Fungal intoxications

- These are caused by consumption of metabolites produced by fungi, when growing in food.
- These metabolites are called mycotoxins.
- Grains, oilseeds, fruits and vegetables are mostly involved if they are stored at high humidity (≥ 0.75) or if they are not properly dried before storage.
- Poor dry storage practices of grains and other foods leads to mould growth and production of mycotoxins.
- Of significance to public health is aflatoxicosis.

Aflatoxicosis

- Aflatoxicosis is caused by aflatoxins produced by the fungi, e.g. Aspergillus flavus.
- Four types of aflatoxins have been described i.e. aflatoxin B₁, B₂, G₁ and G₂. Animals consuming feeds contaminated with aflatoxin B₁ leads to secretion in the milk of aflatoxin M₁ and M₂.

Effects of aflatoxins

- When consumed in large doses, they are lethal in causing acute hemorrhagic syndromes
- Sub-lethal doses cause histotoxic changes
- Long term consumption of small doses cause liver tumors as these are potent carcinogens.

Prevention of aflatoxicosis

- Proper drying and storage of grains and other affected foods
- Quality control of potentially hazardous foods to ensure that they do not contain above the allowable limits of 20 ppb before consumption by use of appropriate analytical tests.
- Use of fungicides as seed dressings to protect stored cereals and other foods like pulses and potatoes against fungal invasion.

CHEMICAL FOODBORNE INTOXICATION

- This is a type of food borne intoxication arising from consumption of food containing poisonous chemicals.
- These may be intentionally or unintentionally added to foods as a result of producing, processing, transporting or storage.
- A number of substances can enter the food chain from the environment and through their use as growth promoters or veterinary therapeutics giving rise to chemical residues.
Chemical substances involved

Chemical food borne intoxication involve the following substances:
- Heavy metals e.g. antimony, mercury, arsenic, fluoride, lead, cadmium, cyanide etc.
- Pesticides and insecticides e.g. DDT, BHC Organochlorines and organophosphates.
- Herbicides
- Fungicides e.g. organomercurials

Chemical substances involved...

- Preservatives e.g. nitrates, nicotinate, etc
- Antibiotics e.g. penicillin, tetracyclines, chloramphenicol etc.
- Radionuclides e.g. cesium, strontium, radium, molybdenum, barium, ruthenium, lanthanum, iodine isotopes etc.

How chemicals enter foods

- Accidental contamination by Heavy metals, Pesticides, and radionuclides.
- Intentional addition e.g preservatives such as nitrite and sodium nicotinate for color preservation and fungicides used as dressing during storage.
- Leaching from containers e.g zinc galvanized containers by acid foods, copper surfaces, lead pipes, asbestos roofs.
- Usage: Presence of such chemicals in food as a result of use of their use in animal and crop husbandry
- Maliciously added to cause harm (is rare).

Clinical signs and symptoms

- Chemical food borne intoxication exhibit a very short incubation period, usually a few minutes to a few hours, with an average of one hour.
- Symptoms are mainly due to effect on gastrointestinal tract and central nervous system and include nausea, headache, convulsions, gastrointestinal irritation, abdominal cramps, vomiting and diarrhea, pallor, cyanosis, blurred vision, sweating, and collapse.
- Other signs may be due to effects on circulatory system.
- Symptoms of radionuclide toxicity depend on dose, time and organ affected.

Preventive measures

- Do not use utensils or containers that are able to leach chemicals such as antimony, cadmium, zinc, copper, etc.
- Use of coloured pesticides and proper storage of the same.
- Prevent contamination of foods when using insecticides.
- Prevent acid foods or carbonated liquids from contact with exposed copper.

