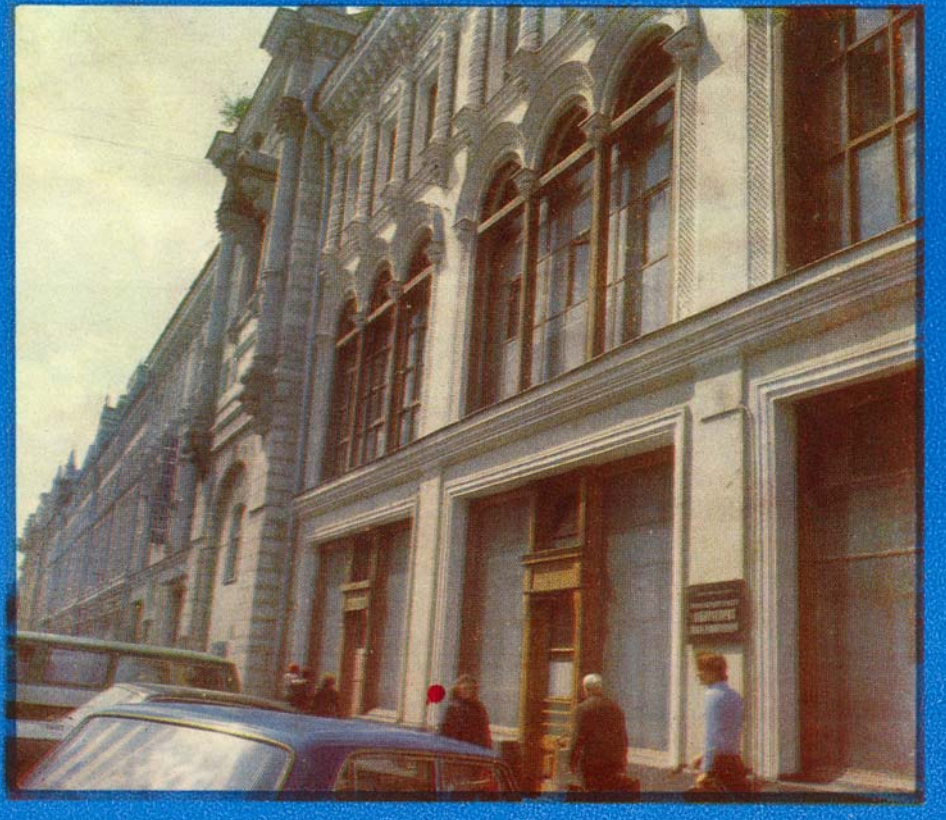
USSR ACADEMY OF MEDICAL SCIENCES

RESEARCH LABORATORY OF GENERAL REANIMATOLOGY



USSR ACADEMY OF MEDICAL SCIENCES

RESEARCH LABORATORY OF GENERAL REANIMATOLOGY

(PROSPECT)

Moscow Meditsina 1984

УДК 616-036.882-08-039.71-074:061.6

Н $\frac{4110000000-215}{039(01)-84}$ заказное издание

The Research Laboratory of General Reanimatology, the USSR Academy of Medical Sciences, was founded by order of the USSR People's Comissariat of Health on August 26, 1936. First it was part of the Institute of Neurosurgery. Academician N. N. Burdenko, outstanding Soviet neurosurgeon and the Institute's director, regarded resuscitation as a new and promising trend of research and actively supported a small group of enthusiasts comprising, besides V. A. Negovsky, founder and permanent chief of the Laboratory and now Academician of the USSR Academy of Medical Sciences, two research fellows, E. N. Tishina-Solovjova and M. I. Shuster, and Engineer V. M. Sambor. Some time later, it was joined by M. I. Telicheva, V. L. Gubar, E. M. Smirenskaya, M. S. Gaevskaya, and A. I. Makarychev. The new Laboratory was first called Special-Purpose Laboratory for Restoration of Vital Processes During Events Similar to Death.

By the time it was founded, certain experimental and clinical experience, though often incorrectly assessed, had been accumulated in the use of certain resuscitation elements. The first monographs (Negovsky, 1943, 1954) provided a detailed analysis of previous works, of their successes and failures. Yet, despite odd publications and some occasionally successful empirical attempts to resuscitate people, there was no systematic theoretical knowledge on resuscitation, lawfulness of resuscitation, indications to it, and scientifically grounded techniques. There existed neither a science of reanimatology, nor a method of resuscitation that would have been convincingly effective and within reach of a large number of physicians.

The tasks of the newly created Laboratory were as follows:

(a) to study the general regularities of extinction of vital functions during dying, and their restoration after resuscitation; from the very start, special attention was given not only to heart and respiration pathology, but to the study of the extinction and recovery of brain functions;

(b) to develop an effective and widely accessible resuscitation technique that would become part of everyday clinical practice, not just a method for occasional use;

(c) to prove that resuscitation is realistic in practical medicine and to overcome the almost absolute scepti-

Academician of the USSR AMS, the USSR State Prizes winner, V. A. Negovsky.

cism and distrust of broad medical and scientific circles for the very idea of resuscitation, and to surmount their resistance against introducing it into practice.

The method of arterial pumping of the blood towards the heart was initially used in resuscitation by Andreev (1913). It was improved and combined with artificial lung ventilation (ALV) involving forcible blowing of air into the lungs by means of bellows. Without this type of ALV, resuscitation frequently proved to be ineffective.

During the few years preceding World War Two, the Laboratory succeeded in obtaining sufficiently convincing experimental evidence showing the above-mentioned tasks to be well grounded and timely. The reality not only of restored heart activity, but also of functions of the central nervous system after clinical death was proved in experiment. In view of the need to run experiments involving bloodloss, a heparin-obtaining technique was developed in the USSR in parallel with the above-said procedure.

The next major stage was to verify in practice the newly developed technique, and this was done during World War Two and in the first post-war years. The experience of resuscitation in the battle area was summarized in a special monograph (Negovsky, 1945). The method of intra-arterial pumping began to be widely used in the treatment of terminal states. At first, bellows were employed for ALV, and the question was raised for the need to commercially

Doctors of medical sciences E. M. Smirenskaya a bowe and M. S. Gaevskaya beline.

Неговскому
Владимиру Александровичу

в 1952 году присуждена Государственная премия СССР
второй степени и присвоено звание

ЛАУРЕАТА ГОСУДАРСТВЕННОЙ ПРЕМИИ СССР

за научные исследования и разработку методов восстановления жизненных функций организма, находящегося в состоянии агонии или клинической смерти.

