiratory responses (total expired ventilation, end-tidal PCO_2) were measured during the immersion experiments with the hope that if significant changes did occur, it might be possible to correlate the number of errors with changes in end-tidal PCO_2. Since the immersion times were similar to those done previously, no assessment of body temperature was made. The subjects were not informed of the water temperatures before any of the experiments. Immersion in either warm or cold water during all the experiments was done in a randomized fashion.

In order to acquaint the subject with the technique of each new experiment, they were given pretest trials in room air. After sufficient practice, the experimental procedure was conducted at room temperature to give the control data to which would be compared the data collected during the water immersions.

1. Experiment I

This experiment was designed to test visual recognition. Thirteen subjects participated in this experiment and were immersed in cold ($15.8^{o}C \pm 0.11^{o}C$) and warm ($33.21^{o}C \pm 0.21^{o}C$) water. Three sets of 25 coloured slides referred to as a Stimulus Set, Test I and Test II were used as stimuli. The slide sets were randomly arranged and presented to include scenery, people, still life, and buildings. The Stimulus Set was shown before immersion in the water; Test I was conducted immediately after removal from the immersion tank, and Test II, 6 min later. Subjects sat in the warm sauna during the interval between Test I and Test II.

The slides were projected by means of a Kodak Ektagraphic Slide

Projector (Model I) onto a wall screen behind the water tank. The exposure time for each slide was 2 sec which was controlled by a shutter timer (Ralph Gerbrands Co., Arlington, Mass.) placed on the projector lens. Although each of the 3 sets contained 25 slides, both Tests I and II contained 12 new slides. Subjects were instructed to look at the slides and respond "yes" if they had seen the slide before, "no", if they had not previously seen the slide and "maybe" if they were uncertain. Thirteen subjects participated in the study and were immersed for 4 min in water at 15.0°C and 33.0°C. Respiratory responses were monitored.

2. Experiment II

During this procedure, also testing recognition, a new Stimulus Set of 25 slides, each exposed for 2 sec, was shown 1 min after the subjects (11) were immersed in the water, at either 13.49°C ± 0.12°C or 32.93°C ± 0.16°C. Respiratory responses were monitored during the immersion period. At the end of 4 min the subjects were removed from the tank and Test I was administered. This set of 25 slides contained 12 new slides. Six minutes later, Test II (also containing 12 new slides) was conducted. The scoring method was similar to that of Experiment I. During the interval between the 2 tests, the subjects sat in the warm sauna.

3. Experiment III

The subjects' ability to acquire information in a cold or warm water environment and retain it in a similar environment was tested in the following manner. Six subjects, whose respiratory responses were measured, were immersed on 2 occasions in water at 13.73°C ± 0.13°C and 34.20°C ± 0.40°C. The new Stimulus Set of 25 slides, each exposed for 0.5 sec, was shown after the first minute of the immersion. Test I, which contained 12 new slides, was conducted at the end of 4 min, while the subjects were in the water. During the 6 min interval between Test I and Test II, the subjects remained in the water. Test II, which contained 12 new slides, was also conducted while the subjects were seated in the tank. The scoring procedure was similar to that previously described in Experiment I.

4. Experiment IV

In order to assess possible intrasubject variation during water immersions, some subjects underwent exposure to either warm or cold water on 3 occasions. Two subjects were immersed in water at 13.93°C ± 0.17°C and 3 were immersed in water 31.62°C ± 0.39°C. No respiratory responses were measured during any experiments. A new Stimulus Set of 25 slides, each exposed for 2 sec, was presented after the first minute of the immersion for each experiment. At the end of 4 min the subjects were removed from the tank and Test I, consisting of 25 slides with 12 new ones, was conducted. Six minutes later, Test II, which also contained 12 new

slides, was presented. Once again, the subjects sat in the sauna during the interval between Tests I and II. The scoring of the tests was done as described for Experiment I.

5. Experiment V

In order to see if the decision making process might be impaired as a result of short term cold water immersion, 11 subjects were seated in cold (13.26°C ± 0.28°C) and warm (32.98°C ± 0.22°C) water for 6 min and then asked to play a simple game, Tic-Tac-Toe (noughts and crosses). Respiratory activity was measured during the immersions. During a 10 min period following each immersion, the subjects sat in the sauna, and played a total of 20 games with the experimenter who always made the first move. In order to offset any writing problem due to a decrease in manual dexterity, particularly as a result of the cold water immersion, the subject indicated where he wished his mark (X or O) to be placed during each turn, by calling a number from an organized chart. This procedure was followed for the playing time after both water immersions. The time required to play each game was noted, as well as the number of wins, losses or ties. The games were scored as follows: +1 for a win; -1 for a loss, and 0 for a tie. As in the previously described experiments, the immersion in either warm or cold water was randomized and the subjects were unaware of the water temperature before entry into the tank.

Some days before the immersion each subject was given a chance to practice the particular technique in the game and each subject played all pre-immersion games with the person who conducted the experiments.

6. Experiment VI

This investigation attempted to separate simple recall from the ability to utilize information. Twelve subjects were immersed for 5 min,

on 2 occasions, in either warm (32.73°C± 0.20°C) or cold (13.54°C ± 0.05°C) water. No respiratory measurements were made during this experiment. After 2 min of immersion they were shown a sequence of 8 sets of randomly arranged 7 digit numbers (ranging from 2 to 9). Each slide was exposed on the screen behind the tank for 1 sec. At the end of each number set, the subjects were requested to perform a specific task; either to recall the 7 digits in correct sequence or do a computation, which involved the subtraction of 2 from each of the 7 digits in proper sequence. They were allotted 12 sec to complete each answer. No verbal instructions were given during the experiment. The subjects were alerted to each task by a light signal easily visible to the subject. A white light indicated that a new set of numbers was to be presented; a red light at the completion of the number presentation indicated a recall task and a blue light at the end of the number presentation indicated a computation task. The red and blue light signals were randomly assigned. Each digit of each set was scored individually and so it was possible to assign some marks for each set. This method is illustrated as follows: a specific number set 3275689 was presented to the subject, the red light was flashed and the subject answered as follows, 3265749. Since 2 digits were out of sequence and one was wrong, the score for this set was 4.

As explained in Experiment V, the subjects were unaware of the water temperature before each experiment. They were also given sufficient practice some days before the water immersion to familiarize them with the procedure. All pre-immersion sessions were carried out by the experimenter.

C. BIOCHEMICAL ASSAYS

1. Blood Alcohol Determinations

Blood samples (3 ml) were stored on ice and analyzed in the Foothills Hospital, Department of Laboratories.

The analysis was done by a standard gas-liquid chromatography technique (Cooper, 1971) for determination of blood alcohol levels and the results were recorded as mg %. The general principle followed in the assay method was as follows: using an autodilutor, blood samples were diluted approximately 1:10 with an aqueous n - propanol internal standard: 5 µl aliquots were injected onto a porous polymer gas chromatography column and the resulting peaks were analyzed using a Hewlett-Packard computer system. The analysis was reproducible to within ± 2%, minimum detectability was less than 5 mg% and linearity was good from 10 to 500 mg% for ethanol.

2. Blood Diazepam Determination

The blood levels of diazepam (Valium) were determined by the gas chromatographic procedures involving electron-capture detection, with slight modification, established by Berlin, Siwers, Agurell, Hiort, Sjöqvist and Ström (1972). In general, the method involved the extraction of diazepam and N-desmethyldiazepam into benzene and analysis by gas chromatography. The procedure allowed for exceptional sensitivity (5 to 10 pcg per injection) with good linear range (≃ 3000 pcg). The analysis was performed in the Faculty of Pharmaceutical Sciences, The University of British Columbia, under the direction of Dr. J.E. Axelson.

3. Dopamine-β-Hydroxylase Assay

The 5 ml blood samples were added to 50 µl heparin containing 150 $mg.ml^{-1}$ glutathione (reduced), the final concentration being

approximately 5 mM. The samples were then kept on ice until centrifugation at 1800 Xg for 20 min at 4°C. The plasma was removed, transferred to new tubes and frozen at -20°C until assayed.

For the dopamine-β-hydroxylase assay (D-β-H) the plasma was partially thawed to permit removal of 20 µl samples and the plasma was refrozen. For fresh blood samples, blood was collected in hematocrit capillary tubes (heparinized) and then centrifuged at room temperature. Twenty µl of the plasma layer were used in the assay.

Several problems became evident in the sampling of the plasma. The amount of plasma taken and delivered by the Oxford sampler showed considerable variation when the volumes delivered were weighed. Also, the sampling of partially thawed plasma samples did not give an aliquot representative of the whole sample as there was concentration of the plasma proteins into definite areas during freezing, e.g. between the ice crystals and the edge of the tube. It was found that much of the variation in D-β-H activity assayed was due to these problems and could be minimized by assaying the amount of plasma protein used in the dopamine-β-hydroxylase assay and then expressing the enzyme activity as units of enzyme per mg plasma protein. This procedure also removes the uncertainty that an observed change in dopamine-β-hydroxylase activity is due to a change in plasma volume (Stone, Kirshner, Gunnels and Robinson, 1974).

The dopamine-β-hydroxylase assay procedure is that of Nagatsu and Udenfriend (1972), with minor modifications. These included more ion exchange resin, the use of a larger washing volume and 500 µl of the reagent solutions instead of 600 µl (L. Bauce, unpublished methods). The standard incubation mixture consisted of 20 µl plasma, 400 µl water

and 500 µl of reagent solution. This solution was premixed before the assay and contained 4 ml of 1 M sodium acetate buffer pH 5, 1 ml 0.2 M sodium fumarate, 1 ml 0.4 M tryamine, 1 ml 0.02 M pargyline in ethanol, 3 ml 0.2 M N-ethylmaleimide, 1 ml catalase (1 $mg.ml^{-1}$ 1500 units) and 1 ml 0.2 M fresh ascorbic acid. The mixture of plasma and reagents was incubated at 37°C for 1 h. A boiled plasma blank and internal standard were run with the samples. The reaction was stopped by addition of 200 µl 3 M trichloroacetic acid (TCA), the tubes were vortex mixed and allowed to stand for 10 min at room temperature. The precipitated proteins were then centrifuged. The supernatant was applied to prepared Biorad AG 50 W X 8 resin H^+ form (200 mg, packed in 0.5 x 15 cm columns). The pellet was washed with 1 ml distilled water and the wash was applied to the column. The pellet was saved for the protein assay. The columns were washed twice with 2 ml distilled water, and the adsorbed amines were eluted with 1 ml 4 N ammonium hydroxide (NH_4OH). The octopamine in the eluate was then oxidized for 2 min with 100 µl sodium periodate ($Na\ IO_4$, 20 $g.l^{-1}$) and the excess periodate reduced with 100 µl sodium metabisulfate ($Na_2\ S_2\ O_5$, 100 $g.l^{-1}$).

The absorbance at 330 nm of the samples against 4 N NH_4OH was recorded. The difference in absorbance of the samples minus the absorbance of the boiled plasma blank was related to the nanomoles (nmoles) of octamine formed during the incubation time (60 min) by means of a standard curve. The amount of protein in the 20 µl plasma sample was determined by a Folin-Lowry protein assay (Lowry, Rosebrough, Farr and Randall, 1951) using bovine serum albumin as a standard. This was done on the pellet of trichloroacetic acid precipitable material. The enzymatic activity of the dopamine-β-hydroxylase in plasma was expressed

as nmoles octopamine formed per mg plasma protein per minute at 37°C. International units for dopamine-β-hydroxylase are μmoles.min^{-1}.l^{-1} at 37°C.

D. METHODS OF STATISTICAL ANALYSIS

Analysis of data from various experiments was accomplished by means of one way analysis of variance, two way analysis of variance, the rank correlation test, linear regression analysis and the level of significance when comparing means was determined by the paired Student's t-test (Weinberg and Schumaker, 1969; Weiner, 1962).

RESULTS

A. FACTORS AFFECTING INITIAL RESPIRATORY RESPONSES

1. Sauna Heating and Cold Water Immersion

The heights and weights of the subjects participating in this portion of the study ranged from 189 to 163 cm and 82 to 53 kg. Table I provides a listing of these characteristics for each of the 12 subjects.

Total ventilation, end-tidal PCO_2, respiratory rate, tidal volume and skin temperature were measured in 14 experiments for these 12 subjects, 6 male and 6 female, who ranged in age from 22 to 54.

When a subject went from room air at a temperature of $21^{o}C \pm 1^{o}C$ into cold water ($8.7^{o}C$ to $21^{o}C$), respiration was altered. In all experiments the initial portion of the immersion was accompanied by a dramatic increase in total ventilation, the gasp response, a degree of hyperventilation, and increases in tidal volume and respiratory rate. Although respiratory rate increased during the first minute of immersion, it quickly returned to pre-immersion values and changes in tidal volume accounted for changes in total expired volume. Figure 4 illustrates a subject's responses to cold water immersion for the variables, with the exception of the respiratory rate, measured in this series of experiments.

As can be seen in the upper panel, there was an immediate increase in the tidal volume from a mean value of 0.76 to 1.14 l followed by a further increase to 1.4 l. This increase was maintained for the duration of the 8 min immersion. End-tidal PCO_2 (mm Hg) fell sharply during the first minute of exposure to cold water and then recovered gradually to 25 mm Hg. This degree of hyperventilation,

TABLE I

Weights and Heights of the Subjects

Subject	Weight (Kg)	Height (cm)
GB	75	177
SM	63	171
SH	60	170
RF	57	159
MD	55	163
JW	53	170
KEC	81	179
CJ	75	185
DM	72	189
RG	70	182
AC	66	179
DS	65	168
Mean ± S.E.M.	66.08 ± 0.75	174.42 ± 0.74

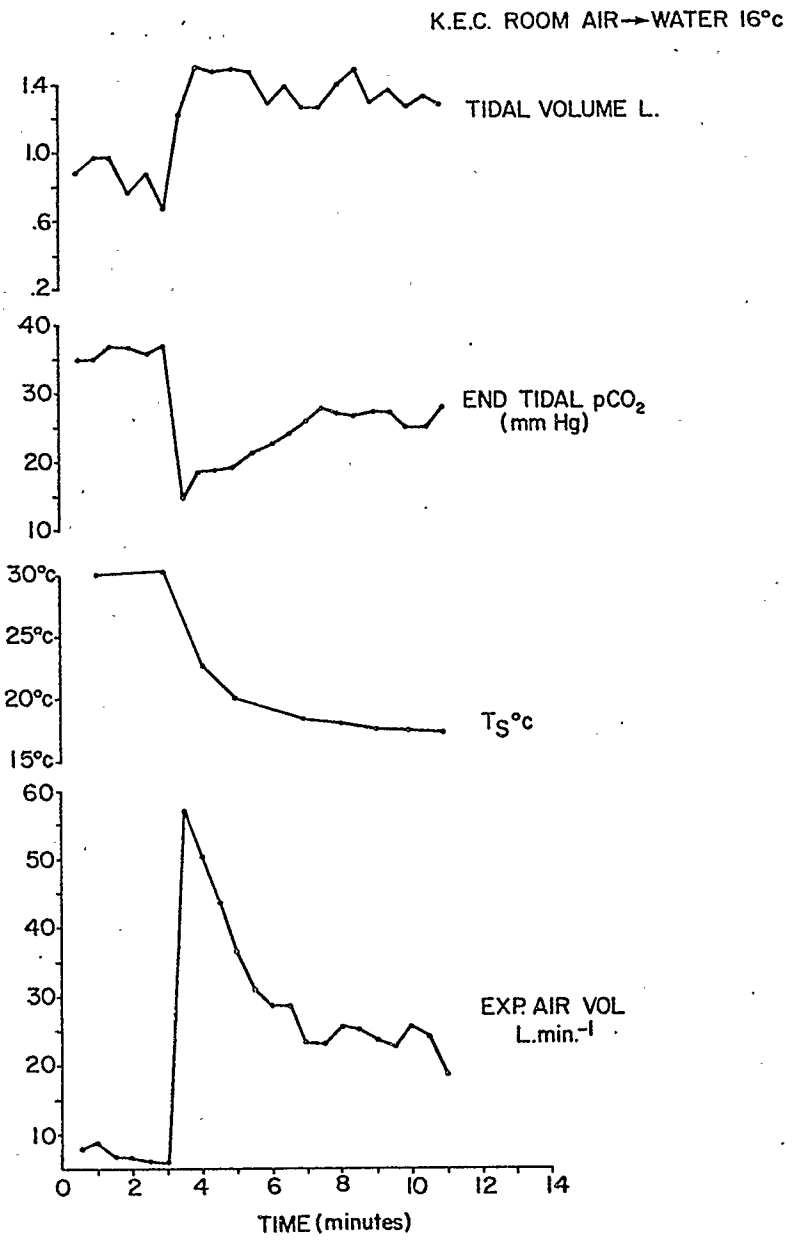

Fig. 4. Effect of immersion in cold water (16°C) after exposure to room air (21°C ± 1°C) on tidal volume (l), upper; end-tidal PCO_2 (mm Hg), upper middle; mean skin temperature (°C), lower middle; total ventilation ($l.min^{-1}$), bottom. Total immersion time - 8.0 min.

was maintained for the next 7 min.

The mean surface skin temperature ($\bar{T}_{SK}$) declined rapidly during the first 2 min of the immersion to 20°C from a resting pre-immersion value of 30°C. The decrease in surface skin temperature for the remainder of the experiment was more gradual and the skin temperature levelled out at 1.5°C to 3.0°C above the water temperature. The expired air volume ($l.min^{-1}$) increased immediately on exposure to cold water from a mean resting value of 7.0 $l.min^{-1}$ to 57.2 $l.min^{-1}$. The rapid return of the gasp response towards pre-immersion values was seen for the next 2 min, followed by a more gradual decline. This particular subject maintained an elevated ventilation (at approximately 25 $l.min^{-1}$) throughout the experiment.

If the subject was heated in a sauna before immersion in cold water (8.7°C to 21°C) the respiratory responses (the gasp response and degree of hyperventilation) were significantly altered. Figure 5 shows one subject's responses to cold water immersion after sauna heating. As noted in the upper panel, there was an increase in tidal volume from a mean resting value of 0.69°C to 1.24°C. A subsequent decrease in tidal volume, to values approximately those of pre-immersion time was evident after the first minute of immersion. However, for the last 3 min of the cold water exposure, a secondary increase in tidal volume was noted. End-tidal PCO_2 decreased to 25.4 mm Hg during the first minute of the immersion time but returned close to pre-immersion values (mean 34.15 mm Hg) for the subsequent 7 min of the immersion. The mean surface skin temperature ($\bar{T}_{SK}$) declined quickly from a pre-immersion resting value of 40°C to approximately 20°C within the first 2 min of the immersion.

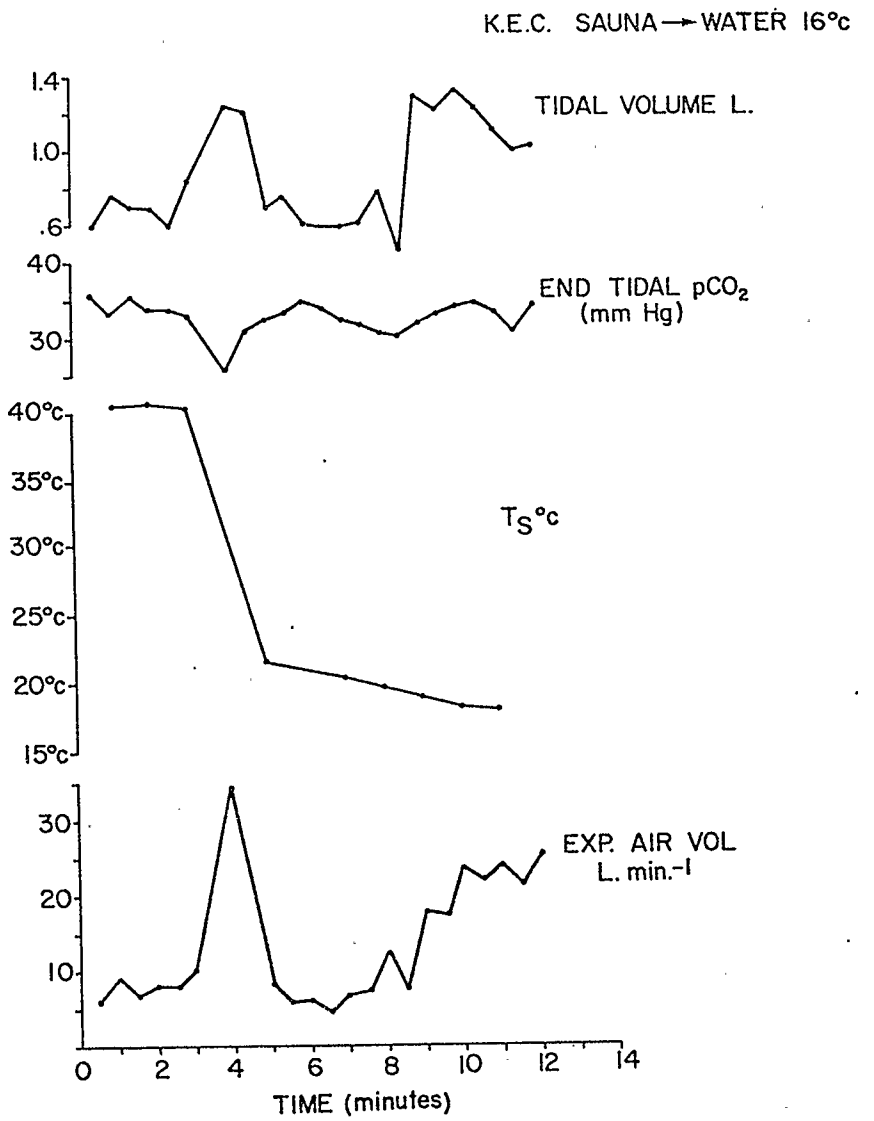

Fig. 5. Effect of immersion in cold water (16^{o}C) after sauna heating on tidal volume (l) upper; end-tidal PCO_2 (mm Hg) upper middle; mean skin temperature (^{o}C), lower middle; total ventilation ($l.min^{-1}$) bottom. Total immersion time - 8.5 min.

The remainder of the immersion time (5.5 min) was characterized by a more gradual decline in mean skin temperature to a level a few degrees above the water temperature. The initial gasp was evident on exposure to cold water as total ventilation increased from a mean resting value of 8.1 $l.min^{-1}$ to 34.3 $l.min^{-1}$. This was followed by a rapid return to pre-immersion levels. However, a secondary increase in total expired volume (to approximately 25.0 $l.min^{-1}$) was seen during the last 3 min of the cold water exposure. This particular response was also seen in 2 other subjects, i.e. in 3 of the 12 participants.

Shivering, as a result of the exposure to cold water at the various temperatures, was noted in most subjects during both experimental procedures, with 3 exceptions. Sauna preheating delayed the onset of shivering from 0.75 to 5.5 min, in comparison to its appearance during the other experimental procedure.

Because of the great degree of biological variability in the absolute changes in the responses to cold water immersion, the significance of the results has been ascertained by considering the mean percentage changes in total ventilation, and end-tidal PCO_2. Figure 6 shows the mean percentage changes in total ventilation during cold water immersion after exposure to room air and sauna heating. A mean percentage change of 530% during the gasp response was evident after exposure to room air, while sauna heating resulted in a mean percentage change of only 240%. A significant attenuation ($p < 0.01$, < 0.02, < 0.05) was seen for the first 5 min of the immersion as a result of the sauna heating. There was no significant difference in the two experimental situations for the remaining 3 min of the cold water exposure.

The mean percentage changes in end-tidal PCO_2 during cold water immersion after exposure to room air and sauna heating are seen in Fig. 7.

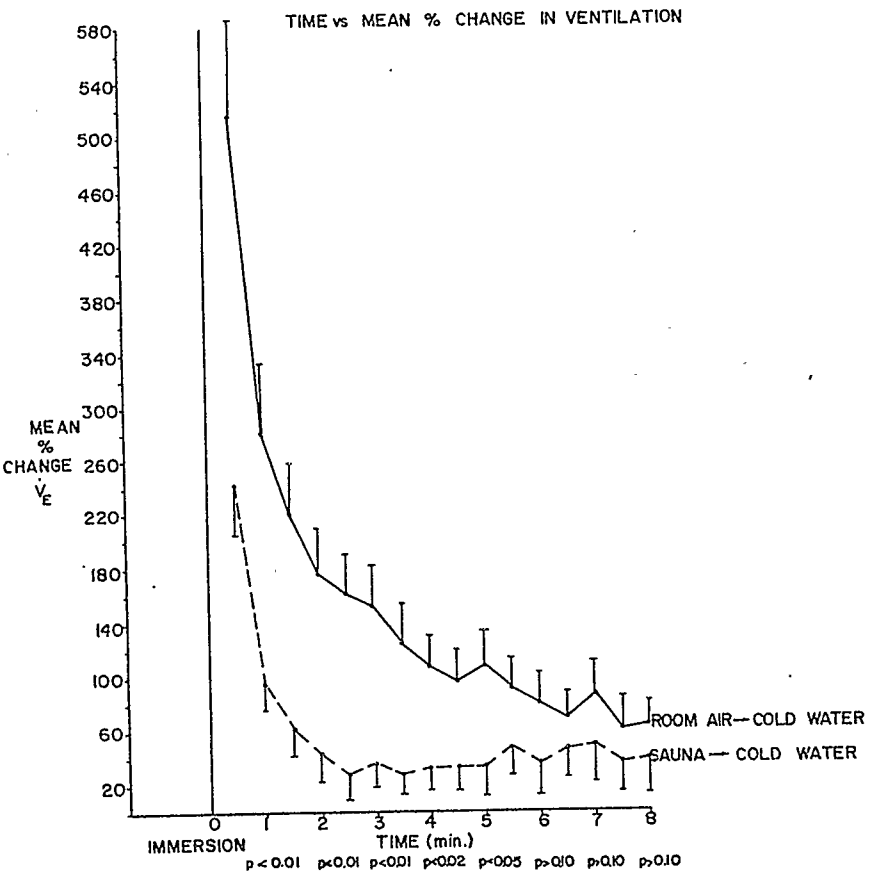

Fig. 6. Mean percentage change in ventilation during immersion in cold water (8.7°C to 21°C) for 8 min. Room air to cold water (——); sauna to cold water (----). N = 14. Vertical bars = ± S.E.M.

After exposure to room air a decrease of -25% was seen during the first minute of immersion and for the next 3 min there was an evident degree of hyperventilation which decreased for the subsequent 4 min of immersion. A mean percentage decrease of -12% in end-tidal PCO_2 was seen during the first minute of water immersion after the sauna heating. An attenuated response was evident throughout the 8 min of this immersion period but only the change seen in the first 3 min was significantly different ($p < 0.01$) from the response obtained during the cold water immersion after exposure to room air.

