ANNUAL REPORT
OF THE NATIONAL POISON CONTROL CENTRE

MILITARY MEDICAL ACADEMY, BELGRADE

2015

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Contents

Review of tables, figures and graphs

Republic of Serbia

According to data of the Statistical Office of the Republic of Serbia (01.01.2015.), Republic of Serbia had 7.114.393 inhabitants (without a data for AP Kosovo and Metohija). Administratively, the teritory of the Republic is divided into 30 districts (Figure 1), with Regional Health Centres in each of them. However, with the exception of the Clinics and the Clinical hospital centers, in a significant extent, they are not adequately staffed and technically qualified for a complete diagnostic and finale care of cases of severe poisoning by chemical substances in humans.

Fig. 1. Republic of Serbia, layout, administrative division

NATIONAL POISON CONTROL CENTRE

National Poison Control Centre (NPCC) is referent institution which provides medical prevention and treatment services for acute poisonings, detection of chemical substances in biological materials, water, soil 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“. The Center is created by integrating clinical and laboratory facilities of the former Clinic for Toxicology of the Military Medical Academy and Department for Medical Care of the Military Technical Institute. Since its inception, the Centre has grown in one of the most prestigious institutions of its kind in Europe in term of its results and capacities.

National Poison Control Center of the Military Medical Academy (NPCC MMA) today has Clinic for Emergency and Clinical Toxicology and Institute for Toxicology and Pharmacology and in its composition is 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. It involves monitoring the incidences of poisoning, seasonal variations in the incidence of poisoning, evaluation of efficacy and safety of antidotes, storage and supply of antidotes. It further involves reporting other health institutions on the necessary measures.

More than half of the employees possess a university degree of various profiles (doctors, pharmacists, veterinarians, chemists), while the nursing staff is specially profiled for the specific requirements in the treatment and care of poisoned patients. The best evidence of the academic potential of this institution is the fact that the various departments of the Faculty of Medicine of the Military Medical Academy employ 4 regular professors, 1 associate professor, 1 assistant professor and 3 assistants from the Center.

Abstract

Introduction: This is the sixth published Annual report of National Poison Control Center of the Military Medical Academy. In it, all available data are elaborated from the Department of resuscitation and triage, Clinic for Emergency and Clinical Toxicology and Department of Toxicological Chemistry PCC MMA. They also contain information about acute intoxications from those health institutions on the territory of the Republic of Serbia, whose reports are timely submitted to the Center.

Methodology: Data of the essential characteristics of patients and types of poisoning, the analytical procedures used to confirm the poisoning, as well as all other relevant indicators, are presented in tables and graphs in the Results chapter. At the end of report, short summary of all poison-related fatalities is presented on page 40. These data are analyzed by a team that consists of three had experienced clinical toxicologists from the Clinic for Emergency and Clinical Toxicology and a toxicological chemistry specialist from the Department of Toxicological Chemistry NCCP MMA. Their work is based on 6-graded RCF (Relative Contribution to Fatality) classification (Section List of Abbreviations and explanations).

Results: During 2015, the Department for reanimation and triage of Poison Control Centre registered 4747 cases. The largest number of them (2466; 51.9 %) were patients registered due to the effects of ethyl alcohol from alcoholic beverages. Abuse of medicaments (1289; 27.2%) was the second and drugs of abuse (442; 9.3%) the third. The highest percentage of cases (over 79.0%) belongs to the working population. After health examination, 682 patients of the total number of patients, were addmited to Clinic for Emergency and Clinical toxicology of the Military Medical Academy. The leading causes of poisoning in hospitalized patients were medicaments, corrosive substances and drugs (70.1%; 10.1%; 6.5% respectively). The lethal outcome was registered in 33 cases.

Conclusion: Acute poisoning by chemical substances, continues to represent one of the major factors of morbidity and mortality in the Republic of Serbia. PCC has, therefore, a great importance in the structure of health services in Serbia. Furthermore, better material and staff support could additionally improve the quality of this institution's work in the future.

NATIONAL POISON CONTROL CENTRE OF MILITARY MEDICAL ACADEMY

In the National Poison Control Center of the Military Medical Academy, medical services for prevention and treatment of poisoning by chemical substances 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 MMA is shown in Figure 2.

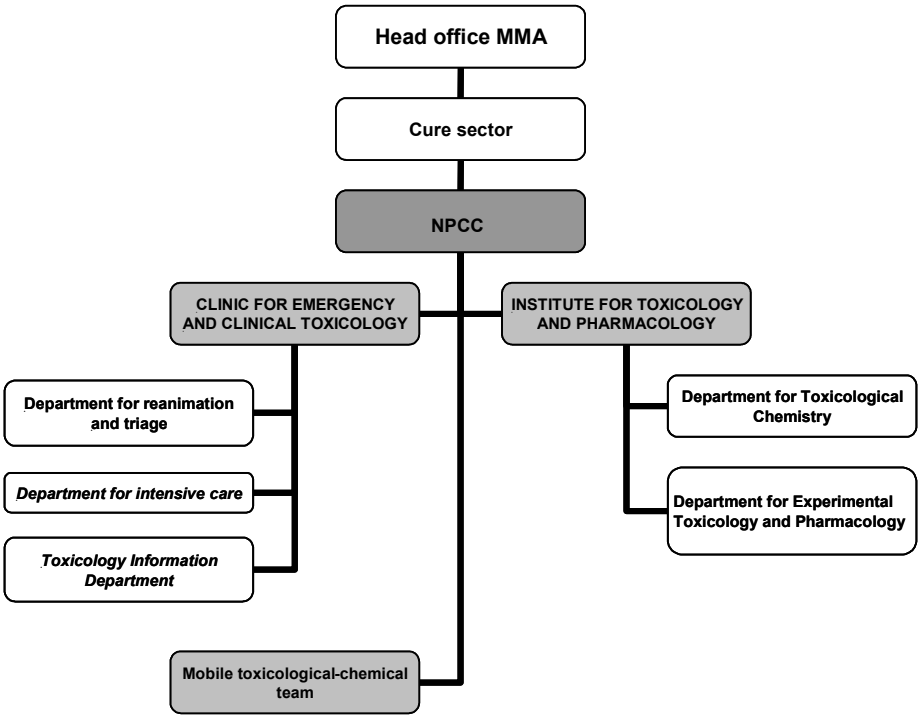


Fig. 2. Organizational structure of NPCC MMA

Clinic for Emergency and Clinical toxicology

The Clinic for Emergency and Clinical toxicology, the only specialized clinical 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. Clinic`s capacity consists of 24 beds with the possibility of increasing the number of patients, if necessary. At the Clinic, patients with acute medicaments, pesticides, corrosives, gases, mushrooms, industrial chemicals and other toxic agents poisonings are treated. The clinic is also responsible for the definitely hospital care and management of acutely poisoned patients in mass chemical accidents. Diagnostic and management of acutely poisoned patients is performed according to clearly formulated protocols, which are in full compliance with the protocols of toxicological centres in the world.

In the previous five-year period, the average annual number of hospitalizations at the Clinic amounted to about 750, with a gradual decline in this number, due to the large scale of definitive ambulatory treatment.

At the Clinic for Emergency and Clinical Toxicology, 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 (DRT), popularly called the Toxicology Ambulance, is located in the Emergency Centre of the Military Medical Academy.

The Department has 6 standard beds intended for the accommodation of patients for outpatient observation. The Department is equipped with 4 vital signs monitors, ECG, defibrillator, aspirator, portable respirator and other necessary equipment, medical supplies and medications. At the DRT medical technicians and clinical toxicologist, are constantly on duty, 24 hours a day performing activities of admission, diagnosis and treatment of patients referred to the Center for Poison Control MMA. Such material and technical equipment, as well as staff training, allow adequate implementation of a number of urgent medical procedures, including procedures of cardiopulmonary resuscitation (CPR).

In the last decade, the annual average number of medical examinations in DRT was around 4000, and in the last 5 years, a trend of steady increase was noted, until this year's 4747th examination.
At the DRT, because of suspicion of acute poisoning, patients are usually transported by car to the emergency service, from public places as well as the different levels of health facilities from the territory of the Republic of Serbia and the region, primarily in the Republic of Srpska. A number of them, come directly into personal arrangement, without any prior contact with health services. In all these cases, the first examination is performed timely, as well as appropriate diagnostic and therapy.
If mild poisoning occures (about 4/5 of the total) at the DRT, after completion of diagnostic and therapeutic protocols and observations, in 6, rarely 12 hours, definitive medical treatment will be finished. In about 1/5 of cases, hospitalization in the Clinic for Emergency and Clinical Toxicology, was indicated, due to severe or moderately severe clinical picture of intoxication.
At the DRT, patients are sent for the toxicological examination without any positive toxicological history, with severely impaired state of health, when rapid differential diagnosis is necessary, to prove or exclude toxicological etiology. Therefore, consultative reviews of other specialists such as ORL, gastroenterologist (endoscopy), neurologists, neurosurgeons, psychiatrists and others are necessary. In that manner in a certain number of cases, toxicological etiology is excluded, other nontoxicological disease is proved, for which patients are sent to other services within or outside VMA, for definitive medical care.

