抗生素的使用

亞東紀念醫院 藥劑部

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抗生素概論

- 感染確定
  - 感染症狀
    - 發燒（fever≠infection）
    - 白血球增加（shift to the left）
    - 血壓下降、尿量減少、紅腫熱痛
- 確認感染部位與鑑定感染原（smear、culture）
- 考慮病患疾病及相關因素
- 制定治療方針與投予抗生素
  - 經驗性治療 (empiric therapy)
    - 病人因素：過敏記錄、感染部位、肝腎功能、其他疾病、使用藥物
    - 藥品因素：藥品動力學、組織穿透性、副作用、花費
  - 殺菌的效力（spectrum）
  - 足夠的濃度（MIC）
- 定期評估治療效果

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抗生素特性

- 抗微生物的類型
  - 殺菌性（bactericidal）
    - Leukopenia、endocarditis、meningitis、osteomyelitis
  - 抑菌性（bacteristatic）
- 抗生素的特性
  - 時間依賴型（time-dependent）
    - β-lactams、glycopeptides、macrolides、clindamycin
  - 濃度依賴型（concentration-dependent）
    - aminoglycosides、quinolones、metronidazole、daptomycin

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常見之革蘭氏陽性菌感染

- Cocci
  - *Staphylococcaus aureus* (金黃色葡萄球菌)
  - Coagulase negative *Staph*
    - *Staph. Epidermidis*
    - *Staph. Saprophyticus*（UTI）
  - *Streptococus pneumoniae* (肺炎雙球菌)、*Strep. viridans*（Catalase negative）
  - Enterococcus
- Rods
  - *Corynebacterium diphtheriae*（白喉桿菌）
  - *Listeria monocytogene*（李斯特菌、meningitis）
  - Anaerobic：*Clostridium difficile*（pseudomembranous colitis）、 Propionibacterium acnes
  - *Mycobacteria*

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常見之革蘭氏陰性菌感染

- Cocci
  - *Neisseria meningitidis*、*Neisseria gonorrhoeae*(淋病奈瑟氏菌)
  - *Moraxella catarrhalis*
- Rods
  - Enterobacteriaceae
    - within and outside：*Escherichia* coli、*Salmonella*（enterocolitis）
    - within：*Shigella*（dysentery）、*Vibriocholerae*（cholera）
    - outside：*Klebsiella pneumonia*、*Enterobacter cloacae*、*Serratia marcescens*
  - *Pseudomonas aeruginosa*、*Burkholderia cepacia*、*Xanthomonas*(*Stentrophomonas maltophilia*)
  - *Helicobacter pylori*(幽門螺旋桿菌)
  - *Legionella pneumophila* (退伍軍人桿菌)
  - Anaerobic：*Bacteroides fragilis*
- Coccobacillus
  - *Haemophilusin fluenzae* (流行性嗜血桿菌)、*Acinetobacter* Sp.

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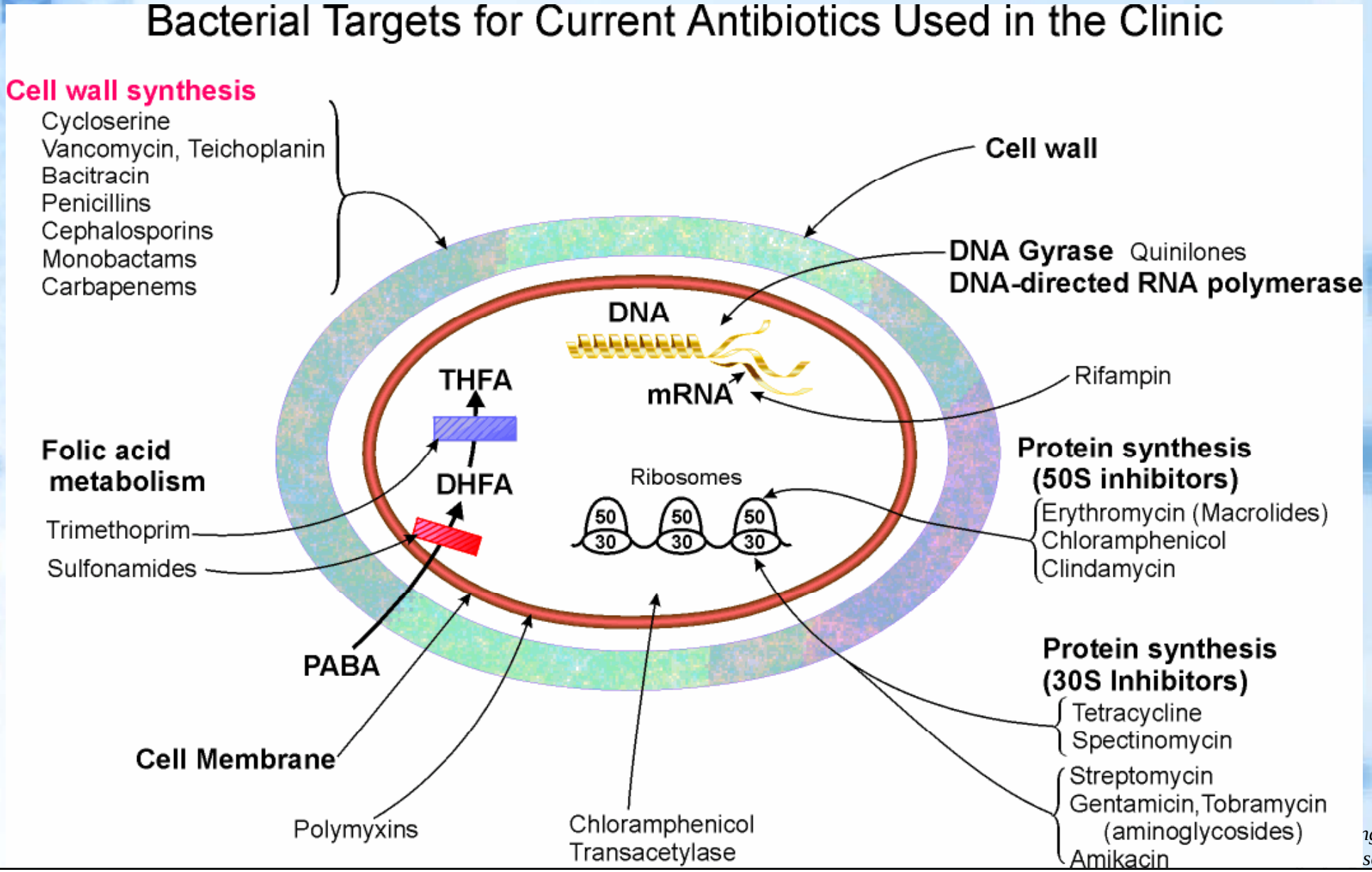
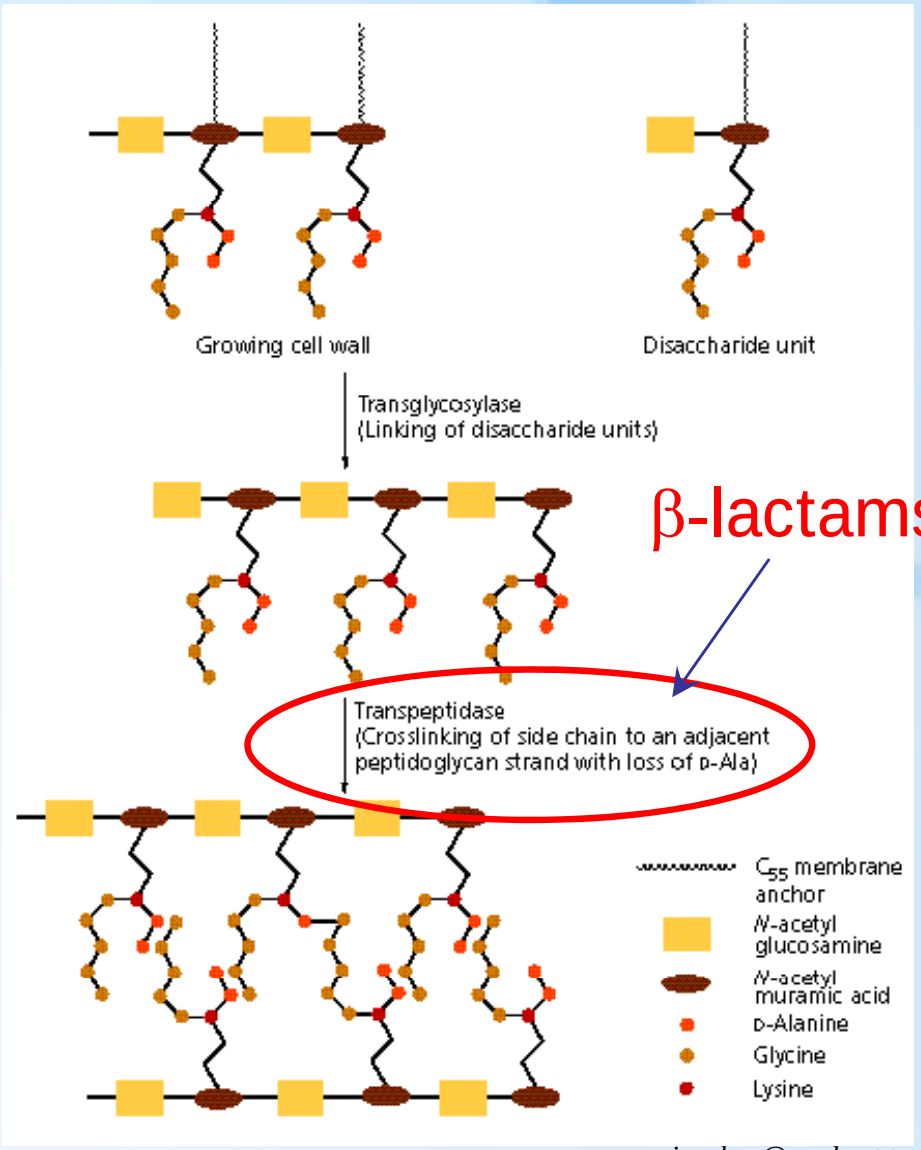
抗生素作用機轉



