Antimicrobial therapy

Prof Ivo Ivić

Bacterial sensitivity to specific antibiotic

Determinants

- MIC- minimal inhibitory concentration

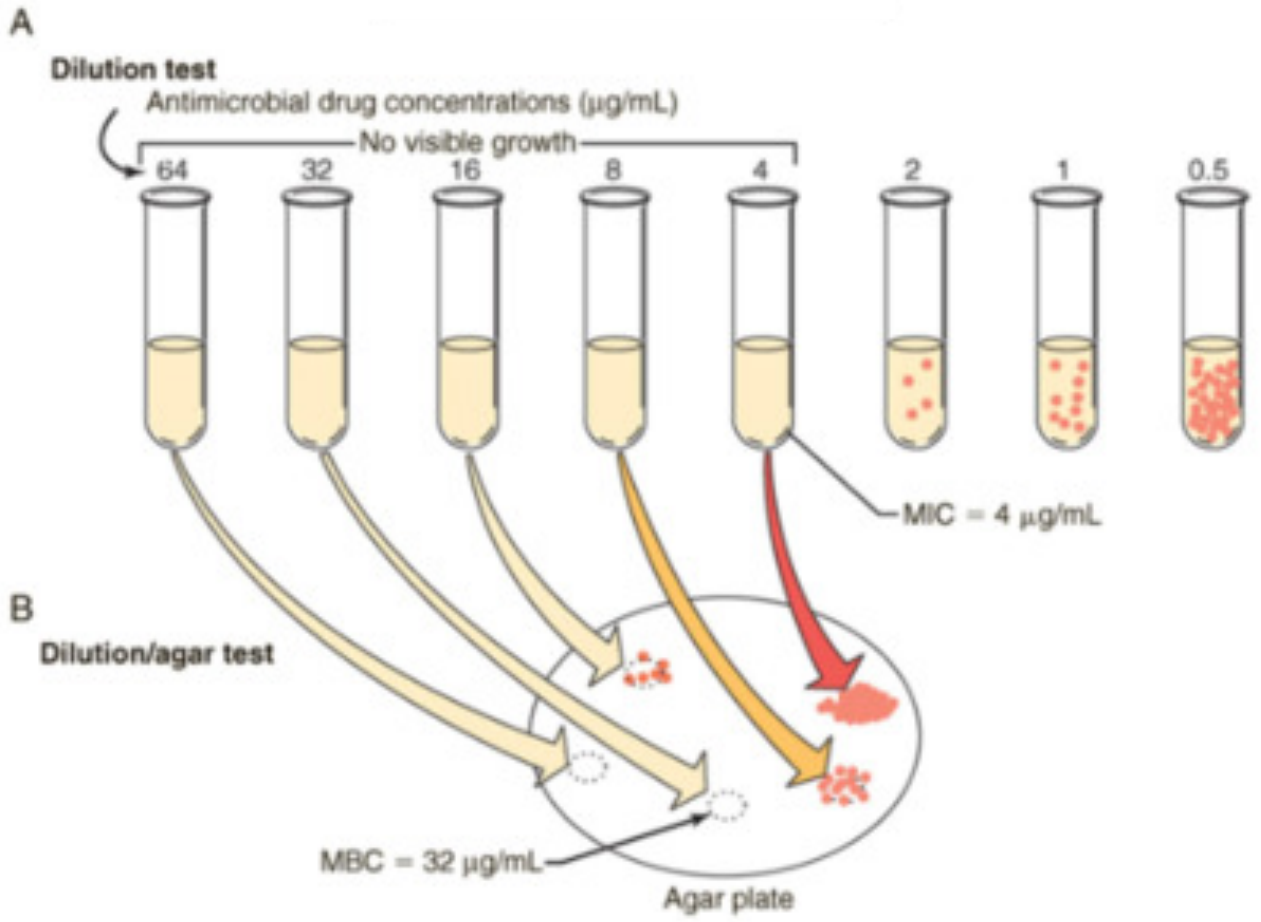
  (inhibit, but does not kill bacteria)

  - disables visible bacterial growth in liquid media (12h)
  - allows growth after inoculation on solid media

- MBC- minimal bactericidal concentrations

  - kills all bacteria
  - no growth after inoculation on solid media

Principles of treatment



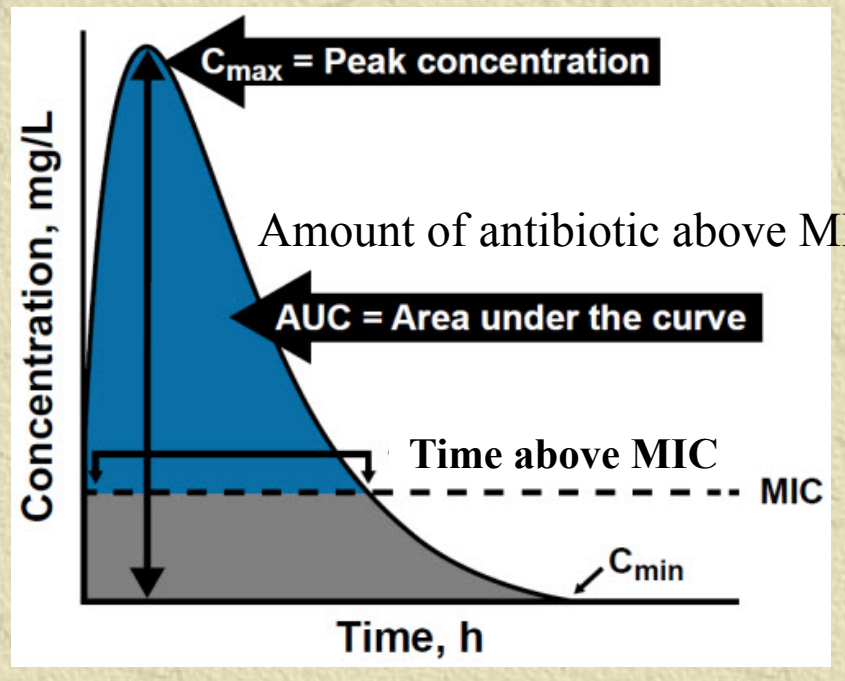
Requirements for treatment success

(using conventional dosage of antibiotic)