During the initial gasp response similar increases in mean percentage changes in tidal volume and respiratory rate occurred during both experiments. Generally, the mean resting tidal volumes while exposed to room air and sauna heating were 0.56 l and 0.70 l respectively. The first minute of cold water immersion elicited an increase of 142% and 79% in tidal volume for the 2 experiments. The mean resting respiratory rate was $13.min^{-1}$ after both exposure to room air and after sauna heating. Mean percentage changes in the respiratory rate during the gasp response included an increase of 158% and 108% for the water immersions after room air exposure and sauna heating respectively.

Subcutaneous fat thicknesses (mm) were determined for 8 of the 12 subjects, by averaging 8 readings ÷ 2 for each subject. The values obtained were as follows: [KEC --7.61; SM --7.15; SH --5.34; DM --5.14; CJ --4.8; AC --3.78; DS --3.75; RG --2.9]. A rank correlation test of these values with the mean percentage changes in total ventilation and end-tidal PCO_2 was done for the first minute of the cold water immersion after exposure to room air or sauna heating. There was no statistically significant correlation ($p > 0.10$) between the respiratory responses and

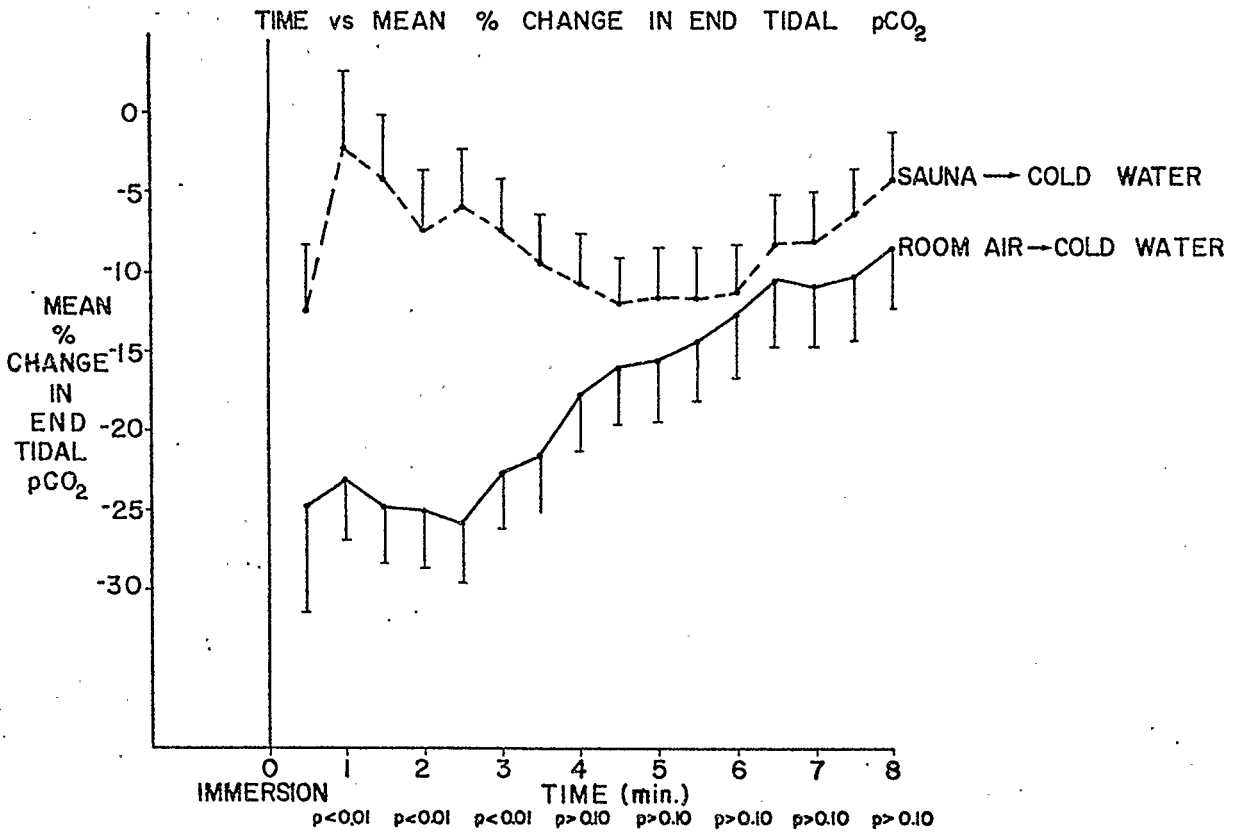

Fig. 7. Mean percentage change in end-tidal PCO_2 during immersion in cold water (8.7°C to 21°C) for 8 min. Room air to cold water (——); sauna to cold water (----). N = 14. Vertical bars = ± S.E.M.

the subcutaneous fat thicknesses.

2. Clothing and Cold Water Immersion

The weights and heights of the 14 subjects, 10 men and 4 women, who participated in this experiment ranged from 84 to 53 kg and 193 to 170 cm. Table II provides a listing of these characteristics for the volunteers.

These subjects, who ranged in age from 22 to 54, wore either a bathing suit only (unclothed) or were dressed as reported in the methods (clothed). The respiratory responses of the unclothed individual subjects when immersed in cold water (13.9^{o}C) were similar to those seen in Fig. 4. When the subjects were immersed, while clothed, the respiratory responses were attenuated. Because of the great variability in the absolute changes, the changes in end-tidal PCO_2 and total expired volume will be given as mean percentage changes.

Figure 8 shows the mean percentage changes in total ventilation during cold water immersion while subjects were unclothed and clothed. Increases of 450% and 350% were seen during the gasp response of the unclothed and clothed subjects. For the first 10 min of each immersion there was a decrease in ventilation to values obtained during pre-immersion time. In contrast, the last 3 min of each immersion were characterized by a slightly increased ventilation. The use of clothing significantly attenuated the gasp response ($p < 0.05$) and there was a significant difference ($p < 0.01$; $p < 0.02$) in the total expired volume from 1.0 to 9 min of the cold water exposure. There was no significant difference between the clothed and unclothed subjects' ventilatory response for the remaining 11 min of the experiment. Swimming movements were performed by the subjects at the end of each experiment and caused an apparent

TABLE II

Height and Weight of Subjects

Subject	Height (cm)	Weight (kg)
A.B.	193	84
R.D.	187	76
B.B.	185	79
R.C.	183	73
M.H.	180	80
K.E.C.	179	81
V.D.	178	66
E.A.	178	72
G.B.	177	75
R.T.	173	62
S.M.	171	67
I.F.	170	64
P.R.	170	64
J.W.	170	53
$\bar{X} \pm$ S.E.M.	178.1 ± 1.89	71.1 ± 2.34

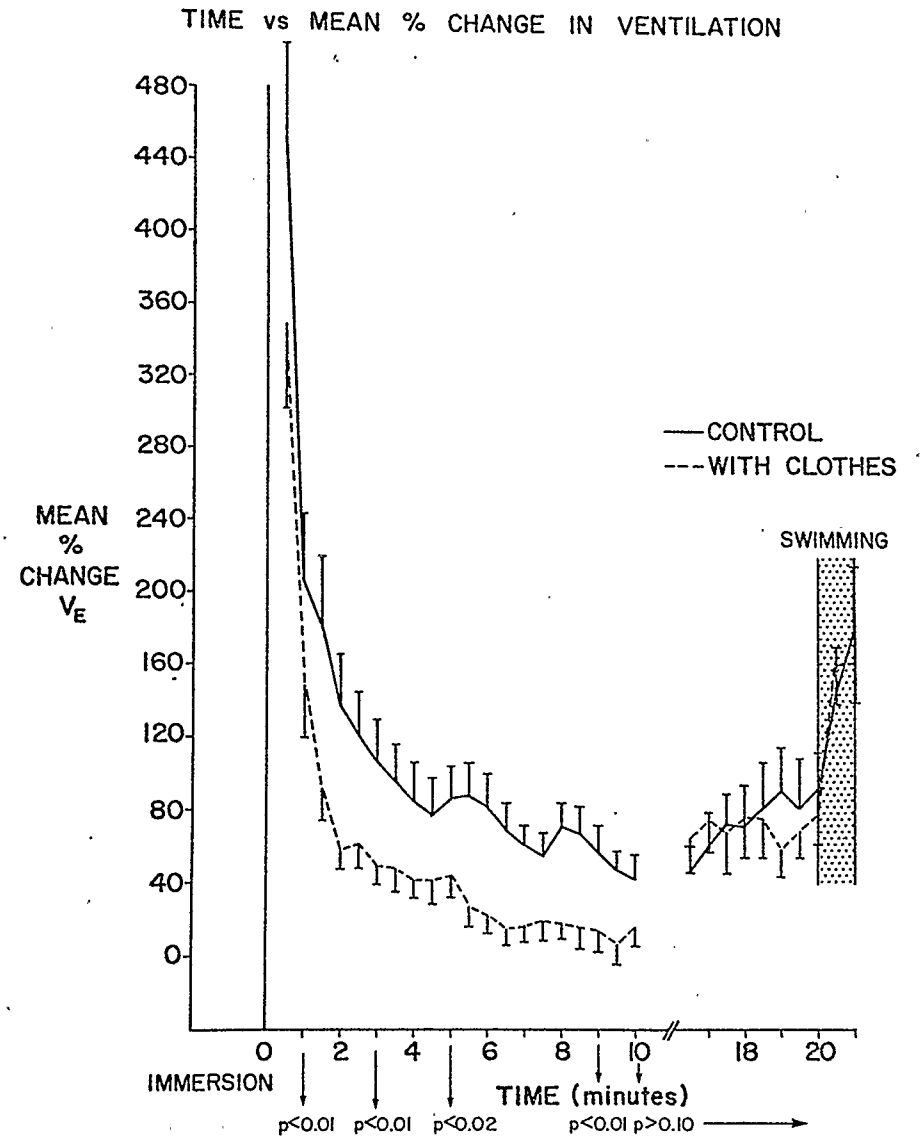

Fig. 8. Mean percentage change in ventilation during a 20 min immersion in cold water (13.9°C). Unclothed, wearing bathing suit (——); clothed (----). N = 14. Vertical bars = ± S.E.M.

increased ventilation. The changes between the clothed and unclothed subjects were not statistically significant.

The mean percentage changes in end-tidal PCO_2 during the two cold water immersions for the unclothed and clothed subjects are seen in Fig. 9. The degrees of hyperventilation, -28% and -26%, for the first minute were quite similar. The end-tidal PCO_2 returned towards pre-immersion values and remained steady for the next 18 min. The only significant attenuation ($p < 0.05$) which occurred as a result of wearing clothing was seen in min 2 and 3. Any changes for the remaining time were not significantly different ($p > 0.10$). Swimming movements at 19.5 min of the 2 immersions precipitated a further decline in end-tidal PCO_2, but these changes were not statistically significant. It was noted that when a subject's responses (PCO_2; $\dot{V}_E$) were monitored for 1 to 2 min after the swimming movements, they quickly returned to the levels observed before swimming.

Mean surface skin temperature changes during both cold water immersions are illustrated in Fig. 10. The mean skin temperature for the unclothed subjects (31.8°C) was significantly lower ($p < 0.01$) than that obtained for the clothed subjects (32.75°C) before the immersion. The mean skin temperatures declined in a similar manner during the first minute of the immersion and reached a value of 24°C for the clothed subjects and 22°C for the unclothed subjects. However, this change was not statistically significant ($p > 0.10$). For the remaining 19 min of the experiment a steady and sometimes slight decline was noted for the unclothed subjects in comparison to the clothed subjects and the differences in the mean skin temperatures were statistically significant ($p < 0.001$; $p < 0.01$). The overall decrease in skin temperatures was

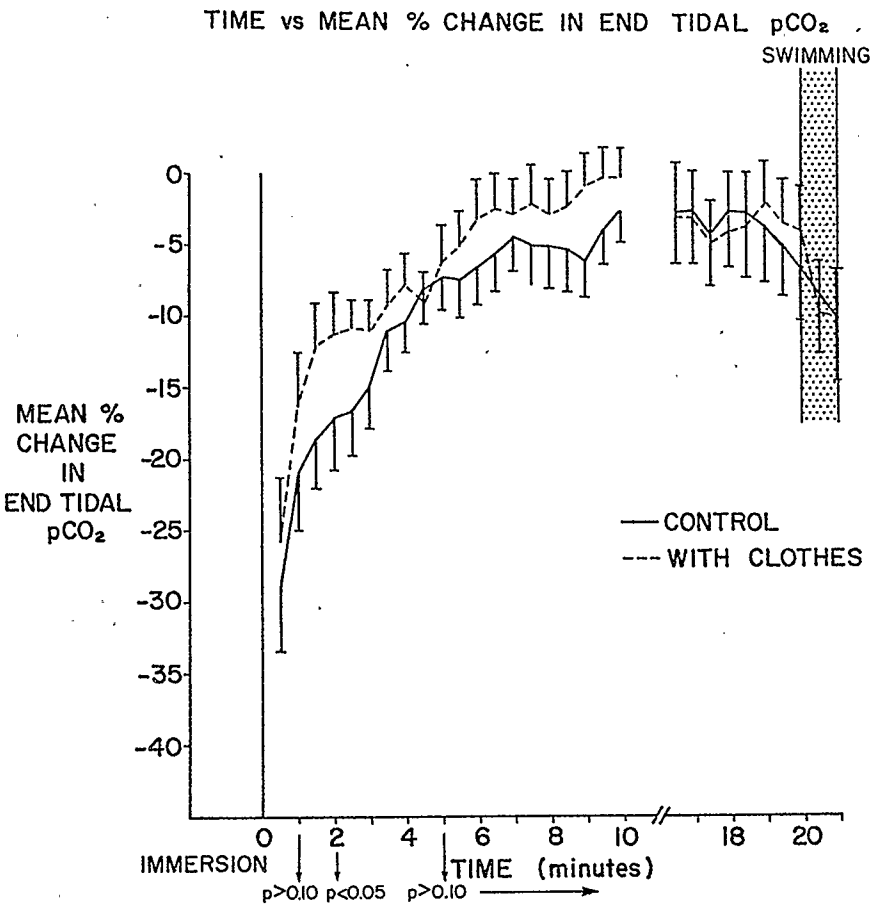

Fig. 9. Mean percentage change in end-tidal PCO_2 during a 20 min immersion in cold water (13.9°C). Unclothed, wearing bathing suit (——); clothed (----). N = 14. Vertical bars = ± S.E.M.

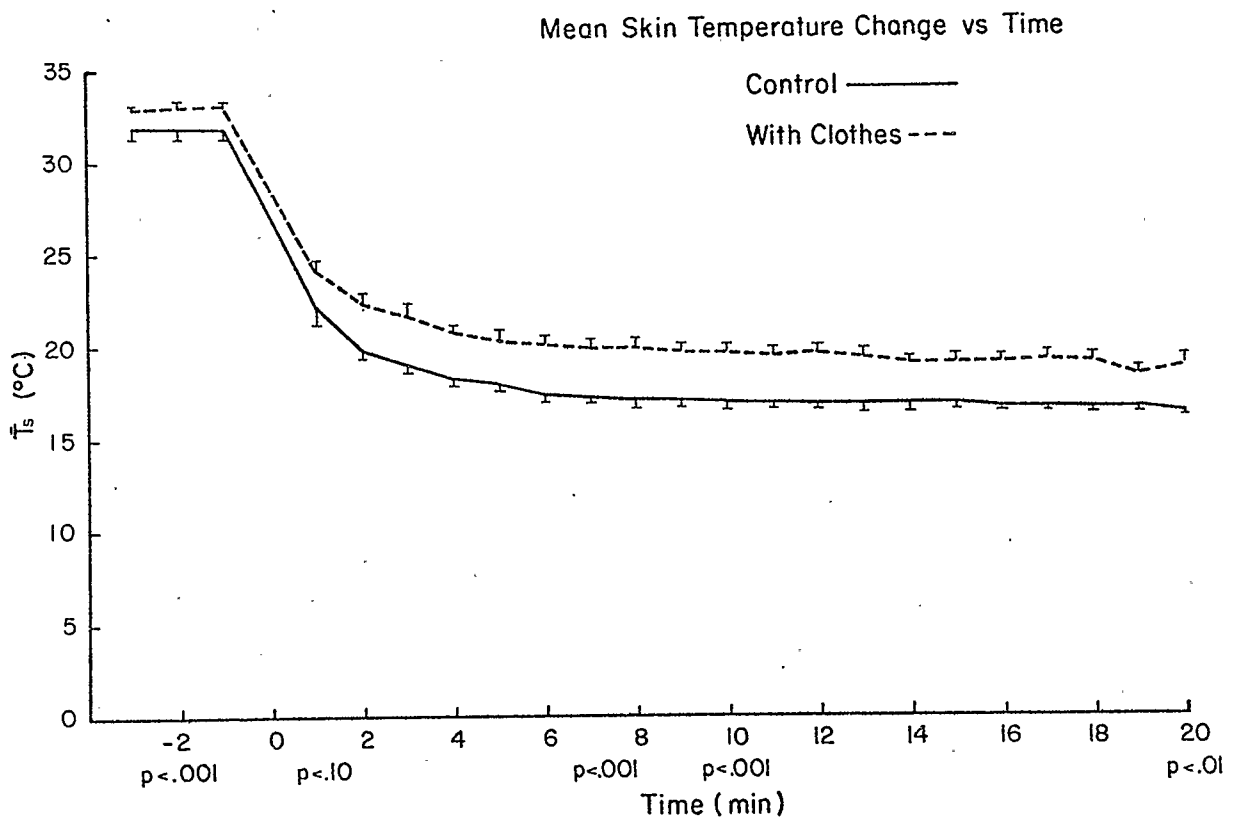

Fig. 10. Comparison of mean surface skin temperatures (^{o}C) during immersion in cold water (13.9^{o}C) for 20 min. Unclothed, wearing bathing suit (——); clothed (----). N = 12. Vertical bars = ± S.E.M.

15.3°C and 14.0°C for the unclothed and clothed subjects respectively. When the subjects were asked to perform swimming movements at min 19 of the immersion, an initial decrease of 0.06°C for clothed subjects and a slight increase of 0.09°C for unclothed subjects was noted. The mean skin temperature was recorded at the end of the swimming movements and an increase of 0.45°C was evident for the clothed subjects, whereas a decrease of 0.25°C was seen in the unclothed subjects. None of these changes was statistically significant ($p > 0.10$).

Figure 11 shows the changes in mean body temperature (aural) during the immersions with the subjects clothed and unclothed. A gradual increase from 36.4°C and 36.49°C to 36.6°C and 36.7°C occurred during the first 10 min of both immersions for the unclothed and clothed subjected respectively. This temperature remained steady for 6 min and a slight decrease was noted during the last 4 min. The final temperatures recorded were 36.61°C for unclothed and 36.65°C for clothed subjects. However, neither temperature returned to pre-immersion values. Although the mean body temperature for the immersion while the subjects wore clothing appeared higher than that obtained during the control immersion, the difference was not statistically significant. Overall, increases of 0.20° and 0.16°C in body temperature were seen when the subjects were either unclothed or clothed during the 2 immersions.

B. ALCOHOL CONSUMPTION AND COLD WATER IMMERSION

1. Immersion in Water at 13.5°C

Thirteen subjects, 8 male and 5 female, ranging in age from 22 to 54, volunteered for this experiment and were immersed in cold water (13.5°C) on 2 occasions. The weights and heights of those subjects

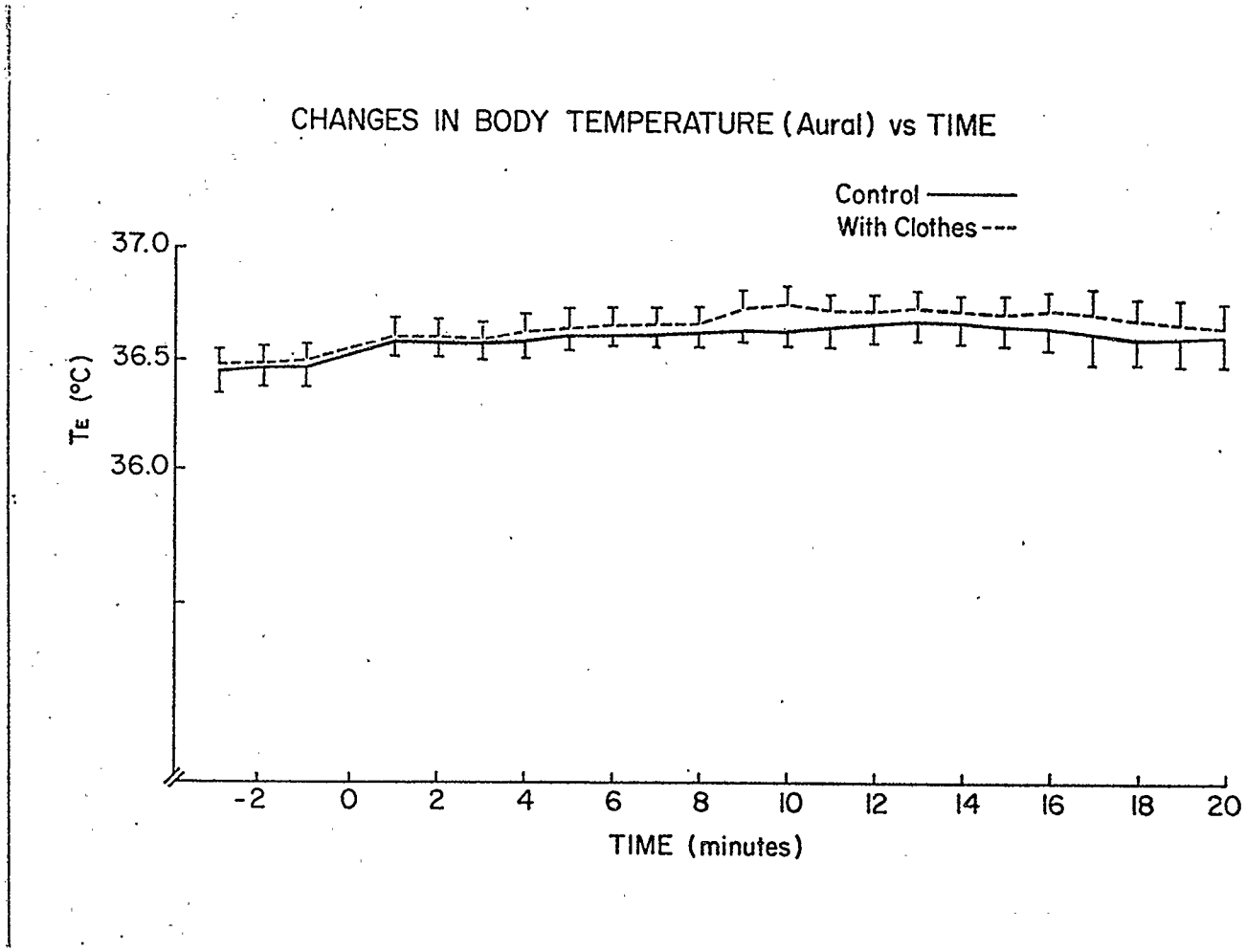

Fig. 11. Comparison of body temperature (^{o}C) as measured aurally during immersion in cold water (13.9^{o}C) while subjects were clothed (----) or unclothed (——). N = 10. Vertical bars = $\pm$ S.E.M.

ranged from 84 to 43 kg and 193 to 157 cm. Table III gives the individual values for each of the 13 subjects.

An attempt was made to have the subjects attain a blood alcohol level of approximately 80 mg.100 ml^{-1}, but, as illustrated in Table IV, a wide range (30 to 175 mg.100^{-1}) was found in the first sample which was taken before entry into the cold water. The second sample, taken 1 h after drinking the alcohol, again showed a wide range (47 to 158 mg.100^{-1}). Six of the subjects had a lower blood level, while 7 subjects had a higher blood alcohol content than that found in the initial sample.

The ventilatory responses measured during the cold water immersion with and without alcohol consumption were compared. Figure 12 shows the mean percentage changes in total ventilation during these immersions. Increases of 450% and 370% were seen during the first minute of the immersion after no alcohol and alcohol consumption. Both recordings returned toward pre-immersion values until the eighth minute of the experiments. The ventilatory pattern remained fairly steady from 8.5 min to the end of the experiment, although the respiratory pattern for the subjects who had consumed alcohol appeared more erratic than that achieved during the control immersion. There appeared to be a slightly attenuated response during the first 3.5 min of the immersion after the subjects had consumed alcohol, but the differences were not statistically significant ($p > 0.10$).

The mean percentage changes in end-tidal PCO_2 during the 2 cold water immersions are seen in Fig. 13. The initial degree of hyperventilation, -25% and -23%, was similar during the immersions without and with alcohol consumption, and in both situations there was a steady return to pre-immersion values for the next 7 min. A plateaued level

TABLE III

Height and Weight of Subjects for Alcohol Experiment

(T_w - 13.5°C)

Subject	Height (cm)	Weight (kg)
A.B.	193	84
R.D.	187	76
G.S.	180	74
K.E.C.	179	81
V.D.	178	66
J.J.	173	65
R.T.	173	62
S.M.	171	67
S.H.	170	60
J.W.	170	53
D.S.	169	65
M.S.	163	55
H.M.	157	43
$\bar{X} \pm$ S.E.M.	174.0 ± 2.63	65.46 ± 3.18

TABLE IV

Blood Alcohol Levels

(T_w - 13.5°C)

Subject	Quantity of Ethanol (ml)	Sample I $mg.100\ ml^{-1}$ (45 min after beginning ingestion)	Sample II $mg.100\ ml^{-1}$ (1 hour 20 min)
R.T.	76.3	175	158
K.E.C.	97.8	130	131
G.S.	90.6	128	146
J.J.	71.1	111	106
V.D.	80.7	110	108
H.M.	39.5	106	99
S.H.	48.9	97	86
D.S.	79.6	70	124
S.M.	54.0	67	78
R.D.	61.2	66	59
J.W.	43.0	63	81
M.S.	44.5	61	75
A.B.	69.0	30	47
		$\bar{X} \pm$ S.E.M.	$\bar{X} \pm$ S.E.M.
		90 ± 11.2	99 ± 9.2

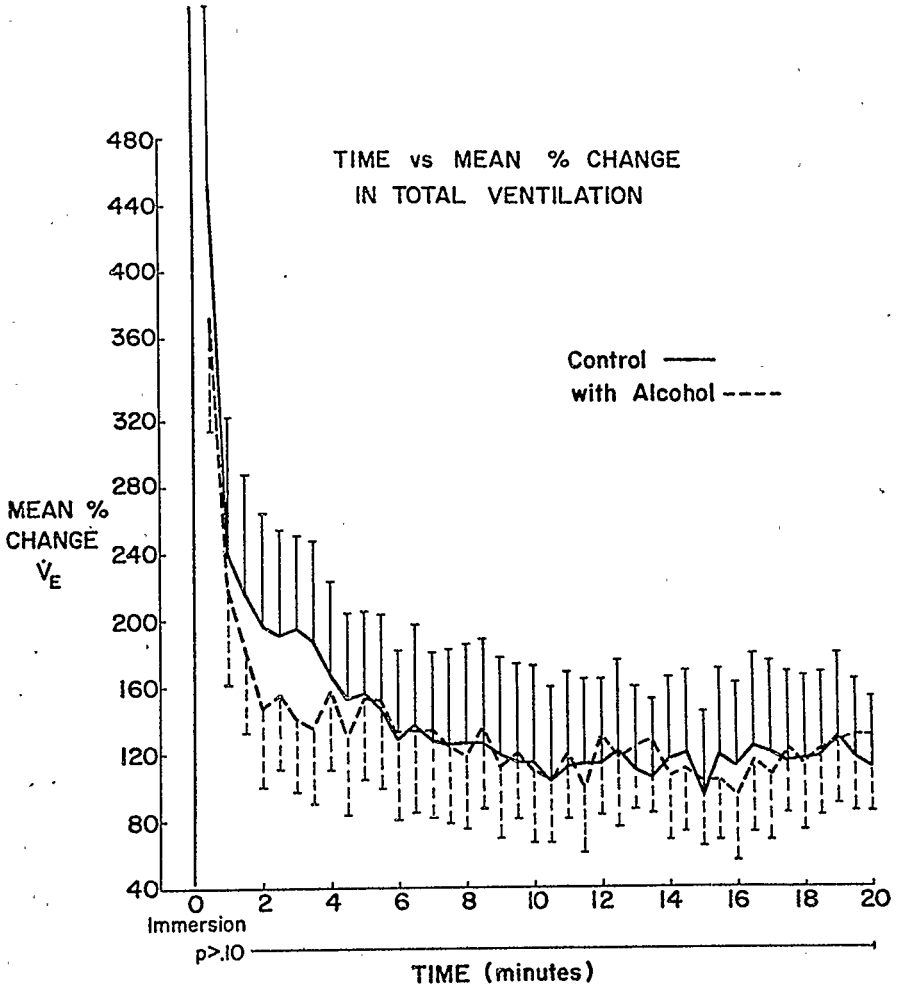

Fig. 12. Mean percentage change in ventilation during a 20 min immersion in cold water (13.5°C). Without alcohol (——); with alcohol (----). N = 13. Vertical bars = ± S.E.M.

