



The history of poisoning: from ancient times until modern ERA

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Abstract

The history of poisoning is one of the greatest chapters of the human history, where curiosity and genius, scientific discoveries and empirical knowledge intertwine with intrigues, crimes, politics, personal tragedies of notabilities, wars and natural disasters. Knowledge of toxic substances is likely as old as the mankind. In the Middle Age, Paracelsus claimed that in the world there is no non-toxic substance that the therapeutic and toxic properties of substances are indistinguishable up to a single parameter—dose. This postulate still belongs among the basic pillars of modern toxicology. Probably, the most ancient way of killing people was poisoning. In addition, the presence of poison in the body of the victim was very difficult to determine, since the symptoms of poisoning were similar to signs of certain diseases. Therefore, the criminals had a big chance to escape the punishment. Nowadays, together with development of toxicology the chance of disclosure of such crimes has increased, however, the progress in the field of design and production of toxic substances has also gone up. Within current contribution we have reviewed the most famous historical cases of poisoning from the antiquity to the present.

Keywords History · Poisoning · Toxicology · Poison

Introduction

What was the secret weapon of weak women, the most powerful men, eternal enemies and close friends? What was the most effective way in conflict solving? The answer is simple—the poison. It would not sound exaggeratedly that the knowledge of toxic agents as well as their utilization is likely as old as the mankind. The history of poisoning is confused and endless. There is probably no scientific area, in which so many outstanding discoveries, sometimes criminal and inhuman, has been made just because of a huge pressure exerted from the side of the most powerful persons of that time.

Prehistory

The utilization of the toxic effect of the simplest poisons on animals and later on man was invented in the prehistoric

era. Cave dwellers noticed that the animals eating particular plants fell dead. Thus, prehistorian people made special grooves on the tips of arrows and darts and soaked them in juice of toxic plants. The most popular poison was curare isolated from the plant *Strychnos toxifera* (*Loganiaceae*). This alkaloid immediately blocked the respiration without poisoning the meat of killed animal. According to the archaeological research, the age of such tools is about six thousand years. Bisset (1992) Gradually, people came to an idea that they can use poisons not only for hunting, but also for killing the enemies. There are several reports that the hunters from the Maasai tribe, who inhabited Kenya several thousand years ago, soaked arrows in extract from *Strophanthus* (*Apocynaceae*) to kill their enemies in war conflicts. (Neuwinger 1996).

Ancient times

One of the oldest literary sources focused on toxicology was the Ebers Papyrus (1550 BC) (Fig. 1). Apparently, this papyrus was only a copy of much older manuscript. Egyptologists suppose that the author of the original one was the legendary Egyptian physician Imhotep at the beginning of the 3rd millennium BC. The oldest pharmacopoeia of ancient Egyptians was discovered in 1872 and included more than 900 medical

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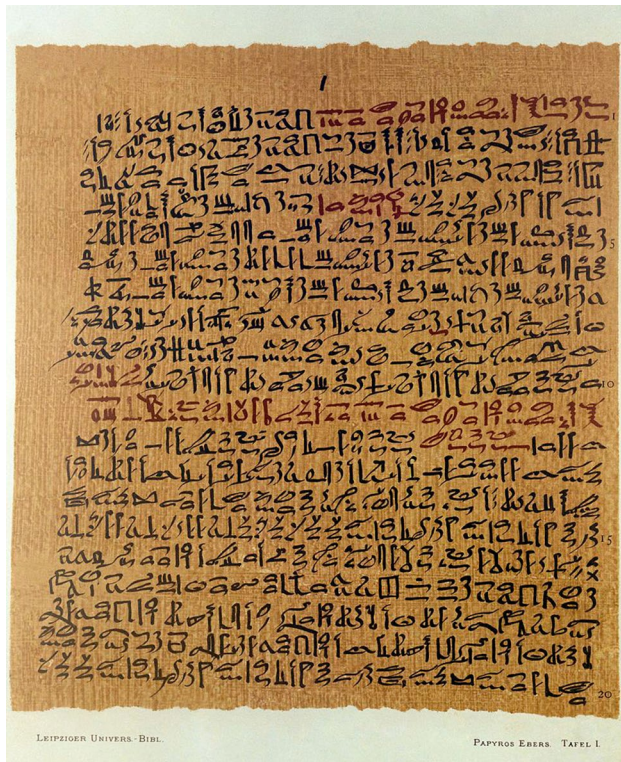


Fig. 1 Ebers papyrus

prescriptions. In this 20.5 m long scroll we could find passages about opium, arsenic trioxide, aconitine, cyanogenic glycosides or an alkaloid isolated from the Calabar beans—physostigmine (Frey 1985). In ancient Africa, Calabar beans (*Physostigma venenosum*, *Fabaceae*) were frequently used as an ordeal poison. Persons accused of the witchcraft had to drink white milky extract of the bean made by crushing of the bean in a mortar and soaking the remains in water. If the accused died, it was considered as a proof of a guilt. If the accused survived, usually due to vomiting up the poison, he/she was acquitted and released (Scheindlin 2010).

