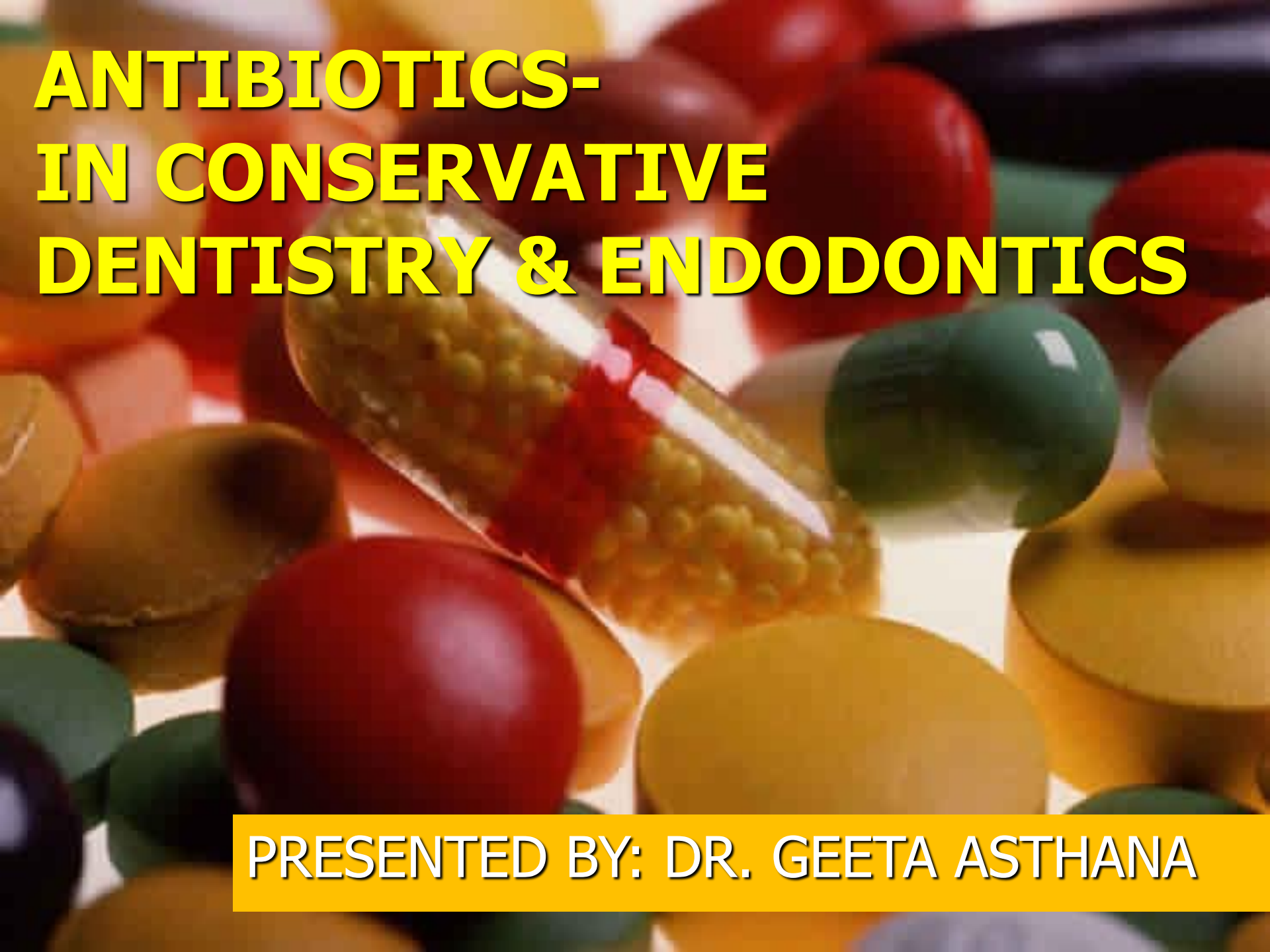


ANTIBIOTICS- IN CONSERVATIVE DENTISTRY & ENDODONTICS

PRESENTED BY: DR. GEETA ASTHANA

- Introduction
- Terminology
- Routes of Endodontic Infection
- Microorganisms found in RCs & associated Endo' lesions
- Significance
- Rationale of Antibiotic Therapy
- Selection of an Antibiotic Regimen
- Duration of Antibiotic Therapy
- Indications for Culturing
- Fundamental Concepts of Antibiotic Therapy
- Use of Antibiotics in Endodontic Rx
- The History
- Definition & Characteristics
- Antibiotic Resistance
- Antibiotic Prophylaxis Guidelines
- Antibiotics-in Action
- Antibiotic Prophylaxis For Infective Endocarditis
- Antibiotic Prophylaxis And Hemodialysis
- Antibiotics & Peritoneal Dialysis
- Preventive Regimens Specifically Systemic Antibiotics for Special Needs patients
- Misuse of Antibiotics
- Myths About Antibiotics
- Classification
- Penicillin
- Cephalosporin
- Fluroquinolones
- Tetracycline
- Erythromycin
- Clindamycin
- Anaphylaxis
- Drug Allergy

- Gell and Coombs reactions
- Penicillin Allergy
- Ampicillin rash
- Antibiotic sensitivity testing
- Ledermix
- Drug Interactions in Clinical Dentistry
- Conclusion
- References

- Dental pharmacotherapeutics is advancing rapidly.

- These therapeutic agents include
  - ✓antimicrobial agents
  - ✓analgesics
  - ✓anti-inflammatory drugs
  - ✓local anaesthetic formulations
  - ✓sedative
  - ✓anxiolytic agents

TERMINOLOGY

- **Chemotherapy** is defined as the use **of synthetic, semi-synthetic** and naturally occurring chemicals that selectively inhibit specific organism causing disease.
- **Antibiotics** are the substances produced by microorganisms, which suppress the growth or kill other microrganims at very low concentration without causing any harm to host. The term antibiotic means "against life".

- **Anti-microbial** agents are the synthetic as well as naturally occurring drugs that attenuate microorganisms.

- **Infection** Invasion and proliferation of bacteria of other pathogenic microorganism **in** body tissues and the reaction of the tissues to their presence.

- **Metastatic or 2° Infection (formerly** known as focal infection) An infection initiated at another site bv microorganisms that have travelled through bloodstream from a focus of infection.

- **Focus of infection:** A localised/circumscribed area of tissue infected with pathogenic organisms (F. Billings. 1904).

- **Bacteremia:** It is the presence of bacteria in the blood stream.

- **Theory of Focal Infection:** A localised or generalised infection caused by bacteria travelling through blood stream from a distant focus of infection.

ROUTES OF ENDODONTIC INFECTION (MICROBIAL INGRESS)

- Microorganisms can reach dental pulp by any of six routes.
- While endodontic therapy is being performed, these routes must be blocked to avoid contamination during treatment.
- Because pulpal remnants and periapical tissues are usually inflammed to some degree during endodontic procedures these areas would be affected adversely **if** micro-organisms are allowed access .
- These routes are:

Through open cavity

due to carious destruction,
traumatic injuries
cooperative procedures.

Through dentinal tubules

- Because most bacteria are smaller than the diameter of dentinal tubules (<4 um), they may reach the pulpal system as a result of salivary contamination or deep carious lesion by passing through the dentinal tubules.

Through gingival sulcus or periodontal ligament:

- Microorganisms or other irritants from PDL may reach the pulp through vessels in apical foramen or accessory canals. In advanced periodontal disease the accessory canals may be opened to bacteria present in gingival sulcus.

Through the blood stream

- In case of existing transient bacteremia. microorganisms are attracted to the dental pulp following trauma or operative procedure that produced pulpal inflammation (*anachoresis*). The damaged/inflammed pulp offers an excellent medium for continued growth *of* microorganisms.

Through a broken occlusal seal or faulty restorations of a tooth previously treated by endodontic therapy

- In such cases studies indicate that micrororganisms from salivary contamination can reach periapical area in less than 6 weeks causing endodontic failure

Through extension of a periapical infection from adjacent teeth

- By far the exposure of dental pulp to microorganisms and other irritants from salivary contamination is the most common route of endodontic infection

MICROORGANISMS FOUND IN ROOT CANALS AND ASSOCIATED ENDODONTIC LESIONS

- Microorganisms from oral cavity, upper respiratory tract, sinus areas, nasopharynx or GIT can gain access to root canal system. But all the invaders of endodontic complex may not reproduce in root canal environment or may not be pathogenic in their new oxygen and nutrient limited setting. On the other hand man\ species that are normal and non-pathogenic residents of oral cavity and gingival sulcus, may become invasive, destructive members producing toxins, enzymes that cause inflammation, tissue necrosis and infection.

AEROBES

- *B. hemolytic (S. pyogens)* non-hemolytic streptococcus, *Enlerococci (S. faecalis).*
- *Staphylococcus aureus* and *S. albus. Pneumococci, B. subtilis, E. coll, Pseudomonas etc.*
- *E. faecalis* has been shown to be one of the most resistant bacteria causing **recurrent** infection in **endodontically** treated cases leading to failure of endodontic therapy

ANAEROBES

- Teeth with necrotic pulps and periapical lesion consists of micro flora rich in obligate anaerobes. Studies by Winkelhoff *et al.* And Sequeira *et al.* show the black pigmented gram negative anaerobes (Bacteroides) as the predominant microorganisms in such cases. They even stated that these are the most predominant bacteria involved in endodontic infection.

- Cocci: *Peptostreptocciis, Peptococcus; Veillonella*
- Bacilli: *Eubacterium; Lactobacilli; Actinomyces; Bacteroides, Fusobacterium*
- Bacteroides includes species of *Porphyromonas* and *Prevolella.* Other anaerobes involved are:
- *Peptostreptococcus Eubacterium Fusobacterium Actinomyces etc.*

Microorganisms found in root canals and associated Periradicular lesions.

Aerobes and their significance

- Alpha- Hemolytic streptococci- most commonly recovered.
- Beta – Haemolytic streptococci and less pathogenic non hemolytic Streptococus, streptococus mitis and streptococcus salivarius

Streptococcus- rigid cell wall

Peptidoglycans

Lymphokine production

Osteoclast activating factor and prostaglandin production

Enhances pathogebicity and symptoms of infectious disease of the periapical tissue.

Lipoteichoic acids

Induce bone resorption

- Enterococci, streptococcus faecalis are also found.

SIGNIFICANCE

- There exists a delicate balance between the invader and the host- that determines health or disease process.
- Various factors like host resistance, number of micro-organisms, their virulence govern the severity of disease process.

- In cases where the host resistance is low or high number of bacteria with increased virulence are present, the normal state of health is disturbed thus causing disease.
- Microorganisms exert certain virulence factors like colonization and invasion of host tissue, evasion of host defence mechanism and ability to cause host tissue damage by release *o*|'certain enzymes, by products, endotoxins, *etc.*

- The apparent presence or absence of microorganisms does not guarantee endodontic failure or success altogether.
- However, the presence of some particular microorganisms, provides an additional source of irritation that must be overcome to gain optimum results.
- Therefore control of microorganisms and their possible substrate must be an objective in every endodontic case.

Rationale of Antibiotic Therapy

- The decision to use an antibiotic agent in managing an odontogenic infection is based on several factors.
- The clinician must first diagnose the cause and determine the appropriate dental treatment that may include multiple modalities, including initiation of endodontic therapy and pulpectomy, odontectomy or surgical or mechanical disruption of the infectious environment. The determination as to whether the conjunctive antibiotic therapy is indicated is based on several factors.

- Because of lack of circulation within dental pulp, the normal host defences (inflammation and immunity) are compromised and the root canal systems become a unique environment to harbour limited group of bacteria.
- Most odontogenic infections are polymicrobial. When the dental pulp is overwhelmed from bacterial attack, a local acute inflammatory response is seen followed by non-specific and specific immunological reactions with the presence of lymphocytes, plasma cells, and macrophages. Eventually PMNs are attracted to the site of damaged tissue.

- An abscess, a fibrocollagenous layer of tissue may form around PMNs in region of infection isolating it from surrounding tissues.
- Because the host may be unable to resorb the abscess and resolve the infection, root canal treatment, extraction or other surgical therapy is needed to remove the cause.

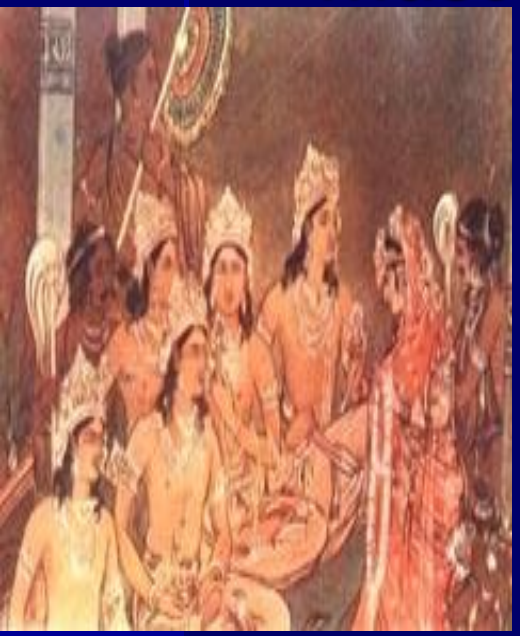
- Further, in some cases, such abscess may be an immunological phenomenon with a non-bacterial cause.The effectiveness of an oral antibiotic as primary and sole treatment for an infection of odontogenic origin is highly questionable because of lack of effective circulation in a necrotic pulpal system or an abscess.

- Because of lack of circulation, systemically administered antibiotics are not effective against the reservoir of microorganisms.
- Likewise a minimum inhibitory concentration (MIC) of an antibiotic may not reach in a space filled with pus.
- The antibiotic moves via a diffusion gradient through the edematous fluid and purulent exudate that accumulates in anatomical space. An incision for drainage will allow drainage of purulent material and improvement of circulation in the area.

- This concept reinforces the idea that surgery of some kind is the primary treatment of an odontogenic infection and that antibiotic therapy is adjunctive care.
- Endorsement of a philosophy of case that the antibiotic administration is low risk and their non-specific use has led to the development of resistance among bacteria.
- Thus antibiotics should not be prescribed as a substitute but as an adjunct to proper endodontic treatment.

