Henry Ford Hospital Medical Journal

Volume 3 | Number 2 Article 2

6-1955

Hypothermia And Artificial Hibernation

Robert D. Dripps

Recommended Citation

Dripps, Robert D. (1955) "Hypothermia And Artificial Hibernation," *Henry Ford Hospital Medical Bulletin* : Vol. 3 : No. 2 , 57-61.
Available at: https://scholarlycommons.henryford.com/hfhmedjournal/vol3/iss2/2

HYPOTHERMIA AND ARTIFICIAL HIBERNATION

Robert D. Dripps, M.D.*

The basic aim of hypothermia and/or "artificial hibernation" is to decrease tissue reactivity and metabolism, and hence permit viability under conditions of reduced supply of nutrients and reduced elimination of waste products. The concept is not new but at least two factors have caused a resurgence of interest in it. The first was the desire to operate upon the open heart — a circumstance under which this organ could not serve as a blood pump until closure was effected. Some means of decreasing the body's need for oxygen, glucose and other nutrients had to be devised, unless an artificial pump — oxygenator of the type proposed by Gibbon[1] or Dennis[2] could be used. The second factor was the synthesis of chlorpromazine by French chemists and the introduction by the French surgeon, Laborit[3], of drug-induced "artificial hibernation" in 1951. Certain physiological, pharmacological and chemical aspects of hypothermia and artificial hibernation will be presented in this paper,

True hibernation in such animals as the golden hamster, dormouse, hedgehog, woodchuck, ground squirrel or opossum differs in certain vital respects from the condition possible to induce in man either with cold or by drugs. The animals listed above can hibernate spontaneously when environmental conditions are proper, and, of even greater significance, can return themselves to normal, unaided. Man cannot do this. Shivering tends to minimize reduction in body temperature in the cold. Anesthesia or use of curarizing drugs are therefore necessary for a reasonably rapid reduction in temperature in man. Once this is achieved, man cannot warm himself, his survival depending upon careful attention to the support of respiration, circulation and reversal of the environmental temperature by attendants. The hibernating animal is self-sufficient; man is completely dependent upon others. Whether a hibernating gland is responsible for these differences remains to be determined.

Physiological Alterations with Cooling

1. *Metabolism*—oxygen consumption decreases progressively with cooling (Fig. 1). At 20° C (68°F) there is a 75 percent reduction in oxygen utilization.
2. *Circulation*—Pulse rate declines steadily as body temperature decreases. Figure 2 illustrates data obtained in the dog (after Ross)[4]. Bradycardia of a marked degree occurs with low temperature. In the hibernating hamster whose usual cardiac rate is 300-400 per minute a pulse rate of 4-6 per minute is common.

Blood pressure likewise falls continuously with body temperature. Figure 3 is compiled from experimental observations in the dog (Ross)[4]. Cardiac output is reduced by about 50 percent at 25° C (77° F). Plasma volume decreases slightly. There is a marked prolongation of the period of systole and isometric relaxation.

Myocardiac irritability increases, and death of the experimental animal or man from ventricular fibrillation is possible when body temperature is below 25° C. A characteristic series of changes occurs in the electrocardiogram as cooling continues. The P wave disappears, the QRS complex widens, is slurred, the S-T segment is evelated and the T wave inverts. Various degrees of heart block are noted; nodal rhythm may occur as well as ventricular extra-systoles.