β-Lactam Antibiotics

- Mechanism
  - attach to penicillin-binding proteins (PBPs) on the inner surface of the bacterial cell membrane, and then interrupting the bacterial cell wall synthesis
- Bactericidal
- Time-dependent



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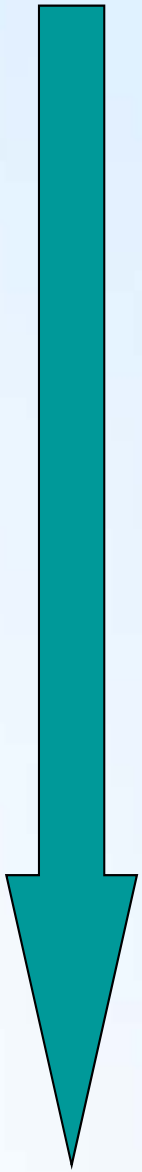
Penicillins

- Natural penicillins
  - Penicillin G
  - Penicillin V
- Aminopenicillins
  - Ampicillin
  - Amoxicillin
  - Bacampicillin
- Carboxypenicillins
  - Carbenicillin
  - Ticarcillin
- Ureidopenicillin
  - Piperacillin



- G(+) cocci、some G(-) cocci

  some anaerobes
- extended G(-) including *E coli*、*Proteus mirabilis*、*Salmonella*、*Shigella*、*Listeria*、*H. influeazae*
- extended to indole-positive *Proteus*、*Enterobacter*、*Provindencia*、*Morganella*、*P. aeruginosa*
- G(-)、anaerobes

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Penicillins

- Natural penicillins
  - Penicillin V(oral)
  - Penicillin G sodium 10MU/vial
  - Penicillin G Benzathine 2.4MU/vial
- Activity
  - *Streptococcus*、*Enterococcus*
  - *Meningococcus*(腦膜炎雙球菌)
  - Syphilis(梅毒)、Actinomycosis(放射菌)、Diphtheria、Anthrax(炭疽)、Listeria
  - Non-*difficile Clostridium* anaerobes
- Ineffective
  - *Staphylococcus*
  - GNB

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Penicillins

- Amino-penicillins
  - Ampicillin sodium
  - Amoxicillin
- Activity
  - *Streptococcus*、*Enterococcus*、*Listeria*
  - Some *E. coli*、*Proteus mirabilis*
  - Some *Salmonella*
- Ineffective:
  - *Staphylococcus*、G(+) anaerobes
  - Other GNB

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Penicillins

- Anti-pseudomonal penicillins
  - Carboxypenicillin：Carbenicillin
  - Ureidopenicillin：Piperacillin sodium 2g/vial
    - Metabolism only in kidney
- Activity
  - *Streptococcus*、*Enterococcus*、G(+) anaerobes
  - Most GNB, including *Pseudomonas*
- Ineffective
  - *Staphylococcus*
  - *Hemophilus*、*Salmonella*、*Moraxella*

