Special Articles

EXTREME HYPOTHERMIA IN VARIOUS ANIMALS AND IN MAN

WITH NOTES ON THE DETECTION OF LIFE AND THE POSSIBILITY OF RECOVERY IN CASES OF APPARENT DEATH FROM EXPOSURE TO COLD

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From the returns given by vital statistics during the past few years it is evident that death from exposure to cold is a fairly common occurrence in countries situated within the North Temperate Zone. In the various territories of the United States, for example, the mortalities from excessive cold have ranged between two and four hundred per year for many years past. It is also well known that a large number of people similarly meet death every year in different parts of Canada. This is clearly shown by the annual Provincial returns, though definite numerical data for the whole Dominion are not available. Of the two extremes of temperature, indeed, it is obvious that man's chief enemy is cold, and, futhermore, if the physical fate of the earth be correctly predicted, this fact must become more pronounced with the passing of time and the coming of later generations.

The present paper deals briefly with a few of the earlier known facts with regard to low temperatures observed in some of the lower types of organisms, and at greater length with some of the more recent observations on those higher animals which normally possess uniform or only slightly varying body temperatures characteristic of elevation of type, and which may thus be very reasonably compared with man in their response to the induction of severe hypothermia. The influence of glandular secretions on body temperature regulation is also discussed. Several instances of extremely subnormal temperatures in man are quoted, and suggestions are presented on the determination of the presence of life and possible recovery in cases where the hand of death may ordinarily appear to have long since passed.

POIKILOTHERMIC ANIMALS AND LOW TEMPERATURES

Some of the lower poikilothermic forms of animal life show remarkable ability to withstand low temperatures. The Arctic explorer Ross[1] repeatedly froze and revived caterpillars (*Laria rossi*), reaching a minimal temperature of −42°C. Other observers have shown that various species of insects survive exposure to a temperature of 40°C. below zero, with no apparent ill effects following. John Hunter[2] found that the body temperature of a fish such as an eel could be reduced to approximately 0°C., and that, though at first it appeared to be dead, recovery took place when the temperature of the surrounding water was raised. Goldfish which were apparently frozen used to be exhibited by Pictet[3] at his lectures, and these could sometimes be revived on gradual thawing.

Frequently in these earlier experiments, however, no very definite records of body temperatures and of general and specific reactions are available. In order to determine with more precison, therefore, the lower temperature limits at which varying types of fishes may still maintain life, and also to observe the effects of extreme temperatures on heart and respiratory rates, on reflex action and on general behaviour, a series of experiments was undertaken by the writer[4] at the Atlantic Biological Station at St. Andrew's, N.B. Briefly, it was shown that fishes could survive exposure to sea water at temperatures from one to almost two degrees below zero for several hours; many reflexes could be elicited during this period, but gradually all vital activities disappeared, and the heart-beat itself was eventually arrested. The body temperature of such fishes (many widely differing species were used) now approximated that of the surroundings; they appeared to be stiffly frozen, and on ordinary observation altogether lifeless. On increasing the temperature of the surrounding water, however, in the course of only a short time, complete resuscitation to normal activity was found to occur.

A particular "order of recovery" has, moreover, been observed in extremely cooled fishes. The heart-beat at first appears, on slight elevation of body temperature, followed by the occurrence of various appendage reflexes, the respiratory reflex (on anal or pectoral stimulation), and, later, by normal respiration, vision, equilibration and natation. It was also shown that the heart of a fish could be frozen for several hours at a temperature of −20° C. and yet, on slowly thawing, recover its normal rhythm. In the cooling of fishes, the heart-beat and the respiratory rates were found to vary according to the body temperature. (See also reference 5.)

It is commonly believed that frogs are often "frozen solid" for long periods during their winter sleep, and still survive, but recent observations fail to substantiate this belief. Cameron and Brownlee[6], for example, in a number of experiments, show that *Rana pipiens* and similar species do not sustain life on the lowering of their body temperature to −1.25° C. for more than one hour.

