

Antimicrobial therapy

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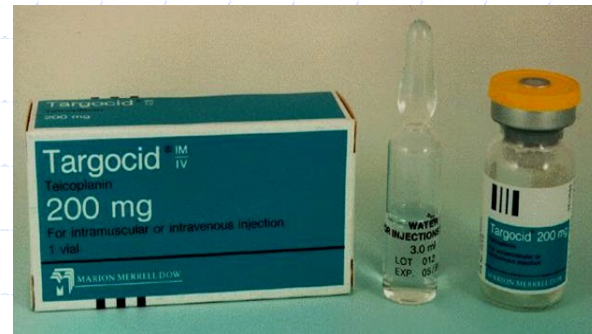
Antibiotics are substances against bacteria

Other groups:

Antivirotics – against viruses

Antituberculotics - against mycobacteria

Antiparasitics – against parasites



Antibiotics are divided due to mechanism of efficacy into 4 groups:

1. Inhibition of cell wall synthesis (betalactames, glycopeptides)
 2. Cell membrane destroy (polypeptides)
 3. Inhibition of NA syntesis (quinolons, imidazols)
 4. Inhibition of proteosyntesis (tetracyclines, chloramphenicol, macrolides, lincosamides, aminoglycosides)
- ◆ Attack against bacterial metabolism (sulfonamids)

Betalactames

- ◆ **Baktericidal, only for growing bacteria**
- ◆ **Often causes allergy**
 - Penicillins (PNC, oxacillin, ampicillin, piperacillin)
 - Cefalosporines (1.- 4. generation)
 - Monobactams (aztreonam)
 - Carbapenems (imipenem, meropenem)

Glycopeptides

- ◆ Reserved for G+ bacteria
- ◆ Vancomycin and less toxic, but more expensive teicoplanin

Polypeptides



- ◆ Ototoxic and nephrotoxic
- ◆ Polymyxin B only local as part of ear drops - Otosporin
- ◆ Polymyxin E – colistin rare used
- ◆ Primary resistance: all G+ bacteria, proteus, providencia, morganelia, serratia etc.

Aminoglycosides

- ◆ Bactericidal, ototoxicity and nephrotoxicity
- ◆ Synergy with betalactames – decrease of toxicity
- ◆ Preparates: Streptomycin only against tuberculosis, gentamicin, netilmicin, amikacin, neomycin with bacitracin = framycetin (neomycin is too toxic, only for local using)

Tetracyclines

- ◆ Broad spectrum
- ◆ Don't use until 10 years (teeth development)
- ◆ Less used

Chloramphenikol

- ◆ Broad spectrum
- ◆ Good penetration to liquor, Hematotoxicity

Macrolides

I. generation: erythromycin, rare used

II. generation: roxithromycin

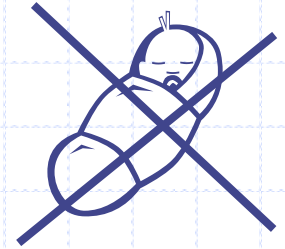
III. generation: clarithromycin, azithromycin –
good intracellular penetration and
longlasting effect, for G+ bacteria

Lincosamides

◆ Lincomycin and clindamycin

◆ Reserved for surgery, good effect to G+
bacteria and anaerobes in addition to
Clostridium difficile – risc of
pseudomembranous enterocolitis

Quinolones



- ◆ Bactericidal
- ◆ Don't use until 15 years (growth cartilages)
- ◆ I. generation (oxolin acid), II. generation (norfloxacin) only for urinary infection
- ◆ III. generation: ofloxacin, ciprofloxacin – also for systemic infection – often used



Analogs of folate acid

- ◆ Sulfamethoxazol in combination with trimetoprim form ko-trimoxazol known as BISEPTOL
- ◆ Bacteriostatic, worse penetrate into tissues

Nitrofurantoin (and nifuratel)

- Effectivity on sugar metabolism. Bacteriostatic, broad spectrum
- For urinary tract infection. Weighty undesirable effect: GIT disorder etc.

