Bodily Reactions to High Temperature

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Man is a homiothermic animal and is capable of operating fairly efficiently over a considerable range of temperature. The brain cells, however, cannot survive long when the blood temperature exceeds 108° F. (41° C.). Such high temperatures cause denaturation of cell constituents.

Heat is produced in the body as a result of chemical reactions occurring in muscle, liver and other active glands. Heat production is increased by physical exertion and fever. Whenever the environment around the body is hotter than the body itself, heat is transferred from the environment into the body by the physical processes of radiation, conduction and convection. Heat stress or strain is the degree of effort required to dissipate the metabolic and exogenous heat (heat gain) to maintain thermal equilibrium. Radiation, conduction, convection, and evaporation are the avenues for heat loss from the body. The part played by conduction is mainly that of transfer between deeper tissues and the skin.

Radiation occurs from about 85 per cent of the body surface, and therefore the posture of the body is of paramount importance in heat regulation when body temperature is high; important also are the temperature of surroundings and surrounding objects and the degree of humidity of the air.

Radiation, conduction and convection can take care of the dissipation of metabolic heat when the environment is cooler than the body. At higher environmental temperatures, evaporation plays a major part in the maintenance of thermal equilibrium. Evaporation of sensible perspiration is continuously carrying away some of the heat from the skin. With increase of heat stress, more sweat for evaporation is required; but sweat merely dropping off the skin does not contribute to heat loss. The relative humidity of the air has an inverse relationship with the rate of evaporation of water from the skin. Increasing air movement greatly augments the rate of evaporation.

The expired air, before leaving the lungs, is warmed to body temperature and is saturated with water vapor. The average daily loss of water from the lungs in the expired air is about 300 ml. This is equivalent to a daily heat loss by way of the lungs of approximately 174 kilocalories (300 × 0.58 = 174).

In addition to heat lost by the vaporization of water in the expired air, there is some loss of body heat in raising the temperature of the inspired air to that of the body. In the presence of dry cool air, heat loss is augmented by increasing pulmonary ventilation.

Changes in body temperature, whether as a result of severe environmental variations or of infectious, metabolic or toxic agents, produce more or less profound effects on the various biologic processes within the body. The heat to which the body reacts may have its origin in extrinsic factors, or internally in metabolic processes.

The ability to withstand high environmental temperature is a good index of a properly functioning cardiovascular system. It is common experience that, during a hot spell, fainting, collapse and even death are often the lot of those with poor cardiovascular reserve.

Effects of Anesthesia and Operation

Knight reported that hyperpyrexia frequently occurred during prolonged operative procedures and had deleterious effects on recovery. Because he believed that the closed anesthetic system raises the patients' temperature, he developed a gas cooler for controlling the rise in body temperature. Bigler and McQuiston reported death of children due to postoperative hyperthermia. Fever developed during operation in over 62 per cent of the children in their series. They were unable to control body temperatures adequately in children by cooling the gases in a to-and-fro absorption system.

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Anesthetics per se interfere with temperature regulation. Under anesthesia the central nervous system and vasomotor and other reflexes are depressed. This means the mechanisms for dissipation and for conservation of body heat do not function normally. If the immediate environment is warmer than the body, body temperature will rise, and if the environment is much cooler than the body, body temperature drops, because the reflexes for conservation as well as for dissipation of body energy cannot be activated efficiently.

In a study of patients undergoing operation under general anesthesia, Clark and his co-workers related body-temperature changes to environmental temperature, humidity and choice of anesthesia system. They did not include in their study any patients in whom signs of shock developed during the operation. Inhalation anesthesia, administered by the endotracheal technique, was used in all cases. They found that when the wet-bulb temperature of the operating room was below 75°F, heat retention was uncommon in adult patients; but above 75°F, heat retention was much more frequent and body temperature rose progressively and sometimes markedly regardless of the anesthesia system used. Whenever heat gain or heat retention by the body occurs, tissue temperature rises. For every degree Fahrenheit rise in body temperature there is an increase of about 7 per cent in metabolic heat production. Patients undergoing operation gain heat from warm objects surrounding them, such as hot pads and the radiant heating effects of operating-room lamps, and retain heat from the wrappings and so forth in which they are tucked on the operating table. Surgical draperies impede heat loss. When a to-and-fro anesthesia system is used, evaporation from the lungs cannot occur because the temperature of the system is higher than that of the exhaled gas and consequently the body gains heat. About 12 per cent of the body’s heat loss is normally dissipated by evaporation of water from the lungs with the warmed exhaled air.

As Clark and co-workers have reported, under conditions of severe external thermal stress, that is, when the temperature of the wet bulb is 75°F or higher, the heat-dissipating mechanisms of the body are overtaxed and heat retention with rise in body temperature is bound to occur. Body temperature tends to rise substantially during prolonged operative procedures no matter what anesthesia system is used. Inadequate hydration augments the temperature rise. Premedication that interferes with sweating contributes to this, and delayed replacement of lost fluids adds its share. These exaggerate the temperature rise, the younger and the smaller the patients are.

In operating rooms with temperatures near 90°F and high humidity during the hot summer months, convulsions have been observed when body temperature has increased rapidly. Fatal outcome was avoided by rapidly reducing the fever and providing maximal oxygenation.

The cells of the liver as well as the cells of the central nervous system are highly susceptible to damage during high fever. Jaundice is a well-recognized complication of fever therapy. Extensive necrosis of the liver has been found at necropsy in those who have died during fever therapy.

Cardiovascular Effects in General

Exposure to a hot environment sufficient to cause a rise in body temperature decreases the ability of animals to survive shock from any cause. In our studies on the effects of external temperature on shock in animals, we found that external temperatures in the neighborhood of body temperature are favorable while anything below room temperature or above body temperature is not only unfavorable but hastens the fatal outcome. In fact, excessive heat in itself produces shock. Excessive heat harms the shocked organism in several ways.

