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PESTICIDES: CURRENT TRENDS IN THE USE AND EPIDEMIOLOGY OF ACUTE POISONING

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Introduction. The widespread use of pesticides, which ensures the sustainable development of agriculture and global economic growth, necessitates the constant monitoring of their harmful effects on human health and the environment.

Objective. To analyze and systemically review scientific publications on the prevalence of acute pesticide poisoning and trends in their use in order to identify the causes and structure of acute pesticide poisoning at the present time.

Materials and methods. A search of the scientific literature is carried out in electronic bibliographic databases in the Russian (eLibrary, CyberLeninka) and English (Web of Science, Scopus, PubMed, Google Scholar, Cochrane Library) languages.

Results. The risks of pesticide poisoning remain high in many countries of the world among both adults and children. In the structure of acute pesticide poisoning, household and suicidal poisoning with organophosphate and halogenated insecticides, anticoagulant rodenticides and pyrethroids are prevalent. Poisonings that occur at mass-, group- and family levels often have fatal outcomes, whether among agricultural workers or urban residents. The problem of acute poisoning with extremely dangerous limited-use substances based on aluminum or zinc phosphide is relevant not only in industrial agriculture, but also under domestic conditions and when working in personal subsidiary farms.

Conclusions. Strengthening controls and ensuring strict compliance with sanitary and hygienic standards of individual and public safety in the storage, use and disposal of pesticides, as well as combating their illegal trafficking, will minimize the risks of acute poisoning involving pesticides under industrial and domestic conditions.

Keywords: epidemiology; pesticides; acute poisoning; toxic effect

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ПЕСТИЦИДЫ: СОВРЕМЕННЫЕ ТЕНДЕНЦИИ ПРИМЕНЕНИЯ И ЭПИДЕМИОЛОГИЯ ОСТРЫХ ОТРАВЛЕНИЙ

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Введение. Широкомасштабное применение пестицидов, обеспечивающее устойчивое развитие сельского хозяйства и рост мировой экономики, обусловливает необходимость постоянного мониторинга их вредного воздействия на здоровье человека и окружающую среду.

Цель. Проведение систематического обзора и анализа литературных данных для выявления характера распространенности, причин развития и структуры острых отравлений пестицидами на современном этапе.

Материалы и методы. Поиск научной литературы выполнен в электронных библиографических базах данных на русском (eLibrary, CyberLeninka) и английском (Web of Science, Scopus, PubMed, Google Scholar, Cochrane Library) языках.

Результаты. Риски развития отравлений пестицидами остаются высокими во многих странах мира как среди взрослого, так и детского населения. В структуре острых отравлений пестицидами превалируют бытовые и суицидальные отравления фосфорорганическими и галогенированными инсектицидами, родентицидами антикоагулянтного действия, пиретроидами. Отмечаются массовые, групповые и семейные отравления, нередко с летальными исходами, как у аграрных работников, так и у городских жителей. Актуальной является проблема острых отравлений чрезвычайно опасными препаратами ограниченного применения на основе фосфида алюминия или цинка не только в производственных, но и бытовых условиях и при работе в личных подсобных хозяйствах.

Выводы. Усиление контроля и строгое выполнение санитарно-гигиенических норм индивидуальной и общественной безопасности при хранении, применении и утилизации пестицидов, борьба с их незаконным оборотом позволят минимизировать риски острых отравлений пестицидами в производственных и бытовых условиях.

Ключевые слова: эпидемиология; пестициды; острое отравление; токсическое действие

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INTRODUCTION

Pesticides (Latin pestis for "taint" and caedo for "to kill") are chemicals or biochemicals used to control pests and diseases of plants, including weeds. Such substances are used in agricultural and forestry production processes, as well as their storage, transportation or trade. Pesticides are also used to control harmful organisms in residential buildings and public places, including vectors of human or animal diseases. Similar substances are also used for plant growth regulation, pre-harvest leaf removal (defoliants) and drying of plants (desiccants), thinning or preventing premature fruit fall. Pesticides may be used in the form of various formulations that include the active ingredient of the pesticide itself or a mixture of active ingredients and excipients (solvents, emulsifiers, surfactants, adjuvants, etc.). The active agent is a biologically active part of a pesticide preparation that directly provides a toxic effect on a harmful organism or on the growth and development of plants. The active principle of a biological preparation of a pesticide (biopesticide) is a microorganism or a product of its vital activity, a chemical is a substance of chemical synthesis [1].

Current trends in the use of pesticides are also associated with the development of new formulations containing nanoscale particles of active substances and a nanocomposite component as an adjuvant for delivery to the target object [4]. While bio- and nanopesticides are considered as an alternative to chemicals as a new generation of effective and safe pesticides, safety criteria for regulating their use have not been sufficiently developed. There are many concerns about the potential risks of toxic effects of pesticides on the environment, as well as on human and animal health [2]. In the near future, despite the growing global market for bio- and nanopesticides, the widespread use of chemical pesticides will continue to dominate [3]. Although making significant contributions to solving hunger problems and preventing of various diseases, pesticides have a negative impact on public health and can lead to the risk of acute poisoning with severe health and even fatal outcomes both under industrial and domestic conditions [4].

The purpose of the study is to carry out a systematic review and analysis of literature data to identify the nature of the prevalence, causes of development and structure of acute pesticide poisoning at the present stage.

MATERIALS AND METHODS

A search for scientific literature was carried out in electronic bibliographic databases in the Russian (eLibrary, CyberLeninka) and English (Web of Science, Scopus, PubMed, Google Scholar, Cochrane Library) languages.

