CERTAIN BODILY REACTIONS TO COOLING THE BRAIN

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The widespread therapeutic application of hypothermia makes it necessary to undertake a broadly based study of the associated phenomena. The usefulness of the method is that by cooling a warm-blooded animal it is possible to interrupt the cerebral circulation for 10 to 30 minutes without causing irreversible changes.

In the last 10 years a large number of investigations of clinical and experimental hypothermia have been carried out. The principal changes taking place on cooling have been described in detail in both Russian and foreign publications [1-5, 7, 10-13, 15].

Experimental cooling is brought about by reducing the temperature of the surrounding air or by placing the animal in a cold water bath. Alternatively the blood may be cooled outside the body by passing it through a coil immersed in a cooling fluid (usually water and ice). The method of covering the animal with a special cooling blanket is also widely used.

Clinically, besides cooling, an anesthetic is also inhaled and many ganglion-blocking neuroplegic substances are given (the so-called "lytic cocktails"). These include promethazine, pethidine, scopolamine, succinyl choline, dimedrol, lidol (demerol), aminasine, promedol, and other substances. Their injection prevents harmful changes occurring and intensifies the action of the physical cooling. However, these substances are not without action on the organism. It has been shown that many complications occurring during cooling and during the recovering from hypothermia may be associated with the poisonous action of large amounts of the essentially toxic substances which make up the "lytic cocktail" [6].

It has been shown experimentally and clinically that for man and animals cooling is most successful at the so-called biological zero (about 30°). If the temperature falls below 26° harmful changes may occur in the cardiovascular and respiratory systems; these are frequently irreversible, and death ensues [3].

The shortcomings of the common method of attaining hypothermia make it necessary to search for new techniques. One approach which seems promising is the selective cooling of the cerebral blood supply, i.e., local cooling of the brain. In spite of its many advantages this method has not been widely used, and very few descriptions of it are available. It has been reported [4, 12, 14] that with this method there is comparatively little disturbance to blood circulation or respiration; it may be possible by these means to avoid the necessity for the injection of ganglion-blocking agents; the degree of anesthesia may be much less, and it may be possible to isolate the brain from the circulation for a sufficiently long period.

We have studied the relationship between the brain temperature and that of the rectum using different methods and degrees of cooling; we have also investigated the effect of the degree of hypothermia of the brain on the cardiovascular and respiratory systems, changes in the different sensory systems, as well as morphological changes in the brain tissue and particularly in its vascular supply.

METHOD

The experiments were carried out on dogs under morphine-ether anesthesia, and on rabbits under urethane. Blood clotting was prevented by injecting heparin. In dogs both carotid arteries, the vagal sympathetic trunks, and the femoral nerve and artery were exposed; in rabbits we used both carotid arteries, the sciatic nerve, and the tibialis muscle. A thermocouple was inserted to a depth of 8-10 mm into the brain through a trepanned hole. A second thermocouple was placed in the rectum. Canuli were inserted into the peripheral and central ends of the cut carotid artery and connected to a coil immersed in a vessel filled with ice. During the cooling, a clamp was placed on the common carotid of the opposite side. In dogs, the femoral artery was connected to a mercury manometer. In rabbits, movements of the tibialis muscle were recorded by means of a lever. The respiration was recorded by means of a hollow needle inserted into the trachea and connected to a Marie's capsule.

A thermocouple was placed at the output of the coil to control the extent of cooling of the blood pass-

ing rostrally in the common carotid artery. Forced circulation was used to speed the cooling.

RESULTS

Experiments on dogs. In all, 25 tests on dogs of both sexes and various weights were carried out: 7 experiments were made at 25°, and 8 at from 25° to 20°. In all cases, the temperature in the rectum fell less than in the brain, remaining higher by 4-6°. In 4 cases the differences amounted to from 7-12°. This phenomenon was encountered only with our particular method of cooling in which the fall in body temperature does not result directly from the cooled blood which is passing directly to the brain. This was demonstrated by measuring the temperature of the blood in the internal jugular vein. There is reason to suppose that the fall in temperature of the body results from reflex control of the rate of trophic processes of the whole body (Fig. 1), the control being exerted by the brain which reduces the metabolic rate. According to our own* and published results, at the onset of cooling the arterial pressure increases by 1-25%.

After a transitory increase, during the cooling the arterial pressure in the brain fell from 120-140 mm of mercury to 900-100 mm, and in some cases when cooled to 25-20° the pressure fell to 70 mm. During recovery from hypothermia, the arterial pressure returned to normal. Six animals were exceptional, and in them the arterial pressure remained at the low level of 60-70 mm for a considerable time. Of these, 4 died, and the remaining two made a slow recovery and remained in a poor condition for a long time.

As the brain temperature fell to 27-25°, there was a weakening of the pressor response to stimulation of the central end of the femoral nerve or the central end of the cut vagus nerve, and also a reduced response from the vascular reflexogenous zones. On cooling the brain below 25°, there was a disturbance of the cardiovascular reflexes which was shown by a reduction in arterial pressure on stimulating the central end of the femoral nerve, and an increased pressure on stimulating the central end of the vagus, while pressure applied to the carotid sinus caused the blood pressure to rise. The response of the heart and changes in arterial pressure occurring in response to stimulation of the peripheral end of the vagus remained unaltered at all temperatures down to the minimum (−20°) which we employed.

Some changes in the pulse pressure occurred during hypothermia and during recovery from it. Usually, with maximal cooling it was reduced by 25-30%; with very rapid cooling when the gradient was above 0.2, the reduction was 50%; during recovery from hypothermia, the pulse pressure returned to its original level.† When the animals were in a poor condition after the hypothermia both the pulse and the arterial pressures were low (pulse pressure 8-12 mm), and this was interpreted as an unfavorable sign.

