The Good, the Bad, and the Ugly  
- mushrooms in medicine  
More of the good - fungi in modern medicine

Antibiotic resistance (e.g. MRSA, the methicillin resistant Staphylococcus). Antibiotic resistant bacteria underlines the importance of bioprospecting and looking for new active compounds.

Cephalosporin is an example of these. Isolated from Cephalosporium (now Acremonium) sp. - effective against Gram- bacteria + can be modified like penicillin.

Antibiotic trials on two bacteria, resistance for one antibiotic present in both.

Horizontal gene flow and the intense selection pressure increases chances for new emerging resistant strains
The Good, the Bad, and the Ugly - mushrooms in medicine

More of the good - fungi in modern medicine

Griseofulvin was first identified as the “curling factor.” The germ tubes of fungi, in presence of griseofulvin grew in spirals and curls. It was first assumed that this too was a cell wall synthesis inhibitor, more specifically, a chitin synthesis inhibitor.

Not true! It was later found out that the mode of action with the griseofulvin was inhibition of $\alpha$- and $\beta$-tubulins into dimers. In brief, griseofulvin appeared to be a antimitotic drug as well as disrupting the cellular transport processes (via the cytoplasmic microtubules).

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Penicillium griseofulvum

The Good, the Bad, and the Ugly - mushrooms in medicine

What is the significance of the antibiotics secondary metabolites in fungi?

They may just be random products that have no evolutionary significance.

However, one should bear in mind that they may have a serious function. Fungi having absorptive nutrition, and few means to find other resources, this might just be the ultimate competitive tool.

Poison your neighbor to assure sole custody of the currently available source.
Last time,…

- We talked about the good.
- *Tolypocladium* and cyclosporin
- *Penicillium* and penicillin
- Homeopathic remedies + polysaccharides
- Penicillin mode of action, its specificity, diversity and development of resistance
- *Penicillium griseofulvum* and griseofulvin.

Fungus of the day - *Gyromitra esculenta*

**Taxonomy:** Phylum (subphylum) Ascomycota  
Order - Pezizales  
Family - Helvellaceae  
Common names - false morel

*Gyromitra esculenta* is an apothecial ascomycete and a member of the order Pezizales known for their operculate unitunicate asci.

*Gyromitra esculenta* apothecium looks like a brown brain with its plentiful folds.

Typical operculate asci with the little lids.
Fungus of the day - *Gyromitra esculenta*

*Gyromitras* fruit at the same time as true morels do. They may also be involved with recent disturbances (fire and clear-cutting), or recent loss of a host tree by, say, a wind storm. However, the evidence for their relationship with a host is lacking.

Both these *Gyromitra* species fruit simultaneously with the true morels (*Morchella elata* here).

Fungus of the day - *Gyromitra esculenta*

We do not know for fact for either false or true morels but the true morels can form mycorrhizas in pure culture synthesis system. This may implicate that the ascomycetous disturbance-related species can be facultative mycorrhizal symbionts.

Ectomycorrhizal structures of *Morchella elata* with *Pinus contorta*. It is unclear whether this happens in nature as well.
Fungus of the day - *Gyromitra esculenta*

The concurrent fruiting of the true and false morels can be problematic since they can at times be hard to tell apart.

In contrast to morels (*Morchella* spp.) *Gyromitra esculenta* is contains a potent, heat-labile toxin, Gyromitrin or monomethylhydrazine (MMH).

MMH is a very cool toxin; its heat-lability (boiling point 87.5°C) allows its removal by cooking or boiling - it is highly volatile. Cook in the kitchen may fall ill whereas the guests may not show symptoms.

MMH must be potent since it or its derivatives are used as rocket fuel.

Fungus of the day - *Gyromitra esculenta*

Despite the toxic effects, *G. esculenta* is sold on many European markets; 2-4% of mushroom poisonings are attributed to *Gyromitras*.

The symptoms from MMH poisoning include nausea, diarrhea and abdominal pains. In addition, one often experiences faintness, loss of muscle control and fever.

In most severe cases, there may be convulsions, coma and - ultimately - death.

It seems that there is a narrow margin of exposure to the toxin resulting in no-effect or symptoms - often some remain unaffected while others may experience severe symptoms.
Today – the Bad

- Producers of fungal toxins that we acquire by ingestion.
- Poisonous mushrooms or fungi that produce secondary metabolites in spoiled food.
- Some, e.g. *Stachybotrys chartarum*, give symptoms when inhaled (hemorrhaging and respiratory irritation).

The Bad - toxic fungi

*Stachybotrys*-story. Cleveland, OH, has been experiencing a number (47 on last count with 16 dead infants) of sick homes. Particularly the children of these families have experienced pulmonary hemosiderosis (symptoms include chronic bloody cough, chest congestion).

The symptoms have been attributed to *Stachybotrys* species whose spores and/or mycelial fragments may cause symptoms like this.

*Stachybotrys* conidiophores and colonized walls. Fungal colonization of wooden structures in homes can get to levels which make evacuation necessary.
The Bad - toxic fungi

*Stachybotrys* is not the only indoor fungus causing problems.