Other antibiotics

Linezolid (zyvoxid) – against resistant staphylococci

Nitroimidazols

- ◆ For anaerobes, for protozoas (*T. vaginalis etc.*)
- ◆ Metronidazol, Ornidazol

Antituberculotics

- ◆ HRZS,HRZE - starting therapy (INH, rifampicin, pyrazinamid, streptomycin, etambutol) + other
- ◆ HRZ,HRE – sequenced therapy

Antivirotics

- ◆ Against herpes – acyclovir...
 - ◆ CMV – gancyclovir, foscarnet
 - ◆ Influenza – amantadin, rimantadin, tamiflu
 - ◆ Antiretrovirus therapy – inhibitors of reverse transcriptase (nucleosid+nonucleosid) , inhibitors of protease – in combination
- Preparates: zidovudin, didanosin ...

Antimycotics

- ◆ Fluconazol, itraconazol, ketoconazol etc. – local (vaginal, skin infection)
- ◆ Amphotericin B – i.v. (in sepsis)

Antiparasitics

- ◆ Against protozoa, helmintes, ectoparasites (moore in parasite capitol)

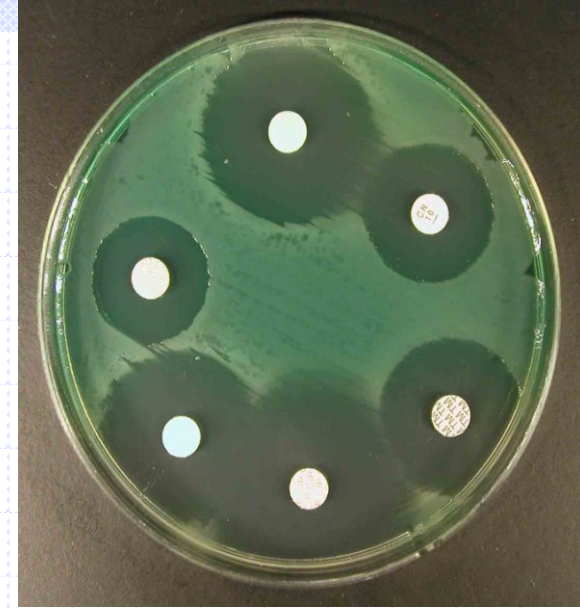
Other preparates

- ◆ Antimalaric: primachin, chlorochin, meflochin...
- ◆ Leprosity: dapson

Susceptibility testing in vitro

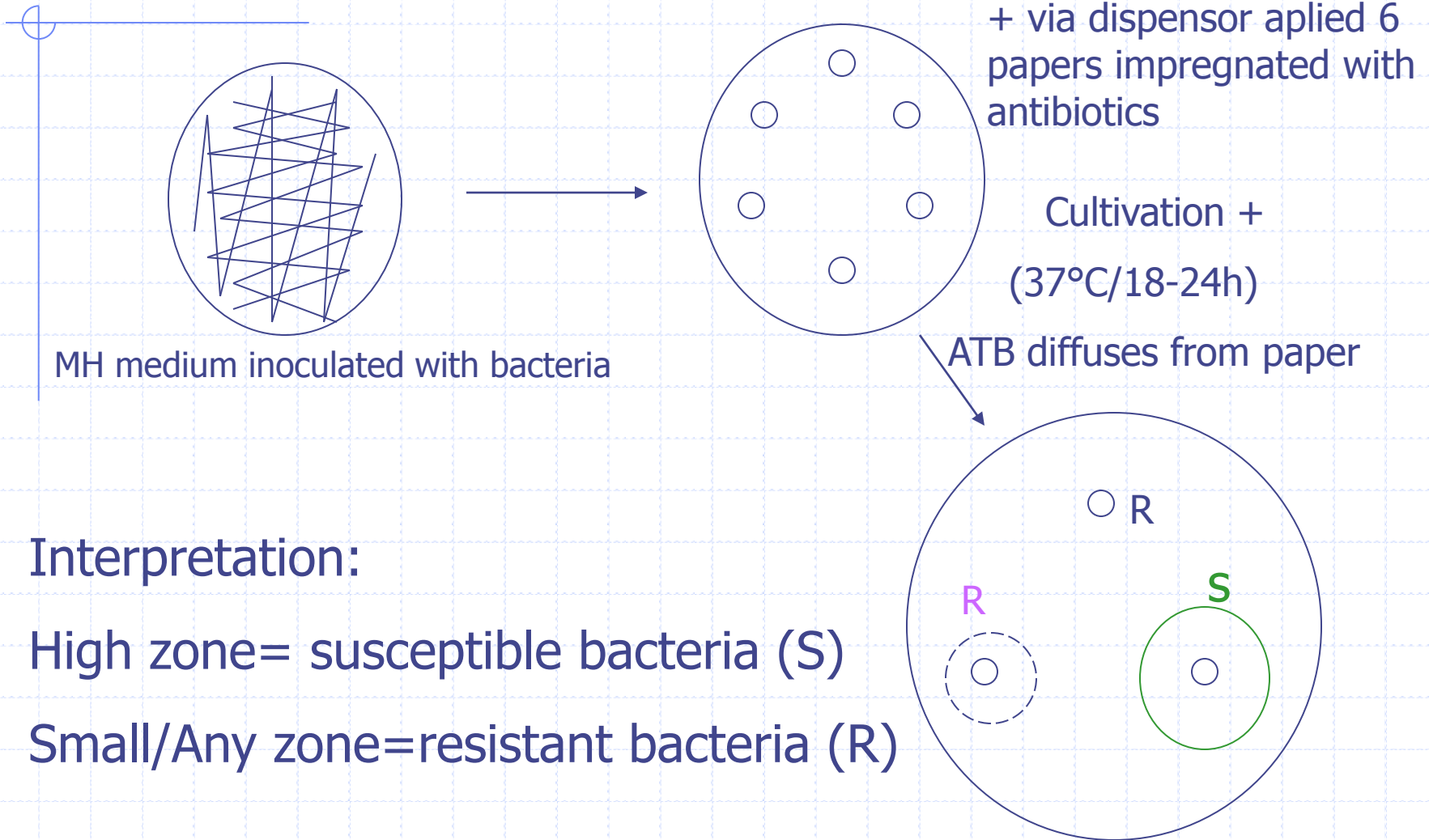
- ◆ Do not correspondent in all cases with effect of therapy
- ◆ Quantitative tests (MIC, E-tests) – in relevant patients
- ◆ Qualitative tests (disc diffusion method) – enough for common cases (susceptible - resistant)

Disc diffusion test



- ◆ MH agar is inoculated with **suspension of bacteria**
- ◆ **Antibiotic discs** (paper impregnated with antibiotics) are applied at MH – **atb diffuse** from disc through agar
- ◆ **Concentration of atb decrease** with distance from disc
- ◆ If microb grow to disc/if there is little zone - is **resistant** (not susceptible)
- ◆ Big zone (higher than defined size) means **susceptibility**.

