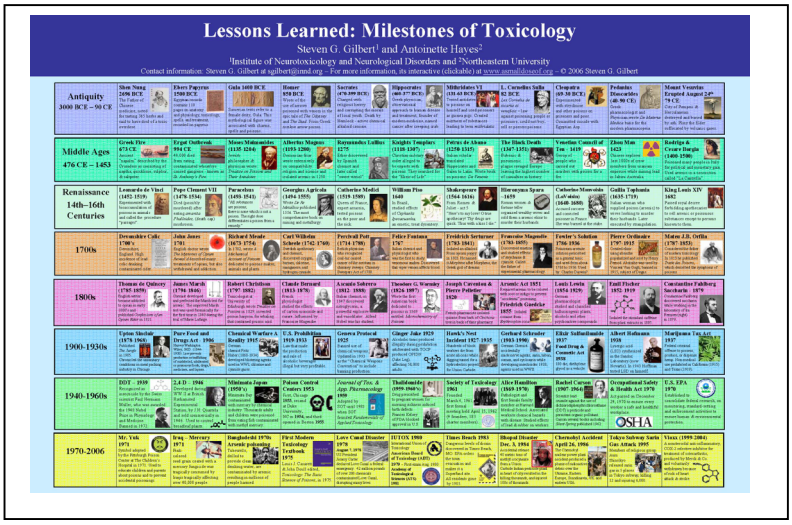
A Small Dose of Toxicology History
Or
An Introduction to the History of Toxicology and Lessons Learned



Chapter 5 in Third Edition of
A Small Dose of Toxicology - The Health Effects of Common Chemicals

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Supporting web sites
web: www.asmalldoseoftoxicology.org - "A Small Dose of Toxicology"

History of Toxicology – Lessons Learned

Introduction - Antiquity

Milestones of Toxicology – interactive poster https://www.asmalldoseoftoxicology.org/milestones-posters

The history of toxicology is rich with personalities, political intrigue, warfare, regulation, and, most importantly, lessons learned. It begins with early humans' need for survival, which required an understanding of the potential hazards of the plants and animals encountered. Early experimentation with plants was driven by an interest in food as well as curing various ailments of body and spirit. Shen Nung, the Father of Chinese medicine (approximately 2695 BCE), who was noted for tasting 365 herbs and dying from a toxic overdose, also wrote an early treatise *On Herbal Medical Experiment Poisons*. This work was modified though the ages and ultimately helped to established China as a leader in herbal medicine.

The Ebers papyrus, an ancient Egyptian record dated from approximately 1500 BC contains 110 pages on anatomy and physiology, toxicology, spells, and treatment. The papyrus has a fascinating history as it changed hands and was lost and found again since it first surfaced in 1862. It documents a wide range of toxic substances including hemlock, the state poison of the Greeks, and aconite, a poison used by the Chinese to tip their arrows.

Early Poisons

An array of poisons were used for assassinations throughout history. Mithridates VI, who was the King of Pontus in Asia Minor 120 BCE to 63 BCE, took increasing concentrations of various poisons in an effort to protect himself from poisoning attacks. Legend has it that Mithridates attempted suicide by poison but failed and ultimately died by the sword.

Some of the first laws related to toxicology were directed at poisons. Sulla (138-78 BCE) created laws such as the *Lex Cornelia de sicariis et veneficis*, which made it illegal to poison people, including prisoners, as well as making it illegal to buy, sell, or purchase poisons.

In the 1400s arsenic became a common poison, sometimes used by women to assassinate an inconvenient husband for his wealth. The trend of using poisons for murder continues to modern times, as exemplified by the 2006 poisoning of Alexander Litvinenko, who was poisoned by exposure to the exotic radioactive alpha-particle emitter polonium 210. There is also increasing concern for the potential use of bio-weapons to kill people or disrupt society. A strain of anthrax, the bacterium *Bacillus anthracis*, killed several people in the US in 1991. Anthrax has an interesting history and was well known as potentially fatal to farm animals and humans. Louis Pasteur developed a vaccine of anthrax in 1881, but research continues to develop and produce more effective vaccines. Unfortunately, the search for more powerful and exotic means of poisoning people continues along with advances in science and technology.

Toxicological Sciences

As scientific methodology advanced, the toxicological sciences became more rigorous. Paracelsus (1493-1541), sometimes called the "father" of toxicology, articulated the now famous saying that “the dose makes the poison”. The first association of an occupational exposure to cancer was made in 1775 by Percival Pott, an English surgeon. He observed that exposure to soot was related to scrotal cancer in chimney sweeps. Mathieu J. B. Orfila (April 24, 1787 - March 12, 1853), a French toxicologist and chemist, is credited with founding the modern science of toxicology, in part through analytical work in forensic toxicology related to the poison of the day, arsenic. Discovery of individual chemicals such as caffeine, nitroglycerin, cocaine, and saccharin increased in the 1800s. This trend accelerated during the 1900s. The Germany military, supported by a robust chemical industry, were the first to use chemical weapons in World War I. On April 22, 1915, the German military released chlorine gas over the battlefield at Ypres Salient in Belgium, killing an estimated 5,000 French and Algerian troops. The start of the chemical revolution was stimulated by World War II, which included the development of very powerful nerve gases. Chemical weaponry stockpiling was an integral part of the

arms race throughout the Cold War, and their destruction has proved challenging, costly, and time consuming. The Chemical Weapons Convention of 1993 outlaws the production, stockpiling, and use of chemical weapons by all signatories. The aftermath of WWII stimulated the development of an array of pesticides and an enormous global chemical industry.