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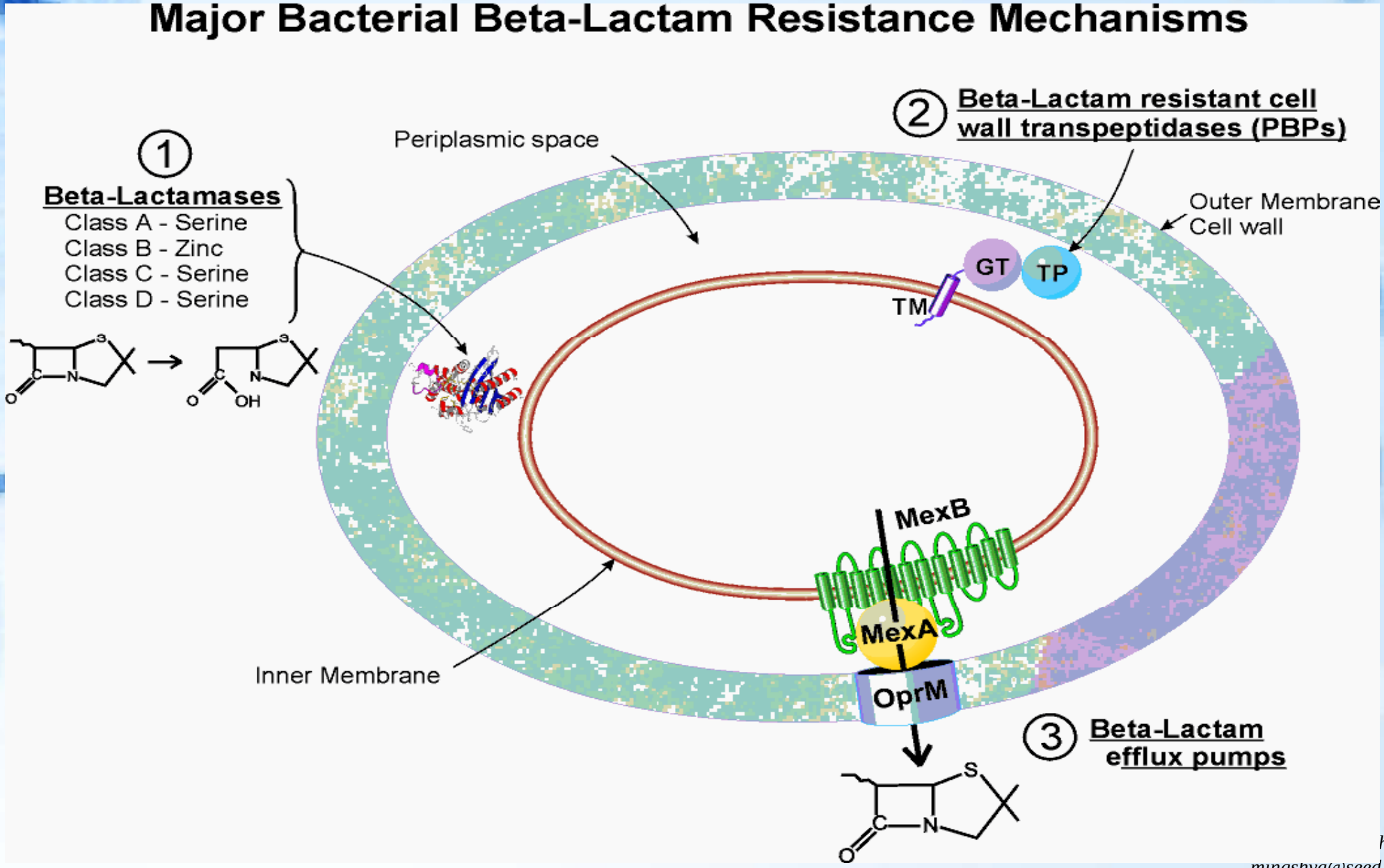
β-Lactam Antibiotics抗藥性



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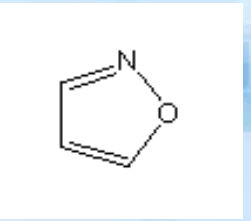
Penicillinase-resistant Penicillin

- Penicillinase-resistant penicillins
  - Methicillin
  - Oxacillin、Cloxacillin、Dicloxacillin、Flucloxacillin、Nafcillin
    - Metabolism only in liver



- Activity
  - Methicillin-Sensitive *Staphylococcus aureus*（MSSA）
  - Less effective for *Streptococcus*
- Ineffective
  - MRSA、*Enterococcus*、G(+) anaerobes
  - GNB

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β-Lactamase Inhibitors

- Mechanism
  - acts as a suicide substrate rendering the β-lactamases inactive through a time-dependent irreversible reaction
  - effective only against plasmid-encoded Ambler class A β-lactamases（except chromosomal Ambler class C β-lactamase）

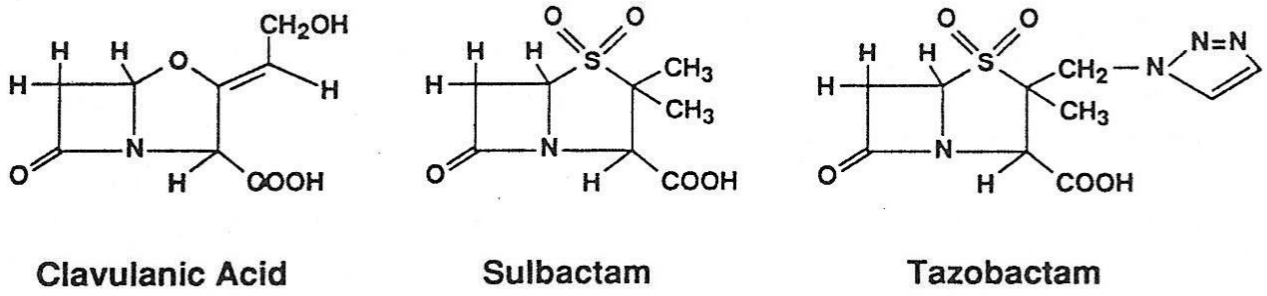

Figure 1. Chemical structures of the various beta-lactamase inhibitors: clavulanic acid, sulbactam, and tazobactam. (*From* Bush LM, Calmon J, Johnson CC: Newer penicillins and beta-lactamase inhibitors. Infect Dis Clin North Am 9:653–686, 1995; with permission.)