Department for intensive care

Department for intensive care is intended for treatment of patients with moderate to severe acute poisoning, who require medical treatment level of intensive care units.
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 treatment and care of patients.
These standard 8 bed positions are equipped with vital functions monitors associated with the central control unit, with the additional possibility of using portable pulse oximeters.
Constantly available devices for mechanical ventilation, aspirators, defibrillators, EKG, enable the implementation of all necessary emergency diagnostic and therapeutic procedures, including those in the context of cardiopulmonary resuscitation.

Spatial and technical conditions, permit the uninterrupted performance of "bedside" additional non-invasive and invasive examinations and interventions, such as echosonography, ORL examination, endoscopy, paracentesis with possible drainage and other procedures.
Within the Clinic, there is a blood gas analyzer, used, if necessary for diagnostics of gas and acid-base status in patients stationed in other units of the MMA, during the non-working hours, weekends and holidays.

Toxicology Information Department

The Section is equipped with "online" computer data-base made by the Sector staff, which contains information about:

- 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, presented to the Centre for a one-year period.

Institute for Toxicology and Pharmacology

The Institute covers numerous preclinical and clinical areas of toxicology and pharmacology which are important in solving toxicological problems in clinical practice.
The 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 is performing toxicological-chemical analyses, aiming rapid, sensitive and reliable detection, identification and quantification of toxic agents in different types of samples (biological material, air, water, soil, 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 (HPLC, GC, UPLC) and spectrometric (UV, VIS, ICP MS).

Department for Experimental Toxicology and Pharmacology

Human resources and equipment of the Department, enable testing of certain pharmacodynamic and toxicodynamic effects of medicaments 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, the production of complex preclinical projects is possible.

Structure of human resources potential of NPCC is shown in Table 1.

Table 1. The Personnel structure NPCC of MMA

Groups	n	%
Doctors	12	17.6
Medical technicians	22	32.4
Specialists of toxicological chemistry	9	13.3
Veterinarians, biologists	4	5.9
Laboratory technicians	12	17.6
Administrative staff	3	4.4
Support staff	6	8.8
Total	68	100.0

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

Mobile toxicological-chemical team

Mobile toxicological-chemical team (MTC) is not an independent organisational unit; it consists of the personnel from all PCC organizational units. MTC team is activated in the case of larger chemical accidents, with the primary task of implementing medical procedures at the scene, in coordination with other relevant departments.

In order to realise these basic purposes, the MTE is equipped and trained to implement a number of activities, among which the most important are:

- Sampling, detection, identification and quantification of chemicals in water, land, air, as well as in biological materials in the field;
- First aid and emergency treatment in field conditions at the location of chemical accidents;
- Organization of medical aspects of triage, evacuation, care and treatment of poisoned victims;
- Consultations about hospital treatment of patients from chemical accidents, admitted to the regional health institution;
- Implementation of specific and nonspecific therapy of poisoned patients during transport to PCC (severe poisoning cases).

Regular activities of members of the Mobile toxicological team that are planned and carried out during the year, are in the function of the preparation and training for the above tasks. These include participation in training courses, demonstration exercises and control activities related to highly toxic chemicals. These activities are carried out by members of the MTE in cooperation with other departments of the Ministry of Defence (MD) and the Serbian Armed Forces (SAF), some civil structures such as the Ministry of Internal Affairs of the Republic of Serbia (MIA RS). In this context, of great importance is a perennial and very meaningful international cooperation, especially with the Organization for the Prohibition of Chemical Weapons (OPCW), whose administrative headquarters is in The Hague.

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 is shown in Table 2. The number of registered cases of poisoning, shown in the table, represents the total number of acute poisoning in the Republic of Serbia based on the data registered in the NPCC (4747) and the available data from 9 regional health care centers in Republic of Serbia (2143).

Table 2. Population in the Republic of Serbia and the number of registered poisoning in 2015

Year	Number of inhabitants	Number of registered cases	Number of cases per 1.000 inhabitants
2014.*	7 114 393	6890	0.96

*Available data, web site of the Republic Institute for Statistics, Statistical Annual Report of Serbia, june, 2016.

Toxicology Information Department

During 2015 in the Toxicology Information Department numerous calls from citizens and medical workers of different profiles are registered. 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
Medicaments	110	8	61	11
Pesticides	54	5	17	2
Corrosives	41	5	12	1
Mushroom	5	7	7	1
Gases	10	3	3	1
Alcohol	14	0	3	2
Drugs of abuse	11	0	4	1
Other	39	14	44	25
Total	284	42	151	44

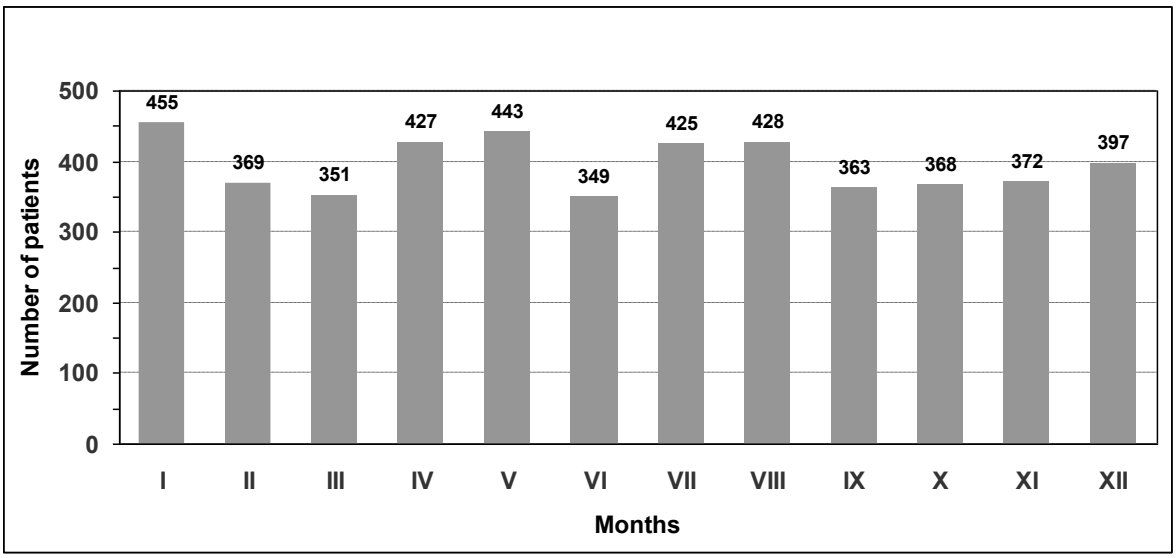
In a one-year period a total of 521 calls were received, 326 calls were related to the presumed poisoning in adults, and 195 in children. Calls from citizens were relatively less represented (86; 16.5%) in relation to the number of received calls from the doctors. In both cases medicaments as a possible etiologic agents predominate, and the character of intentions are suspected as accidental intoxication, especially in children.

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

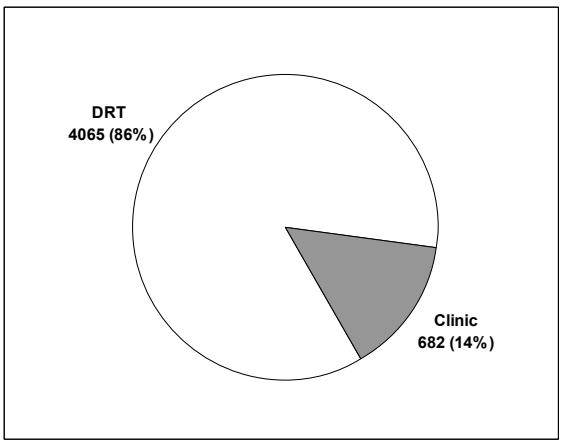
During 2015, in the Department for reanimation and triage of NPCC a total of 4747 patients were examined by a physician, and 682 (14.4%) of them were admitted for hospital treatment in the Clinic for Emergency and Clinical toxicology.

The specified number of outpatient medical examinations, as noted in the introductory section of this Yearbook, confirms the long-term tendency of increasing the volume of activity in the DRT NPCC. As an illustration, data from 2010 can be cited. In 2010 the number was 3996, in 2012 – 4176 and in 2014 – 4415.

Distribution of patients examined by months, is shown in Graph.1, and the relationship of examined (discharged to home) and hospitalized patients in the Graph. 2.

