Environmental Cold and Man

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Ambient cold calls forth a series of responses in homeothermic beasts and man. These efforts to compensate for the environmental factors that increase the rate of heat loss can be categorized, generally, as sympathetic responses. The increased activity of this portion of the neuro-humoral axis results in a mobilization of physiological defenses through the increased release of catecholamines and all the ramifications thereby implied. In addition to specific and nonspecific defense mechanisms, there is increased mental activity, anxiety, and increased muscular movement. When the cold is of sufficient intensity (excessive heat loss), these compensatory mechanisms fail and the "body temperature" continues to fall below normal until metabolic alterations are no longer compatible with life.

The blood serves as the carrier and distributor of heat, flowing from the left ventricle to most organs at a uniform temperature. During circulation through the arteries and arterioles, arterial blood courses in proximity to venous blood and some of the calories from the warmer artery are transferred to the cooler vein by a process of conduction. This counter-current phenomenon has been well documented in those mammals (seals, whales, etc.) existing in cold water but is not so evident in man. Venous blood returning from a region or organ is usually at the temperature of the area drained and individual venous temperatures may vary widely until pooling and heat equalization take place in the major venous conduits and right heart. Temperature regulation is an essential function of the cardiovascular system, though less frequently described, than the nutritional or gaseous exchange function. Just as each organ, structure or tissue has a specific blood flow regulated by chemical needs, so do the optimal temperature requirements exert an influence on perfusion. The body tissues interpose an insulation between the blood supply and the ambient temperature varying in thickness from a microscopical layer of cells in the lungs to the thicker layers of the skin and the ubiquitous adipose layer. Heat is lost from the surfaces via four pathways: (1) conduction, (2) convection, (3) radiation, and (4) evaporation. These share in common the differences in temperature and the area involved, but evaporation depends on addition on the wet bulb temperature of the air. It is not the intent of this review to expand on these factors, rather it is meant to discuss physiologic and metabolic problems. The authors would be remiss if they did not bring to the attention of the reader the excellent reviews on hypothermia by Little, by Burnam and Vandam, by Smith and Stetson, and a symposium on the subject in the Annals of the New York Academy of Medicine for 1959.

A useful concept considers the body as possessing a core maintained at a relatively constant temperature and surrounded by an outer layer of tissue. The temperature of the outer layer may vary considerably according to the external environment, the degree of artificial protection, and the activity of the individual. A gradient of temperature from the inner core to the skin surface is recognized, but Horvath has shown that there may also be considerable variations in temperature in different parts of the core. Thus hepatic temperature may be 1–2° higher than the rectal temperature. The rectal temperature cannot always be regarded as representative of the average deep body temperature. Bazett measured temperatures at various intravascular sites as well as rectally during exercise and demonstrated the marked differences between blood from active muscles and that of the rectum. In ordinary clinical practice, a reading taken

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at the mouth or rectum will supply adequate information relevant to the cause and progress of disease but in induced hypothermia, as cooling proceeds, a reasonably reliable index of cardiac temperature is needed. The temperature of this organ will reflect not only the average body temperature but will largely determine the onset of myocardial depression or development of ventricular fibrillation. Cooper and Kenyon²⁵ made simultaneous measurements of rectal, esophageal and para-aortic temperatures in man. They concluded that the esophageal temperature, taken at heart level, was a good index of cardiac and aortic temperature, whereas rectal temperature was grossly misleading. Severinghaus and Stupfel²⁶ showed that during rapid cooling, the relationship between rectal and other deep body temperatures was not predictable, and that large temperature gradients developed. Clark, Orkin and Ravenstine²² demonstrated at normal temperatures that rectal, nasal or esophageal temperatures were alike but as the body became hyperthermic, the differences in temperature among these three sites increased as the temperature rose.