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Penicillins

- Penicillin + β-lactamase inhibitor
  - Amoxicillin + Potassium calvulanate (Augmentin)
  - Ticarcillin+ Potassium clavulanate (Timentin)
  - Ampicillin+ Sulbactam (Unasyn1.5g/vial)
    - Ampicillin sodium 1g + Sulbactamsodium 500mg
  - Piperacillin+ Tazobactam(Tazocin2.25g/vial)
    - Piperacillinsodium 2g + Tazobactam250mg

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Penicillins常見副作用

- Hypersensitivity (PCN skin test)
  - IgE antibody related：0.004 ~ 0.4% (Penicillin G)
    - Anaphylaxis、early urticaria (< 72 hours)
  - Serum sickness：rare (Penicillin G)
  - Delayed hypersensitivity：4 ~ 8% (Ampicillin)
  - Idiopathic：4 ~ 8% (Ampicillin)
    - Skin rash、fever、late-onset urticaria
- GI tract：2 ~ 5% (Ampicillin)
  - Diarrhea、enterocolitis
- Hematologic
  - Hemolytic anemia：rare (Penicillin G)
  - Neutropenia：1 ~ 4% (Penicillin G、Nafcillin、Oxacillin、Piperacillin)
  - Platelet dysfunction：3% (Carbenicillin、Ticarcillin)

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Penicillins常見副作用

- Hepatic
  - Elevated AST/ALT：1 ~ 4% (Oxacillin、Nafcillin、Carbenicillin)
- Electrolyte disturbance
  - Sodium overload：Ticarcillin
  - Hypokalemia：Ticarcillin
  - Acute hyperkalemia：Carbenicillin
- Neurologic
  - Seizure：rare (Penicillin G)
  - Bizarre sensations (Procaine Penicillin)
- Renal
  - Interstitial nephritis：1 ~ 2% (Methicillin)
  - Hemorrhagic cystitis：rare (Methicillin)

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Cephalosporines

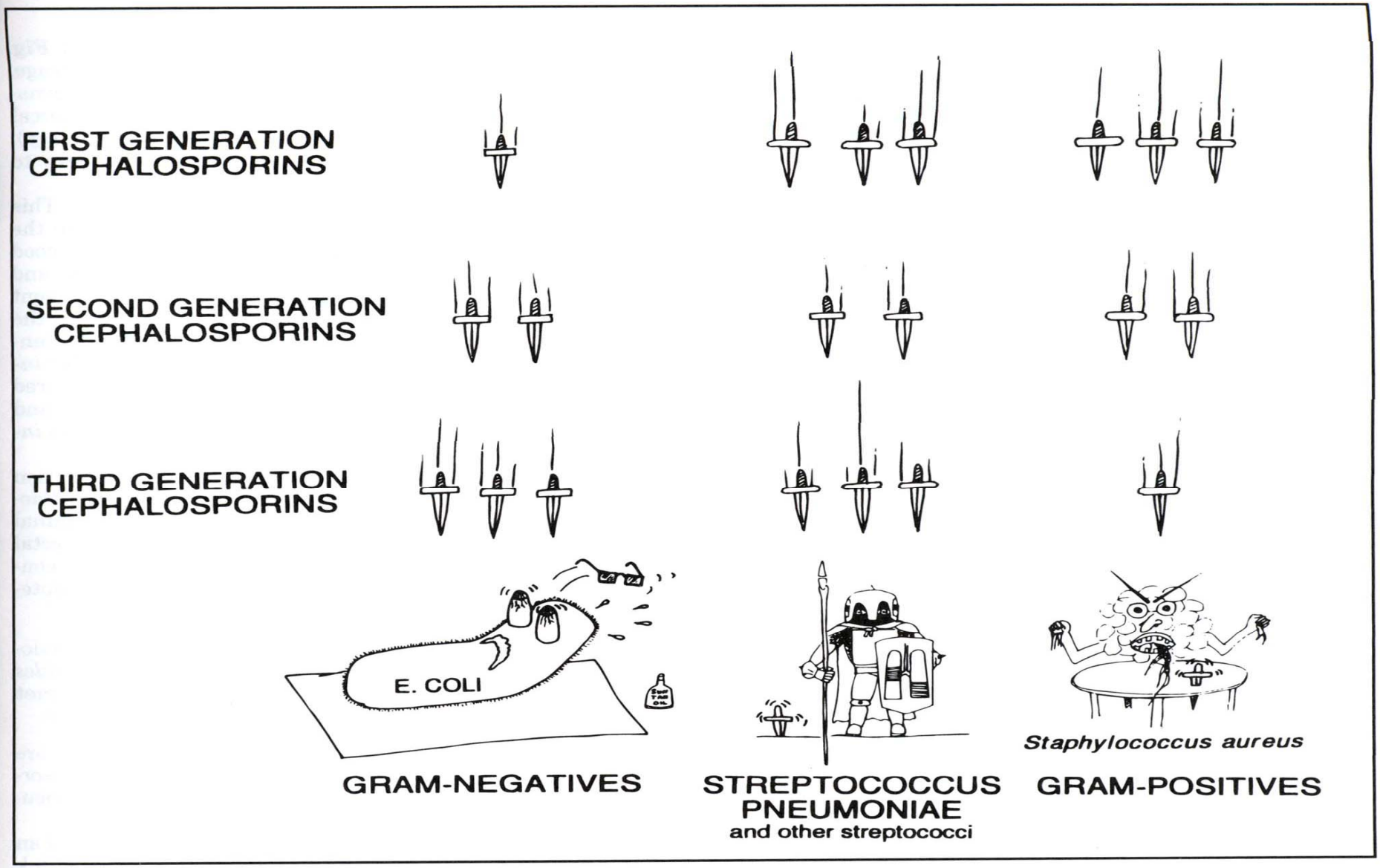

Figure 16-10

Cephalosporines

- First-generation Cephalosporins
  - Cefazolin Sod.（Cefazolin）1g/vial
  - Cephradine Arginine（U-Save A）1g/vial
  - Cephalexin（Keflex）
- Activity
  - MSSA、*Streptococcus*
  - *E. coli*、*K. pneumoniae*、*P. mirabilis*
- Ineffective
  - *Enterococcus*、MRSA
  - Other GNB
  - anaerobes

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Cephalosporines

- Second-generation Cephalosporins
  - True Cephems
    - Cefuroxime Sod.（Zinacef）250/750mg/vial
    - Cefaclor（Keflor）250mg/cap
    - Enhance the anti-GNB effect of 1stCephems
    - Less effective for GPC
  - Cephamycins
    - Cefmetazole Sod.（Cefmetazon）1g/vial
    - With the effect for anaerobes(*B. fragilis*)
- Ineffective
  - *Enterococcus*、MRSA

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Cephalosporines

- Third-generation Cephalosporins
  - True cephem
    - Ceftazidime Sod.（Fortum）500mg/vial
    - Ceftriaxone Disod.（Rocephin）500mg/vial
      - metabolism in kidney(65%) and liver
      - Protein binding＞90%
    - Cefotaxime Sod.（Claforan）500mg/vial
      - metabolism in kidney and liver
    - Ceftibuten（Seftem）100mg/cap
    - penetrate BBB well
  - Cephamycin
    - Flomoxef Sod.（Flumarin）500mg/vial
    - effective for anaerobes and most MSSA