SELECTION OF AN ANTIBIOTIC REGIMEN

- Empirical selection of an antibiotic must be based on one's knowledge of:



  - Micro-organisms commonly involved in endodontic infection and their susceptibility.
  - The site of infection.
  - The drug factors like spectrum of activity, type of activity, relative toxic:?. pharmacokinetic profiles, route of administration, *etc.*
  - Patient factors like age, renal and hepatic status, drug allergy, host immune status, pregnancy, *etc.*

DURATION OF ANTIBIOTIC THERAPY

- The antibiotics should generally be continued for 2-3 days following resolution of major clinical signs and symptoms of infection.
- Following treatment of the source of infection and adjunctive antibiotic therapy, significant improvement in patient's status should be seen in 24 to 48 hours.

- A loading dose is important to provide an initial adequate therapeutic level and a maintenance dose is recommended to prevent the selection of resistant bacteria with high virulence.
- If improvement is not seen within 48 hrs, a reculturing of microbial sample from the foci should be done and a combined use of antibiotics may be recommended.

INDICATIONS FOR CULTURING

- Culturing is rarely required in managing endodontic infections, but at times it is necessary to resolve a progressive infection. Needle aspiration techniques and transfer under inert gas should be used when culturing for aerobic and anaerobic bacteria in oral cavity. An antibiotic is then chosen to treat the predominant microorganism found in culture if empirical therapy has failed.

- The indications for culturing are:
  - Patient not responding to empirical antibiotic therapy after 48 hours and appropriate dental treatment has been completed.
  - The infection is progressing to other facial spaces.
  - The patient is immunocompromised or has a history of bacterial endocarditis and is not responding to empirical therapy.

- In any case empirical antibiotic treatment, when indicated should begin immediately even when a culture is to be taken because of rapid spread of oral infections.

SAMPLE COLLECTION

- Avoid any type of contamination during sample collection.
- Ask the patient to rinse the oral cavity.
- A microbial sample from a RC is taken by first isolating the root with a rubber dam with 5% or 10% iodine tincture.

- Drainage may be sampled with a charcoal-impregnated sterile paper point or aspirated with a 16 or 20 gauge needle.
- The paper point is kept in the RC for 30 sec to absorb the exudate.
- If the exudate is aspirated using a syringe,any aspirated air should be vented from the syringe.

- To sample a dry canal,a syringe is used to place pre reduced transport medium into the canal.
- A file is then used to scrape the canal walls to suspend microorganisms in the medium.

- SUB MUCOSAL SWELLING
- It should be sampled by aspiration before an incision is made.
- After Anaesthesia, mucosal surface is dried, disinfected and a 16 or 20 gauge needle is used to aspirate the exudate.
- If a sample cant be aspirated,a specimen of purulent exudate is collected on a swab after the incision has been made,taking care to prevent microbial salivary contamination.

- The paper point or the aspirate should be taken immediately to the laboratory or injected into pre reduced transport medium like Stuart's or Moller's transport medium

FUNDAMENTAL CONCEPTS OF ANTIBIOTIC THERAPY

- Most effective narrow spectrum antibiotics should be used.
- The causative organism of infection should be identified by culture if possible or needed.
- When used in combination, they should be synergistic and least toxic to patient. f
- A bacteriostatic drug should not be used with a bactericidal antibiotic.
- If possible, bactericidal drug should be professed over bacteriostatic.
- Proper route, dose and duration of antibiotic should be managed.

USE OF ANTIBIOTICS IN ENDODONTIC TREATMENT

- Once the source of infection has been established, dental procedures should be used immediately to disrupt the microorganisms involved.
- Antibiotics should be used as an adjunct and never alone the 1st line if treatment.
- In treatment *of* endodontic infections antibiotics are indicated (as an adjunct) when certain signs and **symptoms** of involvement are evident. These are:

- Systemic involvement
  - Fever> 100°F
  - Malaise
  - Lymphadenopathy
  - Trismus

- Progressive infection (present/suspected)
  - Increasing swelling
  - Cellulitis
  - Osteomyelitis

- Spread to other facial spaces which may lead to:
  - cavernous sinus thrombosis
  - Ludwig's angina
  - mediastinal space swelling, or
  - brain abscess, etc.

THE HISTORY- Lets Discover The Roots

- Although the principles of antibiotic action were not discovered until the twentieth century, the first known use of antibiotics was by the ancient Chinese over 2,500 years ago.[1] Many other ancient cultures, including the ancient Egyptians and ancient Greeks already used molds and plants to treat infections. This worked because some molds produce antibiotic substances. However, they couldn't distinguish or distill the active component in the molds.

ARSPHENAMINE

- Modern research on antibiotic therapy began in Germany with the development of the first modern chemotherapeutic agent - **Arsphenamine**
- **Arsphenamine** is a drug that was used to treat syphilis and trypanosomiasis.
- Sahachiro Hata discovered the anti-syphilitic activity of this compound in 1908 in the laboratory of Paul Ehrlich,
- Arsphenamine was marketed under the trade name **Salvarsan** in 1910.
- It was also called ***606***, because it was the 606th compound synthesized for testing.

PROTONSIL

- **Prontosil**, the first commercially available antibacterial, was developed by a research team at the Bayer Laboratories in Germany.
- The molecule, first synthesized by Bayer chemists Josef Klarer and Fritz Mietzsch, was tested and found effective against some important bacterial infections in mice by Gerhard Domagk, who subsequently received the 1939 Nobel Prize in Medicine.

- Protonsil(a nearly insoluble red azo dye)

  Azo reduction(a kind of bio-activation)

- Sulfanilimide
  - the active portion of the Prontosil molecule, was out of patent
  - cheap to produce
  - easy to link into other molecules
  - soon widely available in hundreds of forms

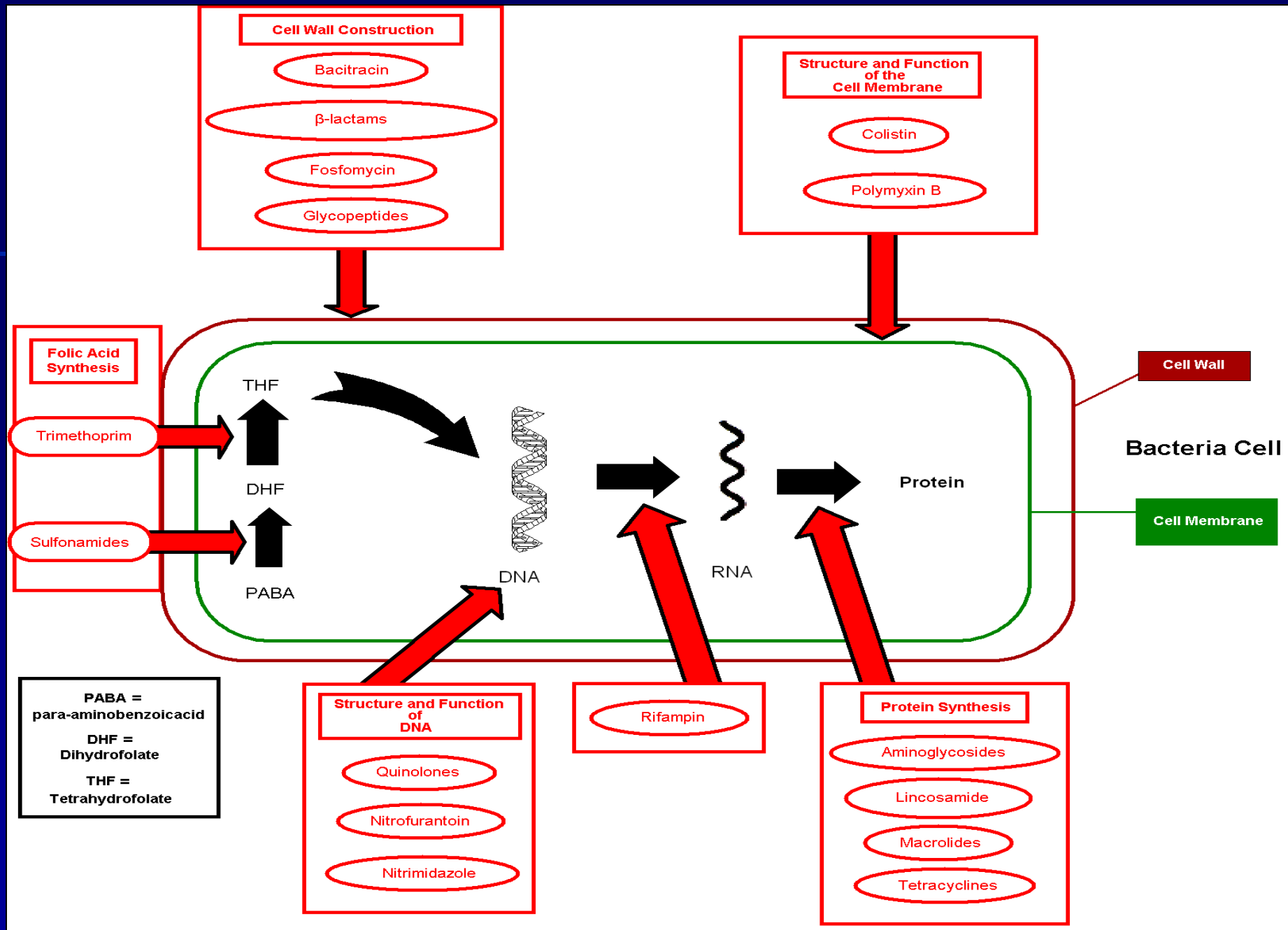
- Antibiotics were further developed in Britain following the discovery of Penicillin in 1928 by Alexander Fleming.
- More than ten years later, Ernst Chain and Howard Florey became interested in his work, and came up with the purified form of penicillin. The three shared the 1945 Nobel Prize in Medicine.
- "Antibiotic" was originally used to refer only to substances extracted from a fungus or other microorganism, but has come to include also the many synthetic and semi-synthetic drugs that have antibacterial effects

DEFINITION & CHARACTERISTICS

- Antibiotics are antibacterial substances produced by various species of microorganisms (bacteria,fungi,actinomycetes) that suppress the growth of other microorganisms

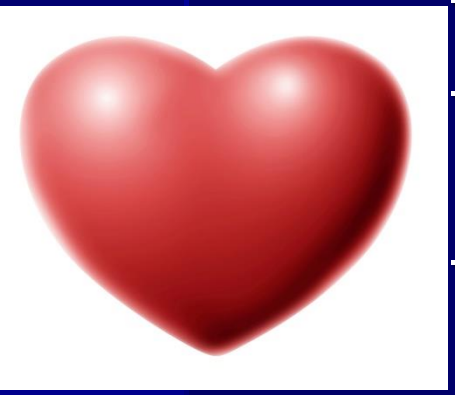
ANTIBIOTICS IN ACTION

ANTIBIOTICS IN ACTION


Cell Wall Construction
Bacitracin
β-lactams
Fosfomycin
Glycopeptides
Structure and Function of the Cell Membrane
Colistin
Polymyxin B
Folic Acid Synthesis
Trimethoprim
Sulfonamides
THF
DHF
PABA
DNA
RNA
Protein
Cell Wall
Bacteria Cell
Cell Membrane
PABA = para-aminobenzoicacid
DHF = Dihydrofolate
THF = Tetrahydrofolate
Structure and Function of DNA
Quinolones
Nitrofurantoin
Nitrimidazole
Rifampin
Protein Synthesis
Aminoglycosides
Lincosamide
Macrolides
Tetracyclines

ANTIBIOTIC PROPHYLAXIS GUIDELINES

BY :-



- AMERICAN HEART ASSOCIATION
- The American Heart Association published its first guidelines in 1955.
- The guidelines for antibiotic prophylaxis was updated in 1990 and most recently in 1997.

Antibiotic prophylaxis is recommended for the following:

- High-risk category
  - Prosthetic cardiac valves, including bioprosthetic and homograft valves
  - Previous bacterial endocarditis
  - Complex cyanotic congenital heart disease (e.g., single ventricle states, transposition of the great arteries, tetralogy of Fallot)
  - Surgically constructed systemic pulmonary shunts or conduits
- Moderate-risk category
  - Most other congenital cardiac malformations (other than above and below)
  - Acquired valvular dysfunction (eg, rheumatic heart disease)
  - Hypertrophic cardiomyopathy
  - Mitral valve prolapse with valvar regurgitation and/or thickened leaflets

Endocarditis prophylaxis is not recommended for the following:

- Negligible-risk category (no greater risk than the general population)
  - Isolated secundum atrial septal defect
  - Surgical repair of atrial septal defect, ventricular septal defect, or patent ductus arteriosus
  - Previous coronary artery bypass graft surgery
  - Mitral valve prolapse without valvar regurgitation
  - Physiologic, functional, or innocent heart murmurs
  - Previous Kawasaki disease without valvar dysfunction
  - Previous rheumatic fever without valvar dysfunction
  - Cardiac pacemakers (intravascular and epicardial) and implanted defibrillators

If you identify with a condition in the high or moderate risk groups, then antibiotic prophylaxis is recommended for the following dental procedures:

- Dental extractions
- Periodontal procedures including surgery, scaling and root planing, probing, and recall maintenance
- Dental implant placement and reimplantation of avulsed teeth
- Endodontic (root canal) instrumentation or surgery only beyond the apex
- Subgingival placement of antibiotic fibers or strips
- Initial placement of orthodontic bands but not brackets
- Intraligamentary local anesthetic injections
- Prophylactic cleaning of teeth or implants where bleeding is anticipated

Antibiotic prophylaxis is not recommended for the following dental procedures:

- Restorative dentistry (operative and prosthodontic) with or without retraction cord
- Local anesthetic injections (nonintraligamentary)
- Intracanal endodontic treatment; post placement and buildup
- Placement of rubber dams, postoperative suture removal, taking of oral impressions, and fluoride treatments
- Placement of removable prosthodontic or orthodontic appliances and orthodontic appliance adjustment
- Taking of oral radiographs
- Shedding of primary teeth

If antibiotic prophylaxis is necessary, the following medications and dosages are recommended by the AHA:

Situation	Medication	Dosage
Standard prophylaxis	Amoxicillin	Adults: 2.0 g; children: 50 mg/kg orally 1 h before procedure
Unable to take oral medication	Ampicillin	Adults: 2.0 g IM or IV; children: 50 mg/kg IM or IV within 30 min before procedure

Situation	Medication	Dosage
Allergic to Penicillin ▪	Clindamycin or Cephalexin or cefadroxil or Azithromycin or clarithromycin	Adults: 600 mg; children: 20 mg/kg orally 1 h before procedure Adults: 2.0 g; children; 50 mg/kg orally 1 h before procedure Adults: 500 mg; children: 15 mg/kg orally 1 h before procedure
Allergic to penicillin and unable to take oral medications	Clindamycin or Cefazolin	Adults: 600 mg; children: 20 mg/kg IV within 30 min before procedure Adults: 1.0 g; children: 25 mg/kg IM or IV within 30 min before procedure

Antibiotic Prophylaxis For Infective Endocarditis-Time For A Rethink?

