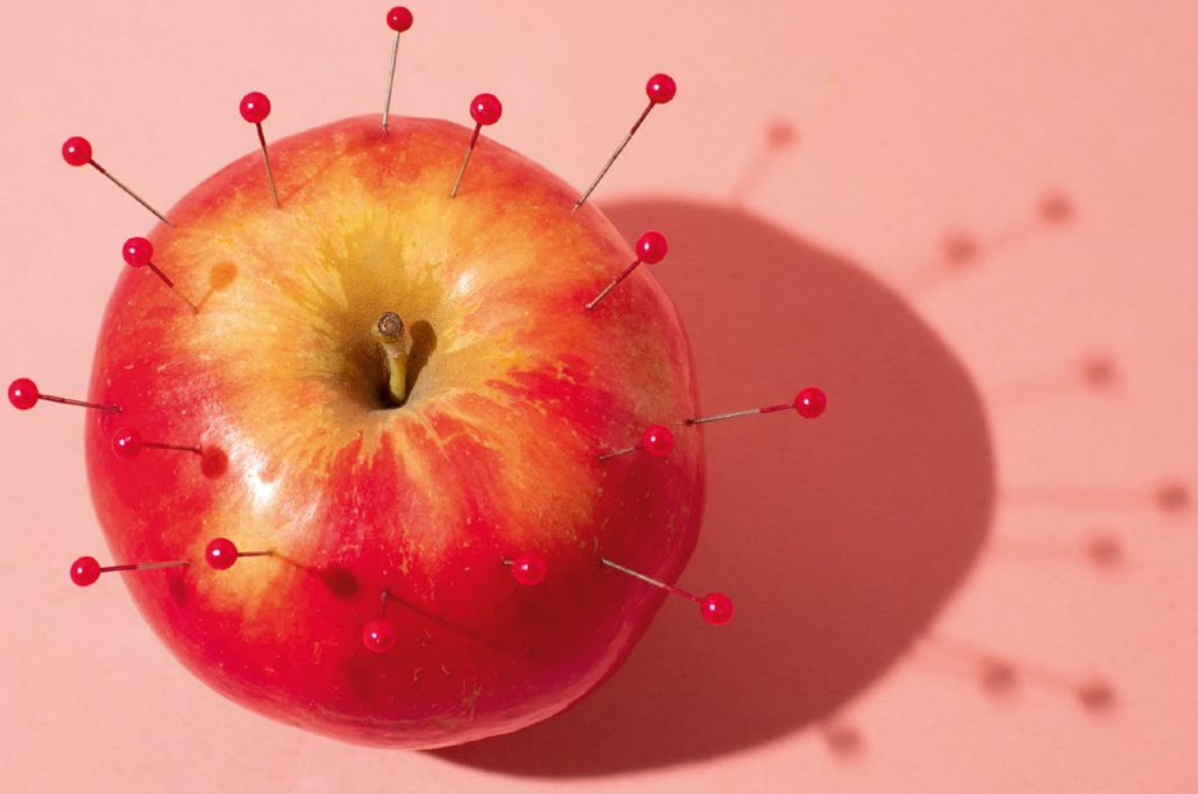
Snow White's red apple



What are poisons and how do they work? A brief exploration of toxicology.

Envy of the beautiful Snow White eats away at the evil stepmother. And so, the offended woman resorts to a ruse and poisons a red apple. When the unsuspecting Snow White eats it, she falls into a death-like sleep. “Snow White and the Seven Dwarfs” is one of the most popular fairy tales by the Brothers Grimm, and the episode with the apple encapsulates many elements associated with the concept of poisons: deception, malice, danger. ‘Poisonous’ – the word has instilled fear since the time of the Brothers Grimm.

The science of poisons, toxicology, approaches its subject with a perspective that is more pragmatic than demonic. It defines a poison (or toxin) as a substance that can harm living organisms, even in small doses. The realm of poisons is large. Public attention is usually focused on man-made potential poisons. These include contamination by microplastics, per- and polyfluorinated alkyl substances (PFAS), and dioxins as well as residues of chemicals or active ingredients of pesticides, such as glyphosate.

NATURE AS A POISONER

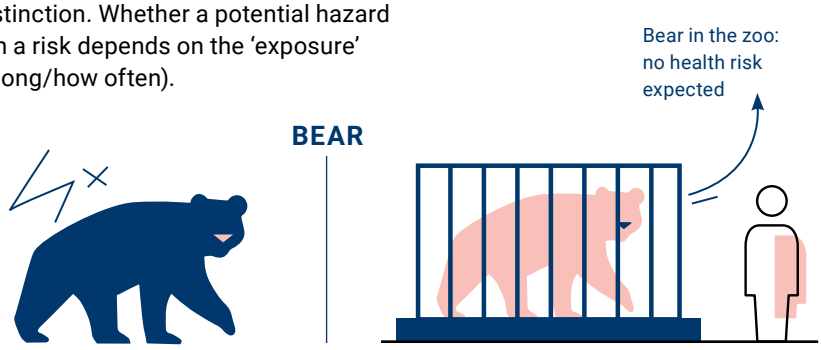
It is easy to overlook the fact that a large (if not the largest) group of poisons comes from nature itself. These chemical compounds are formed by animals, plants and microorganisms to ward off enemies or to capture prey themselves. These are substances that have been “refined” and perfected over the course of evolution to specifically harm other living things. This explains their sometimes immense toxicity. The botulinum toxin secreted by the bacterium *Clostridium botulinum* is the most potent poison known. When injected into a vein or muscle, less than one-millionth of a gram (a microgram) is fatal. It is also a little-known fact that each year, an estimated 81,000 to 138,000 people lose their lives to venomous snake bites.