Председатель Комитета по Ленинским премиям в области науки и техники при Совете Министров СССР
(М. Келдыш)

№ 3028

„6" августа 1962 г.

Ученый секретарь Комитета по Ленинским премиям в области науки и техники при Совете Министров СССР
(Н. Аржаников)

The Diploma of the USSR State Prize winner.

manufacture ALV apparatuses in the USSR. Gradually, the number of successful resuscitations following clinical death began to increase. Even today, with the basic set of emergency resuscitation measures involving closed-chest and direct heart massage and expiratory artificial respiration, one cannot but give credit to the method of arterial centripetal pumping with adrenalin. Its simplicity and high efficiency, especially in hemorrhage, and the possibility of applying it in minimally equipped medical institutions, played a decisive role in changing the attitude of broad medical circles to the very idea of resuscitation. Today, too, it retains its significance in resuscitating patients dying from bloodloss.

In 1946 a provisional clinical group was set up at the Laboratory to start in a clinic headed by Academician A. N. Bakulev, the USSR Academy of Medical Sciences. The Laboratory was gradually winning recognition and support, and medical people began to consider its work important and promising. In 1948 it became an independent institution under the USSR Academy of Medical Sciences, and was named «Laboratory of Experimental Physiology for Resuscitation of the Organism». In 1952 several research workers won USSR State Prize; in the same year the First USSR Conference on Treatment of Terminal States in the Clinic and on Emergency Care was held. It showed the number of physicians and researchers working in the field of resuscitation to be rapidly increasing.

In 1952 the USSR Ministry of Health published the first instructions of the Laboratory on the introduction of resuscitation methods into medical practice. However, the organisation of resuscitation units was still a remote project. In 1955, a new small permanent clinical group was set up in the Laboratory. In 1958, M. D. Kovrigina, the USSR Minister of Health, signed a circular letter to the Union Republics Ministers of Health, recommending to organise units for the treatment of terminal states on the basis of the Laboratory's experience. On the initiative of the Laboratory and with support of the Moscow Municipal Health Department, a small anti-shock unit was organised at the Moscow S. P. Botkin Hospital. It was headed by E. S. Zolotokrylina; N. M. Ryabova, too, took an active part in this work. Clinical results obtained during a year were ponderable enough to convene in 1961 a Moscow City Conference on the first Soviet results in organising a hospital resuscitation service for treatment of patients with severe trauma and hemorrhage. The submitted reports included new facts and concepts that became guides to action for several years to come.

In the early sixties small resuscitation groups were set up under the Laboratory at emergency surgery units of a number of Moscow hospitals (4-th Moscow City Hospital, 29-th Municipal Hospital, and the 13-th Maternity Home).

The situation having improved, a small resuscitation unit was set up in 1962 at the S. P. Botkin Hospital; in 1966 it was reorganized into a large unit. The Moscow Municipal Health Department provided personnel for the service of 20 beds. In addition, a specialized Biochemical Laboratory and a Laboratory for Functional Diagnostics were set up. This marked the establishment of the first full-fledged resuscitation department at a large multi-purpose hospital. The department was originally headed by T. P. Belskaya, Honoured Physician of the RSFSR.

The experience accumulated there permitted to ground the organisational principles of a general-purpose resuscitation service. These principles formed the basis of future (1969 and 1975) USSR Ministry of Health orders under which a modern resuscitation service was organized in the USSR.

The Laboratory initiated the organization of a mobile resuscitation service to provide skilled aid to hospitals and maternity homes that had no resuscitation units of their own. Mobile resuscitation teams staffing Laboratory workers began to operate in Moscow in 1959, and an independent mobile resuscitation centre was set up in 1964. Over the years, it accumulated unique experience. In effect, it was always organically related to the Laboratory's resuscitation service. The Laboratory staff initiated and took part in organizing the first specialized first-aid teams in Moscow.

The new field of medicine started by the Laboratory in 1936 and sistematically developed ever since was named reanimatology (V. A. Negovsky, Intern. Traumatol. Conf. Budapest. Traumatol. Orthop., 1961, 3—4, 259) in 1961; today the term is widely used

Head of the Group for Clinical Pathophysiology and Biochemistry, Senior Research Worker, Candidate of Med. Sci. E. S. Zolotokrylina.

over the world. In the USSR, both the medical speciality concerned with resuscitation and a scientific journal on the problem bear the name of REANIMATOLOGY. In 1977 the Laboratory was given its present name: the Research Laboratory of General Reanimatology, the USSR Academy of Medical Sciences.

ORGANISATIONAL SCHEME OF THE LABORATORY

Today, the Laboratory's staff counts about 84 workers, including 36 research workers and physicians and 24 lab assistants and technicians. Six of research workers are Doctors of Med. Sci. (MDs), and 15 researchers are Candidates of Med. Sci.

The Laboratory incorporates two major research departments, the Experimental and the Clinical Department.

The **Experimental Department** is located at 9, 25th October Str., Moscow, and comparises the following groups:

(a) **Group for General Pathophysiology of Terminal States** (Head: Academician V. A. Negovsky, the USSR Academy of Medical Sciences);

(b) **Group for Pathophysiology of the Central Nervous System** (Head: Senior Research Worker A. M. Gurvitch, MD);

(c) **Group for Biochemistry** (Head: Senior Research Worker L. V. Molchanova, Cand. Biol. Sci.).

(d) **Group for Pathomorphology** (Head: Senior Research Worker G. N. Mirotvorskaya, MD);

(e) **Group for Heart Electrophysiology and Defibrillation** (Head: Senior Research Worker V. Ya. Tabak, Cand. Med. Sci.);

(f) **Group for Experimental Therapy of Terminal States** (Head: Academician V. A. Negovsky, USSR Academy of Medical Sciences).

The CLINICAL DEPARTMENT (Head: Senior Research Worker V. L. Kassil, MD) is located with General Resuscitation Unit at the S. P. Botkin Clinical Hospital, Moscow, and includes:

(a) **Laboratory for Clinical Pathophysiology and Biochemistry** (Head: Senior Research Worker E. S. Zolotokrylina, Cand. Med. Sci.);

(b) **Consulting Room for Functional Diagnostics** (Head: Senior Research Worker N. V. Edeleva, Cand. Med. Sci.);

(c) **Computer Group** (Head: Yu. M. Dovzhenko, Cand. Techn. Sci.).

