St. Anthony’s Fire
Introduction

- **Caused by ergot**
  - A filamentous fungus
  - Genus *Claviceps*
  - Parasitic
- **Found in grains**
  - corn, wheat, barley, oats, rice, and rye
- **Spread via spores**
  - Transported by wind, rain, insects and other animals, or by plant-to-plant contact
Introduction

- Infection of plants can be easily overlooked
  - Mimics the shape of grains

- Fungal form is the most dangerous
  - Causes ergotism
  - Infection usually follows oral consumption of contaminated food ie/ rye bread
Overview

- History
- Signs & Symptoms
- Mechanism of Action
- Drug Interactions
- Treatment
- Therapeutic Uses
- LSD
History

Eleusinian Mysteries

- Religious cult between 1500BC and 396AD
- Cult of Demeter and Persephone promising pleasant afterlife
- Drank ritual drink *kykeon* before having visions of afterlife, hallucinations
- *Kykeon* likely contained ergotized barley
- Extremely secretive, death penalty for revealing secrets and visions
Tollund Man

- Perfectly preserved body found in Danish peat bog, from 400BC
- Rope around neck, likely drowned as ritual sacrifice to earth goddess
- Stomach contained porridge with very high levels of ergot in the barley
- Ergotised porridge likely taken to induce hallucinations before ritual sacrifice
Medieval Ergot Epidemics

- Rhine Valley had many ergotism outbreaks recorded between 7th and 17th centuries, rye bread was staple food
- Became known as St. Anthony’s Fire as monks of St. Anthony specialized in treatment
- Also called *Ignis Sacer* and Holy Fire
- 40,000 deaths in southern France in 944AD
Convulsive ergotism called Dancing Mania, St. Vitus’s Dance, as people screamed, babbled, convulsed, and ‘danced’ in streets: shut down Strasbourg in 1418

Often attributed to demons and madness or divine intervention

Scientific breakthroughs in 1670s when ergotism was connected bread and later to ergotized rye; ergot life cycle identified in 1853
Salem Witch Trials

- 1692 Salem, Massachusetts had a wet harvest, rye bread likely contaminated with ergot.
- 8 girls in Salem experienced hallucinations, convulsions, burning skin sensations.
- Pastor’s daughters affected.
- Immediately accused other women of bewitching them.
Those accused of witchcraft were mostly unpopular, poor, and non-churchgoing.

Over 150 people imprisoned for witchcraft that year.

20 people executed, 5 died in prison.
Salem Witch Trials
Russia

- Ergotism very common until 1945
- Rye bread was staple food in Russia until 1945, when potatoes were planted instead and pesticides/fungicides introduced
- Government statistics show that areas with wet weather and rye crops had outbreaks of trembling, confusion, hysteria, and hallucinations
- 1926, there were 10,000 confirmed cases of ergotism in Russia
Ergot Scare: Pont-Saint-Esprit

- 1951, French town of Pont-Saint-Esprit had 200 people suffering from confusion, hallucinations, ‘madness’, and cold extremities
- 7 deaths and 50 people interred in insane asylums
- Linked to bread
- Misidentified as ergotism, later proved to be mercury poisoning
Signs and Symptoms

- Ergotism can be caused by
  - Acute ingestion of large amounts of fungus
  - Chronic ingestion, usually via contaminated food

- 2 main categories of symptoms
  - Gangrenous
  - Convulsive
Gangrenous Symptoms

- Dry gangrene caused by tissue necrosis
- Fingers and toes are affected first
  - Followed by arms and legs
- Infection may result and can lead to death
- Amputation is often the only solution
- Happens in livestock as well as in humans
Convulsive Symptoms

- Includes tingling sensation in the fingers, tinnitus, dizziness, hallucinations, seizures, nausea and vomiting
- Mental disturbances such as mania, psychoses and delirium may also be present
Kinetics

- Many compounds; absorbed to varying degrees from GI tract
  - Absorption increased in the presence of caffeine (ergotamine)
- Extensively metabolized by CYP450
  - Cinx in liver failure
- Certain drugs inhibit metabolism
  - Protease inhibitors
  - Macrolide antibiotics
Mechanism of Action

- Ergot compounds are structurally similar to the biogenic amines
  - Dopamine
  - Serotonin (tryptophan)
  - Norepinephrine