HYPOTHERMIA IN HIBERNATING FORMS

On the approach of winter certain types of animals retire to their burrows or other shelter, become inactive, and fall into a torpid state. All the activities of the body are greatly reduced, and the temperature generally falls to a point only slightly above that of the surroundings, which, however, is usually several degrees above 0° C. This phenomenon of hibernation is found to occur in many classes of animals, including mammals, reptiles, amphibians, insects, molluscs and probably fishes, but no cases amongst birds have been recorded. The etiological factors connected with winter sleep appear to be not yet definitely established. Hibernating animals are found to emerge spontaneously from their torpor in spring, however, when food supplies are usually available and climatic conditions are more favourable; nutritional economy and environment have therefore been urged by many as the most important considerations.

The attention of many investigators (Walther, Horvath, and others) has, at various times, been directed towards the study of hypothermia in hibernating animals. With a view to studying the reactions of such animals at low temperatures under adequate control, Tait and Britton[7] carried out a number of artificial cooling experiments on the common North American woodchuck. It was found that in some instances the body temperature could be reduced to the extremely low limit of 0°C., at which level the respiration and heart-beat were scarcely if at all perceptible by ordinary means, and the blood pressure, taken with a mercury manometer in the carotid artery, showed a fall of mercury to practically zero from a normal for the animal of about 100 mm of mercury. In several cases respiration really failed before the body temperature reached 0° C., and then artificial respiration was supplied at occasional intervals, while cooling was pushed still further.

It was shown that such severely-cooled animals could be readily resuscitated by artificial warming of the whole body, or in extreme cases by an initial direct application of warm Ringer-Locke solution to the failing, or even to the already stopped, heart. Recovery of the woodchuck was found to occur *spontaneously* after artificially cooling the animal to a deep rectal or œsophageal temperature of 3°C.

Observations which have recently been made by Johnson[8] indicate that body temperatures approximating 0° C. may be found in the ground squirrel during the period of torpidity. Tait[9] also has pointed out that certain excised tissues, particularly the heart, of hibernating animals may continue in activity at very low temperatures. Whereas the excised heart of an ordinary mammal ceases to beat at about 17° C., the heart of a woodchuck is not arrested by any temperature short of freezing.

HOMOIOTHERMIC ANIMALS AND EXPOSURE TO COLD

The influence of low temperatures on true homoiothermic animals was first systematically investigated in the laboratory by Walther[10]. Experimenting with immobilized, non-narcotized rabbits, he found that cooling to a temperature of 20° C. abolished the capacity for spontaneous recovery of the normal body heat, and that artificial warming was necessary in order to effect complete restoration. Cooling below 20° C., he believed, inevitably led to death.

In a series of four experiments on monkeys, Simpson[11] succeeded with the help of anæsthesia in reducing the body temperature of one animal to the low level of 14° C., and in subsequently reviving it by artificial warming. Three other animals similarly exposed to cold did not survive. Further investigation of the condition of cooled animals was made by Simpson and Herring[12], who used cats in their experiments. They stated that at 24° C. the function of the heat-regulating mechanism was suppressed. A temperature of 16° C. was found to be the lowest limit at which cats still showed evidences of life.

That true homoiothermic (non-hibernating) mammals do possess a heat-regulating mechanism which is wonderfully well adapted for dealing with extremely low body temperatures has now been made clear (Britton[13]). Working usually with cats, possessing normally a temperature of 38° C., it was found that cooling really induced a progressive paralysis of the central nervous system. Consciousness disappeared, for instance, at 27° C., the pupillary reflex to light was abolished at 23° C., and shivering was suppressed at 20° C. Of particular interest is the fact that the knee-jerk almost constantly, and one or two other reflexes occasionally, persisted until both rectal and œsophageal thermometers registered only 16° C. In such cases of severe hypothermia the skin and immediate subcutaneous tissues were several degrees colder, and the extremities in some instances were frozen. Both the pulse and apex beat were usually impalpable, and respiratory movements occurred only one to five times per minute, and were sometimes scarcely perceptible; the eyes were half open, the cornea was dull and the pupil usually dilated; the tongue protruded, and the skeletal musculature showed a condition of flaccidity, unless the parts had been really frozen. The animal could be said to be in a state of extreme cold narcosis, since nociceptive stimuli were ineffective, and surgical procedures could be carried on without arousing the least indication of resistance. The presence of the knee-jerk, therefore, and occasionally the anal sphincter (dilatation) reflex on respiration, constituted important signs of life, when on ordinary observation the pronouncement of death would have been made. It may be mentioned that in many particulars the effects of gradual cooling showed a strong similarity to those produced by the induction of anæsthesia.