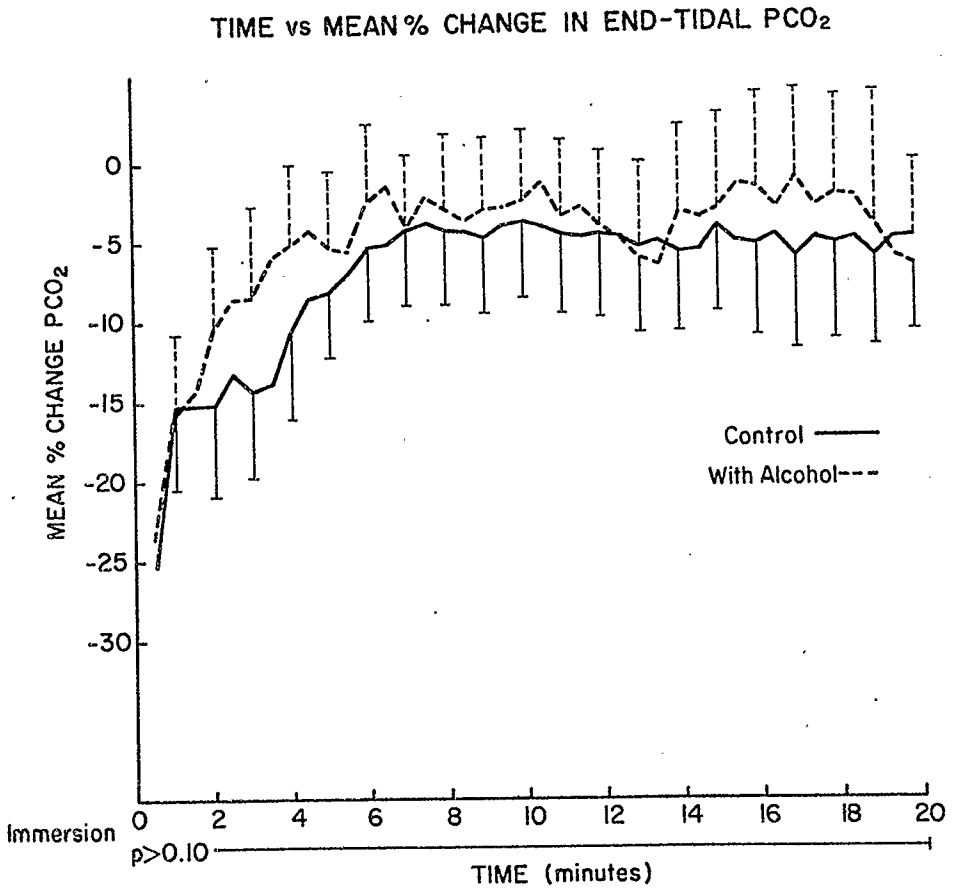

Fig. 13. Mean percentage change in end-tidal PCO_2 during a 20 min immersion in cold water (13.5°C). Without alcohol (——); with alcohol (----). N = 13. Vertical bars = ± S.E.M.

of hyperventilation at approximately -3 to -5% was seen during the remaining 12 min of the immersion. There appeared to be an altered response during the immersion after alcohol consumption but no statistically significant differences were found ($p > 0.10$).

Body temperature was measured both rectally (T_R) and aurally (T_E). The changes during the immersion without alcohol consumption show that the rectal temperature was significantly higher ($p < 0.001$) than the aural temperature in the pre-immersion period and for the first 2 min of the immersion. The aural temperature remained constant for most of the cold water immersion period and a decline was not seen until min 16. In contrast, the rectal temperature showed a steady decline during the time in the cold water, but after the third minute of the immersion, the difference between the 2 temperatures was no longer statistically significant ($p > 0.10$). The overall changes in the 2 measurements were a decrease of $0.92^{o}C$ and $0.11^{o}C$ for the rectal and aural temperatures respectively.

A similar pattern in body temperature changes during cold water immersion was seen after the subjects had ingested alcohol. The differences between the rectal and aural temperatures during the pre-immersion period and for the first 3 min of the immersion were statistically significant ($p < 0.001$). The aural temperature was constant until min 16 when a decrease was evident. There was a decline in the rectal temperature during the 20 min, but after 4 min the differences between the 2 body temperatures were no longer statistically significant ($p > 0.10$). A decline of $1.15^{o}C$ was seen for the rectal temperature and a decrease of $0.22^{o}C$ for the aural temperature.

A comparison of the rectal temperature changes during the

immersions with and without alcohol ingestion is seen in Fig. 14A. From a pre-immersion value of 37.5°C for both experiments a steady decline in the rectal temperature was evident during both immersions and the rectal temperature after alcohol consumption declined more quickly than the rectal temperature obtained without alcohol consumption to final readings of 36.35°C and 36.58°C. The overall change in rectal temperature was a decrease of 0.92°C and 1.15°C for the procedures without and with alcohol consumption respectively. However, the differences were not statistically significant ($p > 0.10$).

Fig. 14B shows the changes in aural temperature (T_E) during both immersion periods. Generally, steady readings were obtained during both experiments until 16 min of the immersion had elapsed; after which time a slight decrease occurred. A slightly faster decline in aural temperature was seen after alcohol consumption, and although the aural temperature was lower in this experiment than without alcohol consumption, the difference was not statistically significant ($p > 0.10$). The change in the aural temperature was a decrease of 0.11°C from a resting value of 36.9°C for the immersion without alcohol and 0.22°C from a pre-immersion reading of 36.9°C for the immersion following alcohol ingestion.

Mean surface skin temperature ($\bar{T}_{SK}$) changes during the 2 cold water immersions are seen in Fig. 15. The mean skin temperature after alcohol consumption was lower (31.6°C) than the mean skin temperature (31.8°C) without alcohol consumption during the pre-immersion period but was slightly higher (0.37°C) during the first 2 min of immersion. These differences were not statistically significant ($p > 0.10$). The fall in the mean skin temperature for both immersion times was similar

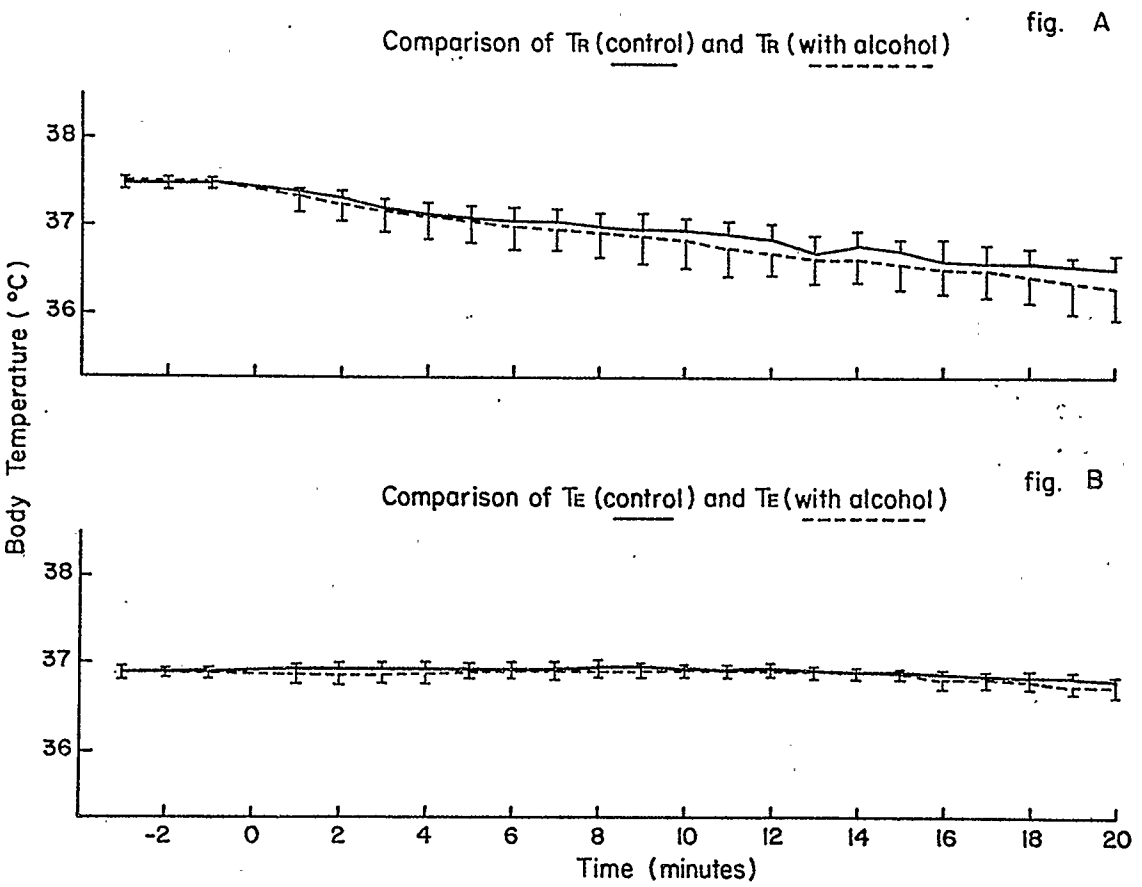

Fig. 14A. Comparison of rectal temperature (T_R) during a 20 min immersion in cold water (13.5°C) with (----) and without (——) alcohol consumption. N = 13. Vertical bars = ± S.E.M.

Fig. 14B. Comparison of aural temperature (T_E) during a 20 min immersion in cold water (13.5°C) with (----) and without (——) alcohol consumption. N = 13. Vertical bars = ± S.E.M.

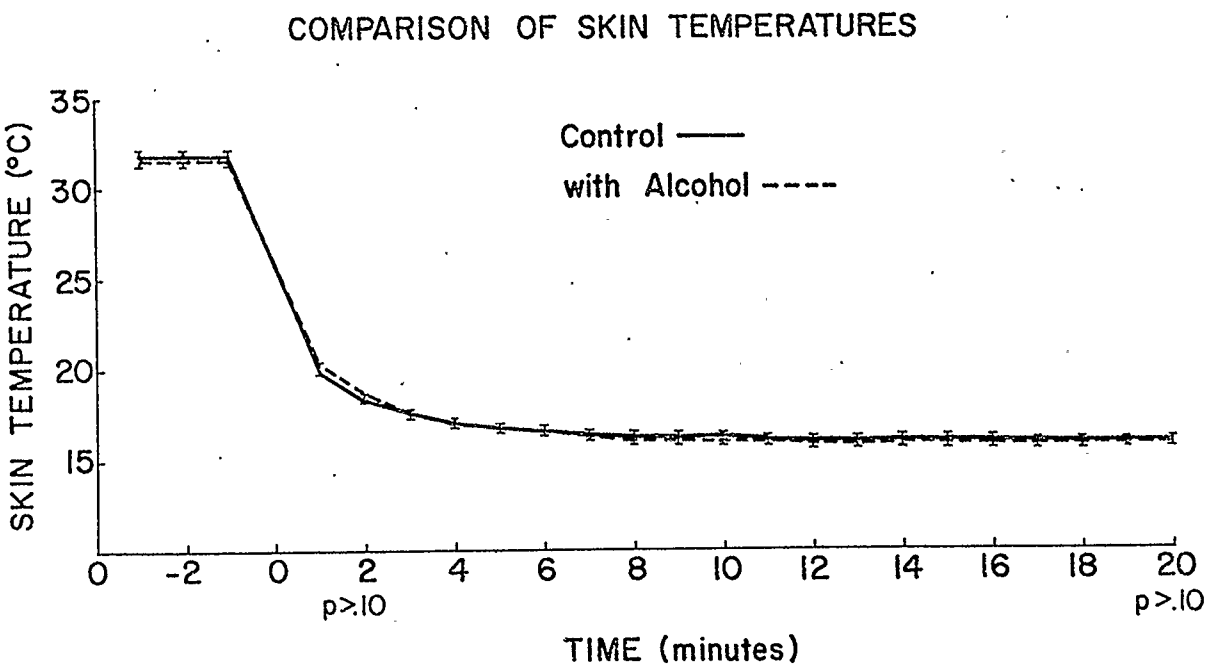

Fig. 15. Comparison of mean surface skin temperature ($\bar{T}_{SK}$) during a 20 min immersion in cold water (13.5°C) with (----) and without (——) alcohol consumption. N = 13. Vertical bars = ± S.E.M.

and no statistically significant differences were noted. The mean skin temperature at the end of each experiment was 2.3°C above the water temperature.

A variable pattern (mild, vigorous, or intermittent) in shivering was observed in the subjects during the immersion periods. The average time for shivering to occur following immersion without alcohol was 2.7 min, while after alcohol consumption, the latency was 3.3 min. Three subjects did not shiver during the control as well as the alcohol experiments. Subjectively, the volunteers found the cold water immersion less uncomfortable after alcohol ingestion.

Oxygen consumption was measured for only 2 of the subjects. As a result of immersion in cold water, there was an increase in oxygen consumption during both immersions from resting values of 0.27 $l.min^{-1}$ and 0.29 $l.min^{-1}$ to a maximum of 0.42 $l.min^{-1}$ and 0.39 $l.min^{-1}$ for the control and experimental immersions respectively. A more steady increase was noted during the immersion without alcohol ingestion. No significant differences were seen in the oxygen uptake during the 2 experiments.

2. Immersion in Water at 22°C

Ten subjects, 4 female and 6 male, whose ages ranged from 22 to 54 participated in this experiment. They were immersed in water at 22°C for 30 min on 2 occasions. Their heights and weights ranged from 193 to 157 cm and 84 to 43 kg. A listing of the individual values is provided in Table V.

The blood alcohol levels attained by these subjects are shown in Table VI. Once again, a wide range (46 to 145 $mg.100\ ml^{-1}$) was evident for the first sample, taken before entry into the water, and

TABLE V

Height and Weight of Subjects for Alcohol Experiment

(T_w - 22°C)

Subject	Height (cm)	Weight (Kg)
A.B.	193	84
G.S.	180	74
K.E.C.	179	81
V.D.	178	66
R.T.	173	62
S.M.	171	69
S.H.	170	60
D.S.	169	65
M.S.	163	55
H.M.	157	43
$\bar{X} \pm$ S.E.M.	173.30 ± 3.32	65.9 ± 4.04

TABLE VI

Blood Alcohol Levels (Tw - 22°C)

Subject	Sample I (mg.100 ml^{-1}) (45 min. after beginning ingestion)	Sample II (mg.100 ml^{-1}) (1 hr 20 min)
K.E.C.	145	154
S.M.	118	98
H.M.	94	96
D.S.	82	114
G.S.	81	119
V.D.	72	98
S.H.	66	81
R.T.	62	99
M.S.	59	78
A.B.	46	69
	$\bar{X} \pm$ S.E.M.	$\bar{X} \pm$ S.E.M.
	82.50 $\pm$ 9.93	100.60 $\pm$ 8.09

the second sample (69 to 154 mg.100 ml^{-1}) taken 1 h after consumption of alcohol. Nine of the subjects had a higher blood alcohol concentration, while only 1 subject had a lower blood alcohol concentration than that found in the initial sample.

The mean percentage changes in total expired volume during both experiments are seen in Fig. 16. Increases of 385% and 260% were noted for the gasp responses during the immersions without and with alcohol consumption. Both recordings show that there was a rapid return of expired ventilation towards pre-immersion values by 2.5 min. For the next 27.5 min the ventilatory pattern for the control immersion was steady at a mean value of 80%. In contrast, the expired ventilation during the immersion after alcohol consumption, showed a continuous decline from 8.5 min, with a sharp decrease occurring at 18.5 min. Thereafter the pattern was steady at a value slightly below 0% change. The attenuated response from 16 to 30 min was statistically significant ($p < 0.01$; $p < 0.05$).

The mean percentage changes in end-tidal PCO_2 during the 2 cold water immersions are seen in Fig. 17. An initial degree of hyperventilation, -20% and -10%, was evident during the first minute of the 2 immersions. The values returned quickly to the pre-immersion readings and during the immersion without alcohol consumption a steady plateau (at approximately -7.5% change) was evident. A similar pattern was seen for the experiment after alcohol consumption and at 17 min into the immersion period a further shift towards pre-immersion values was seen. Although there appeared to be an attenuated response, no differences were statistically significant ($p > 0.10$).

A comparison of the rectal temperature during the immersions

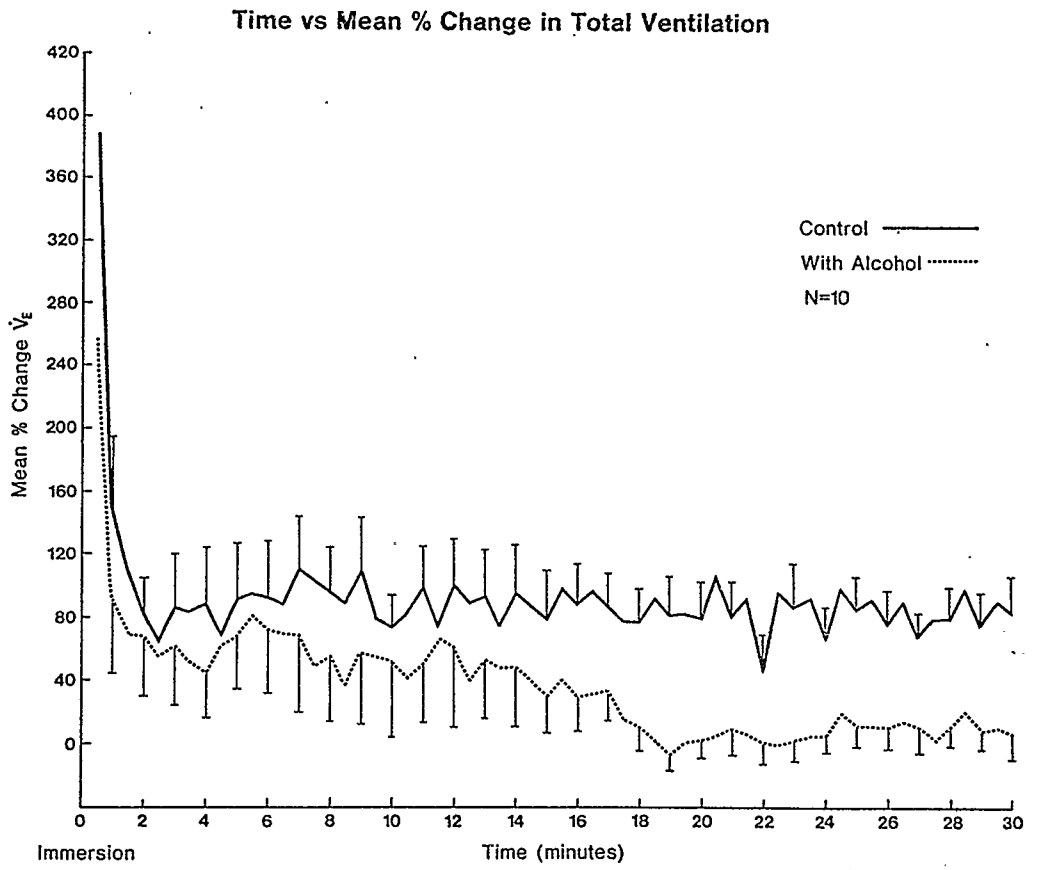

Fig. 16. Mean percentage change in ventilation during a 30 min immersion in water at 22°C. Without alcohol (——); with alcohol (----). N = 10. Vertical bars = ± S.E.M.

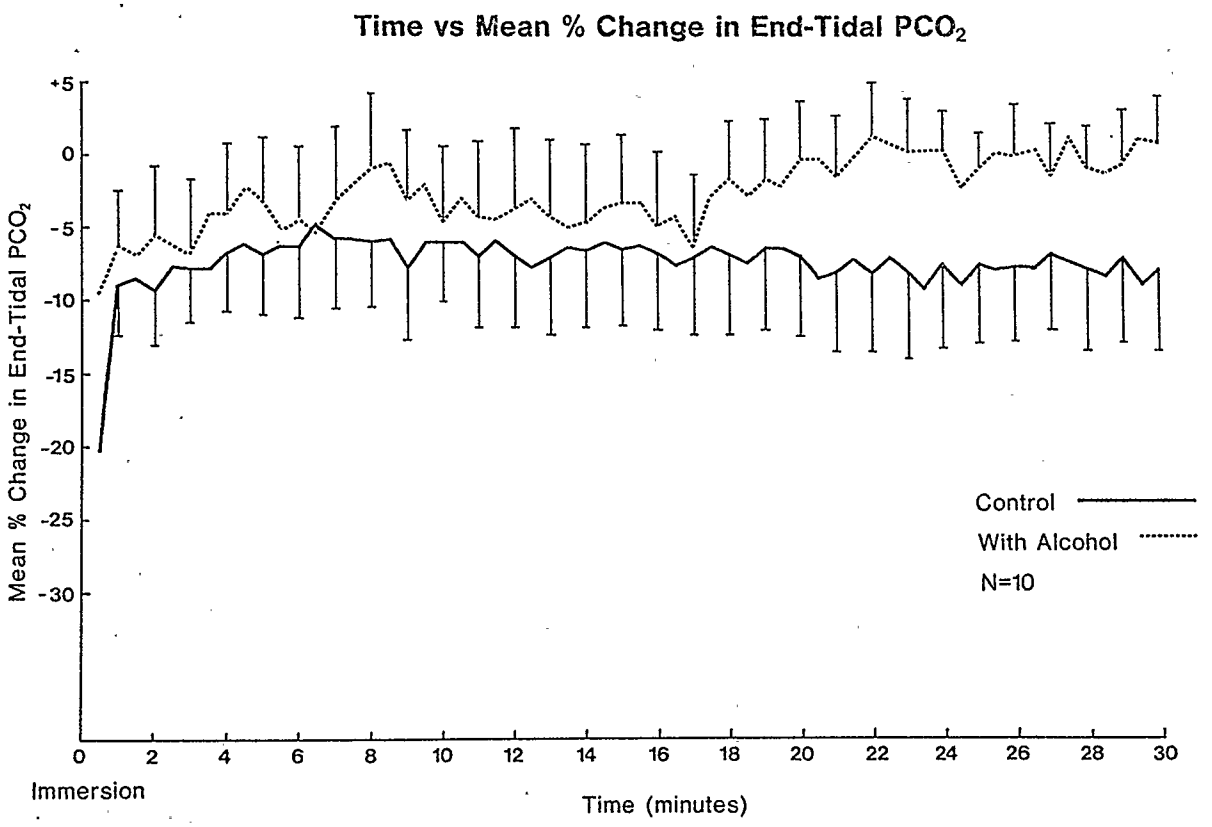

Fig. 17. Mean percentage change in end-tidal PCO_2 during a 30 min immersion in water at 22°C. Without alcohol (——); with alcohol (----). N = 10. Vertical bars = ± S.E.M.

with and without alcohol ingestion is seen in Fig. 18A. The rectal temperature without alcohol consumption was lower (37.29°C) than that obtained with alcohol ingestion (37.35°C) during the pre-immersion time, and a slight increase was noted during the first minute of immersion. Thereafter, a steady decline in rectal temperature was noted during both immersions, with the rectal temperature after alcohol consumption declining more quickly than the rectal temperature obtained without alcohol consumption. This difference was not statistically significant ($p > 0.10$). The overall change in rectal temperature was a decrease of 0.44°C and 0.57°C during the immersions with and without alcohol respectively. Figure 18B illustrates the changes in aural temperature during both water immersions. There was an increase (from resting values of 36.69°C and 36.74°C) during both immersions and generally the aural temperature after alcohol consumption was higher than the aural temperature without alcohol ingestion. No differences were statistically significant ($p > 0.10$). A slight decline was noted in the aural temperature during the control immersion from 22 to 30 min. However, such a change in aural temperature during the immersion after alcohol consumption was not seen until 27 to 30 min. The total change in the aural temperature was a decrease of 0.04°C for the immersion without alcohol and an increase of 0.03°C for the immersion following alcohol ingestion.