(1) It produces a widespread superficial vasodilatation and distribution of blood to nonessential parts and thus counteracts the protective natural reflexes that bring about peripheral vasoconstriction in the skin and neighboring tissues that are so vital in need of blood during the emergency of shock. This protective superficial vasoconstrictor reflex serves to narrow the capacity of the vascular tree to cope with the diminished blood volume (oligemia and hemoconcentration) in shock. In shock, in which the blood volume is signifi-
cantly reduced and concentrated, heating the skin brings the blood to the heated body surface and thus reduces blood flow to vital structures such as the central nervous system, liver and myocardium. Thus, warming the shocked patient excessively defeats the purpose of other treatment designed to augment cerebral, myocardial and hepatic blood flow.

(2) Excessive heat increases the metabolism and the oxygen requirement of tissues. Metabolic activities of tissues are chemical reactions and it is well known that, within certain limits, the greater the increase in temperature the faster the rate of the chemical reaction. In the presence of an already existing anoxemia in shock, overheating the patient necessitates the utilization of more oxygen and hence leads to a more severe anoxemia, which increases capillary damage and capillary permeability.

(3) Excessive heat is likely to increase perspiration and consequently promote dehydration. This, in the presence of hemoconcentration and oligemia already present in shock, creates a vicious cycle the outcome of which is a greater hemoconcentration, which is bound to lead to untoward effects.

Heart Rate and Rhythm

The cardiac effects during hyperpyrexia include a disappearance of the common sinus arrhythmia and its replacement by regular cardiac rhythm. Sinus arrhythmia is the variation in heart rate occurring normally in deep breathing—the heart rate increases during inspiration and decreases during expiration. It is due to alterations in vagal tone during respiration. Both the radiation of impulses from the respiratory center to the cardiac center and the excitation of the vagal stretch receptors from the lungs by infiltration contribute to this reflex variation of heart rate with the inspiratory and expiratory phases of respiration.

The electrocardiographic changes induced by fever are variable and inconsistent. The P-R interval, that is, the conduction time between the atria and the ventricles, is shortened during fever.

Within physiologic limits, the rate of generation and the speed of propagation of impulses are increased by agents that raise the temperature of the body. This means that a greater number of impulses are traveling to the various organs of the heated body. A general rise in body temperature produced from heating increases the heart rate; the metabolic activity of the pacemaker of the heart (sino-auricular node) and the initiation and rate of passage of the cardiac impulses along the conductive system are increased.

In artificially produced fever the pulse rate rises more or less proportionately to the rise in body temperature, in the ratio of about 10 beats to 1° F., much as it does in naturally occurring fever. In studies on the effects of artificial fever, my colleagues and I obtained an average increase of 10.5 heartbeats per minute for every rise of 1° F. in patients. Hill and Flack obtained an average increase in pulse rate of 44 beats per minute for a rise of 2.4° C. (4.3° F.) in rectal temperature. Bazett found with hot baths a mean increase of 37 beats per minute for a rise of 2° C. (3.6° F.).

Philbs and his co-workers attempted to quantify the effects of hyperthermia on the propensity to or resistance against ventricular fibrillation in the dog and monkey heart. Fibrillation was produced by a single square-wave stimulus of unknown strength and duration delivered at a measurable time in the cardiac cycle and applied to a specific area on the heart surface. The influence of hyperthermia with and without coronary occlusion upon ventricular fibrillation threshold was studied in dogs warmed to 40° C. (104° F.). Hyperthermia markedly increased the fibrillation threshold. Occlusion of the anterior descending ramus of the left coronary artery lowered the ventricular fibrillation threshold in hyperthermic animals, but the level still remained above that found in normothermic dogs without coronary occlusion. The monkeys showed an even greater elevation of fibrillation threshold during hyperthermia. In contrast with hypothermia, the very rare development of heterogeneity among individual muscle fibers in the myocardium during hyperthermia partially accounts for the elevation of fibrillation threshold. The maintenance of body temperature at or above normal aids in maintaining normal cardiac action following cardiac arrest or fibrillation.
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Cardiac Output

From his study of the pulse curve by the tachographic method, Bornstein concluded that cardiac output was increased by hot and cold baths; hot baths increased the heart rate but decreased the stroke volume, while cold produced the reverse combination. Baths of less than 40° C. (104° F.) cause little change in cardiac output because the decrease in stroke volume is balanced by the increase in pulse rate. Heymans observed with administration of warmth an increase in cardiac output too great to be accounted for only by an increase in heart rate; an increase in stroke volume was indicated.

In 1957, Burch and Hyman showed that a hot and humid climate increased the output, work and power of the right and left ventricle of normal man at rest, and only slightly increased that of patients with chronic congestive heart failure. In other studies by the same investigators in 1959 to determine whether warm and humid tropical weather would increase cardiac work of patients at rest in bed, the problem was studied during tropical midsummer weather on the same patients in the wards and, for contrast, in a cool air-conditioned room. Cardiac output and right ventricular pressure curves were obtained by means of right heart catheterization. The average cardiac output was 37 per cent greater in tropical weather than in an air-conditioned atmosphere. The increase in output was mainly due to a greater stroke volume with a small contribution from an increase in heart rate. A hot humid environment can increase cardiac work as much as strenuous physical exercise, thus producing considerable stress upon the heart and circulation.

Sancttta and his colleagues subjected 16 patients (eight with and eight without left ventricular failure) to an ambient (room) temperature of 98° F. and a comfortable humidity of 40 per cent for 2 hours. Neither group showed a significant change in cardiac output, nor in minute ventilation, oxygen consumption, or arteriovenous oxygen difference. Both groups showed significant decreases in brachial and pulmonary resistances and in left ventricular work. Warm dry environment is not only nonleterious but may actually be beneficial to certain patients with left ventricular failure.

Blood Volume

Plasma, blood and circulating red-cell volumes are not altered by physical conditioning or by a combination of physical conditioning and heat acclimatization.

