Antiviral, antifungal and anti protozoan agents

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ANTIVIRAL AGENTS

CHARACTERISTICS OF VIRUSES

- DNA or RNA viruses,
- Capsid (protein coat) (nucleic acid + protein coat = nucleocapsid)
- Envelop (lipoprotein, may have antigenic glycoprotein)
- Enzymes - that initiate replication
- Obligate intracellular parasites,
- No cell wall or cell membrane,
- No self sustaining metabolic ability - depend on host metabolic machinery to live & multiply – **difficult to get drugs that are selective for the virus and harmless to the host**

ANTIVIRAL AGENTS

1. Entry inhibitor e.g. CXCR5 inhibitors

2. Uncoating inhibitors - Amatadine, Rimatadine (influenza)
   Pleconaril (rhinoviruses)
3. Viral nucleic acid synthesis inhibitors
   - DNA polymerase inhibitors
   - Reverse transcription
4. Integrase inhibitors

5. Antisense agents – formivisen (CMV)

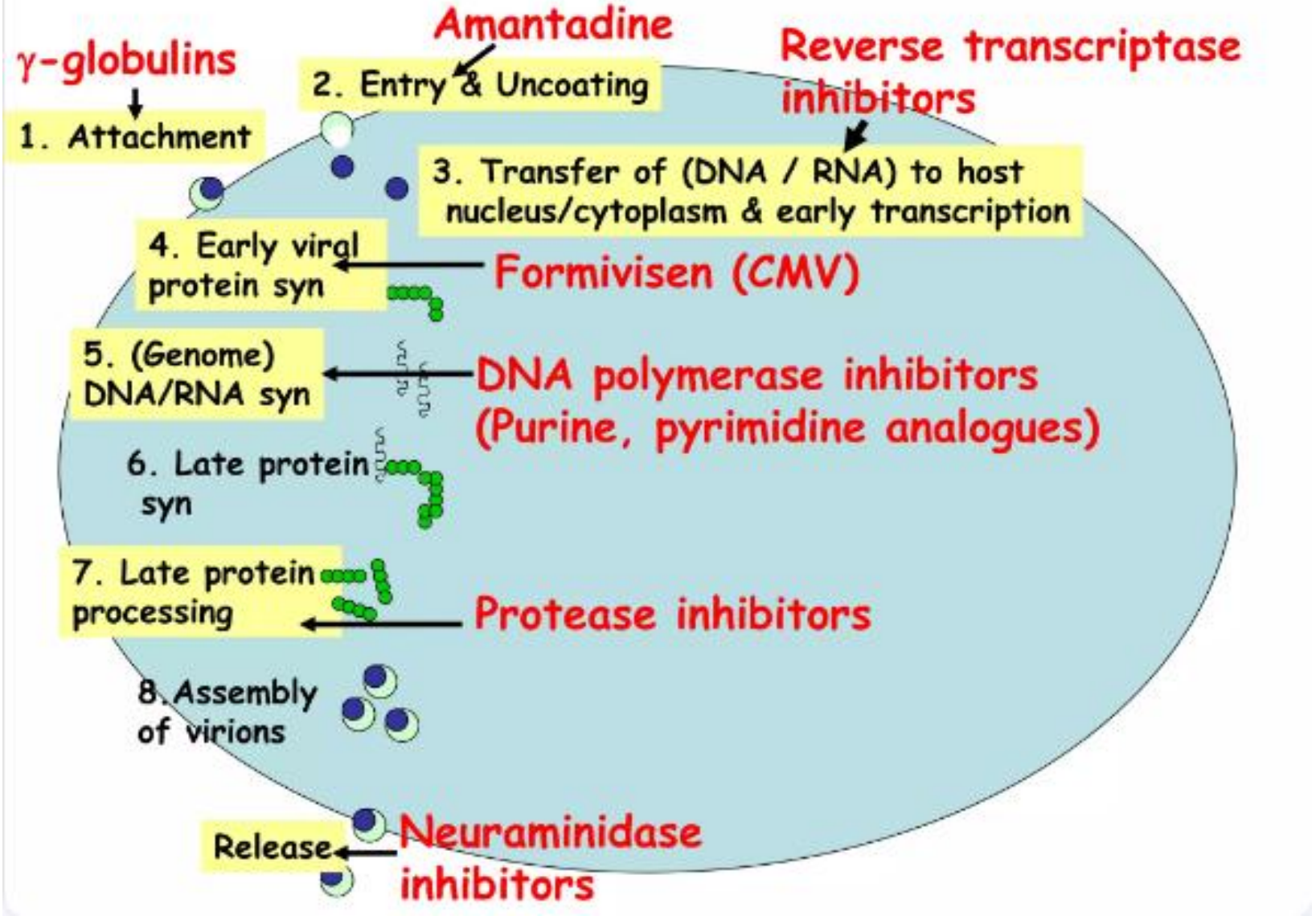
Antisense sequence - is the nucleotide chain that is complementary to the sense sequence.
Antisense molecules recognize and bind to the nucleotide sense sequence of specific RNA molecules, preventing the synthesis of specified proteins.