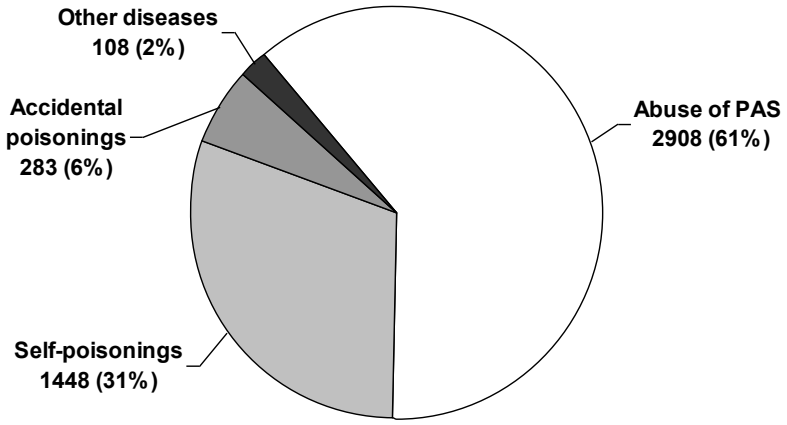


Graph 1. Number of patients examined in DRT, by months



Graph 2. Number and percentage of examined outpatient and hospitalized patients

The most common reason for arriving at the DRT was the suspicion of psychoactive substances abuse – PAS (alcohol and drugs of abuse) and self-poisoning by medicaments, corrosive agents and pesticides (over 90% of all cases). A less common reason for arriving was accidental exposure (Graph. 3).



Graph 3. Basic Distribution of reasons to arriving DRT on intentions characters

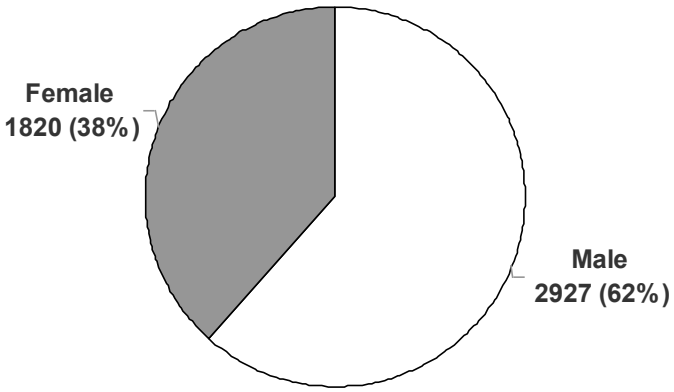
The most common cause for observatioan and treatment in the DRT NPCC was ethyl alcohol with 2466 examinations, 51.9% of the total number of examinations. Agents that followed were medicaments with 1289 examination (27.2%), substances of abuse - 442 patients (9.3%), gases – 189 patients (4.0%), corrosives – 97 patients (2.0%), pesticides – 62 patients (1.3%), mushrooms and plants in 32 patients (0.7%), other agents in 62 patients (1.3%) and 108 patients were without acute exposure and intoxication (2.3%), 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	2466	7	0.3
Drug of abuse	442	44	9.9
Medicaments	1289	478	37.1
Psychoactive	1083	404	37.3
Other drug	206	74	35.9
Gases	189	29	15.3
Corrosive	97	69	71.1
Pesticides	62	22	35.5
Mushrooms and plants	32	10	31.2
Other agents	62	9	14.5
Other diseases	108	14	12.9
Total	4747	682	

From Table 4 (right column), we may conclude the following: analyzed by etiological groups, the highest percentage of indications for hospitalization in relation to the number of examination in the DRT NPCC, registered in corrosive compounds, followed by drugs, pesticides, mushroom (plants). It also suggests that these groups of toxic agents usually cause a clinical picture that required hospitalization of patients. In contrast, a large discrepancy between the number of outpatient examination on one side, and a small percentage of admissions from the other (0.3% and 9.9%) was noted in patients with alcohol and substance of abuse.

Of the total number of examined patients, there were 2927 (61.7%) females and 1820 (38.3%) males (Graph.4).



Graph 4. Distribution of patients by gender (DRT NPCC)

The majority of examined patients, 2171 of them, were in the 19-40 years group (45.7%), followed by 1608 (33.9%) in the range of 41-65 years, which means that the majority of examined and treated people belong to working population (Table 5).

Table 5. Distribution of patients by age (DRT NPCC)

Age groups (years)	n	%
To 18	541	11.4
19-40	2171	45.7
41 - 65	1608	33.9
More than 65	328	6.9
Unknown	99	2.1
Total	4747	100.0

Poisonings are ranked by severity based on PSS (Poisoning Severity Score), shown in Table 6.

Table 6. Poisoning severity expressed by PSS (DRT NPCC)

Poisoning severity	N	%
PSS 0	835	17.6
PSS 1	2829	59.6
PSS 2	468	9.9
PSS 3	287	6.0
Other	328	6.9
Total	4747	100.0

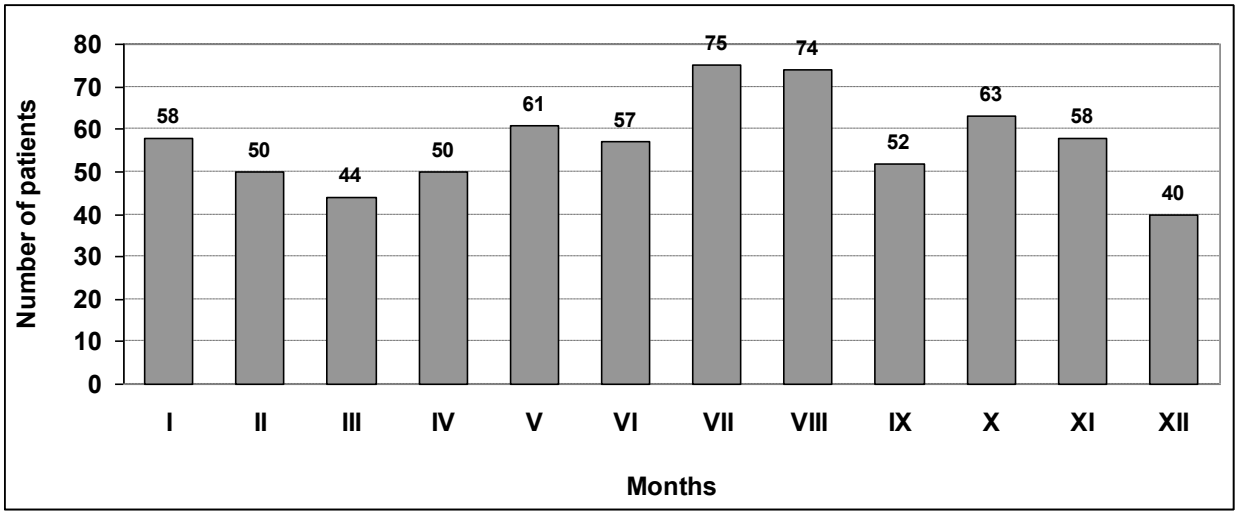
835 (17.6%) people were without any clinically significant signs of poisoning (PSS 0). This data from the table, shows a large number of patients who had anamnestic suspicion of acute poisoning, which was not proven by clinical and additional outpatient diagnostics. The most important reasons for this, lies in the unjustifiably frequent bypassing medical services of primary and secondary rank by patients (accompanied or alone, patients come directly to PCC MMA which is a tertiary institution). This often happens after a phone call to the public emergency services for advise, without prior medical examination, and without consulting a toxicologist who is available on phone (011/36 08 440), daily, round the clock.

Mild poisoning (PSS 1) was registered in 2829 (59.6%) of the total examined and treated patients, moderate (PSS 2) in 468 (9.9%) patients, and severe poisoning in (PSS 3) in 287 (6.0%) patients. In 328 patients (6.9%) no exposure to toxic agents was present. The statement about it, often requires not only safe exclusion of acute poisoning, but also in no small number of cases, diagnosis or reasonable suspicion of others nontoxicological diseases or conditions.

Clinic for Emergency and Clinical toxicology

In the Clinic for emergency and clinical toxicology 682 patients were hospitalized during the 2015.

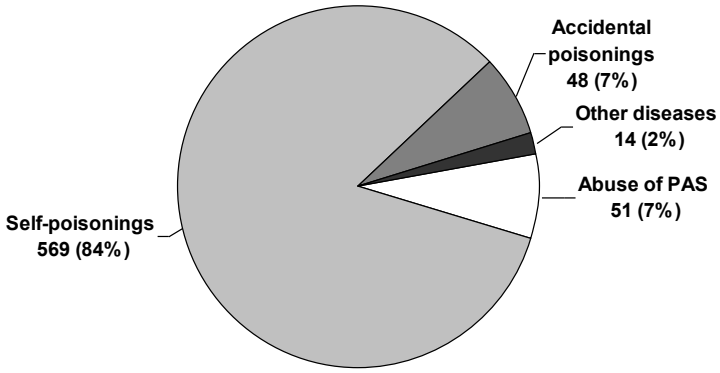
Time dynamics (by months) of admissions to the Clinic for Emergency and Clinical Toxicology shown in the Graph 5.