- to achieve serum antibiotic concentrations above MIC
- to maintain this concentrations for enough long period after adminstration

The lower the MIC, the better the therapy

The greater the AUC, the better the therapy



Bacterial sensitivity to specific antibiotic – antibiogram

- Sensitive
  - low MIC values for specific antibiotic
  - conventional dosage = high probability of cure
- Resistant
  - high MIC values for specific antibiotic
  - therapeutic concentrations not achieveable by conventional or increased dosage

- Intermediate sensitivity
  - MIC values increased (but not high)
  - possibility of treatment failure
  - Increased dosage = sometimes provides therapeutic success

Example

Str.pneumoniae intermediatedly penicillin sensitive

Pneumonia: treatment success with increased dosage

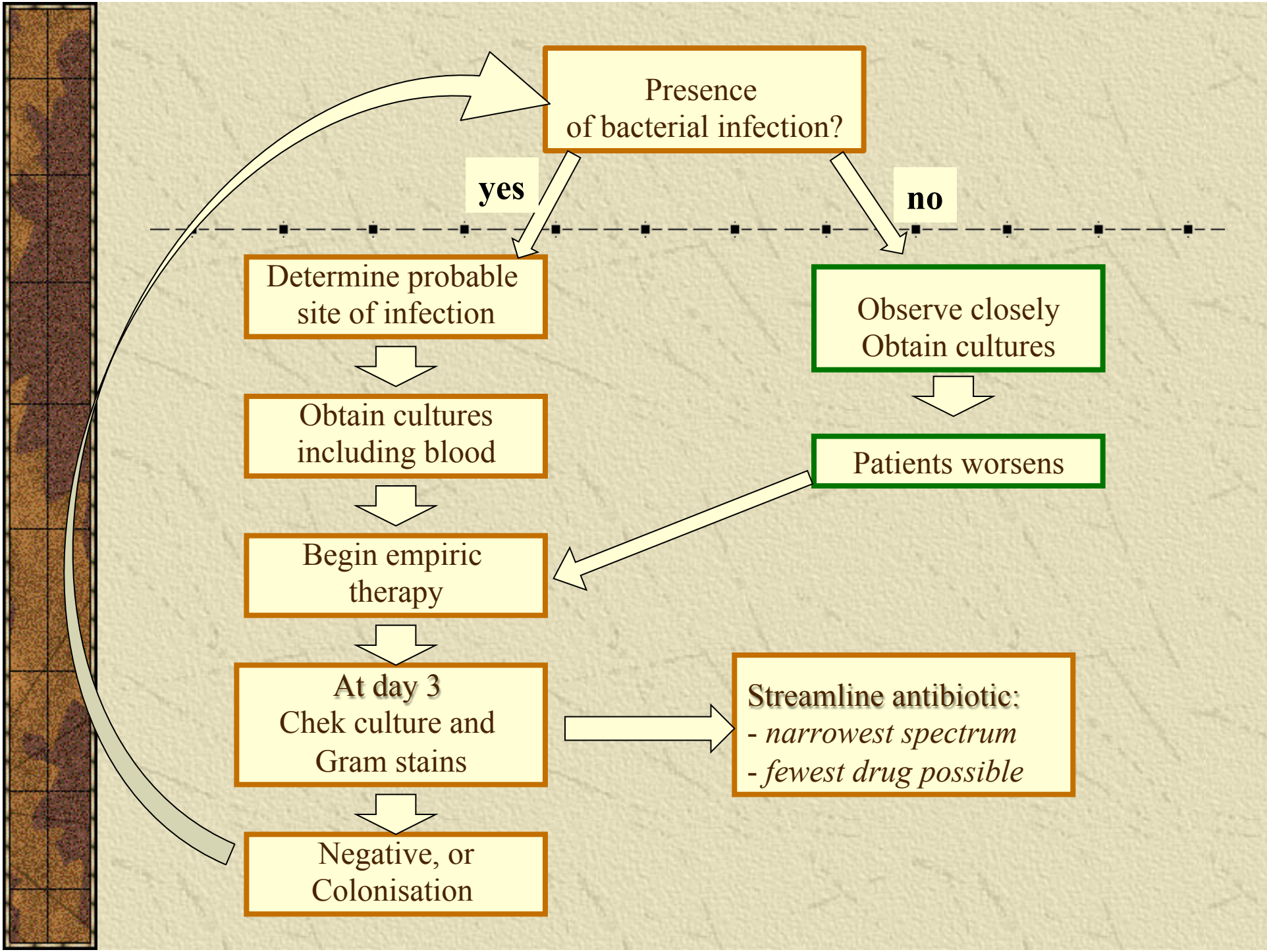
Meningitis: tretment failure even with increaed dosage

Recovery from bacterial infection:
relationship between antibiotic and neutrophils

- Antibiotic:
  - reduces number of bacteria
  - facilitate clearing of bacteria by neutrophils

- At level of 10^2-10^3bacteria/g of tissue
  - Neutrophil clean bacteria without help of antibiotic
  - Usualy, this is achieved after 5 days of therapy

MAKING DECISION FOR ANTIBOTIC THERAPY


Presence
of bacterial infection?
yes
no
Determine probable
site of infection
Obtain cultures
including blood
Begin empiric
therapy
At day 3
Chek culture and
Gram stains
Negative, or
Colonisation
Observe closely
Obtain cultures
Patients worsens
Streamline antibiotic:
- narrowest spectrum
- fewest drug possible

Making decision for antibiotic therapy: Checklist

1. Assess the of possibility of bacterial infection
2. Assess site of infection/pahtogen(s) involved
3. Assess antibotic susceptibility of presumed pathogen
4. Check data about previous antibiotic therapy/resistence
5. Check important predisposing host factors
6. After 3 days select drug with the narrowest antibacterial spectrum

Rational selection of antibiotics

Questions to be answered

1. How broad is antibacterial spectrum of choosen antibiotic?
2. Wether the antibiotic(s) is -cidal or -static?
3. What are the antibotics major toxicities?
4. How is the drug metabolised and eliminated? Is there need for dosign adjustment?
5. What is the price of the antibiotic selected?

