

Antimycotics

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Outline

- ① Introduction
- ② Polyens
- ③ Azoles
- ④ Alylamines and morfolines
- ⑤ Other

Mycoses

- Systemic mycoses

- systemic candidiasis
- cryptococal meningitis or endocarditis
- pulmonary aspergillosis
- rhinocerebral mucormycosis



6/16/73
aspergilloma

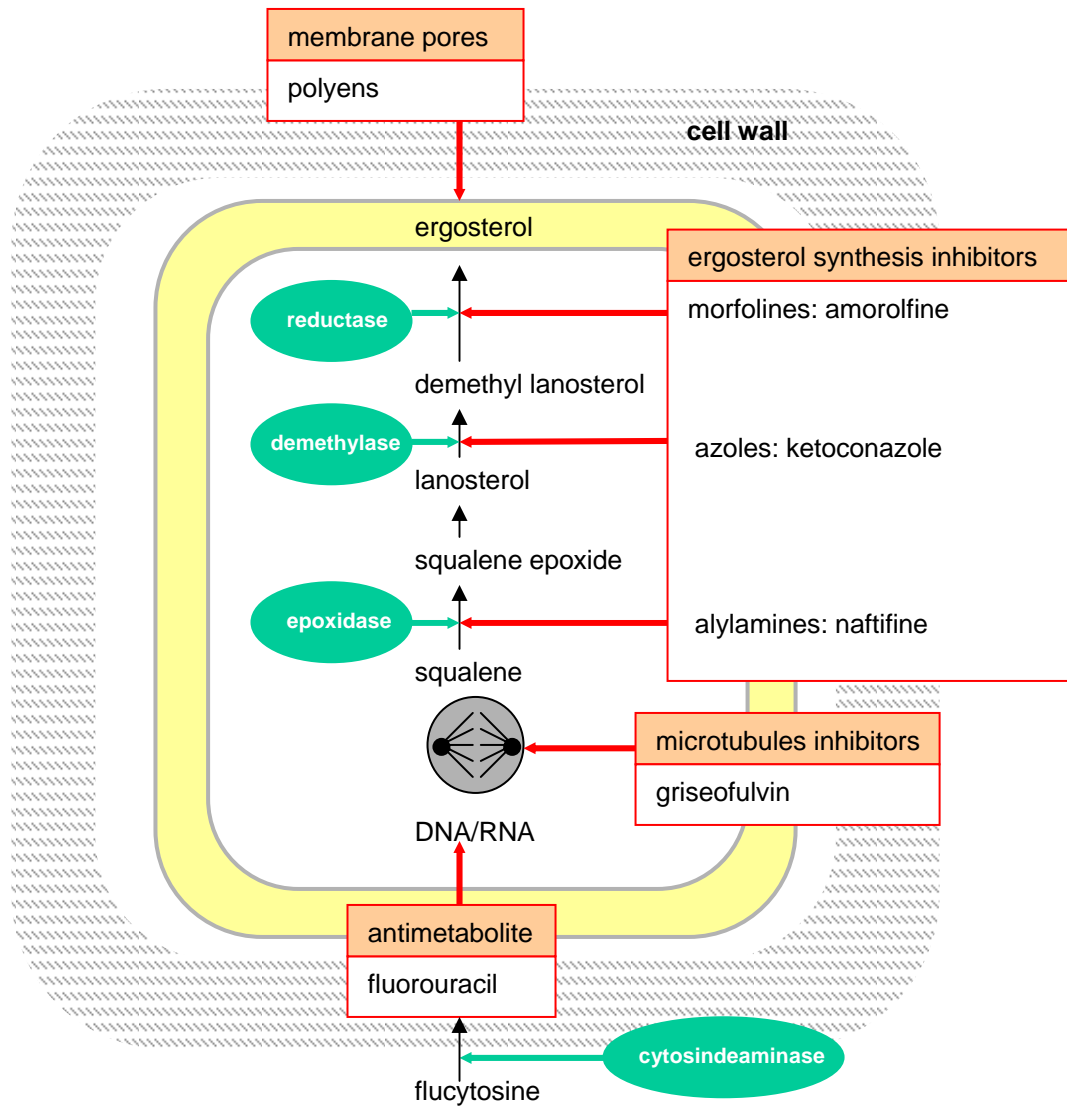
- Superficial mycoses

- dermatomycoses (tinea)
 - trichophyton
 - microsporum
 - epidermophyton
- superficial candidiasis



