OTHER β-LACTAM ANTIBIOTICS Carbapenems Doripenem

 -synthetic β-lactam

 -CSF when the meninges. Ertapenem(IV or IM injection once daily)

 are inflamed

 - excreted by glomerular Meropenem (IV)

 filtration

 Imipenem/Cilastatin(IV)(may provoke seziures)

.

 -Imipenem is compounded with cilastatin to protect it from metabolism by renal dehydropeptidase.

 -Imipenem resists hydrolysis by most β-lactamases, but not the metallo-β-lactamases

 -Impenem active against b-lactamase-producing gram-positive and gram-negative organismsanaerobes, and P. aeruginosa

 -ertapenem is not for P. aeruginosa/Enterococcus species / Acinetobacter species.

 -dose adjusted in patients with renal insufficiency

 Monobactams Azteronam(against the Enterobacteriaceae, including P. aeruginosa.)

- lacks activity against gram-positive organisms and anaerobe

 - use alone in empiric therapy(IV or IM)

 - resistant to the action of most β-lactamase exception (ESBLs)

 - safe alternative for treating patients who are allergic and unable to tolerate penicillins and/or . cephalosporins.

Polymixins (gram-negative bacteria)/

detergent-like effect sulbactam

concentration-dependent

 Proteus and Serratia resistan β-LACTAMASE INHIBITORS tazobactam

polymyxin B (parenteral, ophthalmic, otic, and topical)

 *colistin* (*polymyxin E*).( IV or inhaled) Calvulanic acid

 nephrotoxicity and neurotoxicity -do not have significant antibacterial activity. Instead, they bind to and inactivate β-. . . lactamases, thereby protecting the antibiotics

 -Hydrolysis of the β-lactam ring by enzymatic cleavage or by acid.

 Vancomycin (against multiple drug resistant organisms, such as MRSA and enterococci)

 restricted to topical application/ nephrotoxicity with systemic use.

 treatment of MRSA and methicillin-resistant Staphylo coccus epidermidis (MRSE)

 enterococcal infections.

 vancomycin-resistant bacteria (, Enterococcus faecium and Enterococcus faecalis)

 treat gram-positive infections

 Oral vancomycin treatment of antibiotic-associated colitis

 Intravenous vancomycin is used in individuals with prosthetic

 with the aminoglycosides> treatment of enterococcal endocarditis

 Daptomycin /quinopristin/ dalfopristin and linezolid for the treatment of

 vancomycin-resistant organisms

 resistance can be caused by plasmid-mediated changes or by decreased binding

No-lactam Cell wall Slow IV infusion (60–90 minutes)

Synthesis inhibotors

 Daptomycin (treating infections caused by resistant gram-positive organisms)/ treatment of . . . complicated skin and skin structure infections and bacteremia caused by S. aureus.

* -should *never* be used in the treatment of pneumonia.

 Telavancin (like vancomucin+ disruption of the bacterial cell membrane)

 alternative to *vancomycin, daptomycin(gram(+)+skin infections)/* *last choice for bacterial*

 *pneumonia* (fetal harm/ anticoagulation/ prolong the QTc)

* fosomycin (blocks the enzyme which catalyzes the first step in peptidoglycan synthesis/ for urinary tract infections caused by E. coli or E. faecalis/ cross resistance is unlikely/ oral/ urine and feces/ one-time dose/ parenteral formulation> systemic infections/ adverse> vaginitis
*

Pencillins

 - differ from one another in the R substituent attached to the 6-aminopenicillanic acid residue side chain affects the antimicrobial spectrum

 , stability to stomach acid, cross-hypersensitivity, and susceptibility to bacterial degradative enzymes

 - interfere with the last step of bacterial cell wall synthesis (transpeptidation or cross-linkage)-( bactericidal) “Park nucleotide” accumulates

 - Cell lysis can then occur, either through osmotic pressure or through the activation of autolysins.

 - only effective against rapidly growing organisms that synthesize a peptidoglycan cell wall.

 - inactive against (mycobacteria, protozoa, fungi, and viruses ).