Probably the most famous poisoning of the Hellenistic period was the execution of the Greek philosopher Socrates (470–399 BC) (Fig. 2) who was condemned to drink the extract from hemlock (*Conium maculatum*, *Apiaceae*) (Fig. 3). His death is depicted in detail in Plato's tract *Phaedo* (Hotti and Rischer 2017). The description of poisoning corresponds exactly to the present knowledge of coniine, the main component of hemlock.

The striking progress of the sciences in ancient Greece in the seventh and sixth centuries BC mostly reflected in medicine. Hippocrates (460–377 BC) (Fig. 4), often referred to as the “Father of Medicine”, deprecated to use poisons as murder weapons. Therefore, in *Corpus Hippocraticum*, collection of around sixty medical works strongly associated with Hippocrates, we could find almost no information on



Fig. 2 Socrates execution

this issue. The proof of this statement we can also find in the Hippocratic Oath taken by his disciples. A part of this medical oath was a ban on speaking about the poisons: “Neither will I administer a poison to anybody when asked to do so, nor will I suggest such a course” (Emery 2013).

The death of 32-year-old Alexander the Great (356–323 BC) (Fig. 5) is surrounded by secrets and speculations. As it was ordinary at that time, one of the possible



Fig. 3 *Conium maculatum* (*Apiaceae*)

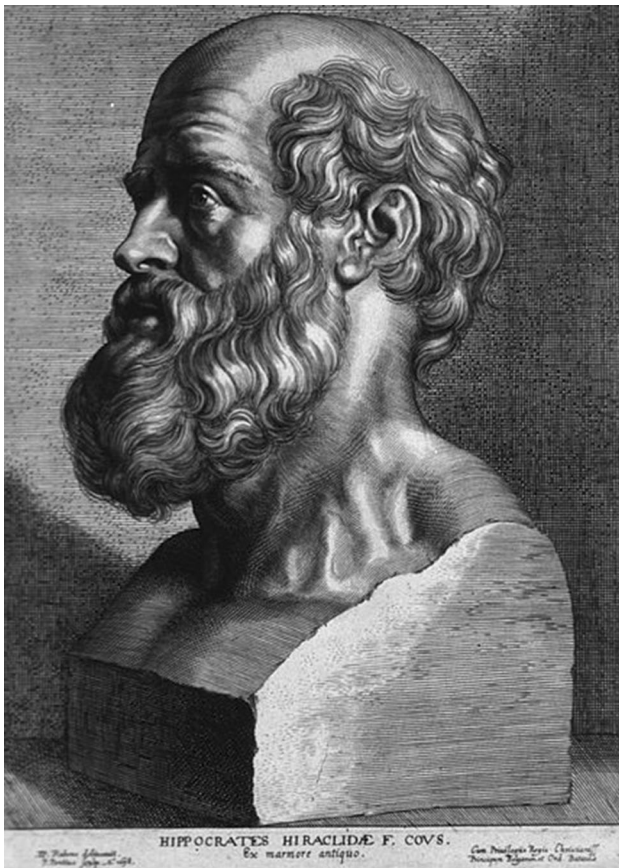


Fig. 4 Father of Medicine Hippocrates



Fig. 5 Alexander the Great

explanations was poisoning. The main suspect in this version was Alexander's wife—Roxana. Allegedly, she used a less known poison, strychnine, to kill her husband. According to the historians of that time, one of the probable reasons of the murder was her jealousy on other women or on Alexander's lover—Hephaestion, who, as historians unanimously claim, he loved more than all his wives.(O'Brien 2003) In Phillip's book "Alexander the Great: Murder in Babylon"

it is written that the intoxication was primarily expressed by excitation and trembling.(Phillips 2012) Then, severe stomach ache, strong convulsions and thirst followed. At night, according to the same source, the King suffered from hallucinations. All aforementioned symptoms resemble the strychnine poisoning. The apparent advantage of this alkaloid was that in the antiquity only a little was known about it, since the plant *Strychnos nux-vomica* (*Loganiaceae*) (Fig. 6) grew exclusively in India. Accidentally, 2 years prior Alexander's death, he and his wife had visited India. According to available sources, it is known that Roxana was very interested in folk customs and traditions. Supposedly, during their journey to the East she had visited a place where local people were consuming low doses of strychnine to induce hallucinations, which they considered as a discourse of the Gods (Phillips 2012).

The study of poisons and searching for effective antidotes was very popular in ancient Greece, since many toxic compounds of various origin were widely used as a mean of removing the enemies. In the second century BC the knowledge about the poisons and antidotes was significantly enriched due to investigations made by the Greek doctor and poet Nikander of Kolophon. Of seventeen prose and poetic works written by Nikander, only two of them survived—*Theriaca* (tract about animal poisons) and *Alexipharmaca*



Fig. 6 *Strychnos nux-vomica* (*Loganiaceae*)

(tract about poisons and antidotes). He did not rely just only on the writings of the philosophers and doctors of that time, such as Hippocrates and Apollodorus, but also on his own observations. It is assumed that Nikander studied the effect of various poisons on prisoners sentenced to death. Based on the data observed, he first classified toxic compounds into specific groups. As universal antidote he recommended linseed tea to evoke vomiting or sucking the animal toxin from the wound by mouth.(Claus 2013).