- IE is a microbial infection involving the cardiac valves.
- The condition is uncommon with a Prevalence of 11-50 cases/million population/year.
- The Prevalence has remained consistent even after the introduction of antibiotic prophylaxis in 1940s.
- Dental procedures esp that results in bacteremia are frequently blamed for IE.

PROCEDURE	PREVALENCE OF BACTERIA
Extractions (Single)	51 %
Extractions (Multiple)	68-100 %
Endodontics (Intracanal Inst')	0-31 %
Endodontics (Extracanal Inst')	0-54 %
PDL Surgery (Flap Procedure)	36-88 %
PDL Surgery (Gingivectomy)	83 %
Scaling & Root Planing	8-80 %
PDL Prophylaxis	0-40 %
Toothbrushing	0-26 %
Dental Flossing	20-58 %
Interproximal cleaning with toothpricks	20-40 %
Irrigation Devices	7-50 %
Chewing	17-51 %

- Oral hygiene procedures & Chewing are responsible for “random” or “spontaneous” cases of bacteremia.
- Such bacteremia are of low grade intensity and of short duration.
- It may well transpire that this bacteremia may be more causative in IE than any Dental Rx.

- Further evidence to support this hypothesis comes from an analysis of cases of IE in which Dental Rx has been implicated as the cause.
- Oral Streptococci cause appx 50 % of all IE cases. Similarly, only 15 % of patients in whom IE has been diagnosed reported Medical/Dental Rx within the previous 3 months.
- It has been estimated that 4% or less of all IE cases are related to dental-induced bacteremia.

- Whether such bacteremia arise from dental Rx or were spontaneous is not discernible.
- OAKLEY (1987) suggested that if spontaneous random bacteria cause 96 % of all cases of IE, then these bacteremia as opposed to thoe arising from dental Rx also may have caused the remaining 4 %.

- Van der Meer et al (1992) & Strom et al (1998) concluded that strict adherence to generally accepted recommendations for prophylaxis might do little to decrease the total no. of patients with endocarditis in the community.
- Strom study founded that dental Rx was no more frequent among patients with IE than control subjects and that among patients with known cardiac lesions (the target of antibiotic coverage) Dental Rx was significantly less common than among control subjects

- Few participants received chemoprophylaxis.
- The author concluded that the lack of a link b/w Dental Rx & IE, together with the rare occurrence of this disease,does not justify the routine use of antibiotic prophylaxis

- Some criticism of the above cited studies have been aired.
- Lancet raised 3 points-
  - (1) Although the no. of cases of endocarditis prevented was negligible in population terms, the effect on individual patients could not be ignored.
  - (2) Concern was expressed at small no. of cases eventually entered into the trial
  - (3) Doubt was expressed over the feasibility of maintaining a sufficiently large trial to settle this question &comment was made that it might be fruitless.

Are the risk for providing antibiotic coverage greater than the risk for contracting IE?

- Most significant adverse event associated with amoxicillin is hypersensitivity reactions.
- These can range from a troublesome rash to a life-threatening anaphylactic reaction.
- 1-10 % of patients report a penicillin allergy
- Chance of an allergic rkn following administration of the drug is in the range of 0.7-5%
- IM-5%prevalence
- Oral Penicillin-0.3% prevalence.
- High dose of oral amoxicillin can cause an allergic rkn rate similar to that of IM Penicillin.

- 400-800 Deaths caused every year by anaphylactic rkn to Penicillin in USA.
- It has been estimated that 1.36 people per million population are likely to die from penicillin anaphylaxis to prevent IE whereas only 0.26 deaths per million population are caused by dental-procedure induced endocarditis.
- Put another way, patients receiving penicillin (amoxicillin) prophylaxis to prevent IE are 5 times more likely to die from an anaphylactic rkn to the drug than to die from contracting endocarditis

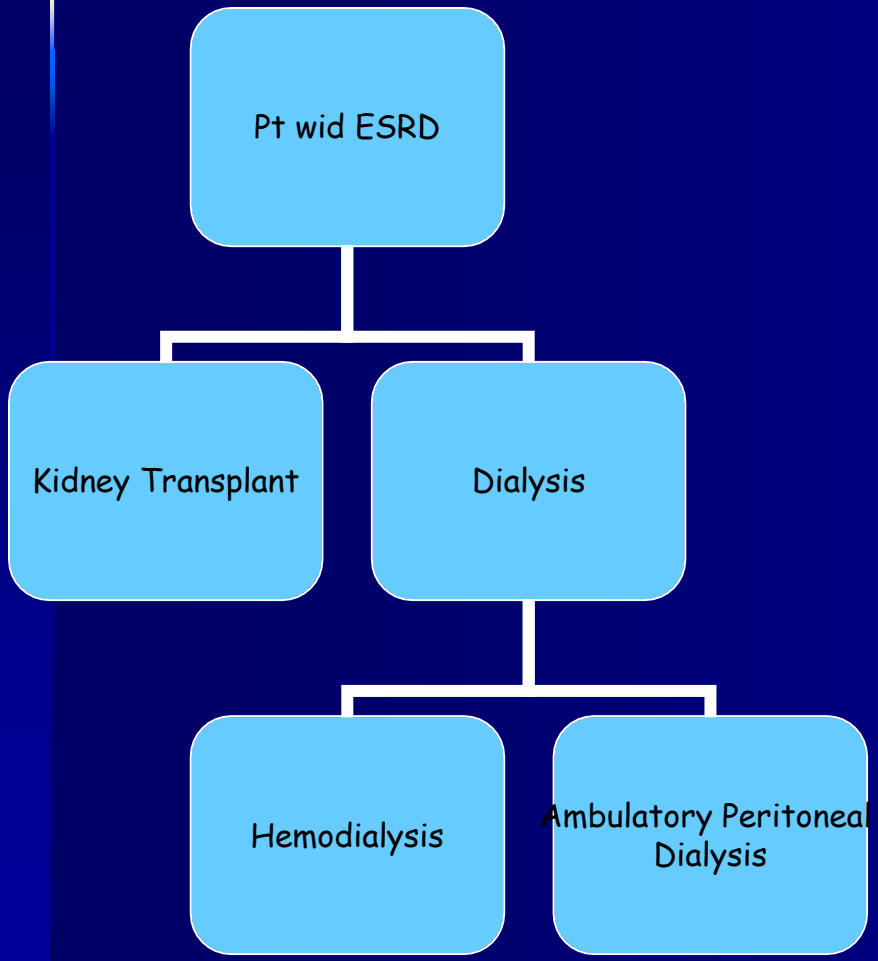
Which way to GO ??

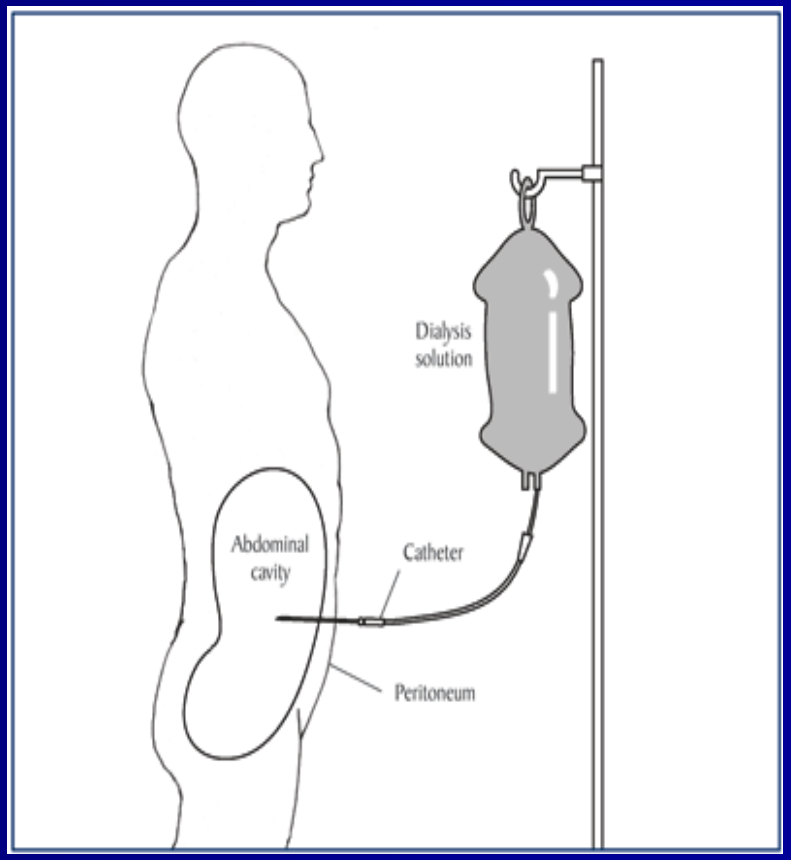
- The Dilemma exists.
- Circumstantial evidence exists on an individual level that coverage confers some benefit.
- Current regimens are likely to remain in place, even if subjected to review and modification.

Antibiotic Prophylaxis And Hemodialysis

- According to ***Dental management of the Medically Compromised Patient,5th ed.,*** "the threat of endarteritis to hemodialysis patients is unknown, and data concerning emboli are scarce.
- AHA cites poor evidence & an apparent low risk for not making a recommendation to provide prophylactic antibiotics.
- Each case should be evaluated individually in concert with the managing physician
- Persual of the AHA's 1997 guidelines for preventing bacterial endocarditis reveals no increased risk for hemodialysis patients.

Antibiotics & Peritoneal Dialysis





- Infection can take place at the site of catheter placement.
- These infections are typically caused by S.aureus.
- Infections of peritoneum can also occur.Peritonitis has been caused during catheter insertion, during dialysate leaks and other invasive procedures.
- It is shown that antibiotic prophylaxis will decrease the risk of peritonitis.
- Because the catheter has no valvular access, there are no immediate concerns with IE prophylaxis. Other possible infections, may occur.
- A medical consult with nephrologist about antibiotic coverage is the best answer

Preventive Regimens specifically systemic antibiotics for special needs patients

- There is a lack of information on the subject in the published literature.
- One has to assume that mental retardation, developmental delay, and old age are not reasons, to use antibiotic prophylaxis
- Unless there is reasonable doubt about the patient's health status or treating a specific ailment such as dentoalveolar infection, avulsion, or PDL, they can be treated from & antimicrobial perspective, as any other patient.

Antibiotics & Pregnant Patients

- A ship under sail and a big- bellied woman,

  Are the handsomest two things that can be seen common.

  -Benjamin Franklin

FDA Classifications for drugs used in pregnant & lactating patients

- A : Controlled human studies- no risk found
- B : Animal studies do not show risk, human studies not adequate or complete yet
- C : Animal studies show risk but benefits overweigh risks
- D : Evidence of fetal risk, benefits may outweigh risks
- X : Risk outweighs benefits

- Penicillin V and Amoxicillin is preferred drug for mild to moderate infections.
- Widely used for many years with no side effects
- No studies show Penicillin to be Teratogenic.
- Amoxicillin widely used without harming the fetus.
- Drug Classes :

  B : Penicillin,Cephalosporins,Erythromycin,Clindamycin

  D : Tetracycline

Timing of Dental Treatment During Pregnancy - From Little and Fallace

- *First Trimester*
  - Plaque control
  - Oral hygiene instruction
  - Scaling, polishing, curettage
  - Avoid elective treatment; urgent care only

- *Second Trimester*
  - Plaque control
  - Oral hygiene instruction
  - Scaling, polishing, curettage
  - Routine dental care

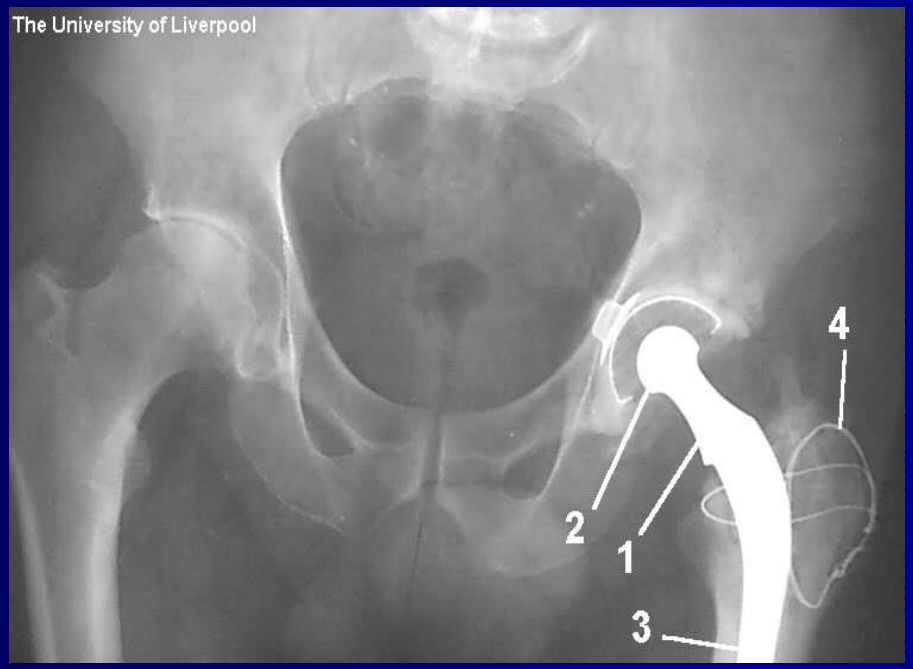
- *Third Trimester*
  - Plaque control
  - Oral hygiene instruction
  - Scaling, polishing, curettage
  - Routine dental care (after middle of third trimester, elective care should be avoided)

ANTIBIOTIC PROPHYLAXIS IN PATIENTS WITH HIP & JOINT PROSTHESIS

- Most joint infections (>66%) are caused by staphylococci & only 4.9 % are related to viridans streptococci of possible oral origin.
- Whether the S viridans infection arose directly from dental treatment or from other sources was not established.
- DNA fingerprinting techniques have not been used to confirm that isolates from infected joints are the same as those found in the mouth.

