

بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ



# MOTTO AND VISION



- To impart evidence based research oriented medical education
- To provide best possible patient care
- To inculcate the values of mutual respect and ethical practice of medicine

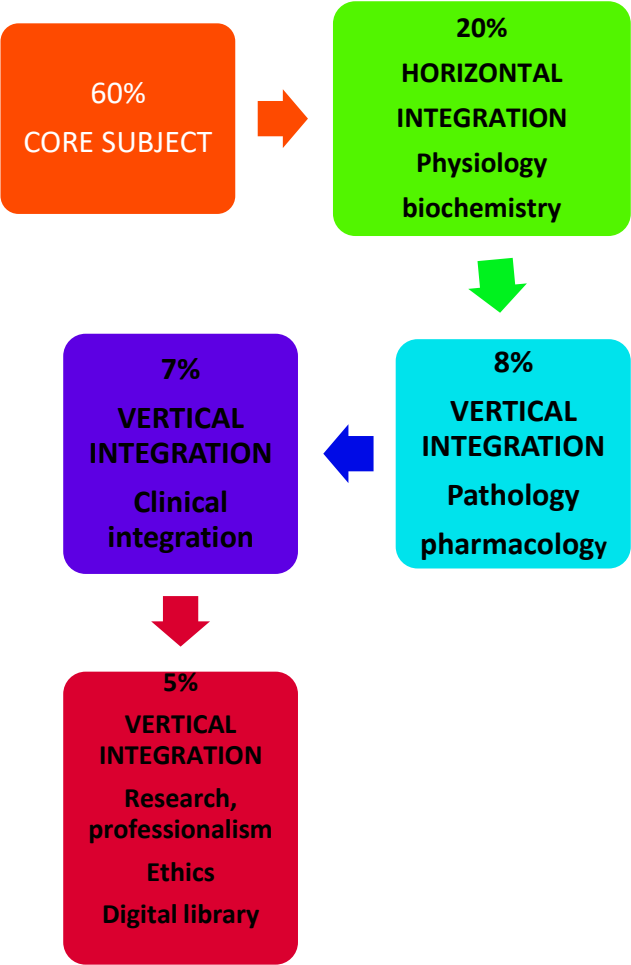
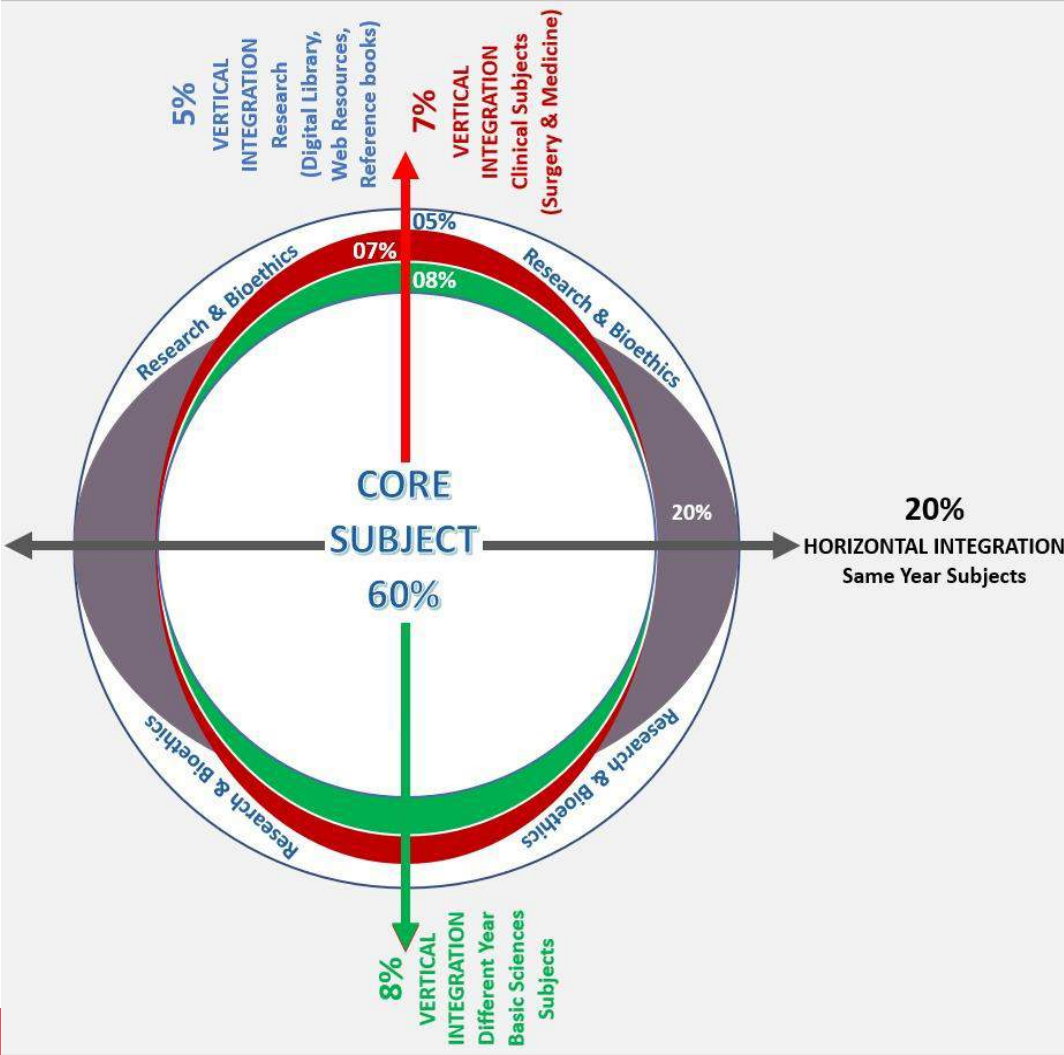


