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Fifty years of the Institute of General Reanimatology of the USSR Academy of Medical Sciences

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Life is the greatest gift; we must safeguard it and struggle for its revival even when it is extinguishing or has just extinguished. Reanimatology is a science dealing with the regularities of dying and reviving, and the prevention and therapy of terminal states. Experimental and clinical study of dying and resuscitation has made it possible to avoid purely empirical research. Earlier development of this science in the USSR has objective historical motives, one of which is the general humanistic tendency of Soviet philosophy, literature, science, and culture. In 1961 at the International Congress of Traumatologists in Budapest, I proposed to call this science reanimatology (from Latin "re" meaning again, and "animare," meaning to resuscitate).

We often say that clinical death is the final stage of dying, and yet resuscitation is sometimes possible. At the same time, clinical death is characterized by so few properties inherent in life that it would be more correct to call clinical death a transitional state from life to death. That clinical death is no longer life but it is not yet death would seem contradictory. There is the struggle between two opposite factors aimed at the extinction of vital functions and combat against this extinction. The task of reanimatology is to reveal the processes leading to dying, as well as those leading to the preservation of life and resistance to dying. To prevent a severe terminal state, to reverse the process of dying at the earliest stage of its development, and to prevent clinical death are the main tasks of reanimatology.

An important development in reanimatology was the formation of the concept of postresuscitation disease, first elaborated by our Institute. After restoration of cardiac activity and respiration, the patient undergoes a specific state which is currently called "a disease of resuscitated organism" or "postresuscitation disease." The elaboration and use of better methods to treat this disease would involve time-consuming research, however necessary and promising. Reanimatology embraces not only problems of resuscitative therapy but also rehabilitation therapy. It involves a special philosophical and methodological analysis of the problems, as indicative of their significance.

As a young physician in the spring of 1936, I wrote a letter to the USSR Sovnarcom (now the Council of Ministers of the USSR) asking for a small staff and place to start studying dying and revival. My request was granted. The laboratory (tiny in the beginning, consisting of only seven people) was organized at the Institute of Neurosurgery, which was then headed by academician N. N. Burdenko. In 1948, the laboratory became an independent body of the Academy of Medical Sciences. In March 1985, in accordance with a decision of the Ministry of Health of the USSR, the laboratory was reorganized as part of the Institute of General Reanimatology of the USSR Academy of Medical Sciences. Our Party and government have always given us support.

Since there were no unified theoretical concepts in reanimatology in the 1940s, many new problems had to be tackled. It is not accidental that the first papers published by the laboratory concerned the extinction and restoration of respiration as well as disturbed metabolic functions during dying and resuscitation. Yet, as early as 1943, a monograph (1) by a Soviet publishing house pertained to the regularities of dying and CNS restoration. This first monograph by our laboratory (2) was translated into English and published in an American journal. During those first years, we mainly restored cardiac activity by centripetal (in the direction of the heart) intra-arterial pumping of blood with epinephrine and glucose under a certain pressure. The principles for this were worked out by A. A. Kulyabko and F. A. Andreev. To restore respiration, we forced air into the lungs using primitive bellows and a primitive metallic intubator inserted into the trachea through the mouth.

During World War II, we asked the Chief Military and Medical Department of the Ministry of Defense to

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send several associates of the laboratory to the front to perform resuscitation. Although occasional successful cases of resuscitation by one or another method (most often by heart massage) had been published, they were outnumbered by failures. Even successful resuscitation as a rule was not assessed from the point of view of the revived brain. On the front, where we resorted to methods previously used in experiments, a number of successive, tormenting failures befell us. Then, we succeeded in restoring all bodily functions including higher nervous activity and were able to discharge wounded soldiers from the hospital in good condition. This work was compiled and published as a book (2). Our experience at the front convinced us that resuscitation must be performed not from case to case but systematically in all dying patients who have no irreversible trauma of the vital organs.

Soon after our return from the front after the war, we set up a small resuscitation department, first at the surgical clinic of academician A. N. Bakulev, then in the Fourth City Hospital, and finally in the hospital named after S. P. Botkin. The successes in elaborating theoretical problems of resuscitation were marked by the first State prize received in 1970.

For many years, the Institute has been investigating the bioelectric activity of the heart during dying and resuscitation. In particular, since the 1940s, our scientists have studied the fibrillation and defibrillation of the ventricles. The theory of ventricular fibrillation created by N. L. Gurvitch (3) is based on the circuit of excitation stimulated by specific peculiarities of the myocardial morphology and the conduction system. From this theory, a basically new method of transthoracic electrical defibrillation of the heart was worked out. This involves the synchronization of excitation by a strong electric impulse induced on the heart. Gurvitch helped to design the first commercial defibrillators which appeared in the USSR in the early 1950s.

Because of the negative effects of electric impulse therapy on the myocardium, ways of lowering the dose of defibrillating charge while preserving its efficacy have been sought (4). A method was found and used as a basis for creating defibrillators generating bipolar impulses.