IT'S ALL ABOUT THE DOSAGE

Intuitively, we tend to categorise substances as good or bad, useful or harmful, healthy or pathogenic. However, anyone who studies toxicology quickly realises that the world of poisons is not divided into good or dangerous, but into high or low doses. This scientifically fundamental insight dates back to the physician Paracelsus, who, as early as the 16th century, stated: “The dose alone makes a thing non-poisonous.” Accordingly, strictly speaking, there is no such thing as a poison per se. “Anything can be toxic, and conversely, anything can be harmless,” explains toxicologist Dr Tewes Tralau. He heads the Pesticide Safety department at the German Federal Institute for Risk Assessment (BfR). What is crucial is the amount of a substance that a person comes into contact with. The toxicological term for this is exposure.

Hazard or risk?

In our everyday language, we often use the two terms synonymously. Scientific risk assessment, however, makes a strict distinction. Whether a potential hazard is associated with a risk depends on the 'exposure' (how much/how long/how often).



HAZARD: describes the potential of something to cause harm to health (hazard potential)

RISK: describes the probability of whether and how severely health can be harmed by something

Here are a few examples: Our body consists of two-thirds water – and yet drinking excessive amounts of water can be life-threatening, as it can cause brain swelling, known as cerebral oedema. Similarly, table salt, which (like water) is essential for life – the body contains half a pound – is deadly if ingested in excess. A dose of 100 to 150 grams a day (about ten tablespoons) can be fatal. On the other hand, the aforementioned "ultra-poison" botulinum toxin is used in extremely low doses to treat nerve and movement disorders (and as a means of smoothing wrinkles).

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WHAT – AND HOW MUCH – LIES WITHIN

There are many methods for detecting toxins in environmental samples, food or bodily fluids. These methods are the focus of analytics, a branch of toxicology. One long-established technique is the immunoassay, where a specific antibody is coupled to the target molecule and is thus "recognised". Chromatography can be used to separate mixtures of substances in a liquid. This makes the individual components visible. The most advanced method is mass spectrometry. During a measurement, a test sample is first electrically charged (ionised). An electrical field then separates its individual components. The resulting 'mass spectrum' provides precise information about the composition of the sample.

Such modern methods can detect the smallest amounts of substances. A toxicologist at Snow White's side would have no problem detecting the stepmother's poison, no matter how tiny the amount. Conversely, however, this also means that the detection of a substance in itself means nothing when it comes to its risk potential. The decisive factor here is always the dose (exposure). Even in today's nano-era, capable of detecting billionths or trillionths of a gram, not every microgram is a macro-risk.

HOW THE BODY DEFENDS ITSELF

As a rule, the human body can defend itself well against potentially toxic substances. This is because it has developed effective “detox” methods over the course of evolution. Probably the best example of this is the enzyme family of cytochrome P450-containing monooxygenases. These proteins generally ensure that toxins are easier to excrete, for example, via the kidneys or bile in vertebrates.

The body's “detoxification centre” is the liver. As the central metabolic organ, it processes 1.5 litres of blood every minute. Almost everything potentially toxic must pass through the liver. Its approximately 200 billion liver cells have a large arsenal of “detox” enzymes. Conversely, their task also puts the organ itself at risk of damage. For example, the toxin from the death cap mushroom can destroy the liver within a few days. Similarly, chronic high-dose consumption of the ethanol in alcoholic beverages often results in irreversible organ damage.

In addition to the liver, potential toxins can put other important organs and processes at risk: the respiratory tract (e.g., asbestos fibres), kidneys (some drugs), bone marrow (e.g., benzene, a hydrocarbon), skin (e.g., nickel) and nerves (e.g., methylmercury) as well as blood formation (e.g., lead), reproductive health and foetal development (e.g., the active ingredient thalidomide, “Contergan”).

Our bodies are two-thirds water – and yet drinking too much water can be life-threatening.