At the extremely low body temperature of 16° C., artificial warming was necessary in order to effect complete resuscitation of the animal. This was found to be best accomplished by the administration of warm and, later, hot water baths, accompanied by artificial respiration as demanded by the animal's condition. No particularly ill results were apparent in those animals which were revived from the most extreme cold narcosis (14° to 16° C.). The administration of ordinary therapeutic doses of such drugs as strychnine and alcohol had practically no effect on the cooled animal, probably because of the very slow rate of absorption by the tissues.

It is particularly noteworthy that a definite thermogenic ability is retained by the highly differentiated animal organism even when it is reduced to the low body temperature of 19° C. The activities of the heart, respiratory muscles, and abdominal viscera, although markedly diminished at this severely subnormal temperature level, are probably wholly responsible for the first small rise in body temperature, even against a *lower* external temperature. Naturally initiated shivering and stepping movements, and an exaggerated muscular tonicity which occurred later, ensured eventual recovery of the animal. A number of artificially-cooled cats showed perfect spontaneous recovery from body temperatures of 19° C. or 20° C. It has also been shown that other homoiothermic animals, including guinea-pigs and dogs, may sustain life, and be recovered from similar remarkably low body temperatures, with no ill effects ensuing. Some further details relating particularly to the heat-regulating mechanism of mammals may be consulted in an article by Barbour[14]. The recent monograph by Pearse and Hall[15] is also exceedingly instructive.

EXTREME HYPOTHERMIA IN MAN

Although the normal variation of body temperature in man is usually within 1° C., many striking differences have been observed in cases of exposure to an excessively cold environment. In some instances the temperature has fallen to approximately 24° C. without a fatal issue. Similar to those conditions occurring in other animals, in man this fall of temperature is accompanied by paralysis of the highest nerve centres and loss of consciousness. The centres in the medulla are later affected, so that respiration is slowed, and the blood pressure falls concurrently with a drop in the pulse rate.

Reincke[16] has recorded numerous cases of hypothermia resulting from the accidental exposure of drunkards to cold air and water. In two individuals the rectal temperature was 30° C. and 24° C., respectively; the patients were unconscious, but under treatment recovered in a day or two. In other cases, with temperatures of 28.4° C., 27° C. and 26.4° C., death followed in about 24 hours. In a case observed by Nicolaysen[17] the rectal temperature was 24.7° C., but the inebriate, who had been exposed the whole night to air at about 6° C. below zero, completely recovered. The temperature of the vagina was 27.9° C. in a woman (quoted by Peter[18]) who had a similar experience; under treatment the temperature rose to 36.3° C. within six hours, and the patient completely recovered.

Weiland[19] has recorded two cases of adults with temperatures reduced to 28.4° C. and 26.6° C. from exposure to cold, the determinations being taken by the rectum several hours before death. In a third case, that of an individual who had been exposed to cold while under the influence of liquor, the rectal temperature was 30.4° C., and yet recovery took place. An observation of a body temperature of 26.7° C. in a man who still retained consciousness was made by Tigerstedt[20] who also discusses other cases in which recovery was made from 24° C. Kohler[21] noted a temperature of 28.2° C. in the rectum of a drunkard, and found that, notwithstanding treatment, it remained low until shortly before the man's death a month later.

In four cases of insanity observed by Lowenhardt[22] the patients often ran about naked in cold weather, and body temperatures as low as 25° C., 29.5° C., 23.7° C. and 28° C. were recorded; in one case the range of temperature for several weeks was from 25° C. to 35° C. All the patients were about sixty years of age; although fairly active they did not take much food, and appeared well.

Recovery in cases of exposure while under alcoholic influence would depend in large measure, of course, on the amount of alcohol taken and the individual resistance, as well as on the particular degree of cooling of the organism. That glandular mechanisms are highly important in connection with the general factor of "individual resistance" is very apparent from what is now to be considered.