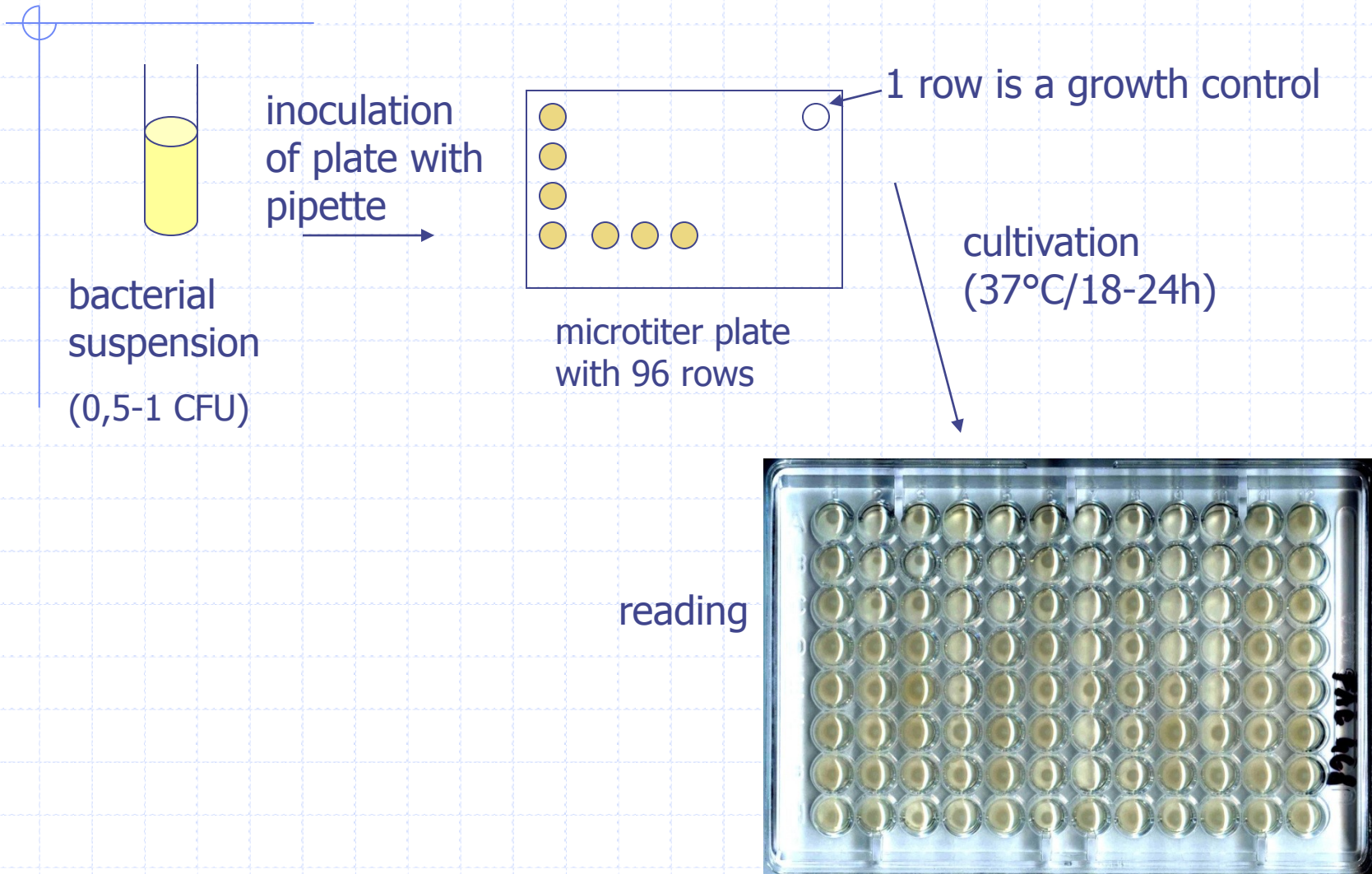
Disc diffusion test



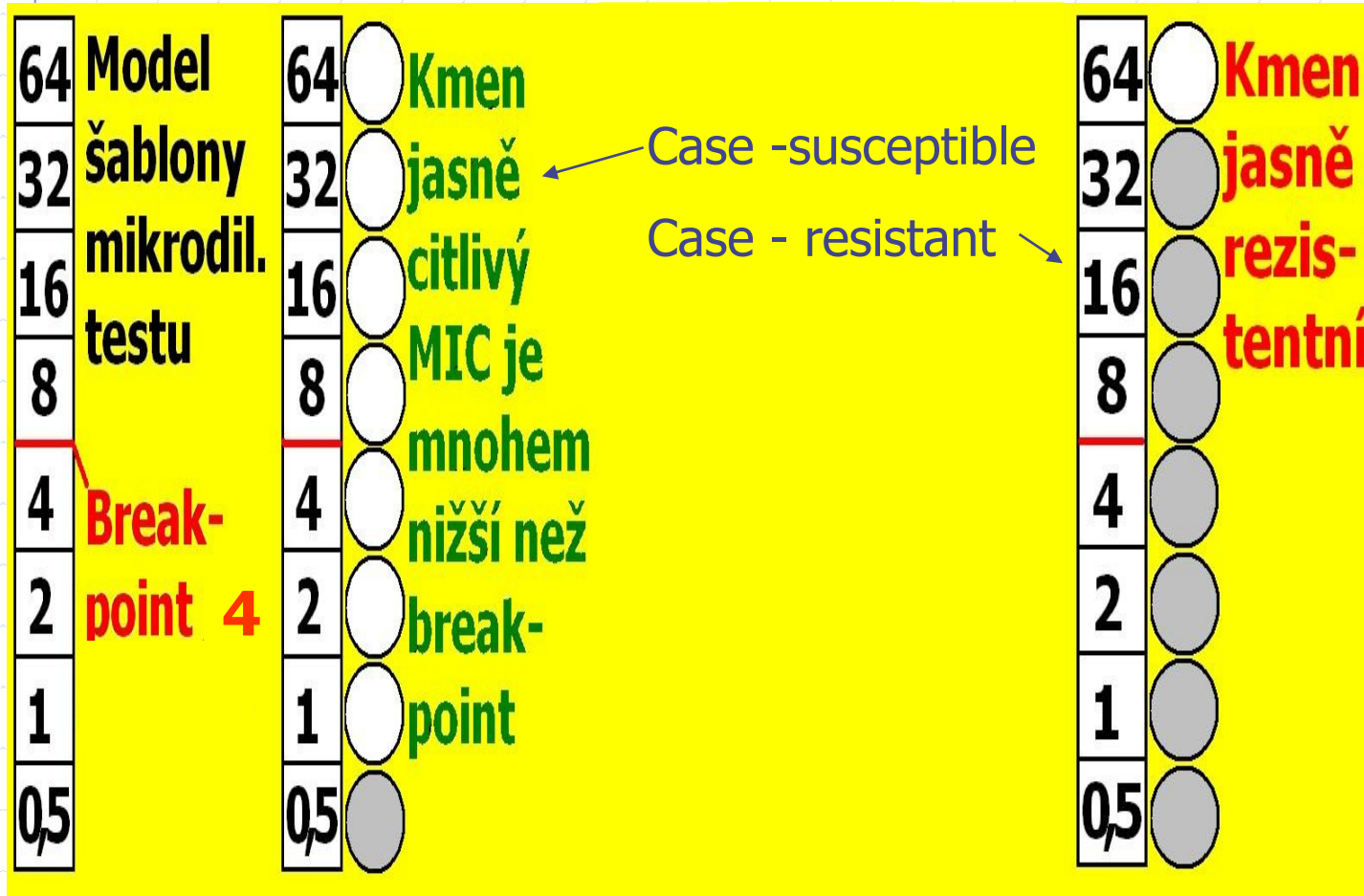
Microdilution test (MIC)

- ◆ MIC is the lowest concentration, which inhibites growth (first clear row)
- ◆ On paper stencil is assigned **breakpoint**. If MIC is lower than breakpoint, bacteria is susceptible. If MIC is higher, bacteria will be resistant
- ◆ 1 plastic plate is used for 1 bacteria, for **12 antibiotics**, in 8 various (decreasing) concentration (*12th only in 7, because corner row upper right is growth control*)

MIC – Material and methods



Interpretation



PEN	AMS	CXT	CLI	CMP	MTR	PEN	AMS	CXT	CLI	CMP	MTR
4	64	128	32	64	64	4	64	128	32	64	KR
2	32	64	16	32	32	2	32	64	16	32	32
1	16	32	8	16	16	1	16	32	8	16	16
0.5	8	16	4	8	8	0.5	8	16	4	8	8
0.25	4	8	2	4	4	0.25	4	8	2	4	4
0.125	2	4	1	2	2	0.125	2	4	1	2	2
0.063	1	2	0.5	1	1	0.063	1	2	0.5	1	1
0.031	0.5	1	0.25	0.5	0.5	0.031	0.5	1	0.25	0.5	0.5

Interpretation of MIC - antibiogram – goes to clinician!