During a voyage from England to the tropical latitudes of Peru, Barcroft and colleagues observed an increase in blood volume amounting to about 17 per cent, which seemed to be correlated with the temperatures within the cabins of the ship. They made no observations on blood volume changes at high altitude. On the relation of external temperature to blood volume, they found that the estimated volume was not constant and that the only factor which it appeared to be correlated was the temperature of the environment, the volume increasing as the temperature rose and decreasing as it fell, and the blood volume being measured by the carbon monoxide method. For estimating the percentage of carbon monoxide in blood, they used three techniques: (1) the reversed spectroscope method of Hartridge, (2) the method wherein the carbon monoxide is evacuated from blood with a blood-gas pump and measured in a Haldane gas-analysis apparatus by means of combustion and absorption of the carbon monoxide produced, and (3) the method of carmine titration. Their explanation for the increase in blood volume was shallow; they simply stated that in a hot climate much of the blood is circulating in the skin and the increase in volume is to preserve the relation between the quantity of vascular fluid and the capacity of the vascular bed that contains it. These explanations were perhaps good in those days but other factors need to be considered today.

Sunderman and his colleagues noted increases during warm weather of 15 to 40 per cent in the blood volumes of three subjects as compared to cold weather. Bazett and his colleagues and Sjöstrand obtained higher blood volumes in summer than in winter. Yoshimura and his co-workers and Tanaka et al. obtained changes in the concentration of various serum and blood constituents (extracellular Na, Cl and Ca, and intracellular...
K and P) studied at monthly intervals throughout the year and concluded that the water content of the serum and blood increases in summer and decreases in winter and that serum Na, Cl and Ca concentrations decrease in summer and increase in winter because of seasonal dilution or concentration of the blood. Serum concentration of P rises in summer and falls in winter while, on the other hand, serum K falls in summer and rises in winter. As the K level follows metabolism, its changes are probably correlated with seasonal changes in metabolic rate.

Dilution of plasma is one of the early responses to sudden exposure to a hot environment. This is demonstrated by decreases in blood solids,20 hemoglobin, and plasma-protein concentration21 and by increases in vapor pressure of the serum.22 Barbour and Gilman23 said that vaporization, whether by the lungs or the skin, is related to the vapor pressure of the body and suggested that it depends on the molecular concentration of the entire milieu intérieur and measured it as the serum vapor pressure. They reported a series of experiments in which cats were exposed to various environments: cold, hot, and excessively hot. The animals were immersed to the neck in a bath at the temperature desired for 10 minutes. Blood samples were taken and serum vapor pressure was determined by the A. V. Hill method. They considered the response to be a reflex mechanism by which cold lowers the vapor pressure and heat raises it. Metabolic responses that increase cellular activity necessitate the entrance of more water into the cell at the ultimate expense of the blood plasma. Calorogenic responses to cold environment serve a dual function in heat regulation: not only heat production but also the prevention of heat loss by evaporation is favored. Heating the skin mitigates against tissue hydration and dulls the sensitivity of the kidney to excess serum water. The mechanism by which this occurs is not known.

In a previous study Barbour and Gilman23 had noted that the serum osmotic pressure increases considerably at the onset of fever (chill period).

The hemodilution on sudden exposure to a hot environment is usually less than 5 percent,24 and, when heat stress is so severe and prolonged as to induce copious sweating, hemodilution is reversed and hemococoncentration supervenes. Anesthesia and transection of the spinal cord abolish hemodilution.25 Barbour and his associates26 attributed the early increase in plasma water to mobilization of water for sweating, the extra water coming from the erythrocytes. Bass and Henschel27 attributed the dilution to influx of extravascular fluid as a result of extensive peripheral vasodilatation occurring during the same period. During induced hyperthermia, the fluid added to the vascular system in rabbits had approximately the same composition as interstitial fluid.28

The finding by Glaser and his colleagues29 of a larger contour of the liver radiologically and a wider radiographic shadow of pulmonary vessels when the skin was cooled than when it was warmed suggests that the lungs and liver contain more blood when the skin is exposed to a cool than to a warm environment.

Blood Constituents

McCUTCHEON40 noted that the rate of locomotion of leukocytes was affected by temperature in a manner similar to that of a chemical reaction; the maximal rate was reached at 40° C. (104° F.). Madsen and Wulf41 observed that the normal blood temperature was optimal for phagocytosis. Krusen42 studied the blood picture before and after periods of artificial fever (temperatures of 104° to 106.8° F.—40° to 41.8° C.) and obtained an average increase of leukocytes from 7,125 per cubic millimeter of blood before fever to 11,289 after fever. After the fever, the number of neutrophils was relatively increased and the number of lymphocytes relatively decreased. Hargraves and Donn43 observed a characteristic postfebrile leukocytosis which was so constant that they felt justified in designating it the "febrile hemogram." They found that the peak of leukocytosis, reaching about 40,000 or more per cubic millimeter of blood, occurred usually several hours after the cessation of fever. It is believed that artificial hyperthermia induced by physical means exerts an effective mobilization of body defenses against disease.

Speakman and his colleagues44 reported that exposure for several days to uncomfortably warm and uncomfortably cold environment in the erect or recumbent position led to a de-
crease in the concentration of plasma protein and hemoglobin in the heat, and to an increase in the cold. Plasma proteins increased when the upright position was maintained and decreased progressively in the recumbent position. No detectable change occurred in hemoglobin in the experiments which lasted several hours.

The relative oxygen saturation of venous blood increases in a hot room, while the arteriovenous difference diminishes.

Exposure to hypoxia and high environmental temperature caused an increase in plasma concentration of corticosteroids in the majority of healthy subjects. Pylkki and Törnbloom suggested that heat releases corticotropin, which depletes cortical hormones in the adrenals and causes a reversible exhaustion of the cortex which plays an essential role in the decrease of serum iron.

