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Creation of Foundations for Emergency Clinical Toxicology Service in Russia

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ABSTRACT The creation of the organizational foundations of clinical toxicology began after its separation in the first half of the 20th century from forensic medicine, pharmacology, and military and industrial toxicology. In this, the research started in the therapeutic clinic of the N.V. Sklifosovsky Research Institute for Emergency Medicine was important, which led to the opening of the country's first toxicological department at the Institute and made it possible to resolve acute poisoning (AP) issues at a new level. The obvious successes achieved in this direction by the employees of the department served as a prerequisite for the creation of Republican and All-Union AP treatment centers on the basis of the N.V. Sklifosovsky Institute, where employees began actively work on the preparation of relevant regulatory documents and the organization of toxicological centers (departments) in the regions. As a result, by the end of the twentieth century, the foundation of the toxicological service was created in the Russian Federation — a network of 44 centers (departments) for AP treatment in 41 regions, which today provide specialized assistance to the population of 50% of the territory of the Russian Federation and serves as the basis for the implementation of advanced achievements in this area.

An outstanding role in the formation of clinical toxicology as a new direction in clinical medicine and the creation of a scientific school of clinical toxicologists belongs to E.A. Luzhnikov, member of RAS.

CONCLUSION Creation of the organizational foundations of urgent clinical toxicology and its formation as an independent scientific and practical direction in medicine, in which a significant contribution belongs to the staff of N.V. Sklifosovsky Research Institute for Emergency Medicine, are closely related to scientific and practical achievements in this area, the prompt response of specialists to the toxicological situation in the country, as well as adoption of the experience gained in the course of organizational and information and advisory activities. At the same time, timely preparation and publication of legal and regulatory documents adjusting practical work in this area are of particular importance.

Keywords: acute poisoning, organization, directive materials

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EH – emergency hospital
CCH – city clinical hospital
ICPC – Information and Consultative Poison Center
HC – Health Committee
MAD – methods of artificial detoxification of the body
MRIEM – Moscow Research Institute of Epidemiology and Microbiology
MSU – medical and sanitary unit
SPTC – Scientific and Practical Toxicological Center
AP – acute poisoning
RAMS – Russian Academy of Medical Sciences
RAS – Russian Academy of Sciences
RCTAP – Republican Center for the Treatment of Acute Poisoning
EMA – emergency medical aid
EA – emergency aid
SAEMA – Station of an ambulance and emergency medical aid
TRCT – toxicological resuscitation and consultative team
CTL – chemical and toxicological laboratory
CTAP – Center for the treatment of acute poisoning
ES – emergency situation
EMC – emergency medical care
FMBA MH RF – Federal Medical and Biological Agency of the Ministry of Health of the Russian Federation

The organization of the emergency clinical toxicology service in Russia is closely related to the improvement of diagnostics, treatment, and the epidemiology of acute poisoning (AP) [1]. The difficulty of studying the state of this issue in Russia, as well as in other countries, lies in the fact that many materials related to this discipline were published under the heading "For official use", as a result of which they became difficult to access for study.

In addition, the lack of specialized departments and trained specialists in the field of clinical toxicology did not make it possible to make accurate diagnoses of AP, to generalize and analyze statistical data on their number and structure. As a result of the creation of a network of centers (branches) of AP, such an opportunity appeared in the form of annual sectoral statistical reporting 1, 2, 3. Based on the data obtained as a result of the release of these documents, the seeking medical attention in the number of hospitalized patients in recent years has reached 123.9–144.4, and together with those who died from poisoning – 152.0–185.6 per 100,000 population. which corresponds to approximately 250,000 patients per year.

The history of clinical toxicology dates back to the middle of the 19th century, its development at this stage took place within the framework of forensic medicine and pharmacology and was associated exclusively with the accumulation and generalization of scientific knowledge about poisons and acute poisonings. The beginning of the twentieth century. characterized by the formation of a pathogenetic approach to the study of the mechanisms of toxicity of toxic substances and the diagnosis of AP. The main method of AP treatment in this period was medication [2–6]. Only taking into account the tragic experience of the First World War, when the problem of AP with chemical warfare agents acquired such a wide sound and reached the state level, the first organizational steps became possible, among them – the creation in 1935 in Leningrad of the Sanitary and Chemical Institute (currently - Institute of Toxicology of the Federal Medical and Biological Agency of the Ministry of Health of the Russian Federation (FMBA MH RF))4.

The solution of issues of domestic AP within the framework of military and then industrial toxicology was initially developed significantly [7, 8], but later became limited, since the main attention was paid to poisonings not found in everyday life as a rule.

With the opening in 1923 of the Sklifosovsky Institute of Emergency Medicine, the study of AP was also started there. In the 30-50s. at XX century this work was most actively carried out in a therapeutic clinic under the guidance of an outstanding clinician, scientist and public figure Academician A.N. Kryukov. Particular attention was paid to AP with mercury, arsenic, and cauterizing agents, which were frequent at that time [9–11]. A significant contribution to the development of diagnostics and treatment of AP during these years belongs to the doctor of medical sciences. O.I. Glazova, who worked under the leadership of A.N. Kryukov and in her works summarized the material concerning

[1] Appendix No. 6 of the report of the poisoning center to the order of the Ministry of Health of the Russian Federation No. 9 dated January 8, 2002, form No. 64.

[2] Statistical report of the Ministry of Health of Russia "Composition of patients with poisoning by drugs, medicines and biological substances, toxic effects of non-medical substances (T36-T65) in the hospital, terms and outcomes of treatment", form No. 14.

[3] Statistical report of the Ministry of Health of Russia "Poisoning by drugs, medicines and biological substances, toxic effects of non-medical substances T36-T65", form No. 57.

[4] Order for the NKZ USSR No. 409 dated 05/23/1935.

more than 250 types of AP, which to a large extent contributed to a significant increase in the role of representatives of the emergency therapeutic clinic in this area [12, 13].