Mean surface skin temperature changes during the 2 warm water immersions are seen in Fig. 19. The mean skin temperature after alcohol consumption was higher (32.15°C) than the mean skin temperature (32.03°C) without alcohol consumption during the pre-immersion period and the first minute (27.42°C vs 27.20°C) of the immersion. These differences were not statistically significant ($p > 0.10$). The decrease in the mean

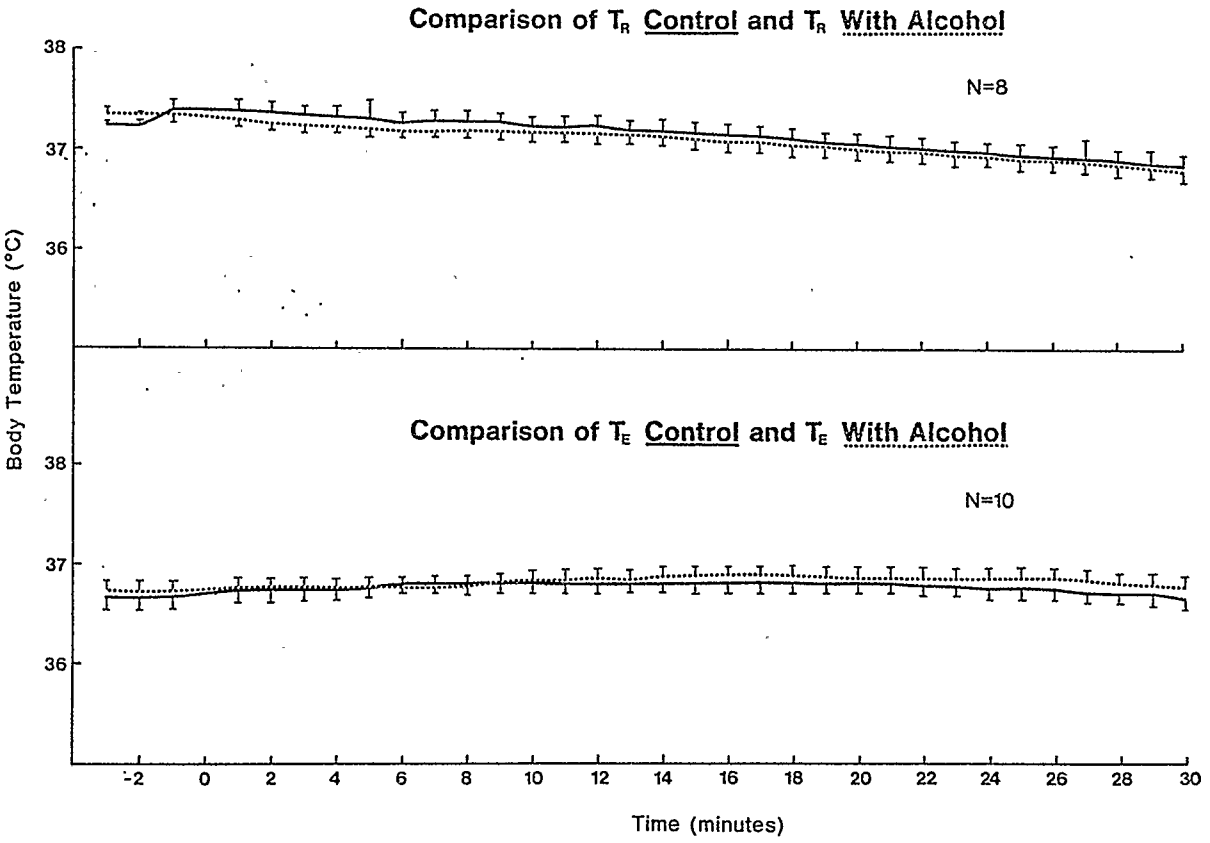

Fig. 18A. Comparison of rectal temperature (T_R) during a 30 min immersion in water at 22°C with (----) and without (——) alcohol consumption. N = 8. Vertical bars = ± S.E.M.

Fig. 18B. Comparison of aural temperature (T_E) during a 30 min immersion in water at 22°C with (----) and without (——) alcohol consumption. N = 10. Vertical bars = ± S.E.M.

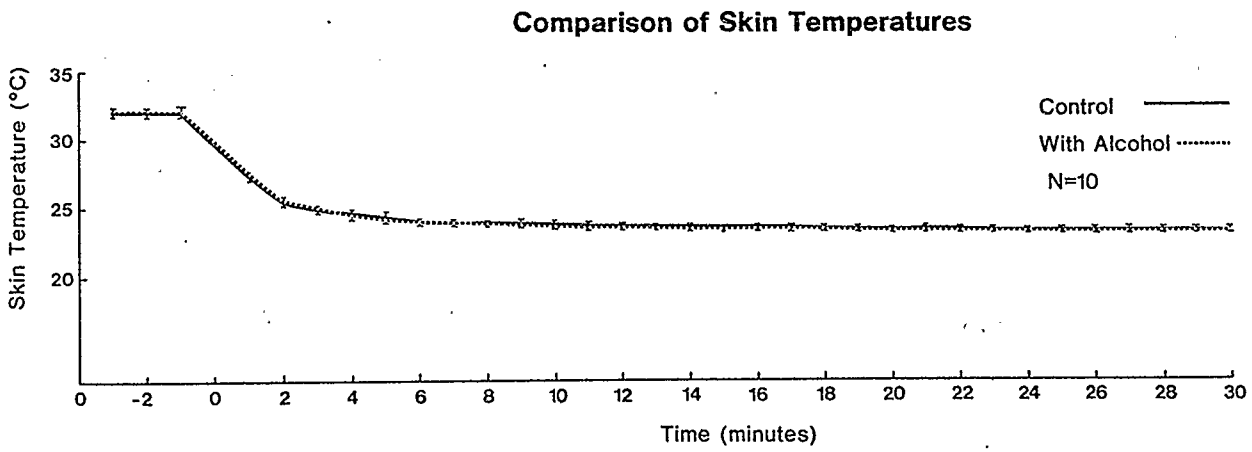

Fig. 19. Comparison of mean surface skin temperature (T_{SK}) during a 30 min warm water (22°C) immersion with (----) and without (——) alcohol consumption. N = 10. Vertical bars = ± S.E.M.

skin temperature for both immersions was similar and no statistically significant differences were noted. The mean skin temperature at the end of each immersion was approximately 1.0°C above the water temperature.

A continuous monitoring of heart rate for the subjects was achieved during both immersions. Although some difficulty was experienced in obtaining clear records at all times, suitable recordings were made from 8 subjects. During the immersion without alcohol the mean heart rate during the first minute of immersion was higher (79 beats.min^{-1}) than that seen during the pre-immersion period (77 beats.min^{-1}) but for the remainder of the experiment the mean heart rate was the same or lower (77 to 72 beats.min^{-1}). The changes were not statistically significant. The mean heart rate during the first minute of immersion after alcohol ingestion was lower (74 beats.min^{-1}) than that observed during the pre-immersion time (79 beats.min^{-1}), and remained lower (77 to 75 beats.min^{-1}) throughout the experiment. Again, no differences were statistically significant.

The variable pattern in shivering during the immersion without alcohol consumption could be described as mild and continuous, with only 1 subject displaying a vigorous response. In contrast to this, a mild, intermittent shivering pattern was generally seen during the immersion after alcohol consumption. The average time for shivering to occur during the control immersion was 6.3 min while after alcohol consumption the latency was 4.3 min. However, during the latter immersion, 2 subjects did not shiver. The subjects usually found the water immersion less uncomfortable after alcohol ingestion. A number of the volunteers also noted that they found the control immersion at 22°C

more uncomfortable than the control immersion in water at 13.5°C.

The oxygen uptake was determined for only 2 subjects during the immersion period. The oxygen consumption during the immersion without alcohol consumption was either the same or slightly lower than the resting value (0.35 $l.min^{-1}$). In contrast, the oxygen consumption during the immersion after alcohol ingestion showed an increase (0.36 $l.min^{-1}$) over the resting value (0.30 $l.min^{-1}$) during 5 to 8 min of the experiment. The samples at 18 and 25 min were lower than the pre-immersion value. The oxygen consumption during the immersion after alcohol ingestion was either higher (0.36 $l.min^{-1}$ vs 0.32 l.min) or lower (0.27 $l.min^{-1}$ vs 0.23 $l.min^{-1}$; 0.28 $l.min^{-1}$ vs 0.32 $l.min^{-1}$) than the oxygen consumption during the immersion without alcohol ingestion. No differences were statistically significant.

3. Immersion in Water at 30°C

Five subjects, 3 male and 2 female, ranging in age from 24 to 35, volunteered for this experiment. Their weights and heights ranged from 74 to 43 kg and 180 to 157 cm. The values for each subject are found in Table VII.

Once again, a variable range (130 to 77 $mg.100\ ml^{-1}$) for Sample I and 136 to 81 $mg.100\ ml^{-1}$ for Sample II was evident in the blood alcohol levels of the subjects. Both samples showed the highest mean blood alcohol levels for any of the experiments, registering 100.6 ± 12.64 $mg.100\ ml^{-1}$ and 114.8 ± 13.94 $mg.100\ ml^{-1}$ for samples I and II respectively. Three subjects showed a higher and 2 a lower blood alcohol level in the second samples. Results are shown in Table VIII.

Body temperatures were measured both rectally and aurally.

TABLE VII

Height and Weight of Subjects for Alcohol Experiment

(T_w - 29.8°C)

Subject	Height (cm)	Weight (Kg)
G.S.	180	74
V.D.	178	66
R.T.	173	62
S.M.	171	69
H.M.	157	43
$\bar{X} \pm$ S.E.M.	171.8 ± 4.52	62.8 ± 5.95

TABLE VIII

Blood Alcohol Levels (Tw - 29.8°C)

Subject	Sample I (mg.100 ml^{-1}) (45 min after beginning ingestion)	Sample II (mg.100 ml^{-1}) (1 hr. 20 min)
S.M.	130	100
R.T.	126	136
H.M.	86	81
G.S.	84	150
V.D.	77	107
	$\bar{X} \pm$ S.E.M.	$\bar{X} \pm$ S.E.M.
	100.6 $\pm$ 12.64	114 $\pm$ 13.94

A comparison of the rectal temperatures is seen in Fig. 20A. A slow, but perceptible decline in rectal temperature was evident during both immersions. Although the rectal temperature after alcohol ingestion appeared to be lower than that obtained during the immersion without alcohol, the difference was not statistically significant ($p > 0.10$). The overall change in rectal temperature was a decrease of $0.36^{o}C$ and $0.45^{o}C$ from pre-immersion values of $37.39^{o}C$ and $37.29^{o}C$ for the experiments without and with alcohol consumption respectively.

The change in aural temperature is seen in Fig. 20B. As noted for previous experiments, a generally steady pattern was maintained once the immersion had occurred. The overall changes were an increase of $0.07^{o}C$ from a pre-immersion reading of $36.65^{o}C$ and a decrease of $0.15^{o}C$ from a resting value of $36.81^{o}C$ for the control and experimental immersions respectively.

The mean surface skin temperature pattern was interesting (Fig. 21). The decline during both immersions was similar but the mean skin temperature elicited during the immersion after alcohol ingestion was apparently lower at all times than the skin temperature during the control immersion. The overall changes were decreases of $1.56^{o}C$ and $1.71^{o}C$ from a resting value of $32.20^{o}C$ and $32.09^{o}C$ during the immersions without and with alcohol consumption. The changes were not significantly different.

Further changes in the respiratory responses were noted during the immersion at this temperature ($30^{o}C$). The alterations in total expired ventilation are seen in Fig. 22. An increase of 170% and 80% was noted during the first minute of each immersion. By min 4 a plateau of approximately 20% and 18% was achieved for the experiments without

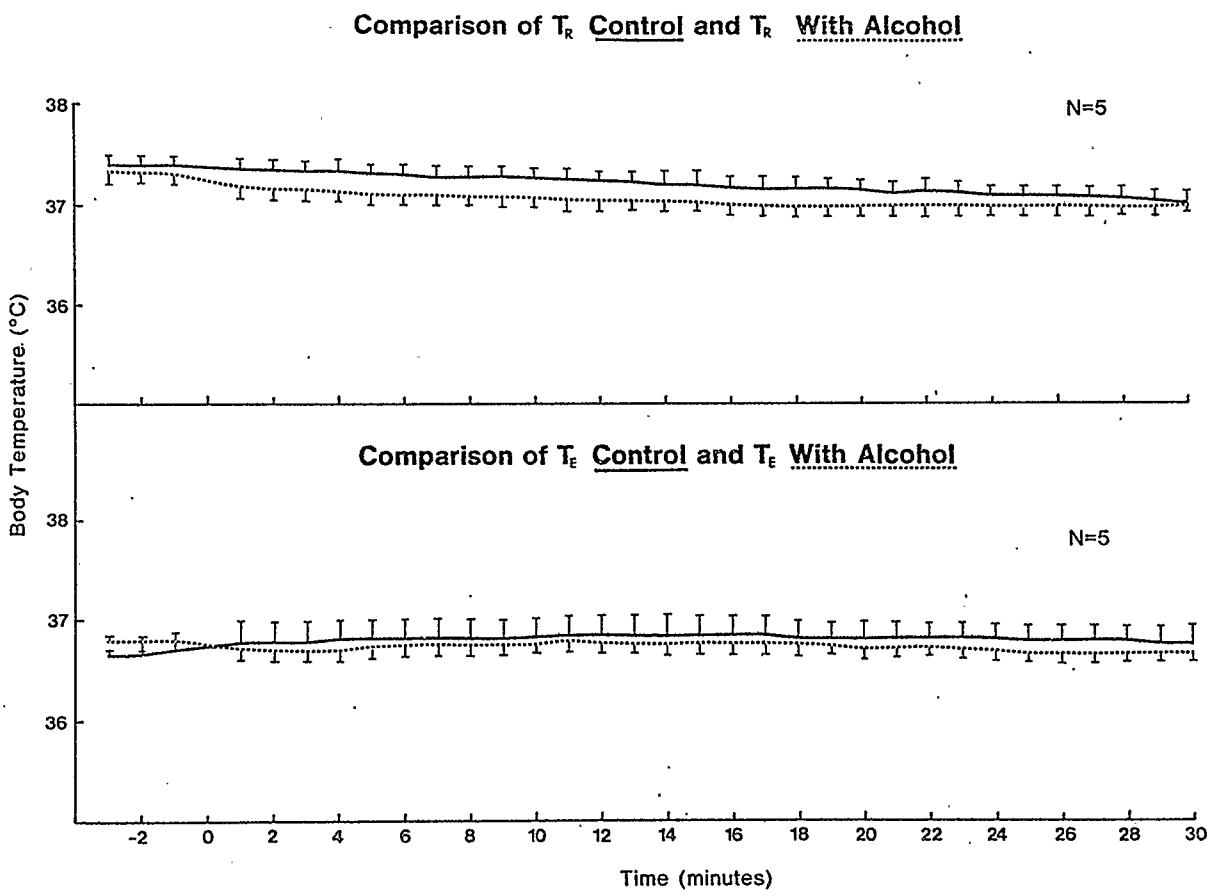

Fig. 20A. Comparison of rectal temperature (T_R) during a 30 min immersion in warm water (30°C) with (----) and without (——) alcohol ingestion. N = 5. Vertical bars = ± S.E.M.

Fig. 20B. Comparison of aural temperature (T_E) during a 30 min immersion in warm water (30°C) with (----) and without (——) alcohol ingestion. N = 5. Vertical bars = ± S.E.M.

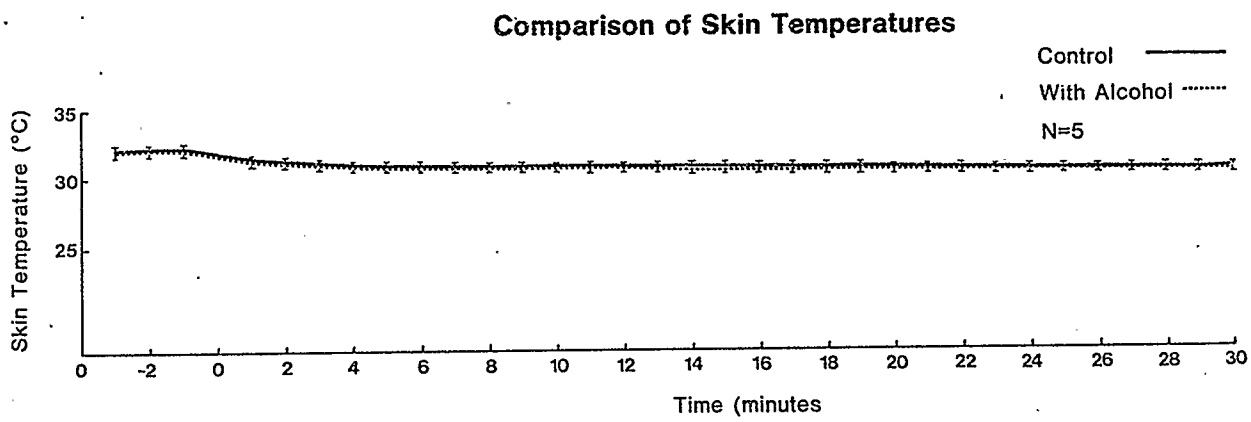

Fig. 21. Comparison of mean surface skin temperature ($\bar{T}_{SK}$) during a 30 min immersion in warm water (30°C) with (----) and without (——) alcohol consumption. N = 5. Vertical bars = ± S.E.M.

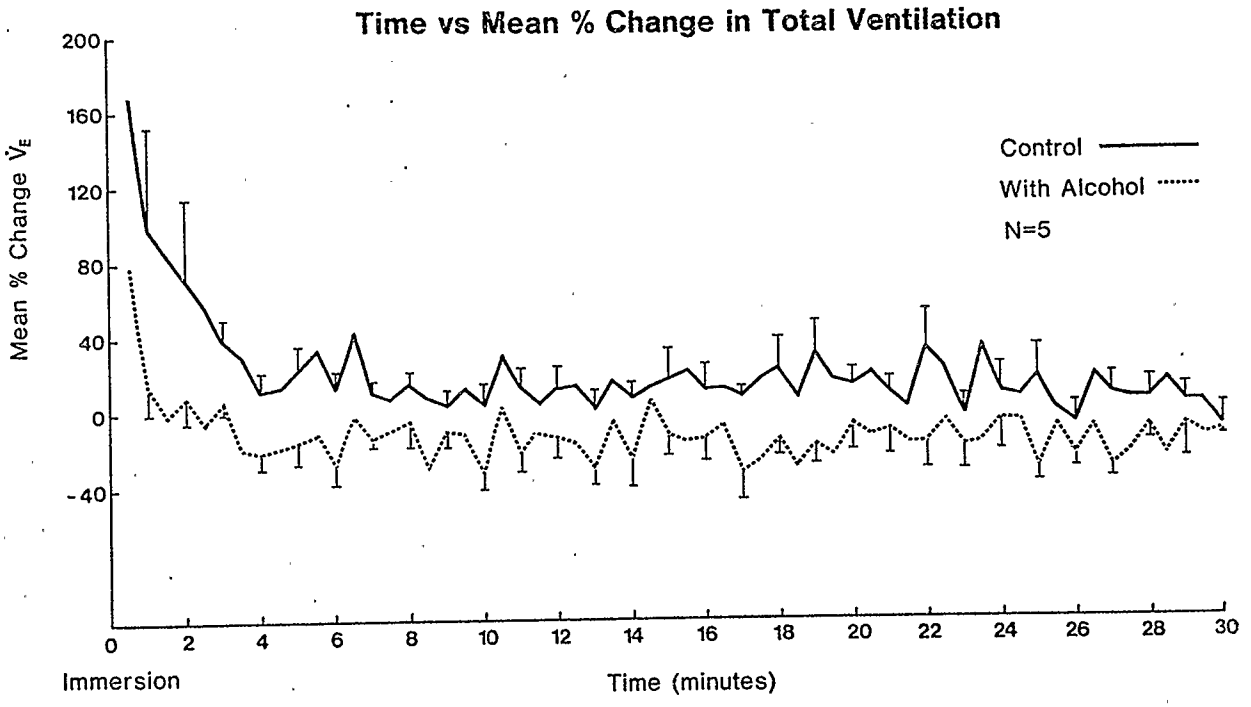

Fig. 22. Mean percentage change in ventilation during a 30 min immersion in warm water (30°C). Without alcohol (——); with alcohol (----). N = 5. Vertical bars = ± S.E.M.

and with alcohol consumption respectively. An erratic breathing pattern was evident during both immersions. An attenuated response was seen after alcohol consumption, but was not consistently statistically significant, e.g. $p < 0.05$, $p < 0.02$, $p < 0.05$, at 4, 5 and 10 min.

Figure 23 shows the mean percentage changes in end-tidal PCO_2. During the initial phase of the control immersion, there was no significant degree of hyperventilation (range from 0% to -5% change). However, as the immersion period progressed this pattern changed and a greater degree of hyperventilation (-7% change) was seen during the last 10 min of the exposure time. After alcohol ingestion, the end-tidal PCO_2 readings were higher (generally steady at +7% change) than during the pre-immersion period. This attenuated response was only significant for min 4 and 30 of the immersion period.

As might be expected, any shivering during these immersions was slight. During the control immersion 3 subjects did not shiver this lack of response was evident for 4 subjects during the immersion after alcohol consumption.

Oxygen uptake was measured for 4 of the 5 subjects. During the 2 immersions the oxygen uptake was either the same or slightly lower than the pre-immersion readings of 0.27 $l.min^{-1}$ and 0.30 $l.min^{-1}$ for the experiments without and with alcohol consumption. There were no statistically significant differences in the oxygen uptake during the immersions without and following alcohol ingestion.

Reliable heart rate recordings were obtained for 4 subjects. During the first minute of the control immersion the mean heart rate increased from 65 to 75 $beats.min^{-1}$ but was lower than the control (ranged from 57 to 62 $beats.min^{-1}$) for the remainder of the experiment.

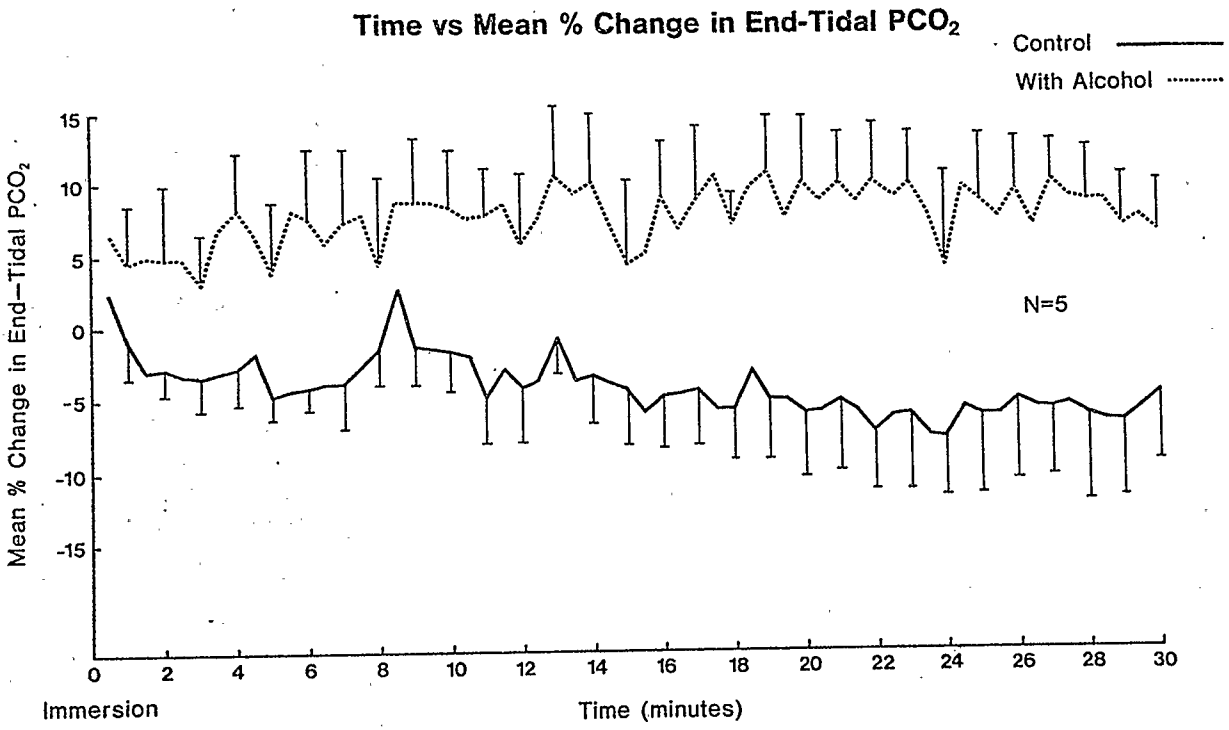

Fig. 23. Mean percentage change in end-tidal PCO_2 during a 30 min immersion in warm water ($30^{o}C$). Without alcohol (——); with alcohol (----). N - 5. Vertical bars = ± S.E.M.

The mean heart rate during the immersion after alcohol consumption was consistently lower (ranged from 57 to 62 beats.min^{-1}) than the pre-immersion reading of 67 beats.min^{-1}. No statistically significant changes in the mean heart rate were observed during the immersions following alcohol or no alcohol consumption.

C. DIAZEPAM AND COLD WATER IMMERSION

Six subjects, 2 females and 4 males, whose ages ranged from 25 to 36, participated in this experiment. They were immersed in cold water (13.5^{o}C) for 20 min. The heights and weights of each subject are listed in Table IX and ranged from 193 to 163 cm and 77 to 57 kg.

Five of the volunteers were given diazepam 5 mg orally and 1 subject (S.M.) was given diazepam 15 mg orally. The control blood samples were taken before ingestion, and the second sample, 1 h later and before entry into the cold water. The third sample was taken after the immersion period and ranged in time from 1 h 30 min to 1 h 50 min after ingestion of the drug. This difference in time was due to difficulty in drawing blood due to the venoconstriction elicited by the cold water.

The plasma levels of diazepam are seen in Table X. A wide range of plasma diazepam concentrations was evident for the subjects. Generally, the control values (time 0) were clear with the exception of subject D.C. who registered a value of 11.35 ng.ml^{-1}. The 5 subjects who had ingested diazepam,5 mg orally, (M.S., D.S., R.T., V.D. and D.C.) showed a variable range (23.68 to 195 ng.ml^{-1}) for the sample taken 1 h after ingestion and immediately before entry into the cold water. The third sample, taken approximately 1.5 h after drug ingestion and after

TABLE IX

Height and Weight of Subjects for Drug Experiment

Subject	Height (cm)	Weight (Kg)
D.C.	193	77
V.D.	178	66
R.T.	173	62
S.M.	171	69
D.S.	169	65
M.S.	163	57
$\bar{X} \pm$ S.E.M.	174.5 $\pm$ 4.61	66.0 $\pm$ 3.02

TABLE X

Plasma Diazepam Concentrations ($ng.ml^{-1}$)

Time (h)	SM	MS	DS	RT	VD	DC
0	0.000	0.000	0.000	0.000	0.000	11.35
0.5	477.0					
1.0	216.96	23.68	32.34	118.55	195.72	142.60
1.5	241.96	144.16	43.85	81.80	192.41	122.06
2.75	266.56					
4.3	190.31					

the subjects had been removed from the water also showed a wide range (43.85 to 192.41 $ng.ml^{-1}$). Of the 5 subjects, M.S. and D.S. showed an increased concentration for the third sample while 3 subjects, R.T., V.D. and D.C., had lower concentrations for this sample. One subject (S.M.) had ingested diazepam 15 mg orally. The highest plasma concentration (477.0 $ng.ml^{-1}$) was seen 30 min after drug ingestion. There was a large decrease in sample 3 (216.96 $ng.ml^{-1}$) with another seen in sample 4 (241.96 $ng.ml^{-1}$) and sample 5 (266.56 $ng.ml^{-1}$) in comparison to the sample at 0.5 h. The sample taken at 4.3 h showed the lowest value (190.31 $ng.ml^{-1}$). The plasma concentrations of diazepam for this subject at 1.0 h (216.96 $ng.ml^{-1}$) and 1.5 h (241.96 $ng.ml^{-1}$) were higher than any plasma concentrations observed for these times in the other subjects.

