ANNUAL REPORT OF THE NATIONAL POISON CONTROL CENTRE

MILITARY MEDICAL ACADEMY, BELGRADE

2014

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Review of tables, figures and graphs

Republic of Serbia

According to data for 2011 (the final results of the census), Republic of Serbia had 7.186.862 inhabitants. Administrative, teritory of Republic is divided into 29 districts. In each of them there are Regional Health Centres, which in the most cases can not provide superior medical care in the treatment of poisoned patients. Geographical layout and administrative division of the country are shown in the Figure 1.

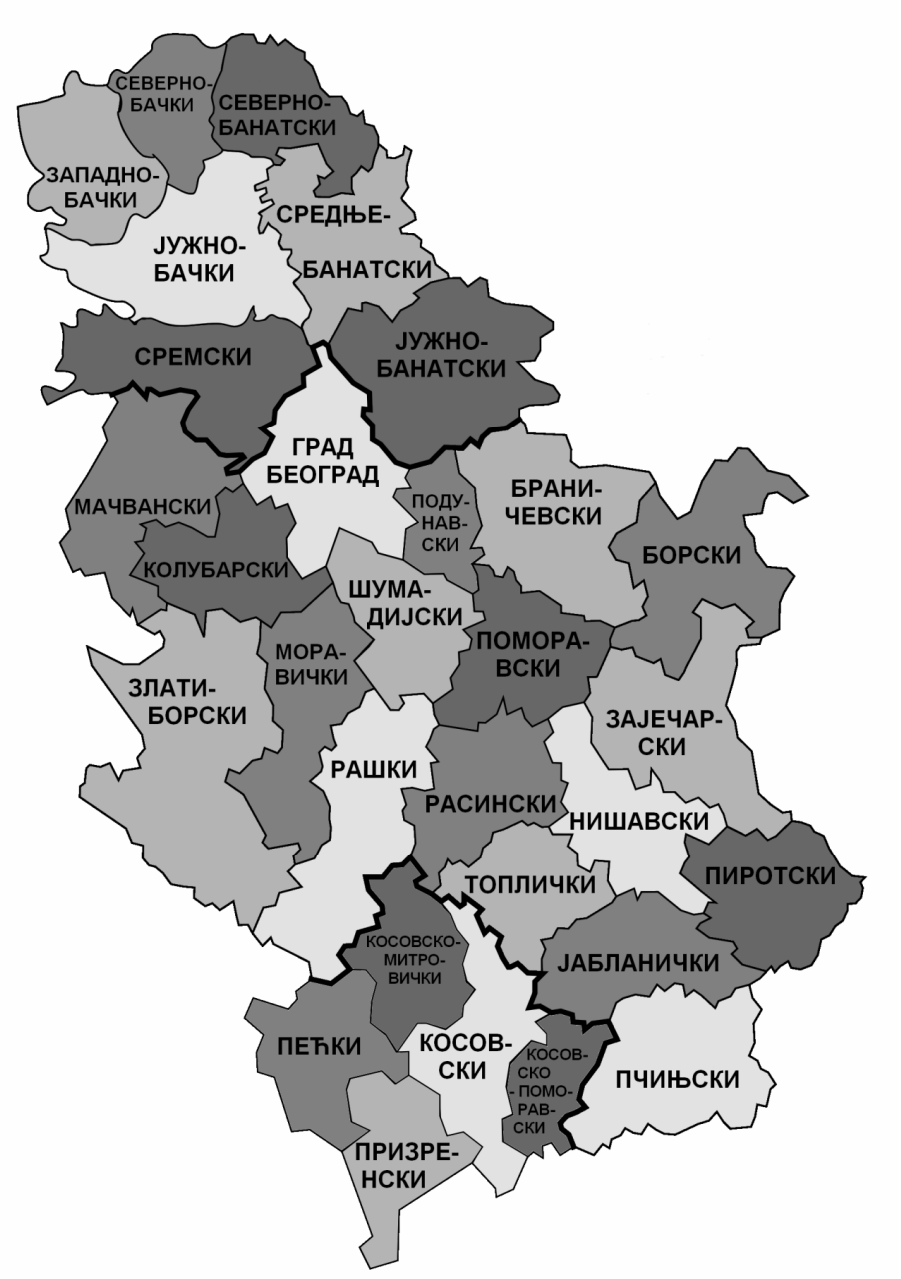

Fig. 1 Republic of Serbia, layout, administrative division

NATIONAL POISON CONTROL CENTRE

National Poison Control Centre (NPCC) is referent institution which provides medical services for acute poisonings, prevention and treatment, detection of chemical substances in biological materials, water, land and air, education in the fields of clinical toxicology and toxicological chemistry, as well as scientific research in the fields of toxicology and pharmacology.

In the Former Federal Republic of Yougoslavia, by relevant normative acts, in the 1997, NPCC was established as a state institution with the task „to organize and provide preventive care measures for poisoning, provide information on the effects of poisons, medical help measures in case of poisoning and eliminate the effects of poisoning“. NPCC is created by integrating clinical and laboratory facilities of the former Clinic for Toxicology of Military Medical Academy and Department for Medical Care of Military Tehnical Institute. From the beginning until today, the Centre has grown in one of the most prestigious institutions of its kind in Europe in term of its results and capacities.

NPCC now has Clinic for Emergency and Clinical Toxicology and Institute for Toxicology and Pharmacology and it also has Mobile toxicological-chemical team, which is activated in the case of larger chemical accidents.

In addition to the treatment of acute poisoning and providing information related to the toxicity of chemical substances, both for medical stuff and for the general public, permanent task of the NPCC is in the field of toxicovigilance- identification of changes in the incidence of poisoning, seasonal variations in the incidence of poisoning, evaluation of efficacy and safety of antidotes, storage and supply of antidotes, and reporting health and other relevant factors on the necessary measures.

More than half of the staff are with the university education of various profiles: doctors, pharmacists, veterinarians, chemists with highly specialized medical technicians. The fact that within the various departments of the Faculty of Medicine of Military Medical Academy work 3 professors, 3 associate professors, 1 assistant professor and 3 assistants from Centre is the best evidence of academic potential.

Abstract

Introduction: This is the fifth published Annual report of NPCC, Military Medical Academy, Belgrade. All available data from NPCC resources were collected and elaborated.

Methodology: Summary demographic data on patient age and gender, reason for exposure, medical outcome, used analytical procedures regarding confirmation of poisoning and all other relevant facts are shown on tables and graphs. At the end of report, short summary of all poison-related fatalities is presented. These data are analyzed by Fatality Review Team (3 clinical toxicologists and 1 analitycal toxicologist). Their work is based on 6-graded RCF (Relative Contribution to Fatality) classification.

Results: In 2014, Department for reanimation and triage of Poison Control Centre registered 4415 cases. Abuse of alcoholic drink was the most prominent reason (51.0% of cases). Abuse of medicaments (27.3%) and drugs of abuse (7.1%) were on the second and third place, respectively. The majority of cases (over 81%) belong to working population. After health examination, 702 patients were addmited to Clinic for Emergency and Clinical toxicology of Military Medical Academy. The leading cause for hospitalisation were medicaments, corrosive substances and pesticides (62.8%, 13.1 and 5.3%, respectively). The lethal outcome was registered in 36 patients.

Conclusion: Poisoning continues to be a significant cause of morbidity and mortality in the Republic of Serbia. NPCC represents a national resource to collect and monitor poisoning exposure cases and improvements of financial and personnel resources would further promote its activity.

NATIONAL POISON CONTROL CENTRE OF MILITARY MEDICAL ACADEMY

In the NPCC of Military Medical Academy (in further text MMA) medical services for prevention and treatment of poisoning are provided, and in modernly equipped laboratory, detection and quantification of numerous chemical substances in biological materials, water, land and air are available. Scientific research in the fields of pharmacology, analitical and clinical toxicology is also performed.

National Poison Control Centre consists of:

- **Clinic for Emergency and Clinical Toxicology**
- **Institute for Toxicology and Pharmacology**

A detailed overview of the organizational structure of the NPCC is shown in Fig 2.

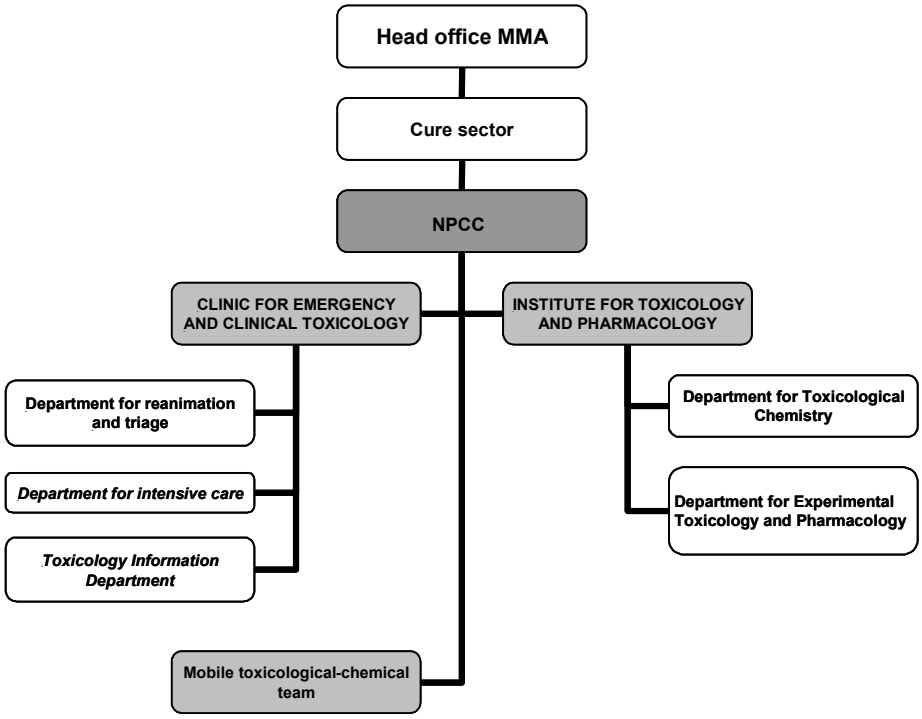

Fig. 2 Organizational structure of NPCC

Mobile toxicological-chemical (MTC) team is not an independent organisational unit but it consists of the personnel from all NPCC organizational units. MTC team is activated in the case of larger chemical accidents.