The Moscow Municipal Mobile Resuscitation Centre (Head: K. P. Kaverina, Cand. Med. Sci.) works in close contact with the Laboratory and its Clinical Department.

The Laboratory has also a **Group for Coordination of scientific Research** (Head: L. G. Shikunova, MD).

The Operation Room is the centre of the Experimental Department. It is there that the basic experiments on dying and resuscitation of animals are performed. They are conducted by researchers aided by a team of specially trained, highly skilled lab assistants. The Operation Room is equipped with modern instruments needed to control the main functions of a dying and resuscitated organism: hemodynamics, lung ventilation, and state of the central nervous system (EEG and brain circulation).

Less complex experiments and special studies are performed in other experimental rooms as well.

The main experimental animals are dogs. Cats, rabbits and rats are also used.

BASIC RESEARCH TRENDS AND RESULTS

During almost fifty years of its existence, the Laboratory has worked in the following directions:

(1) basic studies of the nature of the pathology of terminal states and post-resuscitation conditions in experiment;

(2) clinico-pathophysiological analysis of the mechanisms of the pathology observed when treating patients in terminal states;

(3) improvement of resuscitation methods and post-resuscitation management both in laboratory and clinic, and developpent of resuscitation equipment;

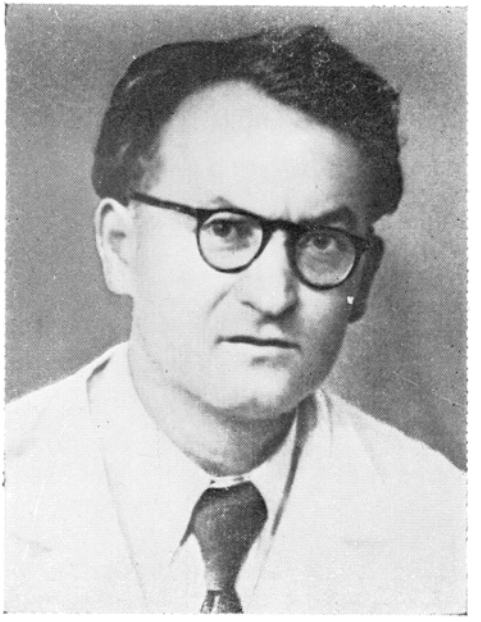
(4) development of principles for organizing a resuscitation service, training of reanimatologists, and publishing instructions and manuals.

The research program of the Laboratory largely involves the study of **general regularities in the extinction of vital functions in dying from different causes.** Relevant works performed over the years were primarily concerned with the functions, metabolism and structure of the central nervous system, particularly with the regularities of extinction and restoration of conditioned—reflex activity, and with respiration system, state of cardiovascular system and hemodynamics, general metabolic disorders. Specific periods in the process of dying were distinguished, and its principal stages were characterized. Besides generally characterizing and typifying the process of dying from bloodloss, electric shock, mechanical asphyxia, drowning, and CO poisoning, the Laboratory researchers:

(1) formulated and substantiated the concept of **clinical death;**

(2) showed the pecularity of the process involved in prolonged dying (prolonged bloodloss): special features of hemodynamic, metabolic and other changes during this kind of dying permitted to make more precise the concept of «**terminal state**», and to ascribe thereto third- and fourth-stage shock in addition to agony and clinical death, and to distinguish the stages of pathological process; by comparing general pathophysiological changes with neurological and pathomorphological ones the Laboratory researchers succeeded in establishing the most vulnerable link the circulatory system and internal organs; thus, grounds were provided for distinguishing somatic and cerebral death (not to mix up with brain death), which characterizes rapid dying;

(3) compared certain characteristics of protein and nucleic metabolism in the brain in rapid and slow dying, and revealed special features of brain pathology in prolonged hypotension that may cause severe and persistent neurologic disorders in patients who had suffered prolonged bloodloss or shock without clinical death;



Author of heart fibrillation theory and of principles of electrical defibrillation of the heart, Doctor of Med. Sci. N. L. Gurvich.

(4) obtained important data when analyzing the dying of the heart; these data formed the basis of the modern theory of ventricular fibrillation without which it would be impossible to determine the principles of and develop modern techniques for effective electrical defibrillation of the heart (N. L. Gurvich);

(5) initiated in recent years the study of the mechanisms of irreversible changes in high-voltage electric injury without ventricular fibrillation, and showed the pathology to be due, in this case, to a most severe intoxication of the crush-syndrome type;

(6) for a number of years, in collaboration with other institutions, have studied maximum permissible duration of high-voltage electric current to develop Soviet Industrial Standards (GOSTs), on which breaking devices in electric safety systems are based.

All these results were most significant in developing suitable resuscitation techniques.

The Laboratory has always shown basic interest for **studying post-resuscitation recovery processes.** Over the years it succeeded in covering, to a certain extent, all the aspects of post-resuscitation conditions. Valuable relevant materials were continuously accumulated for many years: however, the most important general outcome was the development about 15—16 years ago of the concept of **post-resuscitation disease.** Under that concept, the latter is a pathological

Experiment on electrical defibrillation of the heart (Academician of the USSR AMSci V. A. Negovsky, research workers M. S. Bogushevich and V. A. Vostrikov).

Head of the Group for biochemistry, Cand. Biol. Sci. L. V. Molchanova, and lab assistant G. V. Abanina.

state characteristic of an organism that had suffered a terminal state and subsequent resuscitation. The general meaning of the concept of post-resuscitation disease, increasingly recognized both in the USSR and abroad, is that pathological changes in a resuscitated organism are largely due not to dying per se, but to peculiar processes inherent in the post-resuscitation period. The concept opened new and vast horizons for improving prophylaxis and therapy of post-resuscitation disorders.

Among the main results of the study in the special trends the **neurochemical studies** started by M. I. Shuster and M. S. Gaevskaya from the Biochemical Group had major significance. The first stage of those investigations was summarized in a monograph by M. S. Gaevskaya (1963). It chiefly concerned extinction and restoration of energy metabolism in the brain. Subsequentily, M. S. Gaevskaya began studies on amino acid and protein metabolic pathology.

