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EFFECT OF LOW TEMPERATURES ON OSSEOUS AND CARTILAGINOUS TISSUES

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and A. I. Zhigun

Translation of: "Vozdeystviye nizkikh temperatur na kostnuyu i khryashchevuyu tkani", Ortopediya, travmatologiya i protezirovaniye, No. 4, April 1981, pp. 75-78

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16. Abstract

The article discusses the use of extreme cold to treat tumoral afflictions of the extremities. Cryogenic methods and instruments are discussed, and the levels of accumulated knowledge in this area (as well as the areas still in question) are evaluated.

The overall promise for cryogenic methods of treatment is acknowledged, and areas which need further development are noted.

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EFFECT OF LOW TEMPERATURES ON OSSEOUS AND CARTILAGINOUS TISSUES

Ye. Ya. Pankov, G. A. Babiychuk, S. V. Malyshkina and A. I. Zhigun[1]

Low temperatures have long been one of the therapeutic factors in orthopedics. However, only recently has the possibility of evaluating the theoretical bases and practical significance of its use been established, as well as the possibility of determining the immediate prospects for the development of cryomedicine, in connection with the considerable development of cryobiology. /75*

Data on the use of cold as one of the means of therapeutic effect with damage to the tissues of the locomotor system are encountered in the works of Hippocrates, Avicenna and others. However, the concept of "cold", prior to the beginning of the XIX Century, included only the temperature interval slightly below the temperature of the human body. At the present time, several temperature levels of the concept of "cold" are distinguished in medicine, and, in this connection, there are various aspects and areas of its use. If one assumes that the temperature of the human body (36-37°C), as evolutionarily established, is the basic temperature for analysis, then any deviation from the given temperature has a substantial effect on the functional and metabolic condition of cells, tissues and the body as a whole. The region of the temperature interval from +37° to 0°C has been given the name "hypothermic", and the developed state has been called hypothermia. At the present time, there is a number of reports on the fact that this region is of interest for orthopedists and traumatologists [1-3, 7, 8, 11].

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Low temperatures (from 0 to -196°C) differ sharply from the effect of temperatures in the hypothermia region in the mechanism of their effect, and subsequent tissue reaction, and, in this connection, their use is specific.

In the given overview, we have strived to sum up and evaluate the prospects for the utilization of low temperatures in orthopedics.

Temperatures of the given range are utilized in orthopedics and traumatology primarily for conservation of sections of the organs which are insulated from the body (tendons, cartilage, bones), and, secondarily, for a damaging effect on the tissues of the locomotor system with pathologic processes in the body.

Freezing as a method of conservation, utilized independently or in combination with other methods, without a program or according to a specific program, with cryoprotectors or without them, is widely used, at the present time, in many therapeutic and scientific research institutions. There is a series of important theorizing studies on the given question [6, 14, 16, 18, 20, 21, 24], which precludes the necessity of their analysis in the present overview.

Much "younger" and less-studied is the area of use of low temperatures as a local factor of effect on organs, which is associated, on the one hand, with the insufficient level of study of the mechanisms of cryodestruction and reparation in support tissues after the effect of low temperatures, although for other types of tissues, these mechanisms have been studied sufficiently well [22]. On the other hand, it is associated with the insufficient development of technical systems for orthopedic cryosurgery. However, in spite of the difficulties, both theoretical development and practical utilization of low temperatures in this area have sharply intensified in the last decade.

The first studies in this direction concerned the study of the cryogenic effect on tumors. In 1969, American authors [33-35] reported on their results in the treatment of primary and metastatic tumors by the method of cryosurgery. The authors developed the necessary technical devices, and studied the comparative effectiveness of the utilization of low temperatures with intratumoral and extratumoral location of flexible and rigid cold conductors. The condition improved in all patients; however, total cryodestruction of the tumor was not achieved in the greater portion of them. In addition, certain complications developed in some of the patients (spontaneous fractures, necrotization of the skin, osteomyelitis), which the authors associated with insufficiency of experience and imperfection of the technology. Beaupre et al. [25] reported on experiments on the freezing of a tumor, noting that total destruction of the tumoral tissue was achieved with complete cryogenic damage to the tumor and part of the adjacent bone.

A more expanded program of these experiments is presented in the study of Coleman et al. [26]. In experiments on dogs, the authors showed that, after freezing of a tumor, the necrotic tissue is subject to resorption, and the necrotized bone is replaced by newly-formed bone. The authors also established that repeated cycles of freezing have a more effective influence on the tumors.