Activities of MTC team include:

- Detection, identification and quantification of chemicals in water, land, air, as well as in biological materials in the field
- Organisation of care and treatment of poisoned patients
- First aid and emergency treatment in field conditions in collaboration with local health care servicies
- Information support for the hospital treatment of poisoned patients in regional medical centers
- Supportive and symptomatic therapy of poisoned patients during transport to NPCC (severe poisoning cases)

Clinic for Emergency and Clinical toxicology

Clinic for Emergency and Clinical toxicology, the only specialized institution for acute poisoning treatment in the country consists of:

- *Department for reanimation and triage*
- *Department for intensive care*
- *Toxicology Information Department*

Working time of the Clinic is 24 hours, 7 days a week. The Clinic treats patients with acute drug, pesticide, corrosive, gases, mushroom, industrial chemicals and other toxic agents poisonings. It is also responsible for injured and acutely poisoned in mass chemical accidents. Management of acutely poisoned patients is performed according to the clearly formulated protocols, which are in full compliance with the protocols of toxicological centres in the world.
In the Clinic for Emergency and Clinical Toxicology both undergraduate studies (elective course „Clinical toxicology“, Faculty of Medicine of MMA) and postgraduate education within subspecialisation of clinical toxicology are performed.

Department for reanimation and triage

Department for reanimation and triage is used for treatment of patients with mild to moderate poisoning (the most frequent are ethyl alcohol, drugs of abuse etc).

Department for intensive care

Department for intensive care is used for treatment of patients with moderate to severe acute poisoning, who require continuous monitoring of vital functions.
Out of 24 beds in the Clinic for emergency and clinical toxicology, 8 are in the Department for intensive care, but if necessary all capacities can be activated for intensive care.

Department for toxicological information

Department is equipped with a self-made „on-line“ computer database which contains data on:

- Toxic substances and preparations on the market
- Manufacturers and distributors of chemical substances including places of manufacture and storage in the Republic of Serbia
- Cases of acute self-poisoning, occupational and accidental poisoning which are registered in the Republic of Serbia

Institute for Toxicology and Pharmacology

Institute covers numerous preclinical and clinical areas of toxicology and pharmacology which are important in solving toxicological problems in clinical practise.

Institute consists of two organizational units:

- *Department for toxicological chemistry*
- *Department for experimental toxicology and pharmacology*

Department for Toxicological Chemistry

The main task of the Department for Toxicological Chemistry performs toxicological-chemical analyses in order of rapid, sensitive and reliable detection, identification and quantification of toxic agents in different types of samples (biological material, air, water, land, food, general use products, industrial products, etc.).
Urgent toxicological chemical analysis of biological samples of patients admitted for treatment at the Clinic for Emergency and Clinical Toxicology of MMA are of particular importance.
Department for Toxicological Chemistry provides services under the urgent toxicological-chemistry service duty, 24 hours a day. In the case of chemical accidents, the Department participates in the reconnaissance and analytical tasks of Mobile toxicological-chemical team.

Laboratory equipment allows the application of the following analytical methods: physicochemical, chemical, immunochemical, enzymatic, chromatographic (TLC, HPLC, GC) and spectroscopic (UV, VIS, IR, MS, AAS, AES).

Department for Experimental Toxicology and Pharmacology

Human and material potential of the Department allows testing of certain pharmacodynamic and toxicodynamic effects of drugs or poisons in experimental animals. In cooperation with other organizational units of the Institute for toxicology and pharmacology of MMA, as well as clinics and institutes of MMA, production of complex preclinical projects is possible.

Structure of human resources potential of NPCC is shown in Table 1. The way in which the personnel structure is shown to the fullest extent reflects the real state of activities and actions of NPCC.

Table 1 The Personnel structure PCC of MMA

Groups	n	%
Doctors	13	18.6
Medical technicians	23	32.9
Specialists of toxicological chemistry	9	12.9
Veterinarians, biologists	4	5.7
Laboratory technicians	12	17.1
Administrative staff	3	4.3
Support staff	6	8.6
Total	70	100.0

In the event of increased needs of individual organisational units of the NPCC, the necessary personnel are temporarily engaged.

RESULTS

Basic (incomplete) data on the number of registered cases of poisoning and their frequency in relation to the total number of inhabitants of Republic of Serbia are shown in Table 2. The number of registered cases of poisoning, shown in the table, represent the total number of acute poisoning in the Republic of Serbia based on the data registered in the NPCC (4415) and the available data from 10 regional health care centers in Republic of Serbia (2194).

Table 2 Population in the Republic of Serbia and the number of registered poisoning in 2014

Year	Number of inhabitants	Number of registered cases	Number of cases per 1.000 inhabitants
2011*	7 186 862	6609	0.92

*Available data, web site of the Republic Institute for Statistics, Statistical Annual Report of Serbia, March, 2015.

Toxicology Information Department

In the Toxicology Information Department numerous calls from citizens and medical workers of different profiles are registered during 2014. The structure of the calls, in relation to the presumed cause of poisoning is shown in Table 3.

Table 3 Structure of the calls (intoxications of adults and children)

Agents	Adults		Children	
	Calls from the doctors	Calls from the citizens	Calls from the pediatrician	Calls from the citizens
Drug	112	22	132	11
Pesticides	74	26	24	7
Corrosives	37	5	18	4
Mushroom	12	8	15	8
Gases	5	2	2	0
Alcohol	6	3	3	0
Drugs of abuse	4	3	2	3
Other	42	28	66	10
Total	292	97	262	43

In one-year period total of 694 calls were received, 389 calls were related to the presumed poisoning in adults, and 305 in children. Calls from citizens were relatively less represented (140; 20.2%) in relation to the total number of received calls.

Department for Reanimation and Triage of the Clinic for Emergency and Clinical Toxicology

Department for reanimation and triage (DRT) NPCC of MMA is the infirmary where doctors, medical technicians and paramedics, every day of the year, for 24 hours, receive and treat patients exposed to toxic agents. Patients reffered by doctors of Emergency aid service from Belgrade and its surroundings, doctors from the other clinical centers in Serbia and hospitals in Belgrade, doctors from health care centers in Belgrade, were usually transported by ambulance. Numerous patients came for health examination without prior examination by the competent physician - by private or public transport vehicles. During 2014, in the Department for reanimation and triage of NPCC total of 4415 patients were examined by physician, and 702 (15.9%) of them were admitted for hospital treatment in the Clinic for Emergency and Clinical toxicology.

Distribution of patients examined by months, is shown in Fig 3, and the relationship of examined (discharged to home) and hospitalized patients in the Fig 4.

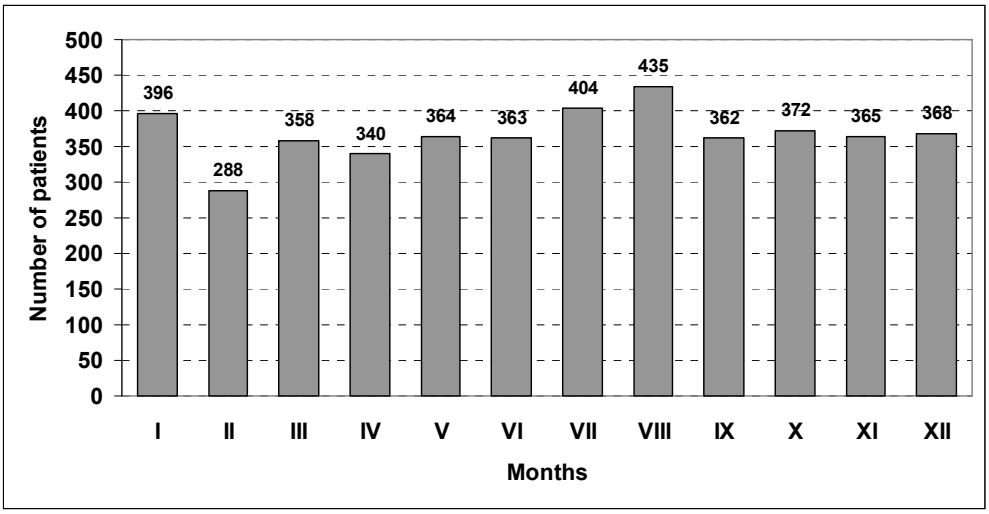

Fig. 3 Number of patients examined in DRT, by months

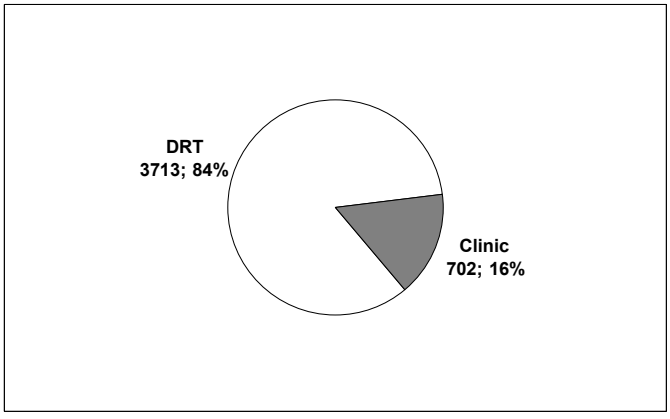

Fig. 4 Number and percentage of examined outpatient and hospitalized patients

The most common reason for arriving to DRT were the suspicion on the abuse of psychoactive substances –PAS (alcohol and drugs of abuse) and self-poisoning by drugs, corrosive agents and pesticides (90% of all cases). Less common reason for arriving was the accidental exposure (Fig. 5).

