Fluroquinolones (Cipro , Levo , Moxi , Nor , O )-floxacin,and Nalidixic acid
\*man-made antibiotic / greater efficacy, a broader spectrum,better safety / tied to Clostridium difficile infection and the spread of antimicrobial resistance /unfavorable effects-antimicrobial resistance-“collateral damage”- third-generation cephalosporins

\*enter through porin channels and affects (1-DNA gyrase(topoisomerase II)-relaxation of supercoiled DNA, promoting DNA strand breakage /2-bacterial topoisomerase IV-chromosomal stabilization during cell division )/ Cross-resistance exists

\*Gram(-) hinibition of DNA gyrase is better while in Gram (+) inhibition of topoisomerase IV is better.

\*Agents with higher affinity for topoisomerase IV(like ciprofloxacin) should not be used for S. pneumoniae infections

\*Agents with higher affinity for topoisomerase II (like moxifloxacin) should not be used for P. aeruginosa infections

\*bactericidal ((AUC/MIC)–dependent killing)/ Bactericidal activity >serum is 30-fold the MIC /

1-gram-negative organisms (Escherichia coli, P. aeruginosa, Haemophilus influenzae)

2-atypical organisms (Legionellaceae, Chlamydiaceae)

3-gram-positive organisms (streptococci), and some mycobacteria (Mycobacterium tuberculosis)

\**Levofloxacin* and *moxifloxacin(respiratory fluroquinolones)-against S. pneumonia that cause (community-acquired pneumonia (CAP)*

*\*Moxifloxacin also has activity against many anaerobes* /

\*Fluoroquinolones are alternatives for patients with β-lactam allergy/not effective against syphilis and N.gonnorrhoea

\*not used for the treatment of Staphylococcus aureus or enterococcal infections/

1-First generation ( nalidixic acid)

2-Secound generation (*Ciprofloxacin* and *norfloxacin)-* *against aerobic gram-negative and atypical bacteria-intracellular penetration-for infections in which a bacterium spends part or all of its life cycle inside a host cell(chlamydia,mycoplasma,mycobacterium)*

*3-third generation(Levofloxacin)-* *increased activity against gram-positive bacteria*

*4-Fourth generation(moxifloxacin)-* *against anaerobic and gram-positive organisms*

*\*treatment of anthrax (bacillus anthractis)-ciprofloxacin and doxycycline*

*\*treatment of UTI (enterobacterspecies)-ciprofloxacin and levofloxacin*

*\*treatment of GI infections (enteric pathogens) including diarrheal illnesses-ciprofloxacin.*

*\*treatment of resistant respiratory infections (S.pneumonea and H.influenzea)-levofloxacin if unresponsive to B-lactamantibiotics /*

*Ciprofloxacin not for pneumonia .*

*\*Norfloxacin-poor oral bioavailability and a short half-life-nonsystemic infections, such as (UTIs), prostatitis, and infectious diarrhea*

*\*Ciprofloxacin-treatment of many systemic infections caused by gram-negative bacilli-against P. aeruginosa-cystic fibrosis patients/*

80% bioavailability, oral and IV /treats Traveler’s diarrhea caused by E. coli as well as typhoid fever caused by Salmonella typhi /

second-line agent in the treatment of tuberculosis / dosed twice daily orextended-release formulation once daily

\*Levofloxacin - prostatitis, skin infections, CAP, and nosocomial pneumonia /excellent activity against S. pneumoniae respiratory infections / 100% bioavailability and is dosed once daily .

\*Moxifloxacin - activity against gram-positive organisms (for example, S. pneumonia)and anaerobes/resistance to Bacteroides fragilis

poor activity against P. aeruginosa / not indicated for the treatment of UTIs .

\*resistance(chromosomal mutations )--mechanism of resistance(1-Altered target - topoisomerase IV and DNA gyrase/2- Decreased accumulation- decreased number of porin, xistnce of efflux pumps)

\* *norfloxacin* is 35% to 70% orally bioavalability / excreted renally(urine) exept moxifloxacin by liver

\* Intravenous and ophthalmic preparations of *ciprofloxacin*, *levofloxacin*, and *moxifloxacin/\** *into all tissues and body fluids*

\* with *sucralfate* *or dietary supplements containing iron or zinc(cations)* *reduce the absorption/*

*\** *Levels are high in bone, urine (except moxifloxacin) kidney, and prostatic tissue (but not prostatic fluid),* *lungs*

*\** *low* *Penetration into CSF exept Ofloxacin / \** *accumulate in* *leukocytes-* *activity against intracellular organisms*

*\** *most antibiotics, the most common adverse effects of fluoroquinolones are nausea, vomiting, and diarrhea*

*\** *patients with central nervous system (CNS) disorders, such as epilepsy, should be treated cautiously with these drugs.*

*\** adverse - *Peripheral neuropathy and glucose dysregulation (hypoglycemia)and phototoxicity(if phototoxicity > discontinuation)*

*Articular cartilage erosion (arthropathy) in immatures/* *tendinitis or tendon rupture in systemic use/* *prolong the QTc*

*\** *avoided in pregnancy and lactation and in children under 18 years of ageand arrhythmias*

*\* Ciprofloxacin* *increase serum levels of theophylline / \*Quinolones raise the serum levels of warfarin, caffeine, and cyclosporine.*

 *Urinary tract antiseptics(methenamine, nitrofurantoin, and the quinolone nalidixic acid ) /\** *concentrated in the urine*

*\*E. coli leading cause then Staphylococcus saprophyticus.*

*\*\** Methenamine *decomposes at an acidic pH in urine producing formaldehyde which is toxic to most bacteria/ \** *orally/* *Bacteria do not develop resistance to formaldehyde/* *Antacids, such as sodium bicarbonate, should be avoided./chronic suppressive therapy to reduce the frequency of UTIs /* not for catheter associated bacteriuria or catheter-associated UTI*/*not for upper UTIs (pyelonephritis)/ Urea-splitting bacteria that alkalinize the urine(proteus) are resistant*/contraindicated in patients with hepatic insufficiency because it produses ammonium ions as well /* *eliminated in the urine/*systemic toxicity does not occur because it only decoposes at urine acidic ph / gastrointestinal distress, although at higher doses, albuminuria, hematuria, and rashes may develop / contraindicated in patients with renal insufficiency / Sulfonamides not used with methamine because (crystalluria and mutual antagonism).

\*\* NItrofurantion (inhibits enzymes and damages DNA - E. coli,gram(+) not gram (-)-hemolytic anemia in G6PD diffeciency/not be used in patients with significant renal impairment or women who are 38 weeks or more pregnant.