Chapter 13.3: Poisons and Toxins

Introduction

Poisons are compounds that function primarily to kill cells. For centuries, poisoning was a feared as a common and effective way of “doing away” with someone. Medieval royalty had food testers, alchemists worried about finding antidotes for poisons, and professional assassins were well stocked in methods to poison an unsuspecting victim. Conspiracy theories about the poisoning of influential people have for centuries accompanied unexpected deaths, although until the development of modern methods of toxicology, death by poison could rarely be proven.

Poisons are an integral part of our everyday lives. Our childhood tales are filled with poisoning cases: Snow White and her poisoned apple and the Grimm’s fairy tale of the Poisoned Combs, to name just two. As has been pointed out in the press, our literature and movies are made far more interesting through the effects of poisons on good and bad characters alike. In literature, poisoning is a common theme with such infamous examples as Shakespeare’s Hamlet, Arthur Conan Doyle’s The Sign of Four, Lemony Snicket’s A series of Unfortunate Events, Robert Graves’ I, Claudius, Agatha Christie’s Cards on the Table, and even Metamorphoses by Ovid (written in 8 AD). The comic movie from the 1940s, starring Cary Grant, called Arsenic and Old Lace tells the tale of two old spinsters who use arsenic and other poisons to help lonely, elderly gentlemen on their way to a happier life. In the classic movie, the Court Jester, Danny Kaye has to contend with the rhyme “The pellet with the poison’s in the vessel with the pestle; the chalice from the palace has the brew that is true!” Even comic book superheroes have derived their powers from a toxic poisoning event: Spiderman, the Mutant Ninja Turtles, Daredevil, and many others. We are fascinated by poisons!

Part of the mystique of poisons arises because they often come from very common, easily obtained sources which may mimic the symptoms of natural diseases and usually leave no traces behind – the magic bullet. The very tiny doses of poisons necessary to cause great harm can usually be disguised in the foodstuffs or drink of unsuspecting victims. Symptoms can develop rapidly or be more insidious and develop slowly over many months, depending upon the way that the poison acts. For example, low doses of arsenic, the so-

Figure 13.3.1. Snow White’s gift poison apple (Disney’s Snow White)
called inheritance powder, results in weakness, confusion, disorientation, digestive problems and other low-grade symptoms in chronic doses. Over time these symptoms, while ultimately leading to death, may simply be attributed to the inevitable decline of a person from natural causes. An entire “cult” grew up in Medieval Europe where would-be assassins were trained in how to use arsenic and other poisons to achieve their political, economic and personal goals. Wives were schooled on how to poison their husbands, businessmen were taught to use poisons on rivals, and challengers even learned how to carefully poison wet nurses with less than lethal doses in order to murder the young heirs that they nursed.

Toxins are distinguished as a special subset of poisons that are produced specifically by living organisms, such as snakes, bacteria (e.g., botulism and tetanus), and certain plants. Sometimes, a further distinction is made by calling a toxin that is injected directly into a victim (as opposed to ingestion) a venom, such as from a snakebite or insect sting (Figure 13.3.3). A venomous organism, such as a black widow spider or a rattlesnake, is one that uses poison to defend itself while a poisonous organism is one that unintentionally causes harm through ingestion, inhalation, or skin contact. So, a snake may be venomous while a mushroom may be poisonous.

Many poisons have both a healing and a harming nature. Arsenic is still used medicinally to treat a variety of problems including cancer and sleeping sickness. Today, accidental and intentional poisoning cases are all too common and form an important part of the work of a forensic toxicologist. The pathologist and toxicologist must understand how various poisons work on the body so as to both recognize the symptoms and to know specifically what to look for to determine if poisoning might have been the cause of death and, if so, whether the poisoning was accidental or intentional.

**Method of Action**

Poisons act in a variety of ways in the human body but, in general, their modes of action can be used to classify poisons into two general categories: corrosive poisons or metabolic poisons.