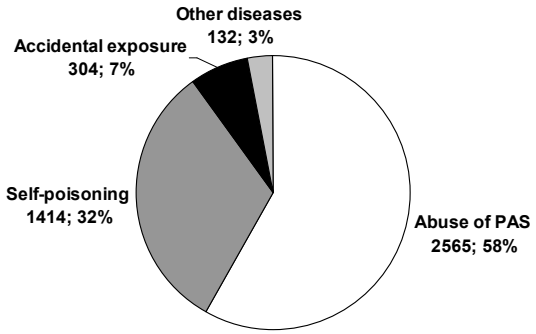

Fig. 5 Reason of arriving to DRT

The most common cause for observatioan and treatment in the DRT PCC was ethyl alcohol with 2253 examinations, 51.0% of the total number of examinations. Agents that followed were drugs with 1205 examination (27,3%), substances of abuse - 312 patients (7.1%), gases – 176 patients (4.0%), corrosives – 120 patients (2.7%), pesticides – 89 patients (2.0%), mushrooms and plants in 64 patients (1.4%), other agents in 64 patients (1.4%) and 132 patients were without acute exposure and intoxication (3.0%), Table 4.

Table 4 The frequency of the dominant causes of piosoning in examined outpatient and hospitalized patients and the distribution of agents in hospitalized patients in relation to single agent

Dominant cause	DRT	Clinic	
	n	n	%
Alcohol	2253	11	0.5
Drug of abuse	312	35	11.2
Drug	1205	441	36.6
Psychoactive	1015	367	36.2
Other drug	190	74	38.9
Gases	176	29	16.5
Corrosive	120	92	76.7
Pesticides	89	37	41.6
Mushroom and plants	64	32	50.0
Other agents	64	7	10.9
Other diseases	132	18	13.6
Total	4415	702	

From the Table 4 (right column), it can be concluded that the highest percentage of patients examined in the DRT PCC, who were admitted to the Clinic, were poisoned with corrosive

substances, mushrooms (plants), pesticides and drugs. It also shows that these groups of toxic agents led to the clinical picture which required hospitalization of patients.

Of the total number of examined patients, there were 1640 (37%) females and 2775 (63%) males (Figure 6).

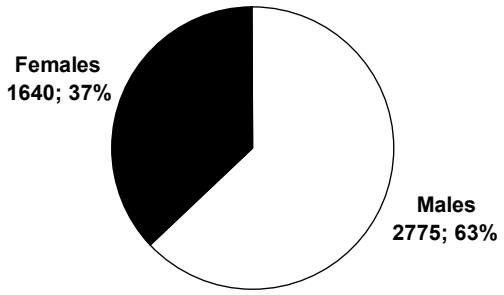

Fig. 6 Distribution of patients by gender (DRT PCC)

The most of examined patients, 1989 of them, were in the group of 19-40 years, then 1602 (36.3%) of them in the range of 41-65 years, which means that the majority of examined and treated persons belong to working population (Table 5).

Table 5 Distribution of patients by age (DRT PCC)

Age groups (years)	n	%
To 18	410	9.3
19-40	1989	45.0
41 - 65	1602	36.3
More then 65	330	7.5
unknown	84	1.9
Total	4415	100.0

Poisonings are ranked by severity based on PSS *(Poisoning Severity Score).* Mild poisoning (PSS 1) was registered in 3286 (74.4%) patients, moderate (PSS 2) in 556 (12.6%) patients, and severe poisoning in 335 (7.6%) patients. Before admission, due to severe general condition, lethal outcome (PSS 4) was registered in 4 patients. In 234 patients (5.3%) there was no exposure to toxic agents (Table 6).

Table 6 Poisoning severity expressed by PSS (DRT PCC)

Poisoning severity	N	%
PSS 1	3286	74.4
PSS 2	556	12.6
PSS 3	335	7.6
PSS 4	4	0.09
Other	234	5.3
Total	4415	100.0

Clinic for Emergency and Clinical toxicology

In the Clinic for emergency and clinical toxicology 702 patients were hospitalized during the 2014. Dynamics of patients admission in the Clinic for emergency and clinical toxicology is shown on the Figure 7.

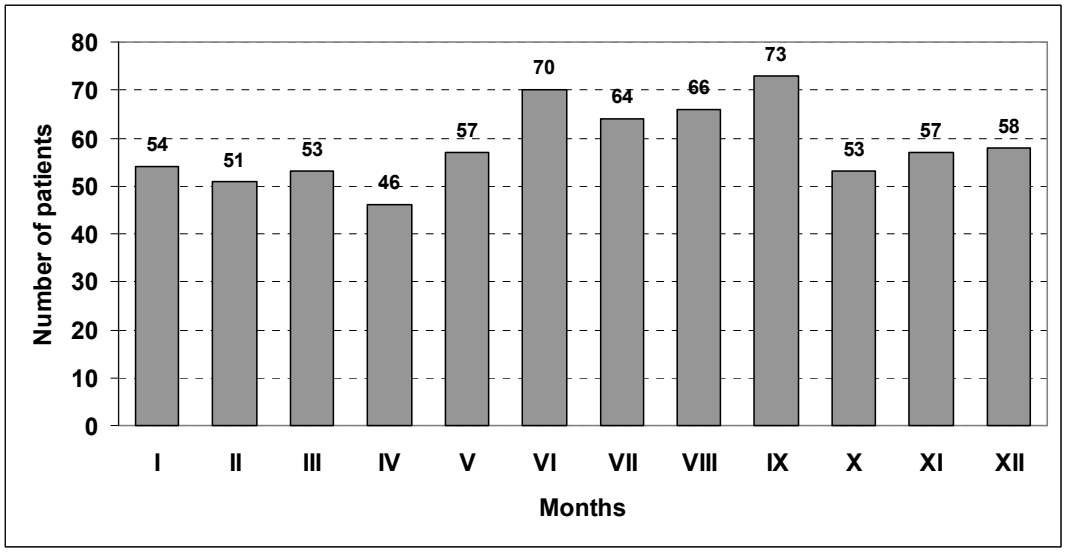

Fig. 7 The number of hospitalized patients in the Clinic for emergency and clinical toxicology, by months

The most common reason for hospitalization was self-poisoning by drugs, corrosive substances and pesticides (more than 80% cases), accidental poisoning (10%), and much rarer psychoactive substances abuse - PAS (alcohol and narcotics; figure 8).

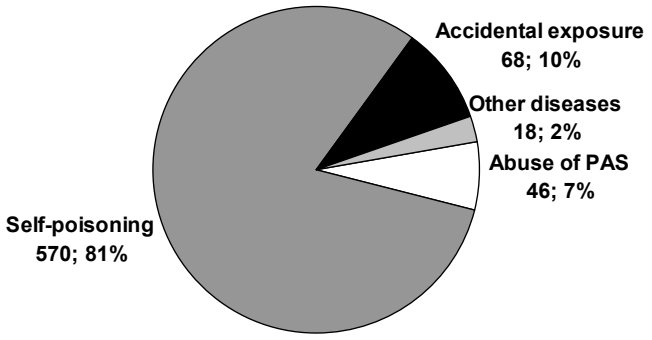

Fig. 8 Reason for hospitalization of patients (Clinic for emergency and clinical toxicology)

Drugs, as a dominant cause of poisoning were the most common agent, in 441 patients (62.0% of hospitalized patients), followed by corrosives in 92 cases (13.0%), pesticides with 37 poisonings (5.0%), drugs of abuse in 35 patients (5.0%), mushrooms and plants in 32 (5.0%), gases in 29 (4.0%), ethyl alcohol in 11 (2.0%), and other toxic agents in 7 patients (1.0%). Other diseases were noted in 18 patients (3.0%), figure 9.

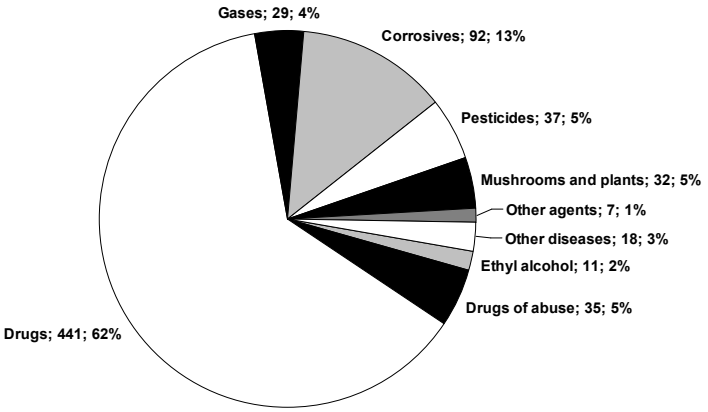

Fig. 9 The percentage distribution of causes of poisoning (Clinic for emergency and clinical toxicology)

According to gender, 282 (40%) males and 420 (60%) females were hospitalized, figure 10.

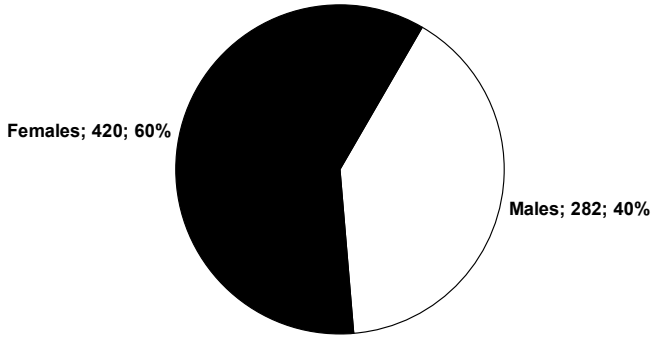

Fig. 10 Distribution of patients by gender (Clinic for emergency and clinical toxicology)

According to the age structure of hospitalized patients, there were 36 (5.1%) persons younger than 18 years, from 19-65 years 561 patients (79.9%), and 105 patients were older than 65 years old (Table 7).

Table 7 Distribution of patients according to age (Clinic for emergency and clinical toxicology)

Age groups (years)	n	%
To 18	36	5.1
19 - 40	284	40.5
41-65	277	39.4
More than 65	105	15.0
Total	702	100.0

Mild poisoning was registered in 349 (49.6%) patients (PSS 1), moderate (PSS 2) in 129 (18.4%), severe poisoning (PSS 3) in 176 (25.1%), and there were 32 (4.6%) cases with lethal outcome (PSS 4) (Table 8). Additional clinical and laboratory analyzes showed that in 16 patients (2,3%) there were no signs of intoxication.