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Cephalosporines

- Activity
  - Not so adequate for MSSA、enhanced activity for *Streptococci*
  - Strong effect for Enterobactereacea
  - Ceftazidime and Cefoperazoneare also effective for *P. aeruginosa*
- Ineffective
  - *Enterococcus*、MRSA
  - More resistant enterobactereacea, such as *Enterobacter*、*Citrobacter*、*Serratia*、*Morganella*(若為有效，應 combine aminoglycosides)

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Cephalosporines

- Fourth-generation Cephalosporins
  - Cefepime HCl（Maxipime）500mg/vial
  - Cefpirome （Cefrom）1g/vial
- Activity
  - Most MSSA、*Streptococcus*
  - Most Enterobactereacea, including *Enterobacter*、*Citrobacter*、*Serratia*、*Morganella*
  - *Pseudomonas aeruginosa*
- Ineffective
  - *Enterococcus*、MRSA
  - Anaerobes

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Cephalosporines常見副作用

- Hypersensitivity
  - Maculopapular rash（1 ~ 3%）、Urticaria、Pruritus
  - Serum sickness：rare (Cefaclor)
  - Eosinophilia：1 ~ 7%
  - Cross-allergenicity with penicillin：3 ~ 7%
- Hematologic reaction
  - Reversible neutropenia：< 1%
  - Thrombocytosis：2 ~ 5%
  - Positive Coombs'test (hemolysisis rare)
  - Coagulation abnormalities
    - Prolonged PT time：Cefmetazole、Ceftriaxone、Cefoperazone、Cefotetan
    - Reduced platelet aggregation：Moxalactam

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Cephalosporines常見副作用

- Gastrointestinal reaction
  - Mild abnormal liver function tests：1 ~ 7%
  - Diarrhea：non-specific / *C. difficile*related
  - Biliary sludge：20% (Ceftriaxone-dose related)
- Nephrotoxicity
  - Interstitial nephritis：rare

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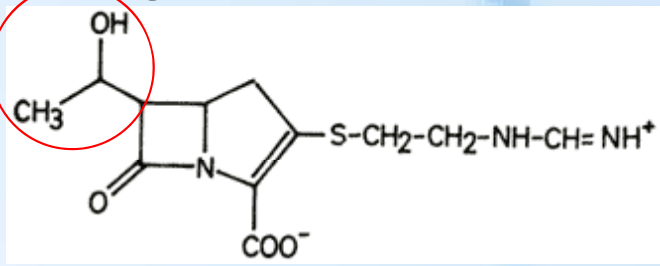
Carbapenems

- Imipenem/Cilastatin（Tienam）250mg/vial
  - Cilastatin Sod.
    - Imipenem will be inactivated in proximal renal tubule by dehydropeptidase, the product will cause the necrosis of proximal renal tubule.
    - Cilastatin is an inhibitor of dehydropeptidase I I
  - 具有右旋（trans）支鏈，增加對β-lactamase的穩定性
  - 副作用：輸注相關症狀（5%），噁心嘔吐（4%），腹瀉（3%），皮疹或發燒（2.7%），痙攣（1.5%）



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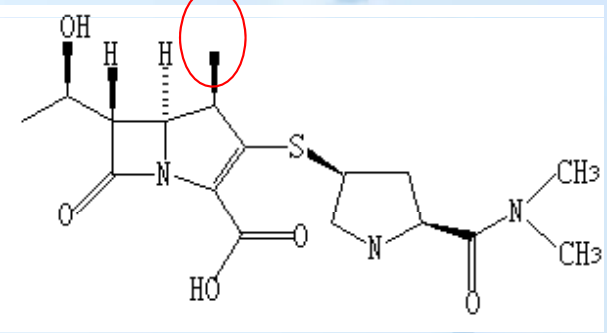
Carbapenems

- MeropenemTrihydrate（Mepem）500mg/vial
  - No be inactivate by dehydropeptidase（第二個碳上多一個-CH_3）
  - Less seizure effect（0.5% vs 1.5%）
  - Meropenem is better than imipenem against GNB（*P. aeruginosa*、*B. cepaciae*）
  - Meropenem is less active than imipenem against GPC（Enterococcus）



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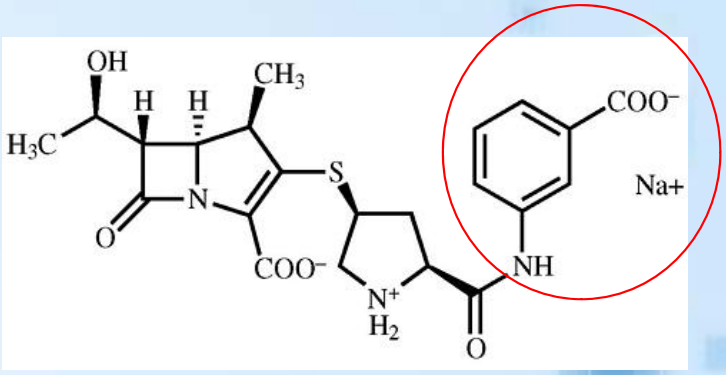
Carbapenems

- Ertapenem（Invanz）1g/vial
  - Benzoate moiety make it high protein bound（＞90%）and increase $T_{1/2}$（4H）
  - Activity
    - Most G(+)、G(-)、anaerobes
    - Poor activity against
      - *Pseudomonas aeruginosa*、*Acinetobacter spp.*
      - *S. maltophilia*、Enterococcus、MRSA、PRSP



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Carbapenem properties

	Ertapenem	Imipenem-cilastatin	Meropenem
Stable to renal DHP1	Yes	No	Yes
Metabolism	Renal	Renal	Renal
Protein bound	~94%	20%	<10%
Half life	4h	1h	1h

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Monobactam

- Monobactam
  - Aztreonam（Azactam）1g/vial
- Activity
  - Most GNB, including *P. aeruginosa*
- Ineffective:
  - G(+)、anaerobes
- Special consideration
  - β–lactam allergy
  - impairing renal function(aminoglycoside)

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Glycopeptides

- Mechanism
  - inhibits cell wall synthesis by binding to carboxyl units on peptide subunits containing free D-alanyl-D-alanine
  - it inhibits peptidoglycan polymerase and transpeptidation reactions
- 藥物動力學
  - 口服幾乎不吸收，需靜脈注射使用
  - 藥效與與達到超過MIC的時間有關
    - 時間依賴型(time dependent)

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Glycopeptides

- Glycopeptides
  - Vancomycin HCl（Vanco）500mg/vial
    - Peak：20-40 μg/ml；Trough：5-15 μg/ml
  - Teicoplanin（Targocid）200mg/vial
- Activity
  - G(+)、MRSA
  - Less effect to *Enterococci*（bacteristatic）
    - 與aminoglycosides合用有加成效果
  - *Clostridium difficile*
    - Vancomycin oral：125mg Q6H for 7-10 days