Recognizing Hazards

With the widespread use of chemicals and other agents such as metals, it became clear that they could cause ecological damage and affect human health. Advances in methods to detect chemicals spurred research on the mechanisms of action of many early chemical formulations. In addition, advances in medicine and toxicological sciences lead to a better understanding of the health effects of chemical exposures on individuals and populations.

Several incidents brought into sharp focus the potential hazards associated with chemical exposures. During prohibition in 1929, alcohol tonic called Ginger Jake was contaminated with tri-ortho cresyl phosphate (TOCP), a paralyzing organophosphate chemical. This incident damaged the nervous systems of an estimated 50,000 people. Alice Hamilton, MD (1869-1970), the first female member of Harvard Medical School, documented the health effects of occupational exposure to chemicals such as lead. In the 1950s mercury was released into the environment of Minamata Bay in Japan. The mercury was taken up by fish in the form of methylmercury and resulted in tragic effects on the developing fetus and even some of the adults that lived in the area and depended on fish in their diet. The publication of Rachael Carson's *Silent Spring* in 1962 marked a turning point in the management of chemicals in the United States and ultimately lead to the banning of the pesticide DDT. In 1978, the contamination of Love Canal in upstate New York vividly demonstrated the consequences of not appropriately managing chemical waste. Industrial accidents such as the 1984 release of methyl isocyanate by a Union Carbide subsidiary manufacturing pesticides in Bhopal, India resulted in the death of thousands and injury of hundreds of thousands. All of these events produced obvious and disastrous to many people and the environment, effecting future generations. The challenge now is to recognize the subtler effects of chemical exposures that might cause cancer or affect the nervous system of children and develop appropriate regulation to prevent delayed or longer-term harm from chemical exposures.

Regulation

The incidents mentioned earlier, and others as well, generated public outrage and political pressure sometimes leading to polices to regulate the use of chemicals. In 1906, the Pure Food and Drugs Act was enacted with the support of the Department of Agriculture's chief chemist Harvey W. Wiley. This act established the basis for the Food and Drug Administration (FDA) to protect consumers from potentially dangerous drugs and food

and stipulated that the consumer be given warning about the toxic or addictive nature of certain products. Most countries adopted the Geneva Protocol in 1925 to limit the use of chemical and biological weapons in warfare. The federal Food, Drug, and Cosmetic Act (FD&C) was passed by Congress in 1938, giving authority to the FDA to oversee the safety of food, drugs, and cosmetics. This policy effort followed the 1937 introduction of Elixir Sulfanilamide, which contained diethylene glycol as a vehicle. Over 100 people, including many children, died when it was distributed and consumed without testing or warnings of the hazard. The Occupational Safety & Health Act (OSHA), passed on December 29, 1970, was intended to ensure every worker a safe and healthful workplace by preventing work-related injuries, illnesses, and deaths. OSHA functions by issuing and enforcing rules (called standards) for workplace safety and health, including exposure to hazardous chemicals. The Environmental Protection Agency (EPA) was officially formed as a result of a law passed in 1970 by the Nixon administration. The EPA would be responsible for maintaining clean air, land, and water and for regulating pollutants in the environment. In the 1990s the European Union moved forward with a more comprehensive chemical use policy through the REACH program (Registration, Evaluation, and Authorization of Chemicals). REACH shifted the momentum and innovation in protecting human health and the environment from the United States to Europe as the European Union embraced a more precautionary approach to managing chemicals.

Conclusion

The history of toxicology provides a revealing window into our scientific understanding of how chemicals affect health and well-being and how society responds to this new information or experience. The interactive poster depicted in figure 1 provides an opportunity for a more in depth exploration of toxicology's fascinating history. Many of the unfortunate lessons learned were translated into regulatory standards to protect human health and the environment.

History of Toxicology Resources

There is a large and ever-growing body of information on the history of toxicology, particularly on the World Wide Web (e.g. www.toxipedia.org). Introductory chapters to major text books are also an excellent source of information.

Web-based References

- Milestones of Toxicology – Interactive Poster – PDF file available online at: < https://www.asmalldoseoftoxicology.org/milestones-posters> (accessed: 4 August 2008).
  The Milestones of Toxicology interactive poster is a clickable pdf file that presents a colorful review of toxicology that allows the user to click on a topic for

additional information. A high-resolution version suitable for printing is also available.

General References

- Wexler, P and Hayes, A. N. The Evolving Journey of Toxicology: An Historical Glimpse. In: Klaassen CD, editor. Casarett & Doull's Toxicology - The Basic Science of Poisons. 9th ed. New York: McGraw-Hill Company; 2019. p. 3-25.
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- Stirling DA. History of toxicology and allied sciences: a bibliographic review and guide to suggested readings. Int J Toxicol 2006; 25(4):261-8.
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