The respiratory patterns seen during the 2 immersions were interesting. The usual gasp response (increase of 280%) followed by a rapid return of ventilation toward pre-immersion values, was seen during the immersion without diazepam ingestion (Fig. 24). From 4 to 20 min the ventilation was steady at approximately a 35% change. During the exposure after drug consumption, a greater gasp was evident (increased to 400%) and an apparent increased expired ventilation in comparison to that elicited during the control experiment (steady at approximately 50%) was seen from 4 to 20 min. None of the differences was statistically significant ($p > 0.10$).

Figure 25 shows the mean percentage in end-tidal PCO_2 during the 2 immersions. The initial hyperventilation (a decrease of -23% during both immersions) with a gradual return toward pre-immersion readings was seen during both exposure periods. After 5 min of the cold water exposure following the ingestion of diazepam, the mean % change in end-tidal PCO_2 was higher than the pre-immersion values (3% change).

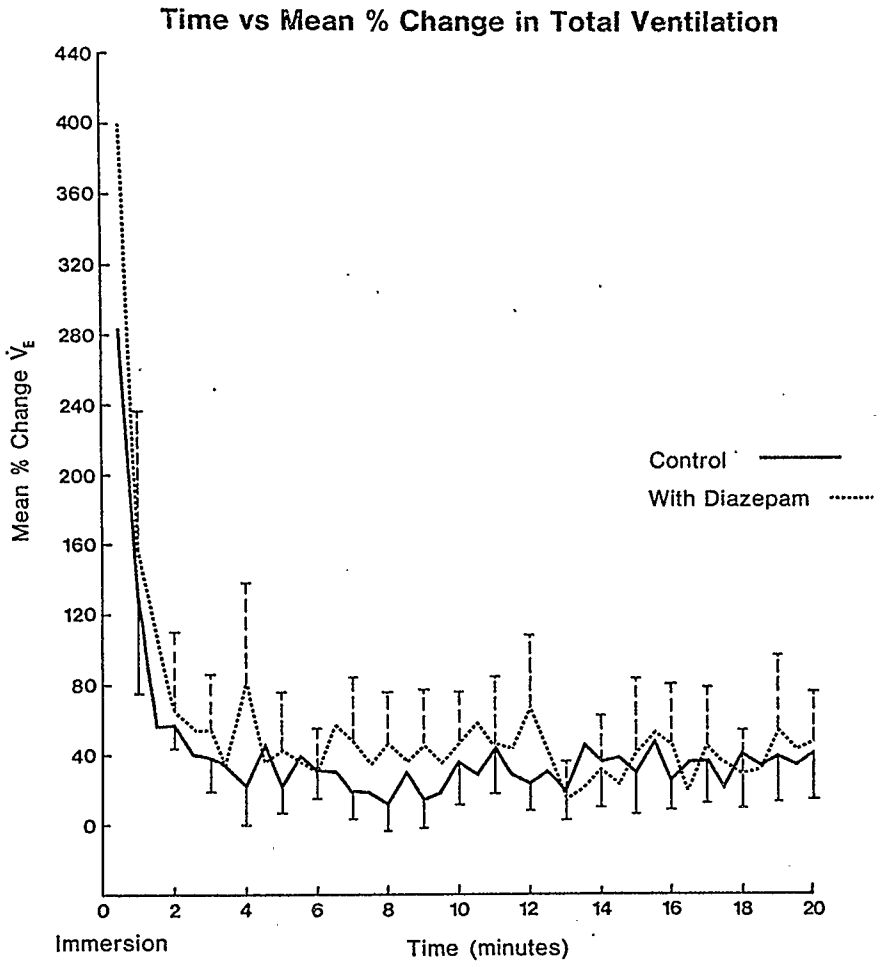

Fig. 24. Mean percentage change in ventilation during a 20 min immersion in cold water (13.5°C). Without diazepam (——); with diazepam (----). N = 6. Vertical bars = ± S.E.M.

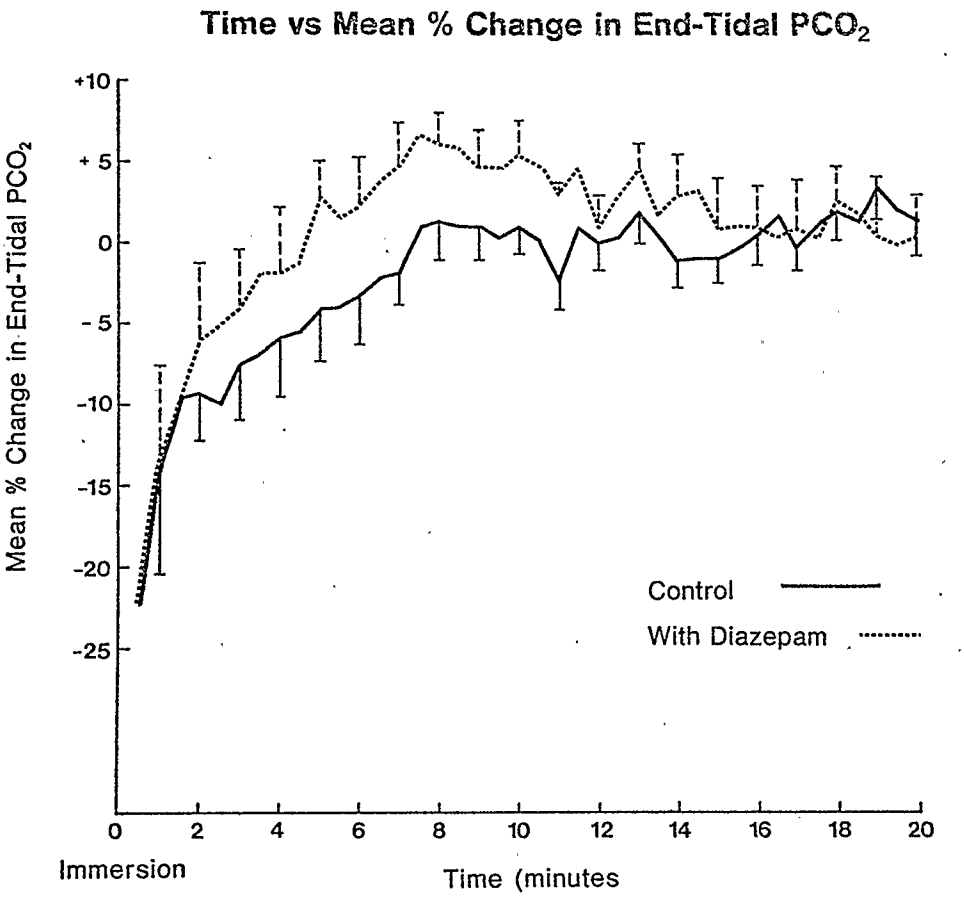

Fig. 25. Mean percentage change in end-tidal PCO_2 during a 20 min immersion in cold water (13.5°C). Without diazepam (——); with diazepam (----). N = 6. Vertical bars = ± S.E.M.

This alteration was generally maintained during the experiment. An apparently attenuated response was evident from 2 to 10 min but towards the end of the immersion periods the end-tidal PCO_2 values closely approximated each other. None of the changes noted was significantly different ($p > 0.10$).

A comparison of body temperature, measured rectally, during the 2 immersions is seen in Fig. 26. The rectal temperature after diazepam ingestion was apparently higher than that observed in the experiment without the drug, during the pre-immersion time and for 7 min of the immersion period, but the differences were not statistically significant ($p > 0.10$). For the remaining 13 min, the decline in the 2 temperatures was similar. The overall changes were a decrease of $0.51^{o}C$ and $0.70^{o}C$ from resting values of $37.33^{o}C$ and $37.43^{o}C$ for the immersions without and with diazepam ingestion respectively.

Figure 27 illustrates the changes in mean surface skin temperatures during the 2 cold water immersions. The mean skin temperature after diazepam ingestion was higher ($32.63^{o}C$) than the mean skin temperature ($32.26^{o}C$) without drug ingestion during the pre-immersion period, but was slightly lower during the first 2 min of immersion. These differences were not statistically significant ($p > 0.10$). The decline in the mean skin temperature for both immersion times was similar for the remaining 18 min and at the end of each immersion period the mean skin temperature was approximately $2.35^{o}C$ above the water temperature.

Oxygen uptake was measured for the 6 subjects during the 2 immersions. During the pre-immersion period the oxygen uptake was the same for the control and the experiment with diazepam ingestion ($0.29\ l.min^{-1}$).

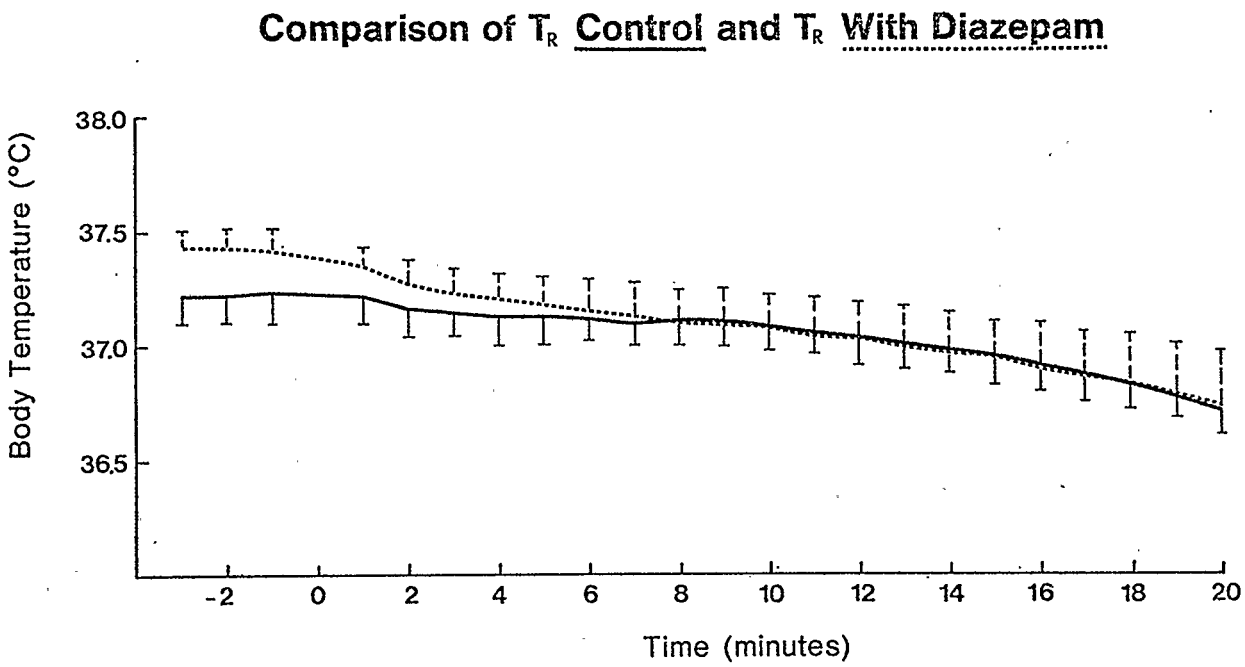

Fig. 26. Comparison of rectal temperature (T_R) during a 20 min immersion in cold water (13.5°C). Without diazepam (——); with diazepam (----). N = 6. Vertical bars = ± S.E.M.

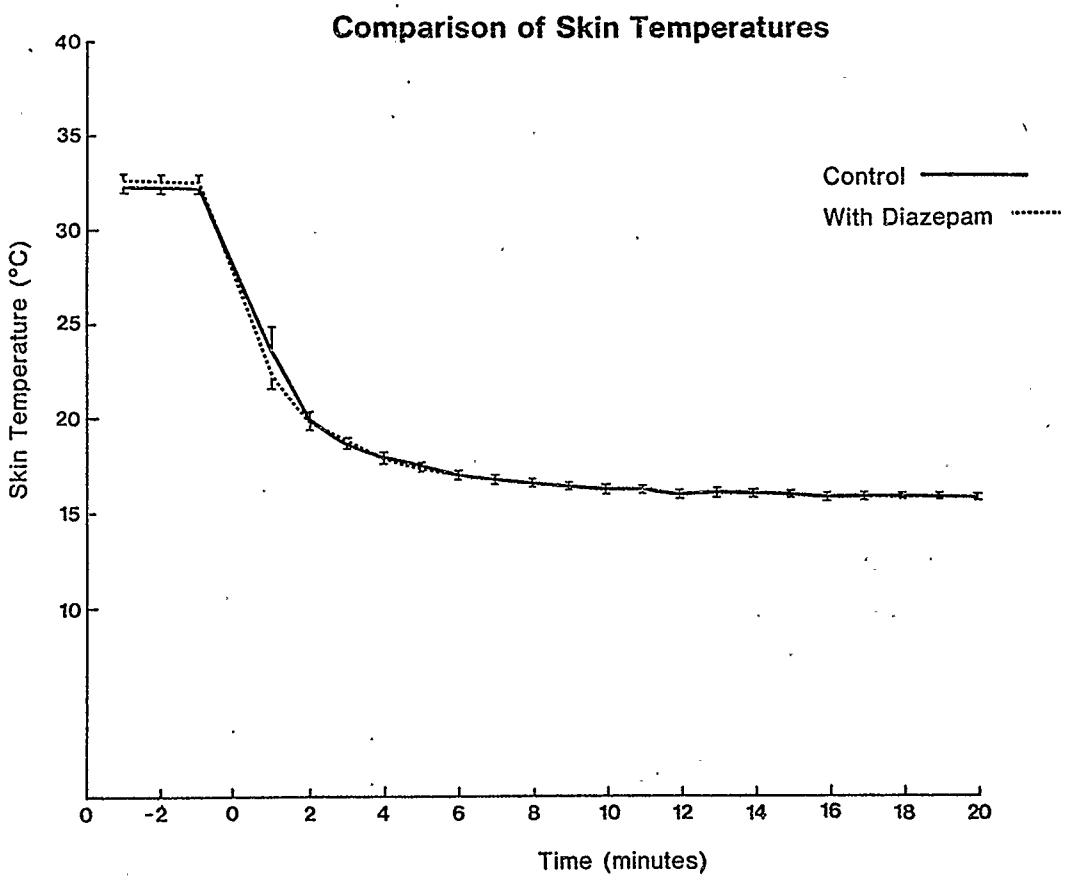

Fig. 27. Comparison of mean surface skin temperature ($\bar{T}_{SK}$) during a 20 min immersion in cold water (13.5°C). Without diazepam (——) with diazepam (----). N = 6. Vertical bars = ± S.E.M.

Immersion in cold water increased the oxygen consumption in both situations. The maximum achieved was 0.41 $l.min^{-1}$ at 25 min of the control immersion and 0.41 $l.min^{-1}$ at 5 min during the immersion following drug ingestion. However, the differences in oxygen uptake which were observed during the immersions with and without drug ingestion were not significantly different ($p > 0.10$).

Reliable heart rate measurements were achieved during both immersions for 4 of the subjects. There was an increased mean heart rate (from 80 to 89 $beats.min^{-1}$) during the first minute of the immersion without drug ingestion. This was followed by a decreased mean heart rate below the control value (range from 69 to 73 $beats.min^{-1}$) for the remaining 19 min. During the immersion following diazepam ingestion the mean heart rate did not change for the first minute (80 $beats.min^{-1}$) and for the remainder of the experiment was lower than the pre-immersion value (ranged from 71 to 75 $beats.min^{-1}$). There was no statistically significant difference in the mean heart rates during the immersions following diazepam or no diazepam ingestion.

Rank correlation tests of the plasma concentrations of diazepam (at 1 h) and the mean percentage changes in total expired volume and end-tidal PCO_2 were calculated for these 6 subjects during the gasp response elicited by the cold water immersion. No significant correlation was found for either response ($p > 0.10$). A similar rank correlation test of the plasma concentration of diazepam (at 1 h) and heart rates was performed for the first minute of the cold water exposure. Again, no significant correlation was observed ($p > 0.10$).

D. DOPAMINE-β-HYDROXYLASE LEVELS DURING COLD WATER IMMERSION

The plasma dopamine-β-hydroxylase (D-β-H) levels for 13 subjects are found in Table XI. Four of the subjects had control samples taken at rest and while exercising the forearm, and only 1 of these (S.M.) required exercise in the water. Nine of the subjects had only 1 control sample taken and this while at rest. Four of these required no forearm exercise while in the water, while 5 required forearm exercise in order to draw the blood samples. A great variation was seen in the control samples without exercise (0.23 to 16.7 units) and with exercise (5.6 to 15.3 units). The results of the first 4 subjects, when compared with the proper control showed that when they were immersed the D-β-H levels were less, but no definite pattern was evident. The next 4 subjects (K.E.C., G.B., D.M., R.C.) required no forearm exercise while in the water. Of these 2 (K.E.C., G.B.) showed lower than control levels of D-β-H while 2 (D.M., R.C.) had higher than control values of D-β-H. The last 5 subjects had only 1 control sample taken (without exercise) and all required forearm exercise while immersed. Of these, 2 (B.D., S.H.) had lower than the control, 2 (A.B., R.T.) exhibited a variable pattern in relation to the control, and 1 (D.S.) had a lower than the control level of D-β-H. The only indication of a probable consistent rise or fall in D-β-H levels during the immersion period was seen in the values for subjects R.C. and D.S.

The change in expired ventilation during the cold water immersion is seen in Fig. 28A. The initial gasp response (increase of 350%) was noted with a return toward baseline values which were steady at 180% change.

TABLE XI

Dopamine-β-Hydroxylase Assay

D-β-H units expressed as nmoles octopamine formed. mg protein^{-1}. 60 min^{-1}

Time (min)	G.S.	J.J.	A.C.	S.M.	K.E.C.	G.B.	D.M.	R.C.	B.D.	S.H.	A.B.	R.T.	D.S.
0 (NE)	16.7	14.1	4.7	10.6	2.9	0.23	2.06	9.7	27.8	12.0	10.0	13.5	3.1
0 (E)	15.3	14.1	5.6	14.2	-	-	-	-	-	-	-	-	-
	NE	NE	NE	E	NE	NE	NE	NE	E	E	E	E	E
1	15.7	11.9	2.4	11.2	2.4	0.27	5.45	9.2	25.9	9.6	9.6	13.7	2.5
2	16.8	12.3	3.7	12.6	2.5	0.23	4.41	14.0	25.3	9.0	8.8	11.5	2.4
3	16.1	14.0	3.9	11.3	2.5	0.11	4.57	14.2	26.5	8.7	9.7	13.8	2.6
4	14.1	12.0	3.2	12.1	2.3	0.26	4.26	16.8	27.0	10.0	9.7	15.9	2.2
10	14.5	11.4	4.3	9.7	2.5	0.22	4.41	16.1	25.3	9.7	10.5	10.2	1.7

(E) Exercise

(NE) No Exercise

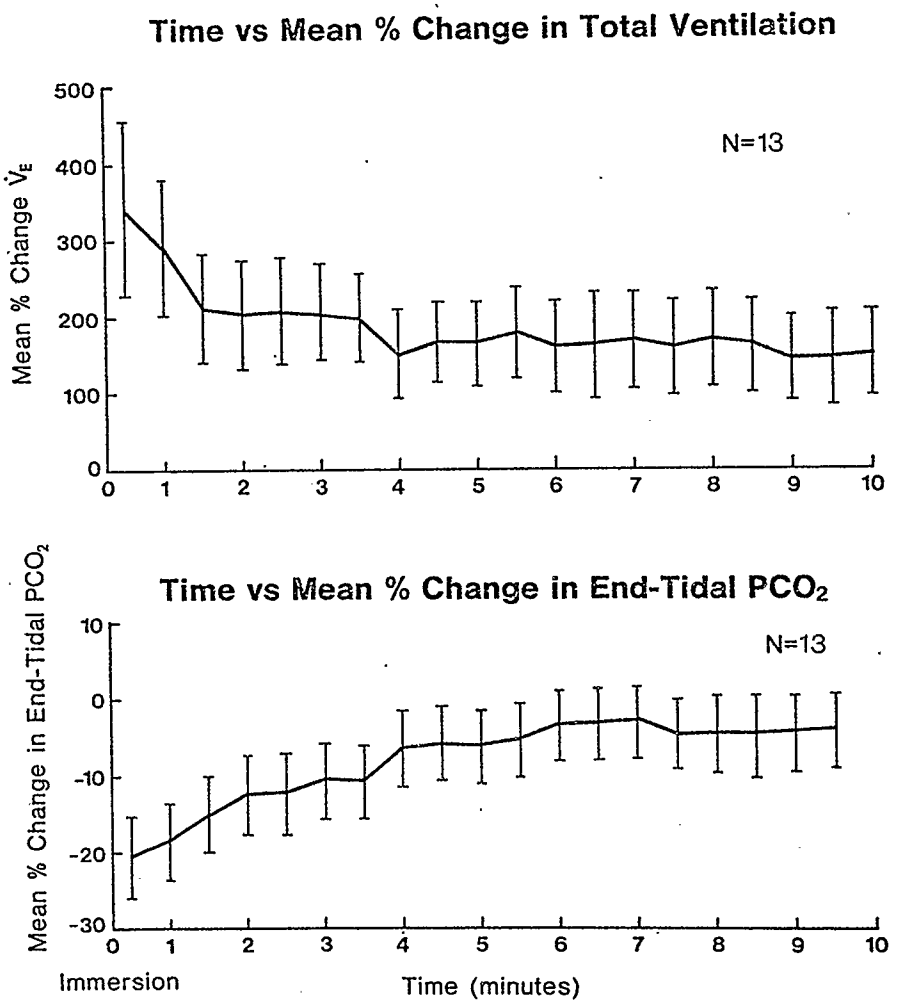

Fig. 28A. Mean percentage change in ventilation during a 10 min immersion in cold water (13.5°C). Vertical bars = ± S.E.M.

Fig. 28B. Mean percentage change in end-tidal PCO_2 during a 10 min immersion in cold water (13.5°C). Vertical bars = ± S.E.M.

Fig. 28B shows the degree of hyperventilation evident during the immersion period. The greatest change in end-tidal PCO_2 was seen during the first 2 min (-20% to -12% decrease) with a gradual return toward pre-immersion values. However, a steady hyperventilatory response (decrease of -5%) was evident during the last 4 min of the experiment.

Figure 29 shows the change in mean heart rate for 8 of the subjects during the cold water immersion. An immediate increase from 69 beats.min^{-1} to 95 beats.min^{-1} occurred during the first minute of immersion with a return towards pre-immersion values throughout the remainder of the experiment. However, at the end of 10 min the mean heart rate was still elevated (82 beats.min^{-1}). The differences were significant at 1, 3, 5 and 10 min ($p < 0.001$; $p < 0.01$; $p < 0.01$; $p < 0.05$) of the immersion.

A rank correlation test of the D-β-H levels (for subjects G.S., J.J., A.C., K.E.C., D.M., B.D., S.H., A.B.) and heart rates was done for the first and third minutes of the immersion period. No significant correlation was obtained ($p > 0.10$).

A similar rank correlation test for both mean percentage changes in total expired ventilation and end-tidal PCO_2 and D-β-H levels was calculated for these 8 subjects for the first and third minutes of the cold water exposure. No significant correlation was evident ($p > 0.10$). When this test was repeated for 13 subjects for the same time intervals of the immersion period, no significant correlation was found between the D-β-H levels and either the mean percentage change in total expired ventilation or end-tidal PCO_2 values ($p > 0.10$).

Seven subjects were immersed in water at 13.7°C; blood pressure

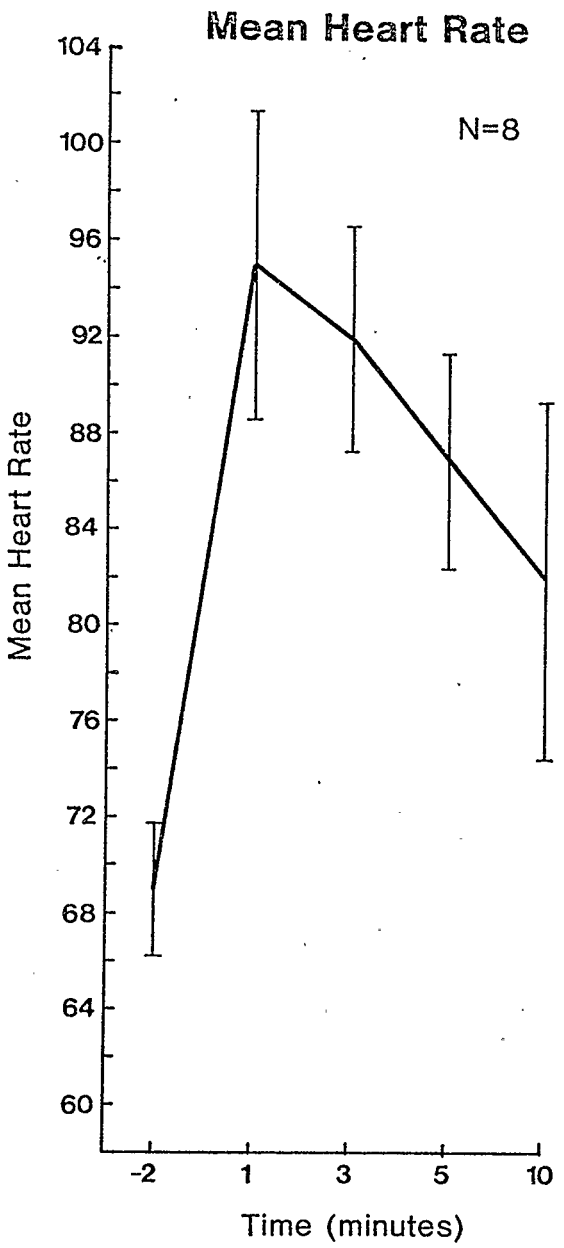

Fig. 29. Mean heart rate during a 10 min immersion in cold water (13.5^{o}C). Vertical bars = ± S.E.M.

was measured and the mean blood pressure (Diastolic + $\frac{\text{Systolic - Diastolic}}{3}$) was calculated for the subjects during the experiment. It appeared (Fig. 30) that an increase in blood pressure (92 to 102 mm Hg) had occurred for the first minute with a gradual decline during the next 10 min. The values evident at the end of the experiment (91 mm Hg) were comparable to the control. None of the changes were statistically significant ($p > 0.10$). However, if the readings obtained for individual subjects during the immersion ($n = 3, 5, 6$ for min 1, 2, 3) were compared with their control values, the mean blood pressure changes were statistically significant for the first ($p < 0.02$), second ($p < 0.05$) and third minutes ($p < 0.02$) of the cold water exposure.