tinea pedis

Physiology



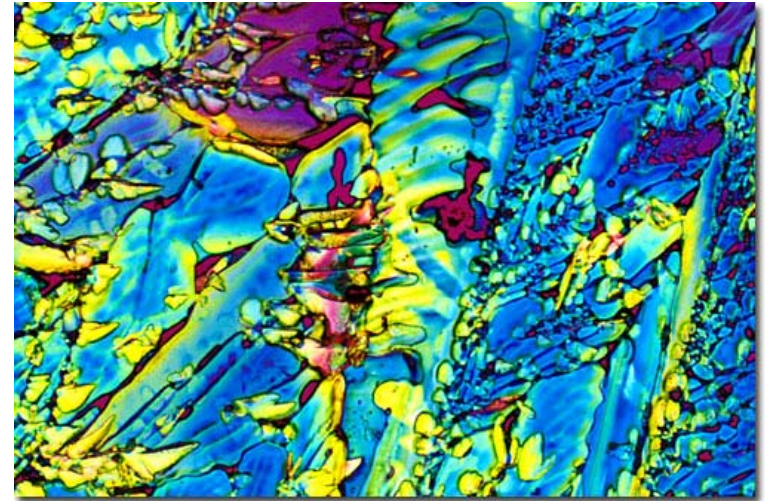
Polyens

- ➊ Introduction
- ➋ Polyens
- ➌ Azoles
- ➍ Alylamines and morfolines
- ➎ Other

Polyens

- Amphotericin B

- antibiotic
- macrolide structure
- binds to ergosterol in membrane
- creates pores - loss of K^+
- combination with flucytosine



amphotericin B

Indications

- severe systemic mycoses
- candidosis (endocarditis, pneumonia, systemic candidosis)
- aspergillosis and mucormycoses - drug of choice
- cryptococcal infections, including meningitis
- coccidiomycosis, histoplasmosis, blastomycosis

Polyens - Amphotericin B

Characteristics

- not absorbed from GIT
- fungistatic
- toxic
 - lipid complexes, β -cyclodextrin, liposomes, nanospheres
- normally does not cross BBB

Side effects

- nephrotoxic
 - renal impairment in 80% of patients
- hypokalaemia, hypomagnesaemia
- nausea, chills, fever, headache
- local reaction - slow i.v. infusion

Polyens

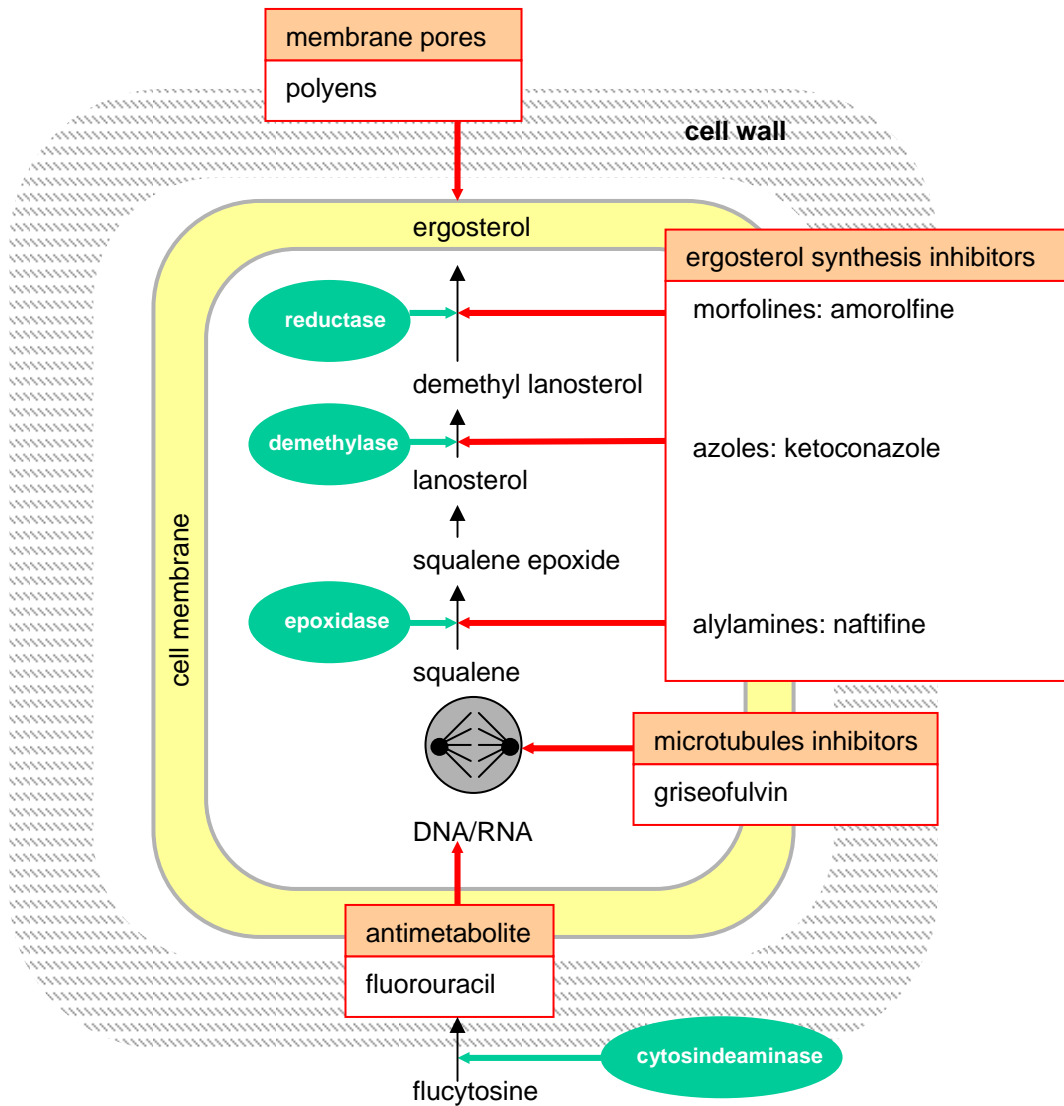
- Nystatin
 - similar to Amphotericin B
 - no absorption
 - highly toxic
 - only local

