Sept 2010
QUESTION 03

Compare and contrast Ceftriaxone and Meropenem with respect to]
- Mechanism of action and spectrum (40% of marks)
- Pharmacokinetics (30% of marks)
- Effect of critical illness on pharmacokinetics and subsequent dosing. (30% of marks)

	Ceftriaxone	Meropenem
	Is a third generation cephalosporin antibitoic	Is a carbopenum antibiotic, used in serious infections only
Spectrum	Gram positive cocci (less than 1st gen) Gram negatives EKP and ES (ecoli, klebsiella, proteus, enterobacter, serratia) No pseudomonal	v.broad spectrum, gram positive, gram negative (incl pseudomonal) and anaerobic coverage (resistant to beta lactamases and cephalsporinases)
Pharmaceutical	Parenteral formulation only in 1g vials	Parenteral formulation only Very expensive (MIMS $1000 per gram)
Pharmacodynamics		
mechanism	Beta lactam ring is incorporated in the baceterial cells walls via penicillin binding protiens, inhibiting cell wall formation	Beta lactam ring is incorporated in the baceterial cells walls via penicillin binding protiens, inhibiting cell wall formation
Pharmacokinetics		
Absorption	Well absorbed when given IM Dose is 1-2g daily or BD	IV route only Dose is 500mg-1g TDS
Distribution	small Vd 0.5L/kg Highly protien bound 85-95% Crosses the BBB, improved with inflam	small Vd 0.3 L/kg Minimally protien bound 2% Crosses BBB with plasma and CSF conc =
Metabolism	minimally hepatic	partially hepatic
Elimination	half life 8 hours enabling daily dosing excreted mostly unchanged in urine and bile	half life 1-1.5 hrs excreted in urine unchanged renal failure significantly increases half life

Changes in critical illness

Distribution

Volume of distribution - important dose loading (LD = Vd x desired concentration)
hydrophilic drugs in sepsis (increased permiability) Vd may increase
lipophilic drugs in obesity may have larger Vd
beta lactams are hydrophobic

Protien binding - albumin is generally reduced in critical illness and this is likely to affect Ceft

Metabolism

minimal change due to lack of metabolism

Elimination

both are excreted in urine mostly unchanged
renal impairment will significantly increase elimination half times (dose reduction required)
protien binding of ceftriaxone reduces CVVH clearance, meropenem is cleared via this method