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Glycopeptides常見副作用

- Vancomycin
  - Nephrotoxicity
    - therapeutic drug monitor (TDM)
      - 最高值（peak）：給藥結束後約一小時抽血
      - 最低值（trough）：下一次給藥前
  - Hypersensitivity
    - red-man syndrome
      - 濃度<5-10mg/ml
      - infusion＜10mg/min
  - Phlebitis

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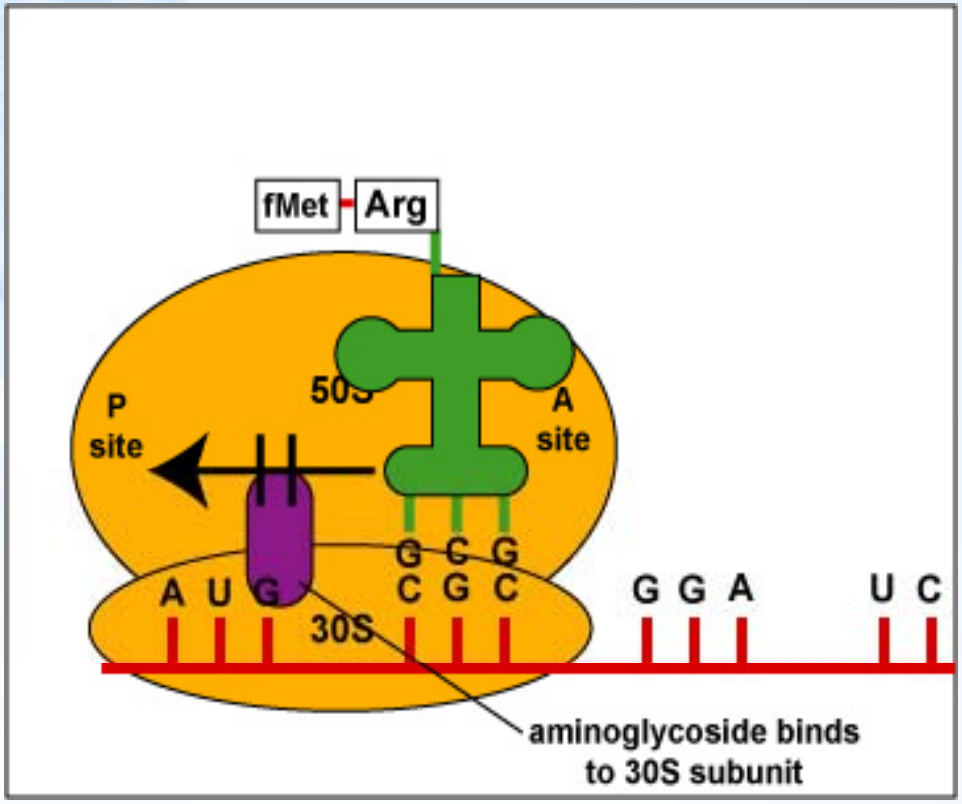
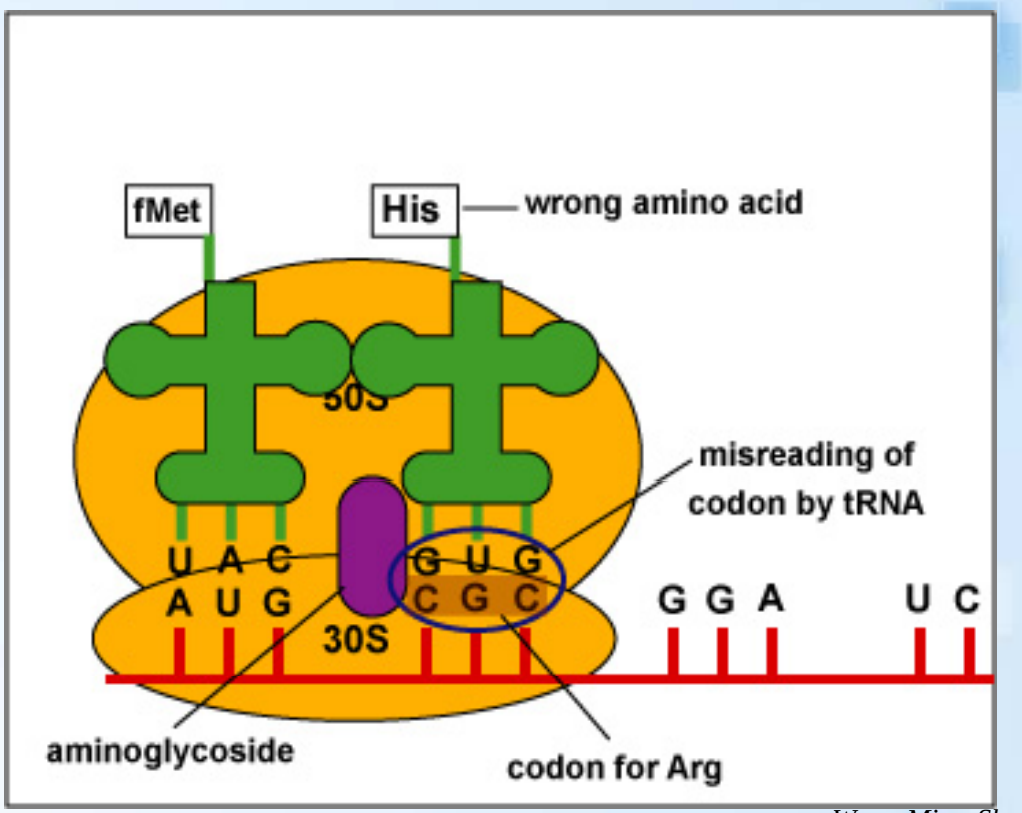
Aminoglycosides

- Mechanism
  - Bactericidal by inhibit 30s ribosomal protein synthesis





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Aminoglycosides

- Aminoglycosides（IBW）
  - Gentamicin Sulfate（Gentamycin）80mg/vial
    - Peak：4-12 μg/ml；Trough：1-2 μg/ml
  - Amikacin Sulfate（Amikin）500mg/vial
    - Peak：15-35 μg/ml；Trough 5-10 μg/ml
  - Kanamycin Sulfate（Kanamycin）1g/vial
  - Isepamicin Sulfate （Exacin）200mg/amp
- Activity（Combinative therapy ）
  - MSSA
  - Most GNB, including *P. aeruginosa*
  - Some Mycobacteria
- Characteristics
  - Concentration-dependent
  - Post-antibiotic effect

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Aminoglycosides

多次投與的血中濃度

藥品	每日劑量（mg/kg）	給藥間隔	最高濃度值（mcg/ml）	最低濃度值（mcg/ml）
Gentamicin	3-5	8小時	4-12	<2
Tobramycin	3-5	8小時	4-12	<2
Netilmicin	3-5	8小時	4-12	<2
Amikacin	15	8小時	15-35	5-10

