

ОЖИВЛЕНИЕ ОРГАНИЗМА  
И ИСКУССТВЕННАЯ ГИПОТЕРМИЯ

OZHIVLENIE ORGANIZMA  
I ISKUSSTVENNAYA GIPOTERMIYA

RESUSCITATION  
AND ARTIFICIAL HYPOTHERMIA



# RESUSCITATION AND ARTIFICIAL HYPOTHERMIA

*by*

V. A. Negovskii

With a Preface by Claude S. Beck, *M.D.*

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Pitman Medical Publishing Co., Ltd.  
46 Charlotte Street  
London, W. 1.

The Russian text was published by Medgiz,  
the State Press for Medical Literature, in Moscow in 1960.  
The translation contains revisions made by the author  
subsequent to the publication of the Russian original.

НЕГОВСКИЙ ВЛАДИМИР АЛЕКСАНДРОВИЧ

**Оживление организма  
и искусственная гипотермия**

*Library of Congress Catalog Card Number: 62-21589*

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## Preface to the American Edition

This work, published in the Soviet Union in 1961, contains 49 illustrations and 336 references to Soviet literature, 110 of which were published before 1950 and 226 since, and some 530 references to the non-Soviet literature. The Soviet scientists have had a long and active interest in resuscitation.

Professor Negovskii is director of the Institute in Moscow where investigations on this subject are carried out. The building is one of a row of typical four-story Moscow residences. In this old and poorly equipped building are some 20 full-time scientists working with great devotion under the direction of Negovskii. The Institute has laboratories for physiology, metabolic studies, histology, a soundproof room for conditioned reflexes, and an area for the development of apparatus for defibrillation and other electrical equipment. A liaison exists between this Institute and the hospitals of the Soviet Union.

Negovskii concludes his introduction with the words:

"Because of the vast scale of research on hypothermia in the Soviet Union and elsewhere, we deemed it imperative to study this problem with particular reference to its bearing on the use of artificial cooling in the treatment of terminal states. At the present time in the study of the pathophysiology and in the treatment of states of agony and clinical death, increasing use is being made of the fact that hypothermia, when properly applied, prolongs the period during which the brain and other tissues can survive general anemia. The need has arisen to summarize the more important findings obtained during research into resuscitation in recent years, and it was this that led the author to write this monograph. If the material it contains proves helpful to those working in the fields of the pathophysiology and treatment of terminal states, the author will consider his object fulfilled."

The content of this book is indicated by the various chapter titles and subheadings.

The following quotations from Chapter 2, *Some Principles Governing the Suppression and Restoration of Respiration*, indicate the

type of material presented:

"We do not yet fully understand those admittedly rare cases in which, despite the late appearance of the first inspiration, the higher divisions of the central nervous system are restored to activity and the dogs survive. Of the 1200 experiments performed in our laboratory during recent years, results of this type were observed in only 14 animals. As a rule the process of dying did not last longer than 12–15 min; clinical death lasted 5 min in 10 experiments, and 6 and 7 min in 2 experiments each. It is interesting to note that, despite the late restoration of respiration in the animals of this group (after 7–8 min and, in one case, after 12 min), the corneal reflexes were restored comparatively early (at the 15th–19th min). In one experiment only were they restored at the 28th min. It is evident that in these animals an early restoration of the functions of the bulbar centers took place, apart from an isolated inhibition of the respiratory center. Notwithstanding this phenomenon, excitation in the bulbar region led to the restoration of the higher divisions of the brainstem, as demonstrated by the early restoration of the corneal reflexes, followed by that of the higher divisions of the brain . . . .

"In contrast to many observations which have been reported, the administration of pure oxygen at the beginning of resuscitation of animals clinically dead for 5 min was found to be less effective than artificial respiration with air. During artificial respiration with pure oxygen, spontaneous respiration was restored late and the animals died. Oxygen was found to be of some value when given only in the later stages of resuscitation, for example, between the 12th and 24th hr of resuscitation, and in small doses . . . .

"These reports of the negative action of oxygen during resuscitation after prolonged clinical death are confirmed by histological investigations. Romanova (1956) examined the brain of 20 dogs clinically dead for about 5 min. Artificial respiration was applied with pure oxygen. In some animals oxygen therapy was used after resuscitation. Fifteen animals died in the course of the first few hours or days, and five were sacrificed 14 to 90 days after resuscitation. Histological investigation revealed both diffuse and focal changes, differing in character depending on the length of survival of the animals after resuscitation."