Brauer and his colleagues found a rapid decrease of liver glycogen, increasing concentration of blood sugar and an increase of lactate during perfusion of the liver at elevated temperatures. Bile flow was accelerated initially when the temperature of the perfusate was raised but then decreased to low levels and finally was completely arrested. These events were accompanied by morphologic changes which included hyaline-body formation and extensive dissolution of the endoplasmic reticulum, and changes in nucleoprotein configuration. Disruption of metabolic patterns, depletion of key metabolites, direct effects of heat on cellular enzyme systems and structural changes are the possible mechanisms that could account for the events occurring during elevated temperature of the perfusate.

Body Fluids and Electrolytes

Thermal sweating is a constant threat to body-water balance. On the other hand, a subject replacing only the water that is lost in sweat becomes depleted of sodium, chloride and potassium, and consequently sweating also becomes a threat to electrolyte balance. When these possibilities materialize, homeostatic mechanisms influence in turn the constituents and the volume of the sweat. When the body is threatened by sodium depletion, the concentration of sodium in sweat falls to a negligible level and sweating does not continue unchecked until severe water depletion results. Leithhead summarized the evidence on sweat-salt retention by considering salt deficiency as the principal stimulus in which aldosterone is an active agent. He presented data showing that the administration of aldosterone had the desired effect on water and salt retention and led to increase in body weight and reduction in urinary output and sodium/potassium ratios. Most patients had smaller sweat losses after administration of aldosterone but felt less comfortable in the heat. Severe water depletion rarely occurs, because it is usually prevented by thirst and water intake.

Salt-depletion heat exhaustion is characterized by fatigue, giddiness, nausea, vomiting, and muscle cramps. In neglected and severe cases, oligemic circulatory failure may occur.

Relative salt depletion, or water intoxication, is the basis of heat cramps. Compared to the findings in salt-depletion heat exhaustion, the biochemical data in the cases of heat cramps are unremarkable; the value for urinary chlorides is diminished or virtually zero, but the amount of sodium, potassium and chloride in the serum during violent cramps is largely within normal limits.

Vascular Reactions

In discussing the effects of hot weather on the heart and circulation, Egger stated that hot weather produces a variety of clinical syndromes and in general lowers basal metabolism, increases blood volume, increases pulse rate persistently, diminishes appetite, and causes weight loss. The first response to heat is dilatation of the vascular bed in the skin, bringing a greater fraction of the total volume of blood to the surface for cooling. The venous return to the heart is diminished by the vasodilatation and blood pressure drops. Egger suggested that compensation is achieved by an increase in heart rate which, if prolonged, results in an increase of the total volume of blood in circulation. He must have meant that prolonged vasodilatation rather than increased heart rate augments the total volume of blood in circulation.

Dilatation of the blood vessels occurs in the peripheral areas of the body whenever they are exposed to heat, so that the blood contained in those areas is much increased. This
demands either an increase in blood volume or a compensatory reduction of the vascular bed in the unheated areas. Bazett observed that heating the entire skin area reduces the peripheral resistance to two thirds or half of normal. In addition to dilatation in the skin in response to heat, there is compensatory constriction in the splanchnic region. The dilatation is accompanied by an increase in blood flow in the heated areas. The mechanisms involved in the production of this vasodilatation include direct effects of heat locally on the vessel wall and reflexly by inhibiting vasomotor tone as well as centrally by the elevation of temperature in the hypothalamus.

In studies on the relation between the onset of sweating and vasodilatation in the forearm during body heating, Love and Shanks suggested that the cutaneous vasodilatation in response to heating is secondary to activity of the sweat glands, and that there is no evidence for separate vascular vasodilator innervation. Hellen and associates reported that in a hot environment a larger increase of blood flow in the forearm was observed in older than in younger men. This was brought about by local vasodilatation and not by increase in perfusion pressure. In older men systolic (or mean) blood pressure rose slightly while in the younger it dropped slightly. The older men displayed much greater local vasodilatation, and they may have had a higher cardiac output.

Senay and colleagues showed that during slowly rising ambient temperatures, digital vasodilatation often preceded that in the forearm skin. Vasodilatation in forearm skin often continued to increase even when local skin temperature had stabilized. Of the multiple factors possibly controlling circulation in the skin of the forearm, the local temperature seemed most important. The maximal vasodilatation in the forearm during heat exposure was not augmented by acetyl-β-methylcholine. The mechanism by which heating the forearm skin produces vasodilatation in the skin as well as in adjacent areas was attributed by Crockford and his co-workers to arterial conduction, being conveyed in the smooth muscle of the vessels of the cutaneous arterial plexus.

Heat, no matter from what source, influences the vascular tree in several ways. First, thermal stimulation of sensory receptors in the skin may bring about vasodilatation through the axon reflex. Since these impulses pass away from the central nervous system, rather than toward it as is usually expected to take place along sensory nerve fibers, Bayliss called them "antidromic impulses." They play an important role in the cutaneous vasodilatation observed in subjects exposed to heat. Furthermore, the sympathetic nerves are believed to contain vasodilator fibers. While perfusing the hind limb of dogs, Burn frequently obtained vasodilatation on stimulation of the lumbar sympathetic chain. He suggested the presence of a general system of vasodilator fibers. Lewis and Pickering presented evidence supporting the existence of sympathetic vasodilator fibers in man. This, however, was refuted by Uprus and his associates.

Second, metabolites liberated in the tissues act as direct vasodilators. Heat increases the speed of chemical reactions occurring in the living organism. The metabolites, liberated at a great rate under the influence of heat, exert their well-known direct chemical vasodilator effect on the small-vessel bed throughout the body. This brings about two definite effects: (1) an increase in the caliber of the blood vessels and (2) an increase in the number of patent vessels; that is, under the influence of heat, vascular channels in addition to those already patent are widely opened up.

