
























































































Lessons Learned: Milestones of Toxicology

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<p>Antiquity 3000 BCE – 90 CE</p>	<p>Shen Nung 2696 BCE The Father of Chinese medicine, noted for tasting 365 herbs and said to have died of a toxic overdose.</p> 	<p>Ebers Papyrus 1500 BCE Egyptian records contains 110 pages on anatomy and physiology, toxicology, spells, and treatment, recorded on papyrus.</p> 	<p>Gula 1400 BCE Sumerian texts refer to a female deity, Gula. This mythological figure was associated with charms, spells and poisons.</p> 	<p>Homer 850 BCE Write of the use of arrows poisoned with venom in the epic tale of <i>The Odyssey</i> and <i>The Iliad</i>. From Greek <i>toxikon</i> arrow poison.</p> 	<p>Socrates (470-399 BCE) Charged with religious heresy and corrupting the morals of local youth. Death by Hemlock - active chemical alkaloid conine.</p> 	<p>Hippocrates (460-377 BCE) Greek physician, observational approach to human disease and treatment, founder of modern medicine, named cancer after creeping crab.</p> 	<p>Mithridates VI (131-63 BCE) Tested antidotes to poisons on himself and used prisoners as guinea pigs. Created mixtures of substances leading to term <i>mithridatic</i>.</p> 	<p>L. Cornelius Sulla 82 BCE <i>Lex Cornelia de sicariis et veneficis</i> – law against poisoning people or prisoners; could not buy, sell or possess poisons.</p> 	<p>Cleopatra (69-30 BCE) Experimented with strychnine and other poisons on prisoners and poor. Committed suicide with Egyptian Asp.</p> 	<p>Pedanius Dioscorides (40-90 CE) Greek pharmacologist and Physician, wrote <i>De Materia Medica</i> basis for the modern pharmacopeia.</p> 	<p>Mount Vesuvius Erupted August 24th 79 CE City of Pompeii & Herculaneum destroyed and buried by ash. Pliney the Elder suffocated by volcanic gases.</p> 
<p>Middle Ages 476 CE – 1453</p>	<p>Greek Fire 673 CE Ancient "napalm" described by the Crusaders as consisting of naphtha, quicklime, sulphur, & saltpeter.</p> 	<p>Ergot Outbreak 994 CE 40,000 died from eating contaminated wheat/rye caused gangrene - known as <i>St. Anthony's Fire</i>.</p> 	<p>Moses Maimonides (1135-1204) Jewish philosopher & physician wrote: <i>Treatise on Poisons and Their Antidotes</i>.</p> 	<p>Albertus Magnus (1193-1280) Dominican friar wrote extensively on compatibility religion and science and isolated arsenic in 1250.</p> 	<p>Raymundus Lullius 1275 Ether discovered by Spanish chemist and later called "sweet vitriol".</p> 	<p>Knights Templars (1118-1307) Christian military order alleged to be experts with poisons. They searched for the "Elixir of Life".</p> 	<p>Petrus de Abano (1250-1315) Italian scholar translated Hippocrates and Galen to Latin. Wrote book on poisons: <i>De Venenis</i>.</p> 	<p>The Black Death (1347-1351) Bubonic & pneumonic plague ravaged Europe leaving the highest number of casualties in history.</p> 	<p>Venetian Council of Ten - 1419 Group of people who carried out murders with poison for a fee.</p> 	<p>Zhou Man 1423 Chinese explorer lost 1000s of crew members from uranium exposure while mining lead in Jabiru Australia.</p> 	<p>Rodrigo & Cesare Borgia (1400-1500) Poisoned many people in Italy for political and monetary gain. Used arsenic in a concoction called "La Cantarella".</p> 