The mechanisms that maintain body temperature are truly remarkable and man can survive after considerable hypothermia. Most mammals, including man, require forced cooling in order to become hypothermic. This state can be induced by exposing the nude subject to lowered environmental atmospheric temperatures, by immersion in cold water, by packing in ice, by refrigeration blankets, or by blood heat-exchangers.¹⁵, ⁸² The possibility of lowering the temperature of the entire body was postulated by Currie²⁸ in 1798. He measured oral temperatures in subjects immersed in water at 7° C. (44° F.) and found an initial fall in oral temperature followed by a slight rise associated with shivering. When the subject was removed from the bath and exposed to air, oral temperature fell an additional 1° to 1.5° C. Currie concluded that the final body temperature was not the sole factor determining ultimate mortality or morbidity but that the duration of hypothermia also had a profound effect. Many similar cases have been described during the past two hundred years. The abhorrent experiments performed by the Nazis at Dachau have been reported in detail by Alexander. Prisoners were immersed in water at temperatures of 2°–12° C. (35°–55° F.) and rectal temperatures taken. There was initial violent shivering followed by intense muscular rigidity which was abolished only at rectal temperatures below 27° C. (81° F.). Consciousness became clouded at 31° C. (88° F.). Rectal temperatures reached 29.5° C. (85.1° F.) after 70 to 90 minutes of cooling; death occurred when rectal temperatures fell to 24°–25.7° C. (75°–78.2° F.).

Hamme³⁰ determined that the critical environmental temperature of a modern European or American lies between 27° and 29° C. This means that for the resting naked man in still air, shivering will be required to balance heat production against heat loss for ambient temperatures below 27°–29° C. Andrus¹ showed that the range of active defense by the unanesthetized rat against cold lay between body temperatures from 36° C. to 30° C. Above 30° C., the metabolic rate was usually increased; below 30°, there was a progressive decline. The greatest fall occurred below 25° C., and cold narcosis or lethargy was encountered in the range from 20° to 13° C.¹² The experiments at Dachau and others showed that the cooling of man or animals resulted in the disintegration of cardiopulmonary function and anoxic death rather than cellular or enzymatic dysfunction. Moreover, the recent investigations of Andrus,¹ Smith,³⁵ and Gollan²⁶ have definitely demonstrated that hypothermia approaching 0° C. is compatible with life in animals and man provided that adequate perfusion is maintained. When respiration and circulatory functions are maintained by mechanical means during cooling, cellular function diminishes gradually in relation to bodily needs. Death does not occur until the cells undergo crystallization or denaturation.³⁵ Popovic,²⁷ in experiments on rats exposed to temperatures from 10°–15° C. for prolonged periods, showed that animals can tolerate limited periods of cooling to the freezing point; if exposure is prolonged, death ensues. Laufman's⁵⁵ classical account of the case of a Negro woman in Chicago is probably the best documented description of survival after accidental exposure to subfreezing temperatures. This woman lay in a drunken stupor,
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all night, at an atmosphere temperature between −18° and −24°C. When rescued the next day, she was pulseless but the heart was beating 12 to 20 times per minute and respiratory rate was 3–5 times per minute. The rectal temperature was 18°C (64.4°F). The extremities were much colder and were so severely frostbitten that it was necessary to amputate the legs below the knees and all the fingers were lost. She was rewarmed slowly, being left naked in a room at 20°C (68°F), and rectal temperature rose at the rate of 1°C per hour. Amazingly, she survived. In this as in other instances the question arises as to whether a high alcoholic blood level favors survival from severe hypothermia or whether the intoxicated merely are more liable to suffer exposure. Thus far, there is no evidence that any human being whose internal temperature has reached the freezing point has recovered.

Despite the considerable number of studies of the physiological effects of hypothermia, there is still very little known concerning either the mean lethal temperature or the exact nature of death in accidental exposure, either to cold water or cold air in man. Adolph and others have established the lethal body temperatures in adult mammals for many species, some of which hibernate. In every instance the result was essentially the same; breathing and pulse slowed and the animals died when the internal temperature was still well above the freezing point of plasma. Molnar investigated the survival times of men in the sea and conducted a study of the factors leading to death. In sea water at a temperature of −1.1°C (30°F.), man would be expected to survive for less than one hour; the time limit increases to about 3 to 6 hours at 15.6°C (60°F.). The curve relating survival time to duration of immersion shows a sharp inflexion between 15.6° and 20°C (60°–68°F.). Above 20°C (68°F.), the maximum time of immersion is greatly prolonged. Hegnauer found the LT₅₀ for the anesthetized dog subjected to immersion hypothermia to be approximately 17°C; for unanesthetized man the temperature appears to be closer to 27°C. A somewhat lower value is obtained in man on exposure to cold air owing to the slower rate of cooling and the more intense shivering reaction. The cause of death in unanesthetized man appeared to be ventricular fibrillation. In the anesthetized dog, death was the result either of ventricular fibrillation at temperatures below 25°C, or asystole in the range of 18°C to 14°C. The mechanism of the bradycardia, asystole or ventricular fibrillation, is still unknown.