And from Chapter 3, *Oxidative Processes and Carbohydrate—Phosphorus Metabolism of the Brain in Terminal Stages*:

"A crucial moment for the metabolism is the terminal pause, *i.e.*, the interval after regular breathing has ceased and before agonal respiration has commenced. At this time the cortex is in a state of

deep inhibition, and the regulation of the physiological functions is performed by the brainstem, largely by the bulbar centers. A more primitive form of metabolism begins to predominate in the brain—namely, glycolysis—and breakdown is more in evidence than synthesis. Creatine phosphate disappears from the brain tissues, the sugar content falls to 59 mg%, while at the same time the lactic acid rises to 101 mg% and the inorganic phosphorus to 18 mg%, and the glycogen content is unchanged. The relative proportions of adenosinephosphoric acids in the brain tissue change in the course of dying; the adenosinetriphosphate content decreases and there is a simultaneous increase in the adenosinediphosphate and adenosinemonophosphate contents (E. A. Nosova). During agony, when the physiological functions are regulated only by the bulbar centers, a further accumulation of lactic acid is observed in the brain tissue, the sugar content falls considerably (25 mg%), and the glycogen breakdown begins. As a result of the compensatory dilution of the blood with tissue fluid, the oxygen capacity of the blood falls by 1.5–2.5 vol%. Although the arterial blood is well saturated with oxygen (at the moment of onset of agony its saturation reaches 97–98%), the reduction in the volume of circulating blood leads to the accumulation of large amounts of incompletely oxidized products of metabolism, in the form of organic acids. A state of nongaseous acidosis develops, and the amount of chemically combined carbon dioxide is diminished.”

Professor Negovskii, in his Conclusion, states that:

“Clinical death changes to biological or irreversible death 10 min or less after cessation of cardiac activity and respiration . . . if the process causing death is prolonged and exhausting this transition takes place in the first minute. In a young and healthy patient this transition is delayed. Cerebral inhibition and excitation affect duration of clinical death as does also depth of anesthesia . . . . Pure oxygen is possibly beneficial in the first 1 or 2 min of clinical death; in the 3rd and 4th min only air is given; oxygen causes death of animals within 24 hr . . . . The cortex of the monkey is more sensitive to anemia than the cortex of the dog or other animals lower in the scale of evolution . . . . According to the law of negative induction, a focus of excitation in the central nervous system induces peripheral inhibition; during resuscitation, however, a focus of excitation arising in the medulla leads to disinhibition of the higher divisions of the brain, and this leads to their excitation, not inhibition . . . . During resuscitation the impulses accompanying both inspiration and expiration disinhibit and excite the respiratory center.

“ . . . The successful solution of resuscitation is bound up with training. We can now state with pride that the ranks of the many

experimental researchers concerned with resuscitation for several years are being swelled by groups of young scientific workers."

The author quotes Lenin as saying "it is all a matter of not allowing ourselves to be satisfied by what we have learned from previous experience, but of going *further and further* . . . to more difficult tasks."

"Concerning the pathophysiology and treatment of terminal states only the crumbs of knowledge have been gathered, only the first stones of the building have been laid . . . . A practical problem is to make the use of resuscitation more widespread. We must aim to ensure resuscitation procedures available in all district and country hospitals . . . .

"During the last 5 years more than 17,500 doctors from every corner of the Soviet Union have gained knowledge concerning terminal states . . . . The time is near when failure of the doctor to take active resuscitation measures will be regarded as a case for legal action . . . . With the growth of our country and the powerful development of our sciences, there is no doubt that research into the treatment of terminal states of life will be extended and intensified. By the united efforts of experimental and clinical workers the battle against sudden death, in which Soviet scientists are deeply committed, will be successfully won."

In our laboratory machine life has been provided in dogs fibrillating for 120 min. Such machine maintenance of life will allow the victim to be transported to a medical center where the heart can be defibrillated and the heartbeat restored. A new medical specialty—Resuscitology—is thus being born.