In ancient times, many legends and myths have grown out of the skills of poisoners and the occupational hazards of political life. One such legend tells about the King Mithridates VI of Pontus (132–63 BC) (Fig. 7). Mithridates was indeed scared of the poisons and poisonings, therefore, he devoted a significant part of his life to searching for a universal antidote. The result of his efforts was a preparation containing more than 36 components. In Roman Pharmacopoeia this preparation even got a special designation “*mithridaticum*”. Apparently, the King believed in his invention so much so he decided to take it every day gaining thus a considerable resistance to various poisons. However, in several cases an advantage can easily become a fatal disadvantage. At an advanced age, Mithridates decided voluntarily to end his life by drinking a cup of non-specified poison. Despite



Fig. 7 Mithridates VI of Pontus

relatively high dose, the King remained alive. Therefore, he commanded a soldier to kill him by the sword, what he eventually did. Based on this legend, the term “*mithridatism*” has been adopted into modern toxicology indicating an increased resistance of an individual to poisons.(Griffin 1995; Valle et al. 2009, 2012).

In ancient Rome, poisons and overall poisonings were very popular. Here, to poison or to be poisoned was considered as a common matter. Even committing the suicide via poison was legalized. If there was a compelling reason, the state power supplied its citizens with aconitine isolated from *Aconitum* (*Ranunculaceae*) or with the hemlock decoction. Several cases are known when a convicted consumed the poison voluntary immediately after the judgement. In Roman Empire getting rid of rivals by the cup of the poison was quite common. Even a special profession was formed—degustator. His duties included tasting of food and drinks before they were handed over the owners. Because of the huge demand on this profession, a special collegium of degustators had been established. In addition, the custom of clinking appeared exactly in ancient Rome. When a cup tapped on another cup, wine spilled from one cup into another (Cilliers and Retief 2014). What was a better guarantee that the enemy would be poisoned as well?

The Emperor Tiberius Claudius Caesar Augustus Germanicus (10 BC—54 AD), also known as Claudius, was married five times. The last wife of 57-year-old Claudius became his niece Agrippina the Younger (15 AD—59 AD) (Fig. 8). Most of all, she desired for getting rid of Claudius son Britannicus and adopting by Claudius her own son Nero from the first husband (Aveline 2004). In October 54, after the dinner Claudius felt bad. In 12 h he died. In imperial Rome mushrooms were very popular. Poor Romans ate the common species, whereas the wealthy citizens of Rome preferred special, bright orange Caesar’s mushrooms (*Amanita caesarea*, *Amanitaceae*). Probably, Agrippina got into the dish with mushrooms the poisonous fly agaric (*Amanita muscaria*, *Amanitaceae*). The symptoms such as blurred vision, bronchoconstriction, profuse salivation, terrible stomach aches and low blood pressure pointed out to the intoxication by the alkaloid muscarine. Nowadays, intoxication with muscarine is successfully treated by atropine, however, 2000 years ago no one knew about this providential antidote (Wasson 1972). The Emperor’s doctor, Aesculapius, decided to induce vomiting in Claudius. Agrippina foresaw this turn of events and prepared in advance the poisoned feather. In poisonous feather preparation, she was probably helped by the famous ancient poisoner—Locusta. So, when the doctor put the feather into the patient’s throat, the murder was completed (Marmion and Wiedemann 2002). After Claudius’ death the Senate canonized him. Nero knowing the whole truth about his stepfather’s death subsequently stated: “The mushrooms are undoubtedly the food of Gods,



Fig. 8 Empress Agrippina and her son Nero

since after eating them Claudius became divine!” (Wasson 1972).

Soon after Claudius’ death, Nero (37–68 AD) (Fig. 8) became the Emperor of Rome. Similarly to his mother Agrippina, Nero quite often used the services of professional poisoners. The next victim had to be Nero’s stepbrother—Britannicus who constituted a constant threat to the new Emperor (Shotter 2014). The first attempt to kill Britannicus failed. Apparently, Locusta unwilling to take a risk on her shoulders prepared weak or slowly acting poison. After this failure, Nero started to hit the poisoner shouting that she had given Britannicus a medicine, not a poison. Locusta tried to persuade him that she had prepared weaker poison intentionally to cover up the tracks since gradual deterioration of poisoned person’s health state more resembles the disease. Subsequently, Nero issued an order to prepare more potent poison directly in his presence. Locusta obeyed. Prepared poisonous mixture was given to a goat which died in 5 h. Finally, the poison was added to water that was used to dilute the wine. Usually, the degustators did not taste it. Soon after the consumption of poisoned wine Britannicus died (Smith 1954). Successful removal of all competitors made 17-year-old Nero the only possible Emperor of Rome. Thus, he decided to give Locusta an extraordinary right—to

educate her own students. However, a few years later, the acquisition of the imperial throne did not bring to Nero the desired happiness. He also consumed, albeit voluntarily, the poison from the hands of his servant. Actually, he was afraid of being brought to Senate and of accepting the death sentence (Shotter 2014).