Graph 5. The number of hospitalized patients in the Clinic for emergency and clinical toxicology, by months

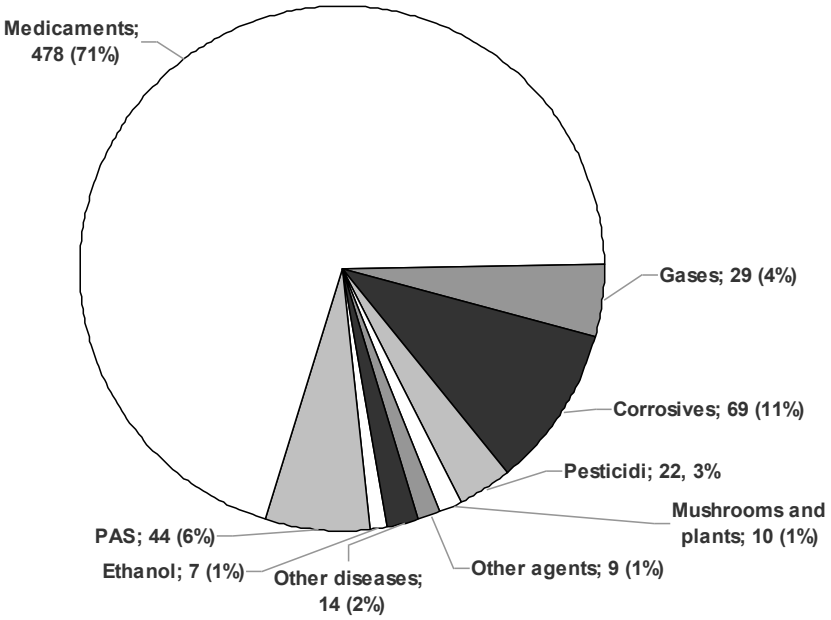
In the previous section, it has already been pointed out, that this number of hospitalized patients, represents 14.4% of the total number of people examined at the DRT and that percentage continues the long-term decrease trend: in 2010 it amounted to 20.5% and in 2014 to 16%. This is undoubtedly one of the indicators of increasing the efficiency and quality of work at the Centre and in full compliance with current intentions of the organization of health services in the developed world.

The most common reason for hospitalization was self-poisoning by medicaments, corrosive substances and pesticides (569 in total; 84.0% cases). On the other side, accidental poisoning and psychoactive substances of abuse - PAS (alcohol and narcotics) appeared in only 48 and 51 patients respectively (by 7.0% for each group), as shown in the Graph 6.



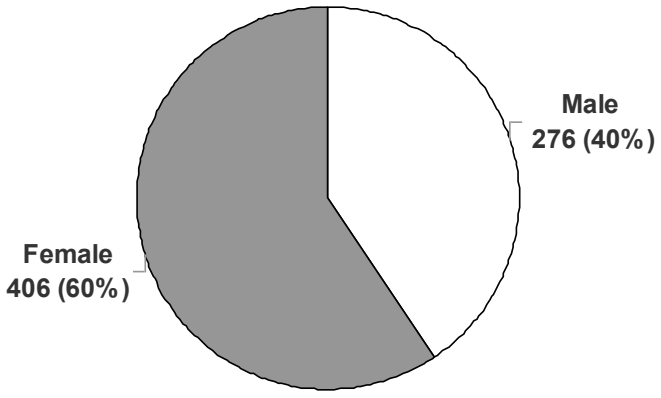
Graph 6. Reason for hospitalization of patients (Clinic for emergency and clinical toxicology)

Medicaments, as a dominant cause of poisoning were the most common agents, in 478 patients (70.1% of hospitalized patients), followed by corrosives in 69 cases (10.1%), substances of abuse in 44 patients (6.5%), gases in 29 (4.2%), pesticides with 22 poisonings (3.2%), mushrooms and plants in 10 (1.5%), other toxic agents in 9 patients (1.3%), ethanol in 7 (1.0%), and other diseases were noted in 14 patients (2.0%), Graph 7.



Graph 7. The percentage distribution of causes of poisoning (Clinic for emergency and clinical toxicology)

According to gender, 276 (40.4%) males and 406 (59.6%) females were hospitalized, Graph 8



Graph 8. Distribution of patients by gender (Clinic for emergency and clinical toxicology)

According to the age structure of hospitalized patients, there were 38 (5.6%) persons younger than 18 years, from 19-65 years 542 patients (79.5%), and 102 patients (14.9%) were older than 65 years (Table 7).

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

Age groups (years)	n	%
To 18	38	5.6
19 - 40	267	39.1
41-65	275	40.3
More than 65	102	14.9
Total	682	100.0

Analysis of the severity of poisoning, of the people treated in our hospital, showed, that no clinically significant signs of poisoning (PSS 0) were present in 30 people (4.4%). Namely, in cases of suspected poisoning with some types of agents, which is characterized by late or delayed manifestation of clinical symptoms of intoxication, the time necessary for an adequate toxicological diagnosis, significantly exceeds the optimal time of outpatient observation. As an example of this, exposure to certain pesticides-rodenticides, mushrooms, some types of medicaments (eg. Lithium), unknown potential corrosive substances and some other substances are given. For these reasons, hospital observation and further diagnostic tests, which usually last up to 48 hours after exposure, are indicated and implemented. The above data, shows the frequency of those cases where acute poisoning has not been proven, despite positive or suspected history.

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

Poisoning severity	n	%
PSS 0	30	4.4
PSS 1	316	46.3
PSS 2	118	17.3
PSS 3	169	24.8
PSS 4	33	4.8
Other	16	2.3
Total	682	100.0

Mild poisoning (PSS 1) was registered in 316 (46.3%) patients, moderate in 118 (17.3%), severe poisoning (PSS 3) in 169 (24.8%), and there were 33 (4.8%) cases with lethal outcome.

Because of other nontoxicological diseases (Table 8), 16 patients were treated at the clinic (2.3%).

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 2466 people were examined (51.9% of all examined). A significantly higher number of males 1876 (76.1%), compared with females 590 (23.9%), was registered. Most were represented patients aged 19-40 years, of whom there were 980 (39.7%); followed by patients in the age range of 41-65 years (894; 36.2%). Patients aged over 65 years made up 197 (8.0%). Significantly, 12.4% (307 patients) were minors.

Mild acute ethyl alcohol intoxication (PSS 1) was registered in 1838 (77.6%) patients, 351 examined patients (14.2%) were with signs of moderate and severe acute intoxication (PSS 2 - 281 i PSS 3 – 70). In 219 (8.9%) people PSS 0 was registered. A total of 56 patients (2.3%) was mistakenly sent due to suspicion of ethyl alcohol intoxication, which were rejected with appropriate diagnostic procedures. We either proved that another toxicological ethiology was present or that a completely non – toxicological condition was present in a significant number of patients.

Due to the acute ethyl alcohol intoxication 7 patients (1.0% of all hospitalized patients) were admitted to **Clinic for emergency and clinical toxicology**. All of them were males, aged 19 to 65 years. In 2 patients a score of PSS 3 was registered, and there has not been a lethal outcome, which could be more firmly connected with ethyl alcohol poisoning.

Medicaments

Due to the acute medicaments intoxication 1289 (27.1% of all examined) patients were examined in the DRT NPCC.

Due to the acute psychoactive drug intoxication 1083 (84.0%) patients, out of them 368 males (34.0%) and 715 (66.0%) females, were examined.

As a dominant cause of poisoning, in most of cases benzodiazepines were detected (723; 66.8%), then antiepileptics with 212 cases (19.6%). Neuroleptics in 104 patients (9.6%) and antidepressants in 44 patients (4.1%) were registered as a cause of poisoning.

In the group of benzodiazepines, the most common cause of poisoning was bromazepam in 366 cases (50.7%), then diazepam (186 cases; 25.7%) and lorazepam (84 cases; 11.6%).

Among the antiepileptics, significantly more frequent in comparison to other was carbamazepine, in 89 (42.0%) patients, then clonazepam in 87 (41.1%) patients, VPA in 20 (9.4%) and barbiturates in 7 (3.3%) patients.

In the group of neuroleptics, clozapine and similar drugs (olanzapine, risperidone) were the predominant cause of poisoning in 61 (58.6%) patients, followed by phenothiazines (30 patients; 28.8%).
In the group of antidepressants, the new-generation antidepressants (SSRI) (26 patients; 59.1%), compared to cyclic antidepressants (8 patients; 18.2%) were a bit more frequent, as the cause of poisoning. Detailed review of number of acute drug poisonings in DRT NPCC was shown in Table 9.
According to age, minors were 90 (8.3%), 920 people (84.9%) were aged 19-65 years and 73 patients older than 65 years (6.7%).
Even with 313 people (28.9%) anamnestic suspicion of intoxication (PSS 0) had not been proven, while mild poisoning (PSS 1) was found in 521 people (48.1%). Moderate poisoning (PSS 2) was registered in 78 (7.2%), and severe poisoning (PSS 3) in 110 patients (10.2%). Sixty one patients (5.6%) were mistakenly sent, due to the suspicion on the acute drug intoxication, which has not been confirmed.

Among the medicaments from other groups, which were the predominant cause of poisoning in 206 examined patients, the most common were analgesics which were the primary agent in 79 (38.3%) patients. NSAID was the cause of poisoning in 47 cases, and opioid analgesics in 31 cases. The predominant cause of poisoning in 68 (33.0%) patients was cardiovascular drugs. Among these group of medicaments as the cause of poisoning, the most common were beta blockers (32 cases), calcium antagonists (11 cases) and ACE inhibitors (21 cases). Sympathomimetic drug poisoning (theophylline and other) was registered in 9 (4.4%), and anticholinergic drug poisoning in 7 (3.4%) patients. Poisonings by other drugs (oral hypoglycemic drugs, hormonal preparations, unknown drugs, etc.) were recorded in 43 (20.9%) patients.
A score of PSS 0 was present in 74 patients (35.9%), signs of mild poisoning (PSS 1) were found in 91 (44.2%) patients, moderate poisoning (PSS 2) in 14 (6.8%) of them, and severe poisoning (PSS 3) in 15 (7.3%) patients. Twelve patients (5.8%) were mistakenly sent because of suspected acute intoxication of drugs, since it has not been proven.