- Natamycin (pimaricin)
 - similar to nystatin
 - local therapy

Azoles

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- 2 Polyens
- 3 Azoles
- 4 Alylamines and morfolines
- 5 Other

Physiology



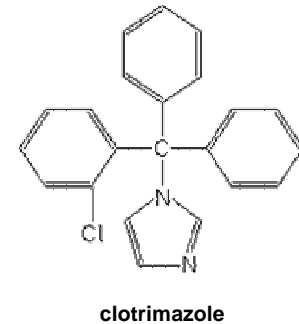
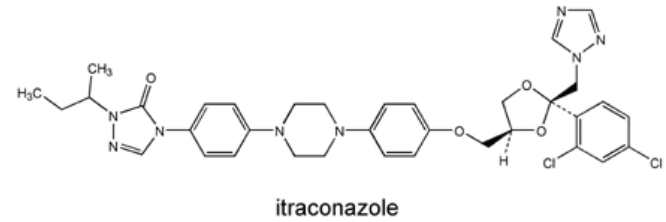
Azoles

- General characteristics & action

- synthetic
- fungistatic
- inhibit fungal CYP450 3A
- alter fluidity of membrane
- inhibit replication
- imidazoles and triazoles

Indications

- topical use (some also have antibacterial activity)
- systemic use – local and systemic mycoses



Azoles

- Miconazole
 - obsolete
- Ketoconazole
 - first azole for oral administration

Indications

- systemic candidosis, coccidiomycosis, histoplasmosis, skin mycosis

Side effects

- nausea, vomiting, hepatopathy, inhibition of steroid hormones production

Interactions

- CYP 3A, needs acid for absorption

Azoles

- Fluconazole

- triazole
- reaches high concentrations in CSF
- can reach fungicidal concentrations

Indications

- first choice for fungal meningitis

Side effects

- better tolerated, GIT, does not inhibit steroids

Interactions

- lower affinity to human CYP 3A

Azoles

- Itraconazole

- triazole, lipid soluble
- variable absorption
- β -cyclodextrin coated particles for IV

Indications

- first choice for fungal meningitis

Side effects

- well tolerated, skin lesions, does not inhibit steroids

Interactions

- CYP 3A inhibition, needs acid (Coca-Cola[®][™])

