

CSB601 – Notes

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Week 2 - Pharmacokinetics

Pharmacokinetics

- Pharmacokinetics – the effect the body has on drugs – how does it get into the body, does the body change it
- Pharmacodynamics – effects of the drug on the body, what it does etc
- ADME
 - Absorption
 - Distribution
 - Metabolism
 - Excretion
- C_{max} = maximum concentration of the drug in the body – used to determine therapeutic benefits
- Half-life ($T_{1/2}$) – time taken to remove half of the drug from the body
- Area under the curve represents total exposure to the drug

Absorption

- Via gut administration – V_{max} low, T_{max} high
- Arterial – greater C_{max} , smaller T_{max}
 - Due to a more direct administration, faster and shorter reaction
- Inhalation – fastest absorption
- Total exposure remains same

Distribution

- Compartments
 - Blood plasma
 - Extracellular fluid
 - Intracellular fluid
 - Fat
 - Other – CSF, Peritoneum, Synovial fluid
- K_c – equilibrium constant – dependant on permeability of barriers, ph of compartments and binding capacity
- V_D – volume of distribution = total amount of drug in the body / concentration of drug in plasma

Metabolism

- Cytochrome – metabolises drugs in the liver via
 - Oxidation
 - Hydrolysis
 - Hydroxylation
- Phase 1 metabolism – hydroxylation via a cytochrome enzyme genotype
- Phase 2 metabolism
- Prodrug – molecule or drug must be metabolised to be useful

Excretion

- Hepatic biliary system – excreted into bile → faeces
- Kidneys – most common

- Clearance of drug = $C_u \times V_u / C_p$
 - C_u concentration in urine
 - V_u = volume of urine produced
 - C_p = concentration in plasma
- Rate of excretion is dependent on the rate of cytochrome metabolism eg fully saturated

