Toxic Outbreaks of Historical Importance

Stephen W. Munday, MD, MPH, MS
Sharp Rees-Stealy Medical Group, Inc.
San Diego Division, CA Poison Control System

Toxic Outbreaks of Historical Importance

- Ergot Alkaloids – 12th Century France
  - Thousands affected (St. Anthony’s Fire due to Claviceps purpurea contamination of grain)
  - Convulsive and/or Gangrenous forms

Lead, England 1700s

- Devonshire Colic
  - Likely caused by lead-contaminated cider
Historical Outbreaks

**Cadmium – Japan ~1910-1950s**
- *Itai-itai* – "Ouch-ouch" disease
- So called due to severe pain from osteomalacia-induced fractures
- Prevalence markedly increased in post-menopausal women.
- Believed to be caused by cadmium-containing mine tailings that contaminated the irrigation water used to grow rice that was eaten by those affected.

**Cobalt – Canada 1960s**
- Beer-drinker’s Cardiomyopathy
- Co added to beer to stabilize the foam
- Associated with cardiomyopathy in alcoholics but not non-alcoholics
- Some have theorized this is due to thiamine deficiency since cobalt affects the thiamine pathway and alcoholics are often thiamine deficient.

**Medicinal disasters: Thallium**
- Location: US
- Date: 1920s-1930s
- Significance: Treatment of ringworm; 31 deaths
Medicinal disasters: Diethylene glycol
- Location: US
- Date: 1937
- Significance: Elixir of sulfanilamide contaminated by DEG caused over 100 deaths due to renal failure

Medicinal disasters: Thorotrast
- Location: US
- Date: 1930s-1950s
- Radiographic contrast agent containing thorium dioxide that was concentrated in the RES including the liver and spleen
- Significance: Hepatic angiosarcoma rate increased over 100 fold

Medicinal disasters: Phenobarbital
- Location: US
- Date: 1940-1941
- Significance: Sulfathiazole antibiotic contaminated with phenobarbital; 82 deaths
Medicinal disasters: Diethylstilbestol (DES)
- Location: US, Europe
- Date: 1940s-1970s
- Used to prevent miscarriages or premature delivery
- Significance: Endometrial/Cervical/Vaginal carcinoma in daughters, Testicular cancer in sons & Breast cancer in users.

Medicinal disasters: Stalinon
- Location: France
- Date: 1954
- Significance: Severe neurotoxicity including cerebral edema from triethyltin – used to treat boils

Medicinal disasters: Clioquinol
- Location: Japan
- Date: 1955-1970
- Used topically and orally as an antibacterial and antiparasitic agent
- Significance: Subacute myelooptic neuropathy (SMON): 10,000 symptomatic with a syndrome that involves sensory and motor disturbances in the lower limbs and visual changes; some had green tongues
- Never noted before or after this period so many are not convinced clioquinol was the cause

Bonus: What’s this?
Medicinal disasters: Thalidomide

- Location: Europe
- Date: 1960s
- Used as a sedative and anti-nausea drug in pregnant women
- Significance: 5000 cases of phocomelia (fore-limb shortening) in Europe; it never was approved in the US

Medicinal disasters: Pentachlorophenol

- Location: US
- Date: 1967
- Used in hospital laundry
- Significance: 9 neonates ill, 2 deaths.
- Presented with: fever, sweating, renal failure and acidosis

Medicinal disasters: Benzyl alcohol

- Location: US
- Date: 1981 (MMWR June 11, 1982)
- Used as a preservative in IV solutions
- Significance: Gasping syndrome / acidosis seen in neonates receiving large amounts of benzyl alcohol via IV solutions
- Disappeared once benzyl alcohol exposure to neonates was limited
**Medicinal disasters: Acetaminophen-cyanide**
- **Location:** Chicago
- **Date:** 1982
- **Significance:** Tampering incident resulted in 7 homicides due to cyanide poisoning

![Acetaminophen molecule](image)

