TEMPERATURE LIMITS OF SURVIVABILITY BY REVERSAL OF CLINICAL DEATH DURING DEEP HYPOTHERMIA IN CERTAIN HIBERNATING AND NON-HIBERNATING ANIMALS

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In demonstrating the survival of rats and susliks after lowering their body temperature to 0° and determining the duration of reversible clinical death [3], we have set ourselves the task of establishing the lowest temperature limit for possible successful resuscitation.

EXPERIMENTAL METHOD

The deepest hypothermia permitting possible resuscitation was determined by complete chilling of the body in experimental animals, i.e., a determination was made of the temperature at which all the organs of the body were almost frozen, but without crystallization of their fluids taking place. This hypothermic state was achieved by immersing the animal, which had been preliminarily chilled to 0° and therefore was in a condition of clinical death, in a 50% solution of glycerine or propylene glycol and then cooling it to much lower temperatures. By controlling the rate of refrigeration of the solution in which the animal was immersed, it was possible to obtain complete supercooling, a condition which could be prolonged until the body temperature of the animal fell below −6 or −7°, after which freezing of the tissues took place. This freezing of tissues was accompanied by a characteristic temperature rebound, the well known result of the liberation of latent heat of crystallization. Our experimental techniques and the results of previous investigations have been published in previous papers [4,5].

EXPERIMENTAL RESULTS

The principal conditions relating to the duration and completeness of supercooling, as obtained from experiments with rats weighing 100 g, are set out in Fig. 1. If animals, which have been preliminarily chilled to a temperature of about 0° (the method of chilling and resusitation have been described previously [3]), are immersed completely in a solution of glycerine, the temperature of which is below −7°, then a considerable temperature gradient arises between the internal organs and the surface of the body. Furthermore, a temperature rebound takes place in the skin after a relatively brief supercooling of the surface, well before the rectal temperature reaches freezing point. The temperature of the internal organs is maintained at the same level (freezing point) throughout the whole process of freezing of the body (see Fig. 1A). Hence, complete supercooling does not take place and the partial supercooling of the peripheral organs is of very brief duration.

By contrast, if the animal whose body temperature is approximately 0° is placed in a vessel of glycerine solution at the same temperature and then gradually chilled to lower temperature (see Fig. 1B), the rate of cooling of internal organs only differs slightly from that of the peripheral organs. Subcutaneous and rectal temperatures fall below freezing point and the whole body undergoes supercooling. As the temperature of the medium falls below −7°, a temperature rebound (i.e., crystallization) occurs in the tissues of the body. However, if the temperature of the medium is kept somewhat above −7°, prolonged supercooling can be maintained as shown in Fig. 1C.

Complete revival of adult (1) and newborn (2) rats, also white mice and susliks, was possible when the body temperature had dropped a few degrees below freezing point only in those cases in which complete supercooling had

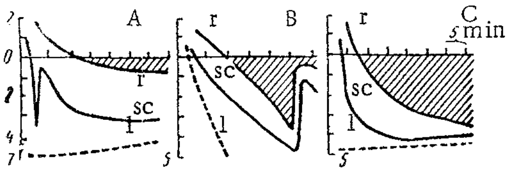

Fig. 1. Partial and complete supercooling of adult rats: r) rectal temperature; sc) subcutaneous; l) temperature of liquid medium. Other explanation in text.

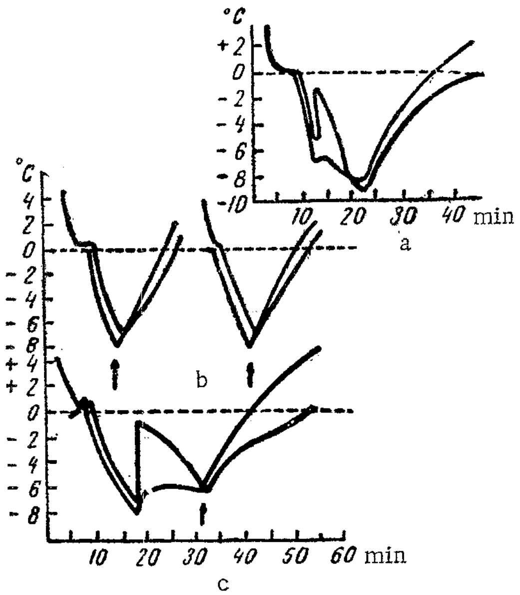

Fig. 2. Supercooling (2 upper graphs) and freezing (lower graph) of newborn rats: b,c) rats; a) frog, Hyla arborea. Narrow curve, temperature of liquid medium surrounding animal; thick curve, rectal temperature (1 cm from surface). Remaining explanation given in text.

occurred. Figure 2 illustrates the results of chilling newborn mice to temperatures below 0° followed by gradual warming, the commencement of which is denoted by an arrow. Figure 2b illustrates the result of completely supercooling two 4-day-old animals weighing 10 g to the lowest possible limits of supercooling (−7.2° in one and −6.4° in the other case). In contrast to the technique used for adult animals, these newborn rats were chilled initially to 0° by immersion in water with ice. The later stages of chilling, as in the case of experiments with other animals, were accomplished with the aid of an ice-salt freezing mixture (about −20°) surrounding the vessel containing the animal immersed in glycerine solution. Uniformity of freezing was achieved by ensuring that the glycerine solution was in continuous movement as a result of the activity of an electric vibrator. The warming up process was begun before the temperature rebound took place, and animals were revived by our previously described resuscitation technique; the newborn rats were then placed with females which continued to rear them normally.