Antibacterial spectrum of some antibiotic groups

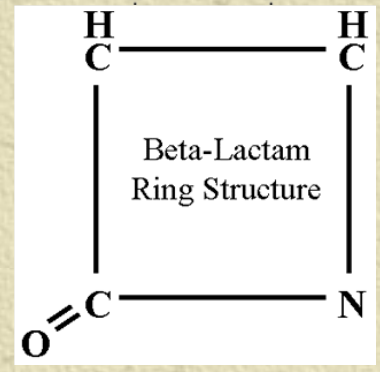
Group	Narrow spectrum	Moderately broad	Broad	Very broad
Penicillins	Penicilin G/V	Amoksicillin	Amoksicillin - calvulanate	Ticarcillin-clavulanate
Cephalosporins	Cefalexine	Cefuroksime - aksetil	Ceftriaxone	Cefepime
Fluoroqiunolones		Cipofloxacin	Levofloxacin	Moksifloxacin
Glycopeptides	Vancomycin			
Macrolides		Azithromycin		
Tetracyclines			Doxycycline	
Carbapenems				Impenem Meropenem

ANTIBIOTICS

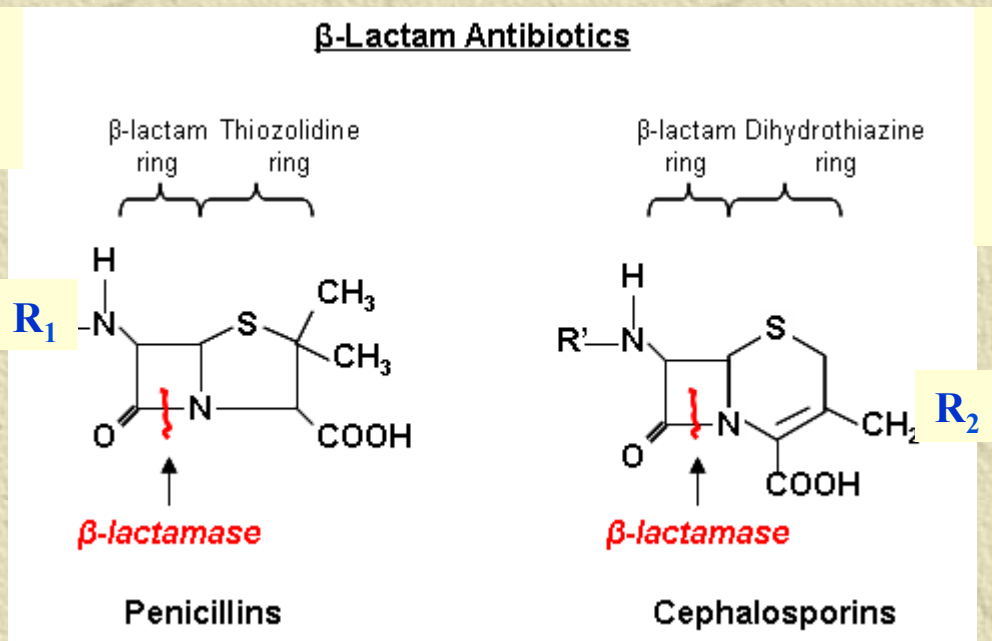
Antibiotic groups:

1. β-lactams
2. Aminoglycosides
3. Glycopeptides
4. Macrolides
5. Ketolides
6. Lincosamides
7. Tetracyclines
8. Chloramphaenicol
9. Quinolones
10. Oxazolidines
11. Streptogramins
12. Daptomycin
13. Metrondiaziol
14. Sulfonamides
15. Trimetoprim
16. Colistin

β-LACTAM ANTIBIOTICS

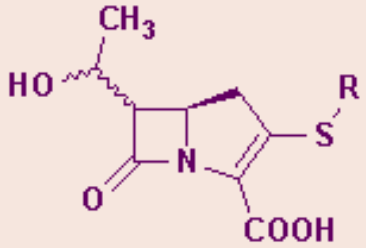


R_1 side chain:
-anibacterial properties

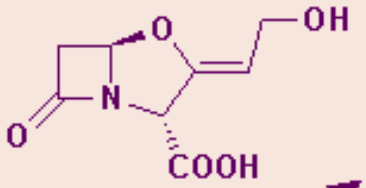


R_2 side chain:
-pharmacokinetics
-metabolism

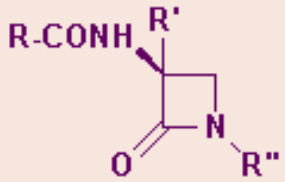
The family tree of ß-lactam antibiotics



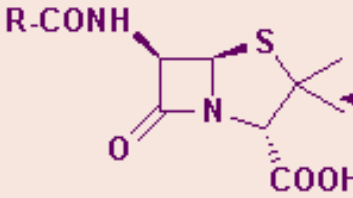
Carbapenems



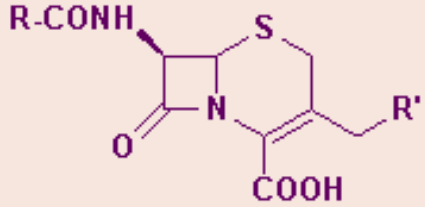
Clavulanic acid



Monobactams



Penicillins



Cephalosporins

Antibacterial mechanism of β-lactams

- Inactivation of cell wall enzymes (PBP-s)