6. Protease inhibitors

8. Release phase inhibitors- neuraminidase inhibitors

9. Immune system stimulation –Interferon alpha (HBV, HBC)

ACTIVITY SITES OF MAJOR ANTIVIRAL AGENTS



Antifungals

SOME PROPERTIES OF FUNGI

1. Yeasts (single cell) or moulds (multicellular)
2. Eukaryotes
3. Cell membrane – has lots of ergosterol
4. Have a rigid cell wall (inner & out layers)- of mannopeptides, β-glucan, chitin, lipids etc

5. Importance of cell wall: agent of attachment to host site, stimulate host immune response, poorly degraded by man
6. Produce spores

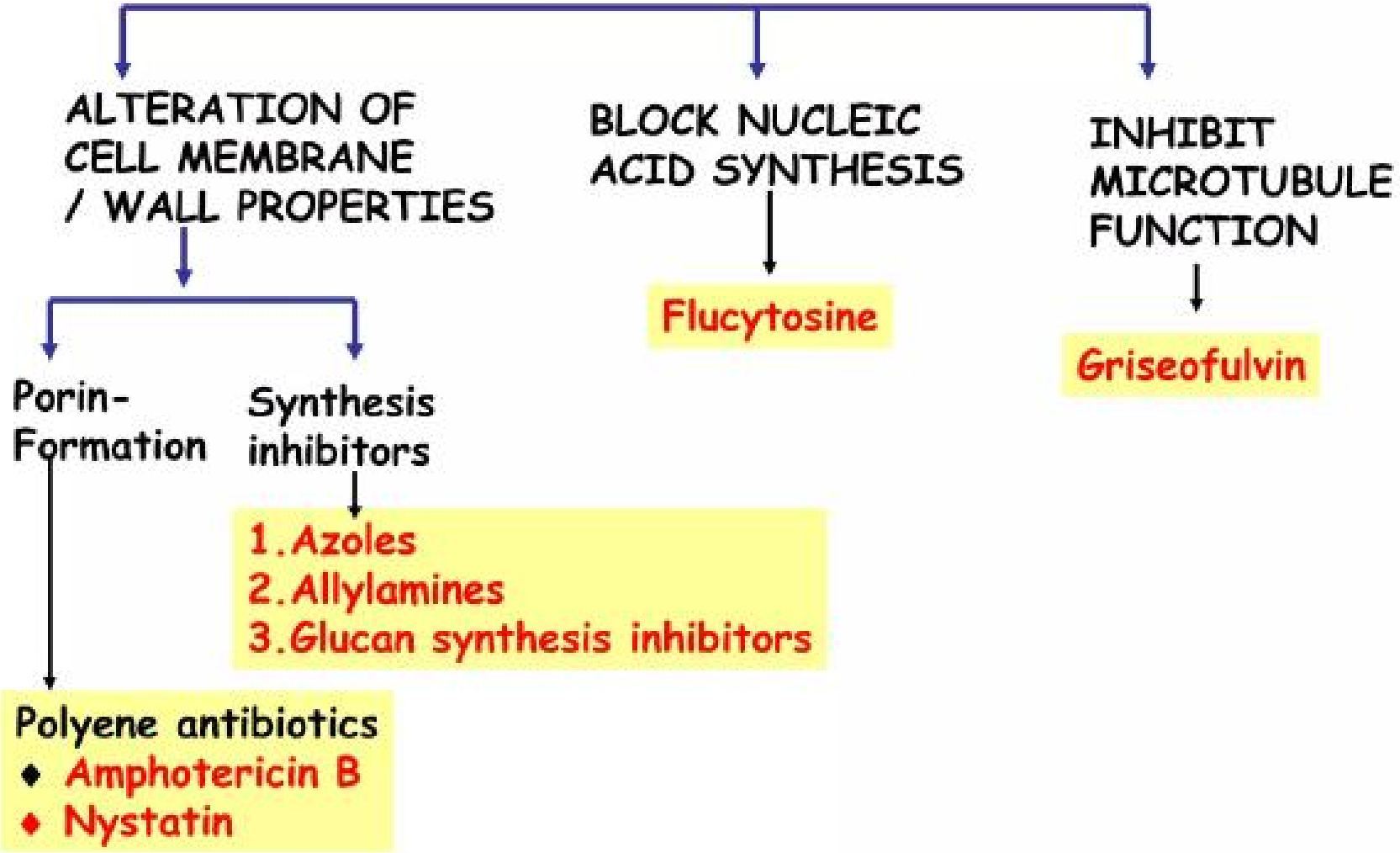
MYCOSES

1. Most fungal infections are superficial (stratum cornea), cutaneous (keratinized layers), or subcutaneous; few but serious infections are systemic (I°) and opportunistic mycoses