Middle age

Also in the Middle Age poisons and poisoning belonged among the important means of achieving political and personal goals. In Europe, poisons were already freely sold in pharmacies. The first attempt to stop free trade with poisons was made in Italy. In 1365 in Siena, apothecaries were forbidden to sell arsenic and mercury to unknown people. In France, a ban on toxic substances was issued in 1662. In Russia, only in 1773 it became forbidden to sell sulphuric acid, amber oil, strong spirits or arsenic (Macinnis 2005). At medieval times, the way of poison administration progressed from trite addition into meal or beverages to more sophisticated ways, such gloves smeared with arsenic paste, poisoned shirts and wigs, poisoned corners of book pages, poisoning of altar paintings, wafer or meek wine. Therefore, also during this historical period, the question of searching for novel poisons and corresponding antidotes remained relevant.

The first real toxicologist is considered to be a Renaissance physician and alchemist of Swiss origin Philippus Aureolus Theophrastus Bombastus von Hohenheim, known as Paracelsus (1492–1541) (Fig. 9). The pseudonym Paracelsus he chose himself and it means “more than Celsus”. Aulus Cornelius Celsus was a Roman naturalist living more than one and a half thousand years before Paracelsus (Grell 1998). Paracelsus’ revolutionary contribution consisted not only in his efforts to interconnect chemistry and medicine, but also in his approach to the studied disciplines. The nicknamed “Luther in medicine” refused to quote ancient texts and preferred to observe the nature and a man by himself. With regard to toxicology, Paracelsus first drew a conclusion that the basis of toxic substances is their chemical action on the organism. He also found out that the therapeutic and toxic properties of substances are indistinguishable up to a single parameter—dose. Thus, according to Paracelsus all compounds are poisons. The aforementioned postulates still belong among the basic pillars of modern toxicology (Borzelleca 2000).

In the Middle Age, Italy and later France were considered the most powerful countries with regard to poisonings. The Queen of France, Catherine de’ Medici (1519–1589) (Fig. 10), nicknamed Queen-Poisoner, perfectly managed the Italian technique of poisoning using it to achieve the desired political goals (Kruse 2003) According to the historical novel of Alexandre Dumas “Queen Margot”, Catherine was



Fig. 9 Paracelsus

involved in the death of her political rival Jeanne d'Albret, the mother of the future King of France, Henry IV (Dumas 2016). Catherine de' Medici gave her an insidious present—poisoned gloves. Within the same novel, Dumas describes the fatal mistake of the old Queen who decided to remove Henry himself after the death of his mother. She issued an order to palm on him a poisoned book about the art of hunting. Unfortunately, this book got into the hands of her own son—King Charles IX who died in terrible agony. Queen Catherine was also known to carry out various experiments on poor and sick people to whom she had given different toxic mixtures. During the experiments, Catherine de' Medici carefully recorded the velocity of the toxic response (onset of the toxic effect), the efficacy of the toxic mixture, the strength of the toxic effect in various parts of the body (organ specificity, site of action) and clinical manifestation of intoxication. Thus, despite the not-so-good reputation of the Queen-Poisoner, she could be considered the first experimental toxicologist in the history (Whyte 2001).

At the same time, Russia kept pace with the rest of Europe. Within the periodic chronicles describing the reign of Ivan IV the Terrible (1530–1584) (Fig. 11) we can find the information about the violent death of the Tsar. Allegedly, Boris Godunov and his companions prematurely



Fig. 10 Queen the Poisoner Catherine de' Medici



Fig. 11 Russian Tsar Ivan IV the Terrible

terminated the life of Russian monarch by bribing the doctor who added the poison in the medicine of the Tsar. However, opening of the tomb and subsequent spectral analysis of the

remains of Ivan the Terrible did not confirm this version. Arsenic and mercury concentrations found in his remains met the standards of that time (Prozorovskii and Kolosova 1970; Payne and Romanoff 2002). In contrast with the Tsar's death, passing of his mother and his second wife looked more like an intentional poisoning. According to the protocol of that time, noble women attending the state events had to whiten their faces with whitening cosmetics. Such make-up contained white pigments based on mercury, arsenic, and lead. Investigation of hair of Tsar's mother revealed high concentration of mercury exceeding the concentration of mercury present in people of that time 1000-times. The same situation was observed in the case of Ivan's 26-year-old wife. Even if these women had been using the whitening cosmetics several times a day, so huge amount of mercury would not accumulate in their hair (Prozorovskii and Kolosova 1970).

The Golden Age of King Louis XIV of France was not associated just with the development of the country, but also with the heyday of occultism, divination and black magic. Poisons came into fashion as a mean of solving conflicts between wealthy and aristocratic families. One of the most popular poison supplier of that time in France was Catherine Monvoisin (1640–1680) (Fig. 12). Among the most desirable products of this poisoner was “*poudre de succession*” (=hereditary powder) (Parascandola 2012). Allegedly, Catherine produced several types of this powder—from those that killed the victim in a few seconds, to poisons that killed



Fig. 12 Catherine Monvoisin

unwanted people very slowly. A frequent client of Madame Monvoisin was also the hot favourite of the Sun King—Marquis de Montespan. According to the historical sources of that time, besides poisons that helped her to remove the competitors she was also ordering the so-called exciting powder for the King (Somerset 2004). However, neither exciting mixtures nor lethal poisons guaranteed her to remain the number one of the King until the end of her life.

