COMBINED ACTION OF MICROWAVE IRRADIATION AND LOCAL COOLING ON LIVING TISSUES

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Experience gained in cryogenic surgery has shown that opportunities for low-temperature destruction of large pathological formations are very limited [12]. A small increase in the volume of necrosis in the frozen region is achieved by increasing the power and improving the geometry of the instrument, by giving repeated cycles of freezing and thawing, and by the combined action of freezing and ultrasound [8, 12]. However, these methods of intensifying cold destruction are not sufficiently effective. Tissues of a living organism have low thermal conductivity (0.38 kcal·m/h/°C), due to their structural and metabolic properties. Water is the main component of all biological systems. However, this water possesses certain specific properties [2, 9, 11]. Investigation [4-6] by calorimetric methods and NMR spectroscopy have shown that water in tissues is heterogeneous in composition and that its orderly arrangement is characterized by the quantity of bound water. The quantity of bound water varies from 0.232 to 0.610 g/g matter for different macromolecules and from 0.15 to 0.46 g of water/g dry weight for different tissues. If the water present in the system is not in its ordinary state, its phase transition (water—ice) will not take place in the regular manner and the greater the deviation in the state of the water from the usual state, the greater will be the difference in this phase transition. In particular, if the water is in a bound state it cannot crystallize at all into ice when the temperature falls [6]. Polymers, ions, and proteins structurize and bind water, modifying its properties. Globular molecules, for example, structurize a much smaller quantity of water than fibrillary molecules. Depending on the magnitude of their structurizing effect on water biopolymers can be arranged in the following order: DNA → collagen → hemoglobin. Ions such as Mg^{++}, Ca^{++}, H^+, Li^+, Na^+, OH^-, Cl^-, hardly change the structure of water at all.

According to data in the literature [4, 5], changes in the degree of "packing" of water or of dipole mobility may be accompanied by strengthening or weakening of molecular bonds. During activity disturbing the "packing" of water the volume occupied by the aqueous phase may be increased and, in turn, this may lead to an increase in size of the water lattice.

The information given above largely explains the considerable resistance of tissues to local cooling. If structure and metabolism, and also the transport function of the microcirculation are taken into account it will be clear that destruction of large volumes of tissues by the cryogenic method is a difficult problem. To overcome this barrier we need to modify the state of the tissues so that they become more sensitive to low-temperature destruction, while preserving its advantages (painlessness, absence of bleeding, freedom from excessive scar formation, and possible immune effects).

The theoretical basis for the experiments described below was a study of the action of microwave irradiation on the tissues of living organisms. The effect of microwave irradiation on living tissues is not uniform, but according to most workers, the point of application of this type of irradiation is the dipole structures, the greater part of which consists of