Metabolism

In general, the initial response of the homeothermic organism to external cold is one that suggests intense sympathetic stimulation: shivering occurs, vasoconstriction is profound, oxygen consumption increases tremendously, respiratory rate is accelerated, the pulse rate is increased, blood pressure is elevated, and there is a significant increase in cardiac output. Behnke exposed himself and two volunteers to aqueous temperature at 5.5°C to 10°C (42°–50°F.). Rectal temperature rose slightly at first, then fell in a linear fashion to 35.8°C at the end of an hour. Metabolic rate increased from 86 kg./Cal./hour to approximately 500 kg./Cal./hour, taking some 30 minutes to reach a maximum. In spite of the great increase in metabolic rate, the net heat loss was still between 30 and 36 per cent after one hour.

That heat production of animals increases with cold has been known for a very long time and dates back to the investigations of Lavoisier and Laplace using animal calorimetry. In his work on temperature regulatory responses wrote about the increase of the metabolism in body tissues in response to cold. This has been confirmed many times. Thermogenic factors in cooling may be divided into two broad categories: those associated with shivering and those arising from other sources. In 1872, Bernard proposed that there exists a nonshivering source of heat production. Subsequent failure to demonstrate its presence led physiologists to discredit its existence; even the support lent by Rubner, Lefevre, Cannon, and others has failed to substantiate this theory.

Between 1900 and 1854 shivering was considered to be the only active mechanism of thermogenesis in the cold. Cold and warm perfusion experiments, and the recent hypo-
thalamic heating experiments performed by Hardy et al.14 demonstrate that warming the hypothalamus inhibits shivering while cooling causes stimulation. The preparation by Keller56 of the poikilothermic dog by selective ablation of the hypothalamus again demonstrated the importance of this region in the regulation of shivering. However, in the intact dog, peripheral stimulation via dermal receptors appears to be a major factor contributing to the shivering process, and the question of how the hypothalamus and peripheral receptors combine to regulate shivering remains a puzzle.21 In rats, Davis59 has shown that under normal conditions of cooling, shivering is stimulated by a fall in skin temperature and that the thermal state of the body core appears to play no major role in either the inhibition or stimulation of shivering. However, in extended experiments with mice, he showed that even though shivering in the normothermic animal is stimulated fundamentally by a falling skin temperature, quantitative regulation is dependent upon changes in core temperature. In the truly hypothermic homeotherm, however, shivering appears to be stimulated entirely by decreased central temperatures. In a study of shivering in nine nude human subjects exposed to atmosphere temperature of 14° C. for a period of 60 to 70 minutes, two pertinent observations were noted. There was a variation in time of onset of shivering from 4 to 55 minutes. The degree of variability in the intensity of shivering in each individual at any moment during the period of exposure exhibited a cyclic or periodic character.

Intensity of shivering is related to the rectal temperature and violent shivering does not start until rectal temperature begins to fall. If body heat production is three to six times the basal level (as is usual during shivering), then at 20° C. (68° F.) and above, the heat loss will be balanced or be less than the body heat production; a fall in central body temperature will not occur. Below 15°–20° C. (59°–68° F.) heat loss will exceed heat production and the deep body temperature must fall. The rate at which the deep temperature falls will be a function of the total insulation supplied by the subcutaneous layer and its initial heat content.74 Most observations on hypothermia suggest that the increase in metabolic rate with cooling does not persist after the rectal temperature has fallen to approximately 35° C. (95° F.). There is a gradual decline, reaching basal values or lower at rectal temperatures from 27° to 30° C. (80°–86° F.). Shivering usually ceases at rectal temperatures from 30° to 33° C. (86°–91° F.) and is succeeded by muscular rigidity. The same sequence has been observed in dogs by Hegnauer and Penrod.47, 40, 50, 54 During rewarming, shivering begins again at rectal temperatures above 30° C. (86° F.). There is debate as to whether the fall in oxygen consumption bears a linear or exponential relationship to the drop in body temperature.14, 83, 55, 79, 88 However, the important fact would seem to be that there is roughly a 6 per cent fall in oxygen consumption per degree centigrade fall in body temperature providing that shivering is controlled.

