Second 2008
VIVA 5

This station is mostly concerned with the pharmacology of drugs acting on the GI tract. What is a prokinetic? This viva explored the candidates' knowledge in relation to the following points Prokinetics, examples of prokinetics, mechanism of action, general pharmacology of metoclopramide GIT secretions Laxatives, mechanism of action of lactulose Octreotide, mechanism of action, general pharmacology, indications for use

"Describe the physiology of gut motility"

dependent on the enteric nervous system, autonomic nervous system and circulating hormones
ENS is the most important
controls the migrating motor complex which takes about 90 mins
Four phases, phase II involves release of motilin
inhibition is via NO and excitation via ACh

"What is a prokinetic and can you give some examples with their mechanism of action"

are drugs which selectively stimulate gut motility function (enhancing coordinated function)

Metoclopramide	is mediated by peripheral antagonism of D2 receptors, selective stimulation of muscarinic receptors, and 5HT4 agonism
Domperidone	D2 agonism
Erythromycin	acts via agonism of motilin
Cisapride	is a SSRI which acts as a prokinetic by activation of 5-HT4 receptors

"Describe the pharmacology of Metoclopramide"

is an anti emetic and prokinetic
is available in oral and injectable forms
mechanism of action is primarily through the antagonism of dopamine receptors, (serotonin also)
side effects include extrapyramidal effects, prolactinaemia, glactorrhoea, acute HTN in phaechromo
rapid oral absorption, variable bioavailability due to differing first pass metab - is up to 95%
moderate Vd 3-5 L/kg, low protien binding
50% liver metabolism by glucuronidation, sulphation, half life 2-6 hours
excretion in the urine, 50% unchanged

"Classify the laxative medications"

Classified according to their mechanism of action
Bulk forming laxatives - non digestable, hydrophilic colloids (metamucil)
Stool softeners - lubricate and allow water to penetrate stool - docusate and glycerine
Osmotic laxatives - draw water into large bowel - lactulose is the most commonly used
Stimulant laxatives - poorly understood mechanisms - Senna (overuse may lead to melanosis coli
Others - chloride channel activators, 5 HT4 agonists, opioid receptor agonists

"Discuss the pharmacology of lactulose"

is a synthetic disaccharide of galactose and fructose
its has osmotic actions in the bowel
reduces ammonia absorption in the gut by causing ionisation NH3 to NH4 and aid with excretion
uses are for constipation and hepatic encephalopathy
relatively safe, concerns in bowel surg due to H2 production, electrolyte imbalances chronically
minimal absorption, remains in GIT
metabolised in the bowel by bacteria to short chain fatty acids, excreted in faeces

"Discuss the pharmacology of octreotide"

is a synthetic analogue of somatastatin
indications are for acromegaly, treatment of gastrointestinal tumours, offlabel oesophageal varacies
action: inhibits serotonin, gastrin, VIP, insulin, glucagon, motilin, secretin release and reduces sphlanic BF
side effects gallstones with chronic use and glucose homeostasis disruption
given parenteraly IV, SC or IM
small volume of distribution
metabolised 2/3 hepatically, half life 2 hours
excretion in urine 1/3 unchanged

Christopher Andersen 2012