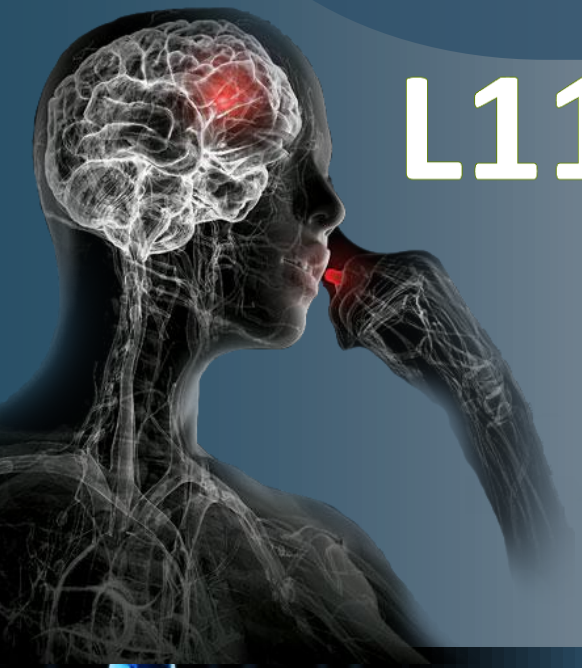
King Saud University

College of Medicine

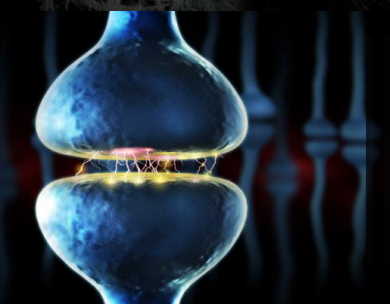
2nd Year, 1st Block

PHARMACOLOGY 433

MED 433 Teams



L11: Drugs used in meningitis

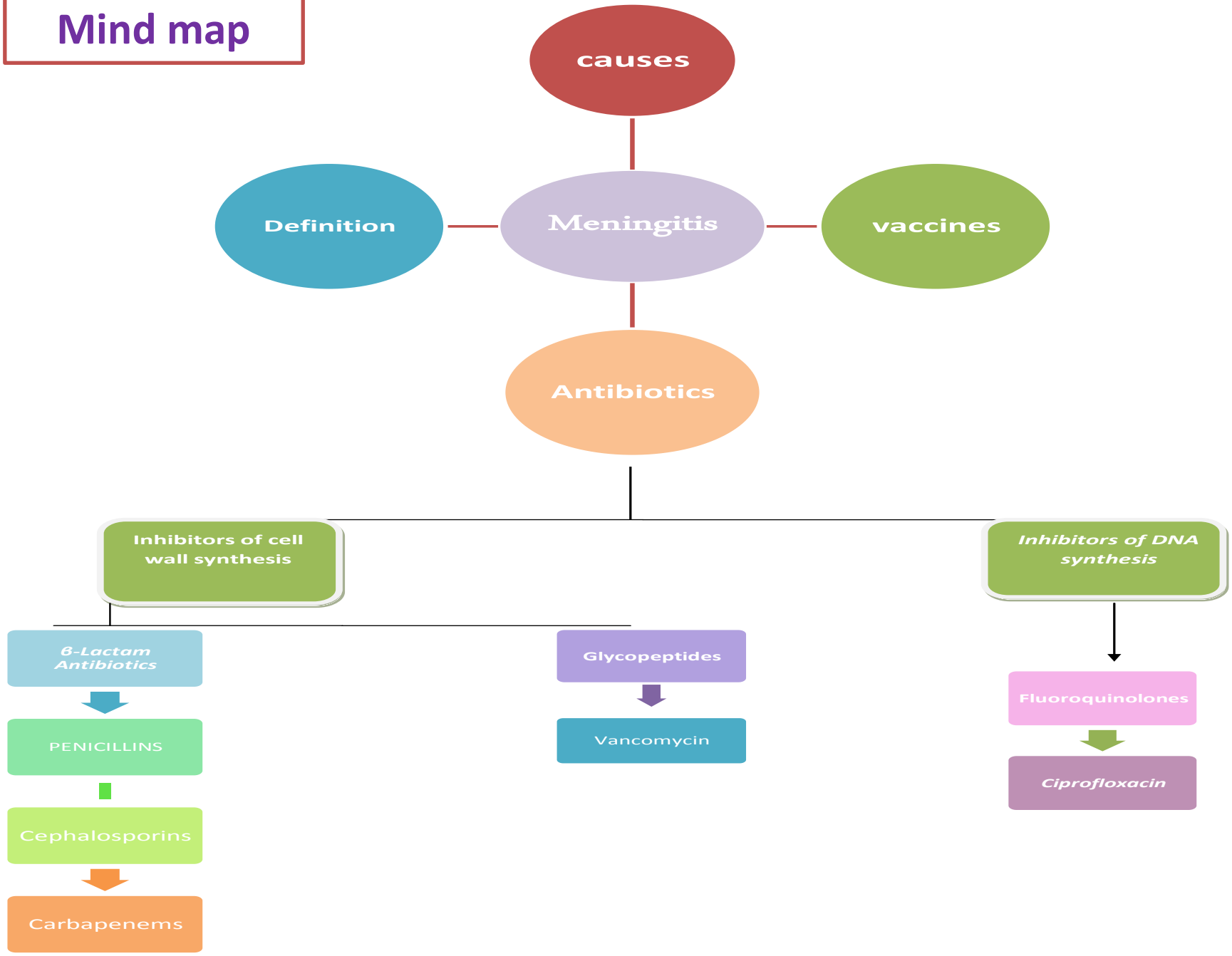


CNS Block

Objectives :-

- ✓ Specify microorganisms causing meningitis.
- ✓ Delineate the therapeutic strategy.
- ✓ Classify the relevant antibiotics used.
- ✓ Expand on the pharmacokinetic and dynamic patterns of each antibiotic and specify its indications, contraindications& adverse effects.
- ✓ List prophylactic measures taken against meningitis.

Mind map


causes
Definition
Meningitis
vaccines
Antibiotics
Inhibitors of cell wall synthesis
Inhibitors of DNA synthesis
β-Lactam Antibiotics
PENICILLINS
Cephalosporins
Carbapenems
Glycopeptides
Vancomycin
Fluoroquinolones
Ciprofloxacin

Meningitis (introduction)

* Definition: It is an inflammation of the protective membranes covering the brain and the spinal cord .

* Causes:-

- ✓ Bacterial: Is a serious, life –threating disease that is caused by an infection of bacteria, like Neisseria meningitides, Haemophilus influenzae, Streptococcus pneumoniae, Listeria monocytogenes, and Mycobacterium tuberculosis.
- ✓ Viral.
- ✓ Parasitic.
- ✓ Non-infectious (as spread of cancer to the meninges).

* Rout of transmission:

- ✓ The bacteria are carried by humans in the nose and throat and spread into the air by coughing and/ or sneezing, And they can be picked by anyone.
- ✓ The pathogens spread from the respiratory tract to the blood stream and to the nervous system and cause bacterial meningitis.

* Symptoms:

- ✓ Fever.
- ✓ Headache.
- ✓ Neck stiffness.
- ✓ Irritability to light.
- ✓ Nausea and Vometing

* Treatment principles:

- ✓ Emergence hospitalization.
- ✓ Antibiotics.
- ✓ Measures for treatment of complications.

* Empiric therapy:

- ✓ Treatment without exact diagnosis (antibiotics are given to a person before the specific microorganism causing an infection is known)
- ✓ Empiric therapy may be changed after the culture sensitivity reports are available.
- ✓ Antibiotic selected must reach the meninges in a adequate quantities.
- ✓ Regimen chosen must have potent activity against known or suspected pathogens in a particular geographical place.