**Medicinal disasters: L-Tryptophan**
- **Location:** US
- **Date:** 1989
- **Significance:** Eosinophilia-myalgia syndrome
  - Scleroderma-like skin changes associated with eosinophilia and myopathy
  - Epidemiologic and chemical evaluation suggested that it **MAY** have been due to contaminated L-tryptophan from a single manufacturer
  - Similar to 1981 Spanish toxic oil syndrome

![Image of skin changes and tryptophan bottle](image)

**Medicinal disasters: Diethylene glycol**
- **Location:** Haiti
- **Date:** 1996
- **Significance:** Acetaminophen elixir contaminated with DEG; renal failure; >88 pediatric deaths

![Map of Haiti and image of DEG](image)
Toxic Outbreaks of Historical Importance

- Methylenedianiline - Epping, England, 1965
  - Contaminated flour caused 84 cases of cholestatic jaundice

- Hexachlorobenzene - Turkey, 1956
  - Wheat seed with fungicide was eaten instead of planted
  - ~4,000 cases of porphyra cutanea tarda

Toxic Outbreaks of Historical Importance cont'd

- PCBs (polychlorinated biphenyls) & PCDFs (polychlorinated dibenzofurans)
  - Japan, 1968: Yusho or Rice oil contaminated by heat-exchange fluid from a leaking pipe
  - 1,600 affected
  - Chloracne, hyperpigmentation and increased liver cancer and reproductive effects
  - Taiwan, 1979: Yu-Cheng (Oil Disease) 2,000 affected
  - Similar to Yusho Effects
Historical Outbreaks

**Toxic Oil Syndrome**
- Spain, 1981
  - Associated with 2% aniline denatured rapeseed oil
  - Sclerodema-like plus eosinophilia and pulmonary hypertension
  - Caused over 600 deaths
  - 1989 Eosinophilia-myalgia syndrome possibly associated with some tryptophan supplements was clinically similar

**Arsenic**
- France, 1828
  - 40,000 with neuropathy due to arsenic in bread and wine
- Staffordshire, England 1900
  - Arsenic-contaminated sugar in beer with 6,000 cases of neuropathy and 70 deaths

**Arsenic**
- Bangladesh/West Bengal India
  - Arsenic contaminated ground water from wells
  - 60 million exposed in Bangladesh alone
  - Over 220,000 in West Bengal affected (skin changes/skin cancer)
Historical Outbreaks

Methyl Mercury
- Minamata Bay, Japan 1930s-1950s
  - Industrial waste contaminated with inorganic Hg was concentrated up the food chain as methyl Hg after being dumped in the bay.
  - Many cases of methyl Hg poisoning in humans & animals who ate seafood from the bay.
- Iraq, 1971
  - Methyl Hg treated seed grain intended for planting was mistakenly ingested.
  - >400 deaths

Minamata Disease

Methyl Isocyanates
- Bhopal, India 1984
  - A series of safety factors that were not appropriately engaged, led to an explosion that released methyl isocyanate.
  - Many humans & animals were acutely affected – skin, mucous membranes and respiratory tract.
  - Estimates vary but thousands died acutely and likely hundreds of thousands were injured (many with residual effects).

Bhopal, India
Historical Outbreaks

**Triorthocresyl Phosphate (TOCP)**
- US 1930-1931 ("Prohibition")
- Alcohol containing patented "medication" ("Jake") from Jamaican ginger was formulated with TOCP and caused upper and lower extremity neuropathy
- Similar to OP pesticides
- 50,000 people developed Ginger Jake Paralysis

**2, 3, 7, 8 TCDD (Dioxin)**
- Seveso, Italy 1976
  - A nearby 2, 4, 5, trichlorophenoxyacetic acid (2, 4, 5 T) facility exploded
  - Chloracne developed in those most exposed
  - No clear evidence of increased cancer risk in this group
  - This industrial accident led to the Seveso Directive (European Community Industrial Safety Regulations)

**Chloracne due to Dioxin Poisoning**

Ukrainian President Viktor Yushchenko