- Cessation of cell wall sythesis
  - during active cell growth and divison

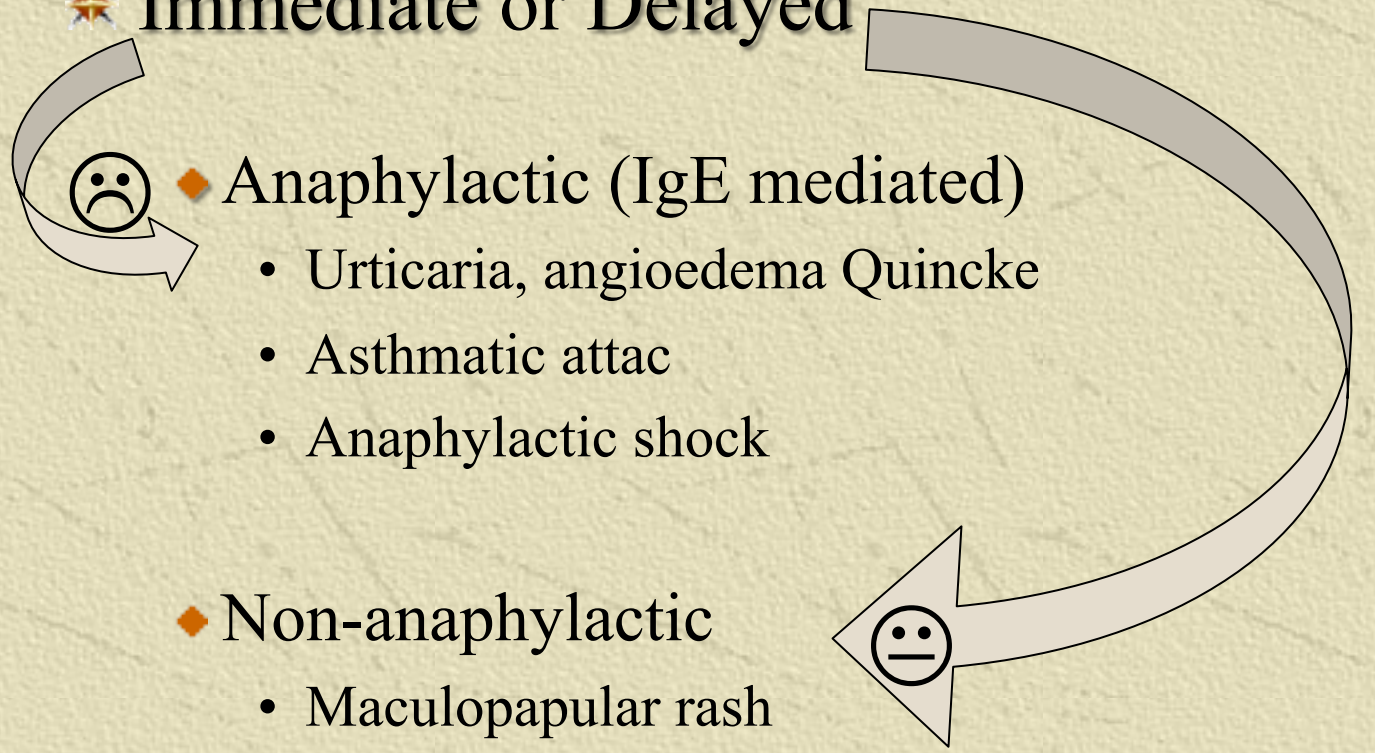
- Cell lysis = bactericidal effect
  - antagonised by bacteriostatic agents

Bacterial resistence mechanisms

- Destruction of β-lactam ring by β-lactameses
  - penicilinases, cefalosporinases, karbapenemases
- Modification of PBP-s
  - lowered affinity for specific β-lactam antibiotic
  - preserved cell wall syntheis

Hipersensitivity to β-lactam antibiotics

- The most common toxicity
- Immediate or Delayed



- Anaphylactic (IgE mediated)
  - Urticaria, angioedema Quincke
  - Asthmatic attac
  - Anaphylactic shock
- Non-anaphylactic
  - Maculopapular rash

Hipersenitivity: Penicillins vs Cephaloporins

- Penicillins
  - 1-10 % allergic reactions
  - 1-7% cross-reactity to cephalosporins
- Cephalosporins
  - 1- 3% allergic reactions
  - rarely anaphylactic

A practical approach in case of pencillin allergy

- Anaphylactic
  - all β-lactams should be avoided
  - or desensitization should be carried out
- Non-anaphylactic
  - another group of β-lactams is allowed

Other β-lactam adverse reactions

- Imipenem: siezures
  - in patients with renal dysfunction
  - less frequent with other karbapenems
- Ceftriaxon: aseptic inflammation of gallbladder
  - drug crystalisation in gallbladder
- Cephalosporins + aminoglycosides: nephrotoxicity
- *Clostridium difficile* diarrhoea

PENICILLINS

Penicillins

1. Natural penicilins
2. Aminopenicilins
3. Penicillinaze-resistent pencillins

   (anti-staphylococcal)

4. Carboxypencillins and ureidopencillins

   (anti-pseudomonal)

1.Natural penicilins (PCN)

- Narrow spectrum
  - *S.pygenes, S. viridans, S.pneumoniae, Neisseria meningitidis*
  - Anaerobic mouth flora
  - *Clostridium perfrigens, C.tetani*, *Leptosipra*
- Short half-life: dosage 3-6 times/day
- Renal excretion: dose adjustment with renal funitton

<u>Preparations</u>

- i.v. : PCN G
- i.m.: procaina PCN G, benzathine PCN G
- p.o.: PCN V-K

2. Aminopenicillins (iv, im, po)

2a. Amoxycillin , Ampicillin

- Moderate spectrum:
  - Gram-positive: *Streptococci., Enterococci, Lysteria*
  - Gram-negative: *E.coli, Salmonella, Haemophilus influenzae* (if β-lactamase sensitive)
- Short half life
- Renal excretion (unchanged)