Table 8 Severity of poisoning expressed by PSS (Clinic for emergency and clinical toxicology)

Poisoning severity	n	%
PSS 1	349	49.6
PSS 2	129	18.4
PSS 3	176	25.1
PSS 4	32	4.6
Other	16	2.3
Total	702	100.0

In the current review only the basic data about the number, gender and age structure of patients and the distribution of different types of poisoning in examined and hospitalized patients are given. In the further text, using similar methodology, the data will be analyzed in relation to the type of chemical agent that caused the intoxication.

Ethyl alcohol

The most common agent due to which patients arrived at the DRT PCC was ethyl alcohol. Due to the acute ethyl alcohol intoxication 2253 persons were examined (51.0% of all examined). A significantly higher number of males 1759 (78.1%), compared with females 494 (21.9%), was registered.

Distribution of patients by age (ethyl alcohol intoxication) is shown in Table 9.

Table 9 Distribution of patients according to age (DRT PCC)

Age groups (years)	n	%
To 18	267	11.8
19 - 40	889	39.4
41-65	887	39.4
More than 65	136	6.0
unknown	74	3.3
Total	2253	100.0

Mild acute ethyl alcohol intoxication (PSS 1) was registered in 1749 (77.6%) patients, 463 examined patients (20.6%) were with signs of moderate and severe acute intoxication (PSS 2 - 353 i PSS 3 – 110), and there was 1 lethal outcome (PSS 4). Forty patients (1.8%) were mistakenly sent, due to suspicion on the acute ethyl alcohol intoxication.

Due to the acute ethyl alcohol intoxication 11 patients (1.6% of all hospitalized patients) were admitted to Clinic for emergency and clinical toxicology. Six of them were males, five females, and they were at the age of 19 to more than 65 years old (there were no patients younger than 18 years). In 3 patients PSS 1 score was registered, and in 8 patients PSS 3.

Drugs

Due to the acute drug intoxication 1205 (27.3% of all examined) patients were examined in the DRT PCC.

Due to the acute psychoactive drug intoxication 1015 (84.2%) patients, out of them 320 males (31.5%) and 695 (68.5%) females, were examined.

Distribution of patients according to age (psychoactive drug intoxication) is shown in Table 10.

Table 10 Distribution of patients by age (DRT PCC)

Age groups (years)	n	%
To 18	69	6.8
19 - 40	478	47.1
41-65	400	39.4
More than 65	68	6.7
Total	1015	100.0

As a dominant cause of poisoning, in most of cases benzodiazepines were detected (688; 67.8%), then antiepileptics with 182 cases (17.9%). Neuroleptics in 99 patients (9.0%) and antidepressants in 46 patients (4.0%) were registered as a cause of poisoning.

In the group of benzodiazepines, the most common cause of poisoning was bromazepam in 313 cases (45.0%), then diazepam (184 cases; 26.7%) and lorazepam (97 cases; 14.1%).

Among the antiepileptics, significantly more frequent in comparison to other was carbamazepine, in 87 (47.8%) patients, then clonazepam in 58 (31.9%) patients, VPA in 22 (12.1%), lamotrigine in 8 (4.4%), barbiturates in 5 (2.7%) and levetiracetam in 2 (1.1%) patients.

In the group of neuroleptics (as a cause of poisoning), clozapine and similar drugs (olanzapine, risperidone) were the predominant cause of poisoning in 59 (59.6%) patients, followed by phenothiazines (28 patients; 28.3%).

In the group of antidepressants, the new-generation antidepressants (SSRI) (28 patients; 60.9%), compared to cyclic antidepressants (14 patients; 30.4%) were a bit more frequent, as the cause of poisoning. Detailed review of number of acute drug poisonings in DRT PCC was shown in Table 11.

Mild poisoning (PSS 1) was found in 808 persons (81.8%). Moderate poisoning (PSS 2) was registered in 91(9.2%), and severe poisoning (PSS 3) in 83 patients (8.4%). Lethal outcome was noted in one patient. Twentyseven patients (2.7%) were mistakenly sent, due to the suspicion on the acute drug intoxication, and the PSS score (percent) was calculated on the total number of 988.

Among the drugs from other groups, which were the predominant cause of poisoning in 190 examined patients, the most common were analgesics which were the primary agent in 51 (26.8%) patients. NSAID were the cause of poisoning in 37 cases, and opioid analgesics in 12 cases. The predominant cause of poisoning in 63 (33.2%) patients was cardiovascular drugs. Among these drugs, as the cause of poisoning, the most common were beta blockers (28 cases),

calcium antagonists (20 cases) and ACE inhibitors (9 cases). Sympathomimetic drug poisoning (theophylline, salbutamol) was registered in 11 (5.8%), and anticholinergic drug poisoning in 10 (5.3%) patients. Poisonings by other drugs (oral hypoglycemic drugs, hormonal preparations, unknown drugs, etc.) were recorded in 56 (29.5%) patients.

Signs of mild poisoning (PSS 1) were found in 152 (80.0%) patients, moderate poisoning (PSS 2) in 18 (9.5%) of them, and severe poisoning (PSS 3) in 19 (10.0%) patients. Lethal outcome (PSS 4) was registered in one patient.

Table 11 The frequency of a single drug as dominant cause of poisoning (DRT PCC)

Psychoactive drug	1015	%	**Other drug**	190	%
Antidepressants			*Analgesics*		
Cyclic	14	30.4	NSAID	37	72.5
SSRI	28	60.9	Opioides	12	23.5
Other	4	8.7	Total	51[2]	100.0
Total	46	100.0	*Cardiological*		
Antiepileptics			Beta blockers	28	44,4
Carbamazepine	87	47.8	Calcium antagonists	20	31.7
Clonazepam	58	31.9	ACE inhibitors	9	14.3
VPA	22	12.1	Antiarrhythmics	4	6.4
Lamotrigine	8	4.4	Cardiotonics	2	3.2
Barbiturates	5	2.7	Total	63	100.0
Levetiracetam	2	1.1	*Sympathomimetics*		
Total	182	100.0	Theophylline	10	90.9
Benzodiazepines			Salbutamol	1	9.1
Bromazepam	313	45.5	Total	11	100.0
Diazepam	184	26.7	*Anticholinergics*		
Lorazepam	97	14.1	Trihexyphenidyl	1	10.0
Alprazolam	56	8.1	Biperiden	9	90.0
Midazolam	13	1.9	Total	10	100.0
Other	5	0.7	*Others*		
Zolpidem[1]	20	2.9	Oral hypoglycemics, hormonal preparations, unknown drugs etc.		
Total	688	100.0			
Neuroleptics					
Phenothiazines	28	28.3			
Butyrophenones	9	9.1			
Clozapine	44	44.4			
Risperidone	7	7.1	Total	56	100.0
Olanzapine	8	8.1	[1] anxiolytic, does not belong to the group of benzodiazepines		
Other	3	3.0			
Total	99	100.0	[2] unknown (analgesics)		

From the total of 702 hospitalized patients, 441 persons (62.8%) were treated due to acute drug intoxication. Among them, 367 persons (83.2%) were hospitalized due to acute psychoactive drug poisoning, and 74 persons (16.8%) due to acute other drug group poisoning.

In the group of patients with acute psychoactive drug poisoning there were 255 females (69.5%) and 112 males (30.5%). Distribution of patients according to age (psychoactive drug intoxication) is shown in Table 12.

Table 12 Distribution of patients according to age (Clinic for emergency and clinical toxicology)

Age groups (years)	n	%
To 18	18	4.9
19 - 40	170	46.3
41-65	138	37.6
More than 65	41	11.2
Total	367	100.0

The most common drugs, as a cause of poisoning, were from the benzodiazepine group (199 persons; 54.2%), antiepileptics (92; 25.1%), neuroleptics (57; 15.5%) and antidepressants (19; 5.2%).

In the group of benzodizepines, the leading cause of poisoning was bromazepam (111 cases), followed by a significantly smaller number of lorazepam (27), diazepam (25), alprazolam (21), zolpidem (9), midazolam (4), and others (2).

Among the antiepileptics, the most common cause of poisoning was carbamazepine (55 cases), followed by VPA (15), clonazepame (13), lamotrigine (5) and barbiturates (4).

Among the neuroleptics, the most common cause were clozapine (35 cases), phenothiazines (13), and then olanzapine (5 cases).

Among antidepressants, as the cause of poisoning, SSRI (10 cases) and cyclic antidepressants (9) were equally represented.

Detailed review of the number of acute drug intoxication at the Clinic for emergency and clinical toxicology is shown in Table 13.

Among the patients hospitalized due to acute psychoactive drug poisoning, mild poisoning (PSS 1) was noted in 211 persons (57.5%), moderate (PSS 2) in 71 persons (19.3%), and severe (PSS 3) in 80 persons (21.8%). In this group of patients 5 lethal outcomes (PSS 4; 1.4%) were registered. The dominant causative agents in 2 cases were antiepileptics and benzodiazepines in 3 cases.

Due to the acute poisoning by other drugs 74 patients, 27 males (36.5%) and 47 females (63.5%), majority of them at the age 19-65 years old (53 patients; 71.6%) were hospitalized.

According to age groups, younger than 18 years were noted in 8 (10.8%), and older than 65 years in 13 (17.6%) cases.

The most common cause of poisoning were cardiovascular drugs. Fortyeight cases of acute poisoning (64.9%) were registered, and beta blockers (22 cases), calcium antagonists (16) and ACE inhibitors (5) were dominant. In the group of analgesics (8 cases), NSAID poisoning were predominant (6 cases).

There were seven pts with acute sympathomimetics poisoning, and 6 of them were acute theophylline poisoning.

Due to acute anticholinergics poisoning 3 persons (2 persons due to acute biperiden poisoning and 1 person due to acute trihexyphenidyl poisoning) were hospitalized.

Other drug poisoning (oral hypoglycemic drugs, hormonal preparations, unknown drugs, etc.) were registered in 8 patients (10.8%). Clinical picture of mild poisoning (PSS 1) in 2 patients (25.0%), moderate (PSS 2) in 3 patients (37.5%), and in 3 cases (37.5%) severe poisoning (PSS 3) were registered.

Three lethal outcomes (4.0%) in patients with acute cardiovascular drug intoxication were registered.

