

# THERAPEUTIC DRUG MONITORING



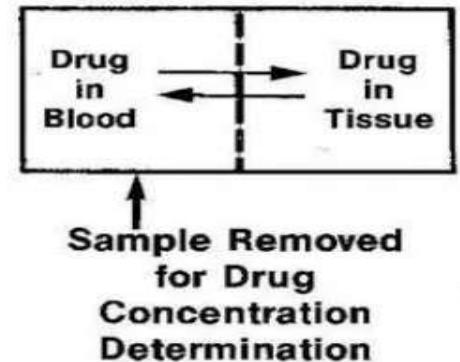
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# What is therapeutic drug monitoring

- Therapeutic Drug Monitoring is measurement of the plasma concentration level of a drug and the coordination of this serum level with a serum therapeutic range.



# Why therapeutic drug monitoring

- Therapeutic drug monitoring can guide the clinician to provide effective and safe drug therapy in the individual patient using serum drug concentration .

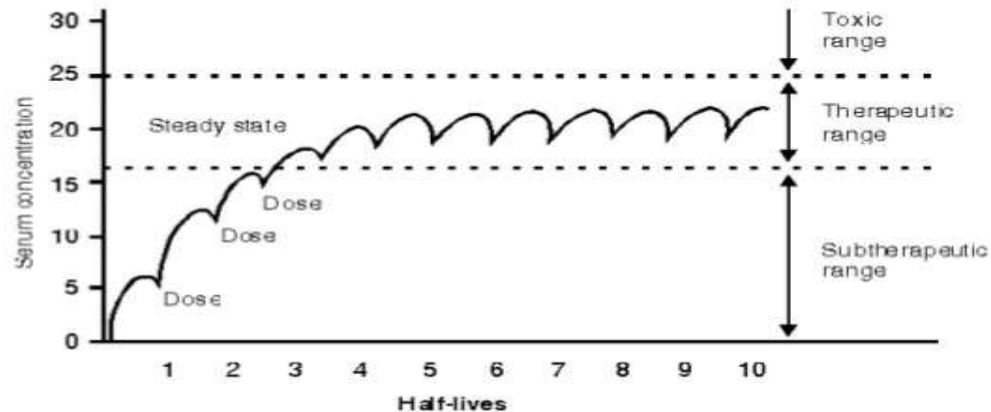


# Why should drug level be monitored ?

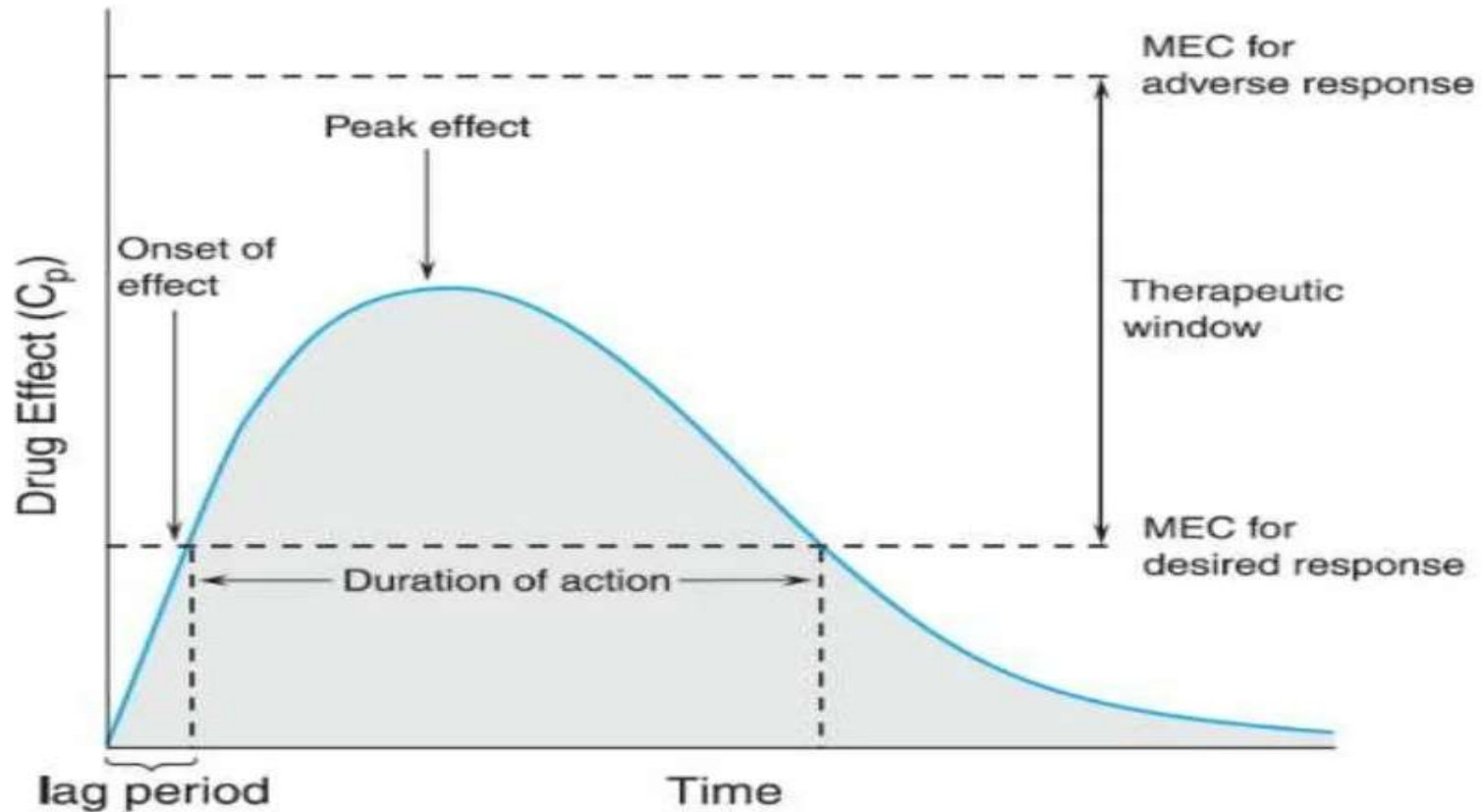
- Certain drugs have a narrow therapeutic range  
In concentrations above the upper limit of the range, the drug can be toxic
- In concentrations below the lower limit of the range, the drug can be ineffective. Not all patients have the same response at similar doses