Preventive measures

- Prevent misuse or avoid use of dangerous additive e.g. sodium nicotinate.
- Education of persons preparing food (e.g. possibility of Zn poisoning).
- Ensure that withdrawal periods are observed after use of pesticides and antibiotics in animal and crop husbandry.
Mushroom poisoning in US

• Every year across the United States, more than 9,000 cases of mushroom ingestion are reported to the American Association of Poison Control Centers.
• Many hundreds of cases of mushroom ingestions occur each year in California.
• Children under the age of 6 years account for a majority of these cases.
• In 85 to 90% mushroom not identified

Mushroom Structure

Features Useful for Identifying Poisonous Mushrooms

• Presence of an annulus (ring) on stalk
• Presence of a volva (cup) at base of stalk
• Scales on cap
• Spore color
  – How to make a spore print
  – Spore morphology
• Staining reactions of spores and cap

Poisonous Mushrooms

• Poisonous mushrooms contain compounds that are toxic to humans and animals.
• Mode of action well known yet generally there are few antidotes available.
• 7 major toxin groups are recognized as poisonous and an 8th toxin group of mainly gastrointestinal irritants.
• Toxins organized into 4 major categories based on physiological action.

Mushroom Toxins

I - Amanitins (Cyclopeptides)
II - Gyromitrin (Monomethylhydrazine)
III - Orellanine
IV - Muscarine
V - Ibotenic acid and Muscimol - already discussed
VI - Coprine
VII - Psilocybin (psilocin) - already discussed
VIII - Gastrointestinal irritants

Group A: Cellular Toxins

• Deadly toxins - also called protoplasmic toxins
• Cause cellular destruction and cell death
• Liver and kidney damage
• Three toxins groups in this category
  – I - Amanitins - Cyclopeptides
  – II - Gyromitrin - Monomethylhydrazine
  – III - Orellanine
Distribution of Amanitins (Cyclopeptide Toxins)

- Amanita bisporigera,
- A. phalloides,
- A. verna,
- A. virosa
- Galerina autumnalis,
- G. marginata, etc
- Lepiota spp
- Conocybe filaris

Destroying Angels
A. virosa and A. verna

Amanita phalloides

- One of the most sensational recent cases was the Oregon poisoning by *Amanita phalloides* that occurred in 1988
- A Korean woman had picked mushrooms that looked similar to ones that she used to pick as a child in Korea
- She had mistaken *Amanita phalloides* with what she thought were edible Paddy Straw mushrooms (*Volvariella volvacea*).
- Out of five people that had eaten these mushrooms, four received liver transplants and will take medication for the rest of their lives, and one was seriously ill, but recovered fully and didn't have to receive a transplant

Galerina autumnalis
Conocybe filiaris

Amanitins (Cyclopeptides)
- Toxins produced by Amanita phalloides (death cap) and Amanita virosa (destroying angel) (and others in this group)
- These two species account for 95% of all mushroom fatalities with A. phalloides causing the most poisoning
- Two cyclopeptide toxin types are phallotoxins and amatoxins

Phallotoxins
- Cyclopeptides (amino acids in a ring)
- Phallotoxins consist of 7 amino acids in a ring
- Cause cell destruction in liver?
- Attack plasma membrane - bind to protein receptors
- Cells leak Ca²⁺ and then K⁺
- Toxin enters cytoplasm and attacks organelles by rupturing lysosome membrane
- Evidence suggests these may not be lethal because it does not appear to be absorbed through the intestine in experimental animal studies

Amatoxins
- 8 amino acids in a ring
- Also cause cellular destruction
- Attacks cells with high rates of mitosis
- First attacks GI tract, produces lesions in stomach which cause initial symptoms - vomiting, severe diarrhea, pain
- Toxin is then absorbed into blood and carried to liver where most of the damage occurs

Amatoxins in the Liver
- Toxin invades nucleus of liver cells
- Destroys nucleolus and inhibits mRNA polymerase, these actions totally stop protein synthesis and lead to cell death
- Toxin circulates to kidneys and attack kidney cells then re-enter blood stream and back to liver
- Amatoxins are LETHAL

General Structure of Amatoxin
Symptoms of Amatoxin Poisoning

- Within 5 to 24 hours - diarrhea, vomiting, and pain (typically 6 to 12 hours)
- Short remission and apparent improvement
- 4 to 11 days later
  - severe liver damage
  - acute kidney failure
  - coma and death