Marcove et al. [30, 32] reported on 25 cases of successful cryosurgery of gigantocellular tumors. Using a double closed probe, the authors used the direct administration of liquid nitrogen to the tumor, under monitoring with a thermomonitor. The temperature in the tumor was reduced to -60°C, and the temperature 2 cm from the tumor — to -21°C. Based on the results of the studies, the authors concluded that the method of cryosurgery makes it possible to avoid amputation more frequently /76
than other methods, specifically radiation therapy.

The report of Williams et al. [40] concerned treatment of primary metastatic tumors of the skeleton and soft tissues in 50 patients. The authors noted a positive effect from the use of low temperatures. Thus, by the middle of the 1970's, a great deal of experience had been accumulated on the use of low temperatures as a destructive factor in the treatment of malignant tumors.

In the last 5 years, a tendency has been noted towards correlation and analysis of studies on the use of low temperatures in orthopedic practice.

Thus, in 1974, Regling [37], correlating the accumulated experience, analyzed the possibiliy of cryosurgery in orthopedic oncology, and indicated that the utilization of low temperatures as a destructive factor started with the studies of Marcove and Miller [34]. The area of use of the cryogenic method may be expanded only with the disclosure of the biological effect of the action of low temperatures on the cells and tissues in the body. The authors noted that one of the positive aspects of the local effect of low temperatures is the presence of a distinct boundary between the area of cryonecrosis and the surrounding tissues, which corresponds to the isotherm with a temperature of 0°C. This makes it possible to rather clearly determine the zone of damage. What is more, it is shown in the study that the development of necrotic changes is accompanied by a weakly-pronounced local inflammatory reaction, and the destruction and thrombosing of the circulatory vessels of small and moderate diameter ensure a definite hemostatic effect. After the cryogenic effect, complete disruption of the conducting of stimulation is noted in the nerves, but a regenerative effect then develops, and total recovery of the nerve function takes place within a period of from 6 months to 2 years, which agrees with the data of Lenz [29].

Some authors [23] noted the substantial property of cryogenic effect as early as the 1960's. They showed that tumoral tissue, subjected to cryogenic treatment and necrotized, evoked the formation of specific antibodies in the body, its own type of antitumoral autovaccination, which lead to suppression of other metastatic foci and the basic tumor.

By analyzing studies on the use of cold for treatment of benign tumors (gigantocellular tumor, ameloblastoma, aneurysmal cyst), Oseburg [36] arrived at a conclusion on the necessity of developing programs for maximal cryosurgical effect on the extremity. For this purpose, he carried out an experiment in which the cold agent (liquid nitrogen), circulated through tubes, acted on the soft tissues of the upper extremity of a rabbit. The minimum temperature in the ulna reached -60°C. After 18 months, the author noted restriction of movement in the joint, and slight atrophy of the muscles. There were no pathological fractures, and the paralysis disappeared within 6-8 weeks. Thus, a gradual regeneration of the tissues by means of replacement of the frozen tissue by newly-formed tissue was noted.

B. Ye. Peterson [12] indicates the hemostatic and anesthetic effect of thorough freezing. What is more, he notes that the method has limited application, because of the impossibility of freezing tissues in a large volume, because of the danger of freezing tissues in a large volume, because of the danger of freezing blindly, and because of the impossibility of effect on the lymphatic barriers.

Generalized in the study of a group of authors, headed by A. A. Pisarevskiy [13], is the experience of the Central Scientific Research Institute of Traumatology and Orthopedics in the use of the cryosurgical method of treatment of bone tumors. In patients with osteodysplasia and benign bone tumors, the focus of affliction was frozen by means of the administration of an elastic cryogenic probe. The necrotic tissue was bloodlessly removed with an ultrasoundinstrument. The authors noted the positive qualities of cryogenic effect — reduction of blood loss and prolonged effect of local anesthesia. They see promise in the combination of cryosurgical and ultrasound instruments.

Of special interest is the study of Walzel [39], in which the state of cryosurgery in 1978 is analyzed, and it is shown that, at the present time, its positive and negative aspects, and its indications and contraindications, have been distinctly crystallized. Specifically, metastatic recurring tumors are an indication for cryosurgery, requiring palliative measures of an anesthetic nature. The author cites 18 sites of localization of tumors (visceral cranium, neck, chest, abdominal cavity, small pelvis and bones) for which a cryosurgical effect was used.

The results of utilization of the cryosurgical method in orthopedic oncology make it possible to assert that one may destroy tumoral or pathologically changed tissue within rather definite limits. In this case, the degree of damage to the tissue may be regulated.

In contrast to other physical factors, the cryogenic effect has definite advantages: simplicity of technology, painlessness of intervention, hemostatic effect, more rapid healing of wounds, minimal number of complications, and absence of side effects.