2b. Amoxycillin-clavulanate , Ampicilin-sulbactame

- Broader spectrum with addition of:
  - Meticillin sensitive *Staphylococcus aureus* (MSSA)
  - β-lactamase producing gram-negative bacteria:
    - *Moraxella catarrhalis,*
    - *H.influenzae,*
    - *Enterobacteriaceae.*

3. Penicillase-resistant penicillins (iv, po)

(methicillin sensitive bacteria)

Methicillin, Cloxacillin, Dicloxacillin

- Very narrow spectrum-
  - Indication: *MSSA, S.pyogenes* (cellulitis)
  - Ineffective against anerobes and gram-negative bacteria
- Short half-life
- Hepatal elimiantion (bile excretion)

4. Carboxypenicillins and Ureidopenicillins (iv)

(tikarcillin) (piperacilin)

- Rezistent to β-lactamase produced by gram-negative bacteria:
  - Pseudomonas, other enterobacteriaceae

Nowdays market- only with β-lactamase inhibitors:

- Tikarcilin-clavulanate
- Piperacilin-tazobactam

Activity aganist:
- Gram-negative bactera
- Anaerobes (+ *B.fragilis*)
- MSSA

Intrabdominal infections
VAP
Mixed soft tissue infections

VAP- ventilator associated pneumonia

CEPHALOSPORINS

	Antibacterial activity of cephalosporins			
	1st generation	2nd generation	3rd generation	4th generation
Gram + cocci	+++	++	++	++
Gram neg. bacilli	+	++	+++	+++
MSSA	++	+	+/-	++
MRSA	-	-	-	-
	Cephalexin Cefazolin	Cefuroxime Cefoxitine Cefuroxim-axetil	Ceftriaxone Cefotaksim Ceftazidim Cefixime	Cefepime

1st generation cephalosporins

- Activity:
  - Streptoccci, MSSA, oral cavity anaerobes
  - CA gram-negative bacilli (*E.coli*)
- Ineffective against
  - MRSA, penicillin-resitant *S.pneumoniae*
  - *H.influenzae*
- Renal excretion
- Do not pass blood-brain barrier
- Good for soft tissue infections

2nd generation cephalosporins

- Similar to 1st generation, wider gram neg.activity
  - *H.influenzae*, *Neisseria sp*, *Moraxella catarrhalis*
- Renal excretion
- Indications
  - Uncomplicated UTI, otitis media
  - Soft tissue infection, pelvic inflammatory disease
- Oral preparation (cefuroxim-axetil):
  - low serum levels
  - expensive

3rd generation cephalosporins

Activity

- Excellent against gram negative bacteria
  - *Neisseria sp, H.influenzae, M.catarrhalis*
  - *Enterobacteriaceae*
  - Ceftazidime: the only active against *Ps.aeruginosa*
- Excelent against gram positive coccci
  - *S.pyogenes, S.viridans*, other streptococci
  - *S.pneumoniae* (including moderately PCN resistant strains)
- **Poor** against *S.aureus* and higly PCN resistant *S.pneumoniae*

3rd generation cephalosporins

- Ceftriaxon- long half life: 1-2 doses/day
  - Other 3.gen.: 3-4 doses/day
- All cross blood brain barrier
- Excretion
  - Renal: for most members
  - Ceftriaxone: hepatal (gallbladder crystals!)
- Indications:
  - CA pneumonia and meningitis
  - UTI and abdominal infections

CA: Community Acquired

3rd generation cephalosporins

PARENTERAL (iv, im)

- Cefotaxime
- Ceftriaxone
- Ceftazidime

ORAL

- Cefexime
- Cefpodoxime proxetil

4th generation cephalosporins (cefexime)

- Resistant to ESBL
- Wide antibacterial spectrum
  - Similar to 3rd gen.cephalosporins

    plus: *Ps.aerurinosa* and MSSA (but not MRSA!)

Indications

- Nosocomial infections (iv)

ESBL: Extended Spectrum Beta Lactamase

5th generation cephalosporins (ceftaroline)

- Antibacterial spectrum
  - Similar to 3.gen.cephalosprins(ceftriaxon)

    plus: MRSA and VISA (vancomyin intermediately restant SA)

- Indications
  - CA pneumonia
  - Complicated soft tissue infections

CARBAPENEMS

Very wide antibacterial spectrum

- Gram negative bacteria, including:
  - ESBL producing strains
  - *P.aeruginosa* (with exception of ertapenem)
- Gram positive bacteria, including:
  - MSSA (but not MRSA)
- Anaerobes

Carbapenems

- Indications (pending results of the microbiology)
  - Severely ill patients with nosocomial infection
  - Severe mixed infections

Carbapenem members

1. Imipenem-cilastatin
2. Etrapenem (1dose/day, inactive against *P.aeruginosa*)
3. Meropenem
4. Doripenem

AMINOGLYCOSIDES

Aminoglycosides

- Derived form *Streptomyces* bacteria
- Bactericidal, but inactive low pH medium

- Post-antibotic effect:
  - Short exposure to antibiotic
    Prolonged suspension of bacterial growth
    (despite falling of antibiotic level below MIC)
  - The higer dose, the longer post-antibiotic effect
  - 1 dose/day is possible

Activity

- Excellent against gram-negative bacteria
- Sinergy with penicillins for:
  - *S.viridans, Enterococcus, P.aeruginosa*
    - But not as monotherapy for them
- Renal excretion
  - deceased creatinin clearance ⇒ dose adjustment

Toxicity

- Nephrotoxicity (usualy reversible)
- Ototxycity (usualy ireverible)
- Avoid aminoglycosides in:
  - Eldery patients
  - Renal disease
  - Patients with liver disease
  - Dehidration and hypotension
  - Combination with cephalosporins, vankomycin, clindamycin, fursemid
- Monitoring of serum levels is reccommended

Aminoglycosides (iv, im)

- Gentamicin
- Amikacin
- Netilmicin

- Tobramycin (topical th- eye infections)
- Streptomycin (tularemia, plague)