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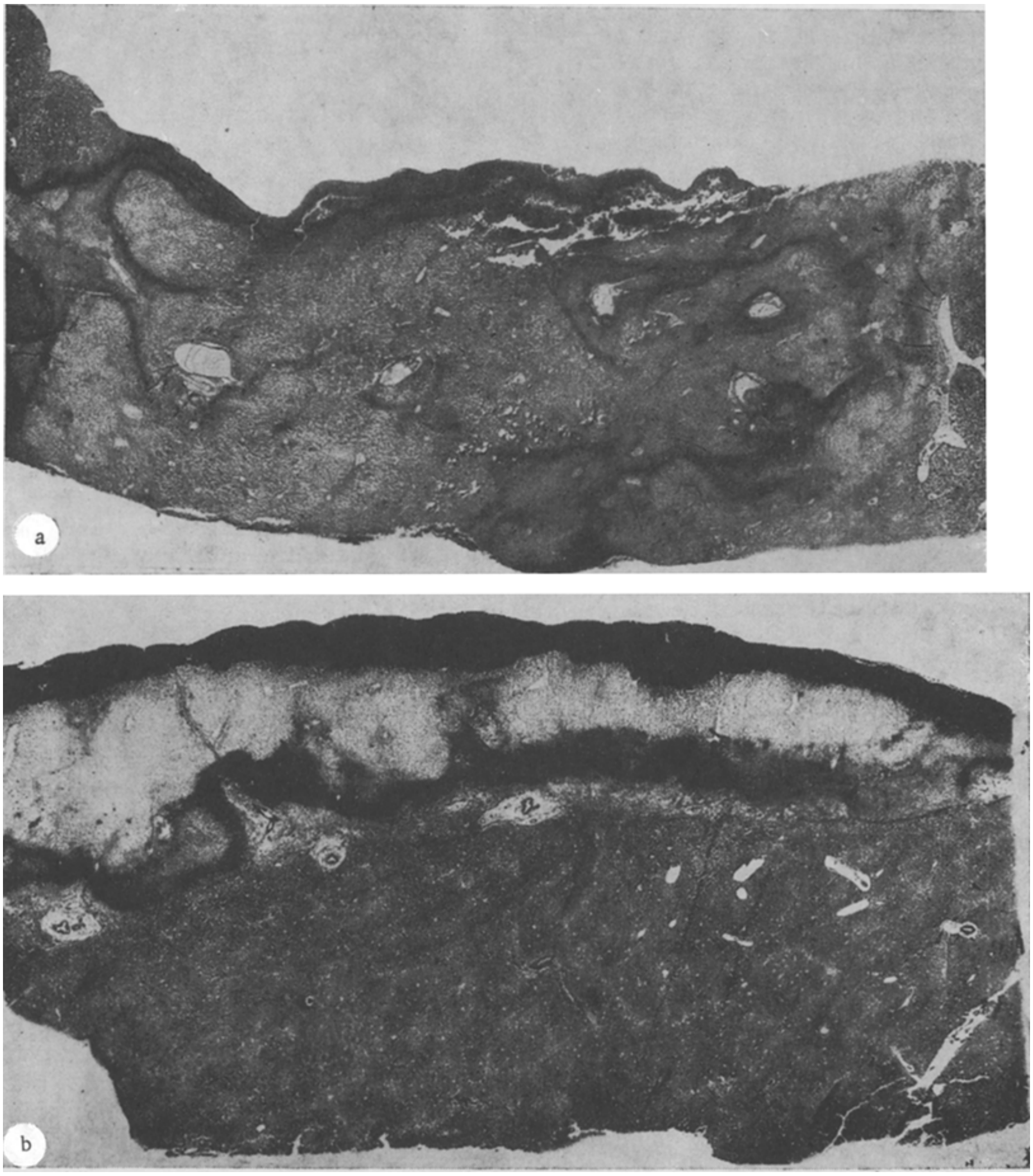

Fig. 1. Preparations of rabbit liver after combined exposure to microwave irradiation and local cooling (experiment) and to cryogenic destruction alone (control). a) Experiment: zone of necrotic changes extends through the whole thickness of the liver; b) control.

bound water [1, 3, 7, 10]. Under the influence of microwaves, polar molecules are brought into an excited state and resonance phenomena arise. A change in the hydration zone and rupture of intramolecular bonds also are possible. All these effects destabilize the structure of the water and make it more mobile and sensitive to various influences.

The action of microwave irradiation thus has a definite point of application which corresponds to the purposes of cryogenic action. Microwave irradiation can be strictly localized and the depth of its action can be controlled by wavelength, allowing for the attenuation factor and the power flux density.

The aim of this investigation was to study combined action of microwave irradiation and local freezing.

EXPERIMENTAL METHOD

Experiments were carried out on the liver and muscles of 36 rabbits, six dogs, and six guinea pigs. The source of microwaves was a standard "Luch-2" physiotherapy apparatus, the diameter of the source was 20 mm, the mean power flux density was 1.2 W/cm^2, and the wavelength was about 12 cm. As cooling device an autonomous cryocautery developed in the Clinic of Pediatric Surgery, with a cooling head 8 mm in diameter and producing a temperature of −160°C, was used. The liver was exposed through a transverse laparotomy under general anesthesia. The vesical lobe of the liver served as the control for cryogenic destruction and the middle lobe was the experimental tissue.

In the course of 3 min an area of the vesicle lobe was frozen (control); this lobe was then returned into the abdominal cavity. The middle lobe was exteriorized (experiment) and exposed to microwave irradiation for 5 min, after which the irradiated area was also locally cooled for 3 min. This lobe was returned to the abdominal cavity and the incision was sutured without drainage.