Azoles - other

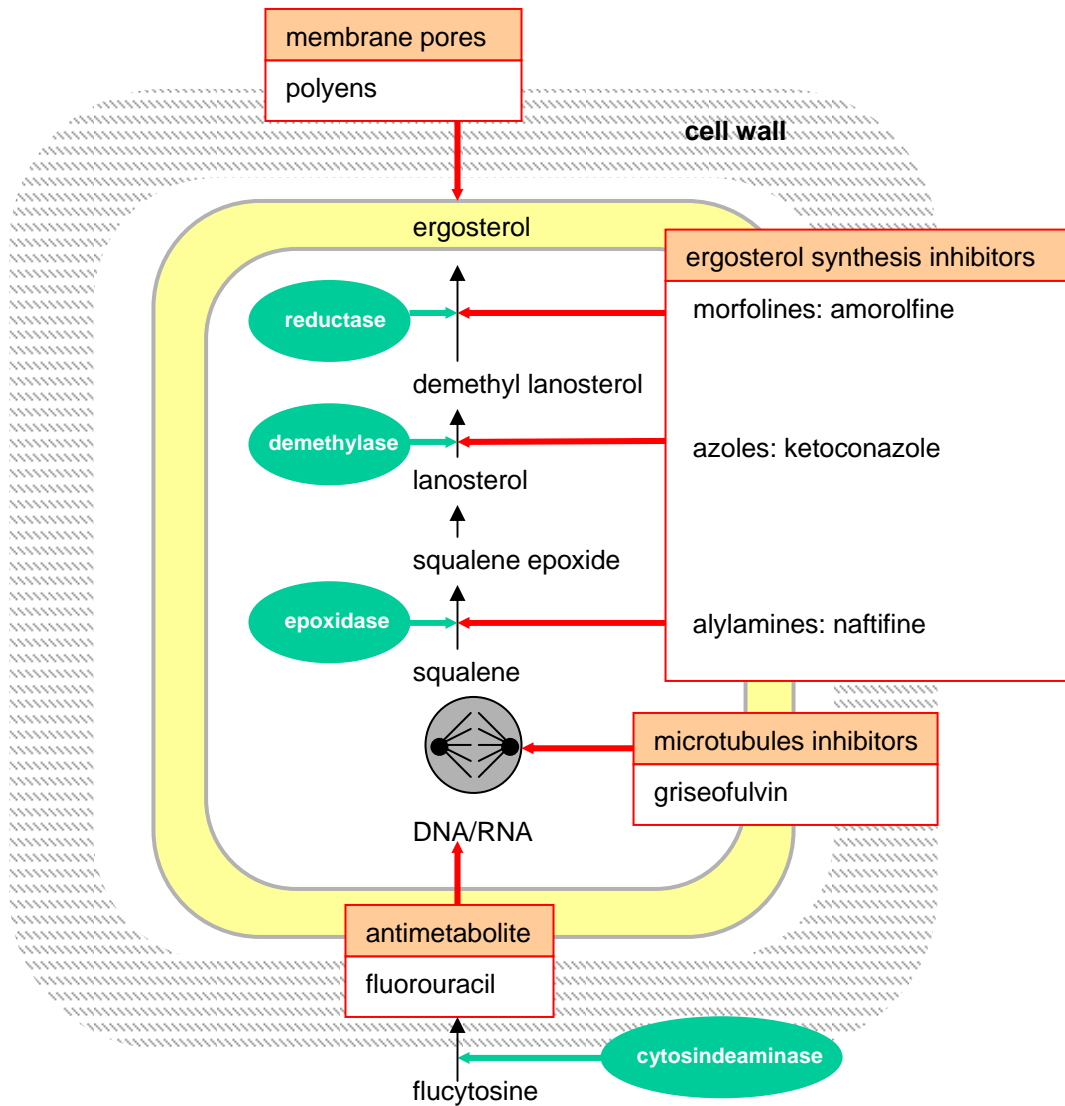
- voriconazole
 - wider spectrum
 - more expensive (VFEND®)
- posaconazole
 - even wider spectrum
 - even more expensive (Noxafil®)
- ravuconazole
 - in clinical trials



