Sea Grant Research Notes
University of Minnesota Sea Grant Program

Number 4

HYPOTHERMIA-INDUCED VENTRICULAR FIBRILLATION

By Lois Jane Heller

Editor's Note: Hypothermia, or lowered internal body temperature, can be caused by exposure to cold water. It is the major factor contributing to one-third of all drownings associated with the increasing use of the oceans and Great Lakes for recreation and transportation. Minnesota Sea Grant Institute has funded research on hypothermia at the Hypothermia Laboratory in the School of Medicine, University of Minnesota-Duluth. The research has addressed aspects of accidental hypothermia of immediate interest to physicians and medics associated with rescue services. Dr. Lois Jane Heller has been one of a team of scientists studying various aspects of hypothermia with Sea Grant support.

Introduction

A major concern of people working on or near water is that of survival in case of accidental long-term immersion with an accompanying drop in body temperature. One of the most severe problems that may occur in these victims of accidental hypothermia is cardiovascular collapse (Brooks 1959; Lloyd and Mitchell 1974). In many cases, as the individual gets progressively colder, the heart rate gradually slows and then stops. Often, however, as the body temperature nears 25-27°C, the heart develops a fatal arrhythmia (ventricular fibrillation), whereby individual muscle cells of the heart contract asynchronously and pumping capability of the heart is eliminated. Ventricular fibrillation is very difficult to arrest and usually requires active rewarming procedures followed by a brief high current stimulus to convert the heart back to normal rhythm (Towne, et al. 1972; Wickstrom, et al. 1976).

The mechanisms responsible for the hypothermia-induced ventricular fibrillation are not well understood. However the studies reported here do shed some light upon the primary causes of this arrhythmia and, furthermore, suggest that certain treatment regimes might be helpful during resuscitation. Such findings should be of applied interest to clinicians who wish to learn more about treating hypothermia.

Methods and Results

There are many factors that contribute to the normal control of the heart's activities. It is difficult indeed to sort out which factors might be responsible for any given change without controlling all other factors. Therefore, in order to eliminate the possibility that changes in nerve activity to the heart or that altered humoral factors precipitate ventricular fibrillation in the cold, all the experiments reported here were performed on isolated rat hearts, perfused through their coronary beds with an oxygenated salt solution resembling plasma and paced by controlled electrical stimulation. A balloon placed in the left ventricle was used to measure the pressure changes that occurred during each beat. Details of this preparation are fully described elsewhere (Heller 1981). Temperature of the perfusate was varied between 37°C and 27°C and characteristics of the heart's mechanical activity were determined.

As the temperature decreased, the spontaneous heart rate decreased (as is shown in Figure 1) and the pressure developed within the left ventricle during each beat increased. These results suggest that the hypothermia-induced slowing of heart rate is likely to be, in large part, a direct result of low temperature on the pacemaker activity of the heart and is not dependent upon altered neural input or hormonal environment.

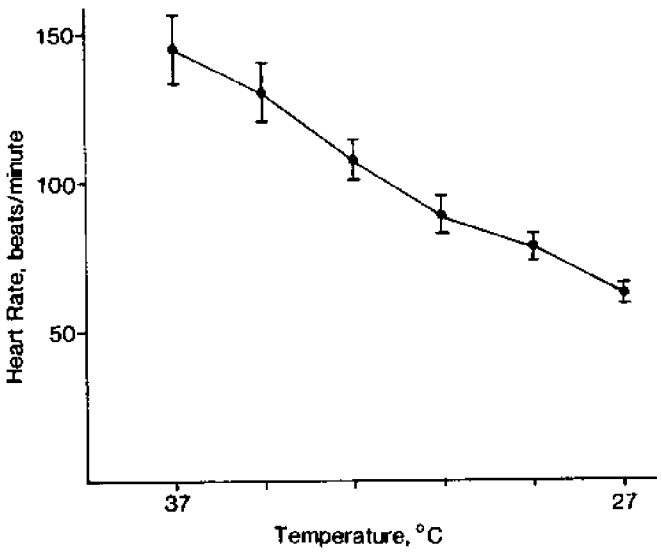

Figure 1 -- Effect of temperature on spontaneous heart rate of isolated perfused rat hearts. n = 24