---

*Professor of Anesthesiology, University of Pennsylvania Medical School

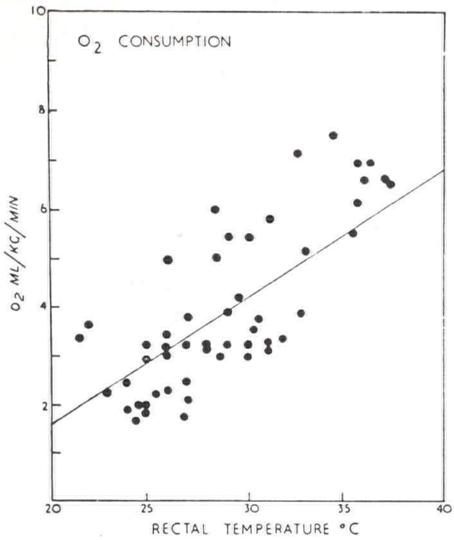


FIG. 1

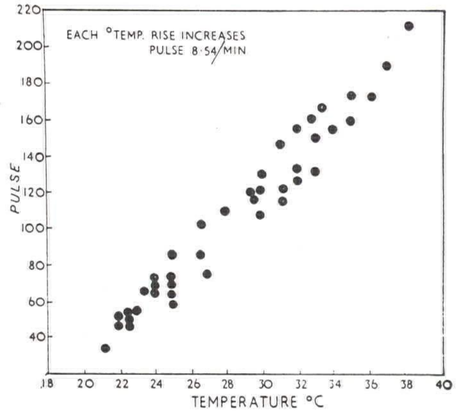
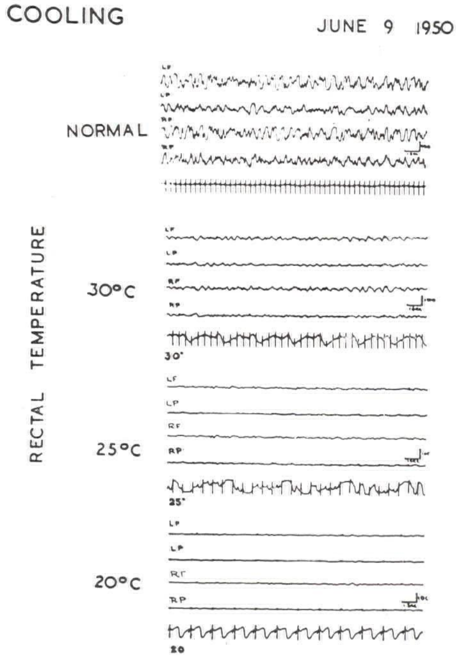


FIG. 2



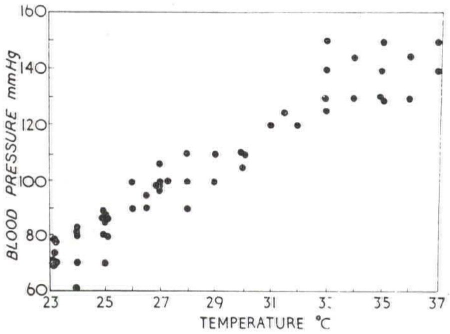


FIG. 3

FIG. 4

The cause of these myocardial and conduction changes is not yet known, but certain aspects have been stressed. Anoxia has been implicated, as has hypercarbia (see respiration below). Potassium loss from the myocardium may occur. There appears to be an imbalance between sympathetic and parasympathetic influences on the heart, with a suggestion that vagal effects are reduced.

Reversal of ventricular fibrillation in the hypothermic state has proven difficult in many instances. Electrical defibrillation, so useful in treating this abnormality at normal body temperatures, has proven of less value during cooling according to some investigators. Swan and co-workers[5] have reported success with prostigmine. Others believe that the heart must first be partially rewarmed before attempts at reversal are made. There seems little question that the heart is one of the weak links of hypothermic man and animals.

3. *Respiration*—Pulmonary ventilation is reduced as body temperatures falls. Spontaneous breathing will usually cease at 20° C. Respiration acidosis with a rise in arterial carbon dioxide tension and a decrease in blood pH developes. These changes can be prevented by artificial ventilation and should never be allowed to develop. Certain clinicians believe that hyperventilation and respiratory alkaloses will reduce myocardial irritability and minimize the likelihood of ventricular fibrillation. Data on changes in lung compliance during hypothermia are not available.

4. *Nevous system*—Electroencephalographic activity is reduced as body temperature falls. Figure 4 indicates that all spontaneous activity ceases at 20° C (68° F). Behavior studies in the post-hypothermic period have failed to reveal changes. Conduction along nerves is reduced and in all probability there is decreased transmission across the nerve-muscle junction. Conduction in non-hibernating animals stops at 10° C., but in hibernating ones is present as low as 2-3° C.