 - Penicillin-binding proteins (PBPs): bacterial enzymes involved in the synthesis of the cell wall and in the maintenance of the morphologic

 features of the bacterium.

 - prevent cell wall synthesis and lead to morphologic changes or lysis of susceptible bacteria.

 - Alterations in some of these target molecules provide the organism with resistance to the penicillins.

 Such as (Methicillin-resistant Staphylococcus aureus (MRSA is susceptible to glycopeptide vancomycin)

 - degradative enzymes (autolysins) in the normal remodeling of the bacterial cell wall.

 penicillin, the degradative action of the autolysins proceeds in the absence of cell wall synthesis.

 - gram positive microorganisms (easily traversed by penicillins)

 - Gram-negative micro organisms (barrier to the water-soluble penicillins/have water-filled channels ( (called porins) to permit entry).

 -Pseudomonas aeruginosa has restrictive porins, making it resistant to many antimicrobial agents.

 -Natural penicillins obtained from fermentations of the mold Penicillium chrysogenum.

 - Natural penicillins and amino penicillins are susceptible to inactivation by β-lactamases (penicillinases).

 - penicillin V is more acid stable than penicillin G/ penicillinase-resistant penicillins have no activity versus gram-negative infections

 - Formulation of ticarcillin or piperacillin with clavulanic acid or tazobactam, respectively, extends the antimicrobial spectrum of these

 antibiotics to include penicillinase-producing organisms(they become penicillase resistant.)( IV / IM)

 - single treatment with penicillin is curative for primary and secondary syphilis

 -\* (Neisseria gonorrhoeae) Silver nitrate drops in the eyes prevent gonococcal ophthalmia in newborns.

 - Penicillinase-producing strains are treated using ceftriaxone, with spectinomycin as a backup.

 . - Stable to acid, permitting oral administration

 -penicillins are negatively charged./ aminoglycosides are positively charged (on prolonged contact > inactive).

 - Natural resistance to the penicillins occurs in organisms that either lack a peptidoglycan cell wall

 (for example, mycoplasma) or have cell walls that are impermeable to the drug./ -Aqquired resistance to the penicillins by plasmid transfer.

 - Gram-positive organisms secrete β-lactamases extracellularly, - gram-negative bacteria confine the β-lactamases in the periplasmic space

 - Decreased permeability to the drug: Decreased penetration/efflux pump/ β-lactamases/altered PBPs

 Are the resistant ways of bacteria againt penicillin

 - oute of administration of a β-lactam antibiotic is determined by the stability of the drug to gastric acid and

 by the severity of the infection

 - Most of the penicillins are incompletely absorbed after oral administration and affect the composition of the intestinal flora.

 - Amoxicillin not appropriate therapy for the treatment of Shigella- or Salmonella-derived enteritis because It is almost completelt absorbed.

 - Absorption of all the penicillinase-resistant penicillins is decreased by food in the stomach

 - penicillase resistant penicillins must be administered 30 to 60 minutes before meals or 2 to 3 hours postprandial

 -cross the placental barrier/ non-teratogenic./ During the acute phase of infection increased amount of drug in

 the central nervous system/ Penicillin levels in the prostate are insuffi cient to be eff ective against infections.

 - Host metabolism of the β-lactam antibiotics is usually insignificant. / penicillin G metabolism in patients with impaired renal function.

 - half-life of penicillin G can increase in the presence of renal dysfunction

 - primary route of excretion is by (tubular) secretory system of the kidney as well as by glomerular filtration

 - Probenecid inhibits the secretion of penicillins thus, can increase blood levels.

 - Nafcillin, dicloxacillin and oxacillin are not eliminated by the kidneys.

 - penicillins are also excreted into breast milk.

 - Penicillin G Does not penetrate into the CNS unless meninges are infl­amed/ Mostly unchanged in urine.