The development of neurochemical research led to the study of changes in the physico-chemical properties of protein and activity of brain hydrolases, and also of cell membrane permeability disorders. Studies of the pathology of brain protein-nucleic metabolism in the post-resuscitation period showed the depth and duration of metabolic disorders, particularly during resuscitation after prolonged hypovolemic hypotension. Neurochemical investigation confirmed that the post-resuscitation pathological process is long, and that a number of new pathological changes in brain metabolism developes in the post-resuscitation period, even 3—4 months after resuscitation.

The Group for Pathophysiology of the CNS likewise studied the peculiarities of post-resuscitation **changes in brain circulation**. Five basic stages were distinguished in the changes of cerebral circulation, and special attention was given to the study of delayed hypoperfusion and secondary hyperperfusion stages. Five types were also distinguished in the restoration of brain circulation, and their correlation with the gravity of post-resuscitation pathology of cerebral function was established.

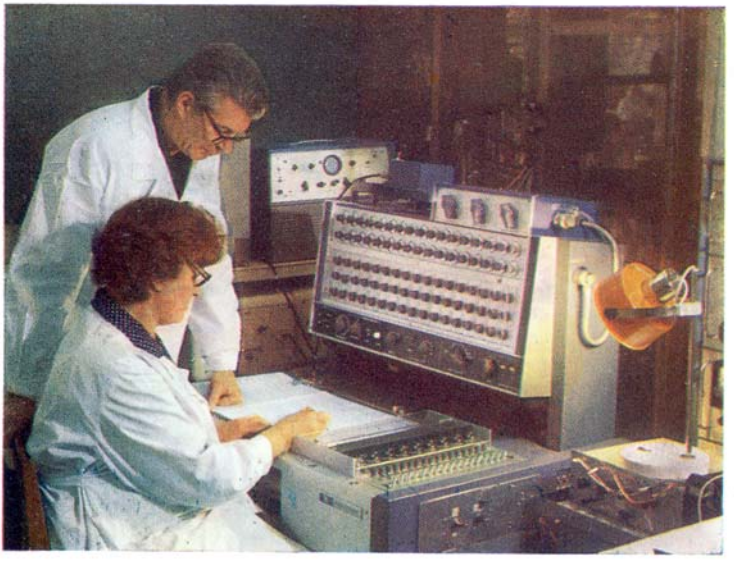
Special attention was also given to the study of the **role of brain edema** in post-resuscitation brain pathology. Experimental studies and the Laboratory's clinical experience have shown that brain edema in post-resuscitation conditions plays but a subordinate role and does not always determine the severity of post-resuscitation neurological disorders. Basing on these investigations, the use of dehydrating agents was sharply restricted in the treatment of patients who had suffered terminal states.

Major attention was also given to the study of CNS **functional pathology.**

The Laboratory's very first monograph (Negovsky, 1943) had already described the general regularities in CNS functions recovery after resuscitation. In subsequent years, post-resuscitation pathology of the central nervous system was the subject of many-sided investigations by the Laboratory's researchers who studied:

Study of general regularities of CNS recovery in resuscitated animals by method of conditioned reflexes (Cand. Med. Sci. T. Ya. Pavlova).

Head of the Group for CNS Pathophysiology A. M. Gurvich, Doctor Med. Sci, and S. V. Tolova, Senior Research Worker, Cand. Med. Sci.



(a) **general regularities in the recovery of higher nervous activity** (conditioned reflexes) in resuscitated animals; internal inhibition processes were found to be particularly susceptible to injury. At the same time, the simplest conditioned reflexes were found to be highly stable during dying;

(b) **general regularities in the extinction and recovery of background electric activity of the brain cortex and subcortical-stem regions, and of evoked potentials** during dying and resuscitation (experiment); two types and a number of variants of post-resuscitation dynamics of electric activity were distinguished; the time and quality factors of EEG recovery were found to correlate with the severity of brain damage. EEG became a permanent and reliable criterion to assess the course of the CNS recovery.

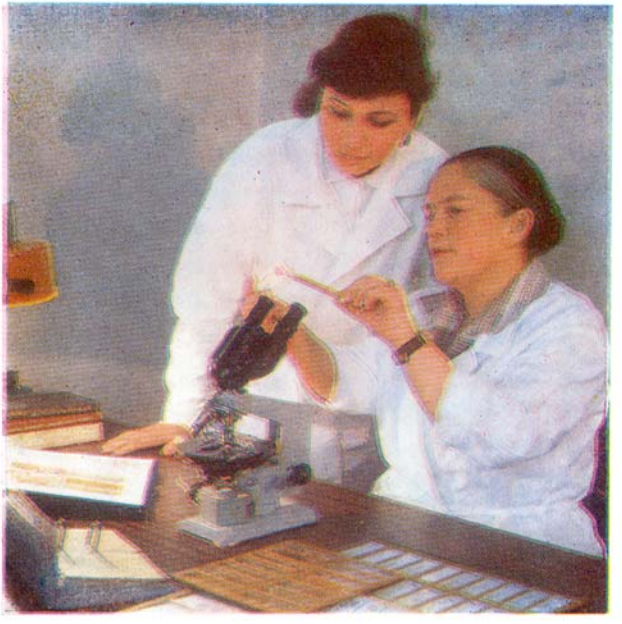
Electrophysiological studies of the CNS provided a number of basically new electrophysiological data which allowed to:

(1) model a rare type of post-resuscitation pathology, that of delayed post-hypoxic encephalopathy, and to begin studying its nature; (2) obtain original data on the nature of the so-called alphacoma in man; (3) prove the active involvement of neurophysiological processes in the mechanisms of post-resuscitation pathology. Other major results of this work included the development of an early prognosis of final results of the CNS recovery, and working out a system for the analysis of functional significance and mechanisms of action of various factors in the post-resuscitation process.

N. P. Romanova, a long-time Laboratory researcher, made a considerable contribution to elucidating the essence and import of pathological processes in the CNS. Her extensive histological studies helped to create principal, fundamental concepts on the post-resuscitation pathology of CNS both in humans and in animals. At present, the Laboratory applies modern quantitative histochemical research techniques (cytospectrophotometry and interferometry). Relevant studies have revealed certain histochemical correlates of delayed post-resuscitation encephalopathies. Another novel result was the description of certain quantitatively determinable compensatory changes in neurons.