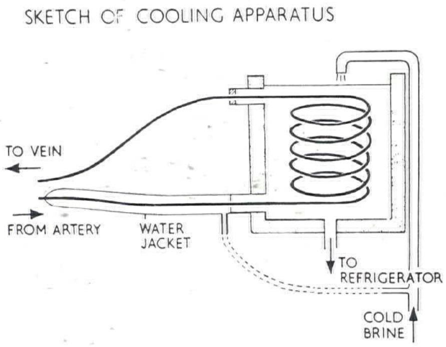
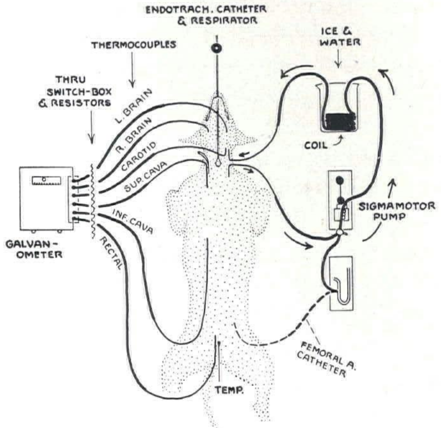


FIG. 5



Differential Hypothermia in the Dog.

FIG. 6

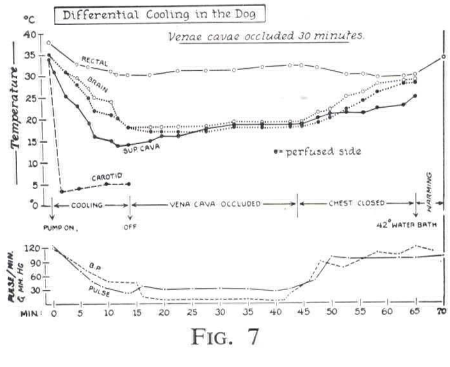


FIG. 7

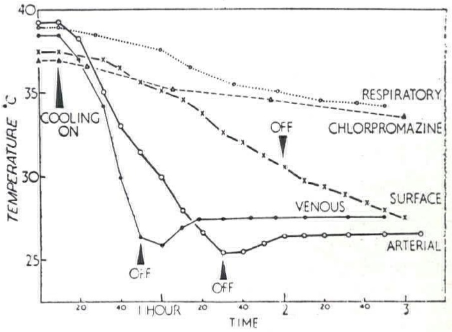


FIG. 8

5. *Stress response*—In hypothermic rats the hypothalamic—pituitary mechanism leading to the release of ACTH in response to stress stimuli is inhibited. The adrenal cortex in such cooled animals, however, remains responsive to the intravenous injection of ACTH. An inhibition of neural transmission of stress stimuli may be responsible for this block.

6. *Kidney*—At 30° C glomerular filteration rate is reduced 50 percent, but urinary output continues during anesthesia and operation on hypothermic man at a rate which cannot be ignored. The accumulation of cool urine in the bladder may interfere with rewarming unless it be removed by catheter.

7. *Blood*—Coagulability of blood decreases as its temperature is lowered, yet clinical evidence of abnormal bleeding tendencies has not been reported. Blood viscosity also increases during hypothermia. The influence of this on cardiac work has not been evaluated.

METHODS OF COOLING

Table 1 lists the common methods of cooling. External cooling of the entire body surface is commonly used. It is slower than direct cooling of the blood, but does not require cannulation of arteries or veins, nor is a pump or oxygenator needed. If an artery is cannulated, it is best to add a pump to the circuit since the heart may have insufficient force at low temperatures to circulate the cooled blood adequately. A schematic diagram of such an apparatus is shown in Figure 5.

TABLE ONE
METHODS OF COOLING

I. External (skin) Surface Cooling—whole organism
    1. Immersion—tub of ice
    2. Ice bags of plastic units containing fluid which is cooled
    3. Blankets with coils—circulating water and Prestone (ethylene glycol)
    4. Deep freeze unit
II. Internal Surface Application — part of organism
    1. Cold fluid poured into thoracic cavity
    2. Balloon in stomach containing cold fluid
    3. Cold fluid or sponges around aorta
    4. Ice water enema
III. Cooling of Blood removed from Body and Returned
    1. Artery to vein through coils immersed in cold fluid (heart acting as pump)
    2. Artery to vein through coils plus booster pump with or without simple oxygenator
    3. Vein to vein—superior vena cava to femoral vein with booster pump.
    4. Vein to artery—femoral vein to aorta at aortic valve with booster pump.
    Can be for whole body or for differential cooling.
IV. Adjuncts to Cooling
    1. Anesthesia
    2. "Curare drugs"
    3. Chlorpromazine