 -Adverse reactions (Hypersensitivity/ Diarrhea/ Nephritis/ Neurotoxicity/ Hematologic toxicities/ Cation toxicity)

 \*Hypersensitivity because of pencilloic acid reaction

 \* Diarrhea because disruption of the normal balance of intestinal microorganisms

 \*Nephritis All penicillins, but particularly methicillin

 \* Neurotoxicity( Epileptic patients are particularly at risk) dosage adjustments minimize the risk for seizure.

 \* Hematologic toxicity (Decreased coagulation/ Cytopenias may occurif greater than 2 weeks of therapy)

 high doses of PiperacillinTicarcillin and Nafcillin,pinecillin G

 \*cation toxicity caused by the large quantities of sodium or potassium that accompany the penicillin

 - patients with mononucleosis who are treated with ampicillin, the incidence of maculopapular rash approaches 100 percent

- cell wall inhbitors alter the permeability > entry of other antibiotics such as (aminoglycosides)> enhanced antimicrobial activity

- any penicillin I didn’t mension his route or admenstration can be taken (oral / IV/ IM)

 penicillins penicillase sensible Natural penicillins penicillin G (Procaine and benzathine ( IM /IV /absorbed slowly )

 (+)cocci \*\*Streptococcus (pneumoniae\* / pyogenes /viridans)\*\*

(narrow spectrum) (-)cocci \*\*Neisseria( gonorrhoeae /meningitides)\*\*

 (+)bcilli \*\*Bacillus anthracis /Corynebacterium diphtheria\*\*

 Anaerobic organisms \*\*Clostridium perfringens)\*\*

 Spirochetes \*\*Treponema :(pallidum (syphilis)/ pertenue (yaws))\*\*

 Penicillin V (stable to acid) (only oral )

 Ampecillin (stable to acid)//if added to sublactam becomes acid

 Not stable but penicillase stable( avalible only parenternal )

 (Ampicillin+sublactam)

 Aminopenicillins

 (entended spectrum)

 -spectrum similar to penicillin G but Amoxcillin (stable to acid) /penicillase resistant if added to

 More effective on gram (-)bacilli (only oral) calvulanic acid (only oral)

 (almost completely absorbed)

 Nafcillin

 Methicillin (toxicity (interstitial nephritis)/ only toidentify resistant strains of S. aureus)

 Penicillase resistant Oxacillin . (Antistaphylococcal) Dicloxacillin (stable to acid)

 - treatment of infections

 caused by penicillinase-

 producing staphylococci

 -no activity versus

 gram-negative

 (very narrow spectrum)

 Ticracellin ( IV / IM )

 carboxypencillins

 Carbenicellin

 Anti-pseudomonal

 -against P. aeruginosa

 - effective against many gram-negative bacilli Piperacillin (most potent)( IV /IM )

 but not against Klebsiella

 . . Ureidopenicillins Azlocillin

 Mezlocillin

Protein Synthesis Inhibitors

\*Target ribosomes and inhibit protein synthesis / \*Bacterial ribosomes:30S,50S / \*mammalian ribosomes: 40S,60S

\*Selectivity for bacterial ribosomes – minimizes adverse effects /\*High concentrations > toxic effects > interaction with our ribosomes

 TETRACYCLINES (30 S – prevent binding of tRNA to mRNA) / (4)\_ (demeclo / doxy / mino / tetra )-cycline

\*should not be used in pregnant or breast-feeding women or in children less than 8 years of age.

\* concentrate intracellularly in organisms / \*Bind reversibly to the 30S / \*Bacteriostatic /\* oral /\* unchanged in the urine

\*gram-positive ( staphylococcus aureus including MRS and streptococcus pneumonia ,bacillus anthracis) and gram-negative (brucella,vibrio cholera , yersenia pestis) , protozoa, spirochetes(borrella bur ,leptospira interrogans,treponema pal), mycobacteria, atypical species(mycoplasma pneumonia,chlamydia , R.reketsii ,clostridium perfringes and tetani)

\*used in the treatment of acne and Chlamydia infections (*doxycycline*) /\*

\*Treatment of cholera (vibrio cholera) includes doxycycline and fluid replacement /\*