At the end of the seventeenth century, firstly in Palermo then in Naples operated the well-known poisoner Teophania, nicknamed Tophana. Reportedly, this Italian was responsible for the death of more than 600 people. Tophana invented an original product called “*Aqua Tophana*” sold in small bottles as “*Manna of St. Nicholas of Bari*”. *Aqua Tophana* had water-like, odourless and colourless consistence. Allegedly, 5–6 drops of this magical water was enough to kill a man. The onset of the toxic effect was gradual—painless, without any sign of fever or inflammation. The death occurred due to the weakness, loss of appetite and incessant thirst. Among the most often takers of *Aqua Tophana* belonged women who desired to get rid of their husbands. Till nowadays, the exact content of *Aqua Tophana* is unknown. According to one source, it was made of arsenic acid with an addition of *Herba cymbalariae* (*Scrophulariaceae*). The other sources claim, that the main component of *Aqua Tophana* was lead acetate solution. Seniora Tophana was eventually sentenced to death and in 1709 burned down (Wexler 2017).

Passing of 35-year-old Austrian composer Wolfgang Amadeus Mozart (1756–1791) (Fig. 13) evoked a number of theories including poisoning. According to the legend, before his death Mozart informed his wife Constanze that he had been poisoned, however, he had not named the killer. Supposedly, lying on the deathbed he uttered that he is composing Requiem for himself (Hirschmann 2001). Based on several versions, the poison used to kill Mozart was *Aqua Tophana*. Nevertheless, currently more acclaimed version inclines to mercury that killed the composer. Several historians claim that in the process of treating himself against syphilis, Mozart wrongly calculated the dose of mercury and died. (Scheidt 1967) In spite of unclear cause of the death, there was a huge number of suspects. The main candidate for the role of murderer was considered the Italian composer Antonio Salieri who envied to more talented colleague (Borowitz 2005). Among all passing versions explaining the demise of the great composer, there was a curious one. This version stated that Mozart was killed by parasitic worms of *Trichinella* family. The source of these parasites were poorly roasted pork cutlets (Dupouy-Camet 2002). Interestingly, the symptoms observed in Mozart completely coincided with the signs of trichinosis.

The death of Napoleon Bonaparte (1769–1821) (Fig. 14) gave birth to various legends and speculations. The health of the ex-Emperor, who was sent to exile on the island of St.



Fig. 13 Austrian composer Wolfgang Amadeus Mozart

Helena, rapidly deteriorated in autumn 1820. He complained of severe stomach aches, weakness and frequent attacks of nausea. A year prior to his death, two Napoleon's servants died under mysterious circumstances. The ex-Emperor was convinced that they were poisoned and that he would be the next victim of the murderers. He died on May 5, 1821. According to official conclusions, the cause of his death was stomach cancer. Reportedly, his father suffered from the same disease as he did (Corso et al. 2000). However, according to conspirologists, the symptoms of Napoleon's death resemble the arsenic poisoning. This assumption has been recently confirmed by the detailed analysis of Napoleon's hair showing almost 40-fold increase in arsenic concentration comparing to normal people of that time (Lin et al. 2004). Several theories have been formed, how the French Emperor could get intoxicated (Hindmarsh and Corso 1998). (1) At those times, addition of green pigment into the wallpaper was quite common. Such green pigment was called Paris Green. From the chemical point of view, Paris Green is copper(II) acetoarsenite. In the humid weather of the island of St. Helena fungi or various microorganisms could convert inorganic arsenic in Paris Green to the organic



Fig. 14 French Emperor Napoleon Bonaparte

forms which subsequently intoxicated Napoleon Bonaparte. (2) The Emperor of France could get a toxic dose of arsenic by life-long holding of the cartridges. The ammunition of that time contained huge amounts of different metals. (3) Another reason why did the hair of Napoleon contained an increased amount of arsenic, could be his wine addiction. The winemakers in the eighteenth and nineteenth centuries dried the wine barrels with a substance based on arsenic. (4) The last theory claims that Napoleon could be poisoned by a mixture of heavy metals. The low doses of arsenic were added him in food and drinks causing severe pain in his stomach. To restrain vomiting, the doctors were giving him potassium tartrate of antimony. Beside aforementioned drug, the physicians prescribed him calomel and orgeat to combat constipation and thirst. The two latter symptoms represent the crucial signs of arsenic intoxication. Calomel is a trivial name for mercury dichloride (Hg_2Cl_2), whereas orgeat was a drink containing bitter almond oil. In acidic environment of

the stomach, such oil hydrolyses to hydrocyanic acid. When calomel and orgeat were mixed in the stomach, mercury cyanide was formed. So, either arsenic, hydrocyanic acid, antimony, mercury cyanide or a mixture of all of them could be the one of the causes on Napoleon's death (Obodovskiy 2015).