- There is little firm evidence to show that dental induced bacteremia can cause hematogenous infection around a prosthetic joint.
- By contrast, there are several studies that show the opposite.
- A review of 21 cases of prosthetic joint infections attributable to a dental procedure identified 1 patient in whom the same infecting organism was grown on culture from the mouth, blood & prosthetic joint

- Whether the bacteremia arose from a dental procedure or occurred spontaneously was never ascertained.



GUIDELINES FROM PROFESSIONAL BODIES

- ADA & American Academy Of Orthopaedic Surgeons (AAOS) jointly state that "Antibiotic prophylaxis is not indicated for dental patients with pins, plates & screws, nor is it routinely indicated for most patients with total joint replacement."
- They do consider that certain immunocompromised patients undergoing high- risk procedures within 2 years of joint replacement or those with a previous history of joint infection might be considered for antibiotic prophylaxis

- A similar view is adopted by the British Orthopaedic Association, but they also advocate antibiotic prophylaxis when dental treatment is complex, extensive & of long duration (>45 minutes).
- British Society for Antimicrobial Chemotherapy (BSAC) takes a different view.
- BSAC does not recommend prophylactic use of antibiotics & further states that exposing patients to the risk for adverse reactions to antibiotics when there is no evidence that such prophylaxis is of any benefit is unacceptable.

ANTIBIOTIC PROPHYLAXIS IN PATIENTS AFTER SPLNECTOMY

- Patients without spleens do not require antibiotic prophylaxis before dental treatments, but a consensus may exist that immunocompromised patients with a white cell count < 500 to 1000 might benefit from antibiotic prophylaxis.

ANTIBIOTIC PROPHYLAXIS IN PATIENTS AFTER BREAST OR PENILE IMPLANT

- There is not even a single documented case of a genetically identical micro-organism from the oral cavity causing an infection of a breast or penile implant.

MISUSE OF ANTIBIOTICS

- Treatment of Nonresponsive Infections
- Therapy of Fever of Unknown Origin
- Improper Dosage
- Inappropriate Reliance on Chemotherapy alone
- Lack of Adequate Bacteriological Information

MYTHS ABOUT ANTIBIOTICS

- Antibiotics are responsible for the decline in infectious disease
- Antibiotics are useful against colds and flu.
- Antibiotics are harmless.
- Doses & Duration of antibiotic treatment should be nonspecific & variable for most odontogenic infection.
- Antibiotics are always indicated when treating dental pain

MYTHS-Contd

- Clindamycin is a first line drug for infections.
- If a periapical radiolucency,sinus tract,fistula or localied abscess is present,antibiotics are always indicated.
- Antibiotics must be given several days before implementation of surgical treatment.
- Indurated soft tissue means drainage is not indicated.
- Overprescription of antibiotic therapy does not occur in Dentistry.

Chemical structure

- **Sulfonamide and related drugs** :
  sulfones- Dapsone (DDS), Paraamino salicylic acid (PAS)
- **Diaminopyramidines**: Trimethoprin, Pyrimethamine.
- **Quinolones**: Nalidixic acid, norfloxacin, Ciprofloxacin
- **Beta lcatam antibiotics**: Pencillins, cephalosporins, monobactams, carbapenems.
  Tetracyclines: Oxytetracycline, Doxycyline.
- **Nitrobenzene derivative** : chloramphemicol.
- **Aminoglycosides:** Streptomycin, gentamycin, Neomycin.
- **Macrolide antibiotics**: Erythromycin, Roxithromycin, Azithromycin.
- **Polypeptide Antibiotics** : Polymyxin B, Bacitracin,
- **Nitrofuran derivatrves:** Nitrofurantoin, Furazolidone
- **Nitroimidozoles** : Metromidazole, Timidazole.
- **Nicotimic acid derivate**: Isoniazid, Ethionamide
- **Polyene antibiotics:** Nystatin, Pyrazinamide.
- **Imidazole derivative:** Clotrimazole, ketoconazole, micomazole.
- Others: Rifampin, cindamyain, Vancomycin, Cyclosporine, Ethambutol.

Mechanism Of Action

- Inhibit cell wall synthesis: Penicillin, cephalosporins, cycloserine,Vanconmycin, Bacitracin.
- Leakage from call membrane- Polypeptides,,Bacitracin, polymyxins. Polyenes – Amphotericin B, Nystatin.
- Inhibit protein synthesis : Tetracyclins, chloramphenicol, Erythromycin, clindamycin.
- Cause misreading of m- RNA code and affect permeability- Aminoglycosides- Streptomycin Gentamycin.
- Inhibit DNA gyrase- Fluoroquinoloues- Ciprofloxacin.
- Interfere with DNA function – Rifampin, Metronidazole.
- Interfere with DNA synthesis- Idozuridine, Acylovir.
- Interfere with intermediary metabolism- sulfonamides, sulfones, Trimethoprim.

Type of organisms against which it acts

Antibacterial : Pencillins, Aminoglycosides, Erythromycin.

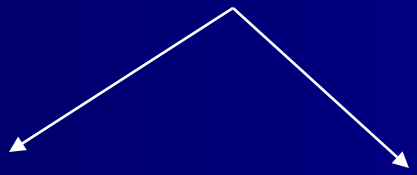
Antifungal: Griseofulvin, Amphotericin B, Ketaconazole.

Antiviral : Idoxuridine, Acyclovir, Amantadine, Zidovudine.

Antiprotozoal: Chloroquine, Metronidazole, Pyrimethamine.

Antihelminthic: Mebendazole, niclosamide.

Spectrum of activity



Narrow spectrum

Penicillin G

Streptomycin

Chloramphenicol

Broad spectrum

Tetracycline

Type of Action

Primarily Bacteriostatic	*Primarily bacteriocidal*
Sulfonamides	Pencillins Cephalosporins.
Tetracyclines	Aminoglycosides Vancomycin.
Chloramphenicol	Polypeptides Ciprofloxacin.
Erythromycin	Rifampin Isoniazid
Ethambutol	Cotrimoxazole.

Primary static drugs become cidal at higher concentrations eg: sulfonamides, erythromycin.

Antibiotics are obtained from

Fungi	*Bacteria*	*Actimomyces*
Penicillin	Polymyxin B	Aminoglycosides
Cephalosporin	Colistin	Tetracyclines
	Bacitracin	Chloramphemicol
		Macrolides.
		Polyenes.

β LACTAM ANTIBIOTICS

- These are antibiotics having a β lactam ring.

Inhibitors of cell wall synthesis

- β- lactam Antibiotic
  - Pencillins
    - Penicillin G
    - Penicillin V
    - Natural Pencillin
    - Methicillin
    - Nafcillin
    - Oxacillin
    - Cloxacillin
    - Dicloxacillin
    - Pencillinese Resistant Penicillin
  - Cephalosporins
    - Ist Generation
      - Cefazolin
      - Cefadroxil
      - Cephalexin
      - Cephalothin
      - Cephapinin
      - Cephradin
    - 2nd Generation
      - Cefoctor
      - Cefamandole
      - Cefomicid
      - Cefotetan
      - Cefoxitin
      - Cefuroxime
    - 3rd Generation
      - Cefixine
      - Cefoperazone
      - Cefotzxime
      - Ceftazideme
      - Ceftizoxime
  - Carbapenems
  - Mpmpbactams
- Other Antibiotics
  - Vancomycin
  - Bacitracin

Pencillin

↓

Ampicillin

Amoxicillin

Extended Spectrum

Carbenicillin

Ticarcillin

Piperacillin

Antipseudomonal

pencillin

Mezlocillin

Azlocillin

Acylureido Pencillin

Structural feature of β-lactam antibiotic.

Widely accepted effective and least toxic antibiotic.

Members of the family differ in 'R' – side chain.

Decides antimicrobial spectrum stability to stomach acid susceptibility to β-lactamases.

MOA

Interfere with transpeptidation or cross-linkage (last step of cell wall syn) – cell lysis then occurs – Bactericidal.

Inactive against mycobacteria, protozoa, fungi, viruses (lack all wall).

Penicillin Binding Proteins

PBP is involved in cell wall syn. → Penicillin inhibits the action and causes lyses.

These target sites altered to produce resistance.

Eg: Methicillin – resistant staphylococcus aureus (MRSA)

Inhibition of transpeptidase

PBPs catalyze formation of cross-links between peptidoglycan chains

Acetolysins

(Participate in remodeling of cell wall)

Penicillin cause disinhibition of autolysis – inhibiting cell wall syn & destruc ting cell wall.

Natural Penicillins

Obtained from fermentations of the mold penicillium chrysogenum.

Other penicillins are semi-synthetic – attachment of R groups to 6-aminopenicillanic acid nucleus.

Active against gm +ve aerobes and most anaerobes.

a)Penicillin G – Benzylpenicillin

gm +ve and gm –ve (cocci), gm +ve bacilli, spirochetes.

Is a salt of either Na or k. (given parenterally).

2-5 million units IM (adult dose).

Acid labile

Repository Penicillin G injections Procaine Peni G. — Longer duration of action

Penicillin G. Benzathine — Insoluble salts of Peni G.

Penicillin G Drawbacks

Poor efficacy

Susceptibility to penicillnase

Narrow spectrum of Activity

Hypersensitivity

b. Penicillin V : Phenoxymethyl penicillin.

Acid stable are given orally only.

Dose : - 500 mg 4 times a day

Peak levels achieved within 30-45 m and drug disappears by 6 hrs after administration.

Used as a potassium salt (large doses → hyperkalemia).

Bacteria – Staphylococcus aureus
Bacteriodes fragils
Haemophilus influenzae

resistant to natural penicillins ↓ i.e susceptible to β-lactamase.

Dose – 125-250 mg 6 hrly

Used in streptococcal meningitis, sinusitis, otitis media.

2. Antistaphylococcal Penicillins (Penicillinase Resistant)

Methicillin, oxacillin, dicloxacillin
Nafeillin, cloxacillin

Vancomycin used against MRSA.

[Toxicity so rarely used]

In treatment of infections caused by penicillinase – producing staphylococci.

3. Extended spectrum penicillins – Aminopenicillins

Ampicillin → More effective against gram –ve bacilli.

Amoxcillin – less incidence of diarrhea.

Amoxicillin :Oral absorption better than ampicillin

Prophylatic dosage in dental treatment.

Orally administered

Ampicillin:

Administered parenterally

Both susceptible to β lactamses

Therefore formulations with β- lactamase inhibitors

Contain a β lactam Ring (with no anti-Bacterial activity) Which binds and Inactivity β lactamase

Sulbactam with ampicillin

clavulanic acid with amoxicillin

extends antimicrobial spectrum

4. Antipseudomonal penicillins: Carbenicillin, Ticarcillin, Piperacillin.

Active against pseudomoans aerogenosa- Mexlocillin and azlocillin

Susceptible to β lactamase breakdown. acylareido pencillins.

Pencillins and Amninoglycosides → combination gives synergistic action.

Alters permeability of bacterial cell wall to facilitate entry of Aminoglycosides to target site.

But not in same infusion fluid (inactive complexes formed on prolonged contact).

Resistance

Natural .R
- organs lacking cell wall
-Impermeable cell wall.

Acquired R
by plasmid transfer that encodes resistance for multiple agents.

Bacteria acquires

Altered PBPs

β lactamase (Pencillmase) Activity

↓ permeability to drug-fail to reach PBPs

Pharmacokinetics : Depends o stability to gastric acid and severityofinfection.

Administration

Methicilin
Carbenicillin
Mezlocillin
Piperacillin Azollicin.

Ampicillin + sulbactam
Ticarcillin + clavulamic acid
Piperacillin+ Taxobactam

Peni V, Ampicillin, Amoxicillin, Clavulonic acid
orally ,others effective by oral Iv or IM

Procaine Pen G IM
Slowly absorbed

Benzathine Pen G
depot forms into circulation.

Well distributed throughout the body , cross the placental barriers (not teratogenic), do not enter bone or meninges unless inflamed.

Excretion

Mainly through kidney.

- Imparred renal function (Naficillin) → excreted through biliary route) .
- Probenecid inhibits pencillin excretion

Pencillin G Pencillinase – resistant penicillin

- Since destroyed in acidic environment in the stomach
  Given 30-60 min before meals or 2-3 hrs postprandially
- Others incompletely absorbed after oral administration and reach intestine in sufficient amounts.
- Metabolism : Insignificant (to certain extend in patients with impaired renal function)

ADVERSE REACTIONS:

- Hypersensitivity
- Diarrhoea
- Neurotoxicity
- Superinfections
- Nephritis
- Cation toxicity
- Platelet dysfunction

THERAPEUTIC USES:

- Pneumococcal Infections
- Streptococcal Infections
- Staphylococcal Infections
- Meningococcal infections
- Rheumatic fever
- ANUG
- Prophylaxis for SABE

CEPHALOSPORINS

-Semisynthetic antibiotics derived from cephalosporim

-C' obtained from fungus cephalosporium.

Classification :

1st generation - cefazolin, cefadroxil, cephalexin

2nd generation - cefuroxime, cefaclor

3rd generation - ceftizoxime, cefixime

4th generation - cefepime, cefpirome

- Structurally and functionally closely related to penicillins.