Figure 2c shows the changes in body temperature (rectal) and the temperatures of the medium immediately adjacent to the animal, as they occur in those cases when freezing (crystallization) of the tissues ensues. The temperature rebound occurs at a body temperature of −7° and is accompanied by a sharp rise to freezing point, after which a slower fall in temperature takes place. The effect of latent heat of crystallization liberation on the surrounding medium at the time when the tissues of the animal freeze is clearly seen on a photomicrograph of the curve.

Attempts at reviving animals which had suffered crystallization of their tissues were unsuccessful. From this point of view and also in relation to the general characteristics of chilling below 0° C, no essential differences exist between the situation in rats and in a poikilothermous vertebrate of the same weight, e.g., the tree frog, Hyla arborea (Fig. 2a).

In Fig. 3 and 4 is set out data obtained from experiments on adult susliks (typical non-hibernating mammals). These experiments yielded results which were not significantly different from those previously obtained with non-hibernating mammals (adult rats) [1].

All the curves illustrated in Fig. 3 resulted from experiments involving revival of animals. In the case of the 205 g suslik, the temperature was reduced without interruption until the time when revival by warming was commenced, whereas in the case of the other 3 susliks the body temperature was maintained at a constant level for 20-30 min after cooling but before revival by warming. The dotted line is based on experimental data relating to 38-g mice, which again responded successfully to revival.

Figure 4 consists of curves showing temperature changes in frozen susliks. In one young suslik weighing 87 g, the temperature rebound at the surface (skin temperature, not shown in figure) took place before the rectal temperature had reached freezing point, where it remained all the time prior to warming up of the animal (c.f. explanation of Fig. 1). In the other cases, the temperature rebound took place after complete supercooling. Figure 4 also shows the various degrees of amplitude of the temperature rebound (from 1 to 4.7°). Attempts at revival were commenced immediately after the temperature rebound. All the animals weighing 205 g, i.e., those which received maximum chilling (to −5.2°) and in which the temperature rebound equalled 4.7°, were temporarily revived but subsequently perished. Animals weighing 87 g, in which the rectal temperature did not fall below freezing point even after the peripheral tissues were frozen, survived for a longer period of time (7 days). One animal weighing 210 g, in which

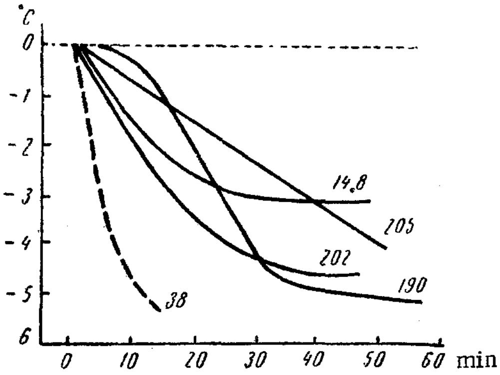

Fig. 3. Supercooling of susliks (rectal temperature). Numbers against curves, weight of animals (in g). Dotted line, chilling of adult white mouse. Curves taken to the moment when the warming up of the animal began (denoted by zero). Rest of explanation in text.

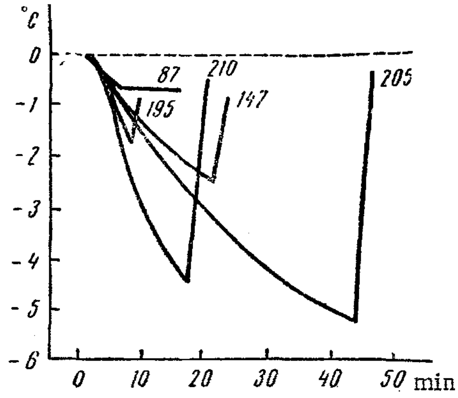

Fig. 4. Freezing of susliks following supercooling (rectal temperatures). Symbols as in Fig. 3. Rest of explanation in text.

the temperature rebound was least of all, died at the end of the warming up process. The rest of the animals survived for about 2 days after the experiment.

Thus, the lowest temperature limit for survival after clinical death occurs at the level beyond which complete supercooling cannot be taken, i.e., about −7°. Our most recent experiments, particularly those with susliks, indicate quite clearly that the duration of the period of reversible clinical death at temperatures below 0° most be prolonged. We have not been able to revive successfully animals chilled to −5° and allowed to undergo a temperature rebound to 0° [3]. The most lengthy period of supercooling after which it has proved possible to bring about successful revival, was 40 min for adult rats. The duration of complete supercooling (down to −5°) which we obtained in our experiments with susliks was of about the same length as the maximum for adult rats, although in this case we were not particularly investigating the limits of duration of clinical death at a body temperature below 0°. It should be noted that, although supercooling avoids the irreversible effect of crystallization, it does not enable the period of reversible clinical death to be prolonged beyond that associated with a temperature of 0°.

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All abbreviations of periodicals in the above bibliography are letter-by-letter transliterations of the abbreviations as given in the original Russian journal. *Some or all of this periodical literature may well be available in English translation.* A complete list of the cover-to-cover English translations appears at the back of this issue.