Pathology of respiration has always occupied an important place in the Laboratory's research, both experimental and clinical. The researchers have completed studies on the changes in the respiratory act structure, described various types of restoration of that structure, and established the efficiency and functional significance of various types of respiratory recovery. Studies of respiration pathology in the post-resuscitation period afforded certain results, important both for the understanding of the mechanisms of external respiration disorders, and for the development of an optimum regimen for the artificial lung ventilation. Thus, data on optimum lung ventilation regimen have been obtained. At the same time large-volume lung ventilation with pronounced hypocapnia at the early stages of resuscitation, was proved to be beneficial. This was explained by

First chief of the Group for Pathomorphology, Senior Research Worker N. P. Romanova, Cand. Med. Sci.



Group for Pathomorphology (G. N. Mirotvorskaya, Doct. Med. Sci and lab assisstant E. V. Tarasova).

neurophysiological investigations devoted to the study of alpha-like post-resuscitation activity of the brain. The work permitted to pose the question on the «neurophysiological cost» of spontaneous respiration at the early stages of resuscitation. It was also important in that it grounded the need to perform artificial lung ventilation till the structure of the respiratory act becomes normal. Experimental studies of ALV and respiration were further developed in clinical investigations.

When studying post-resuscitation **changes in total and regional hemodynamics,** special attention was given to the nature of phasic changes in cardiac output, especially, to the phase of hyperdynamia and that of cardiac output decrease (2—9 hours after resuscitation). Data were obtained on the contribution of changes in blood rheologic properties to post-resuscitation hemodynamics: increased viscosity, higher hematocrit index, disorders of blood coagulation system, and changes in the myocardium and tonus of capacity and resistive vessels.

Important data on post-resuscitation hemodynamics pathology were obtained by the Clinical Department, chiefly when examining patients with severe hemorrhage and trauma. The dynamics of circulatory minute volume was found to have three versions which dictated different therapeutic tactics. A comprehensive study afforded valuable evidence on the perfusion of different tissues, especially of vital organs (lungs and liver), and on the presence of spasms or pareses of peripheral vessels, etc. The data which the clinic obtained on peculiarities in hemocoagulative disorders in the post-resuscitation period (acute fibrinolysis, DIC* syndrome), subsequently taking part in a number of post-resuscitation organ pathologies, present major interest. The Clinical department also studies the functional parameters of hemodynamics by means of modern devices, including computers, to use the obtained data for the improvement of patient management and to specify indications to certain interventions.

Problems concerning **oxygen metabolism and acid—base balance (ABB)** in the post-resuscitation period have been studied ever since the Laboratory was established (E. M. Smirenskaya). ABB disorders inherent in resuscitated animals, irrespective of the cause of dying, have been described, and acidosis was proved to play a role in post-resuscitation pathology (O. N. Bulanova). A number of cardinal facts was established in the clinic on studying ABB and oxygen metabolism dynamics, namely: (1) steadfast development in patients of secondary hypoxia in certain stages and under certain circumstances; (2) role of lung pathology in the development of that hypoxia, primarily of disturbed pulmonary circulation due to disorders in blood coagulative systems and lung vessel tonus; (3) role of blood trans-

---

*DIC — disseminated intravascular coagulation.

port function disorders; (4) possible development of delayed alkalosis in patients, and also its nature and significance. The works contained subtle differentiated analysis of the pathology of changes in ABB and the fluid-electrolyte balance in different sectors of the body and on different stages of pathological process, and had basic importance in developing the existing system of resuscitation units patients' management.

The Laboratory also studied the **state of vital internal organs: lungs, liver and kidneys,** to determine types, degrees and conditions of their possible damage. In recent years, the clinic has been giving major attention to conditions of development of the so-called «shock lungs», one of the main reasons why patients, who survived severe shock-induced terminal states, finally die. Mechanisms responsible for gas exchange disorders during the development of «shock lungs» have been revealed to a great extent: the role of a broken relationship between alveolar ventilation and blood flow in the lungs and true venous shunting of blood flow in the lungs.

For two decades, the Laboratory has **systematically studied the role of endocrine changes** in resuscitation pathology to reveal the dependence of outcome of resuscitation upon the state of the endocrine glands (adrenals, thyroid gland, sex glands, and pancreas), and prove that the state of endocrine functions substantially affects efficiency of resuscitation and the dynamics of restoration of vital functions. The types of post-resuscitation endocrine changes were established and their correlation with the severity of consequences of a sustained terminal state revealed. In the post-resuscitation period, the hormonal profile of the organism was shown to integrally reflect changes in neurovegetative control of endocrine gland activity, and hormone secretion, utilization, inactivation, and excretion.

By modelling favourable and unfavourable types of endocrine changes, the Laboratory researchers succeeded in noticeably affecting the course of the post-resuscitation process to prove that the endocrine system takes an active part in the mechanisms of post-resuscitation pathology.

A highly promising research aspect is the study of **factors of non-specific immunity** in resuscitated organisms. The work is important in connection with the sharply increased sensitivity of a resuscitated organism to infection.

Finally, another major trend in the work of the Laboratory has involved a system of studies that proved the highly significant pathogenic **role of endogenous intoxication** in the pathology of the post-resuscitation period. In the course of these studies, the plasma of resuscitated animals was shown to be toxic.

The significance of numerous pathogenic factors for post-resuscitation pathology was proved by the effect resulting from either removing or alleviating their action by therapeutic measures. The **experimental-therapeutic** research trend provided the following principal results:

1. The possibility of substantially prolonging clinical death (up to 2 hr) by preventive hypothermia was proved to be a reality.

2. It proved possible to prolong clinical death by applying therapeutic potentials involving a number of interventions that correct post-resuscitation pathological distrubances, namely:

(a) by correcting metabolic acidosis;

(b) by raising the arterial pressure level and by unloading the venous system in early resuscitation stages;

(c) by correcting blood rheologic disorders;

(d) by introducing a special set of endocrine preparations;

(e) by employing an artificial circulation apparatus.