**Corrosive Poisons**

Corrosive poisons are substances that act to destroy tissues through a “brute force” approach. These substances physically destroy tissues upon direct contact and usually act immediately. The most common corrosive poisons are strong acids and bases. These chemicals often work to rapidly catalyze destructive reactions in the tissues. Corrosive poisons typically hydrolyze fats, proteins and other biological chemicals by adding the chemical components of water to sensitive bonds – literally digesting biomolecules by breaking the bonds.
larger molecules into smaller ones. For example, large fat molecules are broken into the much smaller molecules of glycerol and carboxylic acids by acid catalyzed hydrolysis reactions (Figure 13.3.4).

Strong acids are quite common corrosive poisons and include sulfuric acid, hydrochloric acid, and nitric acid. Strong bases, sometimes called caustic poisons, include sodium hydroxide, potassium hydroxide, and lithium hydroxide.

Some strong acids, such as sulfuric acid, rapidly dehydrate, or remove water, from tissues with the generation of a significant amount of heat. Cells die quickly when these dehydrating agents rupture cell membranes, denature DNA, and destroy proteins. If enough acid is present, the heat generated can be quite significant and cause thermal destruction of tissues. Some corrosive poisons, such as nitric acid and hydrogen peroxide, act as strong agents, capable of breaking chemical bonds through oxidation.

Luckily, most of the common corrosive poisons usually provide clear warning signals that tell people they have come into contact with a dangerous compound. For example, 0.01% ammonia in the air causes choking and respiratory distress, driving people to seek fresh air. Most acids and bases interact with the nerve endings in the skin to send strong pain signals, alerting the person that immediate action is necessary.

There are some corrosive poisons, however, that don’t provide noticeable warning signals until damage has proceeded rather far and, because of this, are particularly dangerous. For example, hydrofluoric acid (HF), widely used in the electronics and glass industries and produced annually in amounts of over 1 million tons, destroys tissues and bone but usually does not send pain signals upon immediate tissue exposure. This is because HF interferes with normal nerve functioning and it is only when the acid reaches much deeper tissue levels and bone that clear pain signals are first

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\text{Cl}_2\text{C}=\text{O} + \text{H}_2\text{O}(l) \rightarrow 2\text{HCl(aq)} + \text{CO}_2(g)
\]

Figure 13.3.5. (Top) phosgene canisters being used in World War I, and (bottom) the reaction of phosgene (\(\text{Cl}_2\text{C}=\text{O}\)) with water to produce hydrochloric acid (photo: m17mask.com/RedHandbook/003PulmonaryAgents.htm).
perceived by the body. HF is also absorbed more rapidly into tissues than are other mineral acids, making its way to deep tissue levels and into the bloodstream very quickly. Most of the toxicity from HF actually occurs, however, from action of the fluoride ion (F\(^-\)) that binds very effectively to calcium in the blood.

Some corrosive poisons are particularly problematic because of the compounds that they produce in the body, rather than the direct action of the poison itself. Phosgene (Cl\(_2\)CO), a WWI poison gas that is still used in the plastics industry today, is a gas that, when inhaled into the lungs, reacts with the water there to form hydrochloric acid inside the lungs. The body attempts to counteract the presence of the acid in the lungs by diluting it – usually a good response to reduce damage from acid exposure. But in this case, the body rapidly moves fluids into the lungs from other tissues, causing pulmonary edema (fluid in the lungs) that essentially drowns the victim in their in water. Unfortunately, phosgene does not produce well-recognized warning signals upon exposure – it smells faintly of new-mown hay – and the reaction in the lungs is relatively slow. This means that by the time a victim begins to realize that they have been exposed, most of the damage has been done.

Corrosive poisons are often contained in many common household items and are easy to obtain. A few examples are given in Table 13.3.1. These compounds are produced on the megaton quantity annually and their ready availability results in both accidental and intentional exposures.

**Metabolic Poisons**

Metabolic poisons are those that act by affecting the biochemical functioning of cells and tissues. Unlike corrosive poisons, metabolic poisons may not leave any visible marks behind on exposed tissues and may be easily overlooked. These poisons act in many different ways that are ultimately toxic to cells including blocking vital chemical reactions, promoting other damaging reactions, directly decomposing biological molecules, or competing with cells for needed chemicals.