Hearts were also paced at each temperature and certain excitability characteristics were determined. During and immediately following a regular beat, the heart goes through brief phases during which it is first inexcitable (or has decreased excitability) and then is briefly hyperexcitable. These phases are indicated in Figure 2. If the heart is stimulated during the refractory period, there will be no response; if it is stimulated during the hyperexcitable period,

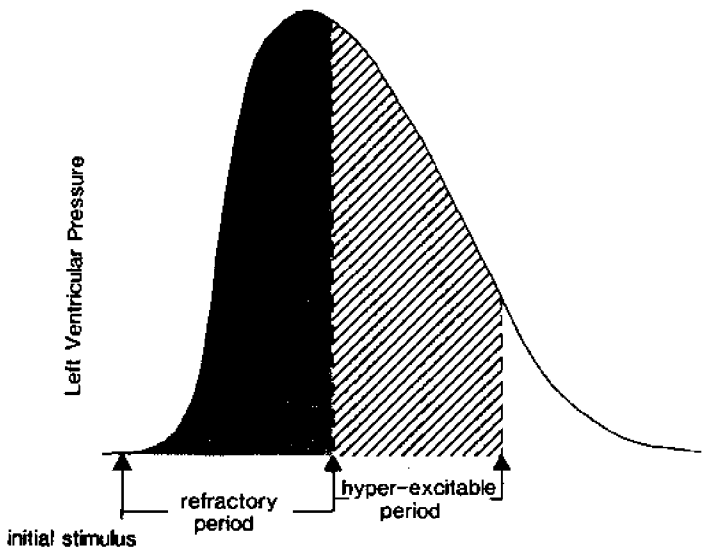

Figure 2 -- Schematic representation of excitability characteristics of the heart during a single beat.

extra beats or even fibrillation may occur. In the present study we determined the duration of these periods by introducing extra stimuli at varying intervals after a regular driven beat and measured the effect of temperature on their durations. The results are indicated in the graph on the left of Figure 3. The points on the graph represent the mean ± SEM of the time after the initial stimulus when the refractory period (open circles) or hyperexcitable period (closed circles) ends. Note that although the re-

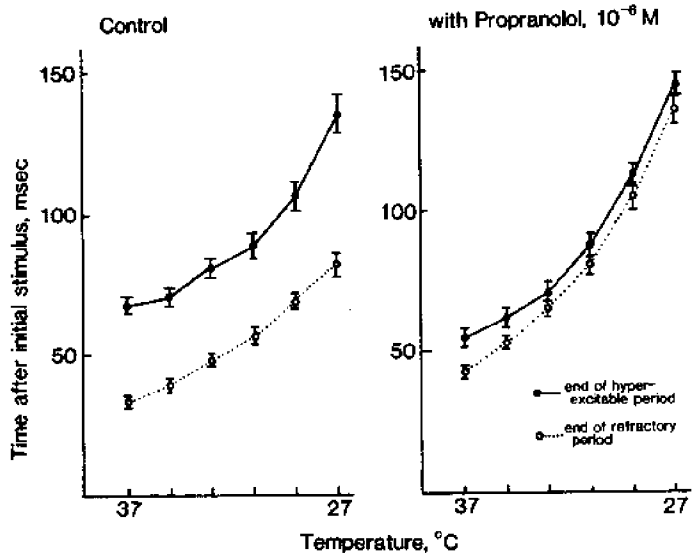

Figure 3 -- Effect of temperature on the duration of the refractory periods and hyperexcitable periods of isolated perfused rat hearts in the absence (left graph) and presence (right graph) of propranolol in the perfusate. n = 24

fractory period increases with decreasing temperature, the hyperexcitable period also increases. (The actual duration of the hyperexcitable period is reflected by the distance between the two lines.) This phenomenon may account for the increased tendency of the hypothermic heart to develop ventricular fibrillation especially if there are external factors that may evoke extra beats that could occur during the hyperexcitable period.