Table 13 The frequency of a single drug as a dominant cause of poisoning (Clinic for emergency and clinical toxicology)

Psychoactive drug	367	**%**	**Other drug**	74	**%**
Antidepressants			*Analgesics*		
Cyclic	9	47.4	NSAID	6	75.0
SSRI	10	52.6	Opioides	2	25.0
Other			Total	8	100.0
Total	19	100.0	*Cardiological*		
Antiepileptics			Beta blockers	22	45,8
Carbamazepine	55	59.8	Calcium antagonists	16	33.3
VPA	15	16.3	ACE inhibitors	5	10.4
Barbiturates	4	4.3	Cardiotonics	2	4.2
Lamotrigine	5	5.4	Antiarrhythmics	3	6.2
Clonazepam	13	14.1	Total	48	100.0
Other			*Sympathomimetics*		
Total	92	100.0	Theophylline	6	85.7
Benzodiazepines			Salbutamol	1	14.3
Bromazepam	111	55.8	Total	7	100.0
Diazepam	25	12.6	*Anticholinergics*		
Alprazolam	21	10.6	Trihexyphenidyl	1	33.3
Lorazepam	27	13.6	Biperiden	2	66.7
Midazolam	4	2.0	Total	3	100.0
Zolpidem*	9	4.5	*Others*		
Other	2	1.0	Oral hypoglycemics, hormonal preparations, unknown drugs etc.		
Total	199	100.0			
Neuroleptics					
Phenothiazines	13	22.8			
Clozapine	35	61.4			
Risperidone	3	5.3	Total	8	100.0
Olanzapine	5	8.8	* anxiolytic, does not belong to the group of benzodiazepines		
Other	1	1.7			
Total	57	100.0			

Drugs of abuse

In the DRT PCC 312 patients (7.1% of all examined) were examined for suspicion on acute drugs of abuse intoxication. According to gender, there were 252 males (80.8%) and 60 females (19.2%).

According to the age groups, distribution of patients (drugs of abuse) is shown in Table 14.

Table 14 Distribution of patients according to age (DRT PCC)

Age groups (years)	n	%
To 18	32	10.3
19 - 40	249	79.8
41-65	27	8.6
unknown	4	1.3
Total	312	100.0

Mild poisoning was noted in 191 persons (61.2%), moderate poisoning in 65 patients (20.8%) and severe poisoning in 42 persons (13.5%).

The lethal outcome was registered in 2 persons (0.6%). Suspicion on the underlying disease was not confirmed for 12 patients (3.8%)

Under suspicion on the heroin abuse 170 persons (54.5%) were examined. According to the age groups, at the age 15-19 were 4 persons (2.3%), 20-24 years 15 persons (8.8%), 25-29 years were 24 persons (14.1%), 30-65 years old 127 persons (74.7%). Mild poisoning had 57 persons (39.3%), 48 patients (33.1%) were with signs of moderate poisoning, and in 39 persons (26.9%) severe poisoning was confirmed. Lethal outcome was registered in 1 person (0.7%). Suspicion on the underlying intoxication was not confirmed for 25 patients (14.7%), and PSS score (percent) was calculated on the total number of 145.

Under suspicion on the marijuana abuse 50 persons were examined (16.0%). According to the age groups, one person was younger than 14 years, at the age 15-19 there were 13 persons (40.6%), 20-24 years old 16 persons (50.0%), 25-29 years old 9 persons (28.1%), 30-65 years old 11 persons (34.4%). Mild poisoning had 29 patients (90.6%), and 3 patients (9.4%) were with the signs of moderate poisoning. Suspicion on the underlying intoxication was not confirmed for 18 patients (36.0%), and PSS score (percent) was calculated on the total number of 32.

Under suspicion on the cocaine intoxication 13 persons (4.2%) were examined. According to the age groups, at the age 15-19 were 2 persons (15.4%), 20-24 years old 3 persons (23.1%), 25-29 years old 2 persons (15.4%), 30-65 years old 6 persons (46.1%). Mild poisoning had 5 patients

(55.5%), and 4 patients (44.5%) were with the signs of moderate poisoning. Suspicion on the underlying intoxication was not confirmed for 4 patients (30.8%), and PSS score (percent) was calculated on the total number of 9.

Under suspicion on the amphetamine intoxication 18 persons (5.8%) of all 312 persons examined on the suspicion on the drug of abuse intoxication) were examined. According to the age groups, at the age 15-19 were 3 persons (16.7%), 20-24 years 7 persons (38.9%), 25-29 years 3 persons (16.7%), 30-65 years old 5 persons (27.8%). Mild poisoning had 11 persons (84.6%), 2 patients (15.4%) were with the signs of moderate poisoning. Suspicion on the underlying intoxication was not confirmed for 5 patients (27.8%), and PSS score (percent) was calculated on the total number of 13.

Under suspicion on the MDMA intoxication (3,4-methylenedioxy-methamphetamine-Ecstasy) 11 persons (3.5%) were examined. According to the age groups, at the age 15-19 were 3 persons (27.3%), 20-24 years old 7 persons (63.6%), and at the age 25-29 was 1 person (9.1%). Mild poisoning had 6 persons (85.7%), and one person (14.3%) had moderate poisoning. Suspicion on the underlying intoxication was not confirmed for 4 patients (36.4%), and PSS score (percent) was calculated on the total number of 7.

For a total of 50 cases (16.0%) of all persons examined under suspicion on the drugs of abuse intoxication, the agent and nature of poisoning were not determined. In this group there were no fatal outcomes, but moderate and severe poisoning were registered in 10 persons (20.0%). These findings indicate the number of intoxication when causative agent (s) could not have been determined with certainty, despite the use of modern analytical equipment. The appearance of new psychoactive substances for which there are still no standardized analytical methods, also aggravates this problem.

In the **Clinic for emergency and clinical toxicology** 35 patients were admitted, thay were all 19-65 years old (working age), which makes 11.2% of the total number of patients examined due to acute intoxication by these agents. According to the age groups, at the age 15-19 was 1 person (2.9%), 20-24 years 4 persons (11.4%), 25-29 years 4 persons (11.4%), 30-65 years old 26 persons (74.3%).

Due to mild drug of abuse intoxication (PSS 1) 3 persons were admitted (8.6%). Moderate intoxication was registered in 9 patients (25.7%), due to severe intoxication (PSS 3) 21 patients (60.0%) were treated, and the lethal outcome (PSS 4) was noted in 2 patients (5.7%).

Due to acute drugs of abuse intoxication 33 males (94.3%) and 2 females (5.7%) were hospitalized.

The most common causative agent in hospitalized patients was heroin (24 persons, 68.6%). According to the age groups, at the age 20-24 there were 3 persons (12.5%), 25-29 years 3 persons (12.5%), 30-65 years old 18 persons (75.0%). Due to moderate poisoning 5 patients (20.8%) were admitted, due to severe poisoning (PSS 3) 18 patients (75.0%), and lethal outcome (PSS 4) was noted in 1 patient (4.2%).

Two patients, one with marijuana abuse (2.9%), and one with MDMA abuse (2.9%) were admitted in the Clinic. The first patient had signs of mild poisoning, and the other had signs of moderate poisoning.

Finally, 9 patients (25.7%) were admitted in the Clinic, and the certain causative agent was not determined. In this group one lethal outcome was registered (anamnestic data indicated that patient was an opiate addict).

Gases

Due to suspicion on acute gas exposure and intoxication in DRT PCC 176 patients (4.0% of all examined) were examined, and 29 persons (16.5% of patients examined due to acute gas intoxication) were admitted for hospital treatment.

According to gender there were 108 males (61.4%) and 68 females (38.6%).

Predominant causative agents were smoke inhalation (54 patients; 30.7%), chlorine fumes from household products (39 patients; 22.2%) and carbon monoxide (35 patients; 19.9%), which represents 72.8% patients examined due to gas exposure and intoxication.

In the other (48; 27.3%) patients, varnishes and solvents (17), vapors of oil and petroleum products (4), base and acid vapors (1+5), and other agents (21) were registered as a cause of poisoning.

According to the age groups, distribution of patients (acute gas intoxication) is shown in Table 15.

Table 15 Distribution of patients according to age (DRT PCC)

Age groups (years)	n	%
To 18	1	0.6
19 - 40	97	55.1
41-65	64	36.4
More than 65	14	7.9
Total	176	100.0

Clinical picture of mild poisoning had 151 patients (91.5%), moderate poisoning 4 (2.4%), and severe poisoning was noted in 10 (6.1%) patients. Suspicion on acute gas intoxication was not confirmed for 11 patients (6.2%), and PSS score (percent) was calculated on the total number of 165 patients.

Among 29 **hospitalized patients** (4.1% of all hospitalized patients), 19 were male (65.5%) and 10 female (34.5%). The most common cause were smoke inhalation, carbon monoxide, vapors of varnishes and solvents, chlorine fumes from household products, unidentified agents (13, 11, 2, 1, 2; 44.8%, 37.9%, 6.9%, 3.4%, 6.9%). The majority of them, 21 patients (72.4%) were at the age 19-65, and 7 (27.6%) patients were older than 65 years. Clinical picture of mild poisoning was found in 19 (65.5%), and moderate poisoning in 2 patients (6.9%). Eight patients (27.6%) had signs of severe poisoning. There were no fatal outcomes in this group.

Pesticides

Due to acute pesticide exposure and intoxication in the DRT PCC 89 patients (2.0% of all examined patients) were examined. According to gender there were 57 males (64.0%) and 32 females (36.0%). Because of the well-known seasonal distribution of this type of poisoning (agricultural work), 51 (57.3%) patients contacted the physician in the period April - July.

Thirtyseven patients, which represent 41.6% of patients examined due to acute pesticide poisoning, were admitted for hospital treatment.

According to the age groups, distribution of patients (acute pesticide intoxication) is shown in Table 16.

Table 16 Distribution of patients according to age (DRT PCC)

Age groups (years)	n	%
To 18	2	2.2
19 - 40	25	28.1
41-65	44	49.4
More than 65	18	20.2
Total	89	100.0

The most of the patients were examined due to suspicion on the acute organophosphorus insecticide and herbicide intoxication (42 cases; 47.2%).

