

**Institute for Microbiology, Medical Faculty of Masaryk University
and St. Anna Faculty Hospital in Brno**

Miroslav Votava

**AN OVERVIEW OF
ANTIMICROBIAL AGENTS – I**

**The 14th lecture for the 2nd-year students
May 18th, 2015**

Prevention, prophylaxis and therapy of infections I – revision

Prevention of infection = avoiding an infection in the future

As the specific prevention of infection serves the vaccination

Prevention, prophylaxis and therapy of infections II – revision

Prophylaxis of infection = avoiding an imminently threatening infection

For the prophylaxis, passive immunization is usually used

Only rarely for the prophylaxis the vaccination is used (e.g. rabies) or the re-vaccination (e.g. tetanus)

Prevention, prophylaxis and therapy of infections III – revision

Therapy of infection

For the therapy the **passive immunization** is used (of course apart from antibiotics); very rarely active immunization by means of autovaccines

Immunization and its types – revision

Immunization	natural	artificial
active	after infection	after vaccination
passive	by transfer of antibodies through placenta and during breast-feeding	after injecting antiserum (immuno- globulin)

Artificial passive immunization – revision

= application of antibodies in the form of
antisera or globulins

Formerly: complete animal sera

Present-day preparations for passive
immunization:

- animal (heterogenous) sera and globulins
(purified and enzymatically split)
- human (homologous) immunoglobulins
 - normal
 - specific

Animal sera and globulins I – revision

Disadvantages:

They are very antigenic

- body tries quickly to get rid of them
- therefore the protection lasts few weeks only

Complications (even after the first application):

- *Serum disease*
- *Anaphylactic shock* (applying adrenalin and corticoids is essential)

Animal sera and globulins II – revision

Examples:

Antirabic serum (antigen used for its production =
for the immunization of animals = inactivated
rabies virus)

Globulin against

botulismus (antigens used for its production
= botulotoxins A, B, E)

gas gangrene (antigens used for its production
= α -toxins of *Clostr. perfringens*,
Cl. novyi and *Cl. septicum*)

viper toxins (antigens used for its production
= toxins of some European vipers,
e.g. *Vipera ammodytes* or *V. berus*)

Human immunoglobulins – revision

Two kinds of human (homologous)
immunoglobulin:

- Normal immunoglobulin
- Specific immunoglobulins

Use:

- For the prophylaxis and therapy of some infections
- As a substitution of antibodies in some types of immunodeficiencies

Normal immunoglobulin – revision

Normal immunoglobulin (formerly called normal gammaglobulin)

Origin: from the mix of plasmas from at least 1000 healthy donors → hence it contains antibodies against all common infections

Examples of the use:

- For the prophylaxis of hepatitis A in contacts with the ill
- At the defects of antibody production
- During therapy of serious infections (special intravenous preparations)

Specific immunoglobulins – revision

Origin: from the plasma of actively immunized donors:

- Human **tetanic** immunoglobulin for the prophylaxis of tetanus
- Immune **antistaphylococcal** plasma
- Ig with high titre of antibody against HBsAg for the prophylaxis of **viral hepatitis B**
- Ig for the prophylaxis and therapy of **chickenpox and zoster**
- Ig for the prophylaxis and therapy of **cytomegalovirus infections**
- Ig for the prophylaxis of **tick-borne encephalitis**
- Ig for the prophylaxis of **rabies**
- monoclonal Ab against **RSV** (in premature newborns)

Nonspecific build-up of immunity – revision

Replacement of missing factors: normal Ig, fresh plasma, transfer-factor from lymphocytes

Immunomodulators: components of common urinary and respiratory bacterial pathogens – e.g. peroral autovaccines, stockvaccines and a vast number of commercial preparations

Probiotics: live non-pathogenic strains of microbes reportedly able to re-establish normal mucosal microflora – e.g. strains of *E. coli*, *Lactobacillus acidophilus*, *Saccharomyces boulardii*

Interferon: for the treatment of hepatitis B and C and some malignancies

ANTIMICROBIAL AGENTS

= drugs used to treat infectious diseases

antibiotics – naturally occurring microbial products

chemotherapeutics – synthetic compounds

Different types of agents:

antibacterial

antifungal

antiviral

antiparasitic

ANTIBACTERIAL AGENTS

Inhibitors of 1) cell wall synthesis

2) protein synthesis

3) nucleic acid synthesis

4) other

1. Inhibitors of bacterial cell wall synthesis

β-lactam agents

**penicillins
cephalosporins
monobactams
carbapenems**

Glycopeptides

**vancomycin
teicoplanin**

Other inhibitors of bacterial cell wall

**e.g. bacitracin
cycloserin
isoniazid**

Penicillins

Acidolabile:

benzylpenicillin (penicillin G)
procaine penicillin

Acidostable:

phenoxymethylpenicillin (penicillin V)

Resistant to penicillinase:

methicillin, oxacillin, flucloxacillin

Aminopenicillins:

ampicillin, amoxicillin, co-amp., co-amox.

Ureidopenicillins & carboxypenicillins:

co-piperacillin, co-ticarcillin

Acidolabile penicillins

Classical benzylpenicillin (penicillin G):

crystalline penicillin G – i.v.

procaine penicillin G – i.m.

benzathin penicillin G – i.m.