Treatment of Amatoxin Poisoning

- No antidote
- Supportive care - pump stomach, restore fluid balance
- Activated charcoal to absorb toxins in stomach
- Plasmapheresis - separate blood, remove plasma, replace with fresh plasma, replace the clean blood in patient
- Liver transplant

Other Treatments

- Several drugs are thought to reduce uptake of amatoxins into liver cells based on animal studies but only anecdotal support is available in humans
  - High dose penicillin G (incredibly high levels)
    - one million units/kg on 1st day and 500,000 units
  - Silibinin (water soluble extract of milk thistle)
    - experimental drug in the U.S. obtainable through FDA

II - Gyromitrin (Monomethylhydrazine)

- Gyromitra brunnea,
- G. caroliniana,
- G. esculenta,
- G. fastigata, G. infula, G. gigas
- Helvella elastica, H. lacunosa
- Paxina spp.
- Sarcosphaera crassa

Morel

- Morchella

False Morel

- Gyromitra

Gyromitrin (Monomethylhydrazine)

- Gyromitra is the false morel
- Gyromitrin in the fungus hydrolyzes to monomethylhydrazine (MMH) - better known as rocket fuel which is highly toxic
- People eat these fungi anyway - MMH is volatile so parboiling will eliminate toxin
- Few fatalities in US but 2 to 4% of mushroom fatalities in Europe from this
Gyromitrin Poisoning
- Resembles *Amanita* poisoning but is less severe.
- Latent period of 6 - 10 hours after ingestion
- Followed by sudden onset of abdominal discomfort (feeling of fullness), severe headache, vomiting, and sometimes diarrhea, pain, cramps
- The toxin primarily affects the liver with additional disturbances to blood cells and the central nervous system - may result in loss of coordination, coma, convulsions

III - Orellanine
- Distribution - *Cortinarius orellanus*, *C. orellanoides*, *C. reainierensis*
- Long latent period of 3 to 14 days - attacking kidneys
- Burning thirst, excessive urination - first symptoms
- Followed by nausea, headache, muscular pains, chills, spasms, and loss of consciousness
- In severe cases, kidney failure may result in death
- Fatty degeneration of the liver and severe inflammatory changes in the intestine accompany the renal damage

Group B - Affecting Autonomic Nervous System
- These toxins affect the autonomic nervous system which controls the involuntary regulation of smooth and cardiac muscles, organs of the GI tract, endocrine system, and excretory system
- Not deadly unless large quantities eaten
- Some edible and sought after
- Two toxin groups (Muscarine and Coprine)

IV - Muscarine
- *Inocybe* species
- *Clitocybe* species
- *Amanita muscaria* and *Amanita pantherina* were previously thought to have contained primarily muscarine - but they contain insignificant amounts

Muscarine Poisoning
- Characterized by increased salivation, perspiration, and lacrimation within 15 to 30 minutes after ingestion
- With large doses, symptoms may be followed by abdominal pain, severe nausea, diarrhea, blurred vision, and labored breathing
- Intoxication generally subsides within 2 hours
- Deaths are rare, but may result from cardiac or respiratory failure in severe cases
- Atropine is the antidote (only one with antidote)

VI - Coprine Distribution
- *Coprinus atramentarius* - inky cap
- Possibly other *Coprinus* species
  - *Coprinus micaceus*
  - *Coprinus fuscascens*
  - *Coprinus insignis*
  - *Coprinus spp.* (some African species)
- *Clitocybe clavipes*
Coproline

- Coprine is an unusual amino acid - a derivative of glutamine - compound is non-toxic unless mixed with alcohol
- A complicating factor in this type of intoxication is that Coprinus atramentarius is generally considered edible (i.e., no illness results when eaten in the absence of alcoholic beverages)

Coproline Poisoning

- Hot and sweaty face, becoming flushed
- Flushing spreading to the neck and chest
- Rapid, difficult breathing,
- Rapid heart rate
- Violent headache
- Nausea and vomiting
- Lasts for 2-3 hours

Group C - Toxins Affecting the Central Nervous System

- V - Ibogaine Acid and Muscimol
- VII - Psilocybin and Psilocin
- Already discussed as hallucinogens
- Remember these can be fatal if enough are ingested