![Figure 13.3.6. CO poisoning action.](http://healthforworld.blogspot.com/2008/11/carbon-monoxide-poisoning.html)
The checklist of how these poisons work is very long but a few examples will serve to show both the range of ways in which these compounds may have their toxic effects and to illustrate the most common modes of action encountered with metabolic poisons.

**Carbon Monoxide** – (mode of action: competition) Carbon monoxide (CO), a colorless, odorless and tasteless gas, is classified as a metabolic poison. Carbon monoxide is produced by the incomplete combustion of organic materials, such as from an improperly working furnace or an automobile with a malfunctioning catalytic converter. These sources may produce large amounts of carbon monoxide without detection or noticeable warning signals to a victim.

Carbon monoxide works in the human body by binding very tightly to the iron center of hemoglobin (Hb) molecules in our red blood cells to form carboxyhemoglobin (COHb). Normally functioning hemoglobin binds only rather weakly to oxygen to form oxyhemoglobin (O₂Hb), the molecule that efficiently transports oxygen from the lungs to the cells where the oxygen is released for use in respiration (converting nutrients into energy). This reversible, weak Hb-O₂ bond allows the oxygen to be released just where it’s needed – a delicate balance between a bond strong enough to deliver the oxygen from the lungs to the cells without losing it *en route* but weak enough to give it up when it reaches its cellular destination, Figure 13.3.6. The problem in CO poisoning, however, is that the carboxyhemoglobin, formed from the reaction of Hb and CO, is over 140 times more stable than the oxyhemoglobin complex. This means that the CO displaces oxygen from the Hb very effectively, bonding more tightly than oxygen, and it is only very slowly released from the Hb. The formation of the very stable COHb, therefore, effectively removes the molecules of Hb from service, greatly diminishing the blood’s ability to deliver oxygen and starving the cells of oxygen. This may not seem like a big problem, but because of the tight bond between CO and Hb, breathing in air containing only 0.1% of carbon monoxide for just four hours converts over 60% of the Hb in blood to carboxyhemoglobin – reducing by 60% the blood’s ability to transport oxygen. CO is not, however, a cumulative poison and, if the exposure is caught in time and the victim is

![Potential Carbon Monoxide Sources in the Home](news.homeenergypartners.com/?p=462)

![“Cherry red” coloration in a non-fatal carbon monoxide poisoning exposure](www.codoh.com/newvoices/nrtkco.html)
given plenty of oxygen to breathe, all of the CO is eventually released from the Hb, allowing it to once again function normally (although permanent damage and death can result from O₂ starvation before the Hb is restored to function).

CO poisoning is a silent killer - it gives no warning signals and can overtake a person either while sleeping or without their notice (Figure 13.3.7). It is also a common method of suicide – neither painful or difficult, the victim just feels sleepy and never awakens. Common in CO poisoning is a “cherry pink” complexion of tissues, shown in Figure 13.3.8, that arises from the bright red color of the carboxyhemoglobin.

**Cyanide** – (mode of action: interfering with metabolic pathways)
Cyanide, CN⁻, is a common chemical used in manufacturing, pest control, electroplating, plastics production. While commonly thought of as the hydrogen cyanide gas (HCN), cyanide is also found in a variety of plants and seeds, especially cherry syrup, flax, apricot pits, cashews, corn, and chickpeas. Even though it is found in these natural sources, accidental cyanide poisoning from natural sources is very rare as very large quantities of the plant matter are required to reach a dangerous level. Cyanide poisoning can occur,

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**Pain Relief Murders**

12-year old Mary Kellerman, who lived in the outskirts of Chicago, awoke one morning not feeling very well and took an extra strength Tylenol capsule to help. Soon afterwards, she died from cyanide poisoning. Nearby, Adam Janus also died from taking cyanide laced Tylenol, as did his brother and sister-in-law who had gathered for the funeral when they took Tylenol from the same bottle of Tylenos that had killed Adam (unknown as the poison’s source at the time). Eventually a total of seven people from the Chicago area died by poisoning from cyanide hidden in Tylenol caplets. To this day, the crime remains unsolved but led to the US Congress passing tough anti-tampering laws.