<p>Renaissance 14th–16th Centuries</p>	<p>Leonardo da Vinci (1452-1519) Experimented with bioaccumulation of poisons in animals and called the procedure "passages".</p> 	<p>Pope Clement VII (1493-1534) Died (possibly murdered) after eating <i>amanita phalloides</i>, (death cap) mushroom.</p> 	<p>Paracelsus (1493-1541) "All substances are poisons; there is none which is not a poison. The right dose differentiates a poison from a remedy."</p> 	<p>Georgius Agricola (1494-1555) Wrote <i>De Re Metallica</i> published 1556. The most comprehensive book on mining and metallurgy.</p> 	<p>Catherine Medici (1519-1589) Queen of France, expert assassin, tested poisons on the poor and the sick.</p> 	<p>William Piso 1640 In Brazil, studied effects of <i>Cephaelis Ipecacuanha</i>, an emetic; treat dysentery.</p> 	<p>Shakespeare (1564-1616) From <i>Romeo & Juliet</i> - act 5 "Here's to my love: O true apothecary! Thy drugs are quick. Thus with a kiss I die"</p> 	<p>Hieronyma Spara ~1659 Roman women & fortune teller organized wealthy wives and sold them an arsenic elixir to murder their husbands.</p> 	<p>Catherine Monvoisin (La Voisin) (1640-1680) Accused sorcerer and convicted poisoner in France. She was burned at the stake.</p> 	<p>Guilia Tophania (1635-1719) Italian woman who supplied poison (arsenic) to wives looking to murder their husbands. Later executed by strangulation.</p> 	<p>King Louis XIV 1682 Passed royal decree forbidding apothecaries to sell arsenic or poisonous substances except to persons known to them.</p> 
<p>1700s</p>	<p>Devonshire Colic 1703's Devonshire, England. High incidence of lead colic drinking contaminated cider.</p> 	<p>John Jones 1701 English doctor wrote <i>The Mysteries of Opium</i> Revealed! described many treatments of opium, but also withdrawal and addiction.</p> 	<p>Richard Meade (1673-1754) In 1702, wrote <i>A Mechanical Account of Poisons</i> dedicated to poisons snakes, animals and plants.</p> 	<p>Carl Wilhelm Scheele (1742-176) Swedish apothecary and chemist, discovered oxygen, barium, chlorine, manganese, and hydrogen cyanide.</p> 	<p>Percival Pott (1714-1788) British physician who recognized coal-tar caused cancer of the scrotum in chimney sweeps. Chimney Sweepers Act of 1788.</p> 	<p>Felice Fontana 1767 Italian chemist and physiologist who was the first to study venomous snakes. Discovered that viper venom affects blood.</p> 	<p>Freidrich Serturner (1783-1841) Isolated an alkaloid from opium poppy in 1803. He named it <i>Morphine</i> after Morpheus, the Greek god of dreams.</p> 	<p>Francoise Magendie (1783-1855) Discovered emetine and studied effects of strychnine & cyanide. Called the father of experimental pharmacology.</p> 	<p>Fowler's Solution 1797-1915 Potassium arsenite solution prescribed as a general tonic and used from about 1786 to 1936. Used by Charles Darwin?</p> 	<p>Pierre Ordinaire 1787-1853 Created elixir using absinthe popularized and sold by Henry Perrod. Absinthe was used by Vincent Van Gogh; banned in 1915, subject of Degas.</p> 	<p>Mateu J.B. Orfila (1787-1853) Considered the father of modern toxicology. In 1813 he published <i>Traite des Poisons</i>, which described the symptoms of poisons.</p> 
<p>1800s</p>	<p>Thomas de Quincey (1785-1859) English writer became addicted to opium in early 1800's and published <i>Confessions of an Opium Eater</i> in 1821.</p> 	<p>James Marsh (1794-1846) Chemist developed and perfected the Marsh test for arsenic. The improved Marsh test was used forensically for the first time in 1840 during the trial of Marie Lafarge.</p> 	<p>Robert Christison (1797-1882) Toxicologist at University of Edinburgh wrote <i>Treatise on Poisons</i> in 1829; invented poison harpoon for whaling that contained prussic acid.</p> 	<p>Claude Bernard (1813-1878) French physiologist studied the effects of carbon monoxide and curare. Influenced by Francoise Magendie.</p> 	<p>Ascanio Sobrero (1812- 1888) Italian chemist, in 1847 discovered nitroglycerin, a powerful explosive and vasodilator. Alfred Nobel was his student.</p> 	<p>Theodore G. Wormley (1826-1897) Wrote the first American book dedicated to poisons in 1869 entitled: <i>Microchemistry of Poisons</i>.</p> 	<p>Joseph Caventou & Pierre Pelletier 1820 French pharmacists isolated cocaine from bark of <i>Cinchona</i> tree in back of their pharmacy.