

- Therapeutic drug monitoring
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- Objectives
- Review the therapeutic monitoring of drugs with low therapeutic indices.
- Indications of Therapeutic drug monitoring.
- Clinical significance of therapeutic drug monitoring.
- Give example of drugs that needs therapeutic drug monitoring.

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Definition of TDM

- Measurement of drug conc. at different intervals in body fluids & tissues
- Maintain relatively constant conc. of medication in bloodstream
- Commonly measurement is in biological matrix of prescribed xenobiotic
- But it may also be of an endogenous compound prescribed as replacement therapy

- **Why TDM ?**

- Major use of measured conc. of drug
 - Individualization of dosage
 - Maintaining plasma conc. within target range

- **Principle**

- ❖ P_D factors:-

- ❖ Max. effect attained in target tissue

❖ Sensitivity of tissue to drug

❖ P_K factors:-

❖ Absorption

❖ V_d

❖ Clearance

Factors determining conc. of drug in plasma & biological fluids:

- **Major sources of pharmacokinetic variability**

- Compliance
- Age
- Physiology
- Disease states
- Drug interactions

- Environmental influences on drug metabolism
- Genetic polymorphisms of drug metabolism
- **Aims of TDM**
- Therapeutic response
- Correlation between drug conc. & therapeutic effects
- Dosage regimen to produce therapeutic effects
- Investigation of therapeutic failure

- **Aims of TDM**
- To monitor ADRs
- Prevention of toxicity
- Diagnosis of poisoning

- Individualization of drug therapy in renal/hepatic disease

- **Situations where TDM is useful**

- ✓ Drugs with narrow therapeutic index

- Digoxin
- Lithium
- TADs
- Antiepileptics
- Antiarrhythmics

- **Situations where TDM is useful**

- ✓ Potentially toxic drugs in the presence of disease

- Aminoglycosides in presence of CRF
- ✓ Drugs where therapeutic effect is difficult to measure
 - TAD
 - Anticonvulsants

- **Situations where TDM is useful**

- ✓ Therapeutic failure- to check patient's compliance
 - ATT
 - Antibiotics
- ✓ Unexpected toxicity with drugs following zero order kinetics
 - Phenytoin

- **Situations where TDM is useful**

- ✓ Toxicity difficult to distinguish from underlying disease
 - Penicillin in pyogenic meningitis

- **Situations where TDM is not useful**

- Drugs whose response easy to measure
 - Antihypertensives
 - Diuretics
 - Anticoagulants
- Drug action due to active metabolite or exists in ‘Prodrug’ form

- **Situations where TDM is not useful**

- Drugs with delayed effects
 - BM depression with anticancer drugs
- ‘Hit & Run’ drugs
 - Aspirin
 - MAO inhibitors
 - Reserpine
 - Omeprazole

- **Situations where TDM is not useful**

- Drugs with irreversible action
 - OPCs
 - Anticholinesterases
- Inflammatory states
 - Basic drugs bind to acute phase proteins

- **Drugs commonly monitored**
- **Disadvantage of TDM**
- Measures both bound & free drug concentration
- Rise in bound form affect results
- Free drug conc. ideal to measure
- **Conclusion**
- Guide to
 - ✓ Efficacy
 - ✓ Avoid toxicity
 - ✓ Compliance
 - ✓ Individualization of dosage