Four years later, however, in Washington state a frighteningly similar scenario began to unfold. Bruce Nickell and, not far away, Sue Snow both died from cyanide poisoning arising from tampered Excedrin tablets. Attention in the case quickly focused on Stella Nickell, Bruce’s wife. She had purchased two bottles of Excedrin from two different stores and both were found to contain cyanide - only three other bottles in the entire state were found to contain cyanide, making it improbable that she had randomly purchased two contaminated bottles from different sources. Other pieces of the puzzle began to fall into place. Stella herself alerted police to the poisoned tablets after her husband’s death even though it was initially attributed to emphysema. Police quickly realized that if Bruce had died of poisoning instead of emphysema, Stella would collect twice the insurance money so it was in her financial best interest to reveal the cyanide-laced tablets. It turned out that Stella had recently bought a large amount of cyanide-containing fish tank algae remover – so much, in fact, that the pet store had to make a special order. A book on poisons was also found in the local library with Stella’s fingerprints on the pages describing cyanide poisoning and she had talked for years about killing her husband.

Stella Nickell was convicted by a jury of murdering her husband and, while serving time, still insists on her innocence.

Many other high profile cases of cyanide murder/suicide have been reported including that of Rosemarie Essa, Jim Jones and the Jonestown murder/suicide of more than 900 people, Hitler’s generals, Rasputin.

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*Photo: Cyanide tablets; [www.cyanco.com/nacn-solid.php](http://www.cyanco.com/nacn-solid.php)*
however, from the use of alternative cancer remedies employing amygdalin (sometimes called bitter almond, laetrile, or Vitamin B₁₇ in the marketplace) that is found in almonds and apricot pits (Note that medical authorities have called this form a cancer treatment one of the worst “cancer quack promotion(s) in history”). Antidotes to cyanide poisoning are available, such as sodium nitrite (NaNO₂) followed by sodium thiosulfate (Na₂S₂O₃), but it must be administered very quickly after the exposure to have any chance of being effective.

Cyanide is a very fast acting poison when introduced into the body, often having a noticeable affect within seconds. Once in the body, it causes asphyxiation (deprivation of oxygen) but in a manner quite different from that of carbon monoxide poisoning. Cyanide interferes with enzymes in the body, particularly with an enzyme called cytochrome c oxidase, so that, even while the cells are receiving a sufficient supply of oxygen from the lungs, they cannot use it – the metabolic pathway for respiration in the cell is shut down by cyanide’s effect upon the necessary proteins and enzymes. High dosages of cyanide can cause death in minutes. A pink complexion similar to that seen in CO poisoning results from the bright red color of a cyanide-hemoglobin complex. Lower doses of cyanide can lead to confusion, vertigo, weakness, and, through accumulation over time, coma and death.

Cyanide poisoning rarely occurs accidentally but is commonly used in both suicide and intentional poisoning cases because of its fast action and ready availability in tablet form.

Heavy Metal Poisons – (mode of action: inactivating enzymes and biomolecules) While there is no suitable, single definition of a heavy metal, they are usually defined in toxicology as elements in the periodic table that fall into the classification of a metal or metalloid. These include arsenic, mercury, lead, cadmium, iron and others. These elements are all around us: in our food, in the air, and in the products that we use. Arsenic gives the green color to “pressure” treated lumber and stops decay,
mercury is found in fluorescent light bulbs and medical vaccines, lead is used in car batteries, bullets and pewters, and cadmium is found in pigments and alloys. Older paints containing lead still present a significant problem when eaten by children. And some of these heavy metal poisons, especially arsenic and thallium, are too often poisons of choice for homicide.

Heavy metals may enter the body in food, from the air, or by direct absorption through the skin. Once in the body, they react with the oxygen or sulfur-containing groups in enzymes to form tightly bound complexes, rendering the enzymes incapable of doing their normal jobs, as illustrated in Figure 13.3.9. These metals accumulate and are not readily eliminated, making repeated low levels of exposure particularly problematic. Symptoms of chronic exposure vary from mild headache and diarrhea to confusion and impairment of motor and language skills. Exposure in young children is especially critical where small chronic amounts of heavy metals may cause significantly impair or impact their mental development. Toxicologists typically measure the amount of heavy metals by either urine or blood analysis.