# **CARBEPENEMS AND MONOBACTAMS**





# PROFESSOR UMAR MODEL OF INTEGRATED LECTURE





# LEARNING OBJECTIVES

- To understand mechanism of action of carbapenems and monobactams
- To know clinical uses of these drugs
- To know adverse effects of these drugs



# S

- Beta lactam antibiotic
- Wide range of spectrum
- Imipenem, Meropenem, Ertapenem, Faropenem, Doripenem

# CARBEPEN



# PHARMACOKINETICS

- Parenteral route only
- Distributes very well
- Cross blood brain barrier
- Renal route of excretion





# BACTERIAL SPECTRUM

- **Gram negative aerobes**
  - Klebsiella
  - Pseudomonas
  - Enterobacteriaceae, Niesseria
- **Gram positive cocci:** Streptococcus pneumoniae
- **Anaerobes**
- **Not effective:** Enterococcus faecium, MRSA



# MECHANISM OF ACTION

Bind penicillin binding proteins



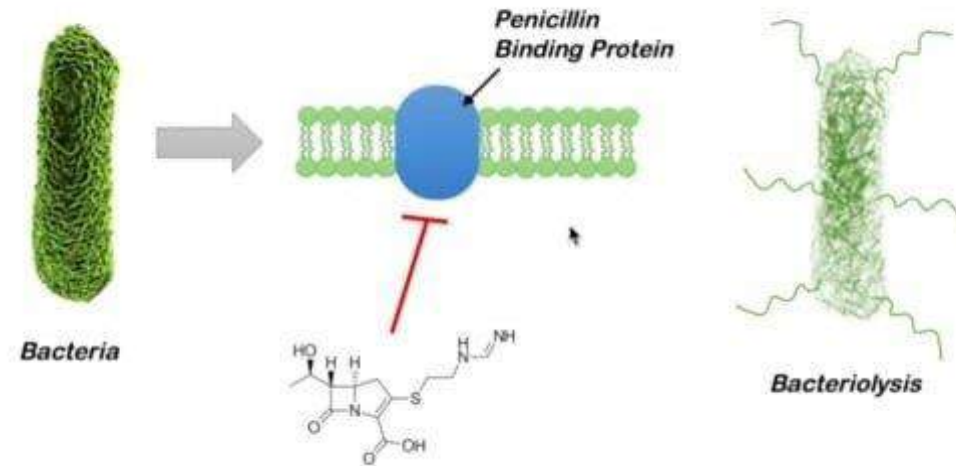
Inhibit cross linking of peptidoglycans



Cell wall deficient bacteria



Undergo lysis: **BACTERICIDAL**





# MECHANISM OF RESISTANCE

- Decreased accumulation due to decreased permeability
- Poor binding affinity for PBP
- Enzymatic inactivation



# CLINICAL USES

- Infections by resistant and multiple organisms
- UTI
- Pneumonia (including resistant streptococci)
- Serious **hospital acquired infections**
- Skin, soft tissues, bone and joint infections
- Pelvic/abdominal infections/sepsis
- Gram negative septicemia