But the following detoxication measures proved most effective: blood substitution and plasmapheresis; maintaining or restoration of liver detoxication potential; washing of cerebral and all other vessels during clinical death with colloid solutions under normo- and hypothermia; extracorporeal detoxication by activated carbon and donor--provided artificial circulation improved for the ends of resuscitation by N. P. Adamenko (A. A. Bogomolets Institute of Physiology, the Ukrainian SSR Academy of Sciences). The last three detoxication methods proved especially effective by permitting to prolong clinical death due to hemorrhage to 16 min — when washing with hypothermic solution with subsequent warming, and to 12 min-when using extracorporeal hemosorption; in regard to drowning in salt water, donor-provided artificial circulation allowed to prolong clinical death to 20—21 min, occasionally to 27 min. Even simpler methods, included in the complex of resuscitation measures, as correction of rheologic disorders, or bigger respiratory volumes of ALV, presently used in the Laboratory, ensure the recovery of neurological functions after 15—17 min of circulatory arrest due to electric injury (heart fibrillation).

The basic significance of these studies is that they prove the concept of pathologic changes developing in the postresuscitation period that can be managed, and that the true limits of clinical death are still to be established.

Thus, basic investigations performed over the years both in clinic and in experiment allowed to form a well-balanced conception of principal processes in a dying or reviving organism and opened wide prospects both for further studies and for the improvement of therapeutic interventions.

From the very start, the **Laboratory's activity has been oriented to medical practice,** with wich it is very closely related. Over the years, the Clinical Department and the Mobile Centre have accumulated considerable experience. Both have developed numerous principles for organizing resuscitation units and for treating patients in terminal states of various etiology. It is in the Laboratory's Resuscitation Department and the Mobile Centre that a new medical speciality has taken shape: a physician-reanimatologist (resuscitologist) who, unlike an anesthesiologist, is fully responsible for the management of a patient. It is in the Laboratory that, owing to the unity of

Workers of the Group for Experimental Therapy A. V. Volkov, V. I. Soboleva, I. S. Novoderzhkina, I. E. Trubina — Cands Med. Sci., lab assistants S. V. Malakhova and T. V. Gavrilova.

In the Resuscitation Department of the Moscow Municipal S. P. Boskin Clinical Hospital, patient rounds: Academician of the USSR AMSci V. A. Negovsky, Senior Research Worker V. L. Kassil, MD, and G. N. Meshcheryakov, post-graduate student.

theory and practice, the Clinico-Pathophysiological Laboratory has been set up as an inseparable part of the Resuscitation Department, which made possible research in clinical conditions. This Laboratory has made a great contribution to the understanding of the essence of resuscitation pathology, particularly in severe hemorrhage and trauma, having promoted the development of the existing set of therapeutic measures.

Systematic research by members of the Clinical Group at the Resuscitation Department permitted not only to introduce into practice the results of experimental sudies, but also to obtain new facts unobtainable in experiment, that considerably expand our knowledge of resuscitation pathology in man. As a result, already in 1966 it became possible for the Laboratory to publish the first Soviet Manual on Resuscitation.

Both theory and practice have shown that the **goal of clinical reanimatology** is not only and not so much resuscitation **per se,** but rather **prevention of clinical death and treatment of patients in post-resusciation states** lasting many days, and even weeks.

Already at early stages, the Resuscitation Department specified the role of the volume of blood loss in the pathogenesis of traumatic shock, and worked out a scheme of transfusion therapy, which in those years contradicted routine practice. A new approach was developed for treating injuries combined with cranial-cerebral traumas, and the traditional unreserved use of dehydration therapy was critically revised. A method of forced diuresis in barbiturate poisoning was introduced into practice in USSR at the same time, a procedure was developed for treating patients with severe forms of acetic acid poisoning.

The Laboratory's Clinical Department has developed a basically novel approach to treatment of metabolic alkalosis, and a system of measures for prevention and therapy of the «shock lung». It has also introduced methods of hemosorption and ultrafiltration and completed the study of other questions of pathogenic therapy of terminal and post-terminal states.

The Clinical Department deserves special mention also for elaborating concrete instructions on optimization of artificial lung ventilation and indications to its continuation in the post-operation period in patients of resuscitation units. Indications were specified for the selection of the basic parameters of ALV in acute respiratory insufficiency of various etiology; for the first time, hyperventilation was shown to be advisable for adapting the patient to the respirator, and the rejection of pharmacological suppression of spontaneous breathing was grounded; the Laboratory researchers also completed a study of the method of ALV with constant positive pressure and established the indications and contraindications thereto. For the first time criteria were suggested for early prognosis of complications and outcome of treatment in patients with acute respiratory insufficiency; at the same time, tech-

Combined use of extracorporeal hemosorption and separate ultrafiltration in clinic. Research worker I. O. Zaks, post-graduate student O. A. Kharkovoy, and internisi G. A. Konovalov.

In the Resuscitation Department of the Hospital. Chief, S. I. Ivanov, and G. V. Alekseeva, neuropathologist.

niques were developed for preventing and treating those complications.

Special mention should be made of the Laboratory's participation in devising methods for electroimpulse treatment of cardiac arrhythmia; as a result, V. A. Negovsky and N. L. Gurvich, together with researchers from the A. V. Vishnevsky Institute of Surgery, USSR Academy of Medical Sciences, won a second USSR State Prize (for 1970).

In recent years, a new trend aimed at **utilizing modern mathematical methods and computers** was started to automate some major aspects in the work of the Resuscitation Department. Comprehensive investigations conducted in co-operation with the USSR Research Centre for Computer Technology, the USSR Research and Experimental Institute for Medical Equipment, and some other institutions, resulted in the development of one of the first Soviet integrated data system in the Laboratory's Clinical Department at the Moscow S. P. Botkin Hospital. The system devices allow to perform work impracticable without a computer. At present, studies of circulation, respiration and the central nervous system have become possible not only for scientific purposes, but for treatment as well, directly in the wards. The system permits to simultaneously record several physiological processes, introduce corresponding data into a computer, and practically immediately obtain a volume of information requiring in usual conditions 3—4 hours of meticulous work by skilled specialists. New possibilities for research work and analysis of case records have appeared.

The following figures characterize the efficiency of the Resuscitation Department. During 22 years of its existence, it admitted 12.475 patients in terminal states caused by different reasons: bloodloss, trauma, eclampsia, peritonitis, myocardial infarction, intoxication, and bronchial asthma, and 8.221 (65.9%) returned to life and work. Among those admitted at last on decades, 350 were in the state of clinical death. Improved resuscitation methods and continued treatment in the post-resuscitation period ware instrumental in creasing the number of patients who recovered after clinical death, chiefly oustide the operation room. Except for cases of injuries incompatible with life, an average of 35 % of the patients recovered after clinical death. Over the years, the efficiency of treatment of clinical death increased from 21.4 to 37.9 %. The Laboratory's system of rehabilitating treatment has reduced to minimum post-resuscitation psychoneurological complications and the degree of psychoneurologic invalidism.