Mild poisoning (PSS 1) was registered in 69 patients (85.2%), moderate (PSS 2) in 2 patients (2.5%), and 8 patients (9.9%) had clinical features of severe poisoning (PSS 3) at the admission. During the admission the lethal outcome was registered in 2 patients (2.5%).

Suspicion on acute pesticide intoxication was not confirmed for 8 patients (9.9%), and PSS score (percent) was calculated on the total number of 81 patients.

In the **Clinic for emergency and clinical toxicology** due to acute pesticide intoxication 37 patients, which represent 5.3% of all hospitalized patients, were treated. The most common toxic agents were from the organophosphorus insecticide group (23 cases; 62.2%). The other pesticides (mainly herbicides) were represented less frequently (14; 37.8%).

According to gender, there were 20 males (54.0%) and 17 females (46.0%).

Distribution of patients according to age (acute pesticide intoxication) is shown in Table 17.

Table 17 Distribution of patients according to age (Clinic for emergency and clinical toxicology)

Age groups (years)	n	%
To 18	0	0.0
19 - 40	8	21.6
41-65	23	62.2
More than 65	6	16.2
Total	37	100.0

Mild poisoning (PSS 1) was registered in 25 patients (67.6%), moderate (PSS 2) in 2 (5.4%), and due to severe poisoning (PSS 3) 8 patients (21.6%) were treated. The fatal outcome was registered in 2 patients (5.4%) treated due to acute pesticide poisoning.

Corrosives

Due to suspicion on the acute corrosive compound poisoning in the DRT PCC a total of 120 patients (2.7% of all examined patients) were examined, and 92 of them (76.7% of this type of poisoning cases) were admitted for hospital treatment. The most common agents were hydrochloric (45 patients; 37.5%) and acetic acid (27; 22.5%). Eight patients (6.7%) were examined due to the NaOH ingestion, 7 persons due to the other acids (5.8%); 6 persons (5.0%) due to the bleach compounds, cleaners (6; 5.0%) and other corrosive compounds (21 persons).

According to gender, 74 (61.7%) persons were females, and 46 (38.3%) males.

According to the age groups, distribution of patients (acute corrosive poisoning) is shown in Table 18.

Table 18 Distribution of patients according to age (DRT PCC)

Age groups (years)	n	%
To 18	5	4.2
19 - 40	31	25.8
41-65	59	49.2
More than 65	25	20.8
Total	120	100.0

Clinical features of mild poisoning (PSS 1) was noted in 55 patients (47.4%), moderate (PSS 2) in 20 (17.2%), and 40 patients (33.3%) had severe poisoning at the admission. During the admission fatal outcome was registered in one patient.

Suspicion on acute corrosive intoxication was not confirmed for 4 patients (3.3%), and PSS score (percent) was calculated on the total number of 116 patients.

In the **Clinic for emergency and clinical toxicology** due to the acute corrosive poisoning 92 patients were hospitalized, which represent 13.1% of all hospitalized patients. The most common ingested agent was hydrochloric acid (42 cases; 45.6%), and then acetic acid (26 cases; 28.3%). Four hospitalized patients (4.3%) ingested NaOH, and other agents (bleach compounds, other acids, other corrosive compounds) in 20 patients (21.8%).

The majority of patients were females (57; 61.9%), and males were 35 (38.1%).

Distribution of patients according to age (acute corrosive poisoning) is shown in Table 19.

Table 19 Distribution of patients according to age (Clinic for emergency and clinical toxicology)

Age groups (years)	n	%
To 18	4	4.3
19 - 40	24	26.1
41-65	46	50.0
More than 65	18	19.6
Total	92	100.0

Clinical features of mild poisoning were noted in 32 persons (34.8%). Due to moderate poisoning 20 persons (21.7%) were treated, and due to severe poisoning 23 persons (25.0%). Lethal outcome was registered in 17 patients, which represent 18.5% of all treated patients.

Mushrooms and plants

Due to acute mushroom and plant poisoning in the DRT NPCC 64 patients, 36 (56.2%) males and 28 (43.8%) females, were examined. In 57 persons (89.1%) there was a suspicion on the acute mushroom poisoning, 5 persons ingested the seeds of the plant *Datura stramonium*, and 2

persons were reportedly ingested plant *Colchicum autumnale* (active substance-colchicine). All mushroom poisonings were accidental, except in the one case of ingestion of mushroom with psychoactive substances.

Persons younger than 18 years were 4 (6.2%), 46 persons (71.9%) were at the age 19-65, and 12 persons were older than 65 years (18.7%). In two cases age has not been noted. Clinical features of mild poisoning (PSS 1) was noted in 34 persons (62.9%), moderate poisoning in 7 persons (13.9%), 13 persons had clinical features of severe poisoning (24.1%), and for 10 persons, it was concluded that there was no ingestion of poisonous mushrooms or plants. Therefore PSS score (percent) was calculated on the total number of 54 patients.

Thirtytwo persons (50.0% of examined patients) were admitted in the **Clinic for emergency and clinical toxicology** for further diagnosis, observation and treatment (19 males and 13 females). Twenty (62.5%) patients were at the age 19-65, 4 younger than 18 years, and 8 persons older than 65 years.

Due to suspicion on the acute mushroom intoxication 26 patients (81.2%) were admitted, 4 patients due to acute *Datura stramonium* intoxication and 2 patients due to suspicion on *Colchicum autumnale* ingestion. Twelve patients (37.5%) had clinical features of mild poisoning (PSS 1), 7 patients had signs and symptoms of moderate, and 13 persons clinical features of severe poisoning.

Other agents

This group consisted of patients (64; 1.4% of all outpatients) who were exposed to or intoxicated with toxic alcohols, various industrial products (organic solvents, detergents, disinfectants) and other agents.

Other diseases

During the 2014 in the DRT PCC and in the Clinic for emergency and clinical toxicology for 132 persons (3.0% of all examined patients) it was concluded that there was some another, non-toxicological etiologic factor.

Department for Toxicological Chemistry

During the 2014 in the Department for toxicological chemistry NPCC of MMA 15170 analysis were done. Analysis were performed according to the requirements of the MMA organizational units, the Army of Serbia and the demands of civil health care institutions. Certain number of analysis was performed as a part of the MMA scientific research projects, but also in order to maintain and improve the quality of analytical procedures. The overall review of the Department work is shown in the Tables 20-26.

Table 20 Analysis performed according to the requirements of the various MMA organizational units and the other Army of Serbia organizational units

Types of analysis	Number	%
Alcohols	1885	35.4
Benzodiazepines	979	18.4
Antiepileptics	351	6.6
Antidepressants	109	2.1
Neuroleptics	65	1.2
Psychoactive substances	209	3.9
Drugs (other)	820	15.4
Metals (Zn, Cu)	150	2.8
Pesticides	265	5.0
RBC cholinesterase	406	7.6
Identification	12	0.2
Others	66	1.2
Total	5317	100.0

Table 21 Analysis performed according to the requirements of the various Army of Serbia organizational units (protocol BIOGNOST)

Types of analysis	Number	%
Psychoactive substances	601	51.9
Alcohols	558	48.1
Total	1159	100.0

Table 22 Analysis performed as a part of the MMA scientific research projects

Analysis	Number
Drugs, pesticides	727
Total	727

Table 23 Analysis performed according to the requirements of the Ministry of Internal Affairs of the Republic of Serbia

Types of analysis	Number
Alcohols	1151
Total	1151

Table 24 Analysis performed according to the requirements of the civil institutions

User/analysis	Number	%
Alcohols	211	4.9
Antiepileptics	674	15.6
Psychoactive substances	423	9.8
Drug	405	9.4
RBC cholinesterase	53	1.2
Metals	34	0.8
Benzodiazepines	131	3.0
Pesticides	60	1.4
Other	21	0.5
Forensic material Alcohol Drug Opiates Others	2305 601 1598 99 7	53.4
Total	4317	100.0

Table 25 Analysis performed as a part of the maintenance and enhancement of quality of the analytical procedures

Types of analysis	Number
Standards, controls, tests (drug, opiates, antiepileptics, pesticides)	2099
Validation of methods (calibration curves)	200
Interlaboratory analysis (drug, opiates, antiepileptics, cholinesterase)	200
Total	2499

Teaching activity

Several teachers and associates of the Department participated in the teaching process at the Faculty of Medicine of MMA. Within the obligatory course Medicinal chemistry and elective corse Phytotherapy 4 teachers and associates were engaged.

During 2014, the scope of accreditation methods was not amended. At this moment the Department is accredited for a total of 73 analytical methods (Table 26).

Table 26 Accredited analytical methods (06.07.2014.)

1. Determination of carbamazepine in serum samples by HPLC-UV method
2. Determination of lamotrigine in serum samples by HPLC-UV method
3. Determination of valproic acid in serum samples by GC-MS method
4. Determination of methadone in urine samples by HPLC-PDA method
5. Determination of methadone in urine samples by LC-MS method
6. Determination of ethanol and methanol in serum, urine and lavage samples by GC-FID method
7. Determination of lorazepam in biological material by HPLC-PDA method
8. Determination of theophylline in biological material by HPLC-PDA method
9. Determination of amoxicillin in biological material by HPLC-PDA method
10. Determination of diazepam and its metabolites temazepam and oxazepam in biological material by HPLC-PDA method
11. Determination of diclofenac in biological material by HPLC-PDA method
12. Determination of bromazepam in biological material by HPLC-PDA method
13. Determination of amitriptyline in biological material by HPLC-PDA method
14. Determination of carbamazepine in biological material by HPLC-PDA method
15. Determination of amoxicillin in biological material by UPLC-MS method
16. Determination of nimesulide in biological material by HPLC-PDA method
17. Determination of diazepam and its metabolites in biological material by LC-MS method
18. Determination of lamotrigine in biological material by HPLC-PDA method
19. Determination of clonazepam in biological material by HPLC-PDA method
20. Determination of sulpirid in biological material by HPLC-PDA method
21. Determination of olanzapine in biological material by HPLC-PDA method
22. Determination of opiates in biological material by LC-MS method
23. Determination of DNOC in commercial and biological samples by HPLC-PDA method
24. Identification of drug of abuse in urine by immunochromatography method
25. Determination of sertraline in biological material by HPLC-PDA method
26. Determination of maprotilin in biological material by HPLC-PDA method
27. Determination of mianserine in biological material by HPLC-PDA method
28. Determination of fluoxetine in biological material by HPLC-PDA method
29. Semiquantitative analysis of drugs and their metabolites- by screening method HPLC-PDA
30. Determination of cholinesterase activity by spectrophotometric method
31. Determination of sulpirid in biological material by LC-MS method
32. Determination of bromadiolone in commercial and biological samples by HPLC-PDA method
33. Determination of warfarine in biological material by HPLC-PDA method
34. Determination of copper in biological material by ICP-OES method
35. Determination of zinc in biological material by ICP-OES method

(extension) Table 26 Accredited analytical methods (06.07.2014.)

