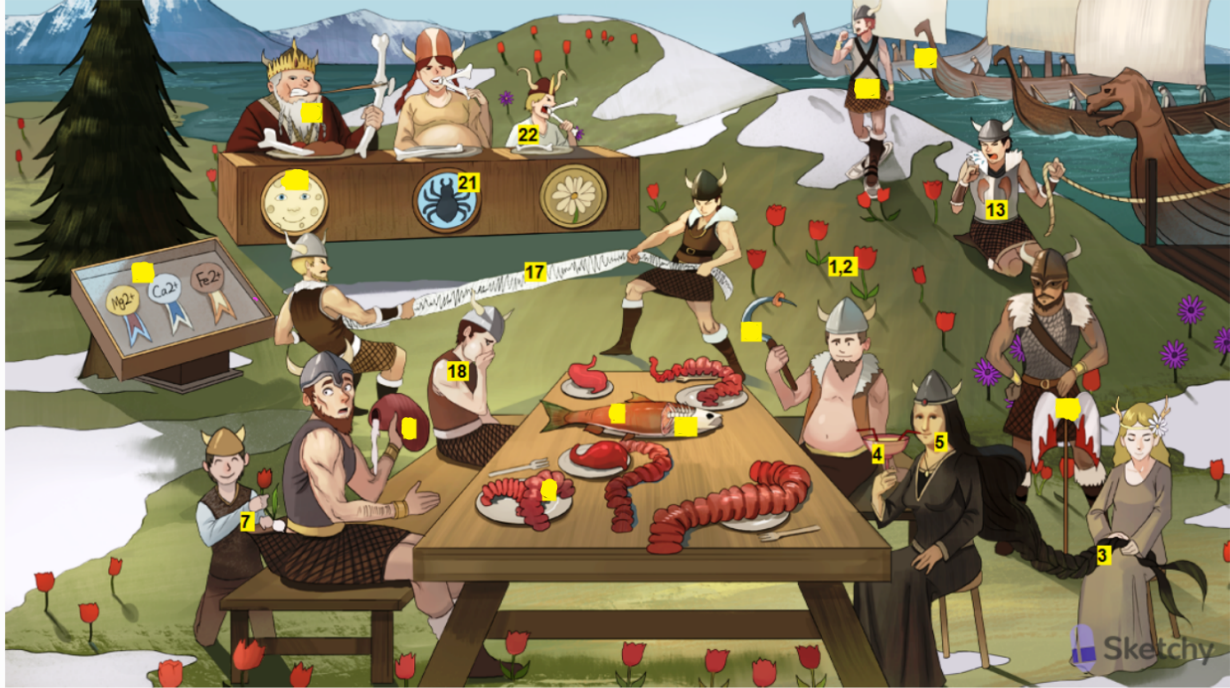


## Pharmacology of UTI

- UTI is an infection affecting part of the urinary system
- It is one of the most commonly occurring bacterial infections, especially in females of childbearing age
- Approximately 60% of females will develop a UTI during their lifetime with about one fourth having a recurrence within a year
- UTIs are classified into upper and lower UTIs
- Upper tract infection, also known as pyelonephritis, is an infection involving the kidneys whereas lower tract infections correspond to bladder infection or cystitis
  
- UTIs are designated as uncomplicated or complicated
  - A-Uncomplicated infections occur in individuals who lack structural or functional abnormalities of the urinary tract that could interfere with the normal flow of urine or voiding mechanism
  - B-Complicated UTIs are usually the result of a predisposing lesion of the urinary tract, such as a congenital abnormality or distortion of the urinary tract, a stone, indwelling catheter, prostatic hypertrophy and obstruction
  
- Most common bacteria involved in the etiology of UTI is E.coli
- Other frequently isolated organisms include Klebsiella pneumoniae, Pseudomonas aeruginosa , staphylococci...
  
- Patients with pyelonephritis may complain of:  
Fever, flank pain, frequency, nausea and vomiting
  
- Patients with cystitis may complain of:  
Burning on urination (dysuria), frequent urination, urgency, suprapubic pain, blood in the urine (hematuria) and back pain
  
- Most effective antibiotics in UTIs:
  - Trimethoprim-sulfamethoxazole (co-trimoxazole)
  - Cephalosporins
  - Quinolones and Fluoroquinolones
  - Nitrofurantoin
  - Fosfomicin...