RESULTS

Current trends in the use of pesticides

Despite restrictions imposed in some countries and a reduction in the use of highly hazardous pesticides, the

global pesticide market has been growing in recent decades. So, while in 1960, about 100 active substances of pesticides were recognized globally, by 2020 there were already about 600 active pesticide substances. Meanwhile, the volume of pesticide used in the equivalent of active substances doubled from 1.5 million tons in the 1980 to 3 million tons in 2020. The leaders in terms of annual pesticide use for the period from 2010 to 2020 were China, the USA and Argentina — about 1.8 million tons, 386,000 tons and 265,000 tons, respectively. In Russia, the pesticide market has quadrupled over this period; by 2020, their use amounted to 187,900 tons [5]. The number of substances included the State Catalog of Pesticides and Agrochemicals Approved for use in the territory of the Russian Federation increased by more than 70% over the period 2010-2015 to comprise around 1800 preparative forms of pesticides as of 2021 [6]. According to analytical studies, the volume of the global pesticide market will reach about 200 billion US dollars by 2031 from 85.12 billion in 2022 [5]. The projected global growth of the pesticide market at the present stage is explained by the need to increase agricultural production due to the growth of the Earth's population as well as tackling phytosanitary risks in agriculture and forestry associated with the introduction, penetration, spread and acclimatization of new insect pest species, pathogens and weeds alien to certain geographical areas occurring as a result of global climate change [5, 7]. In addition, the need to systematically expand and increase the range of constantly updated drugs, the use of mixtures of pesticides with various active substances and the search for new pesticide formulas arises due to the increased resistance of harmful organisms to pesticides, which is universal regardless of the class and type of active substance used [8].

The creation of new forms of pesticides and introduction of technologies for their use often outstrip studies into the effects of their use on human health. Moreover, risks of acute toxic effects of pesticides on humans when used under industrial and household conditions often exceed the prognostic risk estimates of their active substances obtained from experimental animal models [3]. Some authors expect the problem of toxicity of new forms of pesticides to increase in the near future resulting in higher costs associated with their creation [8].

A growing global problem in the international market is the expanded supply of generic pesticides against a background of declining sales of developed and patented substances [8, 9]. In recent years, the proportion of counterfeit pesticide products on the global market has increased by about 25%. Such practices are typically implemented on small farms and the segment of private producers of agricultural products [10]. Counterfeit pesticides, whose composition can be changed both qualitatively and quantitatively, seldom correspond in identity and quality with the active substances and additional components used in officially approved pesticides. Disruption of technological processes during the production of generic pesticides in

clandestine industries significantly increases the risks of acute poisoning when used [3]. In this connection, it may be noted that around 85–90% of all counterfeit pesticides are imported from China and India [10].

The potential hazard presented by pesticides to humans and wildlife is associated with their deliberate introduction into the environment to destroy targeted living objects (pests), which may be spread over vast territories, resulting in their circulation in ecosystems and food chains along with the risk of toxic effects on large segments of non-target wildlife populations [11]. For many years, cases of intentional and unintentional mass poisoning of domestic and wild animals have been reported in almost all countries of the world, including Russia, as a result of inhalation or ingestion of pesticide preparations, including absorption through the skin and transmission through food chains. Toxic effects on animals of banned pesticides and their mixtures used on arable lands in many countries of the world are the rule than the exception, thus necessitating a legal study of this issue and the imposition of criminal and administrative liability for the import, production and use of prohibited pesticides, as well as regulatory violations in the use of permitted pesticides [11, 12].

In recent years, the range of pesticides used has been significantly updated. Mercury-containing, chlorine-containing, highly hazardous organophosphate pesticides, aluminum and zinc phosphides, methyl bromide and other pesticides leading to severe industrial and household poisoning were widely used in the global agro-industrial sector until the end of the 1980s. Thus, in 1971-72 in Iraq, one of the largest mass poisonings of farmers and their family members (6530 were affected, 459 of them fatally) occurred as a result of eating homemade bread made from methylmercury-etched seed grains [13]. In 1967, one of the first cases of poisoning of sailors on a dry cargo ship with methyl bromide used in the practice of quarantine fumigation to kill ticks, nematodes, rodents, pathogens of fungal diseases, was registered. In 1983, the number of reported deaths from poisoning with this fumigant exceeded 950 cases. Methyl bromide was widely used as an agricultural fumigant from the 1930s until the decision to limit its use was approved by the Montreal Protocol on Substances that Deplete the Ozone Layer in 1987. Although the complete prohibition of methyl bromide was planned to apply by 2010, even today it remains one of the main means for fumigation of cargo holds and quarantine treatment of imported products, which can lead to severe cases of poisoning with fatal outcomes [14]. When processing transported goods in containers by sea and storing grain in granaries, extremely toxic aluminum phosphide and magnesium phosphides are used along with other pesticides not included in the State Catalog of Pesticides Approved for Use in Russia, sulfuryl fluoride, formaldehyde, ethylene oxide, 1,2-dichloroethane, dichloromethane (chloromethane), chloropicrin [15, 16].

In industrialized countries, the use of low- and moderately toxic substances has increased, contributing to a decrease in the number of fatal and severe poisonings. However, despite the 2006 decision of the Food and Agriculture Organization of the United Nations to consistently ban the use of especially dangerous pesticides, more than 200 active substances of especially dangerous pesticides are used in many developing countries despite being prohibited for use in European countries and the United States [17]. According to Donley N et al. [18], in the period 2015-2019 unregistered pesticide products containing 26 different highly hazardous organophosphate or carbamate insecticides were produced in the United States for export to 53 countries. At the same time, the US Environmental Protection Agency (EPA) does not provide guaranteed notifications to importing countries (as required by law) about the export of a pesticide recognized as harmful to human health or for which a standard safety assessment has not been conducted. According to some authors, in 72% of the countries importing unregistered pesticides from the United States, acute pesticide poisoning was observed in more than a third of agricultural workers [18].