Third, with a general rise in temperatures of the body, vasodilatation results from central effects. The warmed blood circulating through the heat-regulating centers in the hypothalamus brings about a discharge of impulses to increase the dissipation of heat. Consequently, a generalized vasodilatation is produced and heat loss is increased by radiation, conduction and convection through the skin. The pink color of the skin after exposure to microwaves, diathermy, hot baths or any other source of heat is a manifestation of this generalized cutaneous vasodilatation brought about by local and central mechanisms.

Fourth, there is a tendency for individuals under anesthesia to have circulatory inadequacy and poor venous return in a hot environment. Heat causes dilatation of the capillary bed along with venous engorgement and relaxation and marked arteriolar dilatation. There is sufficient trapping of blood in the
extremities to cause a fall in blood pressure. Elevation of the legs aids in reducing this fall. Warmth relaxes voluntary muscles and reduces muscle tone thus reducing the subsidiary pumping action of the skeletal musculature and contributing significantly to the failure of venous return.

Circulatory adequacy is contingent upon several factors. Important are: (1) the relationship between the blood volume and the capacity of the vascular system and (2) a healthy functional ability to increase cardiac output by increase in both rate and stroke volume. A high ambient temperature, which increases the demand for peripheral distribution of the blood, places additional strain on venous return, heart rate and blood pressure. Muscular activity markedly influences venous return. Under surgical anesthesia, muscular activity is nil and inadequate venous return is something to watch for.

**Blood Pressure**

The effects of external heat and hyperthermia on the blood pressure are varied. In general, external heat in most forms tends to lower the blood pressure and cold tends to raise it. Bazett noted, however, that a bath warmer than 40° C. (120° F.) may cause the blood pressure to exceed normal while a cold bath may occasionally induce a temporary fall followed by a rise. In our studies of artificial fever induced by tub baths, the effects on blood pressure were variable. The systolic pressure increased somewhat in four of 15 subjects, decreased slightly in six and did not change in five. There was some fall of the diastolic pressure in 11 subjects, no change in two and a slight rise in two. Changes in blood pressure as a result of fever induced by the Kettering hypothermy were similar: systolic pressure increased somewhat in five patients, did not change in three and decreased slightly in seven. The diastolic pressure decreased in all except one subject, in whom no change occurred.

The changes in blood pressure result from the interaction of alterations in cardiac output and vasomotor reactions. The rise of blood pressure during exposure to cold is due to increase of cardiac output and to vasoconstriction in the superficial areas of the body. The varying response of blood pressure to warmth is dependent on the degree of vaso-dilatation, the degree of alteration in heart rate, the cardiac output per stroke and per minute, and the pulse pressure. The position of the subject influences venous return and consequently the blood pressure and the differential distribution of the blood to the various parts of the body.

Blockley and Taylor exposed college students to ambient temperatures between 100° and 250° F. with low humidity for short periods. They found that the systolic arterial pressure rose during exposure, but that diastolic pressure was variable. They also noted that (1) the heart rate rose with skin temperature, reaching rates as high as 172 beats per minute, (2) electrocardiographic recordings demonstrated no cardiac changes, (3) the respiratory rate increased to two or three times the resting level, and (4) subjective symptoms were dyspnea, deep irregular respiration, irritability and dizziness.

**Cardiovascular Adjustments**

Edström and his associates observed that in persons with a normal heart the cardiac output did not change at the higher temperatures, but in those with cardiac defects the function of the heart was better owing to diminished active peripheral resistance to blood flow. Improved function in patients with cardiac defects and disappearance of the blue-livid coloration of the skin of hands and feet were among obvious effects. Berenson and Burch noted that when patients with congestive heart failure were exposed to sudden elevation of the environmental temperature and relative humidity, acute attacks of left ventricular failure occurred (cardiac asthma); these were characterized by severe dyspnea, rales, and gallop rhythm associated with apprehension and panic. The patients with advanced cardiac disease were less able to combat the stress of environmental heat than were those without cardiac disease.

Heyer and his associates reported increased frequency of occurrence of myocardial infarction in hot summer months and attributed it to the considerable strain induced by profound physiologic adjustments made to preserve a constant body temperature. These adjustments include increased cardiac work with increased cardiac output, associated with
an increase in blood volume and diversion of blood to the skin to promote heat loss. Patients predisposed to vascular injury by virtue of pre-existing coronary arteriosclerosis may suffer acute myocardial infarction under these conditions. Williams et al.\textsuperscript{66} found that in warmth the major change in hemodynamics was an increase in heart rate with an associated decrease in stroke volume. Neither cardiac output nor arteriovenous oxygen difference was significantly altered. Threefoot\textsuperscript{67} demonstrated a rise of pressure in the superficial veins of normal subjects upon exposure for 1 hour to an environment of 40\(^\circ\) to 45\(^\circ\) C and about 100 per cent humidity.

**Renal Effects**

Traks and Sancetta\textsuperscript{68} reported that renal clearances of mannitol (glomerular filtration rate) and of paraminohippurate (effective renal plasma flow) determined before and after a resting exposure for 2 hours to a warm and dry environment of 98\(^\circ\) F and a humidity of 40 per cent were significantly decreased in patients with left ventricular failure, but not in those with normal hearts.

Byfield and his colleagues\textsuperscript{69} concluded that blood flow through the kidney is rather jealously guarded and not influenced much by other circulatory adjustments, and that therefore slight rises in rectal temperature in a hot environment are not accompanied by any significant increases in renal blood flow. Radigan and Robinson\textsuperscript{70} found that both exercise and exposure to heat stress increased intrarenal resistance and the filtration fraction. Heat decreased the glomerular filtration and exercise decreased it further.

