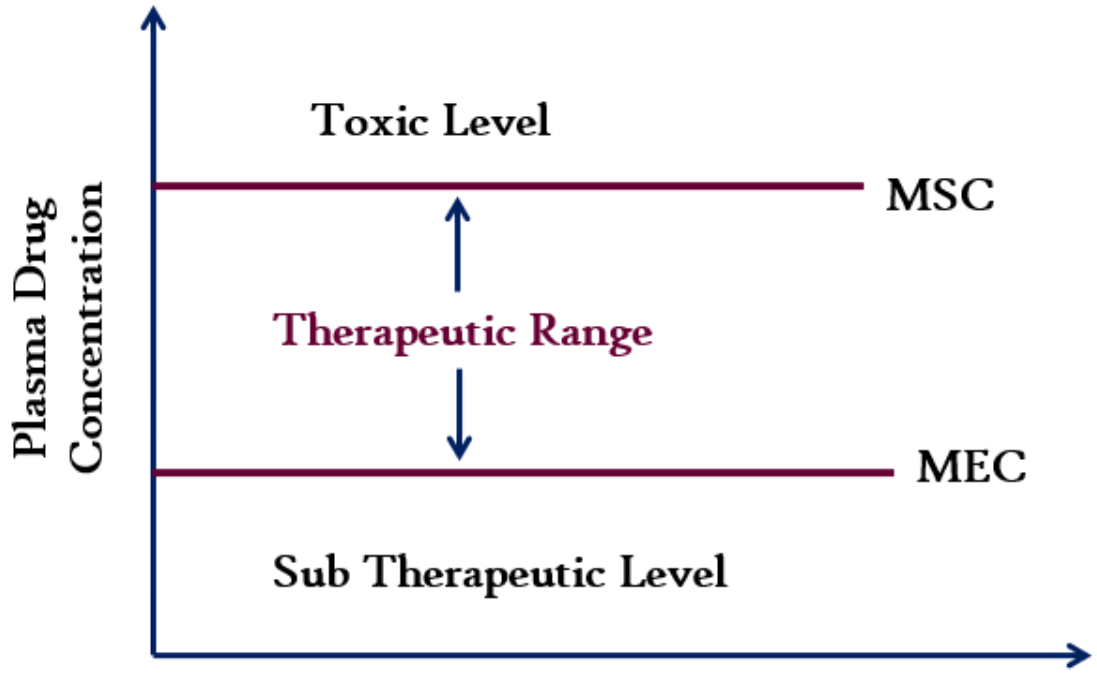
TDM

TDM refers to the measurement and interpretation of principally blood or plasma drug concentration measurements with the purpose of optimizing a patient's drug therapy and clinical outcome while minimizing the risk of drug induced toxicity

Therapeutic drug monitoring (TDM) refers to the measurement of drug concentrations in biological fluids with the purpose of optimizing a patient's drug therapy.

During administration of a dosage regimen, the concentration should be maintained within the therapeutic window.

TDM refers to the tool utilized to individualize dosage regimen by maintaining plasma or blood drug concentrations within the therapeutic range.



CRITERIA OF DRUGS IN TDM

Drug with narrow therapeutic index.

Should have a beneficial concentration response relationship between the blood drug conc. and pharmacological effects