E. FACTORS AFFECTING SHIVERING DURING COLD WATER IMMERSION

1. Deep and Superficial Skin Temperatures at the Initiation of Shivering during Cold Water Immersion After Exposure to Room Air or Sauna Heating

(i) Initiation of Shivering

Twelve subjects, 3 females and 9 males, whose ages ranged from 22 to 55, participated in this experiment. The heights and weights of the subjects ranged from 84 to 45 kg and 193 to 157 cm. The values for each subject are found in Table XII. The subjects were immersed for 10 min in water at 14.3°C after they had been exposed to room air (21°C ± 0.5°C) or sauna heating.

The mean surface skin temperatures and deep skin temperatures at which shivering began, during the immersion after exposure to room air, as well as the subcutaneous fat thicknesses of the 12 subjects, are found in Table XIII. The subjects are listed in the order of the

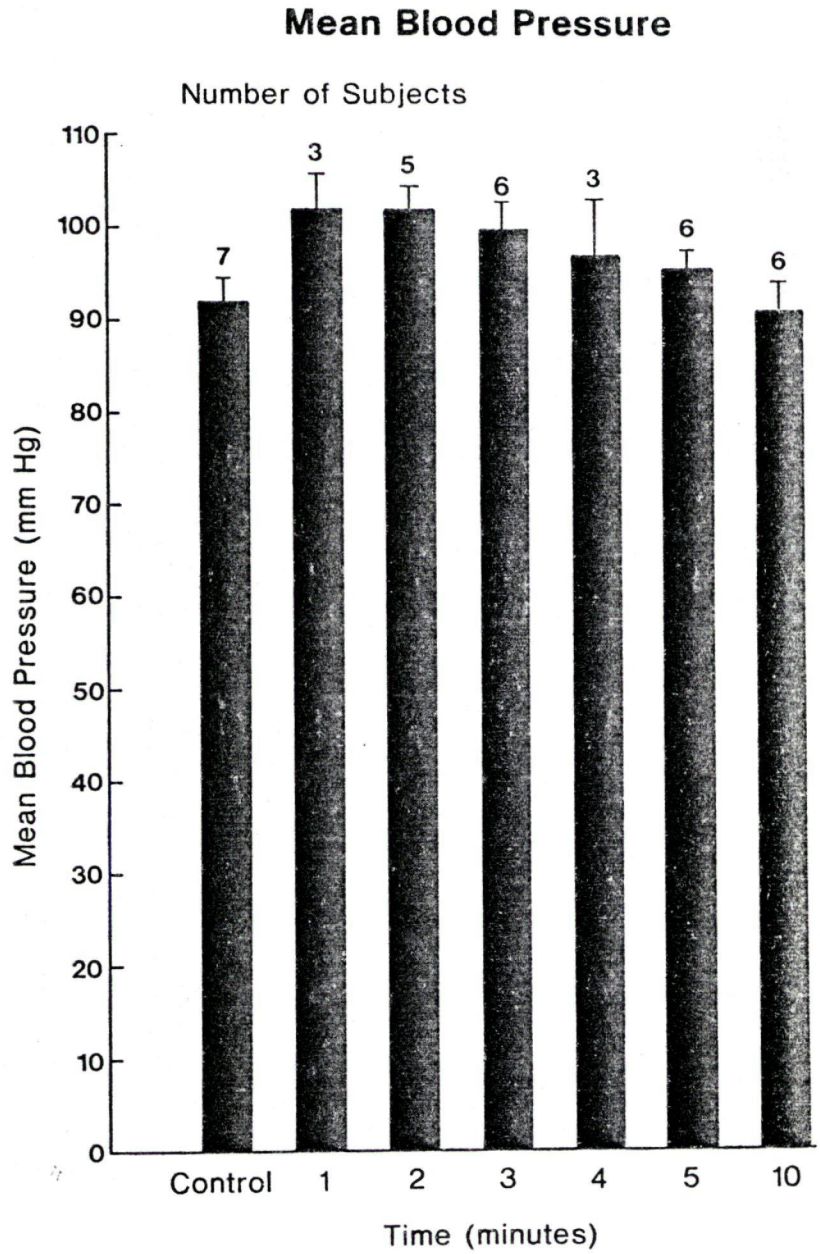

Fig. 30 Bar graphs indicating mean blood pressure changes at specific times during a 10 min cold water (13.7^{o}C) immersion. Number above each bar graph denotes the number of subjects from whom a reading was obtained. Vertical bars = ± S.E.M.

TABLE XII

Heights and Weights of Subjects for Shivering Experiment

Subject	Height (cm)	Weight (kg)
A.B.	193	84
D.C.	193	77
G.S.	180	74
C.M.	182	68
K.E.C.	179	81
A.C.	179	65
V.D.	177	67
R.T.	172	59
S.M.	171	69
S.H.	170	60
D.S.	168	68
H.M.	157	45

subcutaneous fat thicknesses. Shivering was elicited in 8 of the 12 subjects during the 10 min immersion. The deep skin temperature at which shivering began ranged from 18.5°C (A.B.) to 31.9°C (G.S.), while the mean surface skin temperature for 4 of these subjects (K.E.C., D.S., H.M. and A.B.) ranged from 17.11°C (A.B.) to 21.91°C (K.E.C.). Four of the volunteers, 2 females (S.H., S.M.) and 2 males (D.C., V.D.) did not shiver during the 10 min immersion. The deep skin temperatures evident at the end of the exposure time, ranged from 18.8°C to 26.4°C and the mean surface skin temperature ranged from 16.84°C to 19.0°C. One subject (S.M.) remained in the water for 17 min at the end of which time some shivering was evident and temperatures of the deep and mean surface skin were 21.5°C and 16.74°C respectively. For those subjects who shivered during the 10 min immersion the times at which shivering began ranged from less than 1 min (G.S. and A.C.) to 9 min (A.B.). The 4 subjects listed at the end of Table XIII are those who participated in a second cold water immersion. It will be noted that these subjects shivered at times ranging from 1.0 to 4.5 min and at a range of deep skin temperatures (20.6°C to 29.5°C). Two points are interesting: 1/ Subject D.C. shivered at a water temperature of 14.99°C and had a deep skin temperature of 29.5°C, whereas in the first experiment he was immersed in colder water (14.54°C), and his deep skin temperature had declined to 19.5°C, yet he did not shiver; 2/ Shivering in subject S.M. was elicited at the same deep skin temperature (21.5°C) as the first experiment but the response was elicited sooner (at 3.5 min) in the colder water (13.88°C). The other 2 subjects, D.S. and K.E.C., showed different deep skin temperatures (28.2°C; 20.6°C) at which shivering was elicited when compared to the first experiment (19.0°C; 22.1°C). Regression analysis of the deep skin temperature at

TABLE XIII

Surface and Deep Skin Temperatures at which Shivering was Initiated during a 10 min Immersion in Cold Water (14.32°C) after Exposure to Room Air

Subject	Tw °C	Subcutaneous Fat Thickness (mm)	Shivering	T_{DSK} (°C)	$\bar{T}_{SK}$ (°C)	Time at which Shivering Initiated (min)
KEC	14.56	7.61	√	22.1	21.91	1.5
SH	14.59	6.94	-	(26.4)	(16.81)	-
SM	14.71	6.34	-	(23.5)	(17.18)	-
DS	13.58	4.99	√	19.0	20.36	1.5
GS	14.71	4.96	√	31.9	-	< 1
HM	13.95	4.33	√	21.0	20.89	2.0
AB	13.8	4.0	√	18.5	17.11	9.0
DC	14.54	3.92	-	(19.5)	(17.24)	-
AC	14.56	3.78	√	25.5	-	< 1
CM	14.87	3.61	√	28.5	-	1.5
VD	13.33	3.55	-	(18.8)	(19.0)	-
RT	14.61	3.49	√	20.5	-	5.0
DC	14.99		√	29.5		4.5
DS	15.45		√	28.2		1.5
KEC	13.56		√	20.6		1.0
SM	13.38		√	21.5		3.5

the onset of shivering and the subcutaneous fat thicknesses of the subjects showed no significant relationship ($r = -0.28$; $p > 0.10$). A similar analysis of the mean surface skin temperature at the onset of shivering and the subcutaneous fat thicknesses of the volunteers was not statistically significant ($r - 0.30$; $p > 0.10$).

These subjects were heated in the sauna and then immersed in cold water (14.3°C). The mean surface skin temperature and deep skin temperature at which shivering began, as well as the subcutaneous fat thicknesses of the subjects are found in Table XIV. Once again, the subjects are listed in the order of their subcutaneous fat thicknesses. Shivering was evident in 9 of the 12 volunteers during the 10 min cold water exposure. Their deep skin temperature ranged from 20.5°C (A.B.) to 27.5°C (G.S.), while the mean surface skin temperature for 5 of the subjects (K.E.C., D.S., H.M, A.B. and D.C.) ranged from 17.05°C (D.S.) to 24.5°C (H.M.). Three subjects, 2 females (S.H., S.M.) and 1 male (V.D.) did not shiver during the immersion. The deep skin temperatures evident at the end of the exposure time ranged from 20.0°C to 28.6°C and the mean surface skin temperature ranged from 17.0°C to 19.44°C. One subject (S.M.) was immersed for 20 min, at the end of this time some shivering was evident and the deep skin and mean surface skin temperatures were 21.5°C and 16.28°C respectively. The time to shivering during the 10 min immersion ranged from 2.25 to 5 min. Two subjects (A.B., R.T.) shivered at a earlier time than during the immersion after room air exposure, while 6 (K.E.C., D.S., G.S., H.M., A.C., C.M.) shivered at a later time than in the previous experiment. One subject (D.C.) who had not shivered during the immersion after room air exposure shivered at 3 min during the cold water exposure after sauna heating. The 4 subjects listed at

TABLE XIV

Surface and Deep Skin Temperatures at which Shivering was Initiated during a 10 min Immersion in Cold Water (14.36°C) After Sauna Heating

Subject	Tw °C	Subcutaneous Fat Thickness (mm)	Shivering	T_{DSK} (°C)	$\bar{T}_{SK}$ (°C)	Time at which Shivering Initiated (min)
KEC	14.69	7.61	✓	22.5	19.68	5.0
SH	14.69	6.94	-	(28.6)	(19.44)	-
SM	14.81	6.34	-	(23.6)	(17.0)	-
DS	13.53	4.99	✓	25.0	17.05	4.2
GS	14.66	4.96	✓	27.5	-	2.25
HM	13.83	4.33	✓	20.5	24.5	2.3
AB	13.96	4.0	✓	20.5	19.07	4.2
DC	14.41	3.92	✓	26.0	18.95	3.0
AC	14.54	3.78	✓	22.6	-	4.0
CM	14.96	3.61	✓	25.3	-	2.5
VD	13.42	3.55	-	(20.0)	(17.88)	-
RT	14.79	3.49	✓	25.5	-	4.0
DC	14.44		✓	28.0		8.0
DS	14.53		✓	26.5		2.5
KEC	14.12		✓	15.0		6.0
SM	14.72		-	21.0		-

the bottom of Table XIV are those for whom a second deep skin temperature was recorded. Three subjects (D.C., D.S., K.E.C.) shivered while 1 subject (S.M.) did not shiver at the end of 10 min. The time to shivering ranged from 2.5 to 8.0 min at a variety of deep skin temperatures (15.0° to 28.5°C). When these values are compared to the 4 deep skin temperatures listed in Table XIII, all deep skin temperatures at which shivering occurred are lower than those obtained during the immersion after room air exposure, and in each case there was a longer latency to shivering. When these deep skin temperatures are compared to those of the other experiment noted in Table XIV, the values are 1.0°C to 2°C higher for subjects D.C. and D.S. and lower by 7.5°C and 2.6°C for subjects K.E.C. and S.M. Regression analysis of the deep skin temperature at which shivering was initiated and the subcutaneous fat thicknesses of the subjects was statistically significant ($r = -0.57$, $p < 0.05$). A comparable analysis of the mean surface skin temperature at the onset of shivering and the subcutaneous fat thicknesses of the subjects showed no significant relationship ($r = -0.27$, $p > 0.10$).

2. Deep and Mean Surface Skin Temperatures and Ventilatory Responses during Cold Water Immersion after Sauna Heating and Room Air Exposure

Eight subjects (K.E.C., S.H., S.M., D.S., H.M., A.B., D.C., V.D.) had both deep and mean surface skin temperatures measured during both cold water immersions in addition to ventilatory responses. The mean percentage changes in total expired volume during both immersions are seen in Fig. 31. An initial increased ventilation of 420% and 350% was found during the immersions after exposure to room air and sauna

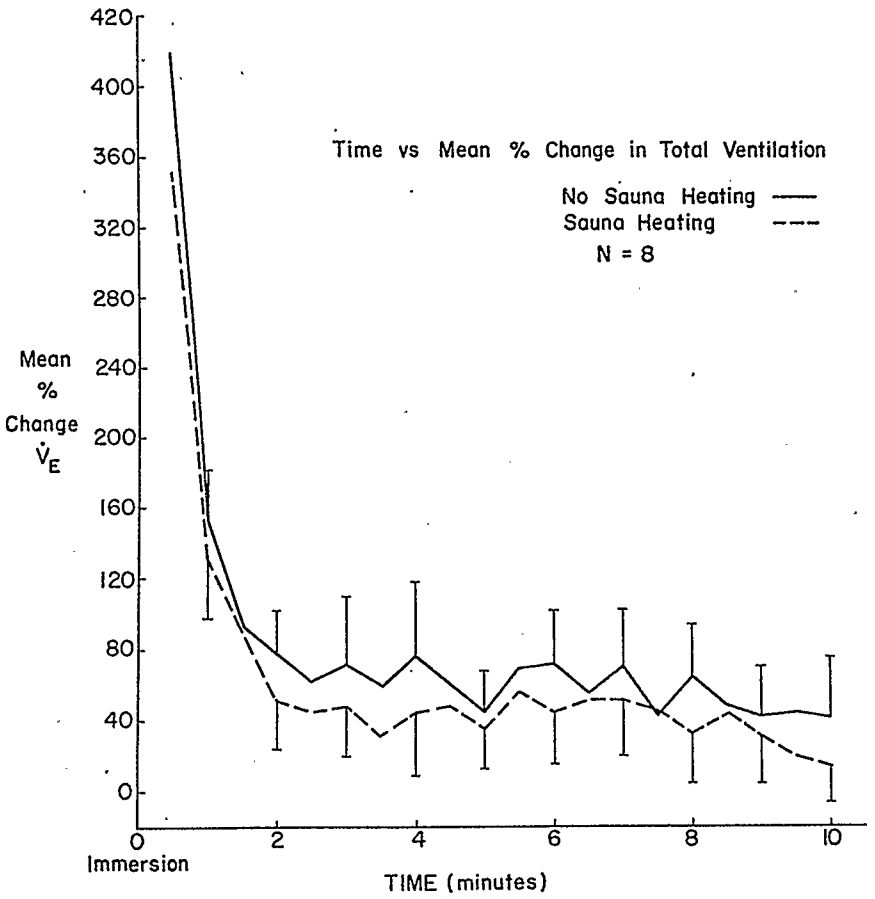

Fig. 31. Mean percentage change in ventilation during a 10 min immersion in cold water (14.1°C). Without sauna heating (——); with sauna heating (----). N = 8. Vertical bars = ± S.E.M.

heating. During both immersions there was a rapid decline toward pre-immersion values and from 2.5 to 8.15 min there was a fairly steady reading at approximately 60% and 40% change. The last 1.5 min of each immersion was characterised by a further decline in expired ventilation. Although there appeared to be an attenuated response after sauna heating, no differences were statistically significant ($p > 0.10$).

A comparison of the deep skin and mean surface skin temperatures during the immersion after exposure to room air is found in Fig. 32A. A similar decline is seen for both temperatures and after the sharp fall during the first minute of immersion to 25.5°C and 23.0°C for deep and surface temperatures, both temperatures remained fairly steady. The mean surface skin temperature declined 14.0°C from a control reading of 31.5°C, while the deep skin temperature declined 13.5°C from a pre-immersion value of 33.5°C. There was no statistically significant difference ($p > 0.10$; $p > 0.05$) between the two temperatures during any time of the cold water exposures.

Figure 32B shows the deep skin and mean surface skin temperatures during the immersion after sauna heating. The mean skin temperature was higher (38.0°C) than the deep skin temperature (35.5°C) during the pre-immersion time. However, during the first minute of immersion the mean skin temperature decreased to the same level (23°C) as it had during the immersion after room air exposure, but the deep skin temperature decreased to only 29.0°C from a resting value of 35.5°C, during the first minute. For the remaining 9 min of the immersion a gradual decline was noted for both temperatures. There was an overall decrease of 20.5°C for the mean skin temperature and 13.5°C for the deep skin temperature. There was a significant difference ($p < 0.001$)

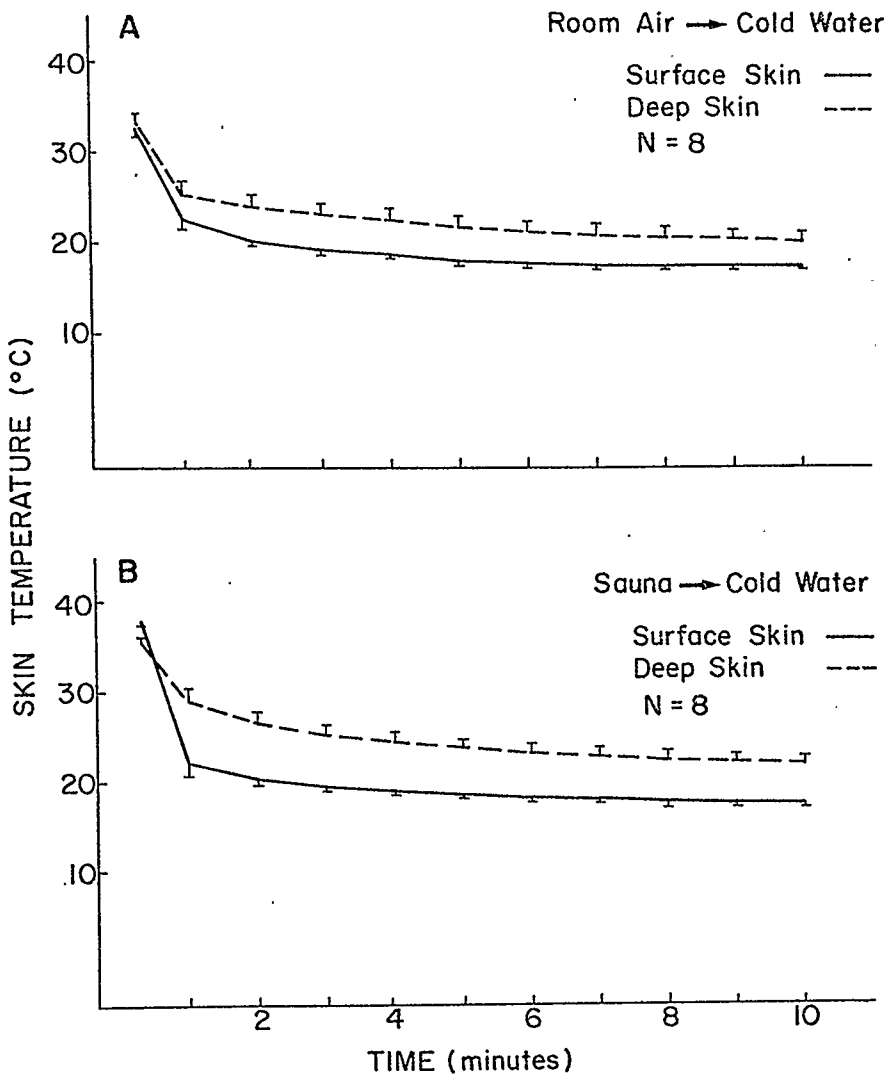

Fig. 32A. Comparison of mean surface skin temperature (——) and deep skin temperature (----) during a 10 min immersion in cold water (14.1°C) after exposure to room air. N = 8. Vertical bars = ± S.E.M.

Fig. 32B. Comparison of mean surface skin temperature (——) and deep skin temperature (----) during a 10 min immersion in cold water (14.1°C) after sauna heating. N = 8. Vertical bars = ± S.E.M.

between the 2 temperatures during the pre-immersion time, at 2 min ($p < 0.02$) and from 3 to 10 min ($p < 0.01$) of the immersion period.

A comparison of the mean surface skin temperature during both experiments is found in Fig. 33A. During the pre-immersion time there was a significant difference ($p < 0.01$) between the 2 temperatures but during the first minute of immersion they decreased to the same level ($23^{o}C$). For the remaining 9 min of the cold water exposure, the patterns of both surface temperatures parallel each other and no further differences were statistically significant ($p > 0.10$). Figure 33B illustrates the deep skin temperature pattern which occurred during both cold water immersions. The deep skin temperature during sauna heating was higher ($35.7^{o}C$) than the deep skin temperature after exposure to room air ($33.0^{o}C$) and remained so, throughout the immersion time. The decrease in both temperatures during the immersion was similar and overall changes of $13.0^{o}C$ and $13.7^{o}C$ were seen after sauna heating and room air exposure respectively. The differences between the 2 temperatures were statistically significant during the pre-immersion period, at 1 min ($p < 0.02$) and from 5 to 10 min ($p < 0.05$) of the cold water exposure.

The rate of change of the deep skin temperature was plotted against the percentage change in ventilation for 8 subjects during the first 3 min (this included half minutes) of the immersion after room air exposure. Figure 34A shows the regression analysis of these data, from which a significant correlation was obtained ($r = 0.58$, $p < 0.001$). The rate of change of the deep skin temperature and percentage change in ventilation for the first 3 min of the cold water immersion after sauna heating are provided in Fig. 34B. Again, some scatter of points was seen but regression analysis of these data also showed a significant

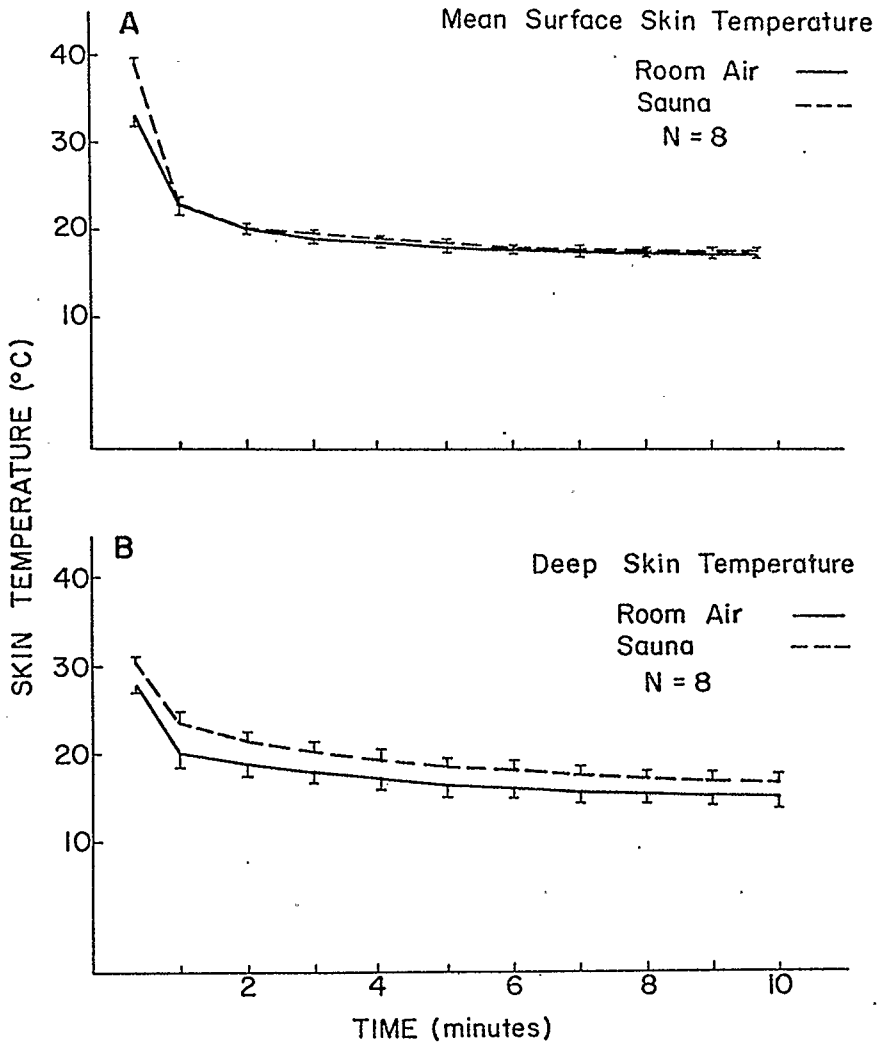

Fig. 33A. Comparison of mean surface skin temperature during a 10 min immersion in cold water (14.1°C) after exposure to room air (——) and sauna heating (----). N = 8. Vertical bars = ± S.E.M.

Fig. 33B. Comparison of deep skin temperature during a 10 min immersion in cold water (14.1°C) after exposure to room air (——) and sauna heating (----). N = 8. Vertical bars = ± S.E.M.