*Strychnine* (mode of action: kills nerve cells – a neurotoxin) – Strychnine is an example of a large class of chemicals called *neurotoxins* –molecules that interfere with the normal functioning of nerve cells. Normal nerve cells operate by turning on and off very rapidly to send electrical signals throughout the body. Different chemicals in a nerve cell turn the signal “switch” on and different chemicals turn it very quickly off, ready
to send the next signal – something like a Morse code for the body. Strychnine and most other neurotoxins work by stopping the nerves from turning off and relaxing after firing, resulting in severe muscle spasms and nerve tiring. Over time, the muscles tire and neurons (nerve cells) “burn out” from prolonged operation. Initial symptoms include paralysis, severe pain, and spasms. The action of strychnine eventually leads to complete exhaustion and failure of the muscles to work, including the muscles needed for pumping the heart and for breathing. Strychnine is used as a pesticide (most commonly as rat poison). There are many classes and types of neurotoxins including the venom from thousands of plants (e.g. horse chestnut and Buckeye tree), animals (e.g., bees, scorpions, spiders, snakes, and fish), and bacteria (e.g., botulinum toxin - the most potent of all known poisons). Chemical warfare agents, the so-called “nerve gases” such as sarin, are also usually potent neurotoxins.

Other Poisons (various modes of action) - Some poisons, while not neurotoxins, act by

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<td>History is full of serial poisoners who ply their trade on unsuspecting victims for personal profit and satisfaction, and the supply doesn’t seem to be slowing. A sample of the hundreds of known cases includes:</td>
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<td>• The Council of Ten in Renaissance Venice poisoned for a fee both for private reasons or to protect the “security of the Republic of Venice”. They sponsored poison training “schools” and maintained a skilled set of assassins on call.</td>
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<td>• Belle Gunness (1859-1908) murdered her husband and two children to collect money to buy a farm in Indiana – she may have murdered all of her children, boyfriends, and husbands. Later, she lived an early version of Arsenic and Old Lace by putting ads in the local newspaper for lonely men, only to dispatch them with poison. After a fire destroyed the farm, the remains of an estimated 49 victims were discovered.</td>
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<td>• Poisoner Donald Harvey was a nurse in the Cincinnati area who became known as the “Angel of Death” when he pleaded guilty to 37 murders. Official estimates place the total number between 37 and 57 deaths. He claimed that he murdered to “ease the pain” of terminally ill patients.</td>
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<td>• Genene Jones, a pediatric nurse in Texas, killed between 11 and 46 children by lethal injection, although she was convicted in 1985 for the killing of just two victims.</td>
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<td>• In 2000, Kristin Rossum poisoned her husband with fentanyl to indulge in a love affair with her boss at the San Diego Medical Examiner’s Office. She staged the death to recreate a scene from her favorite movie “American Beauty” with rose petals and their wedding pictures in bed with him.</td>
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Photos: (Left) Kristin Rossum, (Center) Genene Jones, and (Right) Belle Gunness and her children

emulating important biological molecules but without their beneficial action. For example, dioxins – a class of chlorine-containing organic molecules – mimic hormones in the body and disrupt the myriad chemical reactions controlled by our hormones. These molecules bind to specific sites in cells called receptors and “unlock” access to chemical reactions that may be harmful to the cell. The intentional dioxin poisoning of Ukrainian president Viktor Yushchenko illustrates the devastating effects of these types of biomolecule mimics, Figure 13.3.11.

These are just a few examples of the various modes of operation of common poisons and toxins in the body, and serve to illustrate how they can have their cytotoxic effects (cytotoxic means killing cells). The forensic toxicologist needs to know how these chemicals work, the range of symptoms they produce, and how to detect and measure their presence in the body. The analytical methods used for determining the presence of drugs and poisons will be presented in more detail later in this chapter.