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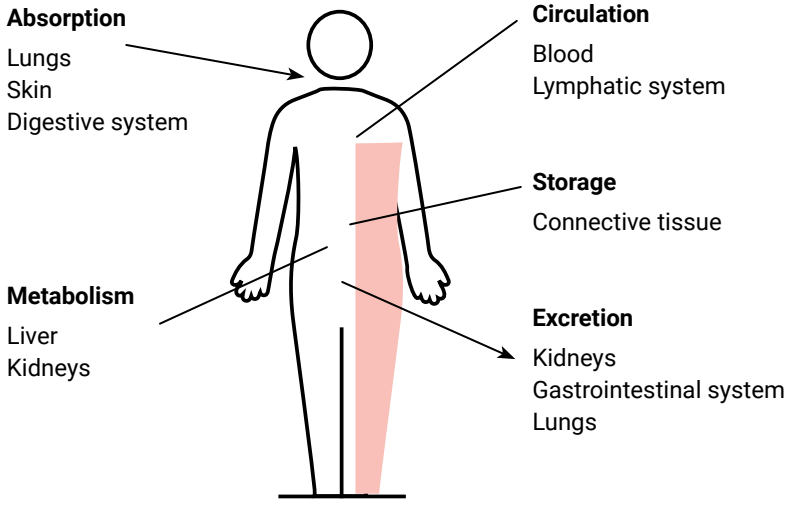
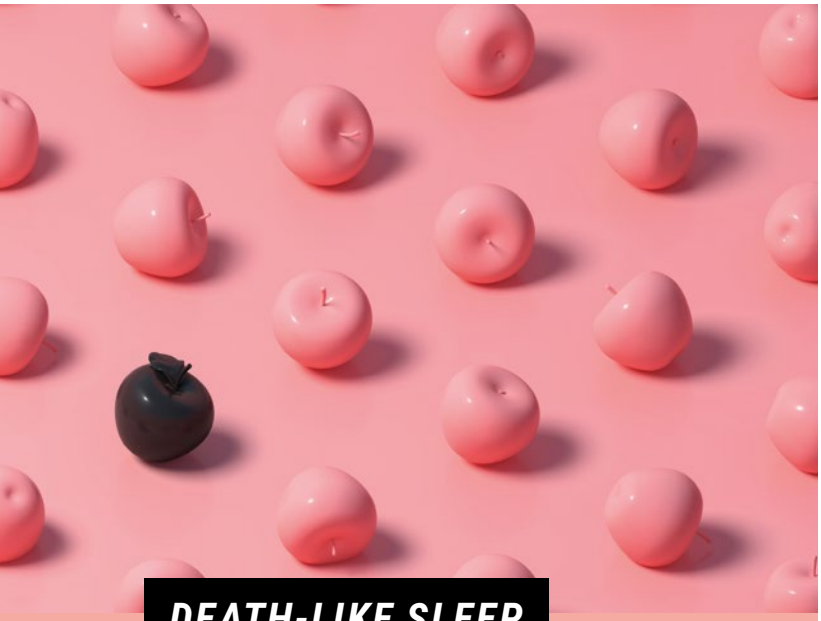
TESTED FOR LIVER AND KIDNEY DAMAGE

There are various methods for determining the possible risk of a toxin. In addition to animal testing, the model that most closely reflects biological reality, there are also animal-free methods, such as cell cultures or more complex cell systems. Epidemiological studies (population studies) are becoming increasingly important. When well-conducted, they can provide clues to the possible causes of disease.

New pharmaceutical active ingredients and chemicals are tested for toxicological health risks before they can be used, approved or authorised. The tests are required by law and manufacturers must submit them to the authorities. The same applies to active ingredients in pesticides.

Toxins in the body – **which processes are affected?**





DEATH-LIKE SLEEP

A case for toxicology

A poisoned apple causes Snow White to fall into a deep unconscious state, medically known as a coma. What substances can cause such a condition? From a toxicological point of view, there are several possibilities. Quite a few natural products and chemicals have the ability to affect the nervous system when given in the right doses. For example, for a long time, chloroform was used as an anaesthetic. Although chloroform was first artificially produced about 20 years after Grimm's fairy tales were published, seaweed and soil fungi also produce the anaesthetic chemical. The royal poisoner may have made use of these natural sources. Another possibility is tetrodotoxin (TTX), the highly dangerous poison of the puffer fish. It paralyses nerves and muscles and is about 100 times more toxic than chloroform. Just a thousandth of a gram is enough to kill a human being. Although puffer fish are rare in our latitudes, worms, frogs, lizards and many other animal species contain TTX – it is often produced by bacteria that live in symbiosis with their hosts. The guiding principle might be: "if you give me poison, you can live with me". The paralysing effect of TTX, for example as a result of poisoning from TTX-containing marine creatures, has been long known to humans and is part of the thrill of eating puffer fish (Fugu) in Japan. If Snow White had been exposed to TTX, she would have been in mortal danger – the fact that she did not swallow the poisoned apple most likely saved her life.

"These substances have been developed, for example, to harm specific fungi or insects," says BfR toxicologist Tralau. "Because of this potential, we have to examine them very carefully."

The tests determine, among other things, whether an active ingredient can cause genetic damage, trigger cancer or have acute or long-term toxic effects. They also examine whether fertility or offspring are harmed, whether hormone-like effects are possible, if the nervous system is affected, or if the skin is irritated. Toxicology has established a dense network to ensure that substances that pose a risk to humans (or the environment) are detected at an early stage. There's no doubt that evil stepmothers would have a much harder time today. —

More information

BfR information
"Plant protection products"

BfR-FAQ
"Difference between risk and hazard"

BfR2GO 1/2024
"Toxicological risk assessment for plant protection products" *(pdf)*