Table 9. The frequency of a single drug as dominant cause of poisoning (DRT NPCC)

Psychoactive drug	1083	%	**Other drug**	206	%
Antidepressants			*Analgesics*		
Cyclic	8	18.2	NSAID	47	59.5
SSRI	26	59.1	Opioides	31	39.2
MAOI	2	4.5	Others	1	1.3
Others	8	18.2	Total	79	100.0
Total	44	100.0	*Cardiological*		
Antiepileptics			Beta blockers	32	47.1
Carbamazepine	89	42.0	Calcium antagonists	11	16.2
Clonazepam	87	41.1	ACE inhibitors	21	30.9
VPA	20	9.4	Nitrates	2	2.9
Lamotrigine	9	4.2	Cardiotonics	1	1.5
Barbiturates	7	3.3	Diuretics	1	1.5
			Total	68	100.0
Total	212	100.0	*Sympathomimetics*		
			Theophylline	8	88.9
Benzodiazepines			Others	1	11.1
Bromazepam	366	50.7	Total	9	100.0
Diazepam	186	25.7	*Anticholinergics*		
Lorazepam	84	11.6	Biperiden	7	100.0
Alprazolam	56	7.7			
Midazolam	10	1.4	Total	7	100.0
Prazepam	1	0.1	Others		
Zopidem[1]	20	2.8	Oral hypoglycemics, hormonal preparations, unknown drugs etc.		
Total	723	100.0			
Neuroleptics					
Phenothiazines	30	28.8			
Butyrophenones	7	6.8			
Clozapine	30	28.8			
Risperidone	3	2.9	Total	43	100.0
Olanzapine	28	26.9	[1] anxiolytic, does not belong to the group of benzodiazepines		
Others	6	5.8			
Total	104	100.0			

From the total of 682 hospitalized patients, 478 people (70.1%) were treated due to acute medicaments intoxication. Among them, 404 people (84.5%) were hospitalized due to acute psychoactive drug poisoning, and 74 people (15.5%) due to acute other drug group poisoning.

In the group of patients with acute psychoactive drug poisoning there were 266 females (65.8%) and 138 males (34.2%). Minors were 20 (4.9%), those at the age of 19-65 years 332 (82.2%) and older than 65 years 52 people (12.9%).

The most common medicaments, as a cause of poisoning, were from the benzodiazepine group (204 persons; 50.5%), antiepileptics (115; 28.5%), neuroleptics (65; 16.1%) and antidepressants (20; 4.9%).

In the group of benzodizepines, the leading cause of poisoning was bromazepam (125 cases), followed by a significantly smaller number of diazepam (33), lorazepam (21), alprazolam (13), zolpidem (10), midazolam (2).

Among the antiepileptics, the most common cause of poisoning was carbamazepine (65 cases), followed by VPA (15), clonazepame (28), lamotrigine (3) and barbiturates (4).

Among the neuroleptics, the most common cause were clozapine (23 cases), olanzapine (22 cases) and phenothiazines (14).

Among antidepressants, as the cause of poisoning, SSRI (13 cases) and cyclic antidepressants (7) were represented.

Detailed review of the number of acute medicament intoxication at the Clinic for emergency and clinical toxicology is shown in Table 10.

Among the patients hospitalized due to acute psychoactive drug poisoning, 9 patients with a score PSS 0 (2.2%) were noted, mild poisoning (PSS 1) in 215 people (53.2%), moderate (PSS 2) in 71 people (17.6%), and severe (PSS 3) in 102 people (25.2%). In this group of patients, 8 lethal outcomes (PSS 4; 2.0%) were registered. The dominant causative agents in 2 cases were antiepileptics and benzodiazepines in 6 cases.

Due to the acute poisoning by other medicaments, 74 patients, 18 males (24.3%) and 56 females (75.7%), majority of them at the age of 19-65 years old (47 patients; 63.5%) were hospitalized. Minors were 14 (18.9%) and older than 65 years 13 (17.6%).

The most common cause of poisoning were cardiovascular drugs. Forty six cases of acute poisoning (62.1%) were registered, and beta blockers (23 cases), calcium antagonists (11) and ACE inhibitors (10) were dominant. In the group of analgesics (13 cases), NSAID poisonings were predominant (8 cases).

There were 7 patients with acute sympathomimetics poisoning, and 6 of them were acute theophylline poisoning.

Due to acute anticholinergics poisoning, 1 person (biperiden) was hospitalized.

Other drug poisoning (oral hypoglycemic drugs, antilipemics, unknown drugs, etc.) was registered in 7 patients (9.4%). A single patient (14.3%) was registered with a PSS score of 0, clinical picture of mild poisoning (PSS 1) in 6 patients (85.7%). In 4 patients (5.4%) lethal outcome was registered, in patients intoxicated analgesics (2), cardiac drugs (1) and sympathomimetic (1).

Table 10. The frequency of a single drug as a dominant cause of poisoning (Clinic for emergency and clinical toxicology)

Psychoactive drug	404	**%**	**Other drug**	74	**%**
Antidepressants			*Analgesics*		
Cyclic	7	35.0	NSAID	8	61.5
SSRI	13	65.0	Opioides	5	38.5
			Total	13	100.0
Total	20	100.0	*Cardiological*		
Antiepileptics			Beta blockers	23	50.0
Carbamazepine	65	56.5	Calcium antagonists	11	23.9
VPA	15	13.0	ACE inhibitors	10	21.7
Barbiturates	4	3.5	Cardiotonics	1	2.2
Lamotrigine	3	2.6	Nitrates	1	2.2
Clonazepam	28	24.4	Total	46	100.0
			Sympathomimetics		
Total	115	100.0	Theophylline	6	85.7
Benzodiazepines			Others	1	14.3
Bromazepam	125	61.3	Total	7	100.0
Diazepam	33	16.2	*Anticholinergics*		
Alprazolam	13	6.4	Trihexyphenidyl	0	0.0
Lorazepam	21	10.3	Biperiden	1	100.0
Midazolam	2	1.0	Total	1	100.0
Zolpidem[1]	10	4.9	Others		
Total	204	100.0	Oral hypoglycemics, antilipemics, unknown drugs etc		
Neuroleptics					
Phenothiazines	14	21.5			
Butirophenoni	1	1.5			
Clozapine	23	35.5			
Olanzapine	22	33.8	Total	7	100.0
Others	5	7.7	[1] anxiolytic, does not belong to the group of benzodiazepines		
Total	65	100.0			

Drugs of abuse

In the DRT PCC 442 patients (9.3% of all examined) were examined for suspicion of acute drug abuse intoxication. According to gender, there were 331 males (74.98%) and 111 females (25.02%).

In relation to the age groups, under the age of 18 years were 72 people (16.3%), in the age of 19 to 40 years 312 people (70.6%) and in the age between 41-65 years, 52 people (11.8%). In six (6) people age was not registered.

Acute intoxication has not been proven (PSS 0) in 76 patients (17.2%), mild poisoning had 233 people (52.7%), 63 patients (14.28%) were with signs of moderate poisoning, and in 45 people (10.0%) severe poisoning was confirmed. Suspicion on the underlying intoxication was not confirmed for 25 patients (5.6%).

Under suspicion of heroin abuse, 225 people (50.9%) were examined. According to the age groups, at the age 15-19 were 8 people (3.6%), 20-24 years 23 people (10.2%), 25-29 years were 40 people (17.8%), 30-65 years old 151 people (67.1%). A score of PSS 0 was registered in 25 (11.1%). 107 people had mild poisoning (47.5%), 50 patients (22.2%) were with signs of moderate poisoning, and in 38 people (16.9%) severe poisoning was confirmed. Suspicion on the underlying heroin intoxication was not confirmed for 5 patients (2.2%).

Under suspicion on the marijuana abuse 50 people were examined (11.3%). According to the age groups, 4 people younger than 14 years (8%) were registered, at the age 15-19 there were 13 people (26.0%), 20-24 years old 11 people (22.0%), 25-29 years old 8 people (16.0%), 30-65 years old 14 people (28.0%). In 21 patients (42.0%) was determined PSS score of 0, mild poisoning had 26 patients (52.0%), and 1 patient (2.0%) were with the signs of moderate poisoning. Suspicion on the underlying marijuana intoxication was not confirmed for 2 patients (4.0%).

Under suspicion of cocaine intoxication 25 people (5.6%) were examined. According to the age groups, at the age 15-19 were 2 people (8.0%), 20-24 years old 3 people (12.0%), 25-29 years old 9 people (36.0%), 30-65 years old 11 people (44.0%). The PSS 0 score was established in 3 people (12.0%), 17 patients had mild poisoning (68.0%), 4 patients (16.0%) were with the signs of moderate and 1 patient (4.0%) was found with signs of severe poisoning.