Thus, the cryosurgical method proved quite effective in the treatment of metastatic and primary tumors, which is indicated by the works of a number of authors [27, 30, 31].

However, in all of these studies, the authors practically did not touch upon questions of the mechanism of effect of low temperatures on osseous tissue; therefore, the pathomorphologic characteristics of the tissues after freezing remained unstudied. In this connection, a slight intensification of experimental developments in this area has been noted in recent years.

Of recent experimental studies in the area of the use of low temperatures, definite interest is represented by studies concerning the reactions of tissues of the intervertebral disk to these effects.

Thus, I. G. Hertsen et al. [4] studied the effect of low temperatures on the tissues of the intervertebral disk. The data of histologic and biochemical studies indicate the advisability of the use of low temperatures for degenerative and /77 dystrophic diseases of the spine (osteochondrosis, deforming spondylosis, spondylolisthesis, and others), in order to obtain the possibility of replacement of the tissues of the intervertebral disk with fibrous tissue.

The mechanism of effect of low temperatures on the tissues of the intervertebral disk was examined by the authors of [9, 10] in studies which were published in 1978. They showed that the effect of low temperatures leads to necrosis of the tissues of the intervertebral disk. Most intensely destroyed is the pulpy nucleus. The fibrous ring is more resistant to cryogenic effect. On the 7th-8th day after the cryogenic effect, reparative regenerations, manifested in the proliferation of cartilaginous cells and new formation of the collagenic fibers, begins to develop. The authors produced fibrosis of the intervertebral disk; however, the cryogenic effect on the pathologically changed tissues remains unstudied.

The dynamics of the histologic changes in the bone with a local cryogenic effect were studied in the experiment of Ye. T. Sklyarenko et al. [17]. The duration of the cryogenic effect on the proximal metaphysis of the tibial bone by the cryogenic probe was from 30 seconds to 3 minutes. By using the methods of thermometry and histologic research, the authors showed that the local freezing leads to the occurrence of a necrotic focus of the bone and the adjacent soft tissues. In the focus of the cryogenic effect, there occurred edema and disruption of circulation with aggregation of erythrocytes in the capillaries, destruction of the walls of the venous sinuses, and others. The authors view these damages as an early element of disruption of microcirculation. This gives basis to think that, in the mechanism of cryogenic destruction of bone, an important role belongs to the ischemic component of the damage. The regenerative processes after cryogenic destruction occur rather intensely. The devitalized section of the bone was subjected to osteoclastic resorption and replacement with new osseous tissue, which did not differ from the normal tissue in its histoarchitectonics.

Interesting data were cited in the study of Simon and Green [38], who studied the effect of low temperatures in the range from -20°C to -80°C on articular cartilage in rats. The authors describe the reaction of the cells and intercellular matter of the articular cartilage, and also note that the cells are more sensitive to low temperatures.

A. B. Rikberg and L. I. Trushkevich [15, 19] have made a definite contributuion to the solution of questions of the mechanism of cryogenic damage of biological structures, specifically osseous tissue. The authors discuss questions of control of the processes of cryogenic damage, and its dissemination in osseous tissue.

One of the shortcomings of all the enumerated studies is the insufficient correlation of the morphologic and biochemical data with the biophysical data.

An important question of the practical utilization of the cryogenic effect is the topography of the cold field, in connection with the pronounced heterogeneity of tissues. At the present time, the overwhelming majority of researchers are citing data on the spherical shape of the zone of freezing [5, 28]. It is probable that the varying structure of the tissues should have an effect on the shape of the zone of freezing; however, there are no concrete data on this question.

One of the unsolved aspects of the given problem is the coincidence of the zone of changes visible to the eyes and the microscopic zones, as well as the existence of definite contradictions in the question of determination of the threshhold of cryogenic sensitivity of osseous and cartilaginous tissues. Certain difficulties in the use of cryosurgery in orthopedics and traumatology are associated with the absence of experimental and technical bases for the use of cryosurgical routines, as well as with the absence of cryogenic instruments, which make it possible to provide an effect on the tissue of the locomotor system which is sufficiently precise, and dosed in intensity and volume. In other areas of medicine (stomatology, dermatology, general surgery), sufficiently good cryogenic instruments have been created, which are utilized in orthopedics; however, they do not make it possible to solve specific methodical problems.

The utilization of low temperatures, even that only associated with a destructive effect, opens definite prospects, and intensive experimental and clinical studies in this area may make this physical factor a valuable treatment instrument in the hands of orthopedic surgeons and traumatologists.

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