- Serotonergic system particularly affected
  - Accounts for many of the convulsive symptoms
  - Similar to symptoms of schizophrenia and epilepsy
Mechanism of Action

- **N/V/D**
  - stimulated serotonin receptors of the GI tract and emetic centres of the brain

- **LSD**
  - a weak partial agonist at 5HT-2 receptors in the brain
  - Results in many of the convulsive symptoms
Mechanism of Action

- All ergot compounds exhibit some vasospastic properties
  - Effects on serotonin and alpha adrenergic receptors in blood vessels

- St. Anthony’s Fire
  - Body feels extremely warm due to constriction of peripheral vessels
Mechanism of Action

- Results in myocardial or peripheral ischemia
  - Gangrene, infection, amputation, death
  - Cinx in CAD, PAD, uncontrolled HTN

- Uterine smooth muscle is also affected by serotonergic and alpha adrenergic effects
  - Contractions may lead to miscarriage or preterm birth
Treatment

- 16th and 17th century folk remedies
  - “green ointment of herbs, earthworms stamped in vinegar, swan or goose dung stamped with the white or yolk of the egg, or doves dung in salad oil”

- Later remedies
  - “British Oil” originally containing bitumen,
  - later preparations with oil of turpentine, oil of rosemary and Barbados tar
Treatment

- Modern-Day Treatment
  - Early detection and immediate discontinuation of exposure vital
  - Severe ischemia may be irreversible

- If overdose is detected early
  - Activated charcoal
  - Gastric lavage if patient is conscious
Treatment

Treatment of hallucinations

- Stopping exposure to toxin usually effective

- Intracranial injection of combination serotonin and cholinergic drugs successful treatment in mice
Treatment

➢ Treatment for ischemia
  • Vasodilators
    • Nitroprusside, nifedipine, captopril, prostaglandins
  • Anticoagulants
    • Dextrin, heparin

➢ In extreme cases of ischemia
  • Regional sympathectomy
  • Hyperbaric oxygen chamber
  • Hydrostatic dilation with balloon catheters
Medicinal Uses

Bromocriptine

- Stimulates D2 receptors in the brain
  - Treatment for Parkinson’s
- Female infertility, abnormal lactation, amenorrhea, hypogonadism, and acromegaly
  - D2 stimulation
- Effective in cocaine withdrawal
- Opiate weaning?
Medicinal Uses

Pergolide

- Anti-Parkinson
- 1000x stronger than bromocriptine
- Inhibits prolactin
- Effects on leutinizing and growth hormone
Medicinal Uses

- Methysergide
  - Prophylactic migraine treatment
  - Activation of 5HT-1D receptors in cranial blood vessels
    - vasoconstriction
  - Linked to retroperitoneal fibrosis
Medicinal Uses

- **Ergotamine**
  - Intermittent treatment of migraines
  - Similar MOA as Methysergide
  - Cinx in pregnant women

- **Migraine treatments are non-selective**
  - Overdose or drug interaction may result in ergotism
  - Triptans are a safer new alternative for migraine treatment
Medicinal Uses

- **Methylergonovine**
  - Used after delivery
  - Initiates strong contractions of uterine smooth muscle
  - Contract the uterus, prevent hemorrhage, promote placental passage
LSD

- Synthesized by Albert Hoffman in 1938
  - Accidentally dosed himself
  - Had the first ‘acid trip’
    - Hallucinations, synesthesias, emotionality, body distortions

- Used as a psychoanalytic drug
  - Was thought to elicit repressed memories
  - Given to alcoholics as part of counselling process
LSD

- Believed to be helpful in treating schizophrenia
  - Tried to map out a ‘model psychoses’ using animals
  - Later realized that schizophrenia and acid trips are very different
  - Therapeutic use discontinued in the ’60s
LSD

➢ CIA

• Attempted to use it for mind control
  • Cold War, Russian spies

• Tested it on unsuspecting civilian and military ‘volunteers’

• Caused mental trauma and suicides in subjects

• No real use was found for it
LSD

- Eventually became accessible to the public
  - Counterculture committed to social change and cultural liberation
  - Timothy Leary’s League of Spiritual Discovery was a church in the ’70s based on LSD use

- Widespread stories of bad trips and flashbacks decreased its use
  - Legislation was imposed prohibiting LSD
LSD

- Today it is part of the ‘party drug’ scene
  - Along with ecstasy and mushrooms
References

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References

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