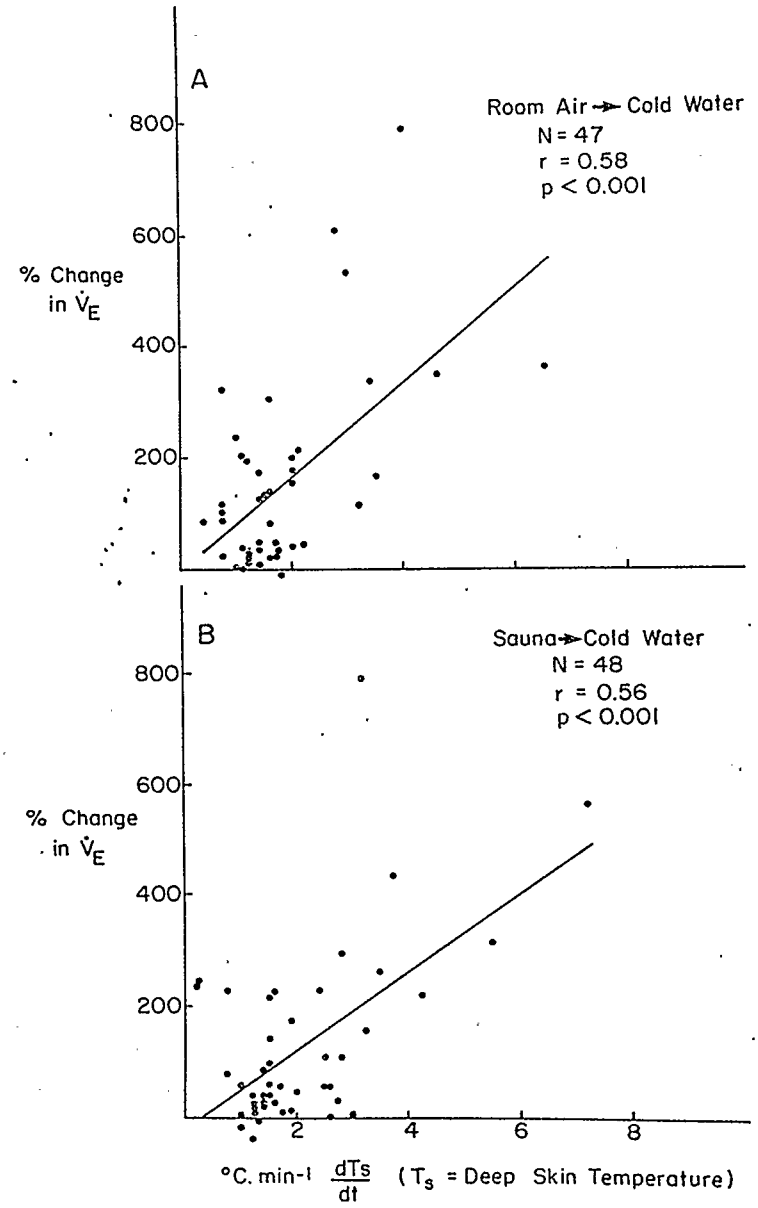

Fig. 34A. Rate of change of deep skin temperature plotted against percentage change in ventilation during 10 min immersion in cold water (14.1°C) after room air exposure. Linear regression line through the points shown.

Fig. 34B. Rate of change of deep skin temperature plotted against percentage change in ventilation during a 10 min immersion in cold water (14.1°C) after sauna heating. Linear regression line through the points shown.

correlation ($r = 0.56$, $p < 0.001$).

The regression analysis of the changes in ventilation and rate of change of mean surface skin temperature during 3 min of the immersion after room air exposure are shown in Fig. 35A. A greater scatter of points was noted and the relationship was not statistically significant ($r = 0.32$, $p > 0.10$). The pattern observed when the rate of change in the mean skin temperature was plotted against the percentage change in ventilation during 3 min of the immersion following sauna heating, is seen in Fig. 35B. Again, a wide scatter of points was evident and no correlation was statistically significant ($r = 0.31$, $p > 0.10$).

The absolute deep skin temperatures and the percentage changes in ventilation obtained during the first 3 min of the 2 immersions were analyzed by regression analysis and no statistically significant correlation was found ($p > 0.10$). A similar analysis of the absolute mean surface skin temperature and percentage change in ventilation during the first 3 min of the 2 experiments likewise yielded non-significant results ($p > 0.10$). A comparison of the temperature gradients (mean surface skin temperature - deep skin temperature) and percentage changes in ventilation during 3 min of the 2 experiments was made. A significant correlation ($r = 0.72$, $p < 0.001$) was evident for the immersion after sauna heating, whereas no degree of significance ($r = 0.29$, $p > 0.10$) was obtained during the immersion following room air exposure.

3. Inhibition of Shivering

Six subjects performed 2 tasks, mental arithmetic and 40% maximum voluntary forearm contraction, while immersed in the cold water

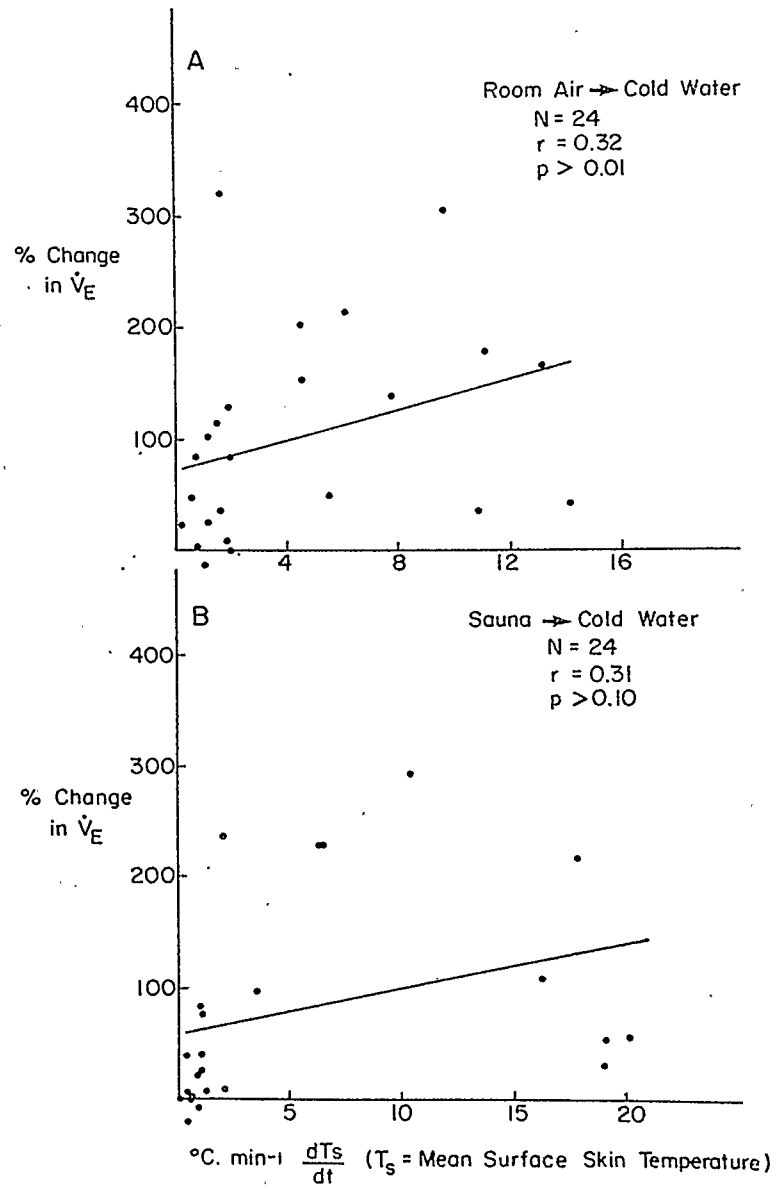

Fig. 35A. Rate of change of mean surface skin temperature plotted against percentage change in ventilation during a 10 min immersion in cold water (14.1°C) after room air exposure. Linear regression line through the points shown.

Fig. 35B. Rate of change of mean surface skin temperature plotted against percentage change in ventilation during a 10 min immersion in cold water (14.1°C) after sauna heating. Linear regression line through the points shown.

(15.1°C). The overall results are found in Table XV. Both Presentations I and II were made up of 4 sets of numbers, presented consecutively. During Presentation I of the mental arithmetic task, 4 of the subjects showed a marked decrease in shivering, 1 showed a slight decrease and in 1 subject there was no change. During Presentation II of this task 2 of the above 4 subjects showed a similar response to that seen in the first task, while 2 others showed only a slight decrease in shivering. Subjects D.S. and J.W. showed a similar pattern to that established in the first test. A more variable response was seen after the isometric forearm grip. Three of the subjects inhibited shivering with a 40% maximum voluntary contraction (MVC), whereas only 1 subject (D.S.) had a similar response with the 50% MVC. The other 2 subjects showed either no change or very slight decrement for part of the time. Neither the 40% or 50% maximum voluntary contraction had any effect on shivering shown by 2 subjects (C.M. and A.B.). The sixth subject (A.C.) showed only a slight decrease in shivering with the 50% maximum voluntary contraction.

Figure 36 shows a typical response during the mental arithmetic task consisting of 3 number sets. An adequate degree of shivering was obtained, and as soon as the subject began the spoken task, which lasted 13, 11 and 10 sec respectively for the 3 sets, the shivering was inhibited. When the task was completed, a similar degree of shivering was once again evident.

A comparable pattern is shown for the 40% maximum voluntary forearm contraction. When shivering had been established, the subject was asked to hold a steady 40% maximum voluntary contraction for 1 min. A typical response can be seen in Fig. 37 and a definite inhibition of

TABLE XV

Shivering, Grip and Mental Arithmetic

Subject	Shivering	Mental Arithmetic Presentation I	Mental Arithmetic Presentation II	Forearm Grip 40% MVC	Forearm Grip 50% MVC
G.S.	✓	↓↓	↓↓	↓↓	→
A.C.	✓	↓↓	↓↓	→	↓
D.S.	✓	↓	↓	↓↓	↓↓
C.M.	✓	↓↓	↓	→	→
A.B.	✓	↓↓	↓	→	→
J.W.	✓	(→)	(→)	↓↓	↓

Decrease in shivering ↓↓

Slight decrease in shivering ↓

No change →

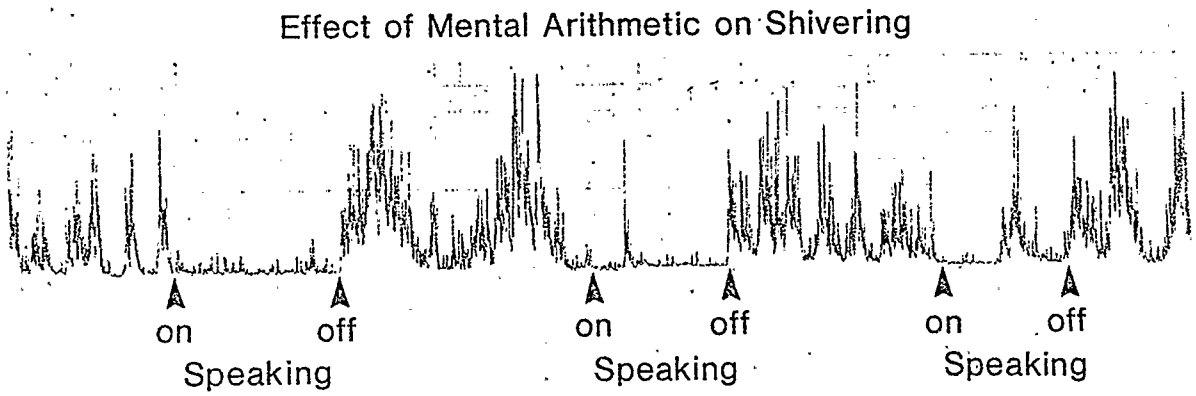

Fig. 36. Inhibition of shivering during immersion in cold water (14.3°C). Mental arithmetic task included consecutive presentation of 4 sets of numbers. Results of 3 sets are shown. Mental arithmetic task time was 12 sec.

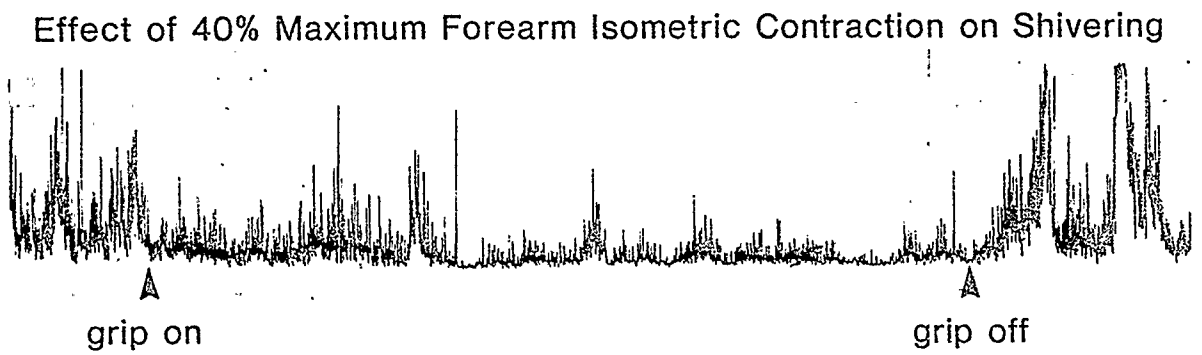

Fig. 37. Inhibition of shivering during immersion in cold water (16.2°C). Performed task was a 40% maximum voluntary forearm contraction held for 1 min.

shivering was found. A response similar to the control shivering was re-established once the forearm grip was relaxed.

F. MEMORY TESTING

1. Experiment I: Stimulus Slide Set Shown Before Immersion

During this procedure the subjects were shown the stimulus set of slides before the warm (33°C) and cold (15°C) water immersions and the tests were conducted after removal from the tank. The number of errors after the 2 immersions was compared with the number made during the control experiment. The totals are given in Table XVI. The results are variable in that 2 subjects had no errors, 3 subjects showed more errors after the warm than the cold water exposure, and 8 subjects showed more errors after the cold water immersion. It appeared that a degree of significance was evident between the number of errors after immersion in warm water and the number obtained for the control experiment (conducted at room temperature). No significant difference was seen in the results from the immersions in the cold water, or in the control vs. the cold water immersion.

2. Experiment II: Stimulus Slide Set Shown During Immersion

The 11 subjects involved in this experiment were shown the stimulus set of slides during immersion in warm (33°C) and cold (13.5°C) water and tested after removal from the tank. The number of errors committed after exposure to warm and cold water and during the control experiment are shown in Table XVII. Four subjects had no errors at any water temperature, while 6 persons showed more errors after cold water exposure. Only 1 subject had more errors after the warm water

TABLE XVI

Number of Errors in Experiment I

Subject	Control	Warm	Cold
1	0	0	0
2	2	4	6
3	1	2	5
4	0	1	1
5	2	6	0
6	1	0	3
7	0	0	0
8	5	6	7
9	1	1	0
10	0	1	1
11	0	0	0
12	0	3	0
13	1	6	1

One Way Analysis of Variance

N = 13; df = 2,24; F = 2.48 (N.S.)

Student's t-test:

Control - Warm - $p < 0.025$

Control - Cold - $p < 0.10$; > 0.05

Warm - Cold - $p > 0.10$

TABLE XVII

Number of Errors in Experiment II

Subject	Control	Warm	Cold
1	1	1	3
2	0	0	0
3	0	0	3
4	0	0	0
5	2	2	4
6	0	3	1
7	1	0	0
8	0	0	0
9	2	2	11
10	2	0	2
11	0	0	5

One Way Analysis of Variance:

N = 11; df = 2,20; F = 4.22 (S)

Student's t-test:

Control - Warm - $p > 0.10$

Control - Cold - $p < 0.05$

Warm - Cold - $p < 0.05$

immersion. There was a significant difference between the number of errors found during the control and cold water exposure ($p < 0.05$) and the number found during the warm and cold water exposure ($p < 0.05$).

The number of errors in Test I and Test II for the control and the warm and cold water exposures was compared by a two way analysis of variance. A significant difference was found between Test I and Test II ($p = 0.05$) and more errors were committed in Test II.

A rank correlation of the number of errors found after exposure to cold water and the mean percentage change in end-tidal PCO_2 values is found in Table XVIII. A correlation existed between the two and generally a greater number of errors was evident for those subjects who showed the greatest degrees of hyperventilation. Results were significant at $p < 0.001$. No such correlation ($p > 0.10$) existed between end-tidal PCO_2 and number of errors for the warm water immersion.

3. Experiment III: All Slides (Stimulus and Test Sets) Shown During Water Immersion

Six subjects were immersed in water at 13.7°C and 34.1°C, and all slides were shown during these exposures. Table XIX gives the results. A wide range (1 to 13) is noted in the number of errors evident during the cold water immersion. A range of 0 to 8 was seen during the warm water exposure. When the 2 water temperatures were compared 4 subjects had more errors during the cold water immersion, while 2 had more errors during the warm water exposure. A comparison of the number of errors made during the 2 water immersions with the control (at room temperature) showed no significant changes ($p > 0.10$).

TABLE XVIII

Experiment II - Rank Correlation of Number of Errors and Mean % Changes in End-Tidal PCO_2 at 13.5°C

Subject	RAW DATA No. of Errors	Mean % Change PCO_2	Subject	RANKED DATA No. of Errors	Mean % Change PCO_2
A.F.	3	-44.96	A.F.	7.5	1
R.C.	11	-38.05	R.C.	11.0	2
M.H.	5	-34.45	M.H.	10.0	3
A.C.	2	-30.32	A.C.	6.0	4
D.M.	0	-29.26	D.M.	1.0	5
D.S.	4	-27.17	D.S.	9.0	6
E.A.	1	-20.76	E.A.	5.0	7
V.D.	0	-16.61	V.D.	1.0	8
H.M.	0	-14.20	H.M.	1.0	9
J.W.	3	-10.74	J.W.	7.5	10
J.J.	0	2.29	J.J.	1.0	11

$N = 11$; $R = -0.93$; $df = 9$; $p < 0.001$

TABLE XIX

Number of Errors in Experiment III

Subject	Control	Warm	Cold
D.N.	3	5	4
D.C.	1	0	1
P.S.	1	0	1
G.B.	3	8	13
R.G.	4	3	2
G.B.	7	4	6

One Way Analysis of Variance:

$N = 6$; $df = 2,10$; $F = 0.59$ (N.S.)

Student's t-test:

Control - Warm - $p > 0.10$

Control - Cold - $p > 0.10$

Warm - Cold - $p > 0.10$

4. Experiment IV: Exposure to Warm or Cold Water for Three Immersions

Three subjects were immersed on 3 occasions to warm (31.6°C) water and 2 were exposed for the same number of times to cold (13.9°C) water. The results are recorded in Table XX. Two subjects had a total of only 1 error and 1 subject made 4 errors during the warm water immersions. The total number of errors during the cold water immersions was 12 and 3 errors for the 2 subjects respectively. No statistically significant difference was found in any of the recorded changes.

5. Experiment V: Game of Tic-Tac-Toe

Table XXI shows the results of this game. The 11 subjects were immersed in 13.5°C and 33.0°C water, and were marked for the number of games played in a 10 min period after the immersions. Marks were awarded as follows: 0 for a tie, -1 for a loss, +1 for a win. A variable pattern was seen. Somewhat surprisingly, a greater number of losses was recorded for 6 subjects after the warm water immersion, when compared to their performance after cold water immersion. Two subjects had a comparable game after the 2 immersions and 2 subjects had more losses after the cold water exposure. Only 1 subject had no errors after either immersion. A significant change was noted between the control and warm water exposure ($p < 0.05 > 0.025$). No other differences were statistically significant ($p > 0.10$).

6. Experiment VI: Mental Arithmetic Task During Cold and Warm Water Immersion

The 12 subjects were asked to perform the mental arithmetic

TABLE XX

Number of Errors in Experiment IV

Subject	Tw. (°C)	Water Immersions (1)	(2)	(3)
1	13.6	6	4	2
2	14.2	0	0	3
3	32.12	1	0	0
4	31.71	1	0	0
5	31.0	2	0	2

One Way Analysis of Variance:

N = 5; df = 2,8; F = 1.0 (N.S.)

TABLE XXI

Number of Errors in Experiment V.

Subject	Control	Warm	Cold
1	0	0	-4
2	0	1	-4
3	-10	-5	-5
4	-4	-3	-3
5	0	0	0
6	-3	-12	-7
7	-6	-8	-4
8	-3	-7	-5
9	-3	-11	-10
10	-1	-4	-2
11	-4	-7	-2

One Way Analysis of Variance:

N = 11; df = 2,20; F = 1.67 (N.S.)

Student's t-test:

Control - Warm - $p < 0.05 > 0.025$

Control - Cold - $p > 0.10$

Cold - Warm - $p > 0.10$

task while immersed in warm ($33^{o}C$) and cold (13.5^{o}) water. The number of errors during each situation (control, warm and cold water) is found in Table XXII. The errors were categorized as relating to either the recall or the computation task and this is followed by the total number. During all 3 situations for all subjects (except #6 in warm water) more errors were attributed to the computation rather than the recall task. In general, no particular pattern emerges, other than to note that the total number of errors, as well as the total for recall and computation, was greater for the immersion during cold water.

However, as shown in Table XXIII, the differences in total number, and recall errors between cold and warm water immersions were not statistically significant ($p > 0.10$). It is interesting to note a degree of significance was approached ($p < 0.10 > 0.05$) for the difference in the number of computation errors between warm and cold water.

TABLE XXII

Number of Errors in Experiment VI

	CONTROL			WARM			COLD		
SUBJECT	R	C	T	R	C	T	R	C	T
1	7	8	15	2	8	10	3	9	12
2	7	13	20	6	9	15	8	12	20
3	8	25	33	13	20	33	11	19	30
4	0	12	12	0	3	3	0	3	3
5	1	4	5	0	4	4	0	4	4
6	2	5	7	5	4	9	0	6	6
7	6	17	23	4	16	20	13	20	33
8	8	7	15	2	3	5	5	16	21
9	0	1	1	0	2	2	0	1	1
10	0	4	4	0	2	2	2	11	13
11	6	21	27	15	16	31	6	17	23
12	1	5	6	2	9	11	4	10	14
	46	122	168	49	96	145	52	128	180

R = Recall; C = Computation; T = Total

TABLE XXIII

Statistical Analysis of Experiment VI Data

Total Number of Errors:

One Way Analysis of Variance

N = 12; df = 2,22; F = 1.50 (N.S.)

Student's t-test:

Warm - Cold - $p>0.10$

Number of Errors in Recall:

One Way Analysis of Variance

N = 12; df = 2,22; F = 0.105 (N.S.)

Student's t-test:

Warm - Cold - $p>0.10$

Number of Errors in Computation

One Way Analysis of Variance

N = 12; df = 2,22; F = 2.54 (N.S.)

Student's t-test:

Warm - Cold - $p<0.10, >0.05$

DISCUSSION AND CONCLUSIONS

A. THE EQUIPMENT AND METHODS

The validity and reproducibility of the responses noted in this work are governed in large measure by the available techniques as well as the biological variations existing among people. Since a major part of the work concentrated on ventilatory responses during cold water immersion, the usefulness of measuring techniques is of paramount importance.

Within the limits of the recording devices it was apparent that a certain degree of reliability was achieved. A calibration-curve for expired ventilation at a constant flow, indicated accuracy of measurement to ± 1.0 $l.min^{-1}$ (in a range of 8 to 112 $l.min^{-1}$) and it was apparent that reproducibility for higher flows was good. Because of the degree of hyperventilation which can be elicited by cold water immersion, it was necessary to know the other limits imposed by the recording devices. It was found that the analyzer could follow changes in PCO_2 to within 1 to 2 mm Hg at flow rates approximating 50 $breaths.min^{-1}$. Above this level there was a decrement in the amplitude of response. On occasion, one or two subjects had respiratory rates and degrees of hyperventilation during the first minute which could not be followed accurately.

Although calibrated gas mixtures were purchased for use in the experiments, the need for recalibration by using a Lloyd-Haldane gas analysis apparatus was recognized. Errors of up to 0.2% CO_2 were found in the commercially prepared mixtures. Calibrations, using either wet (saturated with water vapor) or dry (unsaturated) carbon dioxide, showed that the measurement of end-tidal PCO_2 was valid provided that the

appropriate gas was used to calibrate the instrument. The advisability of using the end-tidal PCO_2 as a measure of arterial PCO_2 must be considered, but animal experiments have proved that the difference between the two measurements varied by only 1.54 mm Hg with a S.D. of ± 1.0 mm Hg and the difference was not significant (Reivich, 1964).

The advantages of using the aural temperature rather than rectal temperature as a more accurate measurement of body temperature, since it closely approximates esophageal temperature has been indicated by Keatinge and Sloan (1975). A close relationship has also been illustrated in a comparison of intra-arterial, esophageal and aural temperatures (Cranston, personal communication).

Surface skin temperature measurements posed some problem in that there was a lag of a few seconds between the actual measurement and the printout by the digitec recorder, even when continuous recording via the machine was used. Each surface skin temperature was read separately and results were averaged after the experiment. There was a rapid and continuous fall in this temperature during the initial minutes of immersion. It does not seem possible that entirely accurate measurements could have been made. It was at this time that the rapid ventilatory changes occurred. It is also probable that the area weighting of skin temperatures, commonly used to compute heat exchanges, may not be applicable for determining reflex physiological consequences of changing skin temperature. This point appears to be supported by investigations of the control of sweating, in which it was found that different areas of the body showed differences in thermal sensitivity, which exerted different effects on the sweating rate (Nadel, Mitchell and Stolwijk, 1973). It is probable that similar areas of thermal sensitivity could be ascertained

in relation to a cold stimulus.

On the other hand, no difficulty was experienced in measuring the average deep skin temperature from 3 sites and a continuous measurement was available. The possibility that there was heat conduction via the shaft of the thermocouple while immersed in water was considered. This was simply tested in the following manner: a suitable steady skin temperature was achieved at a deep skin site and ice was applied to the outer needle portion of the thermocouple. No change in deep skin temperature ensued. When the cold stimulus was applied directly over the skin area in which the thermocouple was embedded there was an immediate decrease in deep skin temperature. One was more concerned with the exactness of replication of chosen sites, because there was no way of proving that the thermocouples were placed at exactly the same depth, in the 3 specific areas, for each person in each experiment. The rate of change of the deep skin temperature was found by drawing tangents to the plotted curves.

B. VENTILATION

Pulmonary ventilation is regulated by neural reflex mechanisms and chemosensitive structures known as chemoreceptors. These chemoreceptors are classed as either central or peripheral and are sensitive to changes in arterial hydrogen ion concentration and to arterial blood alterations of the partial pressures of carbon dioxide and oxygen. A neural network, located in the brain stem pontine and medullary regions, sets the basic breathing pattern. This neuronal organization is responsible for appropriate changes in the respiratory pattern which might be required as a result of information derived from chemoreceptors, higher brain

centers as well as alterations in blood adrenaline levels.

Several factors might be considered as affecting ventilation during cold water immersion. Generally the drive to increased ventilation is considered to be due to massive afferent discharge initiated at the peripheral cold recpetor level (Keatinge and Nadel, 1965). Cold receptors have been found in human skin (Hensel and Boman, 1960) and the range of temperatures in primates and sub-human primates to which they are responsive (generally from 18°C to 34°C with maximum activity at 26°C to 30°C) has been measured (Iggo, 1969). However, this study investigated the hypothesis that these and other factors might be involved e.g. receptors at a deeper skin site or surface skin temperature to deep skin temperature gradient. The evidence would appear to indicate that the primary stimulus to increased ventilation during the first minutes of cold water immersion after sauna heating or exposure to room air, was the rate of change of the deep skin temperature. No similar correlation was seen in the rate of change of mean surface skin temperature and ventilation. The temperature gradient through the skin after sauna heating appeared to have an input into the ventilatory drive under some circumstances. This would seem feasible because after exposure to room air, immersion in cold water would elicit a powerful peripheral vasoconstriction resulting in a small surface skin temperature to deep skin temperature gradient, whereas after sauna heating, the same degree of vasoconstriction would not be evoked and the gradient would be larger. The absolute temperature of neither the deep skin nor the surface skin correlated with the ventilatory drive.