It is obvious that the Soviet Union is placing resuscitation in a showcase for the world to look at. It is obvious also that the world is going to have to look at it. The Soviet scientists have earned an important place in the development of this subject. They have the forward thinking to recognize that a new medical specialty has been created and they have centralized authority to put their ideas across. Where are we in the U.S.A.? We take satisfaction in our individualism. We can be static in our attitudes without being criticized. Indeed the American M.D. does not have to learn. He can walk away from the death scene instead of running to it. We scarcely know that the fatal heart attack can be erased and never recur. We scarcely know that over one half of the coronary victims could be revived if conditions were right at the moment of death. The first defibrillation of a human heart was achieved in America, the first reversal of a fatal heart



attack was accomplished in America, the first application of resuscitation beyond the confines of the hospital took place in this country. Mouth-to-mouth breathing and closed chest pumping of the heart (Crile, 1912) were developed in this country. But it is fair to say that America has not yet awakened to the new future. Our medical scientists seem to be conditioned by the belief that physiological manifestations are necessarily related to morbid disease, which is the basis of the electrocardiogram. Thus the fatal heart attack is produced by injury to muscle and injury current. Our leaders in cardiology are quoted as saying in substance that they do not know "the cause of death after a clean bill of health," i.e., death in a good heart (*Congressional Record*, March 5, 1959, p. A1807). A discussion of coronary artery disease appears in *Modern Concepts of Cardiovascular Disease*, January, 1962. In this article a medical cardiologist refers to anticoagulants and states that "in a word, prevention is to be the battle cry of the future," as though there is nothing else of importance concerning this disease. It seems that our attitudes must be revolutionized, because the experiment is far beyond the clinician. This revolution would be facilitated if we had in this country an Institute for the Study of the Environment of Death. One such Institute (comparable to our many cancer institutes) would focus attention on the prevention of death, the reversal of death, and the complex biological problems of the dying process. There is scarcely any more pressing medical problem. Strange, indeed, that America needs this nudge from Russia—and fortunate that we have had it.

Negovskii's book will find wide usage. It should be in every medical library. Almost every research worker in this area will want it. Clinicians, cardiologists, surgeons, and medical students will find important information in it. It is a research book documented by many experiments and also by many clinical cases. It is more than a manual describing methods. We are pleased to have this work available in English.

Claude S. Beck, M.D.  
Professor of Cardiovascular Surgery  
Western Reserve University



## Preface to the Russian Edition

This monograph summarizes the author's great experience in the field of resuscitation following the publication of his book, "The Pathophysiology and Therapy of Agony and Clinical Death" (1954).

In the present volume the author deals with several currently important problems concerning the pathophysiology and therapy of terminal states, and he closely matches theoretical research with practical problems. Modern ideas on cardiac massage as a method of revival of the action of the heart in terminal states are described at length, and the author's own experience in this field is reviewed. Cardiac massage is combined with other important methods of restoration of the action of the heart, principally with intra-arterial blood transfusion and defibrillation of the heart. The best ways of using these methods in conjunction with each other, depending on the nature of the lethal process, are described.

The author demonstrates the vital importance of early restoration of breathing for the satisfactory resuscitation of the higher divisions of the brain, and the necessity for the use of artificial respiration for this purpose, employing special apparatus.

A section of the book is devoted to the study of the changing pattern of the extinction and restoration of the functions of the central nervous system. It is shown convincingly that the fundamental task of resuscitation is the maintenance of the viability of the brain.

The attention of physicians and physiologists will also be attracted by a large section dealing with the role of hypothermia in prolonging the period of clinical death, *i.e.*, the period of general anemia of the central nervous system. As a result of the use of a comprehensive method of resuscitation, as developed by the author, in conjunction with artificial hypothermia, considerable progress has been attained in the prolongation of the period of clinical death from 5-6 min to 1 hr. Meanwhile, the result of work on the use of hibernation mixtures carried out in Negovskii's laboratory will induce

physicians and pathophysiologists to exercise care in the use of these mixtures when there is the possibility of the development of terminal states.

In a special chapter the author analyzes his experience in the clinical application of his comprehensive method of resuscitation, and gives a detailed examination of the reasons for the possible complications, as well as the factors promoting the efficacy of the method.

The book will be of great interest to workers in anesthesiology, the newly developing branch of medicine, who must be familiar with the pathophysiology of terminal states and must master to perfection methods of their prevention and cure.