- Most resistant to penicillianase than penicillins.

- Bactericidal **(inhibition of cell wall synthesis).**

- They bind to different proteins than those which bind to penicillins since differences seen in spectrum, potency and lack of cross resistance.

Acquired resistance to cephalosporins may be due to

- Alteration of PBPs reducing affinity is antibiotic
- Impermeability to the antibiotic so that it does not reach the site of action
- β - lactamases which distroy specific cephalosporins

Individual cephalosporins differ in their :

a. Antibacterial spectrum and relative potency.

b. Susceptibility to β - lactamase

c. Pharmacokinetics – majority are injected.

some oral – cephadine majority are not metabolized and are actively excreted by kidney and have short half life probenecid inhibits tubular secretion.

Pharmacokinetics – 2nd Gen – well absorbed orally

1st and 3rd – parenteral absorption

excretion by kidney

Adverse effects : Diarrhoea
Hypersensitivity
Nephrotoxicity
Allergic manifestations

Cephalosporins give pain after I.m injection. Well tolerated but more toxic than penicillins.

Disulfiram like effect with cefamandole (accumulation of acetaldehyde)

Therapeutic uses : Alternative to Penicillin G
Respiratory urinary and soft tissue infections typhoid, pencillinase producing staphylococcal infection, septicemia,
surgical prophylaxis, meningitis mixed aerobic infections.

Antibacterial spectrum :

FIRST GENERATION: active against gm positive but weaker against gram negative bacteria.

Cephalothin : First to be used clinically and the prototype member

Active against :

Streptococci [pyogenes viridans], Ecoli
Staphylococci ,Proteus mirabilis
Gonococci ,Salmonella
Meningococci,Actinomyces

Highly resistant to staphylococeal β- lactamase ,therefore mainly indicated in pencillinase producing staphylococcal infection.

Given I.V. (1-2g 6 hrly) – Partly metabolised in lever, excreted through kidney – [t 12 4.5m].

Cefazolin :

More active against Klebsiella and E-coli.
Quite susceptible to staphylocial β- lactamase
Given I.M. [t ½ -2hrs]. Excreted through kidney
In surgical prophylaxis.
Dose – 0.25g 8 hrly (mild cases)
I g 6 hrly (severe cases) I.m
[ORIZOLIN, ALCIZON]

SECOND GENERATION

Well absorbed orally – cefuroxime, cefaclor more active against gm- -ve, with some against anaerobes.

CEFUROXIME : Resistant to gram – ve β lactamases.

Dose : 0.75 –1.5g im or IV 8 hrly.

CEFACLOR– retains significant activity by oral route .

More active than I GEN against

H influenzal, E-colis ,proteus mirabilis.

Dose:250 –1000mg TID.

THIRD GENERATION : Administered parentually

Active against gm –ve enterobactriacea some against pseudomonas.

Highly resistant to gm –ve β- lactamase

Less active on gm +ve cocci.

CEFOTAXIME :

Active against gm –ve and some gm +ve bacteria

Indicated in meningitis, septicaemia, immunocompromised patients.

Dose : 1 –2 gm in or I.V 6-12 hrly

Not active against anaerobes.

CEFTIZOXIME : similar to CEFOTAXIME in antibacterial activity but longer half – life.

CEFTRIAXONE : Distinguishing features : Longer duration of action [t ½ - 8 hr]

therefore administered once or twice daily. Good CSF penetration hypoprothrombinemia and bleeding are adverse effects.

Ceftazidime : Highly active against pseudomonas. Less active against anerobes.

Cefixime : Longer duration of action against H – influenza, strep. pyogenes.

OTHER β- LACTAM ANTIBIOTICS :

A – Carbapenems – Imipenem/Cilastatin

-Broadest spectrum β- lactam antibiotic currently available

-Used in empiric therapy – active against penicillinase.

-Producing gm +ve gm –ve organisms anerobes

-Given IV and excreted through kidney.

-Cilastatin protects imipenem from cleavage and prevents formation of toxic metabolite.

-Adverse effects – nausea, vomiting high levels cause seizures.

B. Monobactams – Aztreonam,

Resistant to action of β- lactamase.

Active against gm –ve rods; not against gm +ve and anaerobes.

Given IV or IM excreted through kidney.

Adverse effects – phlebitis, skin rashes,

A safe alternative for patients allergic to penicillins and /or cephalosporins.

β- LACTAMASE INHIBITORS :

↓

Poses β- lactam ring with no antibacterial activity

↓

Which serve as substrates for β- lactamase

↓

Thus protecting the beta lactam ring of the antibiotic which are the normal substrates.

Eg. Clavulanic acid + amoxicillin

Sulbactam + ampicillin

FLUOROQUINOLONES :

Ist Gen FQ – Norfloxacin, ciprofloxacin ofloxacin, pefloxacin

2nd GEN FQ – Home floracin, parfloxacin amifloxacin

MECHANISM OF ACTION: They inhibit the enzyme bacterial DNA Gyrase –introduction of negative supercoils

PHARMACOKINETICS-Good oral absorption

High Tissue penetrability

Excreted in urine

ADVERSE EFFECTS- Nausea

Headache

Photosensitivity

DOSAGE-Ciprofloxacin;250-750 mg B.I.D

Ofloxacin;200-400mg B.I.D

USES- Typhoid, TB, Bacterial gastroeneritis

Mechanism of resistance :

- Chromosomal mutation
- ↓ Permeability of bacterial

Fluoroquinolones has been slow to develop resistance as resistant mutants are not easily selected.

CIPROFLOXACIN :

Active against a broad range of bacteria, the most susceptible – gm –ve aerobic bacilli (enterobacteriaceae and neisseira)

Gm –ve bacteria – needs higher concentrations.

Highly susceptible

Proteus
E-coli
K – Pheumoniae
Salmonella typhi
N – Meningitidis

Moderately susceptible

staphylococcus – aureus (+ MRSA)
Staphylococcus – Epidermidis

Low to variable susceptibility

Streptococcus pyogenes
Streptococcus faecalis

Notable resistant bacteria

Bacteroides fragilis
clostridia

Remarkable microbiological features of Fluoroquinolones :

- Rapid bactericidal activity and high potency.
- Relatively long post – antibiotic effect on enterobacteriaceae
- Low frequency of mutational resistance.
- Protective intestinal streptococci and anaerobes are spared.
- Active against many β lactam and aminoglycoside resistant bacteria.
- Less active at acidic pH

Pharmacokinetics :

Rapidly absorbed orally; food delayes absorption.

Dose : 250-750mg BID oral [CIPLOX, CIFRAN CIPROBID, CIDROFLOX]

100-200mg IV

Interactions :

- Plasma concentration of theophylline; caffeine and warfarim are increased by ciprofloxacin (also by norfloxacin) due to inhibition of metabolism. (Toxicity occurs).
- NSAIDs may enhance the CNS toxicity of FQs.
- Antacids, sucralfate and non salts given concurrently reduce absorption of FQs.

Uses : Effective against and broad range of infections including those difficult to treat.

Because of widespread bactericidal activity, oral efficacy and good tolerability – extensively used for blind therapy for infections.

- Severe infections – started as I.V then given orally

1. Bone, soft tissue, wound infections.
2. Gram negative septicaemia.

Norfloxacin	**Pefloxacin**	**ofloxacin**
- Less potent	preferred for	more potent
- Not given	meningial	than ciprofloxacin
- When gm +ve	infection	against gm +ve orgns.
- cocci involved infections.		used in systemic and mixed

SULFONAMIDES :

- First antimicrobial agents effective against **pyogenic bacterial infections.**
- Derivatives of sulfanilamides.
- **1. Short acting** (4-8hr) : **Sulfadiazine, sulfisoxazole**
- **2. Intermediate acting (8-12hr) :Sulfamethoxazole, sulfamoxole**
- **3. Long acting (7 days) : Sulfadoxine**
- **4. Special purpose sulfonamides : Sulfacetamide, sulfasalazine silver sulfadiazine.**

BROAD SPECTRUM ANTIBIOTICS

TETRACYCLINES

- Antibiotic with nucleus of 4 cyclic rings.
- Obtained from soil actinomycetes.

Group I	Group II	Group III
Chlortetracycline	Demeclocycline	Doxycycline
Oxytetracycline	methacycline	minocycline
Tetracycline	lymecycline	

- Chlortetracycline in 1948 as aureomycin
- Broad spectrum of activity. (gm +ve cocci and gm +ve bacilli)

MOA : Primarily bacteriostatic, act by inhibiting protein synthesis.

Resistance :

1. Inefficient mechanism to concentrate the drug within the cill.
2. Bacteria pumps the drug out.
3. Production of a protection protein which protect ribosomal binding site from tetracyclines.

PK : Older tetracyclines are incompletely absorbed from g.I.t; absorption is better if taken in empty stomach.

Doxycycline and minocycline are completely absorbed irrespective of food.

Tetracyclines have chelating property – form insoluble and unabsorbable complexes with Ca and other metals.

Milk ,iron preparations, non systemic antacids and sucralfate reduce its absorption.

- Widely distributed in body – bind to bone and teeth
- metabolized in liver, excreted in bile and urine.
- Renal failure doses is reduced except for doxycycline.
- Secreted in milk; Enzymes like phenobarbitone and phenytoin enhance metabolism and reduce plasma half life of doxycycline.

Dosage : Tetracycline 250-500mg QID.

Doxycycline 100mg BID 1st day 100mg every 12-24hrs

Minocycline 200mg initially followed by 100mg BID.

Capsule taken half hr before or 2hrs after food.

Partial cross resistance between tetracyclines and chloramphenicol is noted.

Preparations :

Tetracycline – ACHROMYCIN, HOSTACYCLINE .

Doxyclycline – TETRADOX, DOXYCAPS

Adverse effects : Discoloration of teeth, temporary suppression of bone growth.

Liver damage, kidney damage, super infection (Pseudomenbranous enterocolitis).

Doxycycline and Minocycline – less diarrhoea (small amounts reach lower bowel in active form).

PRECAUTIONS :

1. Not used in pregnancy loctation and in children
2. Avoided with diuretics
3. Used cautiously in renal or hepatic insufficiency
4. Do not mix with penicillins – inactivation occurs
5. Do not inject intrathecally.

Uses :

1. Uses only for those infections for which a more selective and less toxic AMA is not available.
2. Used when nature and sensitivity of infecting organism not known, for initial treatment of mixed infections. (although β lactans and an aminoglyoside antibiotic or a third generation cephalosporin or a FQ is used)
3. Venereal diseases, chlamydial infection, cholera, bruceilosis.

CHLORAMPHENICOL :

- Broad spectrum antibiotic .
- Primarily bacteriostatic , cidal at higher concentrations
- Active against –gm +ve and gm-ve bacteria chalamydia, mycoplasma
- - administered orally and I.V **(oral dose 250 –500mg 6 hrly)**

MACROCIDE ANTIBIOTICS :

Erythromycin :

- First drug of choice as an alternative to pencillin in individuals allergic to β lactum antibiotics.
- From streptomyces erythreus
- Kept in cold to maintain water solubility
- Static at low concentration; but cidal at high concentrations.

MOA : By inhibiting protein synthesis.

Antimicrobial spectrum : Narrow spectrum of activity includes gm +ve and few gm –ve and overlaps with pencillins

- Highly active against – Str. Pyogenes, clostridia
- Str. Pneumoniae
- N. gonorrhoeae

- Effective against the same organisms as penicillin G, so it is used in patients allergic to penicillin.

- Cross resistance observed with macrolides, clindamycin, chloramphenicol.

PK : Erythromycin base is acid labile – so given as enteric coated tablets.

- Food delays absorption by retarding gastric emptying
- Crosses serous membranes and placenta but not BBB.
- Excreted in the bile in the active form.
- Doses is not altered in renal failure
- Pt ½ -1.5hr.

DOSE :250 –500mg 6 hrly (max 8g/day).

Preparations – Erythromcyin base, erythromcycin stearate estolate (acid stable and better

Other members of the family :

Clarithromycin
Azithromycin
Roxithromycin
} show cross resistance with ertythromycin

-Both are stable to stomach acid and is readily absorbed.

Adverse effects : Epigastric distress

Cholestatic jaundice

Ototoxicity

Contraindications and interactions :

1.Not in hepatic dysfunction, as erythromycin acumulates in liver.

2. Erythromycin and clarithromycin inhibit hepatic metabolism of theophylline, warfarin, terfemadine, astemizole, carbamazepine, cyclosporine – lead to toxic drug accumulation.

3. The elimination of a species of intestinal flora which inactivates digoxin, ... greater reabsorption of digoxin.

ROXITHROMYCIN : Semi – Synthetic long acting and acid stable.

Good enteral absorption and tissue penetration , plasma t ½ -12hrs so given twice daily

Better gastric tolerability.

DOSE : 150mg BD 30m before meals.

[ROXID, ROXIBID]

.

CLINDAMYCIN

Introduced in 1970 is a semisynthetic derivative of lincomycin.

MOA is by inhibition of protein synthesis, binding to 50 S submit of bacterial ribosomes. Though bacteriostatic at low concentrations, it is bactericidal at concentrations achieved in vivo.

Important features

1. Has better activity against most strains of S.aureus.
2. More active against most gm +ve and gm –ve anaerobes
3. More restricted antibacterial spectrum that does not include spirochetes, Rickettsia, Mycoplasma and most gram – negative aerobes.

Bacterial Resistance

Mutation in bacterial ribosomes leads to decreased affinty and binding capacity of this drug.

some strains of group A streptococci, peumococci and 15% of staphylococcus aureus have acquired resistance to clindamycin

Gross resistance has been shown between enythronycin and clindamycin but not with any other antibiotics.

Pharmacokinetics

Well absorbed orally even after meals.

Penetrates body tissues and fluids except CSF.

Excellent penetration into the bone makes it ideal for treating infections of bone, such as. Osteomyelitis, purulent osteitis, caused by susceptible organisms. Excreted primarily throu liver; requires reduction dosage in liver diseases.

Superinfection sometimes caused due to alteration in the intestnial microflora.