TABLE TWO
INDICATIONS FOR HYPOTHERMIA

1. Interruption of Blood Supply
    A. Whole Body—during "open" cardiac operations
    B. Regional
        a. Carotid artery—brain operations
        b. Descending aorta
            (1) hepatectomy
            (2) aneurysm
            (3) massive visceral excision

2. Reduce Oxygen Need in Reversible Conditions Causing Hypoxia
    A. Congenital heart disease
    B. Pulmonary, cerebral or peripheral embolus
    C. Acute pulmonary disease
    D. Anemic crises

3. Combat Hyperpyrexia
    A. Thyrotoxicosis
    B. Brain lesions
    C. Heat stroke
    D. Infections

4. Reduce "Stress"—e.g. Anesthesia, Operation
    A. Shock?
    B. "Poor risk" patients?

5. Produce Hypotension
    A. Diminsh operative blood loss
    B. Treat hypertensive crises
    C. Reduce internal hemorrhage e.g., ulcer, varices

If only a single region of the body, e.g. the brain, need be cooled, this can be achieved differentially by an approach illustrated in Figure 6. The success of such differential cooling is indicated in Figure 7 where it can be seen that brain temperature is far lower than rectal temperature. Using such a technique Jensen and co-workers[6] have been able to occlude all blood supply to the brain for periods in excess of thirty minutes with survival of the animals. The utility of this in neurosurgery is obvious when it is realized that at normal body temperatures the brain will be irreparably damaged by complete ischemia after four or five minutes. Similar methods are being applied for operations on the liver. Occlusion of the thoracic aorta high in the chest carries with it a threat of damage to the spinal cord if periods in excess of several hours are attempted.

Efforts have been made to cool the inspired gases with little success. Chlorpromazine alone has also been used in an effort to reduce body temperature. Figure 8 offers a comparision of the rates and degree of cooling achieved by various methods. It is evident that direct blood cooling is most rapid, but external surface cooling of the entire body is of value because of the greater simplicity.

Clinical Indications for Hypothermia

The uses of hypothermia have not yet been defined. Swan has recently listed a number of possibilities, some still in the realm of speculation. These are summarized in Table 2.

The ultimate role of hypothermia in surgery and medicine will depend upon its safety. If further knowledge of the functional changes attendant upon a reduction of body temperature can be translated into increased safeguards for the patient, a considerable number of indications may be developed.

BIBLIOGRAPHY

1. Gibbon, J. H., Jr., and Kraul, C. W.: An efficient oxygenator for blood, J. Lab. & Clin. Med. 26:1803, 1941.
   Gibbon, J. H., Jr.: The maintenance of life during experimental occlusion of the pulmonary artery followed by survival, Surg., Gynec. & Obst. 69:602, 1939.
2. Dennis, C., and others: Development of a pump oxygenator to replace the heart and lungs: An apparatus applicable to human patients and application to one case, Ann. Surg. 134:709, 1951.
   Dennis, C., and others: Pump oxygenator to supplant the theart and lungs for brief periods. II. A method applicable to dogs, Surgery 29:697, 1951.
3. Laborit, H., and Huguenard: L'hibernation artificiele par moyens pharmacodynamiques et physiques en chirurgie, Presse med. 59:1329, 1951.
4. Ross, D. N.: Hypothermia. I. A technique of blood stream cooling, Guy's Hosp. Rep. 103:97, 1954. II. Physiological observations during hypothermia, *Ibid.* 103:116, 1954.
   Cranston, W. I., Pepper, M. C., and Ross, D. N.: Blood reaction during hypothermia, J. Physiol. 125:20p, 1954.
5. Swan, H.: The current status of hypothermia, A.M.A. Arch. Surg. 69:597, 1954.
   Swan, H., Zeavin, I., Holmes, J. H., and Montgomery, V.: Cessation of circulation in general hypothermia. I. Physiologic changes and their control, Ann. Surg. 138:360, 1953.
6. Jensen, R. I., and Jensen, H. P.: Neue Narkoseverfahren in der Neurochirurgie, Acta Neurochirurgica 4:50, 1954.
   Jensen-Pauls, R. I., and Jensen, H. P.: Die Narkose in der Neurochirurgie, Aerztl. Wschr. 8:945, 1953.
   Jensen, H. P., and Jensen, R. I.: Indikation und Kontraindikation der potenzierten Narkose und des sogenannten Winterschlafs in der Neurochirurgie, Anaesthesist 3:156, 1954.