The problem of acute poisoning with extremely dangerous pesticides approved for use in almost all countries of the world (aluminum phosphide, metal bromide, anticoagulant rodenticides), as well as moderately and low-hazard organophosphorus, carbamate, halogenated pesticides, pyrethroids, rodenticides, glyphosates, neonicotinoids and other groups of pesticides, remains relevant [18]. Thus, in 2018 on a dry cargo ship transporting grain treated with aluminum phosphide from Kazakhstan to Azerbaijan across the Caspian Sea, 12 crew members were seriously poisoned with phosphine, three of them fatally. The cause of poisoning of sailors with phosphine released by aluminum phosphide was non-compliance with safety requirements on the ship, as well as the general dilapidation of the vessel in terms of leaky holds etc. [19]. Cases of mass poisoning with anticoagulant rodenticides (vitamin K antagonists) were reported in the USA in 2018 and 2021 [20], as well as in Israel in 2021-22 [21]. Poisoning occurred due to inhalation of synthetic cannabinoids contaminated with these pesticides. As a result of these poisonings, 450 people were injured in the United States, 13 of them fatally, while 98 people were poisoned in Israel, three of them fatally. In Russia in 2019, poisoning with anticoagulant rodenticides as a result of eating sunflower oil made at home from pickled seeds was registered in 80 people, three of whom died [22]. In Uganda, a case of criminal poisoning has been described in seven people with three fatal outcomes as a result of eating bread made from flour contaminated with malathion [23].

According to the data published in a systematic analysis by Boedeker W et al. [4] of the results of 157 scientific studies for the period 2006–2018, the annual number of acute unintentional poisoning in 58 countries amounted to a total of 740,000 cases, including 7446 deaths. According to WHO-registered data from 83 countries for the period 2011–2015, an average of 835 fatal cases of unintentional

poisoning were observed annually, 139 of them in children under 15 years of age. The largest number of unintentional fatal cases of pesticide poisoning recorded by WHO in this period were in Guatemala, Mexico, Japan; in Egypt, Iran, and Mexico affecting children; in Mexico, Brazil, and Japan among farmers [4].

Table 1 shows the countries with the highest number of cases of unintentional fatal pesticide poisoning reported in adults and children in general and separately in children and farmers (industrial poisoning).

According to Table 1, the structure of unintentional fatal pesticide poisoning in the countries that provided information was dominated by domestic poisoning cases, including among farmers. The number of deaths from industrial poisoning among farmers was 8% in Brazil, 7% in Mexico, 3% in Japan, and 0.3% in Guatemala [4]. At the same time, the practice of incomplete accounting and registration of deaths, injuries and occupational diseases among agricultural workers, which is widespread in many countries of the world, is highly dangerous for the life and health of workers in industries both in industrialized and developing countries [24].

Extrapolating the results of a systematic analysis of scientific research data and information on mortality registered in WHO acute pesticide poisoning to the world community, Boedeker W et al. [4] concluded that about 385 million cases of unintentional pesticide poisoning occur annually at the global level with 11,000 deaths — i.e., about 44% of farmers are exposed to the toxic effects of pesticides annually. According to the Environmental Protection Agency, from 10,000 to 20,000 confirmed cases of acute pesticide poisoning affecting agricultural workers are registered annually in the United States. When taking into account cases of non-treatment of victims for medical care and undiagnosed cases of poisoning, the real number may exceed 300,000 per year.

The majority of fatal cases of acute pesticide poisoning occur when substances are taken orally or parenterally administered for suicidal purposes. About 14 million people died from suicidal pesticide poisoning between 1940 and 1980 during the "green revolution" in developing countries — agrarian transformations that included the use of highly toxic pesticides. At the same time, about 50% of fatal suicide poisonings registered in the world during this period were reported in China [25].

The measures taken to prevent suicidal pesticide poisoning in China have significantly contributed to the global decrease in fatal cases of suicidal pesticide poisoning observed since the 1990s, which nevertheless continue to be a serious public health problem [26]. According to WHO [27], currently more than 700,000 people worldwide commit suicide every year. At the same time, pesticide poisoning is one of the most common methods of suicide: one in five suicides is caused by pesticide poisoning. Most of them are observed in rural areas of South Asian countries, mainly involving pesticides based on organophosphate compounds and aluminum phosphide. This is due to the fact that in developing countries, whose economies are based on agriculture, pesticides are a cheap product and are not limited in sale, which contributes to a high risk of fatal poisoning in domestic conditions, including suicidal actions in the presence of crisis or conflict situations. In this regard, the prevention of suicidal pesticide poisoning should be aimed at limiting public access to particularly dangerous pesticides [28]. The reduction in the use and restriction of sales of especially dangerous pesticides (paraguat, metaphosphate, methyl bromide, aluminum phosphide, etc.) led to a significant decrease in the number of all deaths from pesticide poisoning in Japan, Denmark, Republic of Korea, the United Kingdom, the United States, and Taiwan. Thus, in Japan in 2019, 221 fatal cases of pesticide poisoning were registered, which is a 92% reduction from 1986. At the same time,

Table 1. Countries with the highest number of cases of unintentional fatal pesticide poisoning reported to WHO for the period 2011–2015

Countries	Study period	Total number of fatal poisoning cases during the study period			Average annual number of fatal poisoning cases		
		total	children	farmers	total	children	farmers
Brazil	2011–2015	236	29	19	47.2	5.8	3.8
Guatemala	2011–2015	687	43	2	137.4	8.6	0.4
Egypt	2011–2015	366	177	-	73.2	35.4	-
Iran	2013–2015	154	61	-	51.3	20.3	-
Mexico	2011–2015	573	91	40	114.6	18.2	8
South Africa	2011–2015	83	49	-	16.6	9.8	-
Republic of Korea	2011–2015	181	1	-	36.2	0.2	-
Japan	2011–2015	396	0	11	79.2	0	2.2

Table prepared by the authors according to the source [4]

Note: "-" the number of fatal cases of poisoning among farmers is unknown

the number of deaths from unintentional pesticide poisoning decreased by 83.8%. This decrease was due to a decrease in sales of both insecticides based on organophosphates and carbamates, as well as herbicides based on paraquat and diquat [29].