Group D: VIII - Gastrointestinal Irritants

- Large variety of mushrooms contain toxins that can cause gastrointestinal distress, including but not limited to nausea, vomiting, diarrhea, and abdominal cramps
- Symptoms similar to those caused by the deadly protoplasmic poisons - but usually have a rapid onset
- Some mushrooms may cause vomiting and/or diarrhea which lasts for several days

Poisoning in this group

- Fatalities relatively rare - associated with dehydration and electrolyte imbalances caused by diarrhea and vomiting, especially in debilitated, very young, or very old patients
- Replacement of fluids and other appropriate supportive therapy will prevent death in these cases.
- Chemistry of the toxins for this type of poisoning is virtually unknown
 Chlorophyllum molybdites

- Member of the Family Lepiotaceae
- This species is distinctive because gills turn an olive green as the mushroom ages - should be easy to avoid
- However if it is picked when it is still young it can confused with edible members of this family
- Common cause of gastro-intestinal problems

 Chlorophyllum molybdites

Biotoxications

- These are disorders resulting from ingestion of a poisonous substance (a biotoxin) present in the body of a plant or animal.
- Such substances are derived from plants or animals presumably as a result of metabolic activities.
- Only a small proportion of the species of fish and shellfish taken for human consumption throughout the world contain biotoxins.

Animals biotoxications

- This type of intoxication occurs as a result of consumption of poisonous animals.
- Animal tissues may be rendered poisonous by bacterial and enzymatic decomposition, but some are naturally toxic.
- Primary toxicity occurs due to inherent toxicants that arise due to normal metabolic processes.

Animals biotoxications cont.

- Secondary toxicity arises due to external toxicants contaminating animal tissues such as pesticides, heavy metals and drug residues.
- Inherent animal toxins are water soluble and heat labile.
- High concentrations of these toxins are usually found in viscera and dark meats.
- Most human poisoning involves secondarily transvectored toxins.
1. Toxic fishes

- They include puffers, triggerfish and parrot fish. The fish toxin affects the peripheral nervous systems. The fishes may become poisonous by feeding on poisonous marine organisms. A mortality rate of 50% may occur in humans.
- Types of biotoxications associated with fish include ciguatera poisoning, tetraodon poisoning and scombroid toxicity.

2. Mollusca

- Mollusca may either be inherently or secondarily toxic. Poisoning is mainly due to the transvection of dinoflagellate protozoa toxins by the mollusca.
- Mollusca are however not harmed by ingestion of dinoflagellates. Involved toxins are stored in the digestive glands, gills and siphore from where they poison vertebrates.
- Mollusca involved are oysters, mussels and clams, which feed on dinoflagellates and planktons containing alkaloids making them toxic.
Paralytic shellfish poisoning

This results from consumption of shellfish such as oysters, mussels and clams that have become toxic after consumption of toxic dinoflagellate protozoa, which pre-dominantly feed on planktons containing saxitoxin and accumulating the toxin in their tissues. Saxitoxin is heat stable, highly toxic with curare-like activity.

Paralytic shellfish poisoning

The toxin acts by blocking the propagation of nerve impulses without depolarization. Small doses leads to tingling of mouth and lips, while higher doses leads to paralysis, collapse and death. Mortality is about 1-22%. There is no known antidote.

Prevention
1. Avoiding sea foods from waters laden with toxic dinoflagellates.
2. Reduce toxin activity by heating above 100°C. Thorough cooking may reduce 70% of the toxin activity in muscles.

Prevention of animal biotoxications

1. Eating of unknown meats from vertebrates or invertebrates sources is always a threat to the consumer.
2. Local eating customs should be followed and local quarantine regulations strictly adhered to in order to reduce the risk.
3. Avoid sea foods and always heat foods to above 100°C to denature the inherent heat labile toxins that may be present in animal tissues.

3. Poisonous mammals

- Mammals are not commonly inherently poisonous, but secondary toxicity may affect many of them.
- The toxin may be of various types e.g. heavy metals, pesticides, toxic plants, therapeutics, fungal or bacterial toxins.
- Most human poisoning involves secondarily transvectered toxins.