Thanks to the research carried out at the Institute in 1939–1941, the USSR People's Commissariat for Health developed a number of instructions for first aid in emergency conditions, including AP. Order of the Ministry of Health of the USSR No. 525 of August 14, 1946 "On measures to improve the operation of ambulance stations and emergency rooms" [1a] to the director of the Moscow City Research Institute of the SP named after N.V. Sklifosovsky was ordered in 1946 to analyze the service of the population of the USSR with emergency and urgent care for 1945 and to continue this work. This also applied to AP. Данному приказу соответствуют также Regulations on the Institute in 1944 and 1949 [2a, 3a], providing assistance at the institute for acute illnesses and injuries. Based on this, the Institute prepared new instructions for providing assistance with AP [14].

After the death of A.N. Kryukov in 1952 and the creation of two therapeutic clinics at the Institute, AP issues were further dealt with mainly by the 2nd therapeutic clinic, headed by prof. P.L. Sukhinin (Fig. 1).

50-70s of XX century became the years of the formation of clinical toxicology as an independent branch of clinical medicine. The rapid growth of the chemical industry that began then, the chemicalization of the national economy and the creation of new drugs were accompanied by an increase in the frequency of AP and their unfavorable outcomes. Drug treatment of patients in the therapeutic departments turned out to be ineffective, which required new organizational and therapeutic approaches.

In the 60s scientists, including employees of the N.V. Sklifosovsky Research Institute for Emergency Medicine, developed issues of medical care at the pre-hospital stage. On this basis, the USSR Ministry of Health issued order No. 570 of December 23, 1961 "On improving the service of the population with urgent aid and emergency medical care" (together with the "Regulations on the city ambulance station" and "Regulations on specially equipped ambulances of the ambulance station aid "), which streamlined the transition to the provision of emergency specialized medical care, including APs. The list of equipment for the ambulance medical brigade (EMB) has already included equipment for probe gastric lavage.

At the Scientific Research Institute named after N.V. Sklifosovsky, the question of organizing the toxicological department was repeatedly raised. In 1959 the head of the 2nd therapeutic clinic prof. P.L. Sukhinin sent a memorandum to the director of the Institute on the organization of the laboratory of toxicology and made a report on this topic at a meeting of the Scientific Council of the Institute, as a result of which he was instructed "... to carry out work on the organization of this center» [4a, 5a].

The result was the creation in 1961 of a specialized field brigade of the Ambulance and Emergency Medical Aid Station (AEMAS) in Moscow, and in 1962 – the country's first toxicological center as part of the N.V. Sklifosovsky Institute (director – M.M. Tarasov) on the basis of the 2nd therapeutic clinic under the guidance of prof. P.L. Sukhinin [6a]. His primary tasks were the development of specialized methods for the diagnosis and treatment of AP.

This organizational step was logical, given the versatility of the N.V. Sklifosovsky Research Institute for Emergency Medicine, the need for urgent solutions to the diagnosis and treatment of AP, highly qualified personnel, as well as the complexity and high cost of AP treatment. In addition, the inclusion of the chemical and toxicological laboratory (CTL) in the department made it possible to objectify the results of therapeutic and diagnostic measures and conduct scientific research at a high evidentiary level.

The head of the center in the first years of its work was V.N. Dagaev (Fig. 2) [7a].

Fig. 1. Sukhinin Pavel Leonidovich (27.11.1902–1983), Doctor of Medical Sciences, Professor. Since 1955, the head of the 2nd Therapeutic Clinic of the N.V. Sklifosovsky Institute. One of the initiators of the creation of a toxicological department at the Institute on the basis of the Clinic. The first scientific director of this department (1962–1972) and the dissertations written here. He organized research on diagnostics, intensive therapy and long-term consequences of acute poisoning with substances and drugs used in the national economy and everyday life (barbiturates, cauterizing liquids, chlorinated hydrocarbons, pesticides, arsenous hydrogen, pachycarpine, etc.) [15–17]

Fig. 2. Dagayev Viktor Nikitich (26.03.1936–12.12.1994). Scientist, toxicologist, healthcare organizer. Doctor of Medical Sciences (1992). Together with E.A. Luzhnikov he took an active part in the organization of the first mobile specialized toxicological team in 1961, and the first in the country treatment department of acute poisoning on the basis of the N.V. Sklifosovsky Research Institute for Emergency Medicine a year later, heading it from 1963 to 1967

V.N. Dagaev substantiated the principles of clinical toxicometry of AP, taking into account the levels of toxicants in the blood. This approach provided prognostic criteria for the course of AP, contributed to the disclosure of their pathogenesis, made it possible to plan the volume of detoxification therapy and objectively assess its effectiveness. Under the leadership of V.N. Dagayev, the first domestic computer toxicological programs in Russia were created: the expert "TOXICOLOG" and the informational reference "POISON", which are used in many Treatment Centers of AP (TCAP) of the Russian Federation and the CIS countries. He is one of the main organizers of specialized medical care at AP in various regions of Russia. In 1992 V.N. Dagayev achieved the creation and headed the first in Russia Information and Consultative Toxicological Center (ICTC) (currently – the Scientific and Practical Toxicological Center of the FMBA of the Ministry of Health of the Russian Federation), the most important tasks of which V.N. Dagaev considered the creation of a national bank of fundamental data, as well as informatization in the field of clinical toxicology.

From 1967 to 1972, the Center was headed by Cand. med. Associate Professor E.A. Luzhnikov. In 1968, the Center became the Moscow CTAP, which had 25 beds [8a, 9a].

From the very first years of work, the Center carried out intensive scientific and educational-methodical work. Taking into account large volume and importance of that work, already in 1972 at the N.V. Sklifosovsky Institute, a scientific department for the treatment of AP was created, the head of which became E.A. Luzhnikov (Fig. 3) [10a].