GLYCOPEPTIDES

Vancomycin

Teicoplanin

Glycopeptides

- Inhibit cell wall sythesis (peptidoglycan)- bactericial
  - Long half life, postantibiotic effect
  - 1-2 dose/day
  - Unreilable passage through blood-brain barrier
- Activity
  - Gram positive cocci
  - SA, *S.pneumoniae, Enterococcus*, etc.
- Renal excretion
  - Deceased creatinin clearance ⇨ Dose adjustment

Toxycity

- "Red man syndrome" – rapid drug infusion
  - Redness of face and torax
  - Not thrue allergic reaction
  - Rapid infusin- local hiperosmolarity- release of histamine
  - infusion should be slow (1h)

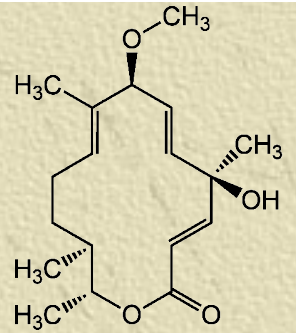
- Rare ototoxicity *and* nephrotoxycity

Limited therapeutic indications

1. MR staphylococci (MRSA and koagulasa neg.)
2. PCN highly resistant *S.peumoniae*
3. Enterocci in patients with PNC allergy
4. *Clostridum difficile* diarrhoea iresponsive to metronidazol (oral therapy)

MACROLIDES AND KETOLIDES

Macrolides and Ketolides



Activ against macrolide resistant bacteria

Macrocyclic lactone ring- basic component

Macrolides

- Erytromicin (natural antibotic)
- Azitromycin (iv, po)
- Claritromycin (po)

One site of action

Ketolides

- Telithromycin (po)

Two sites of action

Mode of action:

Inhibition of protein sythesis

Toxicity (rare, safe groups)

Macrolides

- Gastrointestinal
  - nausea, vomiting, cramps, diarrhoea
  - most often erithromycin
- Prologed QT-interval

Ketolides

- Disturbed accomodation
  - blured vison
- Severe hepatitis
  - very rare

Both metabolised by cytochrome P450

<u>Increase levels of</u>:

- Shrot acting benzodiazepines
- Ritoanvir
- Tacrolimus, ect.

Pharmacocinetics

- Long half life (except eritromycin): 1-2 doses/day
  - Azithomycin: prolonged activity (5 days after cesation)
- Elimination by bile
  - Azithomycin unchaneged
- High tissue concentrations of drugs
  - 10-100 times of serum conc.
- Unsuitable to treat bacteriema/sepsis
- Do not cross blood brain barrier

Anitbacterial spectrum

Vide:

- Gram-positive and –negative bacteria,
- Oral anaerobes
- Intracelluar bacteria
- Mycoplasma, Ureplasma, Chlamidia, Legionella
- Atypical mycobacteria

Treatment indications

- Community aquired pneumonia
  - *S.pneumoniae*- increasing resistence
  - Atypical penumonia- drugs of choice
- *S.pyogenes*
  - increasing resistence
  - reserve for PCN allergy

Treatment indications (continued)

- Atypical pneumonia
- Legionnarie disease
- STD (myoplasma, ureaplasma, chlamida)
- Atypical mycobacteria

- Replacement of penicillin in case of allergy

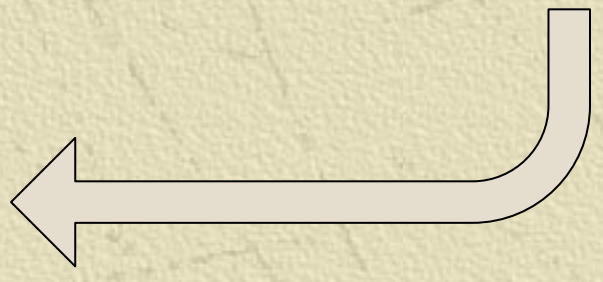
STD: Sexually Transmited Diseases

CLINDAMYCIN (PO, IV)

Mechanism

- Inhibits bacterial protein synthesis
  - the same site of action used by macrolides

- Excretion: liver → bile → stool



- Toxycity
  - Diarrhoea
    - reduction of sensitive flora up to14 postherapy days
    - *Cl.difficile* is invoveded in 50%

Antibacterial spectrum

- MSSA, *S.pneumonae*, *S.pyogenes*
  - for PNC-allergic patients
- Anaerobic bacteria
  - rising resistence of *B.fragilis* **!!**
- Toxoplasma gondii
  - for sulfa-allergic patients

Poor or no activity against gram-negative bactera

TETRACYCLINES

Doxycycline (po)

Tigecycline (po, iv)

Mechanism

- Inhibion bacterial protein synthesis

- Excretion: liver → bile → stool

- Toxycity
  - Photosensitivity- rash
  - Depostion in enemal- teeth discoloration
    - not reccomanded under age of 8 years
  - Benigin intracranial hypertension (headake)

Other antibotics are better !

Antibacterial spectrum

Very wide:

- gram positive and gram negative bacteria
- Anaerobic bacteria

- Intracellular bacteria
  - *Mycoplsama, Ureaplasma*
  - *Chlamida*
  - *Ricketssia*
  - *Borellia*
  - *Brucella*

primary indication

Tigecyclin- the new member

Improved activity against resistant :

- gram positive bacteria
- gram-negative bacteria
  - but not *Pseudomonas* and *Proteus* !!

- Limited indication
  - use as reserve antibiotic
    - multiresistant nosocomial infections

CHLORAMPHENICOL

Chloramphenicol

- Wide spectrum, bactericidal for:
  - *S.pneumoniae, H.influenzae, N.meningitidis*
- Excelent body distribution
  - CSF conc. = 50% serum conc.

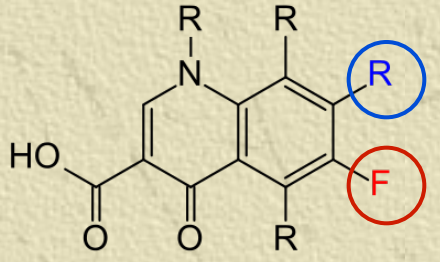
Toxycity

- Aplastic anemia
  - Reason for stopping of production (justified???)