Therapeutic Uses:

Treatment of infections caused by susceptible strains of streptococci, staphylococci, pneumococci, anaerobes (Bacteroides) insensitive to less toxic antimicrobial drugs or where pevicillin or a macrolide (eg : crythromycin) cannot be used. Specially indicated in refractory bone infections.

- Recommended by AHA as an alterbatuve antibiotic (after amocicillin for prophylactic coverage of high risk patients for developing bacterial endocarditis or endarteritis as the result of bactermia caused by dental procedures.
- Given orally or IV; Single dosage makes superinfection less likely.
- Third choice for treatment of orodental infections caused by susceptible organisms when penicillins and macrolides are ineffective.

Adverse effects :

- Gastrointestinal disturbances (diarrhoea, pseudomenbramous cloitis), Superinfections – glossitis, stomatitis, vaginitis.
- Less antigenic than penicillin – allergy ranges from rashes to utticavia, angiocdemia and anaphylaxis.
- Neutropenia, agranulocytosis, thrombocytopevia and thrombophlebitis (IV) has been associated.

Drug Interactions

- Clindamycin, erythromycin and chloramphenicol are mutually antagonistic because of similar binding sites on bacterial ribosome – so never be given concurrently.
- Clindamycin exhibits neuromuscular blocking activity concomitatnt use with sinular drugs should be closely monitored.

PENICILLINS

- Penicillin was the first antibiotic to be used clinically in 1941.
- It was originally obtained from the fungus *Penicillium notatum*
- Present source is a high yielding mutant of *P.chrysogenum*

UNITAGE

- 1 U of crystalline sodium benzyl penicillin=0.6ug of the standard preparation
- Thus 1g=1.6 million Units or
- 1MU=0.6 g

Frequency of symptoms in Anaphylaxis

Urticaria/angioedema	88%
Upper airway edema	56%
Dyspnea or wheeze	47%
Flush	46%
Dizziness, hypotension, syncope	33%
Gastrointestinal sx	30%
Rhinitis	16%

Anaphylaxis

- Onset of symptoms of anaphylaxis: usually in 5 to 30 minutes; can be hours later
- A more prolonged latent period has been thought to be associated with a more benign course.
- Mortality: due to respiratory events (70%), cardiovascular events (24%)

Treatment of anaphylaxis

- EPINEPHRINE (1:1000) SC or IM
  - 0.01 mg/kg (maximal dose 0.3-0.5 ml)
  - administer in a proximal extremity
  - may repeat every 10-15 min, p.r.n.
- EPINEPHRINE intravenously (IV)
  - used for anaphylactic shock not responding to therapy
  - monitor for cardiac arrhythmias
- EPINEPHRINE via endotracheal tube

Treatment of anaphylaxis

- Place patient in Trendelenburg position.
- Establish and maintain airway.
- Give oxygen via nasal cannula as needed.
- Place a tourniquet above the reaction site (insect sting or injection site).
- Epinephrine (1:1000) 0.1-0.3 ml at the site of antigen injection

Treatment of anaphylaxis

- Benadryl (diphenhydramine)
  - H1 antagonist
- Tagamet (cimetidine)
  - H2 antagonist
- Corticosteroid therapy: hydrocortisone IV or prednisone po

Treatment of anaphylaxis

- Biphasic courses in some cases of anaphylaxis:
  - Recurrence of symptoms: 1-8 hrs later
  - In those with severe anaphylaxis, observe for 6 hours or longer.
  - In milder cases, treat with prednisone; Benadryl every 4 to 6 hours; advise to return immediately for recurrent symptoms

DRUG ALLERGY

- Adverse drug reactions
  - majority of iatrogenic illnesses
  - 1% to 15% of drug courses
- Non-immunologic (90-95%): side effects, toxic reactions, drug interactions, secondary or indirect effects (eg. bacterial overgrowth) pseudoallergic drug rx (e.g. opiate reactions, ASA/NSAID reactions)
- Immunologic (5-10%)

Factors that influence the development of drug allergy

- **Route of administration:**

  - parenteral route more likely than oral route to cause sensitization and anaphylaxis
  - inhalational route: respiratory or conjunctival manifestations only
  - topical: high incidence of sensitization

- **Scheduling of administration:**

-intermittent courses: predispose to sensitization

Factors that influence the development of drug allergy-2

- **Nature of the drug:**
  80% of allergic drug reactions due to:
  - penicillin
  - cephalosporins
  - sulphonamides (sulpha drugs)
  - NSAIDs

Gell and Coombs reactions

- Type 1: Immediate Hypersensitivity
  - IgE-mediated
  - occurs within minutes to 4-6 hours of drug exposure
- Type 2: Cytotoxic reactions
  - antibody-drug interaction on the cell surface results in destruction of the cell
  eg. hemolytic anemia due to penicillin, quinidine, quinine,cephalosporins

Gell and Coombs reactions

- Type 3: Serum sickness
  - fever, rash (urticaria, angioedema, palpable purpura), lymphadenopathy, splenomegaly, arthralgias
  - onset: 2 days up to 4 weeks
  - penicillin commonest cause
- Type 4: Delayed type hypersensitivity
  - sensitized to drug, the vehicle, or preservative (e.g. PABA, parabens, thimerosal)

Penicillin Allergy

- beta lactam antibiotic
- Type 1 reactions: 2% of penicillin courses
- Penicillin metabolites:
  - 95%: benzylpenicilloyl moiety (the "major determinant")
  - 5%: benzyl penicillin G, penilloates, penicilloates (the "minor determinants")

Penicillin Allergy

- Skin tests: Penicillin G, Prepen (benzyl-penicilloyl-polylysine): false negative rate of up to 7%

- Resolution of penicillin allergy
  - 50% lose penicillin allergy in 5 y
  - 80-90% lose penicillin allergy in 10 yr

"Ampicillin rash"

- non-immunologic rash
- maculopapular, non-pruritic rash
- onsets 3 to 8 days into the antibiotic course
- incidence: 5% to 9% of ampicillin or amoxicillin courses; 69% to 100% in those with infectious mononucleosis or acute lymphocytic leukemia
- must be distinguished from hives secondary to ampicillin or amoxicillin

ANTIBIOTIC SENSITIVITY TESTING

- This test determines the effectiveness of antibiotics against microorganisms (e.g., bacteria) that have been isolated from cultures.

- Sensitivity analysis may be performed along with:
  - blood culture
  - urine culture (clean catch) or urine culture (catheterized specimen)
  - sputum culture
  - culture from endocervix
  - throat culture
  - wound and other cultures

- **Why is the Test Performed?**
  The test shows which antibiotic drugs should be used to treat an infection.

- **How is the Test Performed?**

  Colonies of microorganisms are combined with different antibiotics to see how well each antibiotic stops them from growing. The test determines the effectiveness of each antibiotic against the particular organism.

- **What do Abnormal Results Mean?**

  If the organism shows "drug resistance" to the antibiotics used in the test, then none of those antibiotics will be effective treatment

LEDERMIX

- It is highly effective anti-inflammatory cortisone derivative combined with a broad range antibiotic (dimethylchlortetracycline)
- Therapeutical results : Rapid relief of pain associated with acute pulpal & PDL inflammations

T

Drug Interactions in Clinical Dentistry

Antibiotics	Interacting drug	Effect and Recommendation
Penicillin V, ampicillin, Cephalexin, Vancomycin	Bacteriostatic antibiotics (erythromycin, tetracyclines, clindamycin)	Bacteruistatuc antibiotic interferes with action of bactercidial antibiotic
Penicillin V, ampicillin Cephalexin	Probenocid	Urinary excretion of the antibiotic is retarded.
Penicillin V, ampicillin Tetracyclins	Oral Contraceptives	Decrease the activity of oral contraceptive drug
Penicillin V, ampicillin	Methotrexate	Urinary secretion of the drugh (methotrexale) inhibited
Ampicillin	Allopurinol	High incidence of skin rash substitute amoxicillin for ampicillin
Erythromycin	Carbamazipine, cyclosporine, warfarin	Erythromycine interferes with metabolism of these drugs

Antibiotics	Interacting drug	Effect and Recommendation
	Chloramphenicol, clindamycin	Avoid concurrent use as erythromycin interferes with antibacterial activity of other agents.
	Drug that cause ototoxicity or hepatotoxicity	Of full course administered, the risk increases.
Erythromycin tetracyclines	Bactericidal antibiotics (penicillins, Cephalosporins	Action of bactericidal agent inhibited.
	Digoxin	Absorption of digoxin is increased
Tetracycline	Antacids, Ca or Mg salts Zn a ferrous sulfate	Absorption of tetracycline is impaired. Spced administriation adviced to avoid simultaneous injestion
	Lithuin salts	Plasma lithiun concentrations increased
	Methoxyflurane	Avoid concurrent use as nephrotoxicity is increased.

Antibiotics	Interacting drug	Effect and Recommendation
Doxycycline	Barbiturates, alcohol, phenytoin, carbamazepine	Hepatic clearance of Doxy is increased. Adjust dose upward or use alternative tetracycline
Oxytetracycline	Insulin	-Hepoglycemic action of oxytetra cycline reduces insulin requrements substitute with anothers antibiotic.

ANTIBIOTIC RESISTANCE

The greatest possibility of evil in self-medication is the use of too small doses so that instead of clearing up infection, the microbes are educated to resist penicillin and a host of penicillin-fast organisms is bread out which can be passed to other individuals and from them to other until they reach someone who gets a septicemia or a pneumonia which penicillin cannot save.

-Sir Alexander Flemming

Herald Tribune

21.09.1999

Death of 4 Children Amplifies Threat From Drug-Resistant Bacteria

By Sheryl Gay Stolberg

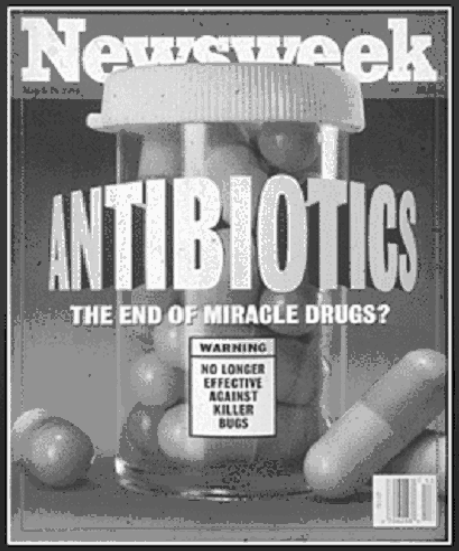
WASHINGTON — More than 200 people in Minnesota and North Dakota have become sick, and four children died, over the past two years after becoming infected with a drug-resistant germ that until recently had been confined to hospitals and nursing homes, federal health officials said Thursday.

The fatalities are the first to be reported in the United States, and are worrisome because they suggest that a lethal strain of *Staphylococcus aureus* may threaten the public. Some cases were reported last year among youngsters in Chicago and Tennessee.

Outbreaks of Community-Associated Methicillin-Resistant *Staphylococcus aureus* Skin Infections — Los Angeles County, California, 2002–2003

During 2002, the Los Angeles County Department of Health Services (LACDHS) investigated three community outbreaks of skin infections associated with methicillin-resistant *Staphylococcus aureus* (MRSA). MRSA commonly has occurred in health-care settings; however, recent investigations of community-associated MRSA (CA-MRSA) have identified infection in various settings, including correctional facilities, athletic teams, and others (CDC, unpublished data, 2002). This report describes investigations of CA-MRSA in Los Angeles County.

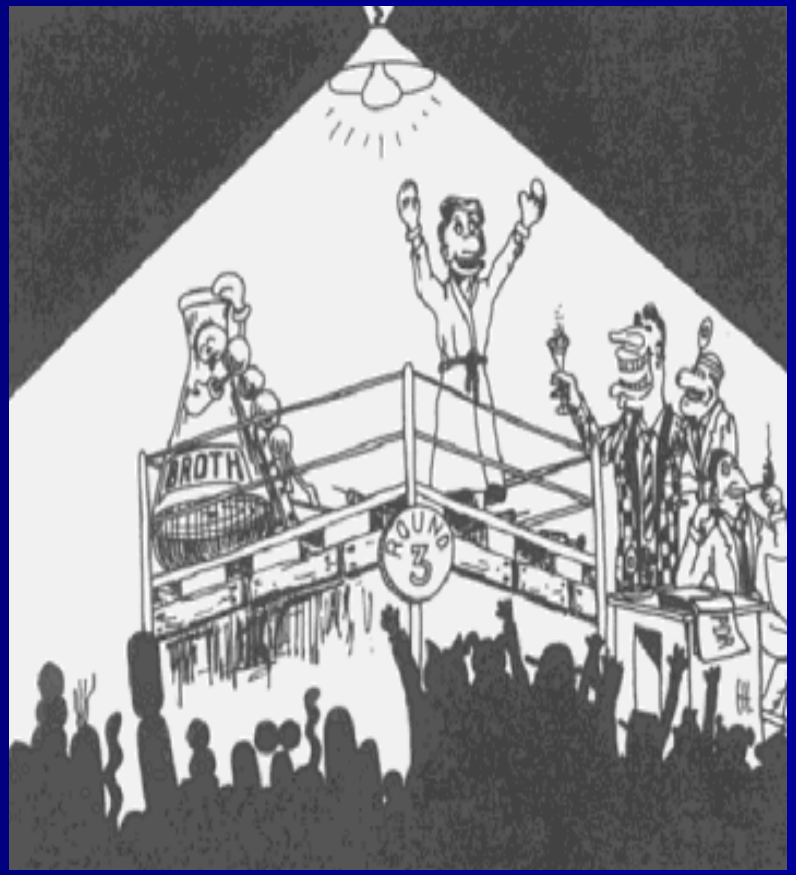
Morbidity and Mortality Weekly Report 2002-2003; 52 (No 05): 88



WHO IS THE WINNER ?

- The microbe always has the last word.