Fig. 3. Luzhnikov Evgeny Alekseyevich (27.09.1934–20.04.2018). Scientist, toxicologist, organizer of the medical toxicological service in Russia, founder of a new scientific field,– clinical toxicology. Doctor of Medical Sciences (1971). Full member (academician) of the Russian Academy of Medical Sciences (RAMS) (2004). Academician of the Russian Academy of Sciences (RAS) (2013). Honored Scientist of the Russian Federation, Laureate of the State Prize of the USSR and Prizes of the Government of the Russian Federation. In 1967-1972, he worked as the head of the Toxicological Center at N.V. Sklifosovsky Institute. In 1970, he was appointed the head of the Republican CTAP and the chief externe therapist-toxicologist of the Ministry of Health of the RSFSR, in 1972–2014, for more than 40 years, he had been the scientific director of the department for the treatment of AP. E.A. Luzhnikov was the main organizer of the specialized toxicological service of a clinical profile in our country, which currently includes 39 acute poisoning treatment centers (departments) in Moscow and the largest cities of the Russian Federation. The founder of the largest and most authoritative Russian scientific school, numbering about 150 scientists, which results have made a fundamental contribution to the development of modern urgent clinical toxicology. In 1986–2016 he had been in charge for the country's first Department of Clinical Toxicology at the Central Institute of Advanced Medicine, CIAM (now Russian Medical Academy of Continuing Professional Education)5

In the 60s and early 80s. the greatest attention was paid to the development of schemes for the diagnosis and treatment of the main nosological forms of AP (organophosphate insecticides, chlorinated hydrocarbons, drugs, acetic acid, etc.), as well as the accelerated elimination of exogenous toxicants from the blood using efferent methods of artificial detoxification (MAD) of the body (blood replacement surgery, sorption-dialysis methods). The early use of MAD became a feature of resuscitation measures in AP and for the first time allowed to radically reduce mortality in the most severe AP, which previously reached 80–100%.

New antidotes have been introduced into the practice of AP treatment, which selectively affect functional systems and, when used parenterally, allow to neutralize poisons in the biological media of the body.

The experience of the department was also used to solve AP issues in children and in forensic medical examination [18–20].

Of particular importance was the work of CTL, where the analytical methods that existed at that time were adapted to the conditions of clinical toxicology. This contributed to the rapid diagnosis of AP, as well as the possibility of an objective assessment of the severity of the disease and the effectiveness of treatment from toxicometric positions. [21].

[5] At present, the department is headed by a student E.A. Luzhnikov prof. Yu.S. Goldfarb

To implement such high results at the regional level, organizational decisions were urgently required. To substantiate them in scientific publications [22–27, etc.] and methodological works [28–30, etc.], the experience of the leading toxicological centers of the country was generalized for a long time. In this period, the First All-Russian Conference on Clinical Toxicology (1968) was of invaluable importance, the main initiators of which were the employees of the CTAP of the Sklifosovsky Institute and which was held within its walls. Thanks to the results of this forum, government decisions were made that contribute to the formation of clinical toxicology as a scientific and medical specialty and the transfer of the experience of the Moscow CTAP to the whole country. So, the collegium of the Ministry of Health of the USSR on April 10, 1969 "On the state and measures for the further development of the toxicological service" made a decision to establish republican toxicological centers in the RSFSR and the Kazakh SSR, and by order of the Ministry of Health of the RSFSR No. 70 dated March 26, 1970, "On measures to further strengthen the toxicological service of the health authorities of the Russian Federation "approved the regulation on the Republican Center for the Treatment of Poisoning (RCTP), created on the basis of the Scientific Research Institute named after N.V. Sklifosovsky. Its main task was to carry out measures in the republic aimed at the prevention, registration and treatment of AP, in connection with which he was charged with organizational and methodological, medical and diagnostic, research, information and educational functions.

To perform these tasks, according to the order, as part of the CTAP of Sklifosovsky Research Institute for Emergency Medicine, the following departments were deployed:

— organizational and methodological department, including a research group for the organization of specialized care, a group for information and prevention of AP, a group of statistics and a group for training and improvement of personnel;

— the clinical department as part of the intensive care unit for 25 beds, the psychosomatic department for 25 beds, the dialysis unit, which was an operating unit for performing surgical methods of extrarenal cleansing (hemodialysis, peritoneal dialysis, etc.) and the experimental therapy unit for testing new methods of treating poisonings;

— forensic chemical toxicology laboratory for the urgent determination of toxic substances in the body with AP by them and performing the necessary biochemical studies during various types of dialysis.

The same order established 13 interregional toxicological centers in large cities, which had a sufficient material and technical base for that time to introduce methods of diagnostics and treatment of AP (Vladivostok, Volgograd, Voronezh, Gorky, Irkutsk, Leningrad, Novosibirsk, Omsk, Perm, Sverdlovsk, Stavropol , Khabarovsk and Chita), and the post of chief therapist-toxicologist was introduced, which was occupied by Ph.D. Associate Professor E.A. Luzhnikov.

The above-mentioned organizational and methodological department of the RCTAP of the Ministry of Health of the RSFSR was established at the Moscow Research Institute of Epidemiology and Microbiology (MRIEM) as a scientific, organizational and methodological department and had 13 staff units (Fig. 4) [11a]. At first, it was led by V.N. Dagaev, and then by V.N. Alexandrovsky.

Fig. 4. Employees of the organizational and methodological department of the Republican Center for the Treatment of Acute Poisoning (RCTAP) (70s) (from right to left, sitting): Dr. Med. Sci. V.N. Aleksandrovsky (head), Cand. Med. Sci. N. Y. Glukhovskaya , Cand. Med. Sci. A.S. Savina; the first on the left (sitting) is the head of the center for the treatment of acute poisoning of the N.V. Sklifosovsky Research Center and RCTAP prof. E.A. Luzhnikov

At the same time, MRIEM included a department for mental prevention of AP, which had 8 staff units and also operated on the basis of the N.V. Sklifosovsky Institute (supervisor – Prof. D. D. Fedotov) [12a].