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Aminoglycosides

- 藥物動力學特性
  - 殺菌效果與血中濃度有關 (濃度依賴型，concentration-dependent)
  - 具有後抗生素效應 (postantibiotic effect)
  - 口服吸收差(Neomycin應用於術前清腸)
  - 半衰期約2小時
  - 極性構造，不易通過生物膜
  - 經由腎絲球過濾排除，堆積於腎皮質可造成腎毒性

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Aminoglycosides

- Once daily Dosing
  - Gentamicin：3-5 mg/kg/day
  - Amikacin：12-15 mg/kg/day
- 立論依據：
  - 殺菌效果與血中濃度有關：高劑量高濃度可達到更快的殺菌效果
  - 後抗生素效應：血中濃度低於MIC亦可持續抑菌
  - 持續血中低濃度：減低藥品在腎臟的累積
- No using once daily dose
  - CLcr< 40 ml/min*
  - Serious burn (>20% TBSA)
  - Pregnancy*、Children*
  - Neutropenic fever
  - Endocarditis、*enterococci*
  - Liver cirrhosis with decompensation*

  (*Avoid aminoglycosides)

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Aminoglycosides常見副作用

- Ototoxicity (irreversible)
  - Cochlear(耳蝸)(auditory、tinnitus)：2-10%
  - Vestibular(前庭)(ataxia、vertigo、vomit)：1-3%
- Nephrotoxicity (reversible if Scr<2-3 mg/dl)
  - 1 week：5-10% rising BUN、Scr (increase 0.5 or > 1.5 mg/dl)、Proteinuria、Oli-or non-oliguria
  - Check renal function 2-4 days periodically
  - Risk：liver cirrhosis、Nephrotoxins(NSAID)、old age、accumulation (within 1 yr)、renal insufficiency
  - therapeutic drug monitor (TDM)
    - 最高值（peak）：靜脈注射30分鐘結束後，30分鐘後抽血
    - 最低值（trough）：下一次給藥前
- Neuromuscular paralysis (reversible、severe)
- Hypersensitivity (rare)

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Quinolones

- Classification
  - First-generation
    - Pipemidic acid、Nalidixic acid (1960s) 、Cinoxacin
    - Spectrum：GNB except *Pseudomonas aeruginosa*
  - Second-generation (add -F ion)
    - Norfloxacin (1986)
    - Ciprofloxacin Lactate（Ciprocin）100mg/bot （1987)
    - Ofloxacin (1991)
    - Enoxacin (1992)、Lomefloxacin (1992)
    - Spectrum
      - GNB involved *Pseudomonas aeruginosa* (Ciprofloxacin)
      - Atypical pathogen、Mycobacteria
      - GPC (incredited)

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Quinolones

- Levofloxacin（Cravit）500mg/bot (1997)
  - L-form of Ofloxacin
- Tosufloxacin、Gatifloxacin (1999)
- Spectrum
  - GNB involved *Pseudomonas aeruginosa*
  - GPC (*Streptococcus pneumoniae*)
  - Atypical pathogen、Mycobacteria
  - Anaerobes

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Quinolones

- Third-generation
  - Trovafloxacin (1998)
  - Moxifloxacin (Avelox) 400mg/bot (1999)
  - Gemifloxacin (2003)
  - Spectrum
    - GPC (*Streptococcus pneumoniae*)
    - GNB except *Pseudomonas aeruginosa*
    - Atypical pathogen、Mycobacteria
    - Anaerobes

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Quinolones

- Pharmacokinetics：
  - High oral bioavailability
    - Chelation：飯前一小時或至少錯開2小時－先服用quinolones
  - High tissue penetration (except BBB)
  - Post antibiotic effect
  - Concentration-dependent antibiotics
    - Cmax/MIC ≥ 8-10 (if ≥ 20, best)
    - AUIC(AUC/MIC)：

	GNB	GPC
Minimum bactericide	≥ 125	≥ 30
Maximum bactericide	≥ 250	≥ 175
Prevent from resistance	≥ 100	≥ 200

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Quinolones常見副作用

- Nausea、Vomiting (2-20%)
  - Less in Ofloxacin and Levofloxacin
- Headache、dizziness、seizure (1-2%)
  - Less in Ofloxacin and Levofloxacin
- Anaphylactic reaction (0.5-3%)
- Hepatoxicity：Increasing liver enzyme (2-3%)
- Musculoskeletal
  - Tendinitis(肌腱炎)、tendon rupture and arthropathy(關節病)
  - 軟骨細胞毒性(動物試驗)
    - contraindication in less 18 y/o children、pregnancy

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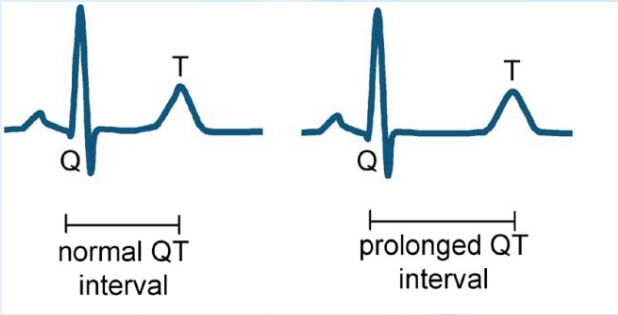
Quinolones常見副作用

- Cardiotoxicity
  - Induced Torsadede pointes by QT interval prolongation
  - High risk in fourth-generation Quinolones
  - mechanism：inhibit hERG* potassium channel
    - delay in ventricular repolarization
    - prolongation of the interval between Q and T waves on the ECG (normal < 440 ms)



* hERG=human *ether-à-go-go related gene*

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Macrolides

- Mechanism
  - Reversible binds to the 50S ribosomal subunit
    - resulting in blockage of the transpeptidation and translocation reactions (bacteristatic)
  - Inhibits RNA-dependent protein synthesis at the step of chain elongation
- Spectrum
  - GPC、GNB (*Helicobacter pylori* 、 *H. influenzae* 、 *Campylobacter jejuni*、Legionella)
  - Anaerobes、Mycobacteria(分枝桿菌)、Mycoplasma(黴漿菌)、Chlamydia(披衣菌)、Diphtheria

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Macrolides

- Drug
  - Erythromycin stearate 250mg/tab(Ilosone)
  - Clarithromycin 500mg/tab(Klaricid)
  - Azithromycin 250mg/tab(Zithromax)
  - Roxithromycin (Rulid)
- Indication
  - 呼吸道感染、皮膚及軟組織感染、生殖泌尿道感染
- Interaction
  - 增加下列藥品血中濃度
    - Theophylline、Carbamazepine、Cyclosporine、Digoxin、Warfarin (not with Azithromycin and Roxithromycin)
  - 與Terfenadine或astemizole併用，可能延長QT interval及造成嚴重心室心律不整