**Respiratory Effects**

The respiratory rate in man is increased with hyperthermia. Sutton\textsuperscript{71} reported an increase of five to six respirations per minute per degree increase in rectal temperature. If the temperature rises rapidly, definite hyperpnea with deep respiration is observed and a real sensation of air hunger is experienced. The hyperpnea causes a marked fall in the tension of alveolar carbon dioxide.\textsuperscript{72} The fall is accompanied by alkalosis.\textsuperscript{72} Landis and his associates\textsuperscript{74} reported rises varying between 0.12 and 0.33 in pH of the blood plasma during experiments with hot baths. The large volumes of carbon dioxide given off as a result of the hyperpnea often increased the respiratory quotient much above unity. Koehler\textsuperscript{78} has shown that alkalosis is maintained in febrile patients. The rise of temperature increases metabolism and lowers the threshold of the respiratory center.

Furman and Lehmann\textsuperscript{75} determined ventilatory equivalents of 26 normal subjects and noted a correlation with temperature and humidity variations. Respiratory efficiency decreased with increasing temperatures and humidities and increased in cooler weather. Traks and Sancetta\textsuperscript{76} exposed 10 rested male patients with chronic obstructive pulmonary emphysema to an ambient temperature of 98\(^\circ\) F and a comfortable humidity of 40 per cent for 2 hours. They noted a significant decrease in brachial arterial pressure but no change in pulmonary arterial pressure. Minute ventilation, oxygen consumption, cardiac output, and calculated work of the right ventricle all increased significantly. They concluded that patients with pulmonary emphysema tolerate a hot environment poorly even though the humidity is low.

Brouha and colleagues\textsuperscript{77} obtained a decrease in pulmonary ventilation in a warm dry environment and an increase in a warm humid one; oxygen consumption was significantly lower in the warm dry environment than at room temperature. Cardiac cost increased and cardiac efficiency decreased in both warm surroundings, whether dry or humid. Cullen and his colleagues\textsuperscript{78} did not find the arterial-oxygen-saturation percentage significantly reduced during the period in which the temperature was elevated (107\(^\circ\) F.) by a Burdick cabinet, but on account of the decreased carbon dioxide content and the increased pH caused by hyperventilation the oxygen partial pressure of the arterial blood could fall as much as 25 per cent.

Hyperventilation produces alkalosis primarily by washing out carbon monoxide. This alkalosis may so interfere with the liberation of oxygen by hemoglobin that insufficient oxygen is released to supply the needs of the tissues. Cullen and his colleagues\textsuperscript{79} showed that the alkalosis present during fever effects a significant reduction in the arterial oxygen tension even in the presence of a normal
arterial oxygen saturation. In the group receiving no oxygen therapy, the arterial oxygen tension fell as much as 25 per cent with the development of the desired level of fever and continued to fall as the treatment progressed. This drop in oxygen tension was compared to that obtained by ascending to an elevation of 17,500 feet. The fall in oxygen tension provides a reasonable explanation for the clinical evidence of oxygen want during fever therapy. The decreased rate of diffusion and the increased demand for oxygen by the tissues because of the elevated metabolism emphasize the deficiency in oxygenation of the tissues and the oxygen want. They explained the clinical evidence of benefit from oxygen therapy during hyperpyrexa on the basis of prevention of reduction in arterial oxygen tension. The administration of oxygen reduced the incidence of restlessness, excitement, mental confusion and tachycardia, which are attributable to cerebral anoxia.

During a study of the physiologic tolerance of men to a variety of hot wet conditions, Jampietro noted that during certain exposures the subjects hyperventilated and exhibited symptoms ranging from tingling of the hands and feet to carpopedal spasm. Heat-induced hyperventilation produces circulatory alterations, acid-base imbalance, neuromuscular alterations and tetany. This tetany may be caused by a combination of factors: decreased tension of carbon dioxide, increased pH of the blood, decreased ionized calcium in the plasma and perhaps other factors. During exposure to a very hot humid environment there is initially a loss of carbon dioxide primarily through the lungs (hyperventilation) and secondarily a loss through the skin (sweat). This loss leads to increase in blood pH. In the production of heat-induced tetany it is the rate of change in pH and carbon dioxide tension, not the absolute change, that is critical. When the rate of change is rapid, compensation is not adequate and the incidence of symptoms is high; but when the rate of change is slower, some compensation occurs and the incidence of symptoms is low. The rapid changes lead to an imbalance between intracellular and extracellular compartments which induces symptoms. The slower changes then allow time for correction of the imbalance and lead to a lower incidence of symptoms. Since the tetany disappears rapidly on removal from the hot environment while body temperature and serum calcium concentration remain for a time at levels attained in the hot environment, the changes in body temperature and serum calcium concentrations are not considered important in the development of heat-induced tetany.

Consolazio and his associates found that the metabolic rate associated with a fixed physical activity is increased in a hot environment.

**Physiologic Adaptation to Heat**

Many factors are involved in endowing the body with a remarkable power of adaptation for existence or even for healthy living in a hot environment. Only the major factors are discussed here.

**Circulation.** Circulatory adjustments bear the main burden for temperature regulation and thermal equilibrium in a hot environment. The blood flow through many parts of the body, including the skin and voluntary muscles, is much increased to aid in conduction, convection, radiation and evaporation, to provide adequate respiratory exchange to the lungs, and to assist in the transfer of fluid to the surface. These adjustments are made by increase in the minute volume of the heart, by alterations in vasomotor mechanisms, and by augmentation in blood volume. During sojourn in a hot environment there is continual struggle between cutaneous vasodilatation to lose heat and vasoconstriction to avoid pooling. The gravitational pooling induced by the erect posture exaggerates the stress on the circulation and so does physical work in a hot environment.

**Sweating.** Perspiration is a major avenue for water and salt loss by the body in a hot environment. The rate of sweating depends primarily on skin temperature; extremely high rates, up to 3 or 4 liters per hour, can occur over short periods. The two responses—peripheral vasodilatation and active secretion of sweat—have a large capacity during heat stress, but the sudden advent of hot weather before acclimatization is sometimes crippling.