There have been suggestions in the literature that plasma levels of catecholamines (norepinephrine and epinephrine) may be increased during hypothermia and may account for the increased susceptibility of the heart to develop arrhythmias (Warner, et al. 1970; Hoffman, et al. 1955). Since, in our preparation, the perfusate does not contain any catecholamines, this mechanism cannot account for the

prolonged hyperexcitable periods found at low temperatures. However, isolated hearts do contain significant amounts of norepinephrine within the sympathetic nerve endings present in the muscle which may be released by the electrical stimulus pacing the hearts (Blinks 1974). In order to determine whether this norepinephrine might be contributing to the excitability characteristics of the heart, the experiments were repeated with propranolol 10^{-6} M, added to the perfusate. Propranolol blocks the effect of catecholamines on β-receptors in the heart and eliminates the usual increase in heart rate or contractile force that occurs in the presence of catecholamines. The results are indicated in the graph on the right in Figure 3.

Propranolol significantly prolonged the hearts' refractory periods and decreased the duration of the hyperexcitable periods at all temperatures. This suggests that the endogenous catecholamines may indeed play an important role in the cold-dependent prolongation of the hyperexcitable period and the development of ventricular fibrillation. Furthermore, these studies strongly suggest that β-blockers such as propranolol may be useful in preventing victims of accidental hypothermia from developing this fatal arrhythmia.

Conclusion

These studies indicate that hypothermia has a direct effect on the heart that is independent of any accompanying changes in neural or humoral input. These changes include a temperature-dependent decrease in duration of refractory and hyperexcitable periods. The increase in the hyperexcitable period that occurs at low perfusate temperatures could account for the increased susceptibility of cold hearts to develop ventricular fibrillation. Furthermore, the ability of the β-blocker, propranolol, to decrease the hyperexcitable periods in these preparations strongly suggests that use of adrenergic-blocking agents should be considered when treating victims of accidental hypothermia.

References

1. Blinks, J.R. 1974. Field stimulation as a means of effecting the graded release of autonomic transmitter in isolated heart muscle. J. Pharmacol. Exp. Therap. 188: 654-667.

2. Brooks, C. McC. 1959. Functional processes in the heart and possible effects of hypothermia. (Symposium) Ann. N.Y. Acad. Sci. 80: 332-383.

3. Heller, L.J. 1981. Isolvolumetric properties of ventricles of spontaneously hypertensive rats. Amer. J. Physiol. (Heart Circ. Physiol.). 240 (9): H927-H933.

4. Hoffman, B.F., A.A. Siebens, P.F. Cranefield and C. McC. Brooks. 1955. The effect of epinephrine and norepinephrine on ventricular vulnerability. Cir. Res. 3:140-146.

5. Lloyd, E.L. and B. Mitchell. 1974. Factors affecting the onset of ventricular fibrillation in hypothermia. Lancet. 2:1294-1295.

6. Towne, W.D., W.P. Geiss, H.O. Yanes and S.H. Rahimtoola. 1972. Intractable ventricular fibrillation associated with accidental hypothermia: successful treatment with partial cardiopulmonary bypass. N. Eng. J. Med. 287: 1135.

7. Warner, W.A., A.H. Anton, T.W. Andersen and L.J. Swofford. 1970. Ventricular fibrillation and catecholamine responses during profound hypothermia in dogs. Anesthesiology. 33: 43-53.

8. Wickstrom, P., E. Ruiz, G.P. Lilja, J.P. Hinterhopf and J.J. Haglin. 1976. Accidental hypothermia: core rewarming with partial bypass. Amer. J. Surg. 131: 622-625.

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This project was sponsored by the Minnesota Sea Grant Institute (under grant NA80AA-D-00114; as project R/S-3) with funds from the National Sea Grant College Program, National Oceanic and Atmospheric Administration, U.S. Department of Commerce and the University of Minnesota.

March 1982