It is possible that an increased sensitivity of respiratory

neurons to the dramatic changes in end-tidal PCO_2 during the first two minutes of immersion could affect ventilation. However, previous experiments, using the rebreathing technique, have shown that there is no increase in the sensitivity of these neurons (Cooper, Martin and Riben, 1976).

Another stimulus to increased ventilation during cold water immersion could arise in the level of circulating adrenaline (Innes and Nickerson, 1975). Unfortunately, it was not possible to measure the plasma levels of this substance in these experiments. However, there was no correlation between expired ventilation, end-tidal PCO_2 and dopamine-β-hydroxylase for the first and third minutes of the immersion. Conclusive evidence regarding sympathetic activity in relation to ventilatory responses was not available since a direct and steady increase in the levels of enzyme activity were not seen. The findings agree with an earlier study (Keatinge and Nadel, 1965) in which no correlation with circulating catecholamines and respiration was found, though their assay was relatively insensitive. The subcutaneous fat thicknesses of the subjects for the initial experiment with sauna heating did not bear any relationship to the severity of the initial gasp response during the water immersion. So far it has not been shown that more obese subjects have a decreased initial response to cold water immersion.

The effect on ventilation of exogenous factors, such as alcohol and diazepam, in addition to cold water immersion were considered. Since large doses of diazepam are required to alter respiratory activity via a central action (Byck, 1975), it was not surprising that no significant effect was noted in this study. It was seen that this relatively low dose

of diazepam had some interesting effects on one individual's responses. This subject (R.T.) was a trained diver and normally his respiratory responses during the cold water immersion were very orderly and regular. However, during the cold water immersion after the drug ingestion, increases in respiratory rate and total expired volume were seen. It is not possible to say emphatically that these changes were directly attributable to the drug, but comparable responses had not been seen for this subject during any other immersion.

Alcohol may augement or depress respiration (Ritchie, 1975). It would appear that the stimulus for increased ventilation as a result of cold water immersion was a primary drive to ventilation at the lower water temperature since no significant changes in ventilation were evident. However, at the higher water temperatures a depressant effect on ventilation was unmasked and significant changes in the ventilatory pattern were seen.

Two different groups, on two different occasions were exposed to sauna heating and cold water immersion. For the subjects of this first experiment it was their first major participation in cold water studies. A significant attenuation of their expired ventilation and end-tidal PCO_2 was evident during the immersion after sauna heating. No measurement of deep skin temperatures was made at this time. When the second group was tested under what were considered the same conditions of immersion, but with a more experienced group of subjects, no significant attenuation of expired ventilation occurred during the immersion after sauna heating. However, in this second experiment, during which surface and deep skin temperatures were measured, the ventilatory responses elicited during the cold water immersions after exposure to ambient

temperature or sauna heating were related to the rate of change of deep skin temperature and temperature gradient rather than surface skin temperatures. Two possible reasons which might explain the inability to reproduce the significant attenuation of ventilation in the second set of experiments are (1) the effect of habituation since this was a more experienced group and (2) the average skin temperature after sauna heating was higher in the first group in comparison to the second group, which might have affected the temperature gradient and/or the rate of change of deep skin temperature to a greater extent and thus a greater and significant attenuation in ventilation was seen.

When clothing was worn during an immersion the initial gasp and subsequent expired ventilation were attenuated. In the resting subject, the layer of water trapped by the clothing and providing a stable micro-environment, would have an insulative value and possibly affect the further rate of change of the deep skin temperature in preference to changes in the surface skin temperature since this measurement was not significantly different from that obtained during the first minute of the control immersion.

In contrast to the statement that the increased ventilation during cold water immersion might be due to stimulation of superficial peripheral cold receptors, it is proposed that the rate of change of deep skin temperature may be a major factor governing ventilatory responses, and in some occasions, the temperature gradient between deep and superficial skin temperature may also be a significant factor. These conclusions would be supported by investigations in which cutaneous

thermoreceptors respond not only to changes in the absolute temperature but perhaps more importantly also respond to rates of change of temperature (Hensel, 1952; Hensel, Brück and Roths, 1973; Maréchaux and Schäfer, 1949). The importance of temperature gradients in affecting peripheral circulation has been pointed out by Kerslake and Cooper (1954), so it is quite possible that these factors could affect ventilatory responses.

C. SHIVERING

Shivering in man exposed to cold appears to be related to skin temperature (Downey, Huckaba and Darling, 1971; LeBlanc, 1954; Wyndham, Williams and Loots, 1968), and it generally occurs at a higher skin temperature for a thin person in comparison to a fat individual. The rapid decrease in surface skin temperature during water immersion does not immediately elicit shivering and it is not known if other, deeper skin receptors might have a part to play. The results show that exposure to cold water elicited shivering in most of the subjects either early or later during the immersion. Both mean surface skin and deep skin temperatures varied, with the deep skin temperature higher than the surface skin temperature. The subjects with less subcutaneous fat generally shivered earlier than the fatter subjects, but this is not true for all cases in that the subject with the greatest fat thickness (K.E.C.) shivered early in the experiment, while the person with least fat (R.T.) took 5 min to shiver. However, their deep skin temperatures were comparable. The fact that two of the subjects who did not shiver after 10 min were

women and had fairly high fat thicknesses does follow what is generally known about the difference in women's reaction to cold in comparison to men (Hardy and DuBois, 1940; Tanaka, 1972). However, since there were only 3 women in the study it is not possible to draw proper conclusions concerning their overall responses to the cold stimulus. Both deep and surface skin temperatures were quite low at this time. However it does not explain why two of the thinner males did not shiver at fairly cold temperatures. One person mentioned above (R.T.) had extensive experience with cold water diving and thus may have been an habituated subject. Reproducibility of results was varied but one subject (S.M.) did have a consistent deep skin temperature at the onset of shivering. The latency to shivering was different during the two immersions which involved measurement of deep skin temperature and in the warmer of the two (14.71^{o}C vs 13.38^{o}C) it took about 15 min in comparison to 3.5 min to reach the deep skin temperature at which shivering occurred. Unfortunately surface skin temperature was measured in only one experiment. Although LeBlanc (1954) had found a relationship between the subcutaneous fat thickness and the surface skin temperature there was no such correlation in this investigation. However that study was done in cold air with a wide range of subcutaneous fat thicknesses in his subjects, whereas the subjects in this study had a narrow range of both skin temperatures and subcutaneous fat thicknesses. There was also no correlation between the deep skin temperature and subcutaneous fat thickness at the onset of shivering. After the subjects were heated and immersed in cold water the onset of shivering occurred later for six of them in comparison to the first immersion, three of the same subjects did not shiver and their deep skin temperatures were higher than those

achieved during the first immersion. For two of the subjects the mean surface skin temperatures were lower than those seen after the immersion following exposure to room air. There was a significant correlation ($p < 0.05$) between subcutaneous fat thicknesses and the deep skin temperature at the onset of shivering. This might imply that as a result of the pre-heating there was a greater heat storage before undergoing the immersion and the greater insulation provided by subcutaneous fat could prevent rapid loss from this acquired store. This might also support the observation that a steady level of deep skin temperature in contrast to surface skin temperature might supply major stimulus to shivering in that if a higher temperature is monitored at that receptor, there would be a difference in the afferent input to the shivering "center" in comparison to that coming in from the surface skin receptor. Reproducibility of results was evident for two subjects and particularly subject S.M. in that a deep skin temperature of 21^{o}C had to be achieved for shivering to occur. This required 21 min immersion on one occasion after the sauna heating. That the longer latency to shivering which occurred during the immersions after alcohol consumption might be due to some vasodilator activity of the alcohol at the level of blood vessels near these receptors is possible. The effect of alcohol on central processing is not known but a subjective feeling of greater comfort was experienced by the subjects after alcohol ingestion and factors other than skin temperature may influence shivering (Wyndham, Williams and Loot, 1968) when it is not required for a lengthy time to maintain body temperature. No effect of diazepam at a central level was evident with regard to the initiation of shivering. Although the data presented here are not conclusive, it would appear that there is some correlation between the deep skin, but not surface skin,

temperature and shivering elicited during cold water immersion. Perhaps a wider range of subjects and repeated experiments would confirm this suggestion.

Consideration of shivering from another viewpoint shows that some factors can attenuate or abolish this response. Some of the findings of this study extend unpublished findings of Cooper, Lind and Petrofsky that an isometric muscle contraction could attenuate shivering. The comparison of two tasks, mental arithmetic and isometric forearm muscle contraction, showed that the mental arithmetic task was more effective in causing a decrement in shivering. Whether this effect implies a greater inhibitory input initiated by the cortical activity attendant upon the mental arithmetic task, in contrast to the input following muscular activity,or whether it might simply reflect the fact that the subjects were not sufficiently practiced in the use of the dynamometer is not known. One experienced subject who participated in the study, but whose data were excluded because his closeness to the experimental hypothesis might have biased his response, consistently showed an abolition of shivering with a 40% or 50% maximum voluntary contraction. What pathways (secondary or primary) might be involved and how they would influence hypothalamic areas concerned with shivering are unknown. However, some investigations by Stuart (1961) have shown that, in cats, septal stimulation of high intensity could evoke or suppress shivering and Kaada (1951) has shown that shivering can be inhibited by electrical stimulation of points on the cerebral cortex. This would imply a secondary modulating influence of this area on shivering in contrast to the primary control exercised by the hypothalamus. In view of the plurality of connections of the hypothalamus with various

areas of the limbic system, and higher brain centers it would not seem out of order to consider that these areas may be exerting some similar modulating influence on shivering.

D. BODY TEMPERATURE

The degree of body heat loss during cold water immersion is governed by many factors. The results obtained here would indicate that neither the ingestion of alcohol, or diazepam, nor the use of light clothing significantly altered the body temperatures observed. Alcohol is a central nervous system depressant and in moderate doses is said to cause cutaneous blood vessel vasodilatation (Ritchie, 1975), and thus may increase heat loss during cold exposure. The results obtained here are in agreement with other reports in which alcohol caused no significant modifications to heat loss during exposure to cold air (Andersen, Hellstrom and Lorentz, 1963) or cold water (Keatinge and Evans, 1960) in resting subjects. However no blood levels of alcohol were reported for these studies. Also the possible effects of alcohol ingestion during warmer water immersions has not been studied. The mean blood alcohol levels of the subjects before each of the 3 immersions were 90 mg.100 ml^{-1}; 83 mg.100 ml^{-1} and 100 mg.100 ml^{-1}. It was hoped to attain a blood alcohol level at about the driving legal limit of 80 mg.100 ml^{-1} and an attempt was made to give an alcohol volume dependent on body size, to control the time of ingestion (20 min) and partially to regulate the metabolic state of the subjects (fasting for 2 h). This was done to insure better alcohol absorption since both rate and efficiency of alcohol absorption are increased in the fasting state (Lin, Weidler, Garg and Wagner, 1976).

However, in spite of these restrictions a wide range of blood alcohol levels was evident both on an inter- and intrasubject basis. Some reasons which might account for this are the actual metabolic state of the subject (Kalant, 1971); hormone levels [although they may not play an important part during acute alcoholic ingestion (Ritchie, 1975)]; the possibility of alternate metabolism by non-alcohol dehydrogenase systems, which may be operative during acute, high alcoholic intake (Lundquist, 1971). Since the rate of alcohol absorption varies for individuals, anywhere from 2 h to 6 h (Ritchie, 1975) and there is an essentially constant metabolic rate, about 10 $ml.h^{-1}$ (Goldstein, Aronow and Kalam, 1974), the variations in the second blood samples might also reflect the above mentioned conditions. Because of the paucity of blood samples, it was not possible to state exactly in which phase of the alcohol metabolism curve the subjects were at the time of the immersion. However it might be inferred that these individuals who showed an increased blood alcohol level in the second sample would be in the absorption phase of the alcohol curve, while those subjects whose blood alcohol levels had decreased might be in elimination phase of the alcohol metabolism curve.

The peripheral vasodilator effects of alcohol are often said to contribute to a serious thermal imbalance if a person was exposed to cold. In view of this the mean skin temperature patterns were interesting. While the relationship of superficial skin temperature to blood flow is non-linear (Cooper, Cross, Greenfield, Hamilton and Scarborough, 1949) and under the conditions of these experiments it would be difficult to give an accurate assessment of blood flow from skin temperature measurements, it would be expected that large changes in skin blood flow would

produce some apparent change in skin temperature. If such an assumption can be made for the first 2 min of the immersion, the vasoconstriction elicited by the 13.5°C and 22°C water after alcohol consumption, was not statistically significant from the vasoconstriction obtained during the immersions without alcohol. It might be concluded that no significant change in skin blood flow occurred with this level of alcohol consumption, any potential vasodilator effect being over-ridden by the vasoconstriction induced by all water temperatures. As a result there was not an increased heat loss during the immersion.

In general the changes in body temperature, measured rectally approximate those of an earlier study (Keatinge and Evans, 1960) but the overall temperature changes during the colder water (13.5°C) immersion showed a greater decline. This difference may be due to diversity of the physical characteristics of the subjects, and the colder water temperature (2°C lower). The rapid changes in rectal temperature seen during the colder water immersions may be evidence of local cooling of the rectum due to the return of cooled blood from the legs via the venous plexuses close to the posterior wall of the rectum rather than an indication of true core temperature. Similar, but less rapid changes in rectal temperature were seen at the higher water temperatures.

Aural temperature closely parallels changes in esophageal temperature during deep body temperature changes (Keatinge and Sloan, 1975) and avoids the lag that rectal temperature shows in relation to true core temperature (Cooper and Kenyon, 1957). Thus, it is probably a more accurate measure of the core changes for these experiments. For these short term immersions the aural temperature was generally constant,

with any change occurring towards the end of the experiment.

The ingestion of alcohol, in the quantities given in these experiments did not increase body heat loss during any of the water immersions since there were no statistically significant differences in rectal, aural or surface skin temperatures during the experiments. The reported blood alcohol levels, therefore would appear not to affect either skin blood flow or central temperature regulating neurones. This conclusion is supported by the recent findings of Kuehn, Livingstone, Limmer and Weatherson (1977). It is possible that blood levels of the order of 200 to 300 mg.100 ml^{-1} might be required to produce such an effect but it was not possible ethically to test this within the confines of this study. It is interesting to note that the immersion following alcohol consumption was considered less uncomfortable and boring by the subjects, with one or two exceptions. Thus, alcohol could minimize the discomfort and panic attendant on a sudden cold water immersion incurred as the result of an accident. Whether this would be an asset in increasing survival chances during a long exposure in cold water is still not clear.

Because of the widespread use of tranquillizers, the possible effect of a single diazepam dosage on body temperature change was investigated. A wide but not excessive range of plasma concentrations was evident after the single oral dosage. This would reflect a degree of variability in the absorption of this drug. The drug levels at the end of 1 h, although not the highest values seen for all subjects do indicate a trend similar to other findings in that highest plasma concentrations are evident within 1 to 2 h (Byck, 1975; Gamble, Dundee and Assaf, 1975) with a biphasic decay pattern seen over an 8 h period.

The fact that only one subject's plasma levels were monitored for more than 1.5 h, precludes any definitive statement regarding the drug kinetics. One comment is in order regarding the ambiguous findings in one subject's control values. This might be due to prior use of diazepam, although subjects were screened regarding drug intake at the time of the experiment, or it may be due to some other plasma constituent. No significant difference in body temperature, measured rectally, or surface skin temperature occurred during the cold water immersion. The drug is not known to have any direct action on blood vessels and quite high doses, given intravenously, are required to affect other physiological systems, e.g. cardiovascular (Byck., 1975). It would appear that diazepam, delivered as a single oral dose does not affect either central temperature regulating mechanisms or cutaneous blood flow thus, no significant change in body temperature was seen.

There were no significant differences in body temperature (aural) during the immersions in which resting subjects were clothed or unclothed, but their surface skin temperatures were significantly higher during the immersion in which they were clothed. Thus, for resting subjects in cold water clothing provides some insulative value. The difference between the results here regarding body temperature and those reported by Keatinge (1960) might be due to the fact that temperature was measured rectally in that study and aurally in our study. From previous discussion, it was seen that significant changes in aural temperature were not usually evident during short term cold water exposures. Whether any significant changes in body temperature would have occurred during any of these experiments, if part of the head had been immersed is not known. However, since this body area accounts for a large portion

of body heat loss when exposed to cold (Froese and Burton, 1957) different changes in body temperature might have been evident.

E. CARDIOVASCULAR RESPONSES

Sudden exposure to cold elicits increased venous and arterial pressures (both diastolic and systolic) as well as pulse pressure and pulse rate (Keatinge and McCance, 1957; Keatinge, McIlroy and Goldfien, 1964). These changes are reported to be due to increased sympathetic nervous activity, rather than to circulating plasma catecholamines because no significant increase in plasma levels of adrenaline or noradrenaline were found (Keatinge, McIlroy and Goldfien, 1964). Since dopamine-β-hydroxylase is stored in nerve terminals and released with noradrenaline when sympathetic nerves are stimulated (see review Axelrod, 1972), changes in the amount of this enzyme in the circulating plasma should reflect changes in sympathetic activity in man. Some investigations have shown that changes in heart rate during exercise (Plantz, Wiethold, Appel, Böhmer, Palm and Grobecken, 1975) and the cold pressor test (Freedman, Ebstein, Park, Levitz, Goldstein, Davis, Chu and Manger, 1973; Wooten and Gordon, 1973) can be correlated with changes in dopamine-β-hydroxylase activity. Some reservation for the reliability of this type of correlation has been registered by Freedman, Ebstein, Park, Levitz, Goldstein, Davis, Chu and Manger (1973). Further confirmatory evidence has come from studies of normal and adrenalectomized persons, since the latter group was found to have normal levels of the enzyme (Noth and Mulrow, 1976). A wide range was evident in the resting values, a finding comparable to other studies (Axelrod, 1972), but the values for dopamine-β-hydroxylase activity do not show a definite

increase during the time of the cold water immersion. Even when individuals were compared to their own control values with or without exercising the arm from which blood was taken and % changes calculated there were no significant increases. The significantly increased heart rate seen suring the immersion is in agreement with earlier findings (Keatinge, McIlroy and Goldfien, 1964) but there was no correlation between this change and the dopamine-β-hydroxylase activity. Since whole body immersion would elicit much stronger sympathetic activity than the cold pressor test at a comparable temperature, the findings are puzzling. Part of the difficulty might be with the assay method, although it is workable and sensitive technique.

In vitro and in vivo studies have shown that dopamine-β-hydroxylase activity in the adrenal medulla is under neural and hormonal control (Ciaranello, Wotten and Axelrod, 1976; Snider, Sahan, Prasad and Fahn, 1977) and require time to be initiated. Since hormonal changes as a result of exposure to cold air occur over hours or days, it is possible that if a consistent increase in plasma dopamine-β-hydroxylase had been present and had correlated with the heart rate that this change would have been due primarily to increased sympathetic nervous system activity. It was intended to measure plasma adrenaline and noradrenaline concentrations, but these samples were lost due to a freezer breakdown. Significant changes in blood pressure during the first 3 min of a cold water immersion have been found but difficulties with the catecholamine assay, said to be able to detect picogram quantities,have prevented me from determining whether these changes are influenced by circulating catecholamines or due to sympathetic nervous system activity as reflected by dopamine-β-hydroxylase activity.

Alcohol did not unduly influence heart rate during any of the water immersions and this confirms the finding of an earlier study (Keatinge and Evans, 1960). Since cardiovascular changes (decreased blood pressure, decreased cardiac output and increased heart rate) are seen only after large doses of diazepam are given intravenously (Byck, 1975) it was not expected that the therapeutic doses given here would have any effect. However it was interesting to note that the usual increase in heart rate seen during at least the first minute of exposure to cold water was not evident during this experiment. It is not possible to say if this was due to an effect of the drug or whether the effect was related to the small number of subjects (4) from whom readings were obtained.

F. MEMORY

Probably the most significant aspect of this study was the fact that when subjects were given a learning task in the water and tested in room air there was a significant difference in their response during the two water immersions and the number of errors correlated well with the degree of hyperventilation sustained by the subjects during the cold water immersion. Whether the decreased cerebral blood flow associated with decreases in end-tidal PCO_2 (Kety and Schmidt, 1948) might interfere with the acquisition of information can only be entertained as a possible exploratory hypothesis. This fact highlights the necessity of repeating this experiment and keeping

the end-tidal PCO_2 constant. Recent experiments (Gibson, 1977) in which the subjects voluntarily hyperventilated, while sitting at ambient temperature and performed short-term memory and digit recall tasks, showed that no cerebral hypoxia was present and there was no significant change in the subjects' performance of the mental task. However these experiments were performed under different circumstances than the one reported here, and it is possible that a measure of state dependent learning was evident. Although a similar degree of hyperventilation was seen in the subjects who were tested in the water, this did not appear to interfere with their performance on the test. Whether the fact that they were tested in the same environment in which they were given the stimulus or whether the smaller number has any effect on the results is not known.

Two of the experiments showed results in which a poorer performance was recorded as a result of immersion in warm water. This finding was unpredicted. It is possible that the subjects were more relaxed during this immersion and did not give full attention to either the visual recognition test or the game during the testing procedure. However, most of them did take longer to play the first ten games after the cold water immersion. It does not seem likely that all subjects felt poorly on particular days for the warm water immersion since another experiment showed that there was no intrasubject variation. It is possible that the subjects were distracted during the testing procedure but care was taken that no disturbances occurred in the laboratory during these times. No precise observations of anxiety were made for any experiments, but under the conditions of the experiments, it probably was not high.

The use of the mental arithmetic task showed there was no significant difference in the subjects' recall ability but there was an indication that perhaps ability to use a previously learned skill (subtraction) might be affected. Whether a greater number of subjects would have shown a greater difference could be explored. The individuals' responses to this experiment were interesting in that they were sometimes concerned about the number of errors made and wondered how their performance compared to others involved in the study. This might imply that a greater degree of concentration was given to the mastery of this task in spite of the cold water immersion.

Although care was taken to randomize the water immersions and to have them spaced over many weeks, some effect of habituation could be present. Repeated cold water immersions are known to cause habituation and decreased physiological responses to this stimulus (Glasser and Whittow, 1957), and localized habituation is evident in man (LeBlanc, Hildes and Héroux, 1960) and rats (Eide, 1971). LeBlanc and Potvin (1966) as well as Lapp and Gee (1967) have shown that as subjects became habituated, as a result of repeated cold water immersions, their performance of a mental arithmetic task improved. However no direct evidence from either the physiological or memory testing data supported the idea of habituation for these subjects. In addition, not all subjects participated in all studies although there was some overlap. The fact that many had participated in cold water studies for at least a year before these experiments were done must be remembered and it is possible that an "unconscious" habituation had occurred.

The one significant experiment implies that a decreased end-tidal PCO_2 which occurred as a result of cold water immersion, might

lead to a decreased ability to either acquire or store information. The first experiment showed that cold water immersion after the learning situation caused no problems. What the possible relationship could be is elusive. One would need to know the actual decrease in local cerebral blood flow at the time and how this low level of end-tidal PCO_2, indicative of arterial PCO_2, could affect neurons possibly involved in any memory activity. It is possible that decreased PCO_2 levels could affect neuronal firing rates since a lowered arterial PCO_2 in the lateral geniculate nucleus altered a unit firing pattern in this area which was initiated by mesencephalic reticular formation stimulation. The spontaneous firing pattern of the single unit was not affected by the decreased arterial PCO_2 (Tatton, 1971). Perhaps a more severe cold water exposure for even these short times and a larger number of subjects would illustrate more clearly some of the possible differences in the other experiments.

Some practical conclusions are evident as a result of this work. Factors such as pre-heating and clothing, can affect the rate of change of deep skin temperature, reduce the initial gasp response and thus decrease the possibility of inhaling water. Although no effect on respiration or body temperature was evident as a result of alcohol or drug ingestion, it is possible that larger quantities or chronic use of these substances would be disadvantageous because of a resultant decrement in motor and intellectual function. Their effect may also be more apparent during a longer water exposure. The point that either motor or mental activity can affect shivering may be important in that a reduced shivering would decrease water movement around the body and prevent some heat loss. Whether this reduction would be detrimental

to adequate heat production during a long term immersion is not known. Because there appears to be a memory deficit as a result of cold water immersion, the reliability of evidence given by an individual in this situation could have implications in the medico-legal area.

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APPENDIX 1

CONSENT FORM

Date_____

I have had explained to me the possible dangers of being immersed in cold water, namely that a rise of blood pressure could occur leading to damage of any weak internal blood vessel, or that irregularities of the heart action might occur. These possibilities, however slight, have been made clear to me. With the clear knowledge of possible harmful effects, I am willing to act as a subject in experiments involving my swimming in cold water, in Dr. K.E. Cooper's laboratory at the University of Calgary, Health Sciences Centre.

Signed_____

(if under 18 years must be signed by parent or guardian)

Signed_____

APPENDIX 2

CONSENT FORM

Date_____

I have had explained to me the nature of this experiment, namely physiological changes with alcohol ingestion and cold water immersion. I have also had explained to me the possible changes in being immersed in cold water, namely that a rise of blood pressure could occur, leading to damage of any weak internal blood vessel, or that irregularity of the heart action might occur. These possibilities, however slight, have been made clear to me. In view of the nature of the experiment, i.e. alcohol ingestion, I shall refrain from operating any motor vehicle or dangerous machinery or equipment for the remainder of the day (or for 5 h) following completion of the experiment. I also understand that my eligibility for this experiment will be void if I am taking any other drugs or medications, or if I have been in the past or am at the present an alcoholic or chronic alcohol abuser. With the clear knowledge of possible harmful effects, I am willing to act as a subject in experiments involving mu swimming in cold water, in Dr. K.E. Cooper's laboratory at the University of Calgary, Health Sciences Centre.

Signed_____

N.B. Persons under the age of 18 years are not eligible to participate in this experiment.

APPENDIX 3

CONSENT FORM

Date_____

I have had explained to me the nature of this experiment, namely physiological changes with the use of tranquillizers (Valium) and cold water immersion. I have had explained to me the possible physiological changes which result from being immersed in cold water, namely, that a rise in blood pressure could occur, leading to damage of any weak internal blood vessel, or that irregularity of the heart action might occur. These possibilities, however slight, have been made clear to me.

In view of the nature of the experiment, i.e. drug (Valium) ingestion, I shall be most careful in all drug ingestion (particularly depressants, e.g. alcohol) and aspirin for 24 h following the experiment, and will refrain from operating a motor vehicle or dangerous machinery or equipment for the remainder of the day (or for 5 h) following completion of the experiment. I also understand that my eligibility for this experiment will be void if I am taking any other drugs or medications, or if I have been in the past or am at the present an alcoholic or chronic drug or alchol abuser. With clear knowledge of possible harmful effects, I am willing to act as a subject in experiments involving my swimming in cold water, in Dr. K.E. Cooper's laboratory at the University of Calgary, Health Sciences Centre.

Signed_____

N.B. Persons under the age of 18 years are not eligible to participate in this experiment.