Modern era

Together with the progress in chemical sciences at the turn of the eighteenth and nineteenth centuries, the principles of the biological action of various chemical compounds have been revealed. In addition, coming up of the Industrial Revolution in the middle of the nineteenth century allowed the synthesis of natural toxins in unlimited quantity. Moreover, novel entities derived from the natural compounds were prepared. Due to all mentioned events, the poisons were gradually losing the mystery associated with them. In the twentieth century there was an enormous increase in the number of synthetic compounds that led to development of modern toxicology as a science. Particularly after the World War II, in parallel with the development of pharmaceuticals, pesticides, polymers and other industrial chemicals, various chemical and biological weapons have been intentionally developed to remove inconvenient people in a more sophisticated way.

Probably one of the most famous persons in Russia of the tsarist times, Grigori Rasputin (1869–1916) (Fig. 15) still attracts many people all over the world. According to historians, he possessed unique magical power, brisk mind and was a devoted servant of the God. All above-mentioned facts are controversial. However, there was something mysterious about this man. One of the most significant mysteries associated with Grigori Rasputin was his inhuman strength and vitality. To kill him the conspirators used potassium cyanide added into the cakes and wine. However, even after the consumption of such tremendous dose of the poison he stayed alive (Fuhrmann 2012). There are four versions explaining the cause of Rasputin's resistance towards one of the most potent poisons of that time. (1) KCN was added into the small cakes and wine. The poisoners probably hadn't taken into account the fact that glucose present in cake and wine neutralizes potassium cyanide by forming a non-toxic substance—cyanohydrin. (2) Rasputin loved garlic. It is generally known that garlic facilitates elimination of the salts of heavy metals from the body. (3) The Russian mystic was very good in hypnosis and self-control. By managing his body, he could slow down the metabolic processes reducing so the need for the oxygen. Thus, the poison acted slowly and the first signs of poisoning appeared just two hours later. (4) The conspirators were given the crystals of citric acid instead of potassium cyanide. This interesting fact was

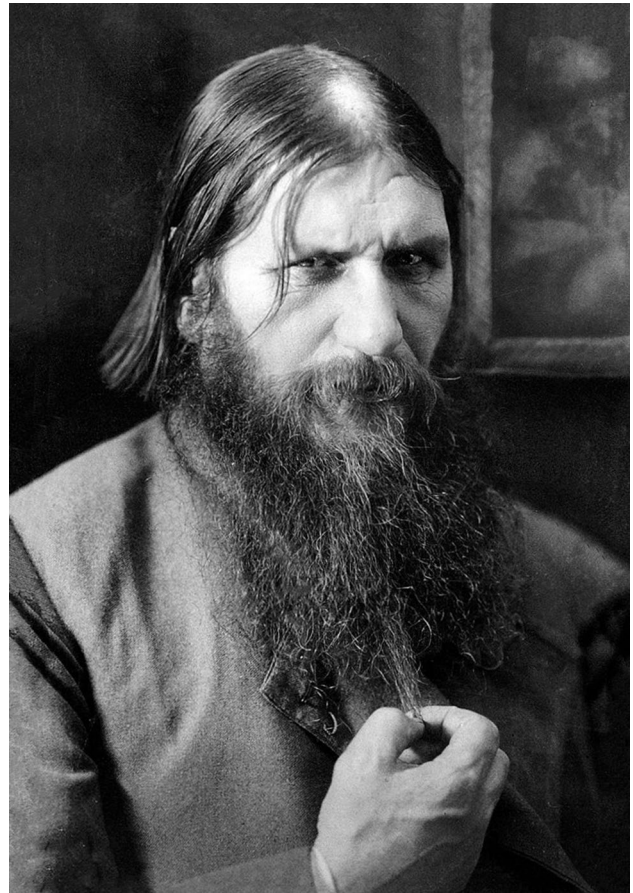


Fig. 15 Grigori Rasputin

revealed by the doctor Lazovert on his deathbed (Harkup 2017).

In the thirties of the twentieth century at the central office of NKVD of the USSR a secret laboratory designated "X" was established. It was patronized by Yagoda and Beria. The main aim of such laboratory were poisons. The toxicologists working there were focused on searching for novel toxic agents whose presence would not be determined from the blood tests nor from the autopsy. The inventions of this laboratory had been tested on prisoners of Lubyanka Internal Prison. Among the most desirable symptoms caused by newly developed substances belonged: heart muscle paralysis, cerebral haemorrhage or blood vessel blockade. According to available sources, one of the victims of this secret laboratory was the Soviet writer Maxim Gorky (1868–1936) (Birstein 2009; Vaksberg 2011).

The lethal dose of potassium cyanide is 6.4 mg/kg. It acts immediately causing tissue hypoxia and affecting the central nervous system. Generally speaking, KCN gets rid the body of oxygen at the cellular level. The members of top Nazi Party of Germany possessed the glass ampoules containing potassium cyanide in the case of defeat. After losing the war,

many of them committed suicide. Among them were: Adolf Hitler and Eva Braun, the leader of the Nazi Schutzstaffel (SS) Heinrich Himmler, Goebbels family including their six children and the leader of the Nazi Luftwaffe Hermann Göring (Goeschel 2009).