PEN (penicillin)...4.....resistant

AMS (unasyn).....2.....susceptible

E-tests (quantitative)

- ◆ Similar to disc diffusion test, but strip is used
- ◆ An increasing concentration of atb is used. Zone is egg like.
- ◆ There is a scale on strip – simply reading



MIC value is 0,75 mg/l (where borderline of zone cross the scale)

Resistance of microbes to antibiotics

- ◆ **Primary resistance:** all strains of bacteria are resistant.
- ◆ **Secondary resistance:** arises unsensitive mutants, by selective antibiotics pressure became dominant

*

MBC (minimum bactericidal concentration) is the lowest concentration, which kills bacteria

Primary bactericid: atb, where MIC and MBC are almost equal

Primary bacteriostatic: atb, where MBC is X-fold higher than MIC - unreal baktericidal effect in human body

Resistance factors detection

◆ Special detection methods for resistance factors (for ex. betalactamase). It can be diagnostic strips (chemical detection of specific enzyme) or other tests (ESBL)

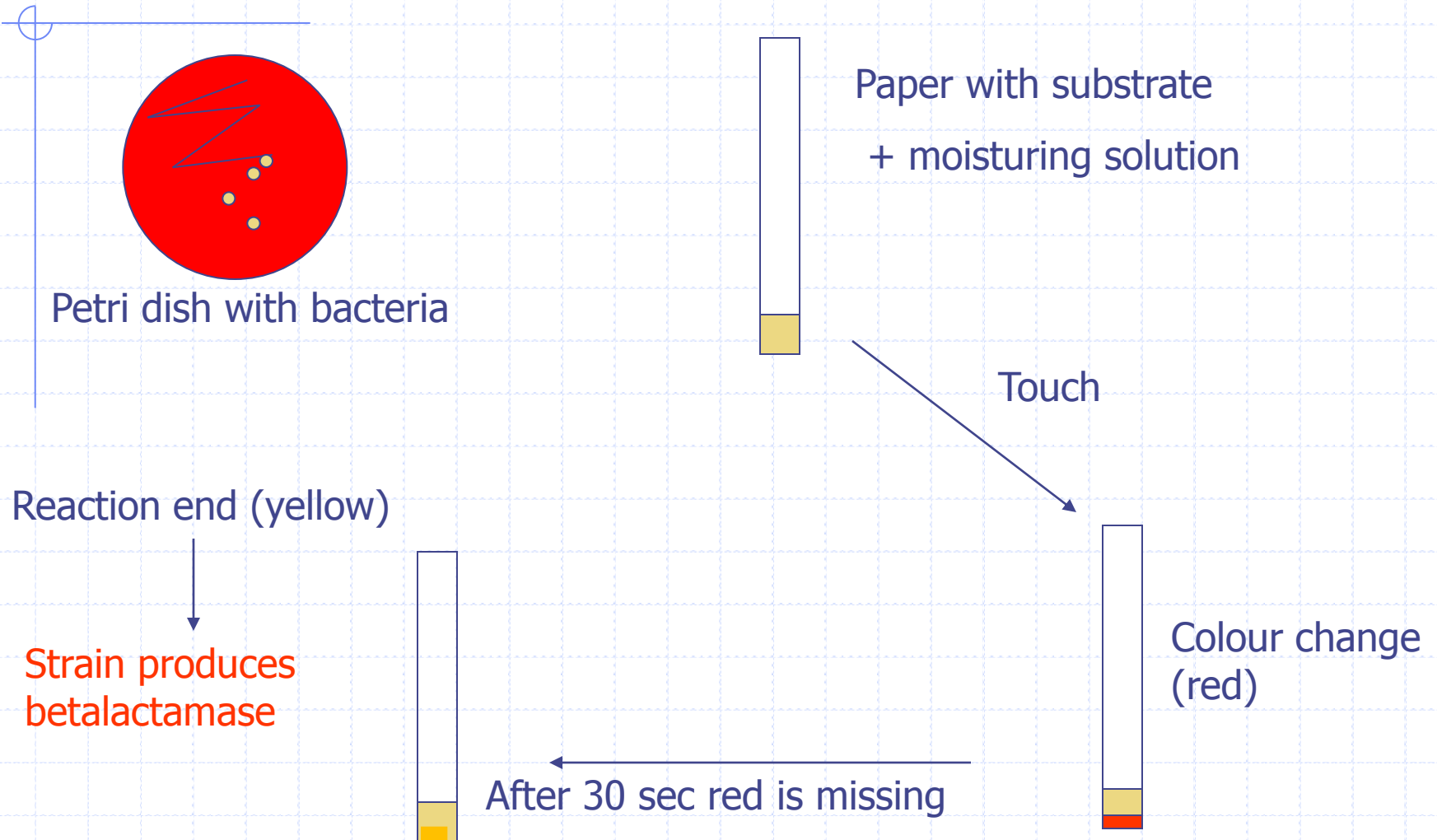
1. Betalactamase testing

◆ In neisseria, *M. catarrhalis*, *H. influenzae*

◆ destroys betalactams

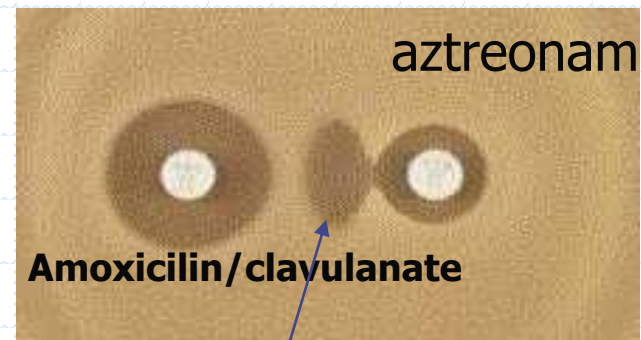
◆ For therapy we use ATB with inhibitors of betalactamase like clavulanate, sulbactam...

Detection of betalactamase



2. ESBL (extended spectrum betalactamase)

E. coli, *K. pneumoniae* etc. produces ESBL, which destroys cheap betalactams. For therapy we use expensive carbapenems, aminoglycosides (toxicity), problem of ICU, big hospitals

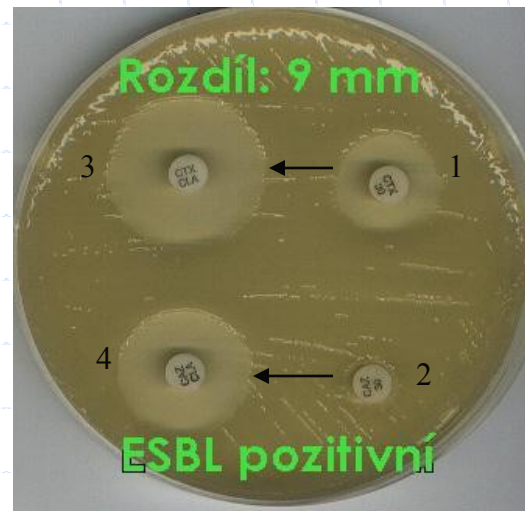


ESBL – screening

- ◆ Inhibition of growth between discs – owing to a synergism of 2-3 antibiotics such as aztreonam, AMC, ceftriaxon

ESBL detection

- ◆ 4 discs: Cefotaxim (1) and ceftazidim (2), cefotaxim with clavulanate (3) and ceftazidim with clavulanate (4)
- ◆ Difference between cefalosporines (1,2) and cefalosporines with clavulanate (3,4) is higher than 5mm



Compare

1 with 3 and 2 with 4