The increase in heat production by metabolic or nonshivering sources of heat, as a defense against cold (called by Rubner, "chemical regulation")79, has been extensively studied by oxygen consumption measurements and by observations of nutritional caloric requirements. Shivering is preceded by an increased "thermal muscular tone," which is detectable as frank shivering. Swift81 studied the increased metabolism in man and was convinced that any increase in metabolism not accompanied by overt shivering must be justly ascribed to increased muscular tension. Burton18 provided further evidence of the existence of "thermal muscular tone" before the onset of shivering, using electro-myographic recordings from the muscles of chilled cats. Finally, the most conclusive work on this subject is the result of an excellent study by Davis and Mayer,29 who were able to show that a nonshivering form of thermogenesis as postulated by Bernard,11 Rubner,76 and Cannon20 does indeed exist. In a series of investigations on rats and using curare for muscular paralysis, Davis and Mayer were able to show that nonshivering thermogenesis of unacclimatized rats is stimulated primarily by central temperature changes. This contributes approximately 45 per cent of the cold-induced increase in metabolism while shivering contributes about 55 per cent.20
Respiration

Pulmonary ventilation increases at the onset of cooling and there is a fall in alveolar CO₂. Subsequently, the minute volume falls, although oxygen consumption increases. After the initial increase, there is a close, and almost linear, relationship between the fall in body temperature and the decrease in respiratory rate and depth. At approximately 24°C, a respiratory crisis occurs, and the respiratory minute volume quickly diminishes to the point of cessation. Severinghaus showed that hypothermia leads to an increase in physiological and anatomical dead space through bronchodilatation; in fact, at 25°C, the anatomical dead space was increased by 50 per cent. There was no difficulty in the elimination of carbon dioxide as had been previously stated, and the distribution of blood flow through the lung was minimally altered. The alveolar-arterial Pco₂ difference remained almost constant with decreasing temperature. Sechzer, in a study on compliance in man during hypothermia demonstrated no alteration in the lung thorax system or in the airway resistance at air flows between 0.5 and 1.0 liter/second. However, Hegnauer and Pendar pointed out that a progressive fall in the pH of arterial blood occurs in hypothermia which results from a depression of spontaneous respiration and that it is accentuated by development of metabolic acidoses. This shift in pH of blood toward the acid side could counteract the effect of decreased temperature on the shift to the left of the oxygen-hemoglobin dissociation curve. Nevertheless, analysis of arteriovenous oxygen differences indicate that the same fraction of oxygen is extracted from the blood at 18°C as at 38°C, suggesting that the tissues need contract no significant oxygen debt during hypothermia. In clinical practice, the magnitude of respiratory depression produced by hypothermia and the temperature at its endpoint, apnea, depend greatly on the choice and depth of anesthesia, the type and amount of premedication and individual patient variation.