</p> 	<p>Arsenic Act 1851 Required arsenic to be colored with soot or indigo to prevent "accidental" poisoning. Friedrich Gaedcke 1855 Isolated cocaine from <i>Erythroxylon coca</i>.</p> 	<p>Louis Lewin (1854-1929) German pharmacologist studied and classified hallucinogenic plants, alcohols and other psychoactive compounds.</p> 	<p>Emil Fischer 1852-1919 Isolated the stimulant caffeine from plant extracts in 1895.</p> 	<p>Constantine Fahlberg Saccharin - 1879 Constantine Fahlberg discovered saccharin while working in the laboratory of Ira Remsen (right) in 1879.</p> 
<p>1900-1930s</p>	<p>Upton Sinclair (1878-1968) Published <i>The Jungle</i> in 1905. Chronicled the unsanitary conditions in meat packing industry in Chicago.</p> 	<p>Pure Food and Drugs Act - 1906 Harvey Washington Wiley, M.D. (1844-1930). Law prevents production or trafficking of mislabeled, adulterated or poisonous foods, drugs, medicines, and liquors.</p> 	<p>Chemical Warfare A Reality 1915 German chemist Fritz Haber (1868-1934) developed blistering agents used in WWI: chlorine and cyanide gases.</p> 	<p>U.S. Prohibition 1919-1933 Law that made the production and sale of alcoholic beverages illegal but very profitable.</p> 	<p>Geneva Protocol 1925 Banned use of chemical weapons. Updated in 1993 as the "Chemical Weapons Convention" to include banning production.</p> 	<p>Ginger Jake 1929 Alcoholic tonic produced illegally during prohibition adulterated with TCCP produced OPIDN (Jake Leg).</p> 	<p>Hawk's Nest Incident 1927-1935 Hundreds of black workers die from acute silicosis while digging tunnel for a hydroelectric project for Union Carbide.</p> 	<p>Gerhard Schrader (1903-1990) German Chemist accidentally made nerve agents; sarin, tabun, soman, and cyclosporin while developing insecticides 1938; agents used in WWII.</p> 	<p>Elixir Sulfanilamide 1937 Food Drug & Cosmetic Act 1938 100 die, diethylene glycol as a vehicle.</p> 	<p>Albert Hofmann 1938 Lysergic acid (LSD) synthesized in the Sandoz Laboratory (now Novartis). In 1943 Hoffman tested LSD on himself.</p> 	<p>Marijuana Tax Act 1937 Federal criminal offense to possess, produce, or dispense hemp. Non-medical use prohibited in California (1915) and Texas (1919).</p> 
<p>1940-1960s</p>	<p>DDT - 1939 Recognized as insecticide by the Swiss scientist Paul Hermann Müller, who was awarded the 1948 Nobel Prize in Physiology and Medicine. Banned in 1972.</p> 	<p>2,4-D - 1946 Developed during WW II at British Rothamsted Experimental Station, by J.H. Quastela and sold commercially in 1946. Used to control broadleaf plants.</p> 	<p>Minimata Japan (1950's) Minimata Bay contaminated with mercury by chemical industry. Thousands adults and children were poisoned from eating fish contaminated with methyl mercury.</p> 	<p>Poison Control Centers 1953 First, Chicago 1953, second at Duke University, NC in 1954, and third opened in Boston 1955.</p> 	<p>Journal of Tox. & App. Pharmacology 1959 Adopted by SOT until 1981 when SOT founded <i>Fundamentals of Applied Toxicology</i>.</p> 	<p>Thalidomide (1959-1960's) Drug prescribed to pregnant women for morning sickness induced birth defects. Frances Kelsey of FDA blocked approval in U.S.</p> 	<p>Society of Toxicology 1961 Founded March 4, 1961 first formal meeting held April 15, 1962 (9 founders, 183 charter members).</p> 	<p>Alice Hamilton (1869-1970) Pathologist and first female faculty member at Harvard Medical School. Associated worksite chemical hazards with disease. Studied effects of lead & rubber on workers.</p> 	<p>Rachel Carson (1907-1964) Scientist lead crusade against the use of dichlorodiphenyltrichloroethane (DDT) a pesticide and persistent organic pollutant. Carson several books including <i>Silent Spring</i> published 1962.</p> 	<p>Occupational Safety & Health Act 1970 Act passed on December 29, 1970 to ensure every worker a safe and healthful workplace.</p> 	<p>U.S. EPA 1970 Established to consolidate federal research, on monitoring, standard-setting and enforcement activities to ensure human & environmental protection.</p> 