The most important section of the work of the organizational and methodological department of the RCTAP was the organization of toxicological centers (departments) in the regions of the country. So, in the decision of the problem commission on clinical toxicology at the Academic Council of the N.V. Sklifosovsky Institute, who supervised the activities of the organizational and methodological department (chairman E.A. Luzhnikov), it was noted that in 1971 the department “carried out a lot of work on the following sections: organizing a specialized service in the RSFSR, on special training of toxicologists for interregional centers and ambulance, under scientific and technical

information on clinical toxicology and on the scientific development of some problems of clinical toxicology. Including the head of the department V.N. Aleksandrovsky organized interregional centers for the treatment of poisoning in the cities Voronezh, Volgograd, Perm, Sverdlovsk»; the letter also mentioned the active organizational, methodological and pedagogical work of the senior researcher A.S. Savina and junior researchers V.N. Dagaev, N. Ya. Glukhovskaya and T.V. Novikovskaya, who worked in this division [13a].

The result of the implementation of the developed principles of diagnostics and treatment of AP throughout the country, especially the early use of the MAD, was a significant decrease in mortality from AP during the first decade of the functioning of regional toxicological centers, created by the above-mentioned order of the Ministry of Health of the RSFSR No. 70 of 03.26.1970.

Thus, decrease in mortality from AP in the toxicology department of Volgograd was from 28% in 1971 to 9.5% in 1980 (3 times), and in the same department of Chita – from 14.3% to 3.5%, respectively (3.5 times). In general, the possibility of reducing mortality in the provision of specialized care at the prehospital stage from 39.1 to 12.4% (3.2 times), overall mortality in OO from 6 to 2.5% (2.4 times), mortality in toxicological hospitals 1.2-10 times or more [31].

A major achievement of the staff of the organizational and methodological department was the preparation of a system-forming order of the USSR Ministry of Health No. 475 of 05/06/1980 "On the improvement of inpatient specialized medical care in acute poisoning", which completed the first stage of the development of the toxicological service in the country and is necessary for a clearer regulation of the creation and operation of toxicological centers and introduction to the nomenclature of the position of a toxicologist. At the same time, the organization of toxicological departments was envisaged already in cities with a population of 500,000 people and above. The order was signed by the Minister of Health of the USSR, academician B.V. Petrovsky, who closely followed the development of a new branch of clinical medicine and personally visited the CTAP of N.V. Sklifosovsky Institute (fig. 5) [32].

Fig. 5. Minister of Health of the USSR Academician B.V. Petrovsky (center) during a visit to the Center for the Treatment of Acute Poisoning (CTAP) of the N.V. Sklifosovsky Institute (70s). E.A. Luzhnikov is on the left, the head of the department of the Center for Children's Education, Candidate of Medical Sciences, V.M. Dvorina is on the right

The results of the conducted studies, the creation of new medical technologies and their widespread introduction allowed raising the diagnosis and treatment of AP to a fundamentally new level and laying the theoretical basis for clinical toxicology, which for many years determined the direction of scientific activity in this area.

This was also largely facilitated by the formation of a new, the largest scientific school in clinical toxicology led by E.A. Luzhnikov in Moscow (along with the school of S.N. Golikov in Leningrad) with the priority of scientific research on the use of the MAD and scientific and organizational work [33]. The main results of the school's activities were the creation of new technologies for the treatment of AP and the organization of an independent toxicological service in Russia in order to improve the results of therapeutic measures at the regional level. These scientific ideas of E.A. Luzhnikov were developed and continue to be developed by his closest students - employees of the N.V. Sklifosovsky Institute professors I.I. Shimanko, K.K. Ilyashenko, Yu.S. Goldfarb, G.N. Sukhodolova, N.M. Epifanova, M.M. Goldin, Dr. med. Sciences S.I. Petrov, V.N. Dagaev, V.A. Matkevich, candidates of medical sciences Yu.N. Ostapenko, M.M. Potskhveriya, as well as prof. V.G. Sentsov (Yekaterinburg) and other specialists.

Taking into account the accumulated experience in the late 1980s and early 2000s, at the CTAP of N.V. Sklifosovsky Research Institute for Emergency Medicine, the idea of improving the treatment of OO due to a complex nonspecific non-drug detoxification approach with the elimination of concomitant endotoxicosis prevailed, in connection with which the technology of complex detoxification of the body was developed and introduced into practice, including the use of sorption-dialysis methods, enteral detoxification and physicochemical hemotherapy - magnetic, ultraviolet, laser and chemotherapy with sodium hypochlorite. A large amount of research was also completed in the field of enteral detoxification with the aim of effectively eliminating the intestinal depot of toxicants and its implementation in relation to the severity of the patient's condition and the type of toxicant [34], which significantly expanded the possibilities of its practical use. It should be noted the fundamental contribution to the development of intestinal detoxification methods, which was made by fundamental research carried out jointly with clinicians in the experimental laboratory of the institute, in those years headed by prof. Yu.M. Galperin [35, 36]. The use of the new therapeutic algorithm was accompanied by a significant acceleration of blood cleansing from exo- and endotoxicants and a sharp decrease in mortality among the most severe patients, the largest during the operation of the CTAP [37–39]. New forms of AP have also been explored [20, 40].

The success of this work was facilitated by the introduction of modern methods of analysis (specific chromatographic and immune ones) into CTL, which significantly increased the range of analyzed substances [41].

The accumulated material served as the basis for the preparation in the indicated period of major works summarizing the results of studies carried out by the country's leading toxicologists (Fig. 6) [38, 39, 43–48, etc.] and promoting their implementation.