GLANDULAR INFLUENCES AND TEMPERATURE REGULATION

A number of workers (see Cushing and Goetsch[23]) have considered that the pituitary gland is of importance in connection with the regulation of body temperature. The results of others[24], [25] are not wholly in accord with this viewpoint, however. That the so-called hibernating gland (*la masse hibernale*) may be a significant factor in relation to winter sleep has also been mooted[26]. Pathological conditions of the thyroid gland, too, have long been known to produce marked effects on oxidative processes, and therefore on thermal regulation in the organism.

The recent observations by Finney, Dworkin, and Cassidy[27] are of distinct significance. They noted that a condition simulating hibernation could be induced in various animals by the combined action of cold and insulin, and that adrenalin and pituitrin readily restored the shivering reflex in cooled animals. Very low respiratory quotients were found during the state of artificial hibernation.

Recent evidence has been presented (Cannon, Querido, Britton and Bright[28]) which indicates that the secretion of the adrenal medulla is very definitely linked up with the chemical control of body temperature. By establishing a known "heat debt" (measured by c.c. of ice water given by stomach tube per kilo weight of animal) it was observed, with the use of the denervated heart of the animal as an indicator, that marked secretion from the adrenal medullary tissues occurred during the discharge of the "debt;" furthermore, similar results were forthcoming on exposure of animals to cold surroundings. Metabolism experiments on man, too, were corroborative of the foregoing. Adrenin secretion probably serves, it is pointed out, as a highly potent calorigenic influence, particularly on the exposure of animals or man to low environmental temperatures.

The effects of medulli-adrenal secretion in reinforcing the heart and circulation, in the stimulation of glycogenolysis to provide increased blood sugar (fuel) for vigorous muscular contraction (thus augmenting body heat), and in the promotion of shivering movements, are emphasized in a paper corroborative of the foregoing[29], in which low body temperatures were studied. When small amounts of adrenalin were injected intravenously into animals in which artificial hibernation had been induced, they were found to stimulate reactions which tended to bring about a re-establishment of the normal body temperature.

Evidence is reviewed and reasons are also presented (Britton[29]) which lead to the belief that a natural autumnal diminution in activity of the highly differentiated adrenal tissues may result, in the case of comparatively (thermotactically) unstable hibernating organisms, in the commencement of winter sleep. Furthermore, the phenomena which are associated with the recovery of animals from hibernation—the rapid rise of body temperature, the remarkable increase in heart and respiratory rates, the augmentation of the blood-sugar level, vigorous shivering, and general stimulation of the arrectores pilorum—and also of artificially cooled homoiothermic animals from low body temperatures, significantly point to increased activity of the medulliadrenal mechanism as the immediate important agency in the thermal restoration process.

DISCUSSION AND NOTES ON RECOVERY FROM EXPOSURE TO COLD

Considering the frequent occurrence of death from exposure to extreme cold in countries within the north temperate latitudes, it is important that the general and specific reactions to cold, as well as the particular condition of the organism at low temperatures, be more thoroughly understood. With this interest in view, an attempt has been made in the foregoing pages to evaluate the condition and effects of extreme hypothermia in man by the consideration and correlation of the various phenomena observed in lower animal types.

It is shown that the lowering of body temperature induces a progressive paralysis of the central nervous system. Consciousness disappears first, followed by the abolition of different reflexes as successively lower temperatures are reached. The effects of cold are, therefore, in many respects similar to those of anæsthesia.

Poikilothermic animals and certain hibernating forms maintain life even when their body temperature has been reduced to 0° C. or slightly lower. The hibernating woodchuck recovers spontaneously from a degree of cold that induces a deep rectal temperature of 3° C. True homoiothermic animals show on the other hand a distinct line of demarcation from other types, in that they may not be cooled beyond 16° C. without death supervening. From this critical body temperature for mammals, including some of the primates, artificial resuscitation to normal may be carried out. At the slightly higher body temperature of 19° C., perfect spontaneous recovery may be effected.

At very low body temperatures the homoiothermic animal, which may be considered as being most nearly allied to man, frequently appears on first examination to be quite lifeless. The cornea appears dull, and the pupil widely dilated and unresponsive to light and accommodation. The heart-beat and respiration may not be perceptible by ordinary methods, and noxious stimulation applied to any part of the body may elicit no response. The condition may be looked upon as one of extreme cold narcosis. The skin and subcutaneous tissues appear very cold and may be frozen, and an *ordinary* rectal or an anal thermometer reading may show a temperature almost approximating zero. It may be said that it is necessary, in order to obtain a true record of body temperature, that the thermometer be introduced either deeply into the œsophagus or to a depth of at least 8 cm. into the rectum. Such a *deep* body temperature will be found considerably higher than that elicited by an ordinary superficial placing of the thermometer.