A need arises to limit use of the new insecticide chlorfenapyr, which, according to the WHO classification, belongs to moderately dangerous pesticides and is used to destroy insects resistant to organophosphorus insecticides. The effect of this drug is similar to bipyridine herbicides (in particular paraquat), which cause a high mortality rate, especially in suicidal poisoning [30].

Currently, 2,4-Dinitrophenol (DNP), which is used sparingly in industry and agriculture due to its pronounced herbicidal, fungicidal and insecticidal effects, has become a serious threat to human health in many industrialized countries. Due to the effective "fat-burning" action of DNP in the USA in the 1930s, biologically active additives for weight loss began to be used on its basis. In 1938, their use was banned due to a number of acute poisoning incidents having fatal outcomes. Since the 2000s, there has been a resurgence in the use of DNP as an illegal drug for weight correction or muscle building in the United States and other countries of the world. The growth of online sales and distribution of this drug has led to an increase in the number of cases of both accidental and intentional fatal poisoning [31].

Epidemiology of acute pesticide poisoning in postsoviet countries

Since the 1990s, traditional forms of farming in post-Soviet countries have radically changed due to the liquidation of state and collective agricultural farms. The reform of the agricultural sector and the creation of small and large farms was accompanied by a significant reduction in the financing of measures to ensure production safety and labor protection, imperfection of regulatory documentation on regulating the activities of the agro-industrial complex, insufficient awareness of agricultural workers and the public about the risks of toxic effects of applied pesticides, as well as an expansion of the list of insecticides, fungicides, herbicides allowed for free sale on the markets, rodenticides and their active use in everyday life and individual household farms [32, 33]. These consequences of reforming the market economy have largely determined the causes and patterns of acute pesticide poisoning.

According to Prodanchuk et al. [32], the creation of unfavorable working conditions on farms in Ukraine was due to the imperfection of the technological processes, the widespread use of outdated equipment and machinery, low-mechanized labor operations, and the predominance of manual labor, especially in the cultivation of sugar beet, orchards and vineyards, as well as the inadequate provision of workers with personal protective equipment. An analysis of the etiology and structure of 647 cases of acute pesticide poisoning in agricultural workers over a 25-year

follow-up period revealed 522 cases (80.7%) of acute poisoning with herbicides based on 2,4-dichlorophenoxyacetic acid, 60 cases (9.3%) of poisoning with organophosphorus insecticides, 36 cases (5.7%) with herbicides based on sulfonylurea, 14 cases (2.2%) — synthetic pyrethroids and 15 isolated cases of poisoning with aluminum phosphide, dithiocarbamates (active ingredients carboxin and thiram), and fipronil (chemical class of pyrazolines). Among the victims, beet growers (76.1% of cases) and (11.6%) winegrowers (11.6%) prevailed; less often, gardeners and workers of warehouses for the storage of pesticides [35]. Registered mass and group poisonings with pesticides accounted for 14.7-43.6% of the total structure of occupational pathology in rural areas. In 90% of cases, poisoning developed as a result of wind-borne distributions of pesticide preparations from neighboring treated areas; less often, in violation of current sanitary rules and hygienic standards.

A retrospective analysis of 287 cases of acute household pesticide poisoning among the adult population of Kiev over the period 1993–2013 revealed a decrease in the number of cases of severe poisoning, among which organophosphate poisoning prevailed (80% of cases). Mortality rates for severe pesticide poisoning remained high and tended to increase. The average annual number of severe pesticide poisoning ranged from 0.25–1.5% in the structure of all severe poisoning of chemical etiology. In contrast to poisoning in rural areas, an increase in the number of severe oral poisonings with synthetic pyrethroids and neonicotinoids, mainly of a suicidal character, was noted in urban conditions. Acute fungicide poisoning during the research period was noted with the use of carbamates, cyprodinils, and copper hydroxide [33].

In the Republic of Moldova, 919 registered non-industrial cases of pesticide poisoning with 58 deaths were detected in the period 2011–2016. At the same time, there was a trend of annual increase in the number of poisoning cases: 2011 — 95 cases (10 of them fatal); 2012 — 118 (9 fatal); 2013 — 173 (15 fatal); 2014 — 199 (13 fatal); 2015 — 122 (5 fatal); 2016 — 212 (6 fatal) [34]. Among the child population in the Republic of Moldova for the period 2014–2018, 231 cases of pesticide poisoning were registered, two of them massive: inhalation poisoning with organophosphorus insecticide Bi-58 affected 58 school-children; a preparation based on aluminum phosphide when used in a subsidiary farm in poisoned people, three of them fatally [35].

An increase in cases of pesticide poisoning was also observed in Georgia from 74 cases reported in 2017 to 236 cases identified in 2019 [36].