In a special place is the first in Russia National Guide to Clinical Toxicology "Medical Toxicology" (2012) edited by E.A. Luzhnikov, who has accumulated advanced views on topical issues of the stationary stage of diagnostics and treatment of AP [49]. Later, thanks to the efforts of mainly specialists from St. Petersburg, the National Guide to the EMA (2017) was created, edited by S.F. Bagnenko with a toxicological section [50].

Fig. 6. Prof. V.G. Sentsov (Yekaterinburg), corresponding member of RAMS, prof. E.A. Luzhnikov (Moscow) and prof. G.A. Livanov (St. Petersburg) on a walk during the All-Russian scientific and practical conference "On measures to improve the provision of medical care to patients with acute poisoning" (Yekaterinburg, September 2002)

The practical steps in this period were the further organization of the CTAP, the introduction of modern technologies for the treatment of AP and the preparation of regulatory documents that made it possible to consistently resolve the existing difficulties in organizing the work of toxicological departments.

To improve the quality of care in AP, the order of the Ministry of Health of the USSR No. 1527 of 20.11.1986 "On measures to improve specialized medical care in acute poisonings" became fundamental, obliging the implementation of both the most effective artificial detoxification for patients with AP and the organization of specialized departments in hospitals, having the appropriate units for the use of hemosorption and hemodialysis, as well as the letter of the Ministry of Health of the USSR No. 02-14 / 118-4 dated 16.12.1987, "On the creation of resuscitation and intensive care wards as part of the departments (centers) of acute poisoning" with addition to it No. 02-14 / 61-14 of 02/15/1988, allowing the creation of such chambers for 6 beds as part of AP departments and regulatory issues of the staffing table.

An important role was played by the information letter of the Ministry of Health of the USSR No. 04-6 / 64-6 dated 03/27/1990 "Organization of inpatient medical care for acute poisonings of chemical etiology", which has been used for many years as the main document and allowed the introduction of anesthesiologists into the staff of toxicological departments – resuscitators and nurses for work in intensive care wards, as well as a nurse for active detoxification methods and a laboratory assistant to ensure the operation of equipment.

As a result, by the end of the twentieth century, the foundation of the toxicological service was created in the Russian Federation – a network of 44 centers (departments) for the treatment of OOs in 41 regions, as a rule, in multidisciplinary hospitals and emergency hospitals (EMC), in which 1235 toxicological beds were deployed today, providing specialized assistance to the population of 50% of the territory of the Russian Federation and serving as the basis for the introduction of advanced achievements in this area (Fig. 7).

Fig. 7. The network of toxicological centers in the Russian Federation in the end of the 20th century

Taking into account the real conditions, the organization of the local educational centers had its own characteristics. So, the Sverdlovsk interregional CTAP, organized in 1973, due to the large number of AP and the complexity of organizational tasks in 1991, was divided into the city center, which remained on the basis of the city emergency hospital, and the regional center – on the basis of the regional narcological hospital of the Psychiatry association, and in it CTAP was created. The Ministry of Health of the Republic of Tuva followed the same path (order No. 144 of 09.06.1993 "On the establishment of the toxicological department of the association "Psychonarcology"). Some CTAP were created at industrial enterprises (orders of the Omsk Regional Department of Healthcare No. 117 of 03.07. 1972 on the opening of the Department of Acute Poisoning and the Health Department of the Administration of Izhevsk No. 94 of 13.04.2007 on the basis of the Medical-Sanitary Unit (MSU) No. 1) "On the organization of the toxicological department in the municipal health care institution "Medical and sanitary unit "Izhmash"), which, however, over time required other organizational decisions (order of the Omsk Regional Department of Health No. 38 dated December 29, 1990 on the transfer of the Treatment department of acute poisoning from the medical unit No. 1 to the Municipal Healthcare Institution "City Clinical Emergency Hospital No. 1" (MUZ GKB SMP No. 1) in Omsk).

In addition, in the Sverdlovsk region, due to its saturation with chemical enterprises in 1991-1992 4 interdistrict toxicological centers were additionally organized; at AP 50% of such patients began to receive specialized care, and not 10%, as it was before, while the mortality rate in the regional center decreased by 6.8 times.

Experts also raise the question of the interaction of the Center for Sanitary and Epidemiological Surveillance with the territorial centers of the State Sanitary and Epidemiological Supervision, disaster medicine, forensic medical examination bureaus, with the departments of the Ministry of Internal Affairs and executive authorities at various levels; it was proposed to create a fundamentally new territorial coordinating body – the Interdepartmental Commission on Chemical Safety of the Population [27, 30, 51–54].

It should be noted the great importance of the scientific and organizational activities deployed in the N.V. Sklifosovsky Research Institute for AP. Issues of ambulance and emergency care at OO were constantly in the focus of attention of the Scientific Council on Emergency Aid, created by order of the Ministry of Health of the RSFSR No. 475 in 1976 under the Scientific Medical Council of the Directorate of Research Medical Institutions of Russia, and the Interdepartmental Scientific Council on Emergency Medicine, which coordinated the work 44 scientific and practical institutions of the Soviet Union, created by the decree of the Presidium of the USSR Academy of Medical Sciences No. 95 of March 22, 1978; the head institution by these orders was determined N.V. Sklifosovsky Institute. Problematic commissions "Acute poisoning" in the composition of these councils was headed by corresponding member of RAMS E.A. Luzhnikov [14].

The work of the councils was carried out within the framework of state comprehensive programs related to the improvement of emergency care and resuscitation in case of emergency conditions and trauma. The results of the research were the substantiation of the staffing standards for providing specialized medical care at AP, the development of organizational principles of urban AP, the study of new forms of AP, the development of new methods of diagnostics and detoxification in AP using equipment of our own design at the prehospital and hospital stages with a high clinical effect and the dispensary system support at AP.

In connection with the reorganization of scientific institutions and the abolition of the Russian Academy of Medical Sciences, the Scientific Council on EMC problems ceased to exist, however, the organization of research on clinical toxicology, which is carried out according to the plan approved by the Scientific Council of the N.V. Sklifosovsky Research Institute for Emergency Medicine, and control over their implementation is currently included in the scope of the Problem-Planning Commission of the Institute "Acute exo- and endotoxicosis".

