Toxicology Through the Ages

The Eber Papyrus
- Ancient Egypt circa 1500 B.C.
- Described poisons such as arsenic, mandrake, hemlock, as well as purgatives such as castor oil and senna
- Senna: "The Guardian of the Royal Bowel Movement"

Toxicology Through the Ages

Poisons and the Hunt
Oubain
- Masai hunters of West Africa used poison tipped darts from Strychnos plant species
- MOA: Inhibits Na/K pump (digitalis like)
- David Livingstone one of the first to describe its use
Poisons and the Hunt

**Curare**
- *Chondrodendron tomentosum* (usual mixed with *Strychnos* species)
- Used by the Indians of Central and South America, first described in 16th century by Spanish explorers
- MOA: bind to motor end plate, inhibits ACh
- Tubocurare, pancuronium, vecuronium

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William Shakespeare (and his love for poisons!)

- The Witches of Macbeth. Act IV, Scene 1
  - “Double, Double toil and trouble...”

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Poison Arrow frogs

- *Phyllobates, Dendrobates*
- Used by natives of Colombia, Costa Rica
- Over 200 toxins identified, most potent is batrachotoxin
- MOA: prevents closure of Na channels
- Arrows dipped in toxin good for 1-2 years
Toxicology Through the Ages

Upas Tree
- Antaris toxicaria
- Native to tropical Asia
- Active: cardiac glycoside
- Medieval travelers warned to stay away from its "noxious fumes"
- Used on arrow tips, used for execution

Solanaceae Family
Mandrake
- Mandragora officinarum
- Active: hyoscine
- Mediterranean Sea
- Root system can look 'human'
- Associated with witchcraft and the black arts
- Used in surgery to dry mucous membranes

Mandrake

Literary references:
- Genesis 30:14; Shakespeare's Henry VI, etc

The Doctrine of Signatures
- Proposed by Paracelsus
- The magical/curative properties of a plant could be predicted from its appearance
**Toxicology Through the Ages**

**Mandrake**

The Legends
- The “Terrible Shriek”
  - Romeo and Juliet (Act IV, Scene III)
- How to harvest mandrake
- The Witch’s broomstick
- Lycanthropy
- The Magloire of France

**Deadly Nightshade**

Atropa belladonna
- Belladonna (beautiful woman)
- Active: atropine
- Blocks ACh (anticholinergic)
- Treated insomnia
- Witch’s brew
- Uses include treatment of OP poisoning, ocular exams

**Jimsonweed**

Datura stramonium
- Active: hyoscine
- Used in slave trade
- Decimated the troops of Mark Anthony in 36 A.D.
- Jamestown epidemic
- Used to treat epilepsy, melancholy, mania
- Abused today for hallucinatory effects
Toxicology Through the Ages

Trial by Ordeal
- Involved administration of a toxic plant extract to a suspected criminal
- Death implied guilt, survival innocence
- Cheating the test
- One plant used was Physostigma venenosa

Toxicology Through the Ages

Physostigmine
- Acetylcholinesterase inhibitor
- Robert Christison and his "experiments"
- Thomas Fraser: discovered that atropine could be used to treat poisoning with physostigmine
- 1875 Ludwig Laqueur: treatment of glaucoma
- 1934 Mary Walker: treatment of myasthenia gravis

Toxicology Through the Ages

Intentional Poisonings
- Began in ancient Greece
- Roman emperor Silla: first law against poisoning
- Punishment:
  - Rich: lose property or exiled
  - Poor: fed to wild beasts
Toxicology Through the Ages

Arsenic
- Used since 2000 B.C.
- Ulcers, parasites, enemas, acne, syphilis, malaria
- Sugar-like appearance
- Tasteless, odorless, colorless
- Favorite poison of the nineteenth century
- "Arsenic and Old Lace"

Toxicology Through the Ages

Arsenic: Victorian England
- Uses: rodenticides, fly papers, coloring agents, agriculture, facial complexion
- Most common poison used in murder
- Anybody could buy it until 1851

Toxicology Through the Ages

Famous Poisoners
- Renaissance - "The Age of the Poisoner"
  - Venice Council of Ten - poisoning service
  - Borgias - Arsenic/phosphorous
  - Catherine de Medici - sick/poor
  - Catherine Deshayes - sold poisons to women who wanted to get rid of their husbands
**Toxicology Through the Ages**