We (1, 5) showed that expiratory artificial respiration usually promoted stable restoration of respiratory functions. The sooner respiration is restored, the more favorable is resuscitation. The respiratory center is similar to a pacemaker for the cortex of the brain: excitation from it spreads to the higher parts of the brain to awaken them. Initially, these pulses are likely to pass through the reticular formation to the cortex, as the subcortex is restored. These mechanisms should be thoroughly studied in the future.

Using electrophysiologic techniques, Tolova (6) showed that, at terminal stages of dying and the initial stages of resuscitation during agonal respiration (gasping), the reciprocal relations between the inspiratory and expiratory centers are disturbed. As a result, the expiratory muscles contract simultaneously with the inspiratory and additional respiratory muscles during inhalation, thus reducing its depth and making agonal respiration ineffective.

During the postresuscitation period, regardless of the cause and duration of clinical death, the respiratory center is the medulla oblongata. The activity of the expiratory center is restored later, and the afferent vagal pulses stimulate the expiratory center, thus promoting the restoration of active exhalation and, therefore, more effective and economical respiration (as far as energy consumption is concerned).

Whether it is expedient to depress or stimulate the reviving nervous system is not yet known. Our earlier studies (7) showed that barbiturates at certain stages of resuscitation had a somewhat positive effect. Yet, recent investigations (8) showed that under both experimental and clinical conditions, barbiturates as a rule might be harmful if the brain has sustained severe hypoxia, i.e., clinical death. At the same time, it is doubtful whether barbiturates used before clinical death (for the sake of prevention) or postresuscitation are useful. Research involving the use of barbiturates in patients after clinical death are now being carried out by Safar and colleagues. The use of stimulants in the resuscitation periods is only in the initial stage of investigation.

In 1953, Gurvitch (9) studied various problems concerning postresuscitation brain pathology. He described the dynamics of restoration of the electric activity of the brain and electrocorticogram-based indices for early prognosis of postresuscitation restoration of the CNS. Also studied were the general dynamics of restoration of cerebral blood circulation during resuscitation and the nature of postresuscitation alpha-coma. Studies on the pathogenesis and treatment of shock lungs as well as rational infusion therapy in reanimation patients were carried out by Zolotokrylina (10). Studies of endocrine disturbances and their correction in dying and resuscitation have been conducted for many years in our Institute by Volkov (11).

Early investigations using a model of 2 to 4 min of clinical death caused by acute blood loss showed that, during dying, conditioned reflexes disappear sooner than unconditioned ones, while upon resuscitation, the reflectory activity of the brain is restored in reverse order. During the postresuscitation period, revived dogs showed such disturbances of higher nervous activity as complete absence of conditioned reflexes, their sharp decrease or perversion, the absence of responses to certain signals, disturbed differentiation, the appearance of hypnotic phases and other symptoms caused by

lowered working capacity of the cortical cells, and disturbed correlation between excitation and inhibition. Active inner inhibition suffers to a greater extent and is restored later than the process of excitation.

Recently, our Institute in collaboration with the Institute of Higher Nervous Activity and Neurophysiology of the USSR Academy of Sciences headed by P. V. Simonov and the Department of Pathological Physiology of Tselinograd Medical Institute headed by V. G. Korpachev obtained new data on the nature of disturbed brain function during the postresuscitation period. It was revealed that disturbances of conditioned reflexes in resuscitated animals persist after neurologic restoration while electrophysiologic indices of cortical activity normalize. Quantitative characteristics of the alimentary instrumental reflex trained in resuscitated rats remain disturbed for several months, whereas the reflexes trained before dying are restored within 1 to 2 wk (12).

Tajibaeva (13) showed that electric stimulation of the lateral pre-optic area related to the positive supporting structures of the limbic system promotes, during the early postresuscitation period, quicker restoration of the self-stimulation reaction and provokes a positive effect on the restorative process.

Research has shown that, along with the reduced energy potential in the brain tissue when dying, there is also inhibition of biosynthesis and lowering of RNA content (14). Hydrolytic enzymes of the subcellular structures of brain tissue are activated, the physicochemical properties of protein molecules change, and generalized disturbances of the molecular structure occur (15). During postresuscitation, the most frequent metabolic disturbances are the permeability of intracellular membranes leading to numerous cerebral pathologic changes (16). Significant changes were revealed in the adenylate cyclase system connected with the receptors and participating in the transformation of the signal transmitted by hormones and neuromediators. A lowering of cAMP caused by neuroendocrine disturbances, changes in monoamine metabolism, as well as reduced sensitivity of the receptors to catecholamines, play important roles along with other metabolic disturbances in postresuscitation encephalopathy (17).

Over the past 10 to 15 yr, attention has been given to toxemia in postresuscitation disease and prospects for combatting it. Russian pathophysiologists A. A. Kulyabko (1902) and later, I. P. Mikhailovsky (1914, 1925) pointed to the importance of autointoxication during resuscitation. Hypoxia and autointoxication during terminal states lead to accumulation of toxic products. The severity of endogenous intoxication and its duration in the postresuscitative period depend on the severity of the terminal state, even when intoxication persists for hours and sometimes days (18, 19). Lately, good results have been obtained with hemoperfusion (hemabsorption), which is not only simple and available, but also temporarily replaces the detoxification systems.