In the Republic of Azerbaijan during the period 2009–2016, the number of acute pesticide poisonings amounted to 806 cases with a mortality rate of 4.22%, of which 436 cases involved organophosphorus insecticides (mortality rate of 5.05%), while 330 cases were connected with rodenticides (mortality rate of 3.64%). At the same time, in the adolescent age group of people aged 15–19,

pesticide poisoning occupied a leading place in the structure of mortality from acute chemical poisoning, amounting to 30.43±9.59% of cases in the children's age group (0–14 years) In second place, 15.63±6.42% involved poisoning by snake venom [40]. In the structure of pesticide poisoning in children, 237 cases of poisoning (5 of them fatal) with organophosphorus compounds accounted for 46.8%, while rodenticide poisonings amounted to 39.2%. All fatal pesticide poisonings in children were caused by ingestion of organophosphate insecticides. The most common organophosphorus pesticides that provoked the development of acute chemical poisoning were neocidol, BI-58 (dimethoate), dichlorvos, metaphos, chlorpyrifos, malathion, and ethoprophos [38].

In Uzbekistan from 2002 to 2019, the number of acute pesticide poisonings accounted for 2.8% of the total structure of chemical injury. At the same time, there was a twofold increase in the number of hospitalized patients with acute chemical poisoning, from 6670 cases reported in 2002 to 13,255 cases reported in 2019, of which poisonings about 30% were diagnosed in children [39].

In the Republic of Belarus, the share of acute pesticide poisoning in the total structure of chemical poisoning was 2% in 2014 and 1% in 2015 and 2016 [33]. In the structure of chemical poisoning with fatal outcome for the period 2016–2018, the total number of cases amounted to 6910, while the proportion of poisoning with the use of agricultural poisons was 0.17% (12 cases, 1 of them in a child), and that of organophosphorus compounds — 0.09% (6 cases) [40].

Epidemiology of acute poisoning in the Russian Federation

While strict hygienic and toxicological assessment of the safety of pesticide use in the Russian Federation [41] has significantly contributed to a reduction the number of acute poisonings, the risks of their development remain high; cases of severe and acute poisonings are still registered annually. Of around 500 active pesticide substances permitted for use in Russia, about 200 have become widespread. The official document containing the list of pesticides and agrochemicals permitted for circulation in agriculture, forestry, communal and personal subsidiary farms and presenting the main regulations for their use is the "State Catalog of Pesticides and Agrochemicals allowed for use on the territory of the Russian Federation" [15].

Pesticides are one of the major production risk factors affecting the health of agricultural workers. Depending on the type of work performed, the a priori occupational health risk of employees in the hygienic assessment of working conditions is estimated in categories from medium to high; the prognostic probability of developing adverse health effects is 50–80% [42]. According to the indicators of acute toxicity (oral, dermal, inhalation) in the the Russian hygienic classification, pesticides

are classified into 4 classes according to the degree of danger: 1 — extremely dangerous; 2 — highly dangerous; 3 — moderately dangerous; 4 — low-hazard. Currently, 17 extremely dangerous commercial pesticide preparations are used: rodenticide preparations based on brodifacoum (Ratticum) and bromadiolone (Bromine-BD, concentrate); insecticide and acaricide preparations based on carbofuran (Hinufur, suspension concentrate); oxalic acid dinitrile (oxalic acid dinitrile, oxalonitrile, cyanogen); methyl bromide (Metabrom-RFO); preparations based on aluminum phosphide (8 preparations) and magnesium phosphide (4 preparations) [15].

When monitoring the causes of acute poisoning of chemical etiology or analyzing the structure and dynamics of acute poisoning, detailed statistical data on cases of pesticide poisoning are generally lacking. Instead, researchers are usually referred to the general group of other or other monitored toxicants, which also includes organic solvents, halogen derivatives of aliphatic and aromatic hydrocarbons, as well as corrosive substances, metals, carbon monoxide, etc. [43]. This omission hinders comprehensive toxicological monitoring of acute pesticide poisoning. However, generalized analysis of published data on the dynamics and structure of acute pesticide poisoning in certain Russian regions permits a rough assessment the epidemiological situation of this incidence and its nosological forms.

Thus, the mortality rate in acute pesticide poisoning of $20.0\pm0.8\%$ in Omsk in 2002 was the leading category in the structure of acute chemical injury; moreover, every fifth case of acute pesticide poisoning was fatal. The significant decrease in mortality by 7.6 times from 2002–2011 is associated with the disappearance of highly toxic insecticides based on organophosphorus and organochlorine compounds from household circulation. Deaths in subsequent years were recorded mainly as a result of acute poisoning with veratrin-based insecticides [44].

During the period 1999–2018, 197 adult patients (0.8% of the total number of hospitalized with acute chemical poisoning) with a mortality rate of 2.1% were treated at the Irkutsk Toxicological Center [45]. The appearance of unusual forms of poisoning was noted, which were characterized by refractoriness to specific therapy and long-term accumulation of a toxic agent.

In the Rostov region during the period 2008–2015, 2261 cases of acute poisoning with pesticides (fumitox, carbophos, rat poison, dichlorophos, chlorophos, hellebore tincture, etc.) were registered, accounting for 7.6% of the total structure of chemical poisoning [46].

Pesticide poisoning in children was registered in St. Petersburg 86 cases for the period 2010–2022 [47]; in Kazan, 15 cases of rat poison poisoning (10 of them children aged 0–3 years) occurred over the period 2018–2021 [48]. In Irkutsk during the period 1999–2018, 191 children were hospitalized with acute pesticide poisoning (the smallest number of hospitalized children (1 case) was

noted in 2003, while the largest (28 patients) occurred in 2018 [48]. The problem of children poisonings with rat poison is currently relevant in Donbas [49].

The number of appeals for the period 2019–2021 to the information and advisory toxicological department of the Golikov Research Center of Toxicology [50] on acute pesticide poisonings amounted to 541 cases (2.3% in the total structure of appeals). The purpose of the appeals in 30% of cases were issues of diagnosis and tactics of treatment of poisoning with organophosphorus insecticides: in 9% of cases — halogenated insecticides; 29% — other insecticides; 7% — herbicides and fungicides; 8% — rodenticides. Unintentional poisoning was observed in 481 (89%) cases (12 industrial and 469 domestic).