\* treatment of rocky mountain spotted fever (R.reketsii) /\*

\* treatment of (chlamydial infections) by doxycycline and azithromycin /\*

\*treatment of lyme disease(spirochetes)-charectarised by bull eye rash –doxycycline/\*

\*treatment of mycoplasm pneumonia by - macrolide , doxycycline/\*

\*Resistance(Efflux pump , Enzymatic inactivation , proteins that prevent binding to the ribosome ) /\*can be resistant to one or all

\*Dairy products or divalent and trivalent cations decreases absorption/\* *Tetracycline* should be taken on an empty stomach

\* Bind to tissues undergoing calcification or to tumors /\* Penetration into body fluids is adequate/\*

\*minocycline and doxycycline achieve therapeutic levels in CSF /\* doxycycline and minocycline: oral and IV/\*

\**Minocyclinealso* *high levels in saliva and tears-* *eradicating the meningococcal carrier state,-* *hepatic metabolism, lesser kidney*

\*all cross the placental barrier and concentrate in fetal bones and dentition/\*

\* Doxycycline- bile into the feces – in renally compromised patients/\* tetracyclines is limited in paediatrics(reason in adverse 2)

\*adverse(1-Gastric discomfort - minimized through coadministration with food or fluids and use of capsules rather than tablets)

2-Effects on calcified tissues - Deposition in the bone and dentition-cause discoloration and hypoplasia of teeth in children

3-Hepatotoxicity – rare - high doses in pregnant women or preexisting hepatic dysfunction or renal impairment.

4-Phototoxicity - Severe sunburn when exposed to sun or UV light - *tetracycline* and *demeclocycline(most frequent)but all can cause*

 Patients should wear adequate sun protection.

5-Vestibular dysfunction(Dizziness, vertigo, and tinnitus) - particularly with *minocycline - Doxycycline may also cause it.*

6-Pseudotumor cerebri - Benign, intracranial hypertension(headache and blurred vision)- discontinuation of the drug treats it

 GLYCYL-CYCLINES (*Tigecycline)(* *Reversibly binding to the 30S ribosomal subunit)*

\* treatment of complicated skin and soft tissue and intra-abdominal infections/\*

\* *methicillin* resistant staphylococci(MRSA),multidrug-resistant streptococci, vancomycin-resistant enterococci (VRE),

extended-spectrum β-lactamase–producing gram-negative bacteria, Acinetobacter baumannii and aerobic organisms.

\* is not active against Morganella, Proteus, Providencia, or Pseudomonas species /\*Resistance- overexpression of efflux pumps

\* IV infusion /\* large volume of distribution > low plasma concentrations > not for blood ifections.

\* biliary/fecal elimination /\* dose reduction in severe hepatic dysfunction/\*

\*adverse(Elevations in liver enzymes and serum creatinine / photosensitivity, pseudotumor cerebri, discoloration of permanent teeth when used during tooth development, and fetal harm in pregnancy like tetracyclines)

\* decrease the clearance of *warfarin* and increase prothrombin time



AMINOGLYCOSIDES (Amikacin/Gentamicin / Neomycin/Streptomycin /Tobramycin) (bind 30S –misreading of mRNA)
\*treatment of serious infections due to aerobic gram-negative bacilli/\* bactericidal / (or interfere with assembly of ribosome)

\* through porin cross the outer membrane , oxygen depenent system transport the drug through cytoplasmic membrane)

\* Concentration dependent /\* target Cmax is (8-10) times the minimum inhibitory concentration ( MIC)/\*

\*postantibiotic effect (PAE)- continued bacterial suppression after drug levels fall below the MIC/\* larger dose- longer PAE(طردي )

\* single large dose given once daily /Pseudomonas aeruginosa, Klebsiella pneumoniae, and Enterobacter sp ( aerobic gram(-)bacilli)

\*Aminoglycosides are often combined with a β-lactam antibiotic(treatment of Enterococcus( faecalis , faecium infective endocarditis).