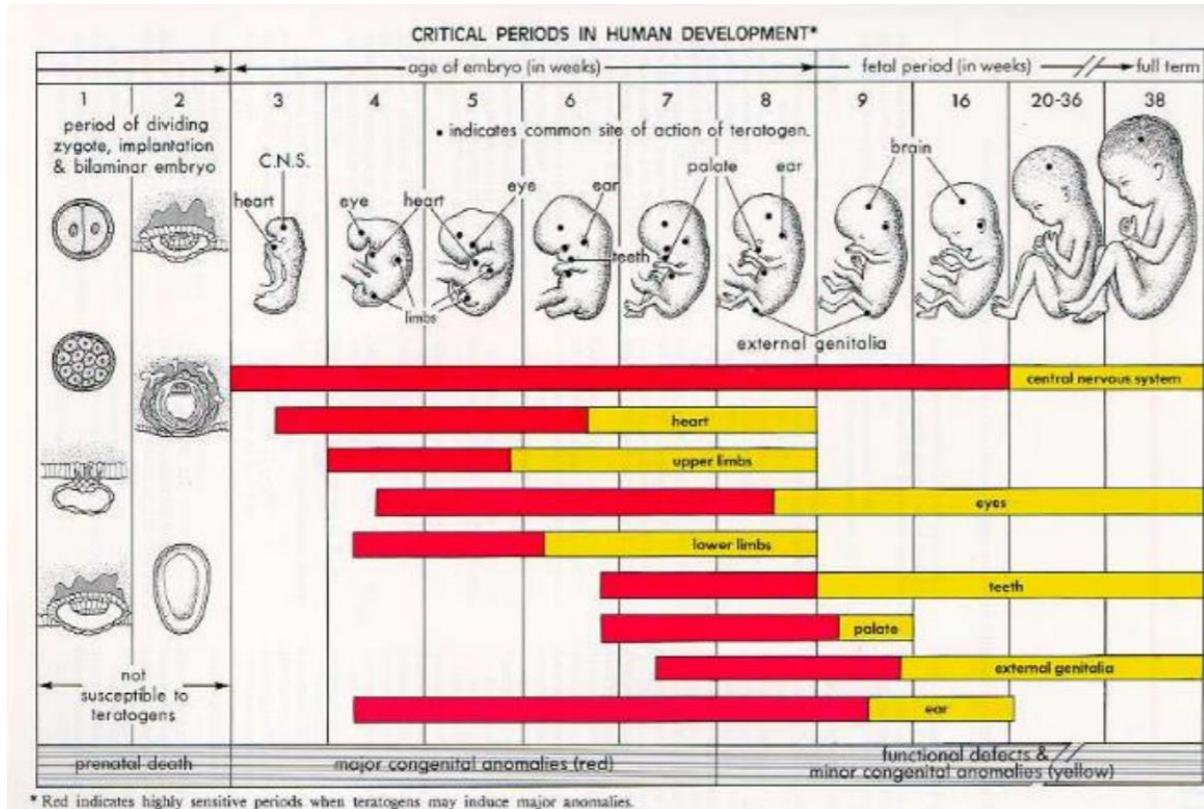
Lecture

- Routes of administration
 - Eye
 - Ear
 - Oral
 - Intranasal
 - Injection (IV,IM,SC,C)
 - Pulmonary (inhalation)
 - Rectal
 - Vaginal (what?)
 - Transdermal
- Pharmacokinetics: administration → absorption → distribution → metabolism → excretion
- Laboratory tests
 - An abnormal test only specifies the probability of a pathological condition
 - Several results required for comparison
 - Abnormalities are suspect

Post Workshop Work

- [Prescribing competencies framework](#) – competencies required for [QUM frameworks](#) (click)
 - Assessment
 - Treatment options
 - Work with patient to develop and implement plan
 - Coordination (with other disciplines)
 - Monitor and review
- Special populations
 - Pregnancy – AMH still good, lactmed for lactation
 - A drug is required to improve baseline congenital risk (2-5%) to be rated safe
 - Physiological changes preconception and antenatal care
 - Pathological changes
 - [Emesis](#) of pregnancy
 - Gestational diabetes
 - Thyroid disease
 - Induced hypertension/[pre-eclampsia](#), after 20 wks
 - 1st- methyldopa, labetalol, oxprenolol
 - Ace and ARB contraindicated in 2/3 trimester
 - [Thrombophlebitis](#) and thromboembolism
 - Infection due to weakened immune system (parasitic)
 - Complicating co-morbidities
 - Asthma
 - Diabetes mellitus

- Depression
 - Higher dose required during pregnancy due to protein binding
 - 1st tricyclic antidepressants
- epilepsy



- drug safety
 - timing of dose, size of dose, risk/benefit to both mother and foetus
 - teratogen – drug causing embryotic malformation
- Categories
 - A – large sample and no increased malformation
 - B1 – limited sample and no increase of malformation, negative animal studies
 - B2- limited sample and no increase of malformation, insufficient animal studies
 - B3 - limited sample and no increase of malformation, positive animal study
 - C – known to cause ill effects but no malformation
 - D – increased malformation or damage
 - X – high risk of damage
- Tips
 - Avoid new medicines, preconception folic acid, no fun drugs
- Geriatric – AMH and AMH grey guidelines are good
 - Polypharmacy issues
 - Increased risk of drug reactions ([see wk1](#))
 - Many drug induced side effects

- 30% geriatric hospitalisation due to drug confusion
- Elderly – over 65 or 50 for abos
- Frail elderly -old with substantial coexisting issues
- Limited trials of over 80 patients
- Renal impairment, monitor if using this route
- Increases CNS sensitivity to benzodiazepines and opioids
- Reduced effects on compensatory mechanisms eg using diuretics
- Increased falls due to drugs

Avoid	
amitriptyline	imipramine
amiodarone	indomethacin
Antihistamines	methyldopa
Benzodiazepines	NSAIDs
dextropropoxyphene	nitrofurantoin
doxepin	oxybutynin
fluoxetine	

- Paediatric
- Renal impaired
 - Function can be reduced in acute illness
 - MI
 - UTI
 - Pre-surgery fluid restriction
- Hepatic impaired
 - Repeated assessment required with psychotropic drugs
- Pharmacogenomic issues