  -LOUIS PASTEUR (1822-1895)



- While *global warming* threatens to bring the skies crashing upon our heads ; *antibiotic resistance*, silent and faceless, is crumbling the ground beneath our feet……

- Without efforts to check and roll back the problem of resistance our world could also go back to the pre-antibiotic era, where thousands died routinely due to simple bacterial infections

MRSA IN EUROPE 2005

- It is estimated that over 50 per cent of antibiotics worldwide is purchased privately, from pharmacies or in the informal sector from street vendors, without prescriptions

Brief History of Antibiotics

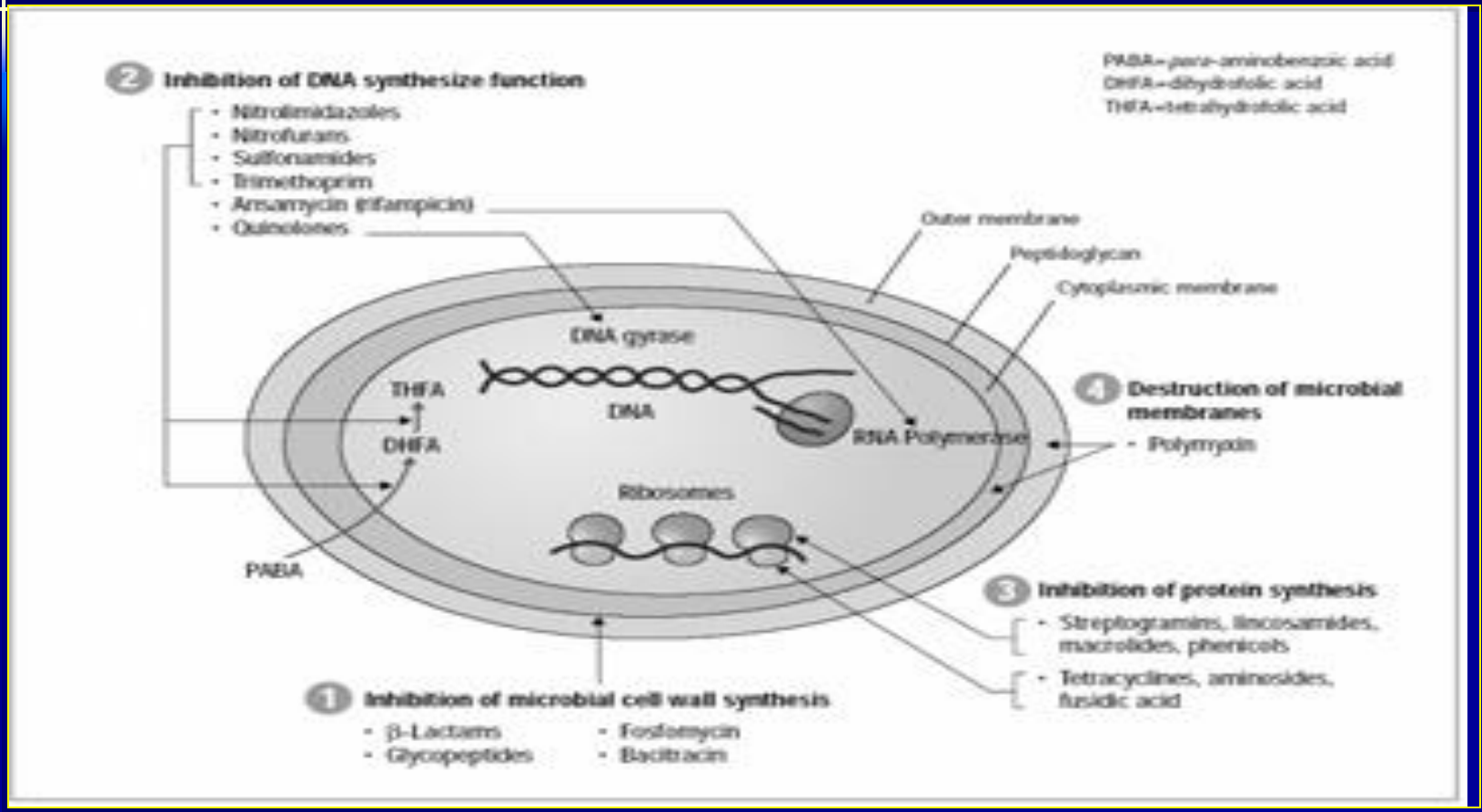
- 1928- Penicillin discovered by Fleming
- 1932- Sulfonamide antimicrobial activity discovered (Erlich)
- 1935- First unsuccessful attempt to use Sulfonamide to treat
- a case of meningitis
- 1943- Drug companies begin mass production of penicillin
- 1948- Cephalosporins precursor sent to Oxford for synthesis
- 1952- Erythromycin derived from Streptomyces erythreus
- 1956- Vancomycin introduced for penicillin resistant staphylococcus
- 1962- Quinolone antibiotics first discovered
- 1970s- Linezolide discovered but not pursued
- 1980s- Fluorinated Quinolones introduced, making then clinically useful
- 2000- Linezolide introduced into clinical practice

Development of Resistance to Newly Introduced Antimicrobials

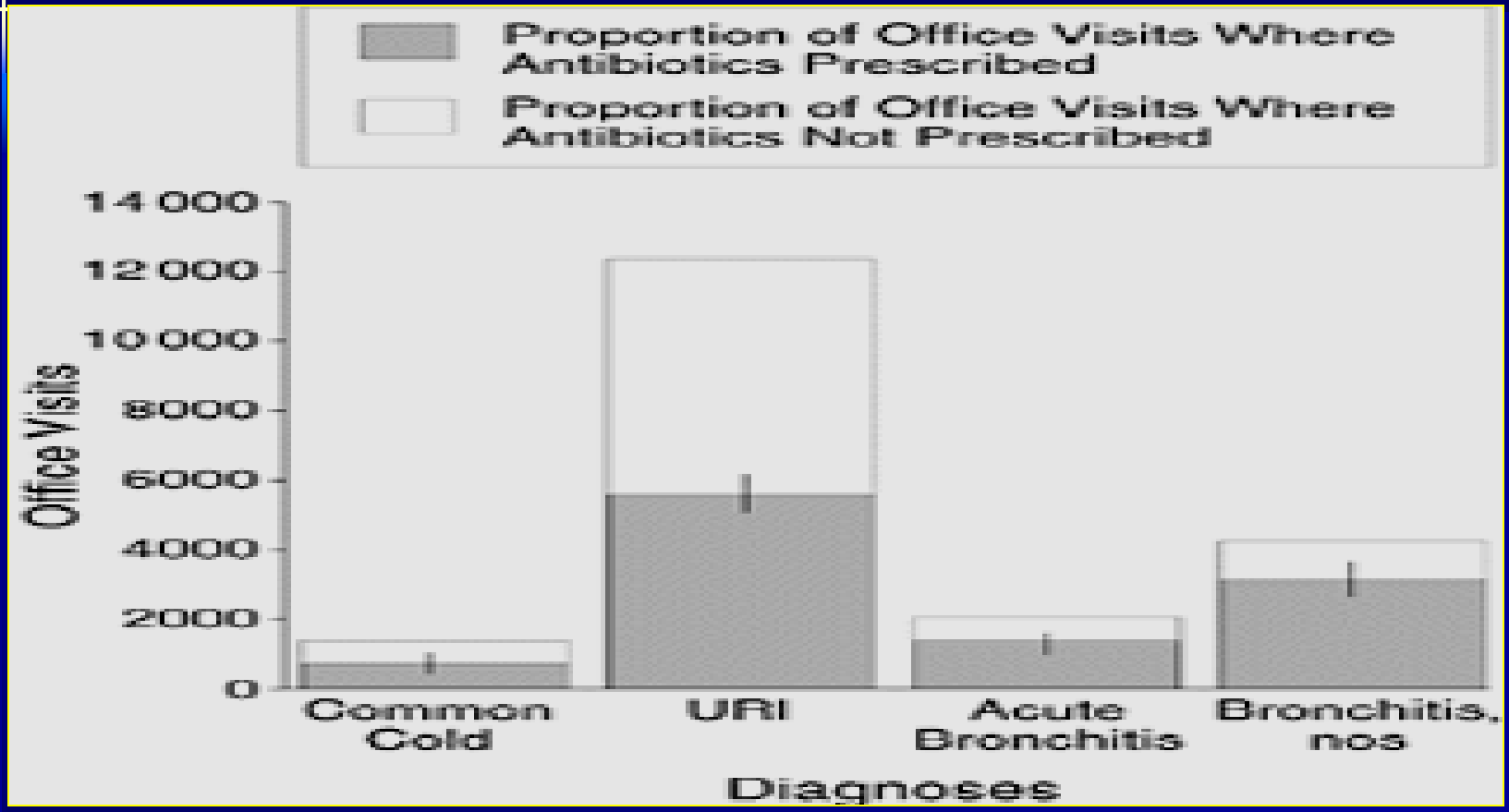
Agent	Year of FDA Approval	First Reported Resistance
Penicillin	1943	1940
Streptomycin	1947	1947
Tetracycline	1952	1956
Methicillin	1960	1961
Nalidixic Acid	1964	1966
Gentamicin	1967	1969
Vancomycin	1972	1987
Cefotaxime	1981	1981 (AmpC β-lactamase) 1983 (ESBL)
Linezolid	2000	1999

Bush K. *ASM News*. 2004;70:282–287.