The most famous poisoning of the twentieth century is considered the assassination of Bulgarian dissident Georgi Markov (1929–1978) (Fig. 16, Holdsworth 2013), who emigrated in 1969 into London. On September 7, 1978, after the evening broadcast on BBC waiting for a bus at the stop on the Waterloo bridge, Markov suddenly felt a sharp pain in his right hip. He looked around and saw a man hurriedly picking up an umbrella from the ground. The stranger speaking with a strong accent apologized him for the situation, caught the taxi and left. At the evening, Markov started to feel bad. He suffered from fever, acute pain in the stomach and severe diarrhoea. The patient's state rapidly deteriorated. The doctors were powerless. Three days later Georgi Markov died in the hospital. The autopsy of Markov's leg revealed a small iridium–platinum capsule with the traces of ricin (Crompton and Gall 1980). Ricin is a plant toxin obtainable from the Castor beans (*Ricinus communis*, *Euphorbiaceae*). The expertise disclosed approximately 450 mg of ricin. Such amount is sufficient to kill at least 6 adult persons. Apparently, he was shot by a stranger from the tip of the umbrella at the bus stop. No one doubted that Markov was removed by the Bulgarian special services because of his active criticism of the communist regime of Todor Zhivkov (Papaloucas et al. 2008). Nowadays, the visitors could see the killing umbrella (Fig. 17) in the Museum of International Espionage in Washington. Such device was endowed by a hidden sting shooting small capsules filled with toxic ricin.

Sarin attack in Tokyo subway (1995) was not the first case of nerve agent misuse by the terrorist organization. Prior to it, in 1994, the same sect Aum Shinrikyo used sarin in Matsumoto, Japan to remove three regional court judges who were overseeing the proprietary lawsuit related to the real-estate purchased by the sect in 1991. Within this litigation,

the sect had only a poor chance to succeed. Thus, the leader and the guru of the sect Shoko Asahara decided to poison the judges. On June 27, 1994 in the afternoon a pick-up transporting sarin, prepared 10 days before, left the starting point at a specified time. However, due to the traffic jam the terrorists arrived to the courthouse too late. The members of the sect were prepared for any situation, so they knew the exact address where the judges resided. They wended there. The terrorists parked their pick-up on a small car park close to the judge residence. Thereafter, Hideo Murai launched the sarin evaporating device becoming thus the first man in the world who used sarin for the terrorist purpose. However, due to unfavourable weather conditions, in particular wind direction, the vapours of sarin reached the houses of people living around. Consequently, seven people died and hundreds were injured (Yanagisawa et al. 1995; Tu 1999; Vale 2005).

The other case of poisoning committed by the same sect was realized in Osaka, Japan in December, 1994. Within this episode, VX agent was used instead of sarin. An inconvenient lawyer was applied the nerve agent on the backside of his neck. Such percutaneous intoxication ended fatally in about 2 weeks. The autopsy of the victim disclosed metabolites indicating the use of VX agent (Tsuchihashi et al. 1998).

Ukrainian politician Viktor Yushchenko (*1954) (Fig. 18) was poisoned by a high dose of 2,3,7,8-tetrachlorodibenzodioxin (TCDD) in December, 2004 during his presidential campaign. According to the detailed analysis, Yushchenko's body contained the second largest concentration of TCDD ever detected in humans (Sorg et al. 2009). The intoxication manifested mainly by the chloracne that significantly deformed the skin of his face (Saurat et al.



Fig. 17 Schema of the umbrella that killed Georgi Markov



Fig. 16 Assassinated Bulgarian dissident Georgi Markov (Photo Reuters)



Fig. 18 Ukrainian president Viktor Yushchenko

2012). Interestingly, the same substance influenced the lives of many Vietnamese people during the War in Vietnam (1955–1975). Within this war the US army used a defoliating substance, so-called Agent Orange. By itself, Agent Orange is relatively non-toxic. However, later it has been revealed that Agent Orange contained traces of TCDD formed in the process of defoliating substance synthesis (Schechter et al. 1995). Such manufacturing error affected the lives of more than 40,000 people in Vietnam (Gough 2013).

The most famous victim of the poisoning of the recent years, the ex-lieutenant colonel of the Russian Federal Service (FSB) Alexander Litvinenko (1962–2006) (Fig. 19, Gander 2016), was killed with polonium. Within several weeks after the incident, in November, 2006, the doctors were persuaded that Litvinenko was poisoned with thallium. However, only 3 h prior his death, the traces of polonium 210 were detected in the urine sample of the victim. Litvinenko died because of acute heart failure (McFee and Leikin 2009). Radioactive polonium 210 in small doses causes the formation of malignant tumours, in high doses it destroys the bone marrow, gastrointestinal tract and other vital organs (Harrison et al. 2007). Allegedly, polonium could get into Litvinenko's organism with tea. A number of suspects were investigated for their involvement in this case. However, there is also a curious version that poisoning of ex-lieutenant colonel was caused by careless handling of polonium. Reportedly, the Russian ex-spy acted as a sales mediator on the trade with radioactive substances (Goldfarb 2010).