\*treatment of tularemia (Francisella tularensis ) gentamicin

\*treatment of INFECTIONS DUE TO ENTEROCOCCI -gentamicin or streptomycin plus vancomycin or a β-lactam such as ampicillin

\*INFECTIONS DUE TO PSEUDOMONAS AERUGINOSA - tobramycin alone or in combination with an antipseudomonal penicillin, such as piperacillin or ticarcillin./\*not oral >because its Highly polar /\*

\*resistance(efflux pumps / decreased uptake / modification and inactivation by plasmid-associated synthesis of enzymes)

\*cross-resistance cannot be presumed / *Amikacin* is less vulnerable to these enzymes/\*

\*All except *neomycin are given parenterally/ \*Neomycin is not given parenterally due to severe nephrotoxicity(given topically for skin or orally for bowel preperations for surgery)/\**low distribution into fatty tissue🡪 doses based on lean body mass(not actual weight)

\*Concentrations in CSF are inadequate so we use intrathecal (IT) route/cross the placental barrier(fetal plasma and amniotic fluid)

\*90% of the parenteral excreted unchanged in the urine /\*Accumulation occurs in patients with renal dysfunction

\*adverse(elderly are susceptible to 1-nephrotoxicity(kidney damage because of retention) and2- ototoxicity(releated to high peak plasma levels and duration-irreversible-affects fetus-risk in patients takingototoxic drugs, such as *cisplatin* or loop diuretics-with streptomycin causes vertigo)3-Neuromuscular paralysis(increase in concentrations (high doses,short time)or administration with neuromuscular blokers- risk in Patients with myasthenia gravis-*calcium gluconate* or *neostigmine* can reverse the block)4-Allergic reactions-dermatitis in topical neomycin) .

 MACROLIDESand KETOLIDES (Azi , Clari , Ery ,Teli)-thromycin / (bind to 50S irreversibly inhibiting translocation)

\*Generally bacteriostatic, (bactericidal at higher doses) /oral/ (may also interfere with transpeptidation)

\**Erythromycin* alternative to *penicillin* in individuals with an allergy to β-lactam antibiotics /\**Telithromycin* –first Ketolide

\*Ketolides and macrolides have similar antimicrobial coverage, ketolides are active against macrolide-resistant gram-positive strains

 \*Erythromycin- against many of the same organisms as *penicillin G*

\*Clarithromycin -Haemophilus influenzae ,intracellular pathogens(Chlamydia*,* Legionella*,* Moraxella, Ureaplasma ,Helicobacter pylori)

\*Azithromycin-against respiratory infections due to H. influenzae and Moraxella catarrhalis/ less against strepto and staphylo )cocci

*Azithromycin* – treats urethritis caused by Chlamydia trachomatis. Mycobacterium avium-treated with *clarithromycin* or *azithromycin*

\*Telithromycin-similar to *azithromycin, least resistance to it*

*\*resistance(inability to take up* /efflux pumps /decreased affinity of the 50S(methylation of adenine in 23S in gram (+) or erethromycin esterases in gram (-))

\*Erythromycin destroyed by gastric acid (enteric coating or easterfied forms)

\**Clarithromycin, azithromycin,* and *telithromycin* are stable in stomach acid and are readily absorbed

\*Food interferes with the absorption of *erythromycin* and *azithromycin / Food increase absorptionof clarithromycin*

\**Erythromycin* and *azithromycin* are available in IV formulations /Erythromycin diffuses into prostatic fluid and all fluids exept CSF

\*All concentrate in the liver /*Clarithromycin, azithromycin,* and *telithromycin* are widely distributed in the tissues

\**Azithromycin* has the longest half-life and the largest volume of distribution/*Erythromycin* and *telithromycin metabolized hepatically*

*\*clarithromycin Interfere with the metabolism of theophylline and antiepileptics /Erythromycin and azithromycin (bile as active drugs*

*\*clarithromycin eliminated by the kidney as well as the liver/*

*\*adverse(1-Gastric distress and motility this can be used in treatment of gastroparesis or postoperative ileus (erythromycin)*