Notwithstanding the foregoing as well as many other indications of the absence of life, it is to be emphasized that perfect restoration of such a severely cooled animal may commonly be effected. Vigilant scrutiny may be demanded in order to detect evidences of respiration, or of the heart-beat. An extremely slight vibration of the precordium may indicate the latter, even when the direct and stethoscopic methods have failed. Movements of the alæ nasæ are sometimes present, and indicate respiratory efforts.

One of the last reflexes to hold out against the paralyzing effects of cold is the knee-jerk. This reaction to patellar (mechanical) stimulation constitutes therefore a valuable sign of the persistence of life. It is to be noted that the reflex may be very slow in initiation and subsidence, even occupying two to four seconds in some cases. The reflex effect on respiration of dilatation of

the anal sphincter may also persist almost until death in cooling. On severe dilatation of the sphincter an asphyxial type of respiration is occasionally produced.

The presence of the more important bodily reactions in the mammal have been noted at various low temperatures as follows:—Knee-jerk, also micturition reflex, 16° C.; anal sphincter respiratory reflex, Achilles-thrust, 17°; stepping reflex, 18°; shivering, 19.5°; flexion reflex, phonation, 20°; corneal, sneezing and swallowing reflexes, 22°; pupillary reflex to light, 23°; equilibrium, sight, smell and hearing, 27.5°; co-ordinated action (walking, etc.), 28°.

Therapeutic doses of drug stimulants such as strychnine and alcohol have slow and relatively slight effects in severe hypothermia, probably because of the low metabolic rate of cooled animals.

The medulli-adrenal mechanism is shown to be specifically concerned in the chemical regulation of body temperature. The remarkable phenomena which are associated also with the awakening of animals from hibernation or from low body temperatures are strongly indicative of increased adrenal secretion. A very potent factor in organic thermogenesis, particularly in emergency situations such as may endanger life, is furnished by the markedly enhanced output from the adrenal glands.

Artificial respiration may usually be practised with success, even after spontaneous respiration has long since failed. Good results have been obtained with the tracheal tube introduced either *per os* or by tracheotomy. Warm baths or packs, gradually increased to higher temperatures within therapeutic limits, and also gastric lavage with warm fluids, are valuable aids to resuscitation.

A number of instances of the recovery of men from low body temperatures are quoted. A striking case on record is that of the resuscitation of an inebriate in whom the rectal temperature after exposure to cold registered only 24° C.

From the evidence herein adduced, showing the exceedingly low body temperatures (far below those observed in the human subject) from which the higher types of animals allied to man (in the thermotaxic sense) may fairly readily be resuscitated, it is indicated that man himself is *potentially* able to withstand much lower temperatures than have hitherto been recognized as compatible with life. It is therefore urged that such therapeutic measures for recovery as are briefly outlined above be immediately instituted in cases of apparent death from exposure to cold.

Considerable evidence has been adduced which indicates the marked calorigenic influence of adrenalin. The intravenous injection of small amounts of the substance has been shown to further remarkably the recovery process in extreme hypothermia. The effect may possibly result from the increased availability of glucose (as fuel) for the tissues, through the mobilization of glycogen from the liver by adrenalin. Injected glucose, indeed, appears to act similarly in accelerating recovery from cold.

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THE DANGEROUS EFFECTS OF WATER.—The dread of water can be traced back to a fairly remote period. In the first quarter of the sixteenth century bathing was considered a strange fad in England. The Grete Herball, printed by Peter Treveris in London, in 1526, gives Galen as the authority for the statement that "Many folke that hath bathed them in colde water have dyed or they came home." The drinking of water seems also to have been deemed harmful at that time and earlier. Prohibitionists will derive cold comfort from this statement, taken from the same herbal: "Mayster Isaac sayth that it is unpossyble for them that drynketh overmuche water in theyr youth to come to ye aege that god ordeyned them." Possibly, the rooted objection of the small boy to having his face washed may, after all, be natural, a sub-conscious "hang-over" from the past.—[ED.]