## Fluoroquinolones: A Nordic Spring



1. Flowers: Fluoroquinolones
2. Mostly red: mainly indicated for gram negative **Broad spectrum (effective against pseudomonas)**
3. Unwinding braid: **inhibit bacterial DNA gyrase (Topoisomerase2)** Inhibitors of microbial DNA synthesis (inhibit bacterial DNA replication)
4. Red bladder cup: **treatment of complicated cervicitis** by( Ciprofloxacin & levofloxacin)
5. Mona Lisa elevating (levo) and sipping (cipro) from Bladder cup: Complicated UTI's, levofloxacin and ciprofloxacin treat UTI caused by Pseudomonas  
Mainly (particularly Ciprofloxacin & levofloxacin) used in complicated UTI's, respiratory infections, invasive external otitis, bacterial prostatitis and cervicitis, bacterial diarrhoea caused by shigella, salmonella and E. coli
7. Flower bulb down pants: **treat acute prostatitis**
13. Rusty lung chest plate: **treatment of respiratory infection**
17. Torsade's strip: risk of **prolonged QT interval (Cardiac toxicity)**
18. Puking guy: **GI Side effects N/V**
21. Tarantula: **teratogenic (carcinogens) – damage to growing cartilage & cant be given during pregnancy**
22. Child gnawing cartilage: **not recommended for children** under 10 years of age  
**interfere with cartilage development**

### Addition :

- 1-Most widely used antibiotics in 2002 but their use has been recently reduced due to toxicity, development of resistance and the introduction of safer new macrolides
- 2-synthetic & bacterocidal

#### •Quinolones are classified into:

- 1st generation  
Nalidixic acid , Pipemidic acid , Oxolinic acid
- 2nd generatipon  
Ciprofloxacin, Ofloxacin , Norfloxacin , Enoxacin , Lomefloxacin , Nadifloxacin
- 3rd generation  
Levofloxacin , Sparfloxacin , Gatifloxacin
- 4th generation  
Moxifloxacin , Prulifloxacin , Gemifloxacin

- 1st generation e.g. Nalidixic acid effective more in G+ve infections and only in UTI's (urinary tract antiseptic). Has little activity against E. coli; Proteus; Shigella, Enterobacter and klebsiella. No effect against Pseudomonas
- 2nd generation exhibit more activity against G-ve bacteria
- 3rd & 4th generations have good activity against pseudomonas and anaerobic microorganisms
- Most widely used quinolones include:  
Ciprofloxacin (2nd); levofloxacin (3rd); moxifloxacin (4th)

3-well absorbed but affected by food containing Ca<sup>++</sup> and iron

- 4- bacterial resistance [bacterial efflux pumps+Production of certain proteins especially by Gram-ve bacteria that can bind to DNA gyrase, protecting it+Mutations in DNA gyrase or topoisomerase
- 5-side effects:photosensitivity and others

## Nitrofurantoin

- Synthetic, bactericidal orally effective antibiotic
- It is effective against G+ve & G-ve bacteria Has good activity against G-ve bacteria particularly E. coli
- Highly effective in UTI's (cystitis) (known as UT antiseptic)

### • Nitrofurantoin MOA (multiple):

- 1-It is converted by bacterial reductases into many reactive intermediates leading to direct damaging effect of bacterial DNA, disruption of RNA and protein synthesis and also interfering with many metabolic processes in bacteria
- 2-Development of resistance to nitrofurantoin is rare, due to multiple sites of action (the bacteria that is sensitive to it remain sensitive forever)
- 3-Pulmonary fibrosis is a major side effect to nitrofurantoin
- 4-Nitrofurantoin is contraindicated in patients with G-6-PD deficiency

## Fosfomycin

- It is a broad-spectrum bactericidal drug
- primarily used to treat lower UTI (cystitis) and occasionally is used for prostate infections
- It disrupts cell wall synthesis by inhibiting phosphoenolpyruvate synthetase and thus interferes with the production of peptidoglycan
- Fosfomycin has a broad spectrum of activity against both gram-positive and gram-negative organisms, including many antibiotic-resistant organisms
- It is available in 3g oral powder dosage form for reconstitution
- Use of fosfomycin is commonly restricted to only a single dose because of rapid microbial resistance

• Fosfomycin is well tolerated but may lead to the following side effects:

- Metallic taste
- Stomach upset
- Dizziness
- Stuffy nose
- Back pain
- Vaginal itching or discharge