Industrial poisoning has been caused by the toxic effects of organophosphorus insecticides, rodenticides, pyrethroids and aluminum phosphide. The general circumstances of accidental poisonings were household (household) work and accidental ingestion (less often). Intentional poisoning was detected in 26 (5%) cases, of which 23 were suicidal (mainly with rodenticides and organophosphorus insecticides, as well as copper chloride, dinitrophenol, permethrin) and one was criminal (oral administration of dichlorvos), while two cases were for the purpose of intoxication (inhalation of dichlorvos). In 34 (6%) of cases, the circumstances of poisoning are unknown. The condition of patients at the time of consultation was satisfactory in 338 (62%) cases; in 111 (21%) — of moderate severity; in 13 (2%) — severe; in 79 (15%) — objectively undetermined. The cause of severe cases of poisoning was oral administration of rat poison (three cases), fenthion (two cases), diazinon, chlorpyriphos, an insecticide of an unspecified class (in one case), as well as inhalation exposure to an insecticide from bedbugs and an unspecified class (in two people), organophosphorus insecticide (in one case).

At the same time, four mass-, five group- and 10 family poisoning cases were registered. In the structure of mass poisoning, about 80 people suffered as a result of eating sunflower oil produced at home from seeds etched with anticoagulant rodenticide; 15 people suffered from inhalation effects of an organophosphorus insecticide and a pesticide of an unspecified class, six

from malathion, and five from an insecticide of an unspecified group. The main cause of family poisoning was inhalation exposure to insecticides from cockroaches, bedbugs and insecticides of unspecified groups. There have also been isolated cases of accidental inhalation poisoning with aluminum phosphide and glyphosates, as well as four cases of oral poisoning with dinitrophenol taken in order to reduce weight.

CONCLUSIONS

The widespread use of pesticides in industrial and household conditions, in which circumstances food, drinking water, and air can become potential sources of toxic effects, leads to serious consequences for the health of the entire planetary population. This increases the risk of acute pesticide poisoning, which has become a priority global public health problem. No part of the human population is completely protected from the adverse effects of pesticides. An analysis of current trends in the use of pesticides and the epidemiology of acute poisoning has revealed global problems of mass death of wild and domestic animals due to intentional and unintentional acute poisoning with permitted and prohibited pesticides and the increased use of counterfeit drugs that increase the risks of acute poisoning. In developing countries, the toxic effects of pesticides are a serious health problem, reaching epidemic proportions in some countries. There are growth trends in cases of pesticide poisoning in Ukraine, Moldova, Georgia, Azerbaijan, and Uzbekistan.

Although strict toxicological assessment of pesticide safety in the Russian Federation has contributed significantly to reducing the number of acute poisonings, the risks of their occurrence remain high. Annually registered cases of severe acute poisoning with pesticides, some having fatal outcomes, mainly involve organophosphate insecticides, rodenticides, veratrines, and aluminum phosphide. Analyzing the causes and structure of poisoning contributes to the optimization of a set of preventive measures to strengthen sanitary control and compliance with hygienic standards of individual and public safety during the storage and use of pesticides.

References

- FAO. The international Code of Conduct for the sustainable use and management of fertilizers. 2019.
 - https://doi.org/10.4060/CA5253EN
- Khamidullina HH, Ryabikova D N. Green pesticides (advantages and problems of implementation). *Toxicological Review*. 2020;3(162):53–6 (In Russ.).
 - https://doi.org/10.36946/0869-7922-2020-3-53-56
- Kumar S, Nehra M, Dilbaghi N, Marrazza G, Hassan AA, Kim KH. Nano-based smart pesticide formulations: Emerging opportunities for agriculture. *J Control Release*. 2019;294:131–53. https://doi.org/10.1016/j.jconrel.2018.12.012
- Boedeker W, Watts M, Clausing P, Marquez E. The global distribution of acute unintentional pesticide poisoning: estimations based on a systematic review. BMC Public Health. 2020;20(1):1875.
 - https://doi.org/10.1186/s12889-020-09939-0
- Tareev AI, Bereznov AV, Smirnov VV, Tareeva A, Kislaya SS. The world market of chemical plant protection products: potential crop losses, trends and prospects of pesticide production for the Russian economy. Food production equipment and technology. 2024;54 (2):310–29 (In Russ.).
 - https://doi.org/10.21603/2074-9414-2024-2-250

 Dolzhenko VI, Laptiev AB. Modern range of plant protection products: biological efficiency and safety. Fertility. 2021;3(120):71–5 (In Russ.).

https://doi.org/10.25680/S19948603.2021.120.13

 PPC Secretariat. Scientific review of the impact of climate change on plant pests — A global challenge to prevent and mitigate plant pest risks in agriculture, forestry and ecosystems. Rome. 2021. FAO on behalf of the IPPC Secretariat.

https://doi.org/10.4060/cb4769en

 Benbrook CM. Why Regulators Lost Track and Control of Pesticide Risks: Lessons From the Case of Glyphosate-Based Herbicides and Genetically Engineered-Crop Technology. Curr Environ Health Rep. 2018;5(3):387–95.

https://doi.org/ 10.1007/s40572-018-0207-y

 Weisner O, Frische T, Liebmann L, Reemtsma T, Ro-Nickoll M, Schäfer RB, et.al. Risk from pesticide mixtures — The gap between risk assessment and reality. Sci Total Environ. 2021;796:149017.