# Therapeutic range/ therapeutic window

- The therapeutic range/ therapeutic window is the concentration range of drug in plasma where the drug has been shown to be efficacious without causing toxic effects in most people.

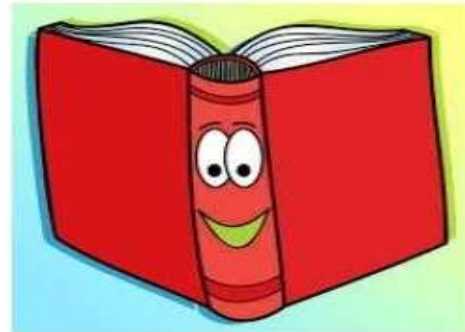


# Therapeutic window



# Where to find information regarding therapeutic range

- Recommended therapeutic ranges can generally be found in the product inserts for drugs that require monitoring.
- They are also available in books such as the Physicians Desk Reference, and articles in the primary medical journals.



# Digoxin

- Plasma concentration –response relationship
  - 0.5 $\mu\text{cg/L}$ : No therapeutic effect
  - 0.7  $\mu\text{cg/L}$ : some  $\uparrow$  in force of contraction of heart
  - **0.8- 2  $\mu\text{cg/L}$ : Optimum therapeutic range**
  - 2 -2.5  $\mu\text{cg/L}$ :  $\uparrow$  risk of toxicity although tolerated in some patients
  - 2.5  $\mu\text{cg/L}$ : Gastrointestinal, cardiovascular and CNS toxicity





# Theophylline

- Plasma concentration response relationship
  - 5mg/L: No bronchodilation
  - 5-10 mg/L: Some bronchodilation and possible anti-inflammatory action
  - **10-20 mg/L: optimum bronchodilation, minimum side effects**
  - 20-30 mg/L: increased incidence of nausea, vomiting and cardiac arrhythmias
  - 30 mg/L: cardiac arrhythmias & Seizures



# Lithium

- Plasma concentration response relationship
  - 0.4mmol/L: Little therapeutic effect
  - 0.4 to 1 mmol/L: Optimum range for prophylaxis of mania
  - **0.8 to 1.2 mmol/L: Optimum range for acute mania**
  - 1.2 to 1.5 mmol/L: Causes possible renal impairment
  - 1.5 to 3 mmol/L: Renal impairment, weakness, drowsiness, thirst and diarrhoea
  - 3 to 5 mmol/L: Confusion, spasticity, convulsions, coma and death