Another way to improve the toxicological care carried out at the N.V. Sklifosovsky Research Institute for Emergency Medicine, there was information and advisory support for the population and medical workers. Initially, this work was one of the aspects of the activities of the department employees - both in the form of telephone consultations and travel to the place of emergency toxicological situations as part of a specialized ambulance brigade to the intensive care and therapeutic departments of Moscow, the Moscow region and other cities of the country, in the latter case - with the help of Air ambulance stations of the RSFSR.

Later, at the initiative of the staff of the toxicology department of the N.V. Sklifosovsky Research Institute for Emergency Medicine [55] by order of the Ministry of Health of the Russian Federation No. 319 dated 07.12.1992 "On the establishment of an information and consultation toxicological center of the Ministry of Health of the Russian Federation" this institution was created (headed by V.N. Dagaev, since 1994 – Yu.N. Ostapenko), since 2011 - the Scientific and Practical Toxicological Center of the FMBA of the Ministry of Health of the Russian Federation (SPTC) (headed by Yu.N. Ostapenko, since 2015 – P.G. Rozhkov), which began to play a large role in solving organizational and other issues clinical toxicology. The content of the information service is round-the-clock advice to doctors with the help of a special file of toxic substances, embedded in an automatic reference installation, and in difficult cases, a specialized toxicological team of the emergency medical service was sent for consultation. The organization of the information service served as the basis for the organization of a similar service in the interregional and Moscow children's toxicological centers.

In addition, the function of the Scientific and Practical Center is to coordinate the activities of toxicological centers and departments throughout the country, as well as monitor the toxicological situation, accumulate and disseminate the information received, and prepare methodological materials. In recent years, the SPTC has also formed a regulatory and legal framework for the organization and functioning of the country's toxicological service, in the development of which the employees of the SPTC took an active part and which was initially based on the results of its activities.

The work of the SPTC was aimed at further improving the provision of assistance to the population of Russia in acute chemical pathology and served as the basis for the emergence of orders of the Ministry of Health of the Russian Federation No. 460 dated December 29, 2000 "On the approval of accounting documentation for toxicological monitoring" and the Ministry of Health and the SR of the Russian Federation No. 152 dated February 21, 2005 d. "On the further development of information and advisory toxicological assistance to the population of the Russian Federation", prepared for the purpose of improving information and advisory toxicological assistance, solving medical aspects of the chemical safety of the population of the Russian Federation, introducing scientific advances in the field of information technology and increasing the efficiency of providing specialized medical care at AP. The same order of the SPTC prescribed methodological assistance to the public health authorities of the constituent entities of the Russian Federation in organizing information and advisory toxicological units,

organizational and methodological management of the activities of newly organized units of this kind, as well as the development of a computer program for accounting and analysis of toxicological consultations.

According to the existing opinion, for the sparsely populated territories of the constituent entities of the Russian Federation, the creation of an SPTC is the only possible way to organize a specialized toxicological service. These centers must also carry out organizational and methodological work within the territory of the subject of the Federation [56].

Meanwhile, the Moscow toxicological service was constantly evolving. Since 1964, the children's CTAP began to function at the city clinical hospital (GKB) № 13 named after. N.F. Filatov. In 1995, due to insufficient bed capacity, an emergency detoxification center was additionally established on the basis of City Clinical Hospital No. 33 (now the Bakhrushin Brothers Hospital) (Head of the center Candidate of Medical Sciences A.S. Livanov). The bed fund and the CTAP of NII SP N.V. Sklifosovsky by the order of the Health Committee (HC) of Moscow No. 448 of August 11, 1997 “On the organization of a city center for the treatment of acute poisoning on the basis of the N.V. Sklifosovsky Research Institute for Emergency Medicine "after the reconstruction of the toxicological building of the Institute, the country's largest urban toxicological center with 100 beds was formed, and it also includes an organizational and methodological office under the chief freelance toxicologist of the Moscow Regional Clinical Center. To date, this unit, which is also a scientific department of the Institute (head – candidate of medical sciences M.M. Potskhveriya), has 73 beds and includes the following departments in its structure: treatment of acute poisoning (scientific), a reception with 4 diagnostic beds, as well as resuscitation and intensive care with a small operating room for emergency detoxification - 15 beds, acute poisoning (rehabilitation) – 30 beds, somatopsychiatric – 24 beds and a chemical-toxicological laboratory. As you can see, there is a significant increase in this subdivision (in comparison with the bed stock in 1965 [14a] – more than 3 times).

As a result, by the end of the twentieth century in Moscow, a developed system of emergency medical care (EMC) at AP was created, including a CTAP for adults and children (109 toxicological and 24 intensive care beds), ICTTs, GKB Nos. 1, 20, 67 and them S.P. Botkin, as well as the visiting toxicological advisory brigade of the EMA station in Moscow, organized back in 1977 according to the decree of the Central Committee of the CPSU and the Council of Ministers of the USSR No. 517 of 07/05/1968 and the order of the Ministry of Health of the RSFSR No. 260 of 18.04.1977 "On additional measures for the organization of emergency medical care for the population in the event of mass accidents and their prevention", among other things, providing for the presence in the TRCT of the Moscow Research Institute named after N.V. Sklifosovsky Specialized Toxicological Resuscitation and Advisory Brigade (TRAB) for the provision of medical care to the population (Fig. 8).