36. Determination of olanzapine in biological material by LC-MS method
37. Determination of sertraline in biological material by LC-MS method
38. Determination of trihexyphenidyl in biological material by LC-MS method
39. Determination of atropine in biological material by LC-MS method
40. Determination of sildenafil in biological material by LC-MS method
41. Determination of colchicine in biological material by HPLC-PDA method
42. Determination of colchicine in biological material by LC-MS method
43. Determination of midazolam in biological material by LC-MS method
44. Determination of gliclazide in biological material by LC-MS method
45. Determination of midazolam in biological material by HPLC-PDA method
46. Determination of gliclazide in biological material by HPLC-PDA method
47. Determination of clozapine and its metabolites in biological material by HPLC-PDA method
48. Determination of paroxetine in biological material by HPLC-PDA method
49. Determination of zolpidem in biological material by HPLC-PDA method
50. Determination of malathion and malaoxon in biological material by UPLC-MS method
51. Determination of diazinon in biological material by UPLC-MS method
52. Determination of dimethoate in biological material by UPLC-MS method
53. Determination of clavulanic acid in biological material by HPLC-PDA method
54. Determination of fluphenazine in biological material by HPLC-PDA method
55. Determination of chlorpromazine in biological material by HPLC-PDA method
56. Determination of opiates in human hair by LC-MS method
57. Determination of diazepam in human hair by HPLC-PDA method
58. Identification of drug and drug of abuse in biological samples by HPLC-PDA screening method
59. Identification of drug and drug of abuse in biological samples by LC-MS screening method
60. Determination of bisoprolol in biological material by LC-MS method
61. Determination of acetaminophen in biological material by HPLC-PDA method
62. Determination of acetaminophen in biological material by LC-MS method
63. Determination of tramadol in biological material by HPLC-PDA method
64. Determination of tramadol in biological material by LC-MS method
65. Determination of atenolol in biological material by LC-MS method
66. Determination of risperidone in biological material by LC-MS method
67. Determination of propranolol in biological material by LC-MS method
68. Determination of propranolol in biological material by HPLC-PDA method
69. Determination of enalapril in biological material by LC-MS method
70. Determination of trazodone in biological material by HPLC-PDA method
71. Determination of trazodone in biological material by LC-MS method
72. Determination of bisoprolol in biological material by HPLC-PDA method
73. Determination of THC-carboxylic acid in biological material by LC-MS method

Department for Experimental Toxicology and Pharmacology

During 2014, members of the Department were involved in the activities of MMA, the Ministry of the Science and Technology of the Republic of Serbia and the other civilian institutions in the country listed below.

1. For the purposes of The Faculty of Medicine MMA University of Defense, one Senior Research Associate of the Department was involved:

- in teaching process at Biomedicine doctoral studies at the following subjects: Pharmacological and toxicological aspects of reactions to stress, Pathophysiological, diagnostic and therapeutic aspects of acute poisoning, Ethics in biomedicine, Experimental models in biomedicine, Molecular mechanisms of action of drugs and poisons and Methodology of preclinical and clinical drug trials;
- in mentoring cadets at the Faculty of medicine of MMA (preparation of scientific publication in the field of experimental pharmacology and toxicology).

2. For the needs of Ministry of Science and Technology of the Republic of Serbia, one Senior Research Associate of the Department has participated:

- in preparation of doctoral dissertation and in the Committee for the defense of the finished dissertation within the scientific project entitled „Development of molecules with antiinflammatory and cardioprotective effect: structural modification, modelling, physicochemical characterisation and preformulation tests (project number: 172041) at the Faculty of Pharmacy in Belgrade;
- in the Committee for the election of candidates from the Faculty of Pharmacy in Belgrade to the position of Teaching Assistant

3. Due to changes in legislation and harmonization with the relevant EU directives, preclinical testing for the needs of various civil institutions in the country could not have been done. Therefore, in the second half of the year started a procedure approved by the Head of the MMA to obtain the necessary certificates for the work of the Ministry of Health and Ministry of Agriculture and Environment of the Republic of Serbia.

After the inspection of the aforementioned ministries inspection teams, the following activities were completed:

-Laboratory of the Department for experimental toxicology and pharmacology as one of the laboratories of the Institute for toxicology and pharmacology from the NPCC and Centre for clinical pharmacology of the Faculty of Medicine, MMA was enrolled as a whole in the National Register of Laboratories, for the activities: the bioavailability and/or bioequivalence, preclinical

trials of drugs for use in human and veterinary medicine, safety testing of substances that are part of the drugs, pesticides, biocides, cosmetics, food additives, industrial chemicals and nanoparticles (Ministry of Health of the Republic of Serbia, decision No 515-04-6396/2014-11 of 08.12.2014.);

- facilities of the Department for performing experiments on animals, has been included in the National Register of experiments on animals as the Institute for Toxicology and Pharmacology, NPCC, MMA (Ministry of Agriculture and Environmental Protection of the Republic of Serbia, decision No: 323-07-04943/2014-05/1 of 17. 12. 2014.);
- the laboratories of the Institute for toxicology and pharmacology NPCC MMA are in the process of obtaining approvals and certificates of Good Laboratory Practice for the activities listed above.

4. Professional training

One doctor of veterinary medicine completed attendance at the academic specialization „Toxicological risk assessment of environmental pollutants“ at the Department of Toxicology, Faculty of Pharmacy, Belgrade.

Senior Research Associate of the Department attended classes in the country and abroad, passed all required exams, and acquired:

- the License for the Advisor for chemicals, in accordance with the Law on Chemicals of the Republic of Serbia, and
- the License for Good Laboratory Practice in accordance with OECD-GLP directives of EU and FDA and EPA regulations of USA.

5. Expansion of activities of the Department

Based on the issued decision on the registration of Laboratory of the Department in the Register for experiments on animal, all the activities for the introduction of 10 new experimental methods were carried out. Thereby to the end of 2014, a total of 30 methods from the field of experimental toxicology, experimental pharmacology and experimental pathology were harmonized with requirements of ISO standards 9001:2008, as well as the Directives of the European Commission 2004/9 and 2004/10, applicable OECD quidelines and the quidelines of the International Conference on Harmonization (ICH).

Selected cases

This section gives a brief overview of 32 cases of patients with lethal outcome whose death was to some extend connected with the causative agent (Table 27).

Table 27 Brief overview of the case of patient with lethal outcome

S. No	Gender	Age (year)	Causative agent	Connection with the cause (RCF)	Case report
1.	F	30	Carbamazepine, citalopram	Undoubtedly proven	Ingestion; coma, acute respiratory failure, hypotension, circulatory failure
2.	M	49	Corrosive agent (acetic acid)	Undoubtedly proven	Ingestion; acidosis, gastrointestinal bleeding, acute respiratory failure, suspected perforation of the stomach, hospitalization shorter than 24 hours
3.	F	78	Corrosive agent (hydrochloric acid)	Undoubtedly proven	Ingestion; severe metabolic acidosis, respiratory and cardiocirculatory failure, hospitalization shorter than 24 hours
4.	M	63	Corrosive agent (acetic acid-kitchen vinegar)	Contributed	Ingestion; mild damage of oropharynx, aspirational bronchopneumonia, atrial fibrillation with rapid ventricular response, sudden cardiorespiratory arrest
5.	F	73	Corrosive agent (concentrated acetic acid)	Undoubtedly proven	Ingestion; hemolysis, gastrointestinal bleeding, acute renal failure, acute respiratory failure, suspected perforation of the stomach
6.	M	55	Corrosive agent (unknown)	Undoubtedly proven	Ingestion; transferred from the other institution 7 days after suspected ingestion, acute renal failure due to which he was on dialysis, aspirational bronchopneumonia, on the second day of hospitalization perforation of stomach was verified, he was operated (*Gastrectomia totalis, Oesophagostomia, Jejunostomia nutritiva)*
7.	M	54	OPI (malathion) Drug (lorazepam)	Undoubtedly proven	Ingestion; patient reanimated in the local institution (condition after resuscitation), expresssed muscarinic effects
8.	F	90	Drug (bromazepam)	Undoubtedly proven	Ingestion; coma, development of complications (bronchopneumonia)
9.	M	85	Drug (carbamazepine, diazepam)	Contributed	Ingestion; development of complications (bilateral bronchopneumonia), development of acute pulmonary edema
10.	F	24	Drug (amlodipine, cilazapril, metformin, gliclazide)	Undoubtedly proven	Ingestion; hypotension, metabolic acidosis, respiratory and circulatory failure
11.	F	43	Corrosive agent (hydrochloric acid)	Undoubtedly proven	Ingestion; severe metabolic acidosis, corrosive damage of the GIT (level III), GIT bleeding, acute renal failure, respiratory and cardiocirculatory failure, suspected perforation of the stomach
12.	M	89	Drug (bromazepam, Dilacor)	Undoubtedly proven	Ingestion; sopor, third degree AV block for which a temporary pace maker was implanted, bronchopneumonia, respiratory failure
13.	M	73	Corrosive agent (Sodium hydroxide)	Undoubtedly proven	Ingestion; gastrointestinal bleeding, respiratory and cardiocirculatory failure, suspected perforation of the stomach
14.	F	83	Drug (diazepam)	Undoubtedly proven	Ingestion; coma, development of numerous complications(bronchopneumonia), respiratory failure
15.	M	57	OPI (malathion)	Undoubtedly proven	Ingestion; expressed muscarinic and nicotinic effects, patient reanimated in the local institution (status after resuscitation)