<p>1970-2006</p>	<p>Mr. Yuk 1971 Symbol adopted by the Pittsburgh Poison Center at the Children's Hospital in 1971. Used to educate children and parents about poisons and to prevent accidental poisonings.</p> 	<p>Iraq - Mercury 1971 Pink-colored seed grain coated with a mercury fungicide was tragically consumed by Iraqis tragically affecting over 40,000 people.</p> 	<p>Bangladeshi 1970s Arsenic poisoning Tubewells, drilled to provide clean drinking water, are contaminated by arsenic resulting in millions of people harmed.</p> 	<p>First Modern Toxicology Textbook 1975 Louis J. Casarett & John Doull edited, <i>Toxicology: The Basic Science of Poisons</i>, in 1975.</p> 	<p>Love Canal Disaster 1978 August 7, 1978 US President Jimmy Carter declared Love Canal a federal emergency. 42 million pounds of over 200 chemicals contaminated Love Canal, disrupting many lives.</p> 	<p>IUTOX 1980 International Union of Toxicology American Board of Toxicology (ABT) 1979 - First exam Aug. 1980 Academy of Toxicological Sciences (ATS) 1981</p> 	<p>Times Beach 1983 Dangerous levels of dioxin discovered in Times Beach, MO. EPA orders the town evacuation and makes it a Superfund site. All residents gone by 1985.</p> 	<p>Bhopal Disaster Dec. 3, 1984 Accidental release 400 metric tons of methyl isocyanate from a Union Carbide Indian pesticide plant in heart of city resulted in the killing thousands, and injured 100s of thousands.</p> 	<p>Chernobyl Accident April 26, 1986 The Chernobyl nuclear power plant accident produced a plume of radioactive debris over the Ukraine, Eastern Europe, Scandinavia, UK and eastern USA.</p> 	<p>Tokyo Subway Sarin Gas Attack 1995 Members of religious group Aum Shinrikyo released sarin gas in 5 places in Tokyo subway, killing 12 and injuring 6,000.</p> 	<p>Vioxx (1999-2004) A nonsteroidal anti-inflammatory, COX-2 selective inhibitor for treatment of osteoarthritis, produced by Merck & Co. and voluntarily withdrawn because of risk of heart attack & stroke.</p> 

Historical Milestones and Discoveries Which Shaped the Toxicology Sciences

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Knowledge of the toxic and healing properties of plants, animals, and minerals has shaped civilization for millennia. The foundations of modern toxicology are built upon the significant milestones and discoveries of serendipity and crude experimentation. Throughout the ages, toxicological science has provided information that has shaped and guided society. This poster presentation examines the development of the discipline of toxicology and its influence on civilization by highlighting significant milestones and discoveries related to toxicology. The examples shed light on the beginnings of toxicology, as well as examine lessons learned and re-learned. This project is also an effort to examine how toxicology and the toxicologist have interacted with other scientific and cultural disciplines, including religion, politics, and the government. Toxicology has evolved to a true scientific discipline with its own dedicated scientists, educational institutes, sub-disciplines, professional societies, and journals. It now stands as its own entity while traversing such fields as chemistry, physiology, and pharmacology. We invite you to join us on a path of discovery and to offer your suggestions as to what are the most significant milestones and discoveries in toxicology. An interactive version of the poster is available at www.asmalldoseof.org.

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