Under suspicion on the amphetamine intoxication 66 people (14.9% of all people examined on the suspicion on the drug of abuse intoxication, amphetamine, metamphetamine and MDMA-(Ecstasy) were examined. According to the age groups, at the age of 14 was 1 person (1.5%), 15-19 were 22 people (33.3%), 20-24 years 17 people (25.7%), 25-29 years 10 people (15.1%), 30-65 years old 15 people (22.7%). In 12 people (18.2%) PSS score 0 was determined, mild poisoning had 45 people (68.2%), 6 patients (9.1%) were with the signs of moderate poisoning, and 3 people (4.5%) had PSS score 3.

A total of 37 patients (8.4%) were examined on suspicion of acute intoxication with synthetic cannabinoids. In this group were people who abused drugs, newly synthesized substances.

Analysis of Distribution according to the age groups, at the age 15-19 were 27 people (72.9%), 20-24 years old 6 people (16.2%), at the age 25-29 was 2 person (5.4%), and at the age of 30-65 was 2 person (5.4%). The PSS 0 score was established in 4 people (10.8%), mild poisoning had 31 people (83.8%). Suspicion on the underlying intoxication was not confirmed in 2 patients (5.4%).

For a total of 39 cases (8.8% of all people examined under suspicion on the drugs of abuse intoxication), the agent and nature of poisoning was not determined. In this group there were no fatal outcomes, but moderate and severe poisoning was registered in 7 people (17.9%). These findings indicate the number of intoxication when causative agent 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** 44 patients were admitted, thay were all 19-65 years old (working age), which makes 9,9% of the total number of patients examined due to acute intoxication by these agents. According to the age groups, at the age 15-19 were 2 people (4.5%), 20-24 years 3 people (6.8%), 25-29 years 8 people (18.2%), 30-65 years old 31 people (70.4%).
PSS score of 0 was registered in 1 patient (2.3%), due to mild drug of abuse intoxication (PSS 1) 2 people were admitted (4.5%). Moderate intoxication was registered in 9 patients (20.4%), due to severe intoxication (PSS 3) 30 patients (68.2%) were treated, and the lethal outcome (PSS 4) was noted in 2 patients (4.5%).

Due to acute intoxication with drugs of abuse 40 males (90.9%) and 4 females (9.1%) were hospitalized.

The most common causative agent in hospitalized patients was heroin (29 persons, 65.9%). According to the age groups, at the age of 15-19 there was 1 patient (3.4%), at the age of 20-24 there were 3 people (10.3%), 25-29 years 4 people (1.8%), 30-65 years old 21 people (72.4%). Due to mild poisoning 1 patient (3.4%) was admitted, due to moderate poisoning 4 people (13.8%), due to severe poisoning (PSS 3) 22 patients (75.9%). Lethal outcome (PSS 4) was noted in 2 patients (6.9%).

One patient was admitted to our hospital due to toxic effects of cocaine (2.3%) and it was severe intoxication. Six patients (13.6%) were hospital treated after the abuse of amphetamines, three with an estimated weight of poisoning PSS 2, and three with PSS 3.
Finally, 8 patients (18.2%) were admitted in the Clinic, and the certain causative agent was not determined. There were no fatal outcomes in this group.

Gases
Due to suspicion on acute gas exposure and intoxication in DRT NPCC 189 patients (3.9% of all examined) were examined, and 29 people (15.3% of patients examined due to acute gas intoxication) were admitted for hospital treatment. According to gender there were 94 males (49.7%) and 95 females (50.3%).

Predominant causative agents were smoke inhalation (76 patients; 40.2%), chlorine fumes from household products (39 patients; 20.6%) and carbon monoxide (24 patients; 12.7%), which represents 7.5% patients examined due to gas exposure and intoxication.

In the other (50; 26.4%) patients, varnishes and solvents (20), vapors of oil and petroleum products (3), base and acid vapors (1, respectively 9), and other agents (17) were registered as a cause of poisoning.
The majority of them, 157 patients (83.0%) were at the age 19-65. Older than 65 years 25 (13.2%) patients were, younger then 18 were 6 (3.2%). PSS score of 0 was registered in 71 patients (37.6%), clinical picture of mild poisoning was found in 81 (42.8%), and moderate poisoning in 12 patients (6.3%). Six patients (3.2%) had signs of severe poisoning. Anamnestic suspicion on the underlying gas intoxication was not confirmed in 19 patients (10.0%).

Among 29 **hospitalized patients** (4.2% of all hospitalized patients), 14 were male (48.3%) and 15 female (51.7%). The most common causes were carbon monoxide, smoke inhalation, chlorine fumes from household products, unidentified agents (12, 10, 6, 1; 41,4%, 34.5%, 20.7%, 3.4%). The majority of them, 22 patients (75.9%) were at the age 19-65, and 6 (20.7%) patients were older than 65 years, and 1 minor (3.4%). PSS score of 0 was registered in 1 patient (3.4%), clinical picture of mild poisoning was found in 15 (51.75%) and moderate poisoning in 7 patients (24.1%). Five patients (17.2%) had signs of severe poisoning. There was 1 fatal outcome in this group.

Pesticides

Due to acute pesticide exposure and intoxication in the DRT PCC 62 patients (1.3% of all examined patients) were examined. According to gender there were 32 males (51.6%) and 30 females (48.4%). Because of the well-known seasonal distribution of this type of poisoning (agricultural work), 39 (62.9%) patients contacted the physician in the period between April and July.

Due to acute pesticide poisoning, 22 patient were admitted for hospital treatment, which represents 35.5% of patients examined.

The majority of them, 51 patients (82.2%) were at the age 19-65. Older than 65 years were 10 (16.1%) patients, and 1 patient was younger then 18 (1.6%). Due to suspicion on the acute organophosphorus insecticide and herbicide intoxication (15 patients; 24.2%) were examined.

In 24 cases (38.7%) a PSS score of 0 was registered, mild poisoning (PSS 1) was registered in 17 patients (27.4%), moderate (PSS 2) in 2 patients (3.2%), and 5 patients (8.1%) had clinical features of severe poisoning (PSS 3) at the admission. Suspicion on the underlying intoxication was not confirmed in 14 patients (22.6%).

In the Clinic for emergency and clinical toxicology due to acute pesticide intoxication 22 patients, which represent 3.2% of all hospitalized patients, were treated. The most common toxic agents were from the organophosphorus insecticide group (8 cases; 36.4% of all pesticides). The herbicides intoxication was represented less frequently (6; 27.3%), the other pesticides were represented in 8 patients (36.4%).

According to gender, there were 10 males (45.4%) and 12 females (54.6%); the majority of them in 77.3% cases were at the age of 19-65 (17 patients). Older than 65 years were 5 patients (22.7%).

PSS score of 0 was registered in 5 patients (22.7%), mild poisoning (PSS 1) was registered in 10 patients (45.4%), moderate (PSS 2) in 2 (9.1%), and due to severe poisoning (PSS 3) 3 patients (13.6%) were treated. The fatal outcome was registered in 2 patients (9.1%) treated due to acute pesticide poisoning.

Corrosives

Due to suspicion on the acute corrosive compound poisoning in the **DRT PCC**, a total of 97 patients (2.0% of all examined patients) were examined, and 69 of them (71.1% of this type of poisoning cases) were admitted for hospital treatment. The most common agents were hydrochloric (38 patients; 39.2%) and acetic acid (19; 19.6%). Twelve patients (12.4%) were examined due to the sodium hydroxide ingestion, 2 people due to the other acids (2.1%); 8 people (8.2%) due to the bleach compounds, cleaners (14; 14.4%) and other corrosive compounds (4 persons; 4.1%).

According to gender, 61 (62.9%) people were female, and 36 (37.1%) male. One minor was registered (1.0%), 73 patients (75.3%) were from 19-65 years, and 23 patients (23.7%) were older than 65 years.

PSS score of 0 was registered in 19 patients (19.65), clinical features of mild poisoning (PSS 1) was noted in 30 patients (30.9%), moderate (PSS 2) in 13 (13.4%), and 31 patients (31.9%) had severe poisoning at the admission. In 4 patients (4.1%) suspicion on the underlying intoxication was not confirmed.

In the **Clinic for emergency and clinical toxicology** due to the acute corrosive poisoning 69 patients were hospitalized, which represent 10.1% of all hospitalized patients. The most common ingested agent was hydrochloric acid (33 cases; 47.8%), and then acetic acid (17 cases; 24.6%). Eight hospitalized patients (11.6%) ingested sodium hydroxide, and other agents (bleach compounds, other acids, other corrosive compounds) in 11 patients (15.9%).

The majority of patients were females (44; 63.8%), and males were 25 (36.2%). At the age of 19-65 years were 53 patients (76.8%), and 16 people were older than 65 years (23.2%).