Circulation

The cardiovascular response to hypothermia has been the subject of considerable investigation inasmuch as progressive cooling leads to cardiac asystole or ventricular fibrillation. The response of the cardiovascular system to hypothermia may be summarized as follows. There is an initial marked peripheral vasodilation with a rise in blood pressure and heart rate. During this stage, the rectal temperature does not fall. If cooling is continued, rectal temperature begins to decline and the heart rate decreases linearly with the fall in body temperature. This is apparently a direct effect of cold on the sinus pacemaker for the slowing is not abolished by atropine or vagotomy. The effect of hypothermia upon cardiac rhythm follows a definite pattern but the effects vary widely from patient to patient. Many factors such as local oxygen supply, hypcapnia, blood pH and electrolyte balance play a role. The usual findings in the electrocardiogram during the temperature range from 32°C to 28°C include: decreased amplitude or absent P waves, increased QRS interval, increased length of ST segment and prolongation and/or inversion of T waves. If the temperature falls below 28°C, varying degrees of heart block may be manifest and ventricular extrasystoles or nodal rhythm may appear. If cooling is continued further, either ventricular fibrillation or cardiac asystole occurs. The smaller the animal's species, the lower will be the critical temperature for cessation of effective cardiac activity. The vulnerability of the heart to ventricular fibrillation in hypothermia has attracted great interest and the subject treated in a number of reviews. Ventricular fibrillation occurs spontaneously below 30°C, frequently without warning, often secondary to myocardial manipulation, during or at the termination of circulatory occlusion. No single etiologic factor or method of control has emerged from many investigations. Metabolic and chemical changes, the physical effect of cold on contractility and nerve conduction, the alterations produced by changes in coronary perfusion and changes in the demands for cardiac work may all be implicated. Two recent suggestions concerning the etiology of fibrillation are: (1) development of a differential in temperature among several areas of the myocardium. Right ventricular mural temperature falls more rapidly than the left,
owing to the return of cooled venous blood. (2) the increased susceptibility of the heart to adventitious stimuli during hypothermia and the development of more rapid impulse transmission due to increased synaptic transmission. Prophylaxis and treatment of ventricular fibrillation under hypothermia with drugs have been ineffective. The use of procaine amide to diminish ventricular excitability has been found harmful. Angelakos investigated the effects of digitalis on the hypothermic heart. Since digitalis and cold exert opposite effects on the refractory period of the myocardium, this may be the basis for the antagonism of cold to digitalis-induced fibrillation. Angelakos concluded that digitalis is not contraindicated in hypothermia and that it is not a factor in the origin of ventricular fibrillation.

Blood pressure falls during hypothermia. During the early cooling period there is a rise in blood pressure but as the body cools, there is a gradual decline. When the rectal temperature reached 25°C, C. in man and in the dog, there is a rapid onset of a severe hypotension followed by ventricular fibrillation. The fall in blood pressure is due chiefly to the reduction in cardiac output, inasmuch as the peripheral resistance in both the systemic and the pulmonary circulations is increased, probably due to vasoconstriction in response to a direct action of cold blood on the arterial smooth muscle.

In conclusion, so long as a normal electrolyte balance can be maintained, and adequate pulmonary gas exchange provided, it is believed that ventricular fibrillation should be an uncommon occurrence at temperatures above 27°C.

Blood

Various features of blood undergo change during deep hypothermia. Viscosity is increased, there is a rather marked rise in red blood cell count, hemoglobin content and hematocrit, and there probably is a loss of plasma from the circulation either as a result of sequestration in minute peripheral vessels or an actual shift of water to the tissues. A fall in leukocyte and platelet counts is commonly seen as a result of sequestration in the liver, spleen, and other sinusoidal areas.

During moderate hypothermia in 10 patients, Bunker and Goldstein found that the concentration of clotting factors remained essentially normal, but the clotting time of various coagulation tests were prolonged.

Central Nervous System

Because of the effect of hypothermia on cerebral blood flow and oxygen consumption, hypothermia has assumed considerable clinical importance in neurosurgery. The accompanying fall in cerebral blood flow amounts to approximately 6 to 7 per cent per degree centigrade temperature or a reduction of 60 to 70 per cent in flow at 25°C. The finding of an unchanged arteriovenous oxygen difference in the presence of a decreased blood flow implies a decline in cerebral oxygen consumption. Reduction in oxygen consumption approximates 50 per cent at 30°C, and is one third of the normal at 25°C.

Of further clinical importance is the effect of hypothermia on brain volume and the extracerebral space within the cranial cavity. Rosomoff and Gilbert believe that hypothermia causes a fall in cerebrospinal fluid pressure and a decrease in brain volume. These changes can be ascribed to a reduction of the volume blood in the arteries and veins and to diminished cerebrospinal fluid formation. The result is the production of a "slack" brain with an increase in the volume of the extracerebral space and improved operating conditions during neurosurgery.

An interesting difference between the hibernating mammal and the nonhibernator is that in the former, nerves continue to conduct impulses almost to 0°C, whereas, in the latter, conduction ceases below 10°C. In man, electrical cortical activity progressively diminishes as temperature falls; at about 18°C electrical silence ensues.