2. Mycoses w/ highest incidence are candidiasis and dermatophytosis
3. Most mycoses are difficult to treat

Antifungals are few 'coz

1. Previously disease burden from fungal infections far fewer than from bacterial infections; increase is due to immunosuppression (HIV, organ transplant)

ANTIFUNGALS



A) POLYENE ANTIFUNGALS

1. AMPHOTERICIN B (Polyene macrolides)

Mxn: Binds to sterols, forms pores and alters membrane permeability leading to loss of cellular constituents especially K+

Selectivity: Fungi have ergosterol while mammals have cholesterol

2. NYSTATIN

Adm; topical or local only (too toxic for systemic use)

Abs: very poor (GIT, other mucus membrane or skin)

Uses

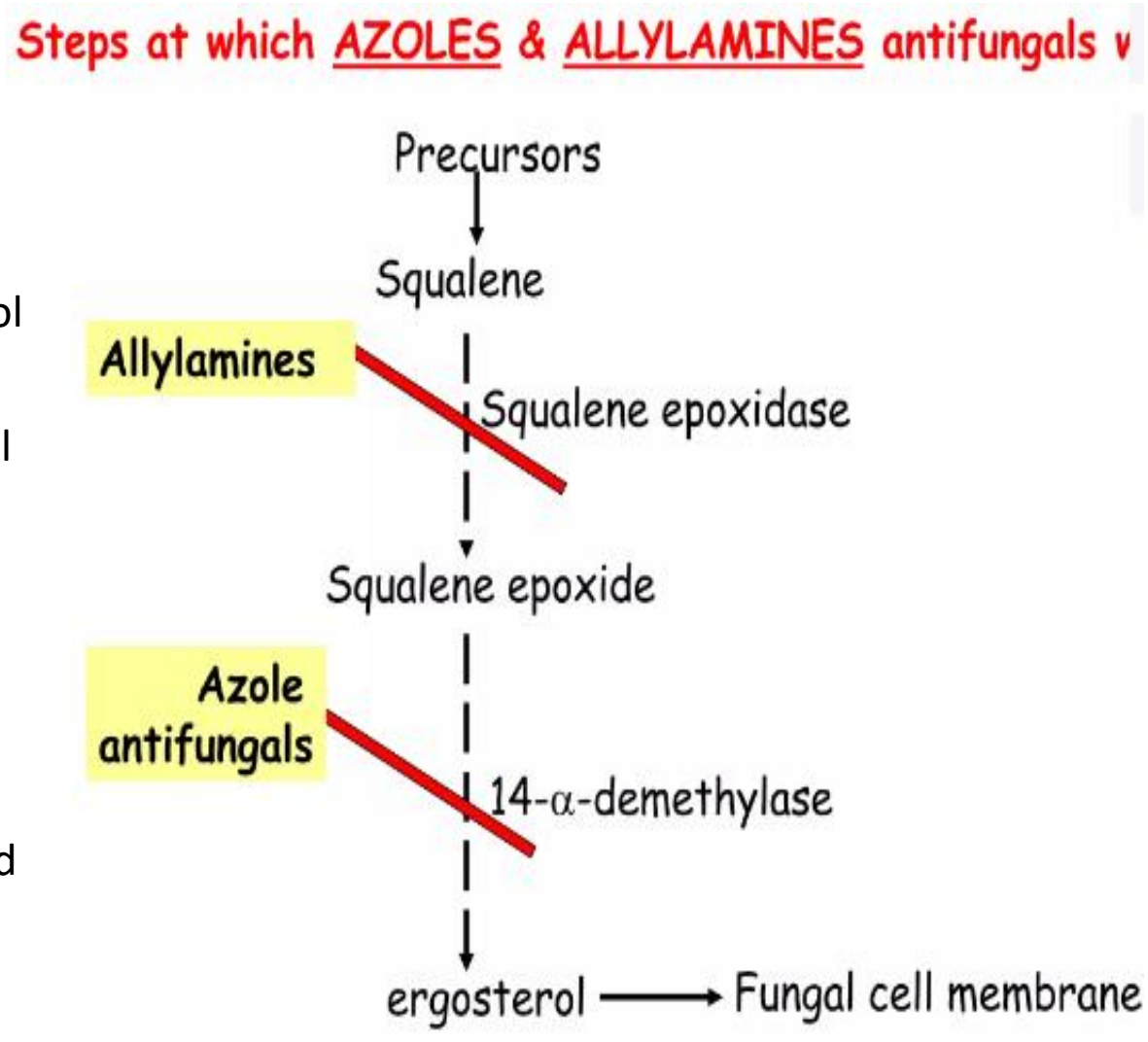
Candida infections – oropharynx, GIT, vagina, skin