(extension) Table 27 Brief overwiev of the case of patient with lethal outcome

S.No	Gender	Age (year)	Causative agent	Connection with the cause (RCF)	Case report
16.	F	81	Corrosive agent (hydrochloric acid)	Undoubtedly proven	Ingestion; severe metabolic acidosis, necrotic lesions of the stomach, respiratory and cardiocirculatory failure
17.	M	68	Suspected intoxication	Unknown	Coma, occlusion *a. basilaris*, ischemia of cerebellum and pons, acute respiratory failure
18.	M	86	Corrosive agent (sodium hydroxide)	Undoubtedly proven	Ingestion; severe corrosive damage of epiglottis, esophagus and stomach, GIT bleeding, respiratory failure, sepsis
19.	M	68	Corrosive agent (concentrated acetic acid)	Undoubtedly proven	Ingestion; hemolysis, gastrointestinal bleeding, acute respiratory and cardiocirculatory failure
20.	F	49	Corrosive agent (hydrochloric acid)	Undoubtedly proven	Ingestion; acute renal failure, acute respiratory and cardiocirculatory failure, suspected perforation of the stomach
21.	F	74	Drug (bromazepam)	Unknown	Observations for the suspicion of intoxication, coma, obstructive pulmonary disease and respiratory failure
22.	M	43	Corrosive agent (concentrated acetic acid)	Undoubtedly proven	Ingestion; severe metabolic acidosis, massive GIT bleeding, suspected perforation of the stomach
23.	M	37	Suspected intoxication	Unknown	Opiate addict, difficult general condition, fever, probably sepsis with multiple organ failure, died 2 hours after admission
24.	M	41	Drug (nifedipine, metoprolol, diazepam)	Undoubtedly proven	Ingestion; coma, hypotension, bradycardia, AV dissociation
25.	M	56	Corrosive agent (hydrochloric acid)	Undoubtedly proven	Ingestion; GIT bleeding, metabolic acidosis, acute respiratory and circulatory failure, acute renal failure, suspected perforation of the stomach
26.	F	70	Corrosive agent (concentrated acetic acid)	Undoubtedly proven	Ingestion; metabolic acidosis, circulatory and respiratory failure, acute renal failure
27.	F	42	Corrosive agent (sodium hydroxide)	Undoubtedly proven	Ingestion; gastrointestinal bleeding, acute respiratory failure, ARDS, pneumothorax, suspected perforation of the stomach
28.	F	72	Corrosive agent (concentrated acetic acid)	Undoubtedly proven	Ingestion; metabolic acidosis, acute renal failure, respiratory and cardiocirculatory failure
29.	F	92	Suspected intoxication	Unknown	Demented patient with impaired swallowing act, aspirational bronchopneumonia and respiratory failure, followed by cardiac decompensation
30.	F	58	Corrosive agent (concentrated acetic acid)	Undoubtedly proven	Ingestion; gastrointestinal bleeding, suspected perforation of the stomach, respiratory and cardiocirculatory failure
31.	M	39	Suspected intoxication	Unknown	Respiratory and cardiocirculatory failure in the former opiate addict. Confirmed bilateral bronchopneumonia with pleural effusion
32.	M	41	Psychoactive substances (opiates-heroin)	Undoubtedly proven	Coma, bilateral bronchopneumonia, acute respiratory failure, severe rhabdomyolysis, severe acidosis

List of abbreviations and explanations

ARI – acute renal insufficiency

ARF- acute respiratory failure

DNOC- dinitro-o-cresol („Kreozan“)

Datura stramonuum (Latin) – tatula (Serbian language), one-year plant, containing atropine, hyoscyamine, hyoscine, scopolamine, stramonin etc.

Drug of abuse- a compound that causes addiction (illegal production and trafficking, prohibited by law)

HPLC/PDA – Liquid chromatography with UV detector (190-400nm)

ISI – Institute for Scientific Information

OPI – organophosphorus insecticides

PAS – psychoactive substances

PSS score - *Poisoning Severity Score* – severity of poisoning

PSS - 0 (asymptomatic)

PSS - 1 (mild)

PSS - 2 (moderate)

PSS - 3 (severe)

PSS - 4 (fatal)

RCF - *Relative Contribution to Fatality* – Relative participation of causative agents in fatal outcome; 6-level scale:

1 – undoubtedly proven

2 – probably

3 – contributed

4 – probably did not contribute

5 – certainly not contributed

6 – unknown

SSRI – *Selective Serotonin Reuptake Inhibitors*

WHO – World Health Organization

PLC/MS – ultra performance liquid chromatography in combination with electrospray ionization and mass spectrometry

VPA – valproic acid, antiepileptic drug and a mood stabilizer

IT support to the PCC work

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Reports of health institutions in the Republic of Serbia

(a summary of the number and basic characteristics of acute poisoning)

The intention of the relatively small team from the Poison Control Centre of MMA, which for the fifth time in a row publishes the Annual Report, was in the number for 2014, to present concisely, but yet detailed, all relevant data related to acute poisoning, which are fully or partially therapeutically resolved at the MMA.

Appreciating own efforts, but also the efforts of many dear colleagues across the country, we tried to, first of all by personal contacts, and on the other ways, get to a structured data on acute poisoning from other health centers in the country.

A number of institutions which are shown below (in alphabetical order), were responded to this invitation.

Since the methodology (classification) of the received data was relatively uneven (some institutions used the ICD classification, a number of health institutions are not able to clearly identify toxins/drugs), we decided, aware of the risks that each transformation causes, to conform collected data to the methodology used in the Poison Control Centre. Time limits and the need to issue a Annual Report on time did not allow us further coordination with other health institutions in the country.

This work we started with a lot of attention, but also aware of the possibility of subsequent errors. We hope that, by this procedure, we did not (inadvertently) created a distorted picture of the situation and characteristics of acute poisoning in the Republic of Serbia.

According to the Law on Health Care (Article 92), Poison Control Centre, among other things, collects and processes data on the effects of toxic chemicals and natural toxins, keeps a register of incidents of poisoning and participates in the formation and supervision of the Central stocks of antidotes in the Republic. By the new Law on health records will be defined the regulations and forms with the necessary data on acute poisoning.

With gratitude to all the people and institutions who have sent us reports, we are firmly committed, that with better cooperation and coordination, the next Annual report would be improved and supplemented with complete reports from other health centres in Serbia.

Appendix 1 Institute for Health Protection of Children and Youth of Vojvodina, Novi Sad

The dominant cause	n	%
Alcohol	43	33.3
Drug of abuse	3	2.3
Drug	43	33.3
Psychoactive Other drugs	21 22	
Gases	1	0.8
Corossives	3	2.3
Mushrooms and plants	1	0.8
Other agents	6	4.7
Unknown	29	22.5
Total	129*	100.0

* Lethal outcome is not registered

Appendix 2 Clinical Centre, Niš

The dominant cause	n	%
Alcohol	606	54.3
Drug of abuse	20	1.8
Drug	315	28.2
Gases	12	1.1
Corossives	42	3.8
Pesticides	88	7.9
Mushrooms and plants	9	0.8
Other agents	23	2.1
Total	1115*	100.0

* 11 lethal outcomes are registered
(corossives-6; pesticides-4; drugs-1)

Appendix 3 General Hospital, Ćuprija

The dominant cause	n	%
Alcohol	36	36.4
Drug of abuse	1	1.0
Drug	46	46.6
Psychoactive Other drugs	36 10	
Gases	4	4.0
Corossives	2	2.0
Pesticides	5	5.0
Mushrooms and plants	2	2.0
Other agents	3	3.0
Total	99*	100.0

* 1 lethal outcome is registered (alcohol)

Appendix 4 General Hospital, Leskovac

The dominant cause	n	%
Alcohol	60	24.1
Drug of abuse	12	4.8
Drug	145	58.2
Psychoactive Other drugs	140 5	
Gases	1	0.4
Corossives	7	2.8
Pesticides	17	6.8
Mushrooms and plants	4	1.6
Other agents	1	0.4
Unknown	2	0.8
Total	249*	100.0

* 10 lethal outcomes are registered
(pesticides-6; psychoactive drugs-2; corossives-1; unknown-1)

Appendix 5 General Hospital, Pančevo

The dominant cause	n	%
Alcohol	70	36.1
Drug of abuse	11	5.7
Drug	24	12.4
Psychoactive Other drugs	16 8	
Gases	6	3.1
Corossives	5	2.6
Pesticides	11	5.7
Other agents	22	11.3
Unknown	45	23.2
Total	194*	100.0

* 1 lethal outcome is registered
(drug of abuse -1)

Appendix 6 General Hospital, Vršac

The dominant cause	n	%
Drug	11	68.7
Psychoactive Other drugs	10 1	
Pesticides	2	12.5
Corossives	2	12.5
Other agents	1	6.3
Total	16*	100.0

* Lethal outcome is not registered

Appendix 7 General Hospital, Zrenjanin

The dominant cause	n	%
Alcohol	62	33.8
Drug of abuse	1	0.5
Drug	48	26.2
Psychoactive Other drugs	40 8	
Gases	5	2.7
Pesticides	8	4.4
Other agents	4	2.2
Unknown	55	30.0
Total	183*	100.0

* Lethal outcome is not registered

Appendix 8 Health Centre, Aranđelovac

The dominant cause	n	%
Alcohol	1	7.1
Drug of abuse	1	7.1
Drug	9	64.3
Psychoactive Other drugs	7 2	
Mushrooms and plants	1	7.1
Other agents	2	14.2
Total	14*	100.0

* Lethal outcome is not registered

Appendix 9 Health Centre, Kosovska Mitrovica

The dominant cause	n	%
Drug	15	55.6
Psychoactive Other drugs	14 1	
Gases	2	7.4
Corossives	2	7.4
Other agents	5	18.5
Unknown	3	11.1
Total	27*	100.0

* Lethal outcome is not registered

Appendix 10 Health Centre „Studenica“, Kraljevo

The dominant cause	N	%
Alcohol	30	17.9
Drug of abuse	9	5.4
Drug	71	42.3
Psychoactive Other drug	63 8	
Other agents	2	1.2
unknown	56	33.3
Total	168*	100.0

* Number of lethal outcomes is unknown