A- Cell wall inhibitors (B lactam antibiotics): subdivided into

1. Penicillins.
2. Cephalosporins.
3. Carbapenems (Imipenem).

1- penicillins

Penicillins (bactericidal)	Broad spectrum	Narrow spectrum
Drugs:	Amoxicillin, and Ampicillin	Penicillin G
Mechanism of action:	Irreversibly inhibits transpeptidase enzyme that catalyze the final step in cell wall synthesis,(Inhibits the synthesis of peptidoglycan layer of bacterial cell wall).	
Pharmacokinetics:	✓ Active against **gram + & gram -** microorganism. ✓ Inactivated by β- lactamase enzyme, now a days combination with B-lactamase inhibitors are available e.g Amoxicillin + Clavulanic acid and ampicillin + salbactum, are more effective against B-lactamase producing pathogens. ✓ acid stable (effective orally). ✓ Can also be given parenterally (I.V or I.M). ✓ Amoxicillin is better absorbed from the gut and not affected by food.	✓ Destroyed by gastric acidity.(given I.V or I.M only) ✓ Inactivated by β-lactamase. ✓ Short acting (4-6 hrs).
Adverse effects:	Hypersensitivity, Diarrhea, Nephritis, and Neurotoxicity (overdoes)	

Penicillin is good for a pregnant woman

2- Cephalosporins

=> 3rd generation: Bactericidal antibiotics. (highly resistant to β- lactamase)

3rd generation	Ceftazidime	Ceftriaxone
Mechanism of action:	Inhibit the synthesis of bacterial cell wall Highly resistant to β- lactamase	
Route of administration:	given by IV infusion.	
Excretion:	Renal route	Biliary route (used in patient with renal disorders)
USES:	**1- Highly effective against Gram –ve bacilli** (used in gram –ve meningitis) 2- Anaerobic microbes.	
	especially in Pseudomonal infections	
Adverse effects:	1- Allergy 2- Thrombophlebitis. 3- Renal toxicity ((overdoes)) 4- Super-infections. ((common))	

3- Carbapenems :

e.g. Imipenem	
Mechanism of action	Bacterial cell wall inhibitors (Bactericidal)
Spectrum	Broad-spectrum (**gram +** & **gram -**)
Resistance	Resistant to most β lactamases except metallo-β lactamase
Pharmacokinetics	❑ Given I.V ❑ Because it is inactivated by the enzyme (dehydropeptidases) in renal tubules, we use an inhibitor (cilastatin) to prevent such inactivation ❑ Penetrates body tissues and fluids including C.S.F.
Adverse effect[1]	1- Nausea, vomiting and diarrhea. 2- Skin rash (at site of infusion) 3- High doses in patients with renal failure may lead to (Seizures)

1- Patients allergic to penicillins may be allergic to carbapenems as well.

B- Other cell wall synthesis inhibitors:

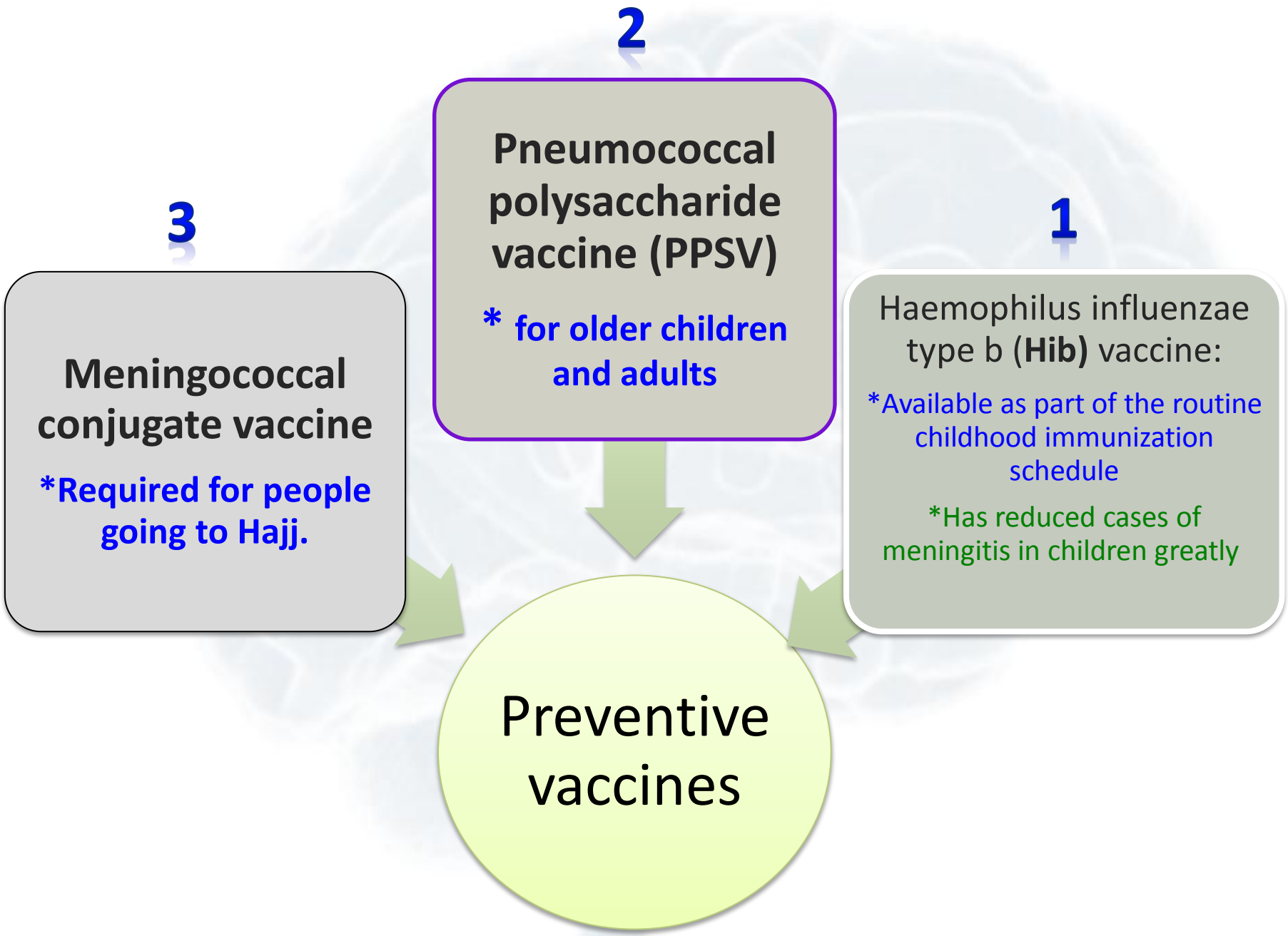
e.g. Vancomycin	
Spectrum	Narrow-spectrum (GRAM +ve ONLY), Bactericidal.
Route of administration	**Given I.V** (Used orally only to treat GIT infections caused by clostridium defficile e.g. colitis)
Adverse effect[1]	1- Thrombophlebitis 2- Ototoxicity[2] 3- Nephrotoxicity[2] 4- Red man (Red neck) syndrome: Manifested by flushing and hypotension due to histamine release caused by rapid injection (minimized if injected slowly) 5-Hypotension
Combination and uses : (reading only)	❑ **With 3rd generation cephalosporins for treatment of meningitis** caused by penicillin resistant pneumococci. ❑ **Used against Methicillin resistant S. aureus (MRSA).** ❑ **With ampicillin or ceftazidime as an initial therapy of meningitis** in infant, elderly and immunocompromised patients .

1- Vancomycin is a toxic drug, we use it **ONLY** when the infection is resistant to other safer drugs.
2- Its toxicity increased when used with **AMINOGLYCOSIDES** (both cause toxicity)

C- Fluoroquinolones:

e.g. Ciprofloxacin (Bactericidal)	
Mechanism of action	Block bacterial DNA synthesis by inhibiting bacterial Topoisomerase II (DNA gyrase)& topoisomerase IV.
Spectrum	**Effective against Gram –ve** and to a little extent against Gram +ve.
Pharmacokinetics	1- Well absorbed orally[1] 2- Penetrates body tissues and fluids including C.S.F (half-life = 3 hours) 3- Highly concentrated in bone, kidney, prostate, lung 4- Excreted through kidney & appear in breast milk
Adverse effect	❑ GIT upset. ❑ Enzyme inhibitor. ❑ CNS effect (Headache , dizziness, insomnia) ❑ Abnormal liver function tests ❑ Skin rash, Photosensitivity. ❑ Cartilage damage (Arthropathy) ❑ Tendon damage (Tendinitis)
Contraindication	1- Growing children (Less than 18 years) 2- Pregnancy 3- Lactation 4- History of epilepsy or CNS disorders.