Spectrum: G+ cocci & rods, G- cocci,

G- spirals

Acidostable penicillins

phenoxymethylpenicillin (penicillin V):

- peroral; **the same spectrum**

Penicillins resistant to staphylococcal penicillinase

Used against infections caused by *S. aureus*

Originally **methicillin**

staphylococci resistant to penicillinase =

MRSA, methicillin-resistant *S. aureus*

Now in use **oxacillin** (but MRSA are also resistant to it)

Combination with ampicillin: **cloxacillin**

Aminopenicillins

Have a broader spectrum:

most strains of *Enterococcus faecalis*

Listeria monocytogenes is more sensit.

Above all many Gram-negative rods:

E. coli, *Proteus mirabilis*, *bordetellae*,
salmonellae, *shigellae*, *hemophilli* & oth.

Amoxicillin (p.os)

Co-amoxicillin (+ clavulanic acid)

Ampicillin (inj. prep. only)

Co-ampicillin (+ sulbactam)

Ureidopenicillins

Broad spectrum:

effective also against *Ps. aeruginosa*

Co-piperacillin (+ tazobactam)

Carboxypenicillins

Spectrum similar to ureidopenicillins

effective against resistant hospital strains incl. *Pseud. aeruginosa*

Co-ticarcillin

Cephalosporins

1st generation (spectrum like ampicillin)

cefazolin

cefadroxil (p.o.)

2nd generation (more resist. to β -lactamases)

cefuroxime

cefuroxime axetil (p.o.)

3rd generation (very effective against G-)

cefotaxime, ceftriaxone

ceftazidime, cefoperazone (*P. aerug.*)

4th generation (also against G+)

e.g. cefepime

Monobactams

Aztreonam (against G- only)

Carbapenems

Imipenem (+ cilastatin = **Thienam**)

for multiresistant strains incl. G+ cocci
and *Kl. pneumoniae* producing **ESBL**,
extended spectrum beta-lactamases)

Meropenem (dtto; diffuses through
inflammed meninges)

Ertapenem (against ESBL-producing strains)

2. Inhibitors of bacterial protein synthesis

Tetracyclines: doxycycline (very broad spectrum)

Chloramphenicol (very toxic)

Aminoglycosides:

streptomycin (now for tbc only)

gentamicin, amikacin (G- rods & staphs)

neomycin (toxic, for topical use only)

Macrolides, azalides, ketolides

Lincosamides

**Newer antibiotics: e.g. oxazolidinons,
streptogramins, glycyglycines etc.**

Macrolides, azalides, ketolides

Macrolides:

Erythromycin (like PNC, + some G- rods)

Roxithromycin (for atypical pneumoniae)

Spiramycin (little toxic, toxoplasmosis)

Azalides:

Azithromycin (better for G- rods)

Clarithromycin (better for G+)

Ketolides:

Telithromycin (even better for G+)

Lincosamides

Lincomycin

Clindamycin

**Both for G+ (except enterococci), anaerobes,
some protozoa**

Streptogramins

quinupristin + dalfopristin (Synercid) (for G+)

Oxazolidinons

Linezolid (G+ incl. MRSA & anaerobes)

Lipopeptides

Daptomycin (kills MRSA)

Glycylcyclins

Tigecyclin (broad spectrum, ESBL
producents)

3. Inhibitors of nucleic acid synthesis

Sulphonamides: sulfamethoxazol (only in comb.)

Pyrimidines: trimethoprim (bacteriostatic), plus sulphamethoxazol = bactericidic co-trimoxazole (most G+ cocci & G- rods, nocardiae, *Toxopl. gondii*, *Pneumocystis jirovecii*)

Quinolones:

nalidixic acid & norfloxacin (urine tract inf.)

ciprofloxacin, ofloxacin (multiresistant G- rods)

Nitroimidazoles: metronidazol, ornidazol (anaerobes & some parasites)

Nitrofurans: nitrofurantoin, nifuratel (urine tract inf.)

Ansamycins: rifampicin, rifabutin (mainly tbc)
rifamixin (travellers diarrhoea)

4. Miscellaneous antibacterial agents

Polypeptids: colistin (some G- rods incl. *P. aerugin.*)
polymyxin B (for local use only)

Antimycobacterial agents (in combinations only)

streptomycin

rifampicin

isoniazid

ethambutol

pyrazinamide

cycloserine

PAS

dapsone (for lepra)

Recommended reading material

Paul de Kruif: Microbe Hunters

Paul de Kruif: Men against Death

Axel Munthe: The Story of San Michele

Sinclair Lewis: Arrowsmith

André Maurois: La vie de Sir Alexander Fleming

Hans Zinsser: Rats, Lice, and History

Michael Crichton: Andromeda Strain

Albert Camus: Peste

Victor Heisser: An American Doctor Odyssey

Richard Preston: The Hot Zone

Mika Waltari: The Egyptian

Richard Gordon: Doctor in the House

Richard Gordon: Doctor at Large

Richard Gordon: Doctor at Sea

Please mail me other suggestions at:

mvotava@med.muni.cz

Thank you for your attention