Kidneys

There is a twofold effect of hypothermia on renal function, one, an indirect effect upon glomerular filtration mediated via the cardiovascular system and the other, a direct effect upon tubular processes. In dogs cooled to 27°C, Moyer et al. measured a fall of 69 per cent in glomerular filtration rate, a fall of 28 per cent in renal blood flow and a de-
crease in the normal tubular reabsorptive capacity for glucose during a reduction of 25 per cent in the mean arterial blood pressure. Despite the changes in glomerular and tubular activity, urinary volume and sodium excretion did not fall, as would have been expected from the same changes at normal temperatures. The behavior of water, glucose and sodium suggested that tubular enzymatic excretory function and absorptive processes were depressed. When norepinephrine was given to raise the blood pressure to normothermic levels, there was no change in the glomerular filtration rate or renal blood flow. Thus, the depressed function was considered due to cold and not to the hypotension.61, 62

Liver

Hallett 63 demonstrated a reduction in splanchnic blood flow and diminution in various liver functions during hypothermia. This decrease in blood flow was accompanied by a decreased oxygen utilization and carbon dioxide production. Of clinical import is the effect of depressed hepatic metabolism on drug detoxification. The half-life of morphine increases from 3.7 minutes at 37° C. to 94 minutes at 24° C., a twenty-three-fold increase in the time necessary for the liver to conjugate the free morphine.64 At the same temperatures the half-life of thiopental is lengthened from forty-six minutes to a span of 185 to 530 minutes.

Hyperglycemia is frequently marked during cooling and may be explained by the inhibition of hexokinase, failure of transfer across the cell membrane or to inhibition of insulin activity. The failure of glucose to enter the metabolic pool may account for the absence of elevation of lactic and pyruvic acids with deliberately produced respiratory alkalosis.61, 62

Acclimatization

Davis,61 in studies on animals, was able to show that shivering activity decreases and disappears with prolonged exposure to cold, while oxygen consumption was maintained well above basal levels. These findings confirmed previous independent observations of Sellers et al.,61 Heroux et al.,61 and Cottle and Carlson 67 that, in the acclimatized animal, increased heat production resulted from nonshivering sources. In man, similar physiological adaptations as a result of prolonged exposure to cold have been observed.61 Ten human subjects were exposed to an atmosphere temperature of 12.5° C. for eight hours daily over a period of thirty-two days. The decrease in shivering activity in the first ten days was dramatic and the fact that the metabolism demand was 33 per cent above basal levels again pointed to the presence of nonshivering sources of heat production in man. Heat loss via the respiratory passages was lessened considerably during acclimatization and accounted for the greater proportion of the diminution in heat loss that occurred. Recent work of Hsieh and Carlson 65 gives some inkling of the important chemical changes that may be taking place during nonshivering thermogenesis. The calorigenic effect of noradrenaline is increased approximately four times in acclimatized rats as compared with the unacclimatized. This finding corroborated earlier work of Cannon,29 whose studies on the secretion of adrenaline in cooled animals led him to state that extramuscular chemical regulation could be explained by the action of this hormone. The pituitary, adrenal and thyroid glands all have been implicated in the increased heat production required to maintain normal body temperature during exposure to cold. Definite evidence does exist that a very active role can be attributed to any one or several hormones produced by these endocrine glands.66 It is reasonably clear, however, that heat production and adaptation are not controlled completely by any one gland as previously thought.

It can be concluded that many can acclimatize to cold by a decrease in shivering by an enhancement of nonshivering thermogenetic mechanisms or by the development of an altogether new mechanism. The frequent observation of an increased oxygen consumption prior to any evidence of shivering 61 supports the belief that nonshivering thermogenesis is an already existing mechanism 28 and that it is increased by acclimatization. Animal data suggest that fat mobilization is necessary for its proper functioning and that noncontracting muscle is an important site of nonshivering heat production. Although shivering is decreased or abolished by acclima-
tization, increasing the cold stress re-elicits the response and supplements nonshivering thermogenesis. It is, therefore, reasonable to conclude that the total heat producing capability of the acclimatized homeotherm is markedly enhanced, resulting in a greater ability to maintain normothermia in extreme cold.

**Accidental Hypothermia**

There is a surprising number of reports of death which can be attributed to or in which hypothermia might have played a contributing role. Many occur in mountaineers (usually called "death from exposure"), or as a result of immersion following shipwreck. In other environments, in exposure following alcoholism, in diseases such as myxedema, hypopituitarism or cerebral vascular accidents, in the air-conditioned environment of the operating room where there is exposure of viscera, and during the intravenous infusion of cold fluids hypothermia may be the underlying factor in unexplained death.