To study the duration of the after-effects of microwave irradiation experiments were carried out by a similar method on six guinea pigs; the only difference was that the experimental lobe of the liver was locally cooled 5, 10, 15, 20, 30, and 60 min after microwave irradiation. The animals were killed 2, 24, 48, and 72 h and 7, 14, and 90 days later. The macroscopic picture was assessed in the experiment and control. Pieces of rabbit liver were taken for histological study 24 and 72 h after the experiment. The aim of the morphological study was to determine the size of the region of tissue destruction in the zone of action of the two factors. To assess the possible effect of these factors on the left (intact) lobe, which was not subjected to either procedure, symmetrical regions of this lobe with respect to the experimental tissues were studied.

EXPERIMENTAL RESULTS

The animals were found to tolerate the operations well and there was no difference in their behavior compared with that of animals undergoing "pure" cryodestruction. The study of the volume of tissue dying as a result of cryodestruction on the liver in the control experiments revealed the usual picture. The zone of necrosis was a hemisphere, which on average did not exceed 12 mm in diameter and 4 mm in depth.

In the experimental lobe, however, the zone of necrosis was 8-10 mm in circumference greater than the control zone, and as regards depth it consisted of a cylinder extending through the whole thickness of the lobe — on average for 2.5 cm.

Calculation of the volumes of necrosis in the control and experimental lobes showed that the volume of dying tissue in the experiment was on average 4-6 times greater than that in the control. In the muscles the zone of destruction in the experiment was on average 3.5 times greater than in the control; similar ratios continued to be found throughout the period of observation. It was also found that if more than 30 min elapsed after microwave irradiation the zones of death in the experimental and control tissues after cryodestruction became practically identical. The after-effect of microwave irradiation thus lasted about 30 min. Hence it follows that cryogenic destruction is best carried out as soon as possible after microwave irradiation. Analysis of the morphological data for the control preparations of rabbit liver after a single application of cryodestruction revealed an area of total, wet, colliquative necrosis with complete destruction of hepatocytes, vessels, and bile ducts. At the boundary between necrotic and intact tissue there was a zone of suppurative demarcating inflammation, containing neutrophilic leukocytes and nuclear debris.

In liver preparations from animals after combined exposure to microwave irradiation and local freezing the zone of necrotic changes extended throughout the thickness of the lobe (Fig. 1). Histological study of the intact lobe after 24 h revealed ill-defined arterial hyperemia, which was no longer present in animals killed after 72 h.

The results are evidence that preliminary exposure to microwave irradiation followed by local freezing can make the latter far more effective. The great increase in volume of necrotic tissues enables the field of application of the method of cryogenic destruction of living tissues to be widened, as a bloodless and painless operation.

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MURICIDITY OF FEMALE RATS DURING PREGNANCY AND LACTATION

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The instinctive activity of animals includes various manifestations of aggressiveness, such as predatory behavior, defense of territory, response to painful stimuli, etc. Starting from 1956 [3] a special form of aggressiveness in rodents, namely muricidity, has been intensively studied. This term is used to describe the ability of rats to attack mice and to kill them. The frequency of manifestation of spontaneous muricidity in rat populations may vary within wide limits depending on the animals' sex, age, and genotype. For instance, populations of brown rats may contain up to 80% of muricidal individuals, whereas rats of the Long-Evans, Wistar, Sprague-Dawley, and August lines as well as noninbred albino rats may have only 45, 30, 5, and 0%, respectively. Muricidal male rats are always more numerous than females. An increase in the number of muricidal individuals is observed in experiments with acute starvation of rats, social isolation, exposure to painful stimuli, and destruction of certain parts of the brain [4-6]. Hypotheses have been put forward to explain the neurophysiological and biochemical mechanisms of regulation of this complex behavior. However, differences in the models used and the contradictory nature of the results do not permit any definite opinion to be formed regarding these mechanisms. Meanwhile the exhibition of muricidity in rats can provide a convenient model with which to study biochemical processes in the brain responsible for functioning of the CNS in general and for instinctive activity of animals in particular.

Considerable changes in the neuroendocrine and biochemical status of female animals take place under natural conditions during the period of rearing and feeding of their young. Accordingly, in the investigation described below, spontaneous muricidity in female rats was studied during the period of pregnancy and lactation.

EXPERIMENTAL METHOD

Noninbred female rats weighing 25-280 g were kept under controlled conditions in the Laboratory Animals Nursery, Academy of Medical Sciences of the USSR. The animals were divided into groups depending on the stage of pregnancy (10, 20, and 23-25 days) and lactation (1, 5, 10, 15, and 20 days), and a corresponding control group also was set up. Muricidity of the female rats was tested by placing one albino mouse with the rat in the cage. The rats were

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