QUINOLONES

(or fluoroquinolones)

1. Ciprofloxacin
2. Gatifloxacin
3. Levofloxacin
4. Gemifloxacin
5. Moxifloxacin



Quinolones = two 6-member rings

- Fluorine addition: = enhanced antibacterial activity
- Piperazin addition = enhanced gram-negative activity

Mechanism: inhibition of bacterial DNA- 2 points

1. foramtion of helix (DNA coiling)
2. division of DNA

Excretion:

- Kidneys: ciprofloxacin, levofloxacin, gatifloxacin
- Liver: gemifloxacin, moxifloxacin

Toxicity

- Tendinitis
- Articular cartilage damage
  - quinolones are not reccommended in children
- A-V blok (prolonoged QT interval)

Ciprofloxacin : antibacterial spectrum

- Gram negative (wide)
  - Primarily for *Pseudomonas*
  - Other gram negative bacteria
    - as alternative drug
    - for prostatitis (high concentrations)
- Intracellular bacteria
  - *Chlamidia, Mycoplasma, Ureaplasma*
    - in case of prostatitis
- Gram positive (narrow)
  - MSSA- bone infections

Respiratory quinolones): antibacterial spectrum (levo-, gati-, gemi-, moxi-floxacin)

Ciprofloxacin spectrum, plus:

- *S.pneumoniae* (even PCN resistant)
- Anaerobic bacteria (gemifloxacin)

- Indications of respiratory quinolones:
  - CAP (community acquired pneumonia)
  - Mixed infections of soft tissue

OXAZOLIDINES

linezolid

linezolid

- Inhitis protein synthesis
- Oral and parenteral preparations
  - wide body distributioin, high CSF concentrations
- Excretion: metabolised in urin
- Toxicity: reversible trombocytopenia (>2 weeks th)

Antibacterial spectrum

- Spectrum: only gram positive bacteria
  - Vancomycin resistant Enterococcus (VRE)
    - major indication
  - MRSA- as alternative drug
  - PCN resistant *S.pneumoniae*- alternative drug

METRONIDAZOL

metronidazol

- Damage of bacterial DNA
- Oral and parenteral preparations
  - Wide body distribution, good CSF penetration
- Excretion by the liver

Toxicity:

- Disulfiram reaction with alcohol consuption
- Sholud be avoided in pregnancy (DNA damage ??)

Antibacterial spectrum and indications

- Anaerobic bacteria
  - major indication
  - usualy with cepahlosporins (mixed infections)
- *Clostridium difficile* diarrhoea
- Genital *Trichomonas vaginalis*

TRIMETROPRIM + SULPHAMETOXASOLE

(TMP+SMX, Cotrimoxasole)

trimeproprim : sulphametoxasol = 1:5

- Sinergistic inhibiton of DNA precursors synthesis
- Oral and parenteral preparations
- Excretion by urine
- Toxicity:
  - Photosensitive skin rash
  - Erythema multiformae and Steven-Johnson's sy.
  - Serum sickness-like disease
  - Hemolytic anemia (in G6P deficiency)

Antibacterial spectrum and indications

- Wide G+ and G- spectrum
- Growing resistence
  - Previously- first choice drug for uncomplicated UTI
  - Nowdays – second choice drug (acording to antibiogram)

- Frist chocie for:
  - *Nocardia asteroides*
  - *Pneumcystis jirovecii*

} Immunocopromised hosts (HIV, immunosupresive th)

OUTPATIENT ORAL ANTIBOTICS

Reccommendations

When?

- higly suspected or proven bacterial infection

Whom to?

- mild to moderately ill patients

Which antibiotic?

- accoridng to reccommendations
  - IDSA- Infectious Disease Society of America
  - ESCMID- European Society of Clinical Microbiology and Infectious Disease
  - CDC- Center for Disase prevention and Control (USA)
  - ECDC- European CDC

For instance …..

- Bacterial (streptococcal) pharyngitis
  - first choice: Penicillin VK
  - PCN allergy: Azithromycin
- Community acquired pneumonia (CAP)
  - first choice: amoxicillin or doxycycline
  - comorbidity: levo- or moxifloxacin