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	Erythromycin (po)	Clarithromycin	Azithromycin	Roxithromycin
劑量	250-500mg q6h for 7-10 days, up to 4 g/day	250-500mg q12h for 7-10days	250mg bid x3 days or 500mg on D1, 250mg qd on D2-5	150mg bid or 300mg qd for 7-10 days
半衰期(T1/2)	1-1.5 hours	3-7 hours	15-40 hours	10 hours
排出	B: 80%, U:15%	B: 60%, U: 30%	B: 60% U: 30%	B: 50%, U: 50%
服用時間	AC	食物不影響生體可用率	AC	AC
主要副作用	胃不適及腹瀉 (20-30%)	噁心 (3%), 腹瀉 (5%), 腹痛 (3%)	噁心 (3%),腹瀉 (3%), 腹痛 (2%)	腸胃不適 (~5%)
藥品交互作用	T↑, C↑ T: theophylline C: carbamazepine	T↑, C↑	T, C, 不改變	T, C, 不改變

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Tetracyclines

- Mechanism
  - Reversible binds to the 30S ribosomal subunit (bacteristatic)
- Spectrum
  - GPC、GNB
  - Rickettsiae(立克次體)、Mycobacteria(分枝桿菌)、Mycoplasma(黴漿菌)、Chlamydia(披衣菌)、Spirochetes(螺旋體)

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Tetracyclines

- Drug
  - Tetracycline 250mg/cap、Doxycycline 100mg/cap、Minocycline 100mg/cap、 Demeclocycline、Oxytetracycline、Chlortetracycline
- Indication
  - 呼吸道感染(包括非典型肺炎)，生殖道感染，全身性感染，其他特殊適應症（胃潰瘍之幽門桿菌治療，青春痘，MRSA-Minocyline）
- Interaction
  - 食物、牛奶、乳製品、鐵劑、制酸劑(含鋁、鎂、鈣)等會與Tetracycline類形成化合物 (chelation)，影響吸收
  - 抗痙攣劑、Cholestyramine會降低Tetracycline類之吸收
  - Tetracycline類會加強Wafarin的抗凝血效果
- Side effect
  - 會造成牙齒變色及骨骼發育不全，禁用於孕婦、授乳婦女、及八歲以下之孩童；光敏感性、肝毒性、暈眩(Minocycline)

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藥品	口服吸收率（%）	食物對吸收的影響	排除半衰期（小時）	腎功能不全對半衰期的影響	排除途徑
Demeclocycline	66	下降	10-17	延長	腎
Doxycycline	90-100	無影響	12-22	無影響	肝膽
Minocylcine	90-100	無影響	11-23	無影響	肝膽
Oxytetracycline	58	下降	6-10	延長	腎
Tetracycline	75	下降	6-11	延長	腎

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Trimethoprim-Sulfamethoxazole (TMP-SMX；Cotrimoxazole；Baktar；Septrin)

- 作用機轉
  - Para-aminobenzoic acid —S→ Dihydrofolic acid —T→ Tetrahydrofolic acid ⟶合成核酸
- 此藥品不會對哺乳類細胞產生影響的原因
  - 細菌細胞之dihydrofolate reductase受抑制的程度為哺乳類細胞的50,000-60,000倍
  - 人體細胞可利用外來的葉酸來源，而細菌細胞不行
- 抗菌範圍
  - GPC、GNB (except *Pseudomonas aeruginosa*)
  - *Pneumocystis*
- Indication
  - 呼吸道感染、尿道感染、預防及治療*Pneumocystis carinii*肺炎（卡氏肺囊蟲肺炎，PCP）

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Trimethoprim-Sulfamethoxazole

- Dosage
  - 分為兩種劑型
    - 80mg TMP＋400mg SMX (single-strength tablet)
    - 160mg TMP＋800mg SMX (double-strength tablet)
  - 大部分的情況下，每天使用兩次雙倍藥效錠，治療期為7-14天（依嚴重程度不同）
  - 治療PCP時需使用較高劑量，每日15-20mg/kg TMP＋75-100mg/kg SMX，分3-4次給予，治療期為21天
  - 預防PCP：每日一顆單一藥效錠或雙倍藥效錠，也可每星期給予三次雙倍藥效錠

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抗厭氧菌藥品－Clindamycin (Cleocin)

- 作用機轉
  - 與細菌核醣體50S結合，抑制蛋白質合成
  - chloramphenicol與macrolides也作用於此位置，若併用會產生拮抗作用
- 抗菌範圍
  - 大部分厭氧菌、GPC (except *Enterococci*)
- 藥動學特性
  - 可到達大部分組織，但無法到達腦脊液（儘管是在發炎狀態下）
  - 腸肝循環及活性代謝物使得clindamycin留在糞便中的時間延長，影響腸道菌叢達2星期之久，易造成*C. difficile*結腸炎

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抗厭氧菌藥品－Clindamycin (Cleocin)

- 適應症
  - *B. fragilis*或是對penicillin有抗藥性之厭氧菌所造成之嚴重感染。可與抗G(－)藥品併用於多菌種感染。
- 劑量
  - 口服：150-300mg q6h
  - 注射：600-900mg q8h
  - 預防細菌性心內膜炎（對penicillin過敏之病人）：手術一小時前給予600mg
  - 肝功能不好需調整劑量
- 副作用
  - 腹瀉、過敏性反應

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抗厭氧菌藥品－Metronidazole

- 作用機轉
  - 破壞細菌DNA
- 抗菌範圍
  - 厭氧G(－)菌，對*B. fragilis*最為有效
- 藥動學特性
  - 口服吸收佳，經肝代謝為活性代謝物，腎臟排除
- 適應症
  - 大部分厭氧菌感染，偽膜性結腸炎，*Helicobacter pylori*（可與氫離子幫浦阻斷劑，tetracyclin，amoxicillin等藥品併用於治療胃腸道潰瘍），Crohn's disease…

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抗厭氧菌藥品－Metronidazole

- 劑量
  - 口服：250-1000 mg q6-12h（1-2g/d）
  - 注射：500mg q6-8h
- 副作用
  - 中樞神經毒性，週邊神經炎，disulfiram-like reaction（噁心，臉潮紅，頭痛，心搏過速，低血壓），胰臟炎，腸胃不適，嗜中性球減少

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Fusidic Acid

- 作用機轉：抑制細菌蛋白質合成
- 抗菌範圍：GPC (include MRSA)
- 適應症：保留於對天然或半合成penicillin產生抗藥性之細菌，通常與其他藥品併用以增加效果並減少抗藥性的產生
- 劑量：480mg tid，肝功能不佳需調整劑量
- 副作用：血栓靜脈炎，腸胃不適

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謝謝您的聆聽!!

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