*2-Cholestatic jaundice/3-Ototoxicity(erythromycin in high doses / azithromycin is irreversible)*

 *\* contradicated in (hepatic dysfunction /hepatotoxicity with telithromycin /prolong the QTc interval -proarrhythmic patients)*

*\*Drug interactions (Erythromycin, telithromycin, and clarithromycin inhibit the hepatic metabolism of a number of drugs/-*

interaction with *digoxin* -eliminates intestinal flora that ordinarily inactivates *digoxin* >greater reabsorption of the drug in enterohepatic circulation

 CHLORAMPHENICOL (restricted to life-threatening infections )(bind reversibly to 50S - inhibits peptidyl transferase)

\*chlamydiae, rickettsiae, spirochetes, and anaerobes/Bacteriostatic (may be bactericidal depends on the dose and organism )

\*Resistance (enzymes that inactivate it , decreased ability to penetrate , binding site alterations )

\* IV / reaches therapeutic concentrations in the CSF /hepatic metabolism to an inactive glucuronide (eliminated in the urine)

\*Dose reductions are necessary in patients with liver dysfunction or cirrhosis / secreted into breast milk > avoided in breast feeding

\*adverse (1-Anemias (dose-related /hemolytic anemia and aplastic anemia-independent of dose),

2-Gray baby syndrome-( Neonates have a low capacity to glucuronidate and underdeveloped renal function -accumulates -interfere with mitochondrial ribosomes - poor feeding, depressed breathing, cardiovascular collapse, cyanosis – Adults in very high doses

\*Drug interactions (Inhibits some of hepatic mixed-function oxidases - blocks the metabolism of drugs such as *warfarin* and *phenytoin*

Spirochaetales spirochaetacea Treponema(Nonpathogenic treponemes (Reiter strain) can be cultured

\*Gram-negative spirochetes,motile anaerobically)( Cardiolipin component of treponemal antigens.)

\*Extremely thin,very long palladium (slender spirals/spiral coils spaced1 μm from one another/

\*periplasmic flagella(axial fibrils, endoflagella) microaerophilic/ from mother to fetus, congenitally,sexually transmitted/

\*Outer sheath encloses axial fibrils Gram or Giemsa stain(not seen) /darkfield microscopy/Intracellular pathogen

\*endoflagella in periplasmic space Staining with anti-treponemal antibodies labeled with fluorescent dyes/

(only outer membrane is in the outside) Cannot be grown in cell-free cultures/ Do not survive well outside of host

\*multiply locally Cause syphilis/ Long incubation period(in it host is non-infectious)/

\*spread to lymph nodes then blood Virulence-(outer proteins for adherence)-(Hyaluronidase-perivascular infilteration

\*spirochetes-regain substance- -(fibronectin coating-antiphagocytotic)/

positive flocculation tests Tissue destruction and lesions result of immune response (immunopathology)

 Primary(syphilis) - papule form ulcer with ("hard chancre“)r ing iroretin

 secoundary- red maculopapular rash, syphilitic اشياء(neph men cho hep)itis

 latent-little or no symptoms(first 4 years-early latent,the rest late latent)

 tertiary- [Gummas](https://en.wikipedia.org/wiki/Gumma_%28pathology%29) in connective tissue /meningovascular, cardiovascular syphilis

 primary is regional while secoundary is generalized lymphadenopathy

 congenital syphilis(from transplacental infection/septicemia in fetus/ widespread

 dissemination/fetuses die, miscarriages result,or stillborn at term or born live-congenital

 syphilis and CNS anomalies)

 tests(Dark field/fluorescent antibody staining/no culture/nontreponemal tests(

 VDRL,RPR)/tremponal tests(FTA-absorbtion/MHA-TP)

 Borrelia (Giemsa Stain /

 \* B.recurrentis-relapsing fever,human resirvior,body louse vector( pediculus)

 \* Borrelia spp-relapsing fever(endemic),rodents and soft shilled tick resirvior

 Vector soft shelled tick(ornithodoros)

 \*B.burgdorferi-lyme disease,hard shelled ticks reservoir and vector(ixodes)others..