The wide range of the problems discussed, the wealth of experimental and clinical data, with the comparison between the author's own results and those reported in the literature, and the very high theoretical standard of the investigations carried out by the author of this monograph and by his group will undoubtedly commend it to those engaged in both clinical and experimental medicine.

Academician A. N. Bakulev

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# Introduction

The increasing attention paid to the study of the mechanisms of dying and resuscitation marks an important stage in the development of scientific knowledge. During the last twenty or thirty years, as a result of a great extension of experimental research, the fundamental patterns of extinction and restoration of the vital bodily functions have been elucidated. A new field of medical science devoted to the study of the pathological physiology and therapy of terminal states, primarily of the states of agony and clinical death,\* has been created. Although the earlier attempts to delay the onset of death were largely nothing more than hopes and dreams, in the present state of science we may begin to tackle the problem of treatment of terminal states in a realistic manner.

Many reports of the revival of human patients after the sudden cessation of cardiac and respiratory activity have been published in the world literature. Besides hundreds of individual articles, several monographs have now been written on this subject.

In prerevolutionary Russia, eminent researchers of the caliber of A. A. Kulyabko and F. A. Andreev had to conduct their investigations into the problem of resuscitation individually, thereby limiting their contributions to the development of this vast and complex field of medical science. Under Soviet rule facilities have been available for more extensive investigation of the problem of resuscitation in close association with practical experience. The humanism of the Soviet system has contributed significantly to the development of these studies. The systematic struggle to save life has real meaning in a country where such a high value is placed on human life. The boldness, the courage, and the pioneering spirit

\*Translator's Note: Inasmuch as the terms "agony" and "clinical death" (which Negovskii uses throughout this book to denote the two stages into which he strictly subdivides the period of impending death) are not usual in Western literature, the reader may wish to turn first to the discussion of their meaning at the beginning of Chapter 6.

inherent in Soviet science were important factors promoting the development and establishment of this new branch of medical science. Finally, the fact that Soviet scientists working in the field of the study of terminal states are guided by the method of dialectical materialism in their investigations has undoubtedly been of some help in the elucidation of the principles governing the extinction and restoration of vital functions.

Interest in this problem has increased considerably in recent years. Claude Beck, a leading American surgeon and research worker in the field of resuscitation, has written that the surgeon who is not competent in the techniques of resuscitation ought not to come near an operating table. This applies with still greater force to the new science of anesthesiology, which is intimately associated with the treatment of terminal states. To paraphrase Beck, we may say that no anesthesiologist who is not familiar with the prophylaxis, the pathophysiology, and the treatment of terminal states should give an anesthetic. Some very pertinent remarks were made on this point at the congress of anesthesiologists held in Zurich in August, 1956, where considerable attention was paid to the question of resuscitation. "The largest number of papers was devoted to the subject of resuscitation," it is stated in the proceedings of the congress, which goes on to say: "In the USA and in some of the larger European cities (Berlin, Hamburg, Cologne, Paris, Rotterdam, and Copenhagen), centers for resuscitation or restoration of breathing have been organized." Many such remarks testifying to the ever-increasing interest of anesthesiologists in the problem of resuscitation could be cited.

It has now been 5 years since our last monograph was published. During this period much new experimental evidence has been collected in the laboratory, supplementing our ideas of the mechanism of extinction and restoration of the functions of the cardiovascular, respiratory, and central nervous systems, and our knowledge of the metabolism in the terminal period. Artificial respiration has been used on a relatively larger scale in resuscitation.

Corresponding with the general level of development of research into terminal states, renewed interest has been shown in cardiac massage, and in the necessity for including it among the methods of emergency resuscitation.

Because of the vast scale of research on hypothermia in the Soviet Union and elsewhere, we deemed it imperative to study this problem with particular reference to its bearing on the use of artificial



cooling in the treatment of terminal states. At the present time in the study of the pathophysiology and in the treatment of states of agony and clinical death, increasing use is being made of the fact that hypothermia, when properly applied, prolongs the period during which the brain and other tissues can survive general anemia.

The need has arisen to summarize the more important findings obtained during research into resuscitation in recent years, and it was this that led the author to write this monograph. If the material it contains proves helpful to those working in the fields of the pathophysiology and treatment of terminal states, the author will consider his object fulfilled.

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