1- Its absorption is impaired by divalent cations such as; iron, zinc or those in antacids as aluminum or magnesium.


2
Pneumococcal polysaccharide vaccine (PPSV)
* for older children and adults
3
Meningococcal conjugate vaccine
*Required for people going to Hajj.
1
Haemophilus influenzae type b (Hib) vaccine:
*Available as part of the routine childhood immunization schedule
*Has reduced cases of meningitis in children greatly
Preventive vaccines

Summary

antibiotics	Spectrum	Mechanim of action	Reaction with β- lactamase enzyme	Side effect
Penicillins	Extended Spectrum 1-Amoxicillin 2-Ampicillin Narrow Spectrum 1-Penicillin G	Inhibits bacterial cell wall synthesis	Inactivated *so use combination with B-lactamase inhibitors	Hypersensitivity Diarrhea Neurotoxicity Nephritis
Cephalosporins: Ceftazidime Ceftriaxone	-effective against Gm–ve Bacilli -Anaerobic	Inhibits bacterial cell wall synthesis	resistant	Allergy Renal toxicity Superinfections
Carbapenems: Imipenem	wide spectrum of activity	Inhibits bacterial cell wall synthesis	Resistant Except: metallo-β lactamase .	Nausea, vomiting, Diarrhea Skin rash
Vancomycin	Gm+ve bacteria	Inhibits bacterial cell wall synthesis	----------	Phlebitis Ototoxicity Nephrotoxicity Histamine release (red man)
Fluoroquinolones: Ciprofloxacin	effective against Gm–ve	Inhibits Bacterial DNA synthesis	----------	-arthropath -Tendinitis

Quiz yourself

Q1: Which one of the following is narrow spectrum penicillin?
A- penicillin G.
B- amoxicillin.
C- ampicillin.
D- B and C.

Q2: What is MOA of penicillins?
A- inhibit bacterial DNA synthases .
B- Inhibit protein synthases.
C- inhibit cell wall synthases.
D- A and B.

Q3: The the ampicillin is effective against which ONE of the following :
A- G+ve.
B- anarobes.
C- G-ve.
D- A and C.

Q4: What are the symptoms of bacterial meningitis?
A- fever.
B- neck stiffness.
C. headache.
D- all above

Q5: In case of bacterial infection with beta lactamase enzyme producing pathogens which combination do we use with amoxicillin?
A- clavulanic acid.
B- salbactam.
C- cilastatin.
D- B and C

Q6: The microbiology lab result for patient suspected to have meningitis reveals Gram –ve which was catalase and oxidase positive, what antibiotic should be described?
A- Vancomycin
B- Flouroquinolones
C- Ceftazidime

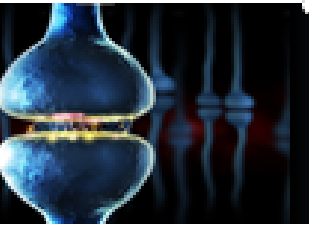
Q7:Which ONE of the following is the optimal choice to be used by Patient with glomerulonephritis:
A- Ceftazidime
B- Ceftriaxone
C- Vancomycin
D- Aminoglycosides

Q8: Which ONE of the following must be combined with cilastatin to prevent its inactivation:
A- Penicillin G
B- Ceftazidime
C- Vancomycin
D- Imipenem

Q9: Which ONE of the following is known to cause red man syndrome
A- Ciprofloxacin
B- Vancomycin
C- Imipenem
D- Ceftriaxone

Q10: During her second trimester of pregnancy, A 34years old women was diagnosed with meningitis, which ONE of the following is contraindicated
A- Ciprofloxacin
B- Penicillin G
C- Cephalosporins
D- Imipenem

Answers: 1-A 2-C 3-D 4-D 5-A 6- C 7- B 8- D 9- B 10- A



CNS Block

PHARMACOLOGY 433

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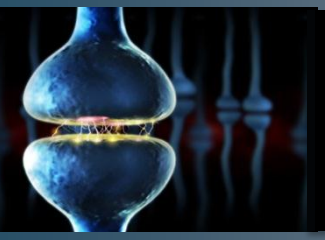
We hope that we made this lecture easier for you

Good Luck !



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