Yasser Arafat (1929–2004) (Fig. 20) died in 2004 at the age of 75 in Parisian hospital Percy. French doctor who had been treating him for several weeks could not determine the exact reason of the rapid deterioration of his health state and subsequent death. The version of possible poisoning of Arafat with radioactive substance arose after passing of



Fig. 19 Russian ex-spy Alexander Litvinenko (Photo Getty Images)



Fig. 20 Palestinian leader Yasser Arafat

the former FSB agent Alexander Litvinenko. The results of forensic examination conducted by Swiss experts from the Institute of Radiophysics and the University Centre for Forensic Expertise in Lausanne confirmed that the death of Palestinian leader Yasser Arafat resulted from the radiological poisoning (Froidevaux et al. 2016). Previously, the media reported that he could have been poisoned with polonium. The inter-Arab television channel, Al-Jazeera, informed that the content of radioactive polonium in the remains of Arafat exceeded the norm by 18-times (Zemskova et al. 2015; Froidevaux et al. 2016). In the case of Litvinenko, the suspicious fell on Russian special services, whereas in case of Arafat on Israeli one. Both, Moscow and Jerusalem, strictly denied any connection with the death of the former FSB officer and the leader of Palestine, respectively.

Kim Jong-Nam (1971–2017) (Fig. 21, Fielding 2017), a half-brother of the North Korean leader Kim Jong-Un, was killed by 2 women on February 14, 2017 at the Kuala Lumpur airport, Malaysia. According to the autopsy of the victim, he was poisoned by an extremely toxic nerve agent—VX. South Korean military experts allege, that sarin and VX agent belong among the main goals of the North Korean chemical weapon program. However, Pyongyang denies this fact (Paddock and Sang-Hun 2017). VX agent numbers among the most toxic artificially synthesized substances and can occur in the form of binary chemical weapon. Such technology involves two or more non-toxic chemical precursors of the lethal weapon physically separated from each other. Firing the munition removes the barrier between the precursors that react with each other to form the intended agent (Wiener and Hoffman 2004). It is highly likely that each woman was bearing a particular precursor of the binary weapon. By touching the victim's face, these two components reacted in situ on skin of Kim Jong-Nam leading to



Fig. 21 Kim Jong-Nam (Photo AP Photo JoongAng Sunday via JoongAng Ilbo, Shin In-seop)

formation of VX agent. According to a video record, the two mentioned women immediately after the attack ran to the public toilet probably to remove the traces of the chemicals from their bodies.

On March 4, 2018, a nerve agent Novichok was allegedly used in an attempt to assassinate the former GRU (Main Intelligence Directorate) officer Sergey Skripal (*1951) and his 33-year-old daughter Yuliya. They were found unconscious on a bench near a shopping centre in Salisbury, UK. Thereafter, being in a coma, they were urgently transported into the local hospital with a suspicion of being poisoned by a nerve agent. On March 12, 2018, British Prime Minister Theresa May stated in the parliament: “Either this was a direct action by the Russian state against our country, or the Russian government lost control over the potentially catastrophically destructive substance and allowed it to fall into hands of others” (BBC News 2018). The Russian Federation refused this blame. The nerve agents Novichoks were developed in 1970’ by the USSR as a reaction to English/American invention of VX agent. The mode of action of above-mentioned substances is similar to other members of nerve agent family—irreversible inhibition of enzyme acetylcholinesterase (Halamek et al. 2011). The Western world learned about the existence of the Novichoks just in 1992 from one of the defectors who emigrated to the USA. The scientist claimed that these substances exert higher or at least similar toxicity as VX agent (Mirzayanov 2008). A significant danger associated with mentioned compounds consists in a nescience of their exact structure, since such molecules as well as their toxicity profiles have not been published yet. So everything that we have in our hands today are just claims of the defectors. However, if the alleged substances are real, the inventors of such nerve agents brilliantly circumvented the Chemical Weapon Convention (CWC), since none of the

representatives of the Novichok family nor their precursors are under control of this document (<http://www.opcw.org> 2018). In conclusion to Salisbury incident, since this case is still under investigation it is too soon to indicate the real offender to avoid criticism and controversies.

Conclusion

Current review indicates that cases of deliberate removal of unwanted persons by means of poison have been known since the ancient history. In the antiquity, the main way to poison an enemy was by adding plant or animal toxins into food and drinks. In the Middle Ages, the progress within this area moved forward. Inorganic toxic compounds prevailed. Moreover, such substances were applied more sophisticatedly, i.e., by poisoning of the gloves, page corners, wigs, etc. However, there was something similar within both mentioned historical periods—the fact that poisons was strongly associated with mystery, black magic and occultism. Additionally, there was one more intermingling feature—usage of poisons for unfair purposes had not been usually proven. Thus, criminals had a big chance to escape the punishment. The rise of toxicology as an independent scientific discipline was a key breakthrough in this field. Since that time, people were able to determine specific organic and mineral toxins. Such progress was not associated just with the analysis, but also with chemical synthesis of novel toxic substances that were applied by very refined devices, such as in the case of assassination of Bulgarian dissident Georgi Markov. Nowadays, among the best-informed professions within this area belong toxicologists, secret services and/or military components. The purpose for which the toxic substances are used has also changed from mere removal of undesirable individuals to mass intimidation, terrorism and false accusation. However, by looking back in time, there is one fact that persisted many thousands years—poisons of various origin were/are/will be considered unconventional type of weapon.

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