Fig. 8. Members of the toxicological resuscitation and advisory team, the station of ambulance and emergency medical care in Moscow (late 70s – early 80s). Y.N. Ostapenko is on the left

For the organization of the toxicological service in Moscow, the normative legal documents of the city level were of great importance. Order of the KZ of Moscow No. 474 of 17.10.2002 "On the provision of urban medical and preventive institutions with drugs for antidote therapy of acute chemical poisoning" approved a temporary regulation on the Bank of drugs for antidote therapy of AP, organized at the Scientific Research Institute of the SP named after. N.V. Sklifosovsky. The creation of the aforementioned EMA system at AP, which provided both specialized and non-core medical institutions of the city, was consolidated by the order of the DZ of Moscow No. 44 dated January 30, 2006 "On the procedure for providing medical care in case of exogenous chemical poisoning in Moscow". For the organization of the service, union and republican orders were also taken into account.

The result was continuity in the work of the prehospital stage, general hospitals and toxicological centers and the successful solution of urgent organizational and treatment-diagnostic tasks (the earliest start of specialized toxicological care, complex detoxification of the body, etc.). Already in the first years of work, the lethality of the leading types of poisoning in the toxicological department of the N.V. Sklifosovsky Research Institute for Emergency Medicine decreased 1.7 - more than 4 times, and in the children's toxicological center – more than 10 times. Since all the doctors of the Regional Clinical Hospital underwent specialization and continued to work directly in the departments of the Center, realizing a clear continuity in the treatment of patients with this pathology at all stages of providing them with medical care, among patients served by these teams, hospital mortality in case of poisoning with the most toxic substances turned out to be significant (in 1.8–2.8 times) lower compared to the results of line brigades.

Thus, by the beginning of the XXI century. in Moscow, a unique model of specialized medical care at NGOs was formed, the principles of which and the new technologies developed were introduced throughout the country. This is confirmed by the data on the therapeutic activity of the CTAP of Russia (table).

Table

Frequency of application of various detoxification methods in toxicological centers of the Russian Federation (according to reports from 22 centers)

Detoxification methods			
	2004	2005	2006
Enhancing Natural Detoxification	% to the total number of centers		
Cleansing the gastrointestinal tract	100	100	100
Enterosorption	100	100	100
Intestinal lavage	13	24	25
Dialysis filtration methods			
Hemodialysis	91	90	91
Ultrafiltration	65	67	67
Hemofiltration	48	48	48
Hemodiafiltration	35	43	48
Sorption, apheresis			
Hemosorption	78	82	95
Plasmapheresis	83	95	95
Physio - and chemohemotherapy			
Ultraviolet Hemotherapy	83	86	86
Laser hemotherapy	48	62	62
Magnetic hemotherapy	26	26	26
Ozone hemotherapy	9	13	13
Indirect electrochemical oxidation of blood by sodium hypochlorite	57	65	65

As can be seen from the table, in CTAP, as a rule, with increasing activity, advanced detoxification technologies are used.

A consequence of the organizational work at the present stage was a further decrease in mortality from AP in the Russian Federation as a whole – from 4.14 to 3.69% in 2006-2008, and the frequency of deaths from AP over 8 years (2000-2008) – from 59,1 to 47.5 per 100,000 population [49].

Among the important indicators of the effectiveness of achievements in a particular medical specialty is the quality of medical care in emergency situations (ES). Attention was paid to medical care during mass AP from the very beginning of the organization of the toxicological service.

Already at the end of the 60s. it was assumed that additional places could be deployed at the Scientific Research Institute for the provision of toxicological aid in the event of massive chemical injuries (order of the director of the N.V. Sklifosovsky Research Institute for Emergency Medicine No. 28a dated 26.03.1966, “On deployment in the event of admission of patients with poisoning of the chemical etiology beds at the Institute ") [15a].

By order of the State Institution of Health of the Moscow City Executive Committee No. 399 of 15.07.1970 "On measures to improve emergency care for diseases of chemical etiology" [16a] to the chief physician of SAEMA L.B. Shapiro was instructed to equip 30 emergency medical teams with medications and property for visiting cases of chemical etiology, and in the event of massive cases of diseases of

chemical etiology, ensure hospitalization, first of all, in the following hospitals: named after Botkin, Institute of Emergency Medicine named after N.V. Sklifosovsky, GKB No. 1 named after Pirogov, city hospitals No. 6, 53, 70, Children's city hospital No. 13 named after Filatov. The order also prescribed the appropriate equipping with medicines and property of a number of medical institutions of the city, admission departments of the designated hospitals and “to organize on the basis of the toxicological center of the Sklifosovsky Research Institute for Emergency Medicine, training of doctors and nurses in emergency care for patients with AP of chemical etiology».

In the early 90s to improve medical care for the population of Moscow in case of emergencies, 200 beds and 15 dialysis places were reserved in the city's clinics. By 2000, within the framework of the EMA, it was envisaged to deploy from 1410 to 2850 places in the clinics of the capital in emergencies associated with chemical damage.

Scientific research was also crowned with the successful introduction of new methods of AP treatment into the practice of emergency medical services and rescue teams in case of mass poisoning, which led to an improvement in the provision of medical care to seriously injured persons [57–59]. In particular, for a number of years, research on the organization of assistance in case of mass poisoning was carried out in the department of disaster medicine of the Institute, created in 1987 on the initiative of the director of the Institute prof. V.G. Teryaev (headed by V.N. Aleksandrovsky). One of the most serious work of the department was associated with the maximum approach of the beginning of medical care to the time of an emergency with the help of appropriate equipment with medical transport and the formation of mobile medical teams [60, 61].

Experience has shown that when providing medical care in a hospital in order to increase its throughput, traditional treatment methods may deviate from the generally accepted indications for their use and the volume of their implementation. It is also advisable to create stocks of equipment and medicines for various methods of treatment, especially efferent ones. In addition, it is necessary to ensure round-the-clock work of medical, technical personnel and medical and diagnostic equipment [62].

The experience of advisory work related to the elimination of the medical consequences of chemical emergencies also indicates the need to attract additional forces and means of medical organizations of the territory where the chemical accident occurred (with the appropriate order of the management body of its health care): the Center for Disaster Medicine for the evacuation of victims, CTL of Bureau of Forensic Medicine for emergency laboratory diagnostics and hemodialysis departments.

