



Southern African HIV Clinicians Society

3rd Biennial Conference

13 - 16 April 2016
Sandton Convention Centre
Johannesburg

**Our Issues, Our Drugs,
Our Patients**

www.sahivsoc.org
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WOMEN VS Drugs

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Pharmacological Concepts

- **Pharmacokinetics**
(P/K): what the body does to a drug

- ✓ Absorption
- ✓ Distribution
- ✓ Metabolism
- ✓ excretion

- **Pharmacodynamics**
(P/D): what the drug does to the body

- ✓ Due to competition at receptor sites OR activity of more than one drug on the same physiological system
- ✓ Effect may be antagonistic (d4T-AZT), synergistic, additive (ddl – d4T), shared toxicity (ganciclovir and AZT)



Drug Interactions

- Occur when either the P/K or P/D effects of one drug is altered by administration of a concomitant drug or other substance (such as food)
- Are a source of variability in drug response
- These are graded responses that are dependent on the concentration of the interacting substance and on dose and time

Drug-Drug Interactions

- P/K interactions are more common and more difficult to predict
 - drug metabolism is complex!
- Clinically significant drug interactions – are generally those that produce at least a **30% change** in P/K parameters

Pharmacokinetic Variability

- Key Principle: the same dose does not produce the same concentration in all patients because of interpatient differences in P/K variables
- Factors that can exaggerate P/K variability
 - ✓ Drug-food interactions
 - ✓ Drug-drug interactions
 - ✓ Drug-disease interactions (altered GI, renal and hepatic functions)
 - ✓ Sex differences in P/K
 - ✓ Pregnancy
 - ✓ Genetic differences in P/K

Cytochrome P450 (CYP) Enzyme System

- CYP 450 is mainly responsible for drug metabolism
 - expressed in the liver and in enterocytes of small intestine
 - CYP1, CYP2 and CYP3 particularly important in human drug metabolism
 - The above further divided into individual isoenzymes (eg: CYP3A4)
 - A drug metabolised by the P450 system will be a substrate of one or more isoenzymes. A drug may also act as an inhibitor or inducer of these isoenzymes

Cytochrome P450 (CYP) Enzyme System

Substrate	Substance metabolised by enzyme
Inhibitor	<p>Inhibits metabolism of substrate by enzyme. Due to direct competition, typically involves a single or few CYP isoenzymes Inhibition tends to occur quickly, this can be used therapeutically Inhibition effects disappear when the inhibiting drug is metabolised</p>
Inducer	<p>Due to upregulation of many CYP genes, resulting in an increase in the numbers of many CYP isoenzymes. In general maximal effect is apparent within 14 days and disappears within 14 days</p>
Properties of all 3	Eg: EFV

Drug-Drug Interactions



Efficacy and safety can potentially be compromised by 'Drug-Drug Interactions'

Why are drug interactions so relevant in HIV medicine?

- Polypharmacy
- NNRTIs and PIs big culprits
 - Inhibition and/or induction of CYP450
 - Inhibition of P-glycoprotein (key drug efflux pump)
 - Inhibition=increased concentration
 - Induction=sub-therapeutic drug concentration



Drug-Drug Interactions

- Some interactions are useful
 - Ritonavir 'PK Boosting' of PIs
- Some are so marked that co-administration is contra-indicated, usually
 - Enzyme induction/inhibition by ARV
 - Enzyme induction/inhibition by co-administered drug
- Some can be managed with dose adjustments
 - Maraviroc
 - Interactions impacting PIs and NNRTIs – statins, methadone, warfarin



Birth to one year: Baby Chen



- HIV PEP
- Anti-infectives
- Paracetamol
- Colic drops
- Traditional medication
- Immunisations

1 to 12 years: Little Nandipha



- Immunisations
- Anti-infectives
- Psychiatric drugs (eg: methylphenidate)
- Chronic medication

13 to 24 years: Tempestuous Adya



- Anti-infectives
- Recreational drugs
 - Tobacco
 - Alcohol
- Contraceptives
- Psychiatric drugs
- Chronic medication

25 to 30 years: Beautiful Reflexive



- Anti-infectives
- Traditional medication
- Multi-vitamins
- Drugs to increase/decrease lactation
- Psychiatric drugs
- Drugs specific to pregnant women
 - HPT drugs
 - Anaesthetic drugs
 - Analgesia

30 to 45 years: Sassy Celia



- Anti-infectives
- Contraceptives
- Chronic medication
- Weight loss drugs
- Homeopathic and other non-western medications
 - Beating fatigue/ stress etc
- Fertility boosting drugs and those associated with fertility treatment

45 TO 65 YEARS: CLASSY CLARE



- Anti-infectives
- Chronic diseases
- HRT
 - Including homeopathic meds for HRT
- ART
- Oncology drugs
 - Including analgesia/anti-emetics

65+ years: Angry Agatha

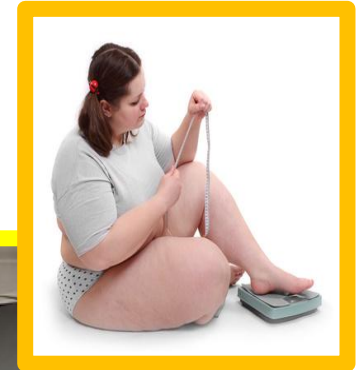
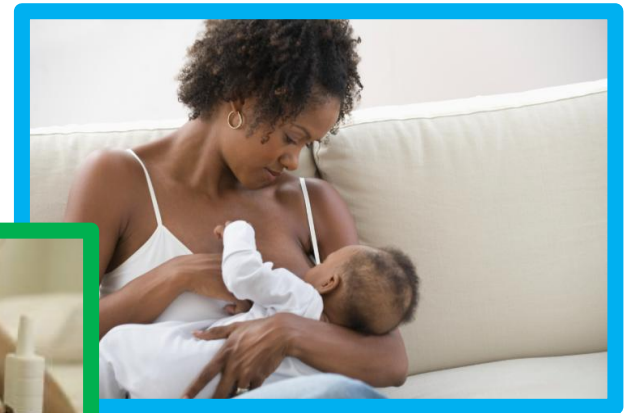


- Chronic diseases
- Medication associated with illness
 - Anti-infectives
 - Anaesthetic
 - Fractured bones
 - Dye's for radiological studies

65+ years: Blissfully-unaware Beatrice



- Osteoporosis
- Vitamins (eg: calcium)
- Psychiatric drugs
 - Dementia



References and acknowledgements

- Handbook of HIV Medicine, 2nd ed. Wilson D, Cotton M et al. 2008. Oxford University Press Southern Africa, Cape Town.
- South African Medicines Formulary, 8th ed. Division of Clinical Pharmacology, Faculty of Health Sciences, University of Cape Town. 2008. Health and Medical Publishing Group, Claremont.
- Dr Pappie Majuba, Chief Medical Officer, Right to Care



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