PSS score of 0 was registered in 2 people (2.9%), and 23 patients (33.3%) had clinical features of mild poisoning. Due to moderate poisoning 13 people (18.8%) were treated, and due to severe poisoning 20 people (29.0%). Lethal outcome was registered in 12 patients, which represent 17.4% of all treated patients of corosive intoxication. At the same time, it represents 36.4% of all deaths at the Clinic in 2015. which once again, confirmed a multi-year trend of constantly, the highest rates of mortality, in this group causes of poisoning.

Mushrooms and plants

Due to acute mushroom and plant poisoning in the **DRT PCC** 32 patients, 15 (46.8%) males and 17 (53.2%) females, were examined. In 24 people (75.0%) there was a suspicion of acute mushroom poisoning, 5 people ingested the seeds of the plant *Datura stramonium*, and 3 people consumed unidentified fungi (plants). All mushroom poisonings were accidental.

People younger than 18 years were 3 (9.4%), 26 people (81.2%) were at the age 19-65, and 3 people were older than 65 years (9.4%). PSS score of 0 was registered in 7 people (21.9%), clinical features of mild poisoning (PSS 1) was noted in 8 people (25.0%), moderate poisoning in 1 person (3.1%), 2 people had clinical features of severe poisoning (6.2%), and for 14 persons, it was concluded that there was no ingestion of poisonous mushrooms or plants (43.7%).

Ten people (31.1% of outpatient examined patients) were admitted in **the Clinic for emergency and clinical toxicology** for further diagnosis, observation and treatment (8 males and 2 females). Six (60.0%) patients were at the age 19-65, 3 younger than 18 years, and 1 person older than 65 years.

Due to suspicion of acute mushroom intoxication 5 patients (50.0%) were admitted, 5 patients due to acute *Datura stramonium* intoxication. Six patients (60.0%) had clinical features of mild poisoning (PSS 1), 1 patient had signs and symptoms of moderate, and 2 people clinical features of severe poisoning. One person was concluded to have no poisonous mushrooms or plants ingestion.

Other agents

This group consisted of patients (62; 1.3% of all outpatients) who were exposed to or intoxicated with toxic alcohols, various industrial products (organic solvents, detergents, disinfectants) and other agents. The **DRT PCC** registered 53 cases, the **Clinic for Emergency and Clinical Toxicology** an additional 9 cases. In 2 patients were registered lethal outcome (PSS 4). In one case analytically is proved the presence of the ethyl and methyl alcohol, and in second methyl alcohol only.

Other diseases

During the 2015, in 108 people (2.3% of the examined patients) were concluded that it was some other, nontoxicological etiologic factor. At the **DRT PCC** 94 cases were registered, and 14 in the **Clinic for Emergency and Clinical Toxicology**.

Department for Toxicological Chemistry

During the 2015 in the Department for toxicological chemistry PCC of MMA 18203 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 were 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 11-17.

Table 11. Analysis performed according to the requirements of the various MMA organizational units and the other Serbian Army organizational units

Types of analysis	Number	%
Alcohols	2005	38.1
Benzodiazepines	1005	19.1
Antiepileptics	360	6.8
Antidepressants	121	2.3
Neuroleptics	72	1.4
Psychoactive substances	278	5.3
Medicaments (other)	831	15.8
Metals (Zn, Cu)	171	3.2
Pesticides	110	2.1
RBC cholinesterase	261	4.9
Identification	7	0.1
Others	42	0.8
Total	5263	100.0

Table 12. Analysis performed according to the requirements of the various Serbian Army organizational units (protocol BIOGNOST)

Types of analysis	Number	%
Psychoactive substances	1145	84.4
Alcohols	211	15.6
Total	1356	100.0

Table 13. Analysis performed as a part of the MMA scientific research projects

Analysis	Number
RBC cholinesterase	351
Total	351

Table 14. Analysis performed according to the requirements of the Ministry of Internal Affairs of the Republic of Serbia

Types of analysis	Number
Alcohols	1333
Total	1333

Table 15. Analysis performed according to the requirements of the civil institutions

User/analysis	Number	%
Alcohols	235	3.2
Antiepileptics	720	9.8
Psychoactive substances	582	7.9
Medicaments	420	5.7
RBC cholinesterase	60	0.8
Metals	36	0.5
Benzodiazepines	152	2.1
Pesticides	71	0.9
Bioequivalence (ALIMS)	2500	34.2
Others	36	0.5
Forensic material	2507	34.2
Alcohol	720	
Medicaments	1672	
Opiates	110	
Others	5	
Total	7319	100.0

Table 16. Analysis performed as a part of the maintenance and enhancement of quality of the analytical procedures

Types of analysis	Number
Standards, controls, tests (medicaments, opiates, antiepileptics, pesticides)	2181
Validation of methods (calibration curves)	200
Interlaboratory analysis (medicaments, opiates, antiepileptics, cholinesterase)	200
Total	2581

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 2015. the Department is accredited for a total of 68 analytical methods (Table 17).

Table 17. Accredited analytical methods (06.07.2015.)

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

(extension) Table 17. Accredited analztical methods (06.07.2015.)

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

Department for Experimental Toxicology and Pharmacology

During 2015, 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 which are 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 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 515-04-3723/2015-11 of 08.07.2015.);

- 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, PCC, 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 PCC MMA are in the process of obtaining approvals and certificates of Good Laboratory Practice for the activities listed above.

4. Professional training

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

- the License for Good Laboratory-Clinical Practice in accordance with directives of EU and FDA regulations of USA;
- the License for Good Clinical Practice in accordance with directives of EU and FDA regulations of USA;
- the License for Informed consent in accordance with directives of EU and FDA regulations of USA;
- the License for Study protocol in accordance with directives of EU and FDA 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 all reported experimental methods were carried out. Thereby to the end of 2015, 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).

Mobile toxicological-chemical team

During 2015, MTC team and its members participated in planning, preparation, implementation or medical support of numerous activities and tasks:

- Exercise demonstrations of the Training center of the Serbian medical army corp in MMA “Spring 2015“ and „Autumn 2015“;
- The multinational CBRN exercise "Balkan response 2015", Training field „Ravnjak“ – Krusevac;
- Training exercise for inspectors of the Organization for the Prohibition of Chemical Weapons (OPCW) in the CBRN training centre – Krusevac;
- The number of different activities whose holders with other services of MO and SA, related with highly toxic agents.

Selected cases

This section gives a brief overview of 33 cases of patients with lethal outcome whose death was to some extend connected with the causative agent (Table 18).

Table 18. 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	57	Corrosive agent (hydrochloric acid)	Undoubtedly proven	Ingestion; transferred from other institutions 5 days after ingestion; corrosive damage to the esophagus and stomach III degree with acute respiratory failure, pneumothorax and bronchopneumonia. On the tenth day of hospitalization massive gastrointestinal bleeding.
2.	M	27	Heroin	Probably did not contribute	Multi-year opiate addict in a poor general condition, arrived without vital signs, reanimated. He did not show the presence of opiates morphine and other structures PAS.
3.	F	91	Corrosive agent (Sodium hydroxide)	Contributed	Accidental ingestion; patients with dementia, EGDS not done, during hospitalization stable vital parameters without developing complications; lethal outcome 11 days of hospitalization.
4.	F	23	Carbon monoxide	Undoubtedly proven	Transferred from another institution, more than 12h after found in the car in the garage, in a coma, respiratory and circulatory insufficient. NMR findings pointed to severe brain damage from a massive brain edema.
5.	M	91	Corrosive agent (hydrochloric acid)	Contributed	Accidental ingestion; demented patients, treatment is complicated bilateral bronchopneumonia, gastrointestinal bleeding; lethal outcome 11 days of hospitalization.
6.	F	65	Corrosive agent (concentrated acetic acid)	Undoubtedly proven	Ingestion; severe poisoning with metabolic acidosis, ARI with respiratory and cardiocirculatory failure.
7.	F	80	Corrosive agent (concentrated acetic acid)	Undoubtedly proven	Ingestion; severe metabolic acidosis, respiratory and cardiocirculatory failure, symptoms and signs of gastrointestinal bleeding.
8.	M	65	Ttheophylline	Undoubtedly proven	Ingestion; coma, the development of complications (epi status, ARF, aspiration bronchopneumonia, gastrointestinal bleeding.
9.	F	71	Corrosive agent (hydrochloric acid)	Contributed	Ingestion; the development of complications (bronchopneumonia).
10.	M	46	DNOC (herbicide)	Undoubtedly proven	Ingestion; ARF and cardio circulatory insufficiency.
11.	F	62	Corrosive agent (concentrated acetic acid)	Undoubtedly proven	Ingestion; severe metabolic acidosis, corrosion GIT III degree, GIT bleeding, ARI, respiratory and cardiocirculatory insufficiency.
12.	M	84	Clozapine, bromazepam	Undoubtedly proven	ingestion; coma, bilateral bronchopneumonia, respiratory insufficiency.
13	F	45	Clozapine	Undoubtedly proven	Ingestion; coma, aspiration bronchopneumonia, sudden cardiac and respiratory arrest.
14.	F	59	Corrosive agent (hydrochloric acid)	Undoubtedly proven	Ingestion; metabolic acidosis, cardiocirculatory shock, suspected perforation.
15.	M	56	Massive cerebral infarction	Certainly not contributed	Sent because of a suspicion of acute intoxication drugs (clozapine, benzodiazepines); MSCT angiography confirmed massive cerebral infarction.