**Acclimatization.** Acclimatization to heat means the process of adaptation that develops
during exposure of man to an environment hotter than that to which he is accustomed. It enables him to live and increase his capacity to work in heat without distress. It requires about 10 to 20 days. Before adaptation to a hot environment subjects may collapse, with high rectal temperature and evidence of peripheral circulatory failure, on the first day of exposure to heat while doing a work load. After exposure for about 10 days to a hot environment, the same work load can be completed without any circulatory difficulty and with much less rise in rectal temperature.

Various studies have demonstrated that acclimatization involves changes in the functions of the cardiovascular system and of the sweat glands. Men working effectively in a hot climate maintain an increased volume of plasma and extracellular fluid and an increase in cardiac output and in peripheral circulation. Reflex shunting of blood to the surface of the body increases the temperature gradient between it and the environment. Working in a hot environment imposes a heavy burden upon the cardiovascular system of unacclimatized men. They undergo acute peripheral vascular collapse through severe diversion of blood to the periphery and this leads to rapid pulse, decreased stroke volume, severe postural hypotension, and evidence of peripheral vascular engorgement as manifested by flushing of the face, neck and chest, and by edema of the nasal mucous membranes and of the hands and feet. Fully acclimatized individuals produce larger volumes of sweat which in dry heat aid greatly in eliminating body heat through evaporation. Another important phenomenon of acclimatization is the reduction in the concentration of salt in the sweat of the acclimatized subjects.

Dill and his colleagues reported a progressive decline in the concentration of sodium and chloride in sweat during the first 6 days of a 20-day stay in the desert. The average chloride concentration fell from 18 mEq. per liter on the first day to 12 mEq. by the sixth day with little change thereafter. By use of more refined methods these findings were later confirmed by some workers and by others who acclimatized men under laboratory conditions. Lee and his associates could not confirm these findings because they did not observe a decrease in sweat chloride during repeated daily exposures to heat. The progressive drop in concentration of sweat chloride could be prevented by adequate intake of salt and it was concluded that the drop was due to the development of chloride deficiency from excessive loss of salt in the sweat.

Saha and associates found that men working in a hot environment, even though they have access to drinks, often failed to maintain water balance, and developed dehydration which, whenever it exceeds 2 per cent of body weight, limits performance and increases pulse rate and rectal temperature beyond desirable levels. While subjects were working in high ambient temperatures, sudden changes in position from horizontal to vertical showed poor circulatory adaptation as judged by delay in recovery of pulse rate and by the transient giddiness experienced.

Eichna and his colleagues concluded that acclimatization to work in heat is apparent on the second day of exposure (at 90° F. and 95 per cent relative humidity), and is complete in 7 to 10 days. Acclimatization to heat is associated with an increase in total peripheral resistance and a reduction in peripheral blood flow. Heart rate and heart output are also reduced. Acclimatized man works in a hot environment with a lower heart rate, a lower skin and rectal temperature, a more stable blood pressure and less discomfort than when unacclimatized. Lack of adequate intake of water, lack of rest and physical fitness, and the taking of alcohol impair performance of acclimatized men in a hot humid environment. Circulatory adjustments in severe heat by acclimatized men consist of a marked reduction in total peripheral resistance due to vasodilatation in muscle and skin, and an increase in heart output, heart rate and pulse pressure.

Conn studied the mechanisms of acclimatization in tropical-climate rooms. The sweat volume was 5 to 7 liters per day but the salt concentration decreased with acclimatization from 3.0 g. to less than 1.0 g. per liter by the tenth day. This means a saving of 10 to 14 g. of salt per day. Furthermore, the renal mechanism for salt-saving was invoked during the early days of exposure to heat, but was relieved of the salt-saving function when the sweat glands took it over.
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The need for salt conservation to enable man to cope with a hot environment constitutes the initial as well as the continuing stimulus for increased secretion of aldosterone, the salt-saving steroid, from the adrenal cortex.

Ladell and Shepherd confirmed these ideas when they disrupted the salt-saving process in adaptation by orally administering 300 mg. of spironolactone which inhibited the action of aldosterone and doubled the amount of sodium chloride lost in the urine, and salt concentration in the sweat increased to levels that exceeded those observed on the very first day of exposure to heat.

Increased rates of sweating, decreased concentration of salt in the sweat, altered sensitivity of the thermoregulatory center and increased blood volume are the various responses on which acclimatization to heat is explained. Adjustments in cardiovascular function are most important in adaptation. Changes in blood volume expedite rapid transfer of body heat to the surface. Increased rates of sweating and decreased salt concentration in sweat increase evaporative cooling and improve the ability to maintain salt balance. According to Bass and his associates, protection against circulatory disturbances rather than against elevated body temperature is the basis for the dramatic responses in acclimatization to heat. Suddenly exposed to a hot environment without any chances for becoming acclimatized, an individual is prone to succumb since the cardiovascular system and the sweat glands have not had time to make the necessary adjustments. Prolonged standing and muscular inactivity put an extra strain on the vasomotor system and increase the risk of syncope.

Maintenance of fluid balance in a hot environment is of paramount importance. Unless water is replaced in quantities equal to those lost in sweat and urine, the ability to tolerate heat is impaired even in the acclimatized individual. In the presence of water deficit, sweat secretion is suppressed and a greater strain is imposed on the thermoregulatory mechanisms. Salt deficiency may lead to a form of dehydration which may or may not be associated with muscle cramps. Dehydration from water deficiency alone or in combination with salt deficiency is an important etiologic factor in heat exhaustion. Uncompensated body losses of water and salt impair the thermoregulatory mechanisms and seriously handicap an individual in a hot environment.

In their studies on acclimatization of man to hot environments Bass and his associates noted that successful acclimatization was attained within the first week, during which sweat glands progressively excreted more water relative to the solutes, with little change thereafter. There was an isotonic expansion of the extracellular fluid which was accomplished by renal retention, during the first 4 days, of sodium and chloride in excess of the amounts required to support the sweat losses of these electrolytes. Plasma volume increased proportionately to a greater extent on the fifth day than did extracellular fluid volume. This was accompanied by an increase in total quantity of circulating proteins. The changes in total body water and in intracellular water were inconsistent. Potassium left intact cells in excess of the amount made available from tissue breakdown during the heat period. Values for plasma magnesium did not change significantly.