The infant and newborn are especially susceptible to a cold environment because the large surface area in relation to body mass allows for increased heat loss by conduction, convection, radiation and evaporation. In the delivery room, the premature child and the newborn are particularly vulnerable and atelectasis of the newborn has been attributed to hypothermia. Under general anesthesia, the reactive sympathetic responses and shivering are depressed. While McQuiston thought mild hypothermia (95°F.) was desirable, deeper degrees of hypothermia are usually undesirable unless for specific surgical procedures. Hackett found during neurosurgery that the number of infants with rectal temperatures below 97°F. was considerably increased in the air-conditioned operating room. The infants with lowest temperatures were slow to resume normal feeding postoperatively. Infants undergoing prolonged intrathoracic or intra-abdominal surgery may develop temperatures ranging from 26.5° to 29° C. (80-84° F.) in a similar environment. The homeostatic temperature control is not well developed in the newborn and other defense mechanisms have not matured, hence shivering response is unreliable at less than two years of age.

Anesthetic agents and techniques also exert their influence. Morales et al. reported that the temperatures of patients on refrigeration blankets fell 1° Farenheit every 20–25 minutes with thiopental anesthesia, every 15 minutes during high spinal anesthesia and every 10 minutes with a combination of thiopental and curare. Spinal anesthesia prevented shivering in the anesthetized area and curare likewise forestalled shivering. The anesthetic agent per se may alter temperature balance during general anesthesia. Thus halothane is said to disturb the heat regulatory mechanism more than ether. Other agents interfere with heat regulation through ganglionic blockade and production of vasodilatation.

Mann and Elliott described a number of infants, usually born prematurely, brought into the hospital with a "cold syndrome." These infants were lethargic, had low body temperatures, signs of upper respiratory tract infection, edematous extremities, and florid complexes. There was a high mortality. The principle postmortem finding was pulmonary hemorrhage. The development of this syndrome was attributed to low environmental temperatures. Almost all the cases occurred during the winter months but the mechanism was not clear. In another study on premature infants, Silverman et al. showed that there was a higher mortality in infants exposed in cooled isotherms. Of the survivors, the infants in the warm isotherms had axillary temperatures averaging from 1.9° to 2.6° C. higher than those in the cool isotherms.

**Conclusions**

Knowledge of basic physiological and pathological consequences of body cooling is far from complete and the interplay with anesthetic depression is likewise not clear. Most of the knowledge in this field has been gleaned from the deliberate cooling of patients for surgical operation or the treatment of medical conditions in which respiratory and circulatory abnormalities, and cerebral edema had already developed. The few isolated reports of the direct environmental effects of cold per se have been cited in this review. The importance of shivering and the role of nonshivering thermogenesis in acclimatization of man has been the subject of considerable debate. The
manner in which animals adapt or adjust to cold has acquired new significance and accounts in no small part for man's ability to survive against environmental cold.

References


RESPIRATORY DISTRESS SYNDROME Synthetic l-alpha-lecithin was administered by inhalation to eleven infants suffering from respiratory distress. The l-alpha-lecithin was delivered by microaerosolization, at a concentration of 0.25 per cent in a mixture of equal volumes of propylene glycol and water. This was done with the aim of decreasing the alveolar surface tension. In eight of the treated infants who survived, the respiratory distress was alleviated. The working hypothesis of this study was based on the consideration that in hyaline membrane disease the formation of the membrane itself might be considered secondary to the increase in surface tension and to its direct or indirect effects on liquid exchanges at the alveolar surface. Both this inferential reasoning and the demonstrated effect of surfactants on alveolar stability justify the approach of trying to lower surface tension in lungs when it is abnormally high. The use of dipalmitoyl lecithin to reduce the surface tension to values near those normally observed does not imply that this substance is the normal intrinsic pulmonary surfactant. Its effective surface-active properties and its lack of interference with the normal formation of the pulmonary surfactant were the main reasons for its use. (Robillard, E., and others: Microaerosal Administration of Synthetic Beta-Gamma-Dipalmitoyl-L-Alpha-Lecithin in Respiratory Distress Syndrome, Canad. Med. Ass. J. 90: 35 (Jan. 11) 1964.)