Main causes of terminal states in patients treated by the Mobile Centre physicians were massive blood-loss during delivery, eclampsia, peritonitis, sepsis, myocardial infarction with cardiac rhythm disorders and cardiogenic shock, lung edema, respiratory insufficiency, and comas of various etiology. By the end of 1981, a total of 9.897 patients were treated, 6.633 (69 %) of them having been discharged after recovery. Among the latter, 152 had suffered clinical death, and 47 (30 %) of them recovered, which is rather a good result accounting for the given conditions.

Being a unique institution of its kind, the Resuscitation Mobile Centre disposes of observations, analysis of which has allowed to determine the peculiarities of patient management in massive bloodloss, and suitable therapy and resuscitation tactics in coagulopathic hemorrhages during delivery. The Centre's materials were used to specify the therapeutic and resuscitation tactics in patients with obstetric and gynecological pathologies. Great experience was also accumulated in treating cardiac arrhythmias, which made possible the development of methods of electroimpulse therapy in critically ill patients. The use of the methods gives an almost 100 % effect. For the first time in the work of mobile resuscitation teams, cardioversion was treated with electronarcosis. The technique of its application in these conditions has been developed by centre's researchers.

The Centre's experience in research and practice allowed to expand the possibilities for and indications to the transfer of patients with impaired vital functions to specialized units for performing hemodia-

lysis, extracorporeal circulation, and prolonged ALV; for transporting patients previously regarded untransportable; and for working out a safe procedure of connecting patients to ALV with continued anesthesia and intravenous infusions in the ambulance. A total of about 900 patients were transported, and none died on the way.

SCIENTIFIC PUBLICATIONS

The Laboratory's research work is reflected in 19 monographs, 16 brochures, 9 volumes of collected articles, 1.300 scientific papers, and 76 theses, including 16 doctorates. The Laboratory workers were initiators and active participants in developing first Soviet apparatuses for artificial lung ventilation and impulse defibrillators. They won two USSR State Prizes and received ten patents. They were also awarded several medals and diplomas of the USSR Exhibition of Economic Achievements.

SCIENTIFIC GUIDANCE AND ORGANIZATION WORK

The Laboratory published 9 instructive letters and instructions, and also **Fundamentals of Reanimatology,** a manual that has already run 3 editions. Since 1958, the Laboratory's researchers have regularly delivered lectures on current problems of reanimatology, these lectures are designed to improve the skills of physicians assigned to resuscitation and intensive care units. At present, they lecture at advanced courses * for anesthesiologists and reanimatologists. The Laboratory trains post-graduates as specialists in reanimatology.

Since 1976, the Research Laboratory of General Reanimatology of the USSR AMSci., heads two Soviet National Research Committees: «Critical and Terminal States» and «Fundamentals of Reanimatology». Prospective research plans have been developed for both subjects, and over 40 Soviet research institutions and medical institutes took part in the work.

The Laboratory has sponsored 6 conferences and symposiums, 4 of them – international.

INTERNATIONAL CONTACTS

The Laboratory has stable and continually developing relations with scientists and research centres in both socialist and capitalist countries. The relations are promoted through participation in conferences, congresses and symposiums abroad; through participation of foreign scientists in meetings organised by the Laboratory in the USSR; and through mutual visits to research centres, organisation of joint research, and exchange of reprints.

The Laboratory maintains its closest contacts with Poland and the German Democratic Republic through regular exchange of research workers. There are also contacts with Bulgaria, Czechoslovakia, and Romania. In socialist countries, contacts are most close with Prof. M. Mossakowsky, Corresponding Member, Polish Academy of Sciences; Prof W. Jurczyk (Poland), Prof. M. Meyer (GDR), Prof. U. Strahl (GDR), Prof. S. Saev (Bulgaria), Prof. E. Stoyanov (Bulgaria). In general, relations with scientists from capitalist countries are also quite extensive. Fruitful contacts are

---

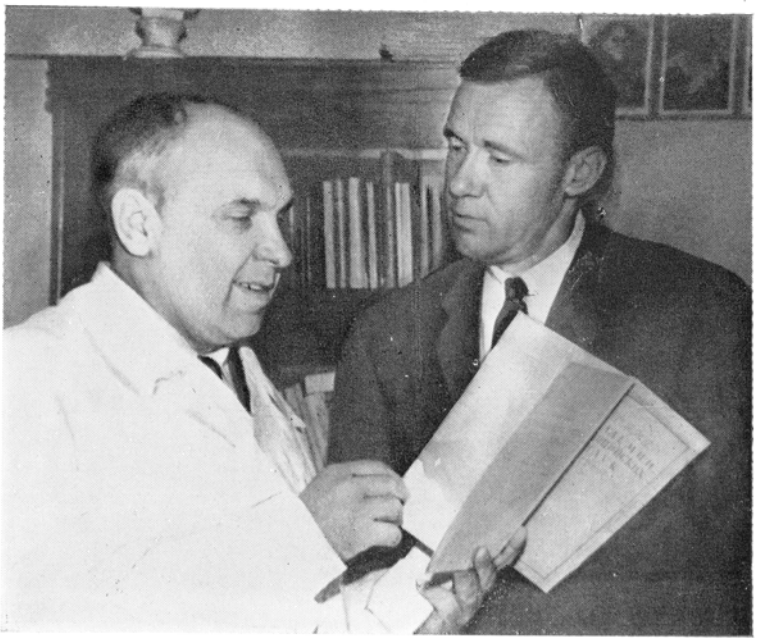
* The Central Institute for Advanced Training of Physicians, the Chair of Anesthesiology and Reanimatology.

International Symposium on Postresuscitation Pathology of the Brain, Moscow, 1978.

Foreign scientists in the Laboratory.

Academician of the USSR AMSci. V. A. Negovsky and Professor P. Safar (USA).

Academician of the USSR AMSci. V. A. Negovsky and Professor H. Stephenson (USA).



maintained with Prof. P. Safar, Prof. H. Stephenson, Prof. R. White and Prof. I. Klatzo (the USA); Prof. K.-A. Hossmann and Prof. H. Hirsch (West Germany); Prof. O. Norlander, Prof. B. Siesjö, and Prof. D. Ingvar (Sweden); Prof. H. Laborit and Prof. A. Milhaud (France); Prof. G. Giron and Prof. C. Manni (Italy); Prof. P. Prior (Great Britain); and many others.