(extension) Table 18. Brief overview of the case of patient with lethal outcome

S. No	Gender	Age (year)	Causative agent	Connection with the cause (RCF)	Case report
16.	M	55	Methyl alcohol	Contributed	Treated for registered elevated levels of methyl alcohol, without metabolic acidosis and other signs of acute intoxication; sudden cardiac arrest.
17.	F	73	Chlorpyrifos, cypermethrin	Undoubtedly proven	Ingestion; severe poisoning with the development of quadriplegia and numerous complications, prolonged MV.
18.	F	74	Fentanyl, bromazepam	Probably	The patient was treated from malignant disease, it was difficult general condition, respiratory and cardiocirculatory insufficiency.
19.	M	26	Sepsis, septic shock	Certainly not contributed	Received in bad general condition, phlebothrombosis, sepsis, metabolic acidosis, bilateral bronchopneumonia, ARI.
20.	M	88	Bromazepam	Undoubtedly proven	Ingestion; severe poisoning, the development of infectious complications.
21.	F	43	Corrosive agent (concentrated acetic acid)	Undoubtedly proven	Iingestion; hospitalization of less than 24h; metabolic acidosis, GIT bleeding, respiratory and cardiocirculatory insufficiency, ARI.
22.	F	90	Diazepam, bisoprolol	Undoubtedly proven	Ingestion; coma, the development of complications (bilateral bronchopneumonia).
23.	M	39	Heroin	Undoubtedly proven	Coma, bilateral bronchopneumonia, ARI, acidosis severe degree.
24.	F	36	Corrosive agent (concentrated acetic acid)	Undoubtedly proven	Ingestion; metabolic acidosis, circulatory and respiratory insufficiency, ARI, GIT bleeding.
25.	M	77	Bromazepam	Probably	Untreated extended malignant disease, coma, severe poisoning with delayed recovery of consciousness and the development of complications.
26.	F	77	Corrosive agent (hydrochloric acid)	Undoubtedly proven	Iingestion; hospitalization of less than 24h; metabolic acidosis, acute respiratory and circulatory insufficiency, ARI, GIT bleeding, suspected perforation of the stomach.
27.	F	77	Corrosive agent (potassium permanganate)	Contributed	Accidental ingestion; dementia; aspirational bronchopneumonia, atrial fibrillation, acute respiratory insufficiency.
28.	F	40	Medicaments (metoprolol, bromazepam, mianserin)	Undoubtedly proven	Ingestion; difficult poisoning, reanimated to arrival, hospitalization is shorter than 24 hours.
29.	M	60	Methyl alcohol	Undoubtedly proven	Ingestion; coma, metabolic acidosis severe degree, the cardiovascular and respiratory insufficiency.
30.	F	79	Medicaments (diazepam)	Undoubtedly proven	Ingestion; extended untreated malignant disease, coma, respiratory failure.
31.	M	89	Medicaments	Certainly not contributed	Perennial dementia, chronic heart failure.
32.	M	82	Medicaments (diazepam)	Undoubtedly proven	Ingestion; extended malignant disease, coma, bronchopneumonia, respiratory insufficiency.
33.	F	80	Medicaments (tramadol, haloperidol)	Probably	Ingestion; gangrenous changes on both feet, coma, respiratory failure; hospitalization is less than 24 hours.

List of abbreviations and explanations

ARI – acute renal insufficiency

CBRN – chemical, biological, radiological, nuclear

ARF – acute respiratory failure

ACE inhibitors – angiotensin-converting enzyme inhibitors

Ca inhibitors – calcium channel inhibitors

NPCC – National Poison Control Center

DNOC – dinitro-o-cresol („Kreozan“)

Datura stramonium (Latin) – tatula (Serbian language), **jimsonweed** or **Devil's snare,** other common names: hell's bells, devil's trumpet, devil's weed, *tolguacha*, Jamestown weed, stinkweed, one-year plant, containing atropine, hyoscyamine, hyoscine, scopolamine, stramonin etc.

DRT – Department of resuscitation and triage

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

EGDS – oesophagealgastroduodenoscopy

EU – European Union

FDA – U.S. Food and Drug Administration

GC – Gas chromatography

GIT – gastrointestinal tract

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

ICH – International Conference on harmonisation - International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use

ICP-MS – Inductively coupled plasma mass spectrometry

ICP-OES – Inductively Coupled Plasma Optical Emission Spectrometry

ISI – Institute for Scientific Information

CPR – Cardio-pulmonary resuscitation

Lethality – the ratio of deaths to the total number of patients suffering from certain diseases

MAOI – Monoamine oxidase inhibitors

MCT team – Mobile chemical-toxicological team

MD – Ministry of Defense

MIA – Ministry of Internal Affairs

MMA – Military Medical Academy

MSCT – multi-slice computed tomography

NMR – Nuclear magnetic resonance

NSAID – Non-steroidal anti-inflammatory drugs

OECD – Organisation for Economic Co-operation and Development

OFI – organophosphorus insecticides

OPCW – Organisation for the Prohibition of Chemical Weapon

PAS – psychoactive substances

PSS – Poisoning Severity Score – severity of poisoning, 5-point scale:

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

SAF – Serbian Armed Forces

SSRIs – Selective Serotonin Reuptake Inhibitors

WHO – World Health Organization

UV VIS – Ultraviolet-visible spectroscopy

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

VPA – Valproic acid or Valproate

IT support to the NPCC 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 sixth time in a row publishes the Annual Report, was in the number for 2015., 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 an 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 Health Centre „Lučani“, Guča

The dominant cause	n	%
Medicaments	3	23.1
Psychoactive Other	3 0	
Gases	2	15.4
Corossives	2	15.4
Other agents	3	23.1
Unknown	3	23.1
Total	13*	100.0

* Lethal outcome is not registered

Appendix 2. Health Centre „Čačak“, Čačak

The dominant cause	n	%
Alcohol	1	20.0
Gases	2	40.0
Corossives	2	40.0
Total	5*	100.0

* Lethal outcome is not registered

Appendix 3. General Hospital,Čačak

The dominant cause	n	%
Alcohol	84	45.2
Drug of abuse	2	1.1
Medicaments	76	40.9
Gases	7	3.8
Pesticides	5	2.7
Corossives	9	4.8
Other agents	3	1.6
Total	186	100.0

Appendix 4. The Institute for Health Protection of Mother and Child of Serbia „Dr Vukan Čupić“

The dominant cause	n	%
Alcohol	7	3.6
Drug of abuse	4	2.1
Medicaments	86	44.3
Psychoactive Other	33 53	
Gases	2	1.0
Corossives	20	10.3
Pesticides	7	3.6
Mushrooms and plants	3	1.5
Other agents	65	33.6
Total	194*	100.0

* Lethal outcome is not registered

Appendix 5. General Hospital, Ćuprija

The dominant cause	n	%
Alcohol	7	12.7
Drug of abuse	2	3.6
Medicaments	36	65.5
Psychoactive Other	26 10	
Gases	1	1.8
Corossives	5	9.2
Pesticides	2	3.6
Other agents	2	3.6
Total	55*	100.0

* 1 lethal outcome is registered (corossives)

Appendix 6. General Hospital, Leskovac

The dominant cause	n	%
Alcohol	96	31.1
Drug of abuse	3	1.0
Medicaments	157	50.8
Psychoactive Other	150 7	
Gases	5	1.6
Corossives	16	5.2
Pesticides	20	6.5
Mushrooms and plants	5	1.6
Other agents	4	1.3
Unknown	3	1.0
Total	309*	100.0

*6 lethal outcome is registered (pesticides - 2; corossives - 4).

Appendix 7. General Hospital, Pančevo

The dominant cause	n	%
Alcohol	50	30.9
Drug of abuse	13	8.0
Medicaments	74	45.7
Gases	4	2.5
Pesticides	5	3.1
Other agents	6	3.7
Unknown	10	6.2
Total	162*	100.0

* Lethal outcome is not registered

Appendix 8. General Hospital, Vršac

The dominant cause	n	%
Alcohol	9	25.7
Medicaments	20	57.1
Psychoactive Other	17 3	
Pesticides	1	2.9
Corossives	1	2.9
Other agents	3	8.6
Unknown	1	2.9
Total	35*	100.0

* Lethal outcome is not registered

Appendix 9. Toxicology ambulance of the Emergency Center, Clinical Center of Vojvodina

The dominant cause	n	%
Alcohol	722	61.0*
Drug of abuse	72	6.2
Medicaments	339	28.6
Psychoactive Other	293 46	
Gases	6	0.5
Corossives	12	1.0
Pesticides	5	0.4
Mushrooms and plants	1	0.1
Other agents	16	1.3
Unknown	11	0.9
Total	1184	100.0

***** High percentage of people, in whom, as the dominant agent of poisoning, ethyl alcohol was registered (medical history, laboratory confirmed), is the result of the fact that these peopleare in a high percentage in addition to ethyl alcohol, used medicamnets (above all those with influence of psychoactive) and various substances of abuse.