3. NATAMYCIN

Spectrum: Aspergillus, candida

Poor oral abs, given locally (inhalation, topical, oral, vaginal tablets)

- Azoles exert their action by inhibiting the C14α demethylation of lanosterol in fungi, which interferes with the synthesis of ergosterol in the fungal cell membrane.
- Allylamines are fungicidal, and their mechanism of action is competitive inhibition of squalene epoxidase, blocking conversion of squalene to lanosterol, leading to squalene accumulation and ergosterol depletion in the cell membrane.



Flucytosine (5-FC)

- Flucytosine (5-FC) is a synthetic antimycotic compound, first synthesized in 1957.
- It has no intrinsic antifungal capacity, but after it has been taken up by susceptible fungal cells, it is converted into 5-fluorouracil (5-FU), which is further converted to metabolites that inhibit fungal RNA and DNA synthesis.

- **Griseofulvin** is fungistatic, however the exact mechanism by which it inhibits the growth of dermatophytes is not clear. It is thought to inhibit fungal cell mitosis and nuclear acid synthesis. It also binds to and interferes with the function of spindle and cytoplasmic microtubules by binding to alpha and beta tubulin.

GLUCAN SYNTHESIS INHIBITORS

ECHINOCANDINS: *Caspofungin, Micafungin, Anidulafungin*

Mxn: Inhibitors of β-glucan synthase thus defective fungal cell wall resulting in osmotic lysis

INTRODUCTION

- Protozoal diseases are highly prevalent in tropical countries.
- They infect both human and animal populations.
- They are malaria,Amoebiasis, Balantidiasis,Giardiasis, Trichomoniasis,Tripanosoniasis, Leishmaniasis etc..,

ANTIPROTOZOAL AGENT-CLASSIFICATION

- Drugs which used for the treatment of protozoal diseases are called as Antiprotozoal agents.

Based on chemical structure:Antiprotozoal agents are classified as:

1.Natural compounds-Emetine Hcl

2.Imidazole derivatives- Metronidazole,Ornidazole,Tinidazole

3.8-Hydroxy quinolines-Clioquinol,Iodoquinol

4.Miscellaneous compounds –Diloxanide Furoate ,Carbarsone

Emetine

- It is also called as protozoal poison as it prevents protein synthesis &protein elongation.
- Also used to treat balantidial dysentery &Fluke infestations such as fascioliasis & paragonimiasis.

MOA OF METRONIDAZOLE

- Metronidazole undergoes microbial reduction of 5-nitro group.
- The reactive intermediate metabolic products produced are nitroso group,hydroxylamino group,nitroxide,amino group.
- These groups will covalently binds with DNA of the microorganism and causes lethal effect to the protozoa.

Quinolines

- The quinoline-containing antimalarial drugs, chloroquine, quinine and mefloquine, are a vital part of our chemotherapeutic armoury against malaria.
- These drugs are thought to act by interfering with the digestion of haemoglobin in the blood stages of the malaria life cycle.