https://doi.org/10.1016/j.scitotenv.2021.149017

- Boyko OA, Ivanov SL. Tariffication in counterfeit and counterfeit plant protection products: determinants and counteraction measures. Citizen and law. 2021;1:42–51 (In Russ.).
 EDN: FRKNGD
- Valverde I, Espín S, Gómez-Ramírez P, Sánchez-Virosta P, García-Fernández AJ, Berny P. Developing a European network of analytical laboratories and government institutions to prevent poisoning of raptors. *Environ Monit Assess*. 2022;194(2):113. https://doi.org/10.1007/s10661-021-09719-2
- Matishov GG, Staheev VV, Savitsky RM. Application of rodenticides and the mass death of animals in the south of Russia. Science of the South of Russia. 2024;20(1):77–84 (In Russ.). https://doi.org/10.7868/25000640240110
- Bakir F, Rustam H, Tikriti S, Al-Damluji SF, Shihristani H. Clinical and epidemiological aspects of methylmercury poisoning. Postgrad Med J. 1980;56(651):1–10.
 - https://doi.org/10.1136/pgmj.56.651.1
- Afandiyev INO. Mass Occupational Phosphine Poisoning of a Dry-Cargo Ship Crew: A Case Report. Iran J Public Health. 2022 Jun;51(6):1428–31.

https://doi.org/10.18502/ijph.v51i6.9700

- The State catalog of pesticides and agrochemicals approved for use in the territory of the Russian Federation. Part I. Pesticides. M.:2024 (In Russ.).
- 16. Golovan TV, Tonkonog VV, Arestova YuA. Security problems of customs officials during the inspection of containers treated with fumigants. Problems of social hygiene, health care and the history of medicine. 2022; 30(4):592–599 (In Russ.).
 - https://doi.org/ 10.32687/0869-866X-2022-30-4-592-599
- 17. Parra-Arroyo L, González-González RB, Castillo-Zacarías C, Melchor Martínez EM, Sosa-Hernández JE, Bilal M, Iqbal HMN et. al Highly hazardous pesticides and related pollutants: Toxicological, regulatory, and analytical aspects. Sci Total Environ. 2022;807(3):151879.

https://doi.org/ 10.1016/j.scitotenv.2021.151879

 Donley N, Bullard RD, Economos J, Figueroa I, Lee J, Liebman AK et.al. Pesticides and environmental injustice in the USA: root causes, current regulatory reinforcement and a path

- forward. *BMC Public Health*. 2022;22(1):708. https://doi.org/10.1186/s12889-022-13057-4
- Afandiyev INO. Mass Occupational Phosphine Poisoning of a Dry-Cargo Ship Crew: A Case Report. Iran J Public Health. 2022 Jun;51(6):1428–31.

https://doi.org/10.18502/ijph.v51i6.9700

 Feinstein DL, Hafner J, van Breemen R, Rubinstein I. Inhaled synthetic cannabinoids laced with long-acting anticoagulant rodenticides: A clear and present worldwide danger. *Toxicol Commun.* 2022;6(1):28–9.

https://doi.org/10.1080/24734306.2022.2025690

21. Bar N, Lopez-Alonso R, Merhav G, Naaman E, Leiderman M, Ilivitzki A, et.al. Radiological findings in poisoning by synthetic cannabinoids adulterated with brodifacoum. *Eur Radiol*. 2024;34(7):4540-9.

https://doi.org/10.1007/s00330-023-10496-4

- Galstyan GM, Davydkin IL, Nikolaeva AS, Vekhova NI, Pavlova ZE, Ponomarenko IS, Klebanova EE, Savchenko VG. Outbreak of mass poisoning with anticoagulant rodenticides. *Russian journal* of hematology and transfusiology. 2020;65(2):174–89 (In Russ.). https://doi.org/10.35754/0234-5730-2020-65-2-174-189
- 23. Kwesiga B, Ario AR, Bulage L, Harris J, Zhu BP. Fatal cases associated with eating chapatti contaminated with organophosphate in Tororo District, Eastern Uganda, 2015: case series. BMC Public Health. 2019;19(1):767.

https://doi.org/10.1186/s12889-019-7143-0

- Rakitskiy VN. Prognostic risk of toxic effects of pesticides on the health of workers. Occupational medicine and industrial ecology. 2015;(10):5–7 (In Russ.).
 - EDN: <u>UMUIOF</u>
- 25. Karunarathne A, Gunnell D, Konradsen F, Eddleston M. How many premature deaths from pesticide suicide have occurred since the agricultural green revolution? *Clin Toxicol (Phila)* 2020;58(4):227–32.

https://doi.org/10.1080/15563650.2019.1662433

- Preventing suicide: a resource for pesticide registrars and regulators (who.int)
- 27. Preventing suicide: a resource for media professionals. https://www.who.int/publications/i/item/9789240076846
- Gunnell D, Knipe D, Chang SS, Pearson M, Konradsen F, Lee WJ, Eddleston M. Prevention of suicide with regulations aimed at restricting access to highly hazardous pesticides: a systematic review of the international evidence. *Lancet Glob Health*. 2017;5(10):e1026-e1037.

https://doi.org/10.1016/S2214-109X(17)30299-1

- Eddleston M, Nagami H, Lin CY, Davis ML, Chang SS. Pesticide use, agricultural outputs, and pesticide poisoning deaths in Japan. Clin Toxicol (Phila). 2022;60(8):933–41.
 - https://doi.org/10.1080/15563650.2022.2064868
- Cheng J, Chen Y, Wang W, Zhu X, Jiang Z, Liu P, Du L. Chlorfenapyr poisoning: mechanisms, clinical presentations, and treatment strategies. World J Emerg Med. 2024;15(3):214–19. https://doi.org/10.5847/wjem.i.1920-8642.2024.046
- Holborow A, Purnell RM, Wong JF. Beware the yellow slimming pill: fatal 2,4-dinitrophenol overdose. BMJ Case Rep. 2017;(1):1–4.
 - https://doi.org/ 10.1136/bcr-2016-214689

- 32. Prodanchuk MH, Balan GM, Bubalo NM, Zhminko PH, Kharchenko OA, Bahlei YA. The problem of acute pesticide poisonings of agricultural workers in ukraine under the conditions of the new business patterns. Wiad Lek. 2019;72(5 cz 2):1083–6. EDN: BOKECL
- 33. Kurdil NV, Zozulya IS, Ivashchenko OV. Features of acute pesticide poisoning in urban conditions. *Emergency medicine*. 2015;3(66):37–42 (In Russ.).