The sick-building syndrome entails a number of common indoor fungi which inhabit wet construction materials and can cause respiratory problems, especially in those of us otherwise susceptible to asthma.

*Stachybotrys* has attracted spotlights mainly because the recent fatalities among infants. Possibly, the necessary toxic load is related to bodyweight: infants are first to suffer.

*Alternaria spp.* are common airborne fungi. They take advantage of wet, cellulose containing substrates such as your walls.

**The Bad - toxic fungi**

Other common indoor molds

Additional fungi that can be responsible for respiratory disorders at home would include *Alternaria, Penicillium, Aspergillus*, even *Cladosporium* when present in larger numbers.

Conidia and conidiophores of *Alternaria, Penicillium, Aspergillus* and *Cladosporium*.
More of the Bad...

- Fungi are common contaminants of food.

- We already know a few of these. Ergotism was covered with the perithelial ascomycetes.

- We will look into these very briefly: *Aspergillus* and *Fusarium*

The Bad - toxic fungi
The Bad - food spoiling fungi with toxins

*Aspergillus flavus* story: In 1960, thousands of turkeys died mysteriously. The turkeys hemorrhaged and had necroses in their livers.

It was concluded that the common denominator was peanut meal used to feed the poultry. The peanuts were colonized by *Aspergillus flavus* (toxin called aflatoxin).

What made aflatoxin so phenomenal was the fact that it was a very potent carcinogen.

This discovery coincided with UN program to promote high-protein peanut products to prevent protein deficiency in developing countries.
The Good, the Bad, and the Ugly - medical mycology

The Bad - food spoiling fungi with toxins

Another set of compounds worth mentioning here are the trichotheceines - mycotoxins of *Fusarium* spp. and *Tricothecium*.

*Fusarium* spp. in particular are often involved with various problems: oesophageal cancer, hemorrhagic syndrome, blood clotting failure and “hole in the head syndrome” in horses, emesis and oestrogenic syndrome of pigs.

Read more in Carlile et al. p. 441.

**The Bad - toxic fungi**

The other Bad fungi - poisonous macrofungi

Although we inhaled loads of spores everyday, ingested fungal toxins are better known and more of a concern. Generally, we can group the poisonous fungi into eight different types.

We will take a look at these one at a time.
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Group I: Amatoxin and phyllotoxin (cyclic peptides) containing species.

Examples: Amanita spp., Galerina spp.

Symptoms: 6-24h after ingestion - abdominal pain, upset stomach; then short remission after which recurring pain with liver and kidney dysfunction, coma and death.

Treatment: Induce vomiting, IV to maintain electrolyte balance, follow and line up for organ transplants.

The Good, the Bad, and the Ugly - medical mycology

Group II: Orellanin (cyclic peptides) containing species.

Examples: Cortinarius spp.

Symptoms: Delayed 3-14 hours after ingestion; acute or chronic kidney failure which can result in death.

Treatment: Induce vomiting, dialysis, follow and line up for organ transplants.
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Group III: Gyromitrin (monomethyl hydrazine - MMH) containing species.

Examples: Gyromitra spp.

Symptoms: 6-12h after ingestion - abdominal pain, upset stomach, loss of coordination, coma and death.

Treatment: Induce vomiting, IV to maintain electrolyte balance, treat seizures.

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Group IV: Muscarine containing species.

Examples: Amanita muscaria, Clitocybe spp.

Symptoms: Profuse perspiration, blurred vision, slow pulse and low blood pressure, recovery usually within 24h.

Treatment: Induce vomiting, atropine to maintain pulse and blood pressure, IV to maintain electrolyte balance.
Group V: Ibotenic acid and muscimol (mycoatropines) containing species.

Examples: *Amanita muscaria, Amanita* spp.

Symptoms: Up to 2h after ingestion, dizziness, delirium, hyperactivity, staggering, followed by deep sleep, recovery within 24h.

Treatment: Induce vomiting, IV to maintain electrolyte balance, antidepressants or balancers (diazepam) may be needed.

Group VI: Psilocin and psilocybin (indole derivatives) containing species.

We should all know what these are

*Psilocybe cubensis*  
*Psilocybe cyanescens*  
*Gymnopilus spectabilis*
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- medical mycology

Group VIII: Mixed bag of gastrointestinal irritants.

Examples: *Agaricus* spp.

Symptoms: Gastrointestinal irritation

Treatment: General supportive measures, induce vomiting as needed.

To sum this up...

• Fungi can cause problems through respiratory track (*Stachybotrys* and common allergens *Alternaria, Penicillium etc.*)
• You can also be affected via food stuffs (*Fusaria* and *Aspergillus flavus*)
• Finally, there are a few poisonous macrofungi.
This wraps up the bad.

• We contemplated on the airborne and ingested fungal toxins and covered a few examples of those. I leave it up to you to read more in the food spoilage and its ramifications to our well being.
• Next time, we will contemplate on the Ugly - the mycoses.