# ADVERSE EFFECTS

- **GIT:** Diarrhea, nausea, vomiting
- **CARDIOVASCULAR:** Edema
- **NEUROLOGICAL:** Headache, Seizures
- **DERMATOLOGIC:** Rash and Pruritis
- **HEMATOLOGICAL:** Anemia, thrombocytopenia, Neutropenia





# IMIPENEM

- Prototype of carbapenems
- Extremely potent
- Extremely broad spectrum
- $T_{1/2}$  is 1 hour
- Forms metabolites toxic to renal tubules



# LIMITATION OF IMIPENEM

- Rapid hydrolysis by renal **DEHYDROPEPTIDASE**
- Combined with **CILASTATIN**, a potent inhibitor of dehydropeptidase





# M E R O P E N E M

- Similar to imipenem
- Not destroyed by renal dehydropeptidase
- Risk of seizures is less than imipenem



# ERTAPENEM

- Similar to imipenem
- Less risk of seizures
- Not useful against *pseudomonas aeruginosa*
- Longest half life (4 hours) amongst carbapenems so given once daily





# CARBEPENEMS

	IMIPENEM	MEROPENEM	ERTAPENEM
Dosage form	IV	IV	IV/IM
BBB penetration	YES	YES	NO
Seizures	Most	Less	Less
Pseudomonas cover	YES	YES	NO
Pregnancy category	C	B	B
Dosing frequency	Every 6-8 hours	Every 8 hours	Once daily



# MONOBACTAMS

- Aztreonam, tigemonam, Nocardicin
- AZTREONAM is prototype
- Mechanism of action is similar to other beta lactam antibiotics
- **BACTERICIDAL**
- No cross sensitivity to other beta lactam antibiotics



# PHARMACOKINETICS

- Oral Bioavailability is poor
- Given IV/IM
- Inhalational: for cystic fibrosis due to P. Aeurogenosa
- Achieves therapeutic concentrations in CSF in presnce of inflamed meninges
- Excreted in urine



# BACTERIAL SPECTRUM

- **AEROBIC GRAM NEGATIVE** bacteria
- No activity against gram positive bacteria or anaerobes





# CLINICAL USES

- Resistant UTIs
- P. Aeruginosa infections
- Meningitis resistant to cephalosporins
- Used in patients allergic to penicillins or cephalosporins



# ADVERSE EFFECTS

- Skin rashes
- Rise in liver transaminase



# HOW TO ACCESS DIGITAL LIBRARY

1. Go to the website of HEC National Digital Library.
2. On Home Page, click on the INSTITUTES.
3. A page will appear showing the universities from Public and Private Sector and other Institutes which have access to HEC National Digital Library HNDL.
4. Select your desired Institute.
5. A page will appear showing the resources of the institution
6. Journals and Researches will appear
7. You can find a Journal by clicking on JOURNALS AND DATABASE and enter a keyword to search for your desired journal.



## FURTHER READING

- Vázquez-Ucha JC, Arca-Suárez J, Bou G, Beceiro A. New carbapenemase inhibitors: clearing the way for the  $\beta$ -lactams. International journal of molecular sciences. 2020 Dec 6;21(23):9308.
- Li YY, Wang J, Wang R, Cai Y. Double-carbapenem therapy in the treatment of multidrug resistant Gram-negative bacterial infections: a systematic review and meta-analysis. BMC infectious diseases. 2020 Dec;20:1-3.



# END OF LECTUE ASSESSMENT

- Which of the following carbapenems is known for its broad spectrum activity against both gram positive and negative bacteria?
  - Aztreonam
  - Imipenem
  - Amoxicillin
  - Vancomycin





# END OF LECTURE ASSESSMENT

- A patient with history of severe penicillin allergy requires treatment for a gram negative bacterial infection. Which of the following drugs would be safest option for this patient?
  - Imipenem
  - Meropenem
  - Aztreonam
  - Ertapenem



# END OF LECTURE ASSESSMENT

- Which carbapenem is used in combination with cilastatin to prevent its degradation by renal dehydropeptidase?
  - Meropenem
  - Doripenem
  - Faropenem
  - Imipenem



# BIOETHICS

- Protect and promote the health of patients and the public
- Provide a good standard of practice and care –
- Keep your professional knowledge and skills up to date
- Recognize and work within the limits of your competence



**THANK YOU.**