EDN: <u>UAUBSZ</u>

34. Mancheva TS. Pynzaru YuV, Sandulyak EV. Analysis of acute unprofessional pesticide poisoning in the Republic of Moldova in the period 2011-2016 Proceedings of the Republican scientific and practical conference with international participation. Health and the Environment. Minsk; 2017 (In Russ.).

EDN: YRFTHI

35. Mancheva TS. Acute poisoning in children in the Republic of Moldova. Proceedings of the international scientific and practical conference. Health and the Environment. Minsk; 2019 (In Russ.).

EDN: SHLMTU

36. Kobidze TS, Gerzmava OX, Kereselidze MT, Tsetskhladze N. Chemical trauma. Some features of the provision of specialized toxicological care to the population of Georgia. Conference proceedings of the scientific and practical conference Janelidze Readings. St. Petersburg; 2021 (In Russ.).

EDN: KPDYIP

37. Efendiev IN, Bunyatov M O, Akhundova MT. Lethal poisoning in Azerbaijan: epidemiology, risk factors and possible ways of prevention. *Eurasian journal of clinical sciences*. 2019;2(2):1–9 (In Russ.).

https://doi.org/10.28942/ejcs.v2i2.82

38. Efendiev IN. Poisoning with substances of anticholinesterase action. *Eurasian Journal of Clinical Sciences*. 2021;3(1):1–8 (In Russ.).

https://doi.org/10.28942/ejcs.v3i1.98

39. Khadjibaev AM, Alakaev AA, Stopnitsky RN. Clinical toxicology in the Republic of Uzbekistan. Twenty years of experience working as part of the emergency medical care system. Emergency medical care. Proceedings of the 20th All-Russian Congress. St. Petersburg;2021 (In Russ.).

EDN: KYCJHB

40. Borisevitch S, Grishenkova L, Bohdan A, Borovikova L. Structure and dynamics of acute poisoningswith lethal outcome in the republic of Belarus in 2016–2018. *Laboratory Diagnostics. Eastern Europe.* 2020;9(4):375–87.

https://doi.org/10.34883/PI.2020.9.4.003

41. Rakitskii VN, Tereshkova LP, Chkhvirkiya EG, Epishina TM. Fundamentals of ensuring the safe application of pesticides. Health Care of the Russian Federation. 2020;64(1):45–50 (In Russ.).

https://doi.org/10.18821/0044-197X-2020-64-1-45-50

- 42. National report. On the state of sanitary and epidemiological well-being of the population in the Russian Federation in 2020. Moscow: Federal Service for the Oversight of Consumer Protection and Welfare; 2021. 256 p. (In Russ.).
- Litvinova OS, Kalinovskaya MV. Toxicological monitoring of the causes of acute poisoning of chemical etiology in the Russian Federation. *Toxicological Review*. 2017;1(142):5–9 (In Russ.). https://doi.org/10.36946/0869-7922-2017-1-5-9
- 44. Sabaev AV. Mortality dynamics according to the data of the Center for acute poisoning in Omsk for 2002–2011. Siberian Medical Journal. 2013;18(3):79–81 (In Russ.). EDN: QIWPWV
- Zobnin YuV, Tretyakov AB, Nemtsova AA, Perfiliev DV, Dragunov MA. Acute poisoning in adults and children in Irkutsk in 1999–2018. Baikal Medical Journal.2019;159(4):46-55 (In Russ.). https://doi.org/10.34673/isma.2019.36.86.011
- 46. Aydinov GT, Marchenko BI, Sinelnikova YuA. Acute chemical poisonings as an index of the system of socio-hygienic monitoring in the Rostov region. *Hygiene and Sanitation*. 2018;97(3): 279–85 (In Russ.).

https://doi.org/10.18821/0016-9900-2018-97-3-279-285

- 47. Udaltsov MA, Pshenisnov KV, Aleksandrovich YuS, Kaziakhmedov VA, Ironosov VE. Epidemiology of acute poisoning in pediatric practice. *Russian Journal of Anesthesiology and Reanimatology*. 2024;(2):58–66 (In Russ.).
 - https://doi.org/10.17116/anaesthesiology202402158
- 48. Kamalova AA, Gorina GA, Kadyrova YuA, Nizamova RA, Zainetdinova MSh, Kvitko EM. Acute poisoning in children: a retrospective analysis of cases. *Toxicological bulletin*. 2022;30(6):351–8 (In Russ.).

https://doi.org/10.47470/0869-7922-2022-30-6-351-358

- Ostrovsky IM, Naletov AV, Lennart TV. Modern features of poisoning in children of Donbass. Bulletin of Emergency and Reconstructive Surgery. 2020;5(2):126–9 (In Russ.).
 EDN: <u>IUXIWF</u>
- 50. Rozhkov PG, Gasimova ZM, Bukharin YY. Retrospective analysis of requests for information and advisory toxicological assistance on issues of acute pesticide poisoning for the period 2019–2021. Proceedings of the International University Scientific Forum. Practice Oriented Science UAE–RUSSIA– INDIA. 2024.

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