**Aconitine**
- Aconitum napellus
- First mentioned in Greek mythology, Ovid
- Wolfsbane, monkshood
- Very popular in ancient Rome, eventually made illegal to cultivate
- Increases uptake through Na channel, arrhythmias, depressed respirations

**Universal Antidote**
- King Mithridates VI of Pontus
  - Repeatedly poisoned as youth
  - Mithridatum - developed by Roman RPhs, 36 ingredients
  - Drank it every day
  - Tried suicide in later years but found out he was “poison proof”

**Cocaine**
- Erythroxylon coca
- Used for over 2000 years
- Incas developed first cocaine plantations
- Believed that it was supplied by the gods to satisfy hunger, forget misery, increase vigor
- Only used by the elite of the tribe
Toxicology Through the Ages

Cocaine
- Brought back to Europe
- 1814: Sir Humphrey Davy hoped it would be a food substitute
- 1884: Sigmund Freud and Über Coca - cure for morphine addiction
- 1884: Carl Koller - cocaine as an anesthetic, used in eye surgery

Merck, Parke-Davis - first drug companies to start manufacturing cocaine
- Carl Ludwig Schleich - spinal anesthesia
- Uses of cocaine began to be reported for other types of surgery e.g. rectal surgery, used extensively in dentistry also

Deaths and serious complications began to be reported soon after use escalated
- Medical community caught off guard - difficult time with concept of coca vs cocaine
- Early on most problems were usually due to physicians administering too much cocaine during procedures
- By the turn of the century, recreational use tended to cause more problems esp. addiction
- Magnon’s Syndrome - feeling of small animals crawling across or out of skin
Toxicology Through the Ages

Cocaine in Literature

- R.L. Stevenson: *The Strange Case of Dr. Jekyll and Mr. Hyde*
- Conan Doyle: *Sherlock Holmes in The Sign of Four*

Toxicology Through the Ages

Jekyll and Hyde
- Buying a "A particular salt" – cocaine
- Felt "A deadly nausea... a horror of the spirit" – commonly seen with use (esp. first timers)
- "ten times more wicked" – aggression
- "hair growing thickly" upon hands – feeling of skin crawling
- "the evil side was less robust" – addict appearance

Toxicology Through the Ages

Coca Cola
- Developed by a pharmacist in Atlanta circa 1887
- Originally called Pemberton's French wine coca
- Cured physical and mental exhaustion
- Prohibition led to removal of wine and replaced with sugar syrup
Toxicology Through the Ages

Coca Cola
- Contained 100 mg cocaine/gallon or 1.5 mg/oz
- Also contained extracts of Cola nitida which acted as a caffeine source
- Cocaine removed 1904
- Government tried to get company to change name but 'Coca cola' and 'coke' had become household names

Toxicology Through the Ages

Opium
- Papaver somniferum
- Used by Sumerians as early as 4000 B.C. as remedy for colicky child
- Milky exudate of seed capsule contains 25% opium alkaloids (17% morphine, 4% codeine)

Toxicology Through the Ages

Opium
- Many uses early on but primarily as antidiarrheal and to induce sleep
- 16th century: Paracelsus advocated use as analgesic (laudanum)
- 1804: Armand Sequin isolated morphine
- 1853: hypodermic needle
**Toxicology Through the Ages**

**Heroin**
- 1874: Alfred White: developed diacetylmorphine
- 1898: Bayer markets heroin as a cough remedy
- High addictive properties not realized initially

**Ergot Alkaloids**
- Claviceps purpurea
- 600 B.C. - Assyrians wrote of noxious pustules in grain, noxious grasses that cause women to "drop the womb"
- 994 A.D. - Aquitania, France: 40,000 people die from contaminated grain

**Toxicology Through the Ages**

**Ergot alkaloids**
- Toxic effects: delirium, seizures, vasoconstriction, gangrene
- Middle Ages: St. Anthony’s fire
- Salem Witch trials
- Used as an abortifacient, assist in childbirth, control postpartum hemorrhage
- MOA: interfere with serotonin reuptake centrally; partial alpha adrenergic agonist
- Uses today: ergonovine - stimulate uterine smooth muscle; ergotamine - vascular headaches