Of great importance was also the information and advisory activities of the toxicological center, which was one of the first to organize round-the-clock informing doctors and the population on the diagnosis and treatment of AP, including mass ones.

The unique experience of the staff of the N.V. Sklifosovsky Research Institute for Emergency Medicine, including those related to public health services, was perceived by specialists and, despite the organization of a special disaster medicine service, it remains in demand and has found its application in the work of the institutions of this service [63].

After the collapse of the USSR, in connection with the loss of the Union's orders, there was a need for new regulatory documents regarding assistance with AP, corresponding to modern realities. Of a certain importance in this was the holding of the collegium of the Ministry of Health of the Russian Federation on September 14, 1999, at which the relevance, results of the organization and the state of assistance with AP in the Russian Federation were considered, moments in the development of the toxicological service that require a solution were highlighted. In particular, it was envisaged to intensify scientific and practical activities, in which the CTAP played a significant role, the issues of expanding the CTAP network and teaching clinical toxicology in higher educational institutions were considered.

A milestone was the order of the Ministry of Health of the Russian Federation No. 9 dated 01/08/2002 "On measures to improve the organization of toxicological aid to the population of the Russian Federation", which consolidated the existing system of toxicological assistance in the country and outlined the priorities for its further development, including information and advisory assistance, which, by virtue of its specificity may be available throughout Russia. The order details the activities of the toxicology department.

This served as an impetus for the creation of new CTAP, since it made it possible to set the tasks of providing medical care in AP at a new organizational level, for the first time on a legal basis including in the composition of a toxicological center (department) resuscitation and intensive care units (wards) with a small operating room for emergency detoxification and allocating for this separate positions of a toxicologist, a paramedical worker and a medical assistant for carrying out artificial detoxification, the basis of which, among other things, was the many years of experience in the treatment of AP at the N.V. Sklifosovsky Institute.

Much attention was paid to the organization of chemical and toxicological studies in the clinic. In the above-mentioned information letter of the Ministry of Health of the USSR No. 04-6 / 64-6 dated 03/27/1990, for the first time, it was also recommended to create chemical and toxicological laboratories as independent departments working around the clock, presented standard standards and also for the first time indicated the standard of chemical and toxicological studies for one inpatient with AP, which was later enshrined in the aforementioned order of the Ministry of Health of the Russian Federation No. 9 dated 01/08/2002, which includes the "Regulations on the organization of the activities of the chemical and toxicological laboratory of the center (department) of acute poisonings». It should be noted that such a laboratory was created as part of the toxicology department of the N.V. Sklifosovsky Research Institute for Emergency Medicine, already at its opening in 1962.

Orders of the beginning of the XXI century. were taken as the basis of the draft Procedure for the provision of medical care in AP, designed to be a guiding normative document determining the content and dynamics of the development of toxicological services in Russia in accordance with the international level, which was enshrined by order of the Ministry of Health of the Russian Federation of 15.11.2012 No. 925n “On the procedure for providing medical care to patients with acute chemical poisonings", developed in accordance with the Federal Law of November 21, 2011 No. 323-FZ "On the basics of protecting the health of citizens in the Russian Federation”. In this order, medical care is structured, and with regard to severe forms of AP it was prescribed that “if it is necessary to provide medical care with the obligatory use of extracorporeal detoxification methods (hemodialysis, hemosorption, etc.), patients with acute chemical poisonings are transferred to the center (department) of acute medical poisoning", and "in the event of complications requiring specialized treatment, patients with acute chemical poisonings are transferred to the appropriate department of a medical organization according to the profile of

the disease (complications)". A number of provisions of this order also became possible thanks to the many years of experience of the CTAP of NII SP named after N.V. Sklifosovsky.

In addition, as a result of the generalization of the experience of providing medical care at AP at the prehospital stage, mainly by specialists from St. Petersburg, a number of orders appeared regulating the activities of ambulance teams in this area[6, 7, 8, 9, 10].

It should be noted the importance of training specialists in the field of clinical toxicology in improving the quality of medical care in AP. In particular, this activity was carried out on the basis of the toxicological department of the N.V. Sklifosovsky Research Institute for Emergency Medicine within the framework of toxicology cycles for ambulance and emergency physicians, resuscitation departments of medical institutions in Moscow and other cities, employees of interregional toxicological centers. In addition, hundreds of ambulance doctors and specialists of intensive care units were trained in the workplace every year. Short-term cycles were conducted for doctors and paramedics of special units (4th Main Directorate of the USSR Ministry of Health, Civil defense), the USSR Ministry of Defense and medical schools.

The historical aspects of the training of scientific and medical personnel, the emergence of a new medical specialty and the birth of clinical toxicology as an independent scientific discipline are a separate page of research, which we are currently engaged in.

CONCLUSION

Creation of the organizational foundations of urgent clinical toxicology and its formation as an independent scientific and practical direction in medicine, in which a considerable contribution belongs to the employees of the N.V. Sklifosovsky Research Institute for Emergency Medicine, are closely related to scientific and practical achievements in this area, the prompt response of specialists to the toxicological situation in the country, as well as the dissemination of the experience gained in the course of organizational and information and advisory activities. At the same time, timely preparation and publication of regulatory documents governing practical work in this area are of particular importance.

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[7] Order No. 1392н of 12.24.2012 "On approval of the standard of emergency medical care in case of poisoning with alcohol, organic solvents, halogen derivatives of aliphatic and aromatic hydrocarbons".

[8] Order No. 1393n of 12.24.2012 "On approval of the standard of emergency medical care in case of poisoning with carbon monoxide, other gases, fumes and vapors".

[9] Order No. 1114n of 20.12.2012 "On approval of the standard of emergency medical care in case of drug poisoning".

[10] Order No. 1448n of December 24, 2012 "On approval of the standard of emergency medical care in case of poisoning with substances of neurotropic action".

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