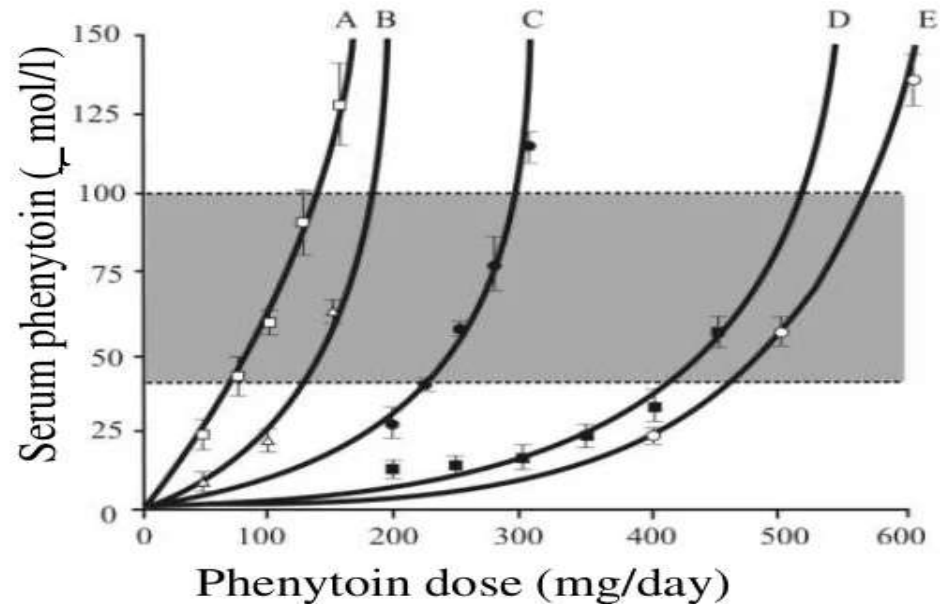
# Phenytoin

- 0.5 mg/L: No therapeutic effect
- 5 to 10 mg/L: Some anti-convulsant action
- **10 to 20 mg/L: optimum concentration for anticonvulsant effect**
- 20-30 mg/L: Nystagmus, blurred vision
- 30 mg/L: Ataxia, drowsiness, coma



# What are indications of TDM

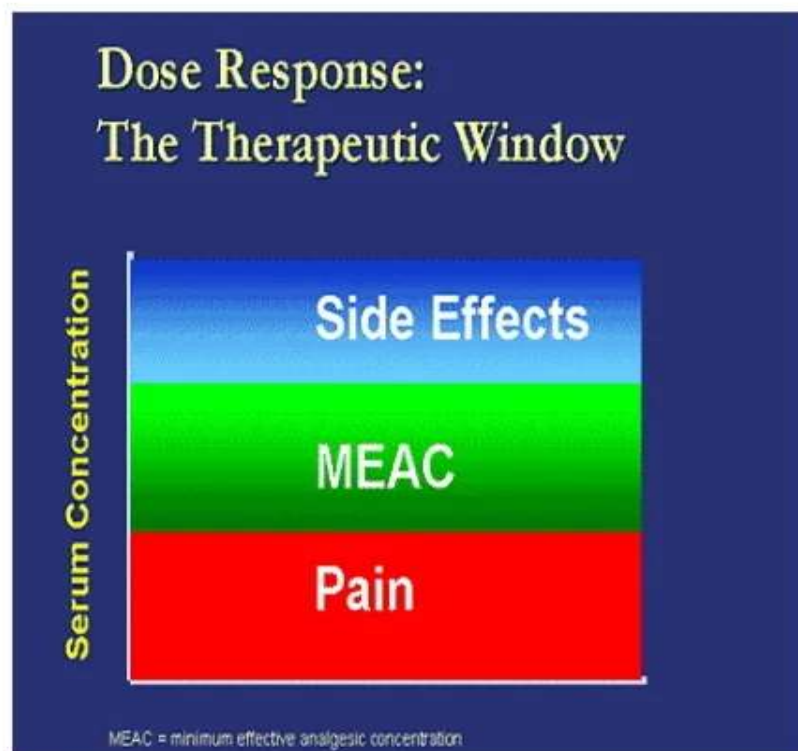
1. Drugs for which relationship between dose and plasma concentration is unpredictable, e.g Phenytoin



(from A. Richens and A. Dunlop, Lancet ii:247, 1975)