Clinical Entities due to Excessive Heat. Excessively hot environment may bring about the following clinical entities: heat cramps, heat exhaustion, and heat stroke or heat pyrexia.

Heat cramps are due to excessive loss of salt in sweat, which upsets the balance of ionic sodium, potassium, magnesium and calcium in the blood and body fluids and induces painful contractions (cramps) of skeletal muscles, especially those of the abdomen and legs. The body temperature is not changed much and the condition can be easily relieved by the administration of salt.

Heat exhaustion results from excessive environmental heat and is characterized by giddiness, loss of appetite, headache, vomiting, profuse sweating, syncope, dyspnea and sometimes "prickly heat."

Heat pyrexia or heat stroke is the most severe of the effects of excessive environmental heat; perspiration ceases, the skin becomes hot and dry, body temperature rises, usually above 106° F. (41° C.), and delirium, coma, convulsions, and circulatory collapse may follow. The mortality rate can be as high as 80 per cent. It is diagnosed in persons who, in the absence of sepsis or disease, are found in ex-
cessively hot weather in a confused state with stupor, convulsions and coma plus a dry hot skin and very high body temperature.

Heat stroke is more frequently encountered when the environmental temperature remains high for long periods and the humidity is also high. Increasing age (more than 40 years), diffuse arteriosclerosis, acute alcoholism, and coexistent disease are predisposing factors.

The following sequence of physiologic mechanisms underlies the production of heat stroke. Initially, sweating ceases and heat loss becomes inadequate since only insensible perspiration, which is very meager, remains. Consequently, heat pyrexia supervenes. Congestion, edema, and petechial hemorrhages in the region of the aqueduct and the ventricles of the brain and extensive degeneration of neurons have been observed. Similarly, extensive degeneration in the heart, liver, lungs and kidney has been encountered. In severe cases, acute circulatory failure has been observed. Since high body temperature is the basic cause for the clinical manifestations of heat stroke, the treatment is directed effectively toward rapid reduction of the hyperpyrexia by use of ice-water baths with vigorous rubbing of the skin till the temperature decreases and becomes stabilized.

When the heat loads exceed normal thermoregulatory capacities, as in heat stroke in man or at times even in the course of a febrile illness, serious tissue damage can occur at temperatures not too much above physiologic levels.

**Summary**

In high environmental temperature, heat is transferred to the body by the physical processes of radiation, convection and conduction, so that ultimately the body temperature rises. Changes in body temperature, whether as a result of severe environmental variation or of infectious, metabolic or toxic agents, produce more or less profound effects on the various biologic processes within the body and on the body systems. The production and rate of locomotion of the leukocytes are increased and a definite leukocytosis occurs. The cardiac changes during hyperpyrexia include shortening of the P-R interval, increase in heart rate, increase in cardiac output, elevation of fibrillation threshold, and greater tendency for fainting, collapse and even death for those with poor cardiovascular reserve if the environmental temperature becomes high suddenly and is of sufficient duration.

The first response to heat is dilatation of the vascular bed in the skin, bringing a large fraction of the total volume of blood to the surface for cooling. The venous return to the heart is diminished as a result of the vasodilation and there is a drop in blood pressure. Compensation is achieved by an increase in heart rate and, if the condition lasts long enough, results in an increase in total volume of blood in the circulation and an increase in blood flow. A hot humid environment produces a considerable increase in cardiac output, cardiac work and stroke volume in normal subjects and a definite but lesser increase in patients with congestive heart failure. Such an environment places considerable stress upon the heart and circulation, with a greater frequency of occurrence of myocardial infarction.

The changes in blood pressure occur as a result of interaction of alterations in cardiac output and vasomotor reactions. The varying response or blood pressure to heat is dependent on the degree of vasodilatation, the degree of alteration in heart rate, the cardiac output per stroke and per minute, and the pulse pressure. The position of the patient influences venous return and consequently the blood pressure and the differential distribution of blood to the various parts of the body.

The influence of high temperature on the vascular tree is exerted through the axon reflex promotion of metabolites, and the temperature-regulation centers. Individuals under anesthesia in a hot environment tend to have circulatory inadequacy and poor venous return. Heat increases the capacity of the capillary bed, with venous engorgement and relaxation and marked arteriolar dilatation. There is sufficient trapping of blood in the extremities to lower blood pressure. Elevation of the legs aids in reducing the fall in blood pressure. Warmth relaxes voluntary muscles, reduces muscle tone, and annuls the pumping action of the skeletal musculature, thus contributing significantly to the failure of adequate venous return.
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High temperature increases the respiratory rate and can bring about dyspnea, deep irregular respiration, irritability and dizziness, and a sensation of air hunger. The hyperpnea causes a marked fall in the tension of alveolar carbon dioxide and a tendency toward alkalosis. The rise in temperature increases the metabolism and lowers the threshold of the respiratory center; with increasing temperature and humidity, respiratory efficiency decreases. Patients with pulmonary emphysema tolerate a hot environment poorly. Pulmonary ventilation and oxygen consumption decrease in such an environment.

Prolonged sojourn in a hot environment increases the plasma concentration of corticosteroids, owing to release of corticotropin (ACTH), which leads to decrease of sodium and chloride in the sweat and greater re-absorption of sodium by the renal tubules. Acclimatization to a hot environment leads to a slower heart rate, lower skin and rectal temperature, and more stable blood pressure, and less discomfort. Adjustments in cardiovascular function and secretion of the sweat glands are important in adaptation to a hot environment. Increased rates of sweating, decreased concentrations of salt in the sweat, altered sensitivity of the thermoregulatory center, and increased blood volume are the various responses in the adjustments of acclimatization. Maintenance of fluid and electrolyte balance are of paramount importance in a hot environment.

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