Alylamines and morfelines

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Physiology



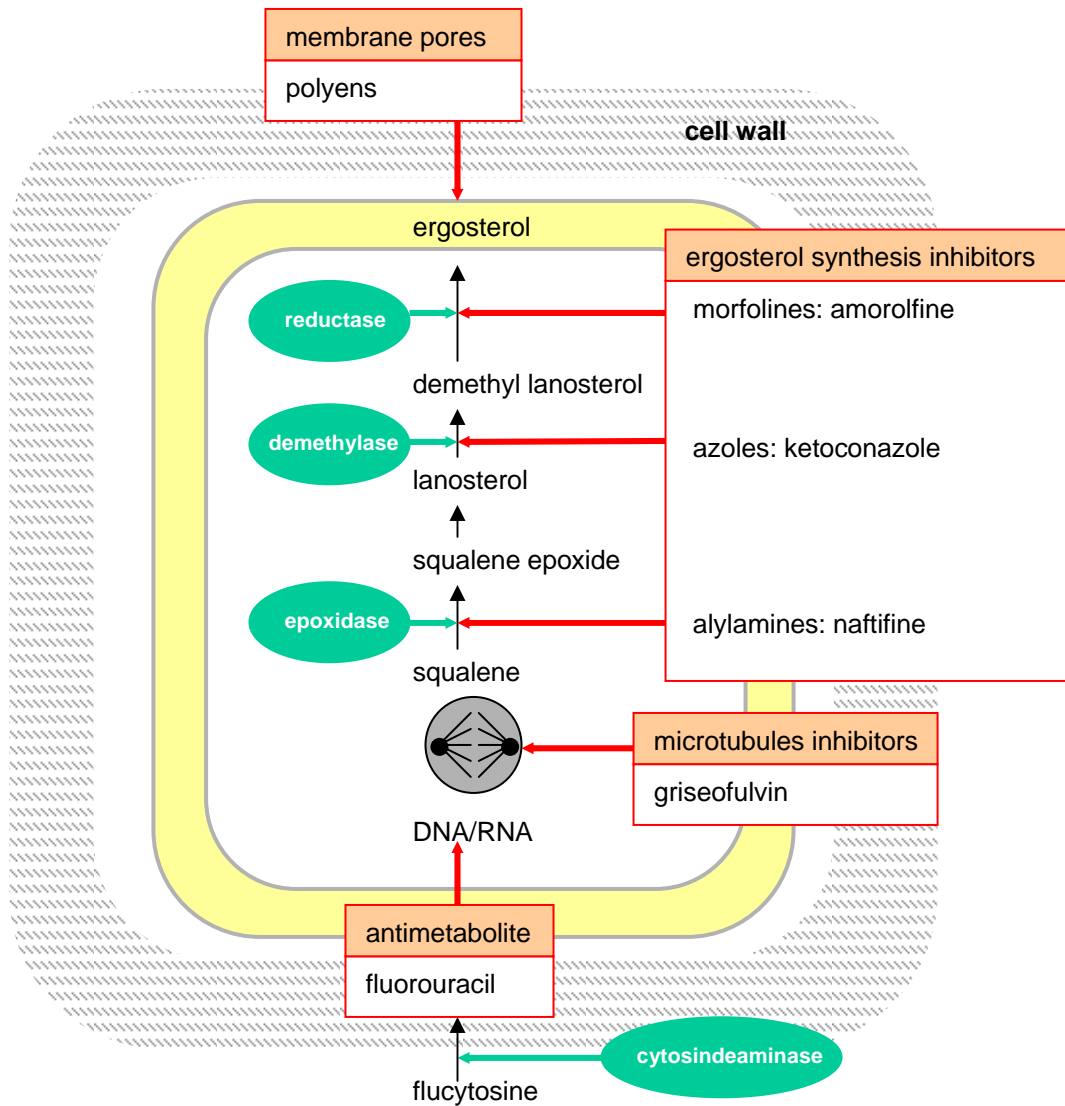
Aylamines and morfelines

- **naftifine**
 - local, fungicidal, wide spectrum
 - antiflogistic effect
- **terbinafine**
 - similar to naftifine, also oral form,
 - keratinophilic
- **amorolfine**
 - good penetration into nails
 - used in the form of a lacquer

Other

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Physiology



Others

- **griseofulvin**
 - local infections, given systemically
 - obsolete, treatment needs to be very long

- **flucytosine**
 - cytosindeaminase inhibitor (cytosine → uracil)
 - good effect on candida
 - 10g daily
 - well tolerated, mild side effects
 - beneficial combination with amphotericin B

Others

- **casprofungin**
 - inhibits cell wall synthesis
 - wide spectrum
 - poor oral absorption
 - long half life - 1 dose/day
- **other...**
 - pradimicin, nikkomycins
 - sordarins
 - GCSFs
 - vaccines?

thank you for your attention