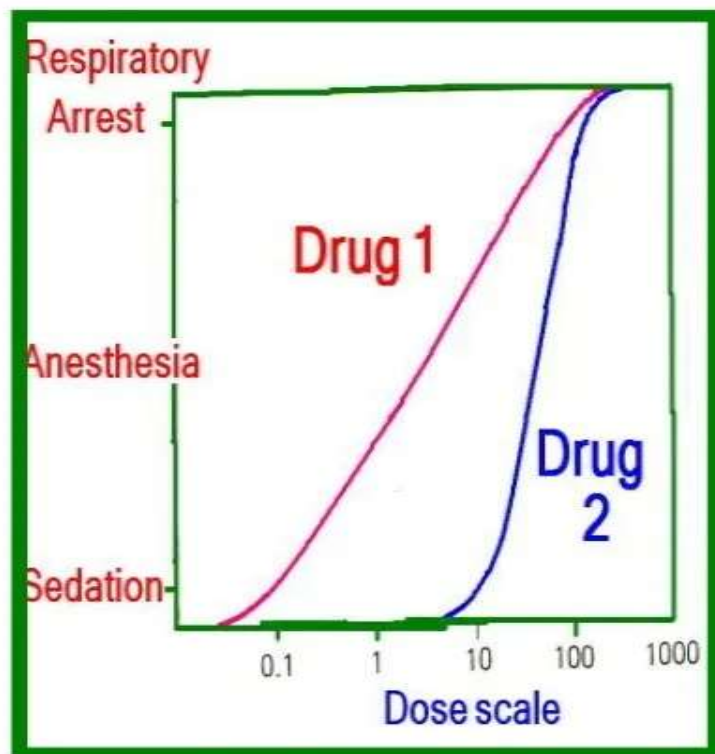
# Indications

2. Drugs with a **narrow therapeutic window**:- measurement of plasma concentrations of such drugs will allow dosage alterations to be made in order to produce **optimal therapeutic** effect or to avoid **toxic effects**.



# Indications

3. Drugs with steep dose response curve for which a small increase in dose can result in a marked increase in desired or undesired response e.g. theophylline.



# Indications

4. To evaluate compliance of patient
5. Drugs for which there is difficulty in measuring or interpreting the clinical evidence of therapeutic or toxic effects:-  
Nausea & vomiting occur in both **digitalis toxicity** & **congestive heart failure**.
6. For diagnosis of suspected toxicity & Determining drug abuse

# Indications

7. Renal disease: Alter the relationship between dose & the plasma concentration. Important in case of digoxin, lithium & aminoglycoside antibiotics.
8. When another drug alter the relationship between dose & plasma concentration e.g. plasma concentration of lithium is increased by thiazide.



# Drugs not suitable for TDM

- Drugs that are used for treating diseases of which their clinical end points can easily be monitored, e.g., BP, HR, cardiac rhythm, blood sugar, blood cholesterol and triglycerides, urine volume, body temperature, pain, headache, etc.
- Drugs whose serum concentrations do not correlate with therapeutic or toxic effects.
- Drugs with less complicated pharmacokinetics.
- Drugs having wide therapeutic index
- Hit and run drugs: omeprazole, MAO inhibitors