V. A. Negovsky, Head of the Laboratory, has been elected honourary member of the Polish Society of Surgeons and Anesthesiologists; Doctor **honoris causa,** Medical Academy in Poznan; Corresponding Member, Academy of Sciences and Literature in Toulouse, France; and Corresponding Member of the Society of Clinical Medicine, GDR. The research workers of the Laboratory have published 153 articles and 12 monographs abroad, and V. A. Negovsky's books have been published in Poland, Yugoslavia, GDR, Romania, Holland, the USA, West Germany, Italy, Great Britain, and Spain.

Doctor of med. Sci. **A. M. Gurvitch**

MONOGRAPHS

Gaevskaya M. S. Biochemistry of the Brain in Dying and Resuscitation of the Organism. — Moscow: Medgiz, 1963. — 206 p. (in Russian). English publicatior: New York, 1964.

Gurvitch A. M. Electric Activity of Dying and Recovering Brain. — Moscow: Meditsina, 1966. — 210 p. (in Russian).

Gurvitch N. L. Fibrillation and Defibrillation of the Heart. — Moscow: Medgiz, 1957. — 252 p. (in Russian).

Gurvitch N. L. Basic Principles of Heart Defibrillation. — Moscow: Meditsina, 1975. — 232 p. (in Russian).

Kassil V. L., Ruda M. Ya. A Guide to Intensive Therapy in internal diseases. — Moscow: Meditsina, 1976. — 224 p. (in Russian); Kiev: Zdorov'ya, 1979. — 213 p. (in Ukranian).

Kassil V. L., Ryabova N. M. Artificial Lung Ventilation in Reanimatology. — Moscow: Meditsina, 1977. — 238 p. (in Russian).

Negovsky V. A. Restoration of Vital Functions of the Organism in Agony or Clinical Death. — Moscow: Medgiz, 1943. — 170 p. (in Russian).— English publication in **Amer. Rev. Sov. Med.**, 1945, vol. 2, 3.

Negovsky V. A. Experience in Treatment of Agonal States and Clinical Death in an Army Region. — Moscow: Medgiz, 1945. — 94 p. (in Russian).

Negovsky V. A. Agony and Clinical Death: Pathophysiology and Therapy. — Moscow: Medgiz, 1954. — 254 p. (in Russian); Romanian edition: Bucharest, 1955; Polish edition: Warsaw, 1956; German edition: Berlin, 1959; Dutch edition (certain chapters), 1954.

Negovsky V. A. Artificial Respiration Devices (Practitioner's library). — Moscow: Medgiz, 1959, 80 p. (in Russian).

Negovsky V. A. Resuscitation of the Organism and Artificial Hypothermia. — Moscow: Medgiz, 1960. — 302 p. (in Russian); English edition (revised and enlarged): New York, 1962, and London, 1962; Spanish edition (revised and updated): Madrid, 1967.

Negovsky V. A. Indirect Heart Massage and Expiratory Artificial Ventilation. — Moscow: Sovetskaya Rossiya. 1966. — 216 p. (in Russian).

Negovsky V. A. (Ed.). Fundamentals of Reanimatology — Moscow: Meditsina, 1966. — 397 p. (in Russian); Serbo-Croatian edition: Belgrade-Zagreb, 1970.

Negovsky V. A. (Ed.) Fundamentals of Reanimatology. Second edition, revised and updated. — Moscow: Meditsina, 1975. — 360 p. (in Russian). Third edition, revised and updated: Tashkent, Meditsina, 1977, 600 p. (in Russian).

Negovsky V. A. Urgent Problems of Reanimatology. — Moscow: Meditsina, 1971. — 215 p. (in Russian).

Negovsky V. A., Gurvitch A. M., Zolotokrylina E. S. Post-resuscitation Disease. — Moscow: Meditsina, 1979. — 383 p. (in Russian), 2nd ed. — revised and completed, Elsevier, Holland, 1983 (in English).

VOLUMES OF COLLECTED ARTICLES

Clinical Pathophysiology of Terminal States. Abstracts of Papers Delivered at the Symposium. December 6—8, 1973. — Moscow. — 168 p. (in Russian).

Current Problems of Experimental and Clinical Reanimatology. Materials of the Visiting Session of the Laboratory of Experimental Physiology for Resuscitation of the Organism, USSR Academy of Medical Sciences. May 13—15, 1974; Volgograd, 1974, 84 p. (in Russian).

Current Problems of Reanimatology (for the 70-th birthday of Academician V. A. Negovsky, USSR Academy of Medical Sciences). Eds. P. D. Gorizontov and A. M. Gurvitch. — Moscow: Meditsina, 1980 (in Russian).

Current Problems of Reanimatology and Hypothermia. Materials of the Symposium on the Use of Deep Hypothermia in Terminal States. September 15—19, 1964 Ed. by Prof. V. A. Negovsky. — Moscow: Meditsina, 1964, 142 p.; English edition; New York, 1965.

International Symposium on **Postresuscitation Pathology of the Brain.** Moscow, November 27 — December 1, 1978. Abstracts of Papers. — Moscow, 1978. — 184 p. (in Russian).

Problems of Reanimatology (Clinical reanimatology). A Scientific Review. Ed. by V. A. Negovsky. — Moscow, 1969. — 162 p. 'USSR Ministry of Health and VINITI) (in Russian).

Recovery Period Following Resuscitation. Pathophysiology and Therapy in Experiment and in Clinic. Transactions of the Symposium, November 25—28, 1968. — Moscow: Sovetskaya Rossiya, 1970. — 327 p. (Laboratory for Experimental Physiology of Resuscitation of an Organism, the USSR Academy of Medical Sciences); (in Russian).

Second Soviet National Conference on the Pathology and Therapy of Terminal States. December 7—9. 1961. Abstracts of Papers. — Moscow: Medgiz, 1961, 88 p. (Sponsors: USSR Ministry of Health and USSR Academy of Medical Sciences); (in Russian).

Transactions of the Conference on the Pathophysiology and Therapy of Terminal States in the Clinical Treatment and Practice of Emergency Medical Care. December 10—12, 1952. — Moscow, 1954. — 210 p. (in Russian).

Заказ № 1228 Типография № 32

Meditsina