The four main mechanisms of antibacterial action

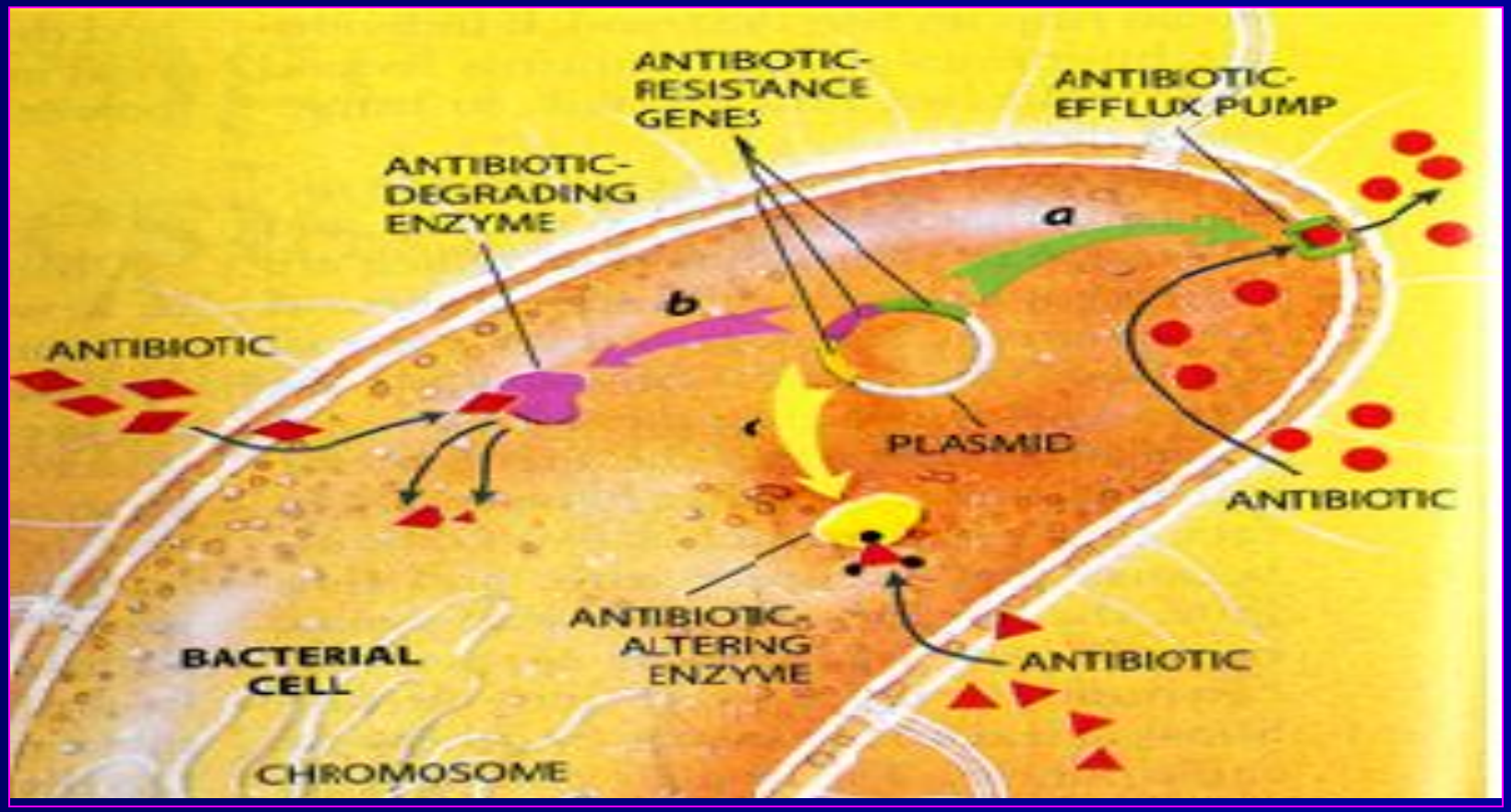


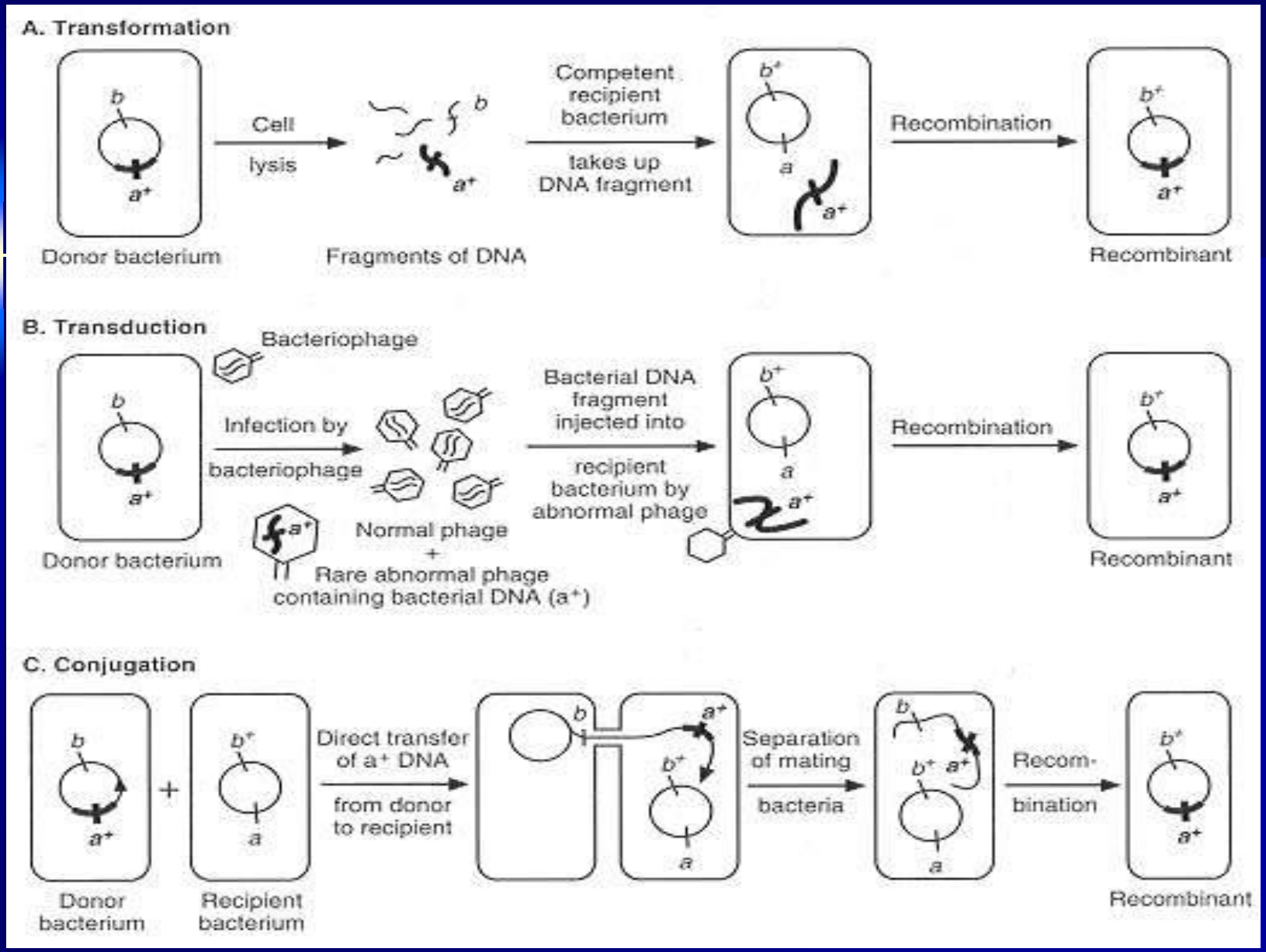
Prescriptions for upper respiratory infections in children and adolescents: National Ambulatory Care Survey 1992



Nyquist *et al. JAMA*

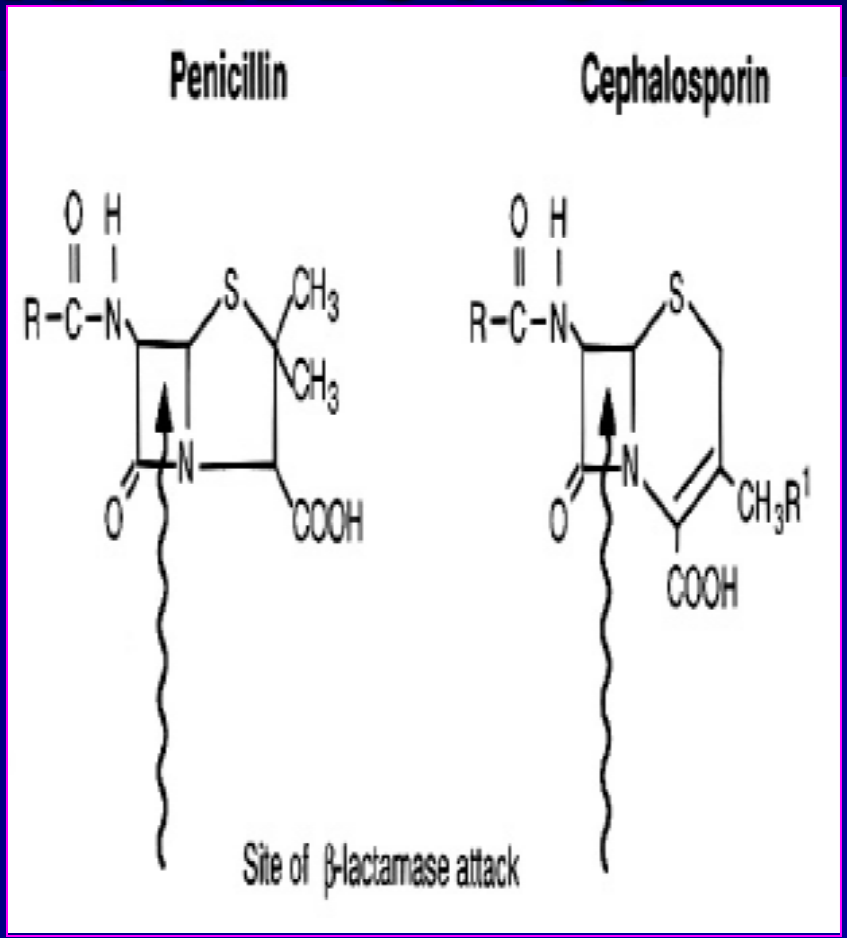
Mechanisms of Antimicrobial Resistance




A. Transformation
b
a+
Donor bacterium
Cell
lysis
b
a+
Fragments of DNA
Competent
recipient
bacterium
takes up
DNA fragment
b+
a
a+
Recombination
b+
a+
Recombinant
B. Transduction
Bacteriophage
b
a+
Donor bacterium
Infection by
bacteriophage
a+
Normal phage
+
Rare abnormal phage
containing bacterial DNA (a+)
Bacterial DNA
fragment
injected into
recipient
bacterium by
abnormal phage
b+
a
a+
Recombination
b+
a+
Recombinant
C. Conjugation
b
a+
Donor
bacterium
+
b+
a
Recipient
bacterium
Direct transfer
of a+ DNA
from donor
to recipient
b
a+
b+
a
Separation
of mating
bacteria
b
b+
a+
a
Recom-
bination
b+
a+
Recombinant

MECHANISM OF MICROBIAL RESISTANCE TO ANTIBIOTICS

- ENZYMATIC ANTIBIOTIC INACTIVATION
  - β lactamases : β lactams
    (penicillins, cephalosporins)
  - Acetyltransferases :
    (aminoglycosides.chloramphenicol, streptogramins)



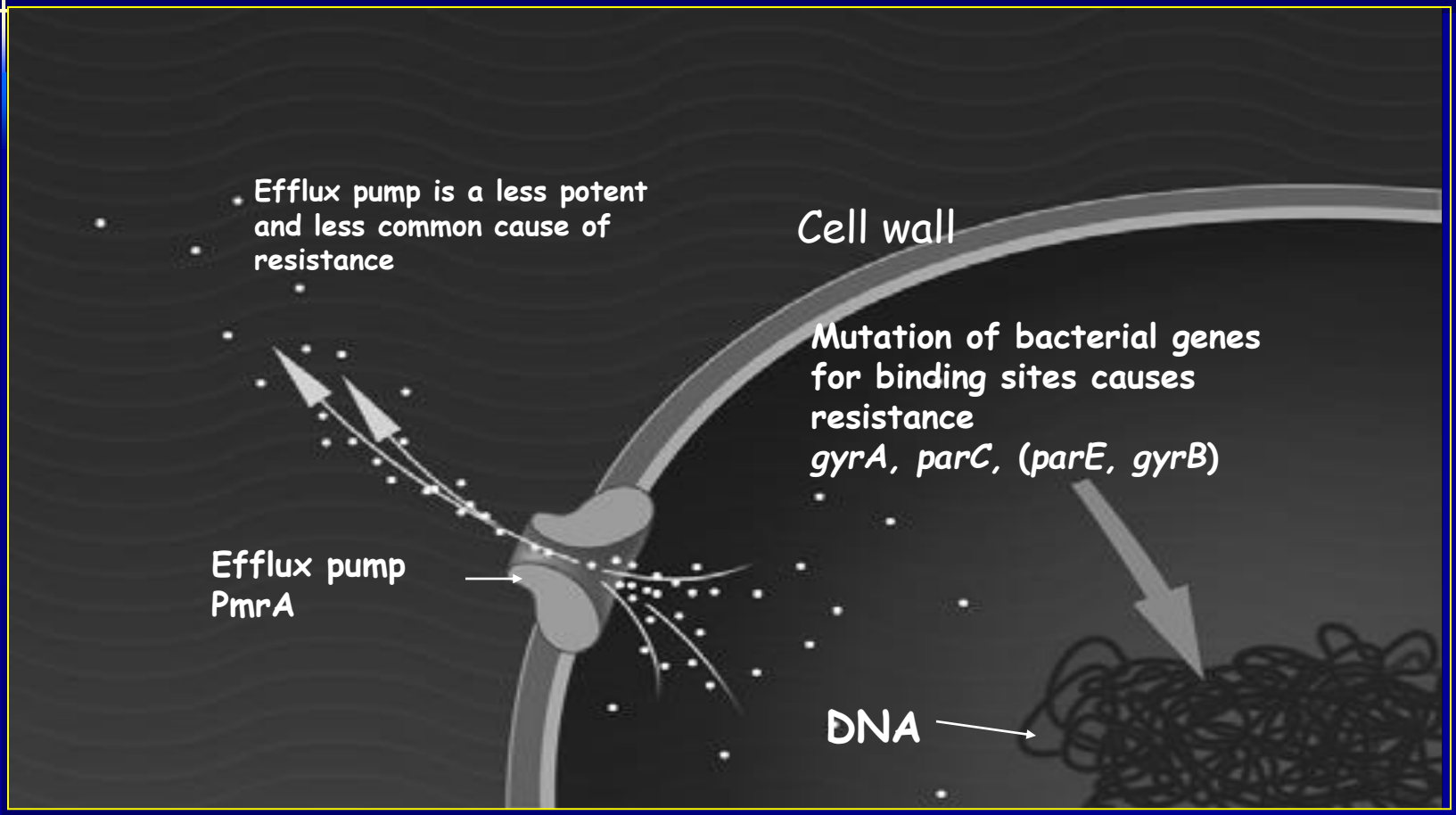
Splits the amide bond hydrolyzing the β-lactam ring

- Modification/Protection of target sites
  - Modified penicillin binding proteins : β lactams
  - Altered DNA gyrase & topoisomerase IV : Fluroquinolones
  - Altered RNA polymerase : Rifampin
  - Methylation of anadenine of 23SrRna :Erythromycin, Clindamycin, Streptogramins
  - Alteration of 16SrRNA : Tetracycline
  - Altered tetrahydrofolate & dihydrofolate reductase : Sulfonamides & Trimethoprim
  - Substitution of terminal peptidoglycan alanine with lactate : Vancomycin & Teicoplanin

- Limiting antibiotic access to microbial cell
  - Altered outer membrane porins reduced membrane transport: Most antibiotics
- Active efflux
  - Antibiotic efflux proteins : Tetracycline, Fluoroquinolones

- Failure to activate antibiotics
  - Deceased flavodoxin production : Metronidazole
- Development of alternate growth requirements
  - Production of auxotrophs : enterococci
- Overproduction of target sites :
  - Hyper-beta lactamase production : enteric bacilli

Mechanisms of Resistance to Fluoroquinolones



CONCLUSION

- Microbes will leave us alone if we leave them alone & stop forcing them to invent new ways to survive (after all they have 3.5 billion years of practice).
- This can be accomplished by reducing our use of antimicrobials to the level where they are necessary for our survival & not merely for Dr & patient comfort.

- Antibiotics are "societal drugs" that affect microbial resistance not only in the person taking the drug but also everyone else, because resistance genes are easily passed via personal contact, fomites & human & animal refuse.

- When antibiotics are used , 6 events may occur with only 1 being beneficial : When the antibiotic aids the host defenses to gain control & eliminate the infection
- Alternatively, the antibiotic may cause toxicity or allergy, initiate a superinfection with resistant bacteria, promote microbial chromosomal mutations to resistance, encourage resistance gene transfer to susceptible species, or promote the expression of dormant resistance genes.

WITH ANTIBIOTICS, NO PERSON IS AN ISLAND

References

- (1) In Search For Endodontic Pathogens:Suchitra U, KUNDABALA M, Shenoy MM- KUMJ 2006, Vol4,No4,Issue 16,525-529
- (2) Antibiotic Prophylaxis in dentistry:A Review & Practice recommendations- JADA Vol 131 March 2000 366-374
- (3) Endodontic intervention versus oral antibiotic therapy in the management of endodontically compromised situations-2 case reports- Endodontology Vol 16 2004 2-6
- (4) Infective endocarditis-a critical review – British Dental Journal,9Dec 2000,Vol 189,No 11,
- (5) Beyond Antibiotics-Keith Sehnert and Lendon Smith
- (6) The Dental Clinics Of North America (Dental Therapeutics), Oct 2002, Vol 46,No 4
- (7) The Dental Clinics Of North America (Infection, Infection Control, & Dentistry, Part2), Oct 2003, Vol 47,No. 4
- (8) Infective Endocarditis – a critical review. BDJ, Dec 2000, Vol 189, No 11,Page 66

References..Contd

- (9) Infective Endocarditis, dentistry, and antibiotic prophylaxis; time for a rethink? (BDJ, Dec 2000, Vol 189,No 11, page 610-616)
- (10) Antibiotic prophylaxis for patients with joint prostheses - still a dilemma for dental practitioners (*British Dental Journal* 2003; Volume 194, No. 12, pages 649-653.
- (11) Patients with artificial joints: Do they need antibiotic cover for dental treatment? (Australian Dental Journal 2005, 50, S45-S53)
- (12) Antibiotic resistance in general dental practice—a cause for concern? Journal of Antimicrobial Chemotherapy (2004) **53**, 567–576


THANK YOU