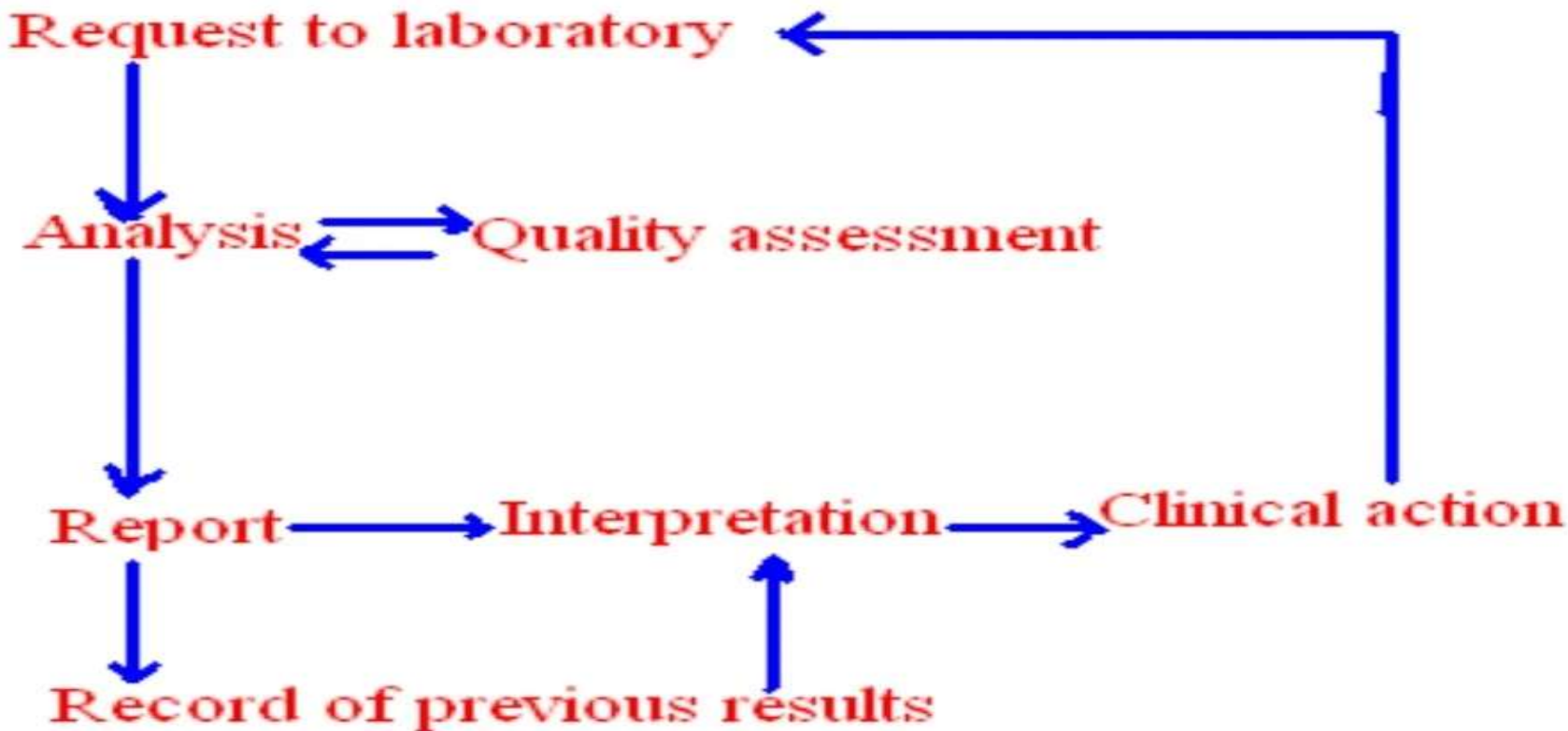
# Clinical significance of TDM

1. Maximizes efficacy
2. Avoids toxicity
3. Identifies therapeutic failure
  - Non compliance, subtherapeutic dose
4. Facilitates adjustment of dosage
  - New dose = Old dose X Desired  $C_{ss}$ /Old  $C_{ss}$
5. Facilitates the therapeutic effect of drug by achieving target drug concentration
6. Identify poisoning, drug toxicity and drug abuse

# Examples of drugs requiring TDM

- Digoxin: 0.8 -2  $\mu\text{cg/L}$
- Theophylline: 10-20 mg/L
- Gentamicin: 2-12 mg/L
- Lithium: 0.8-1.2 mmol/L
- Phenytoin: 10-20 mg/L
- Carbamazepine: 4-12 mg/L
- Ciclosporin: 100-200 ng/ml
- Vancomycin
- Procainamide

■ The management of therapy using plasma concentration



# REQUEST FORM OF TDM

Patient Name.....  
Date..... HN.....  
Age..... Sex.....  
Wt..... Ht.....  
Ward..... Ordered  
by..... Phone No.....

**DRUG LEVEL  
REQUESTED.....**

**REASON FOR REQUEST :**

- Suspected toxicity
- Compliance
- Therapeutic confirmation
- Absence of therapeutic response

Please indicate when level is needed :  
within h                      within - h                      stat  
others.....

**TIME AND DATE OF LAST DOSE :**

Date..... Route : IV, IM, SC, PO, Others.....  
Time..... Dose.....  
Freq.....

**THIS DRUG LEVEL IS FOR :**

Trough or predose level                      **SAMPLING TIME :**  
Date.....  
Time.....

Peak level                      Date.....

# Can drug concentration in other fluids of body be measured

- Yes
  - Urine: benzodiazepines
  - Sweat: cocaine & heroin
  - Saliva: marijuana, cocaine, alcohol
  - Breath: alcohol



# Summary

- TDM is monitoring of plasma concentration of drug for individualization of dose in patients
- Mainly indicated for drugs having narrow therapeutic index, or to check compliance and titration of dose
- Most common drugs to undergo TDM are anticonvulsants, lithium, digoxin, gentamicin

**THANK YOU**