 Sign- expanding area of redness on the skin- lesion -(erythema migrans)/ flu-like

 Symptoms/ arthralgia and arthritis(late)./tick saliva or by regurgitation

 #Relapsing fever- spirochetes in spleen,liver,kidneys ,GI tract,CNS.

 Incubation (3-10)d/ Afebrile (4–10 days,absent from blood) /ferible stage(blood)

 Leptospira interrogans ( causes leptospirosis / corkscrew-shaped )

\*leptospirosis-headaches, muscle pain , fever ,bleeding from the lungs , meningitis/ Can cause renal faliue ( interstistium

-renal tubulers-tubular lumen-nephritis and necrosis- hypovolemia-dehydration).

rodent vector spread it by urine /eyes and mouth and wounds are sites of entry.

Rickettsia

\*poorly with the Gram stain / grow only in the cytoplasm of eukaryotic / Intracellular Gram negative rod bacteria/

\*contain DNA, RNA, enzymes and ribosomes / binary fission/inhibited by antibiotics/animal and arthropod reservoirs

\*arthropod vectors(ticks,mites,lice,fleas) / humans are accidental hosts) / genera:( *Orientia (scrub typhus)*/ Coxiella(*C. burnetti-* Q fever ,*)/ Ehrlichia, Bartonella,rekettsia) /* *seen with Giemsa stains/* *Require growth co-factors/*not grow on artificial media / All, except Coxiella, are transmitted by arthropods / *R. rickettsii* invades the endothelial cells that line the blood vessels.

\*Rocky mountain spotted fever - R.rekettsii(filopodium focal lysis of endothelium) - tick vector(Ixodid)/ Incubation(2-6)d after it maculopapular rash / common in summer/ rash will become petechial/ death during second week due to kidney or heart failure.

\*rickettsialpox - R.akari - mite vector

\* scrub typhus - O.tsutsugamushi(budding of endothelium) – mite vector

\* Epidemic typhus(Brill-Zinsser disease) – R.prowazekii(lysis of endothelium) – louse vector – human resirvior/intense fever,rash after (7-14) which is restricted to the chest and abdomen, Diagnosis: Indirect immunofluorescent assay

\* murine endemic typhus – R.typhi – flea vector

\*other diseases are caused by C.burnetti by inhalation of aerosols

\*spread is hematogenous and lymphatic/none exit in man/kidney failure ,Enencephalitis,pneumonitis,rash)

\*bacterium escapes from the phagosome.

\*Q fever – cause by C.burnetti - Transmission: Tick (only to animals), aerosols, infected milk (to human)/human infection with contact/ Highly contagious /entry by aerosols / spreas is hematogenous / none exit /pneumonitis,endocarditis,granulomas.

proliferate in the respiratory tract/ Febrile illness/ rash is rare / Non seasonal / Antigenic variation / spore-like form allows it to survive in extracellular environment / Acute diseases / Chronic diseases(endocarditis, hepatitis, pulmonary disease, and infection of pregnant women)

\* Weil-Felix test – for [*Rickettsia*](https://en.wikipedia.org/wiki/Rickettsia) and non-motile [*Proteus*](https://en.wikipedia.org/wiki/Proteus_%28bacterium%29) /[*Rickettsia prowazekii*](https://en.wikipedia.org/wiki/Rickettsia_prowazekii), [*R. typhi*](https://en.wikipedia.org/wiki/Rickettsia_typhi) react with *P. vulgaris* OX19

R.[*Orientia*](https://en.wikipedia.org/wiki/Orientia_tsutsugamushi) , [*tsutsugamushi*](https://en.wikipedia.org/wiki/Orientia_tsutsugamushi) reacts with [*P. mirabilis*](https://en.wikipedia.org/wiki/Proteus_mirabilis)OXK / poor [sensitivity and specificity](https://en.wikipedia.org/wiki/Sensitivity_and_specificity) /

\*spotted fever in weil test reacts with OX19 and OX2 at same level