Experiments on rabbits. In all, 21 tests on adult animals of both sexes weighing from 2-4 kg were made. A total of 13 experiments was made in which the brain was cooled to 25°, and 8 with cooling from 25-20°. The principal purpose of the experiments was to enable changes in skeletal muscle occurring during brain cooling to be recorded. We measured the temperature changes in the brain and rectum, the threshold of stimulation of the tibialis muscle, its chronaxy, and the pessimum frequency for suprathreshold stimulation. In most experiments, with brain temperatures of 25° and below there was a reduced excitability to direct stimulation, the muscle chronaxy was increased on average from 0.18 to 0.38 m/sec and there was a reduction in the critical pessimum frequency from 100-200 to 60-80 cps. During recovery from hypothermia, these quantities returned to their original values. The changes we observed therefore did not differ from those occurring when the whole body is cooled. It would appear that the small degree of change observed in these experiments is due to the comparatively small functional alteration in the lower parts of the central nervous system. This circumstance represents one of the advantages of isolated brain cooling.

Histological studies. The brains of animals which succumbed shortly after the experiment and also those of animals which survived cooling and were killed 3-4 days afterward, were examined histologically.

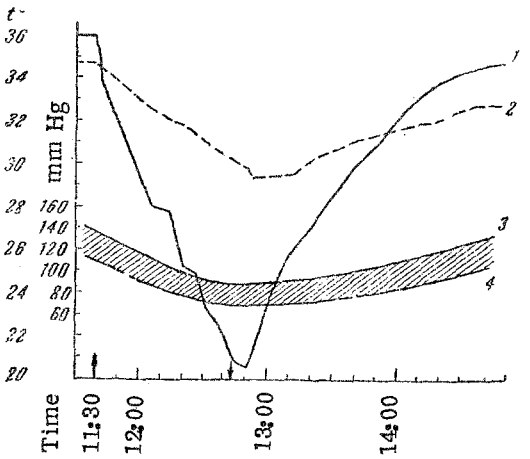

Fig. 1. Changes in temperature and arterial pressure in a typical experiment. 1) Brain temperature; 2) temperature in rectum; 3) maximal arterial pressure; 4) minimal arterial pressure. The onset of cooling is shown by an arrow (↑) and the end by the arrow (↓).

* N. N. Tkachenko assisted in some of the experiments.

† By the gradient of hypothermia we mean the number of degrees of temperature fall of the brain per minute.

The preparations were stained in Nissl's stain for nerve cells and by Eres' method for capillaries.

Investigations were made of the cerebral cortex, basal ganglia, and medulla. It was found that rapid cooling at a gradient greater than the 0.2 (which caused severe postcooling symptoms) was associated with many profound changes in the nerve cells. These were of various kinds; they were graded, and in some cases irreversible. In some cases the cells were swollen, there was often a perinuclear edema, the protoplasm was vacuolized, some of the giant pyramids were crenated and their nuclei eccentric. When the animal died shortly after the experiment, there was a pronounced perinuclear edema, the cells were strongly crenated, the apical outgrowths were greatly swollen, the Nissl substance was almost completely dissolved, and in some of the cells the protoplasm was vacuolized.

In spite of their diversity, all these changes can be included under the general heading "ischemic damage" [9]. We are led to this conclusion by the fact that in cases where there was well marked damage to the nerve cells there were also more or less well shown alterations to the capillaries, particularly in the medulla. On staining by Eres' method, it could be seen that the capillary plexus was much more reduced in those animals which died shortly after the experiment than in those which survived the hypothermia unharmed.

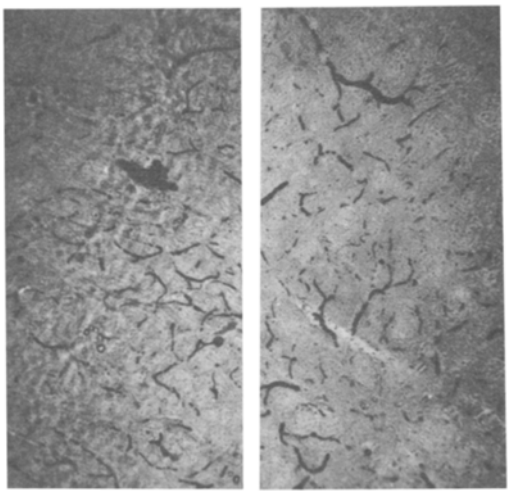

Fig. 2. Capillaries of the medulla in the dog. Stained by Eres, magnification 8 × 8. a) In an animal which tolerated cooling; b) in one which died shortly after cooling.

Figure 2 shows a comparison between drawings of the capillaries of an animal which tolerated hypothermia and another which died shortly after the cooling experiment. One of the causes of death from hypothermia is disturbance of compensatory regulation of function by the central nervous system. It appears that this functional disturbance is in large part brought about by disturbance of the cerebral circulation.

SUMMARY

Isolated cooling was applied to the brain of dogs and rabbits. When it was cooled to 20°, the body temperature did not drop below 30°. This favors the course of hypothermia. Respiration and cardiovascular tone is sufficiently maintained during the whole period of cooling. There is little change in properties of skeletal muscle. When low temperatures are reached, and particularly when the outcome is lethal, considerable changes are observed in the cerebral nerve cells and in the capillaries. The capillary changes may be the cause of those occurring in the nervous tissue.

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