ANTIFUNGAL AGENTS

Antifungal agents

Polienes

- Amphotericin B

Azoles

- Fluconazole
- Ketoconazole
- Itraconazole
- Posaconazole
- Voriconazole

Echinocandins

- Caspofungin
- Anidulafungin
- Micafungin

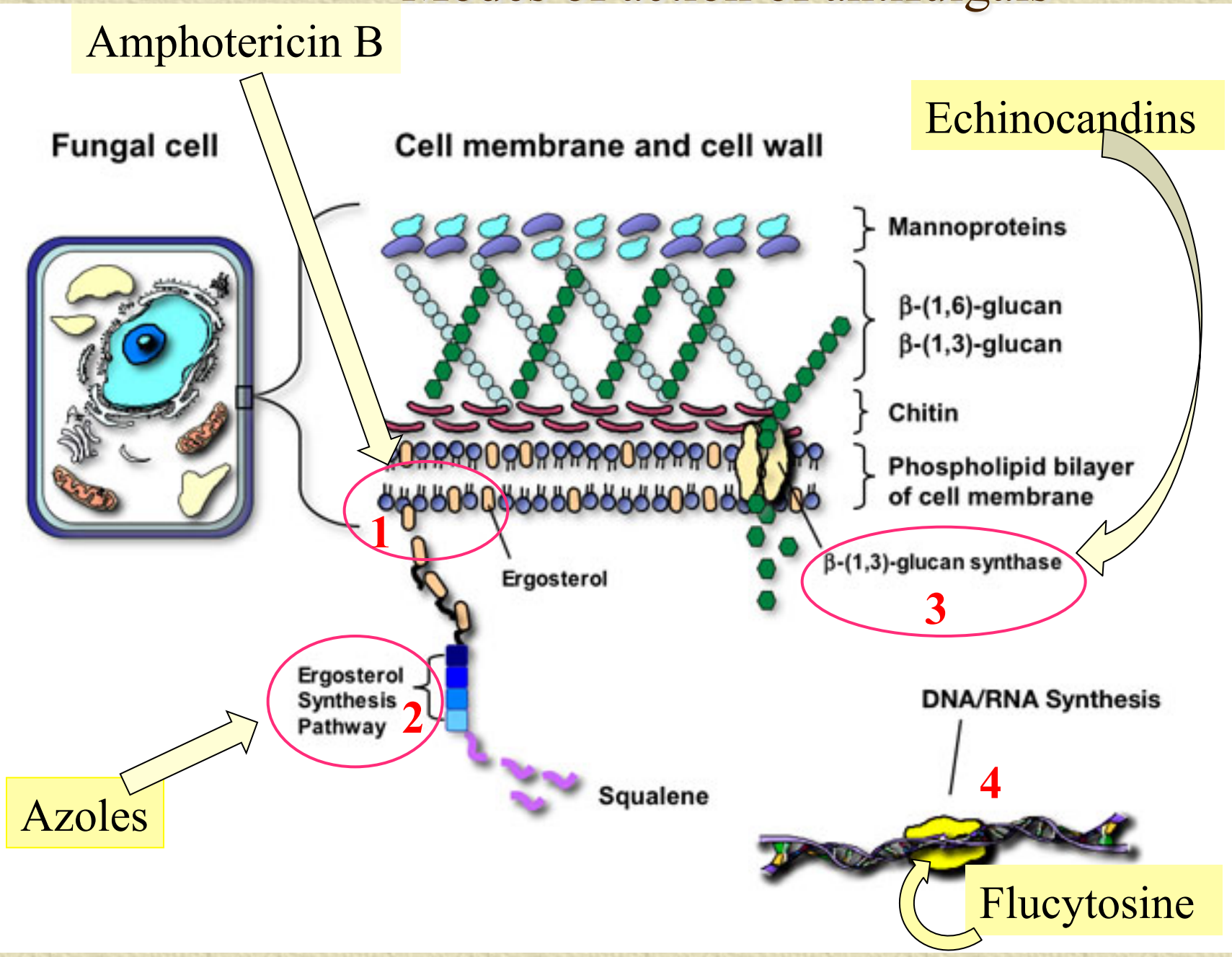
Others

- Flucytosine
- ect…..

Modes of action of antifulgals

1. Polyenes
   - ergosterol binding = disrupted membrane synthesis
   - fungicidal
2. Azoles
   - inhihibition of ergosterol synthesis pathway
   - fugnistatic
3. Echinocandins
   - Blocking of cell wall synthesis (β-glucan)
4. Flucytozine
   - Imapirment of DNA and RNA synthesis

Modes of action of antifulgals



AMPHOTERICIN B (AB)

Toxicity

- Nephrotoxycity- usualy reversible
  - Reduced by hydration
- Fever during infusion, reduced by:
  - Slow infusion (few hours)
  - Corticosterid premedication
- Phlebitis
  - Usually CVC required

Preparations of AB

All intravenous, same antifnugal spectrum, but:

1. ABD- amphotericin B deoxycholate
   - The most nephrotoxic. The cheapest.
2. Lipid-complex AB
   - Less nephrotoxic. More expensive.
3. Liposomal AB
   - Almost non-nephrotoxic. Extremely expensive.

Antifungal spectrum and indications

Systemic infections (but not CNS):

- most *Candida*
- *Aspergilus*
- *Cryptococcus*
- *Histoplasma*
- *Blastomyces*
- *Coccidiomyces*
- *Zygomyces*

AZOLES

Toxicity

- Generaly minimal
  - gastointestnal complaints
  - reversible liver enzymes elevation
- Ketoconazole
  - reduced libido
  - severe hepatitis
- Voriconazole
  - transient loss of vision during the first few infusions

Antifungal spectrum and indications

Systemic (including CNS) infections

and extensive local infections (iv, po)

- Posaconazole and Voriconazole
  - wide spectrum, the same as AB
    - very expensive
- Flukonazole, Itraconazole
  - Inactive against *Aspergilus*

ANTIVIRALS

(OTHER THAN ANTI-HIV AGENTS)

Ribavirin

Interferon-α

Neuraminidaze inhibitors

RIBAVIRIN

Mechanism of action

- Interference with m-RNA
- Not clearly understood

Toxicitiy

- Oral- reversible hemolytic anemia
- Areosol- bronchospasm

Pharmacokinetics

- Excretion by the liver and kidney

Indications

- RSV bronchiolitis
- Lassa hemorrhagic fever (Lassa virus, Arenaviridae)
- Chronic hepatitis C
  - only combined with interferon-α

INTERFERON-α (INF-α)

- Natural occuring antiviral cytokines

Mechanism of action

- enhances immunological kiling of virus-infected cells
- poor activity against DNA viruses

- Pharmacokinetics (sc, im)
  - long half-life: 2-3 doses/week
  - Pegliated form (PegINF-α): 1 dose/week

Toxicity

- Fever
- Irritability, depression, somnolece
- Bone marrow supression
  - neutropenia, thrombocytopenia

Indications

- Chronic hepatitis C
  - Combined with ribavirin
- Chronic hepatitis B
- Kaposi sarcoma (HHV-8)
- Condyloma acuminatum (HPV)

NEURAMINIDAZE INHIBITORS (oseltamivir, zanamivir)

Mechanism of action

- inhibit enzim important for budding:
  - release of influenza virus from infected cell
- effective within first 48h of disease

Toxicity

- Zanamivir (aerosol)- bronchospasm
- Oseltamivir (po)- safe

Indications

- Complicated influenza A and B
  - with penumonia
- Influenza in high risk patients
  - Therapy of uncomplicated influenza
  - Prolonged prophylaxis (half doze)