Naturally, restoration of adequate blood volume is necessary. Particularly important is the prevention of prolonged hypotension during dying so as to restore CNS functions even after the shortest period of clinical death. Without preliminary improvement of blood circulation (for instance, by heart massage), defibrillation of the myocardium usually proves ineffective.

Lately, attention has been given to the diagnosis of heart failure, assessment of the functional status, and compensatory reserves of the myocardium in patients after terminal states. Studies (20) have shown that in most of these patients indices of myocardial pump function had no previous critical values, whereas variables reflecting myocardial contractile activity significantly decreased. According to the data obtained, functional myocardial disturbances of the left and right heart are unambiguous, being dependent on the type of pathology and degree of pulmonary hypertension.

Early turn-off of artificial respiration, especially when the cortex has not yet fully regained its functions, is a new hypoxic attack on the reviving brain, worsening the forecast of resuscitation and delaying restoration of brain function. EEG changes, especially a shift to slow oscillations, show earlier and greater reliability than changes in hemodynamics, pneumogram, and acid-base balance indicating that ventilation should be shut down (21).

During the postresuscitative period, we must control heart function, respiration, and metabolism, and, most important, actively restore brain function. The restoration of other organs and systems and the normalization of metabolic functions are all directed at reviving the brain. Otherwise, resuscitation becomes senseless. A peculiarity of postresuscitation disease is the absence of adequate cortical regulation of physiologic functions. After having sustained hypoxia during dying (especially in clinical death), the not fully resuscitated cortex cannot exert its regulatory action for a long time, and at the beginning of the restorative period, restore the somatic functions. This necessitates early therapeutic measures capable of preventing or alleviating postresuscitation encephalopathy, and accelerating psychoneurologic stimulation and social readaptation.

The sooner the cortex and higher CNS functions are restored, the sooner the patient comes out of the comatose state with fewer complications. If cortical functions are restored more slowly, the disturbed somatic functions normalize more slowly, leading to greater complications, such as septic states. Alekseeva (21, 22) demonstrated a direct correlation between the duration of brain disturbances in comatose patients and the

degree of their psychoneurologic decompensation at 6 to 12 months. The longer the period of unconsciousness, the longer the period required to reverse the pathologic processes. Thus, disturbed consciousness up to 7 days in patients after circulatory arrest (as on the operating table) or massive blood loss and prolonged hypotension leads to CNS restoration in 50% of cases. If consciousness remains disturbed for over 3 wk, the patients may develop a marked psychoneurologic deficit and deep dementia or "Apallic syndrome."

Throughout the existence of our Institute, we have tried to establish close ties with scientists abroad. Reanimatology is so complex that its success can only be achieved by joint efforts of scientists all over the world. Thus, we have joined research with academician M. Mossakowsky, Prof. W. Jurczyk and their colleagues (Poland), Prof. M. Meyer, Dr. U. Strahl and their colleagues (East Germany), Profs. C. Manni, G. Giron, R. Vizioli, and their colleagues (Italy), Profs. O. Norlander, M. Holmdahl and their associates (Sweden), Profs. P. Safar and H. Stephenson (USA), and some others.

Our struggle for saving a life makes sense only if we live in peace, and prevent nuclear and space wars. Our recent disaster at the Chernobyl nuclear power station is comparable with what a nuclear war could bring about, which would totally annihilate humanity. As J. Galbrait well put it: "Under these conditions no one will distinguish between the ashes of capitalist countries from those of socialist countries" (23).

Studies of CNS inhibition and excitation are likely to remain the key problems related to brain neurodynamics. It is still crucial to search for ways to prevent or sharply decrease encephalopathies in patients after terminal states.

Studies of dying directed at combatting unjustified death have specific traits of humanism and love for life. Great is the grief of people who have lost relatives or loved ones, and the thought that some of them could be saved fills a reanimatologist with optimism and faith in the significance of their studies. According to the great Russian scientist, K. E. Tsiolkovsky, "Earth is the cradle of humanity, but humanity cannot stay in the cradle forever." We have witnessed the birth of cosmonautics and a Soviet citizen, Yu. A. Gagarin, was the first to fly in space. Since the beginning, man has always known death but at one time, man stopped regarding death as totally unmanageable. As reanimatology develops, the number of preventable deaths grow as we are able to treat diseases successfully.

I am delighted that young physicians and scientists with new ideas, vigor, and steadfastness take a keen interest in reanimatology; this is important to the successful development of our young science. Undoubtedly, many mysteries of dying and reviving will be solved by our joint efforts. As a scientist, I would like this medical field to be broadened and deepened. Life is our greatest gift. We must continue to struggle for people standing on the brink of life and death. Here lie the meaning and the aim of our science (24).

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