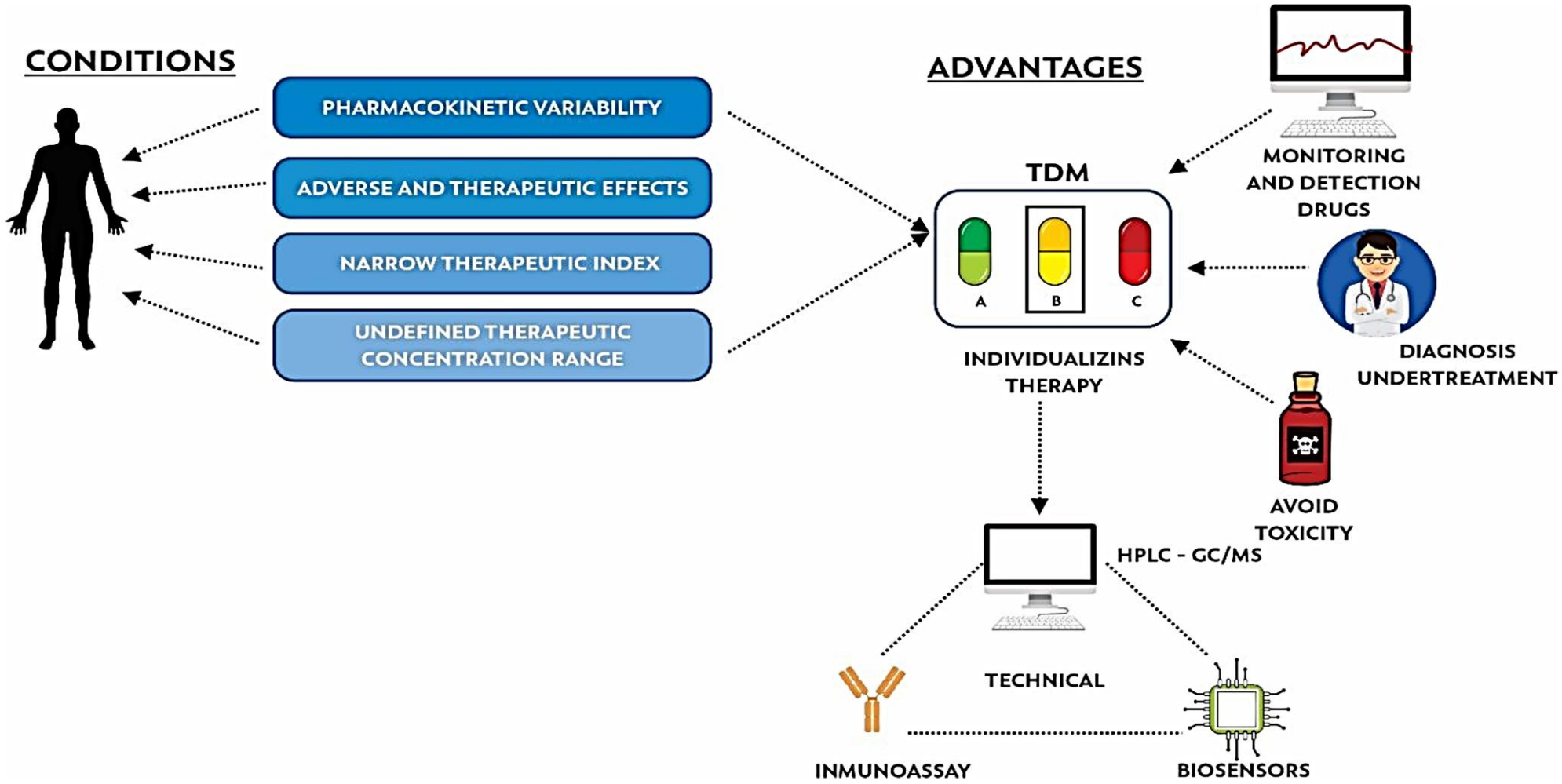
There should be no easily measurable physiological parameter

INDICATIONS

1. Patients with inadequate clinical response
2. Drugs with unpredictable dose-response curve (phenytoin-non-linear kinetics)
3. Drugs which exhibit poor and erratic absorption
4. Drugs which exhibit relatively wider inter-individual variation in drug metabolism
5. Patient exhibiting the signs and symptoms of toxicity (Theophylline intake and persistent nausea)

6. To minimize the risk of toxicity (oto/nephrotoxicity-aminoglycoside)
7. To identify the poison and to determine the severity (paracetamol poisoning)
8. Drugs where signs of over dosage or under dosage are difficult to distinguish.
9. Drugs which are administered in the presence of gastrointestinal, hepatic or renal disease
10. When patients are receiving multiple drug therapy
11. To assess medication compliance (seizure control)

CONDITIONS TO PERFORM TDM



CLINICAL APPLICATIONS

To confirm adequate serum concentrations where clinical response is inadequate: TDM can be used to assess the appropriateness of dosing regimen to maintain the minimum conc. required to exhibit efficacy

To avoid drug toxicity: maintaining a drug within the therapeutic range can help to minimize the risk of toxicity

To individualize dosing of some drug with an unpredictable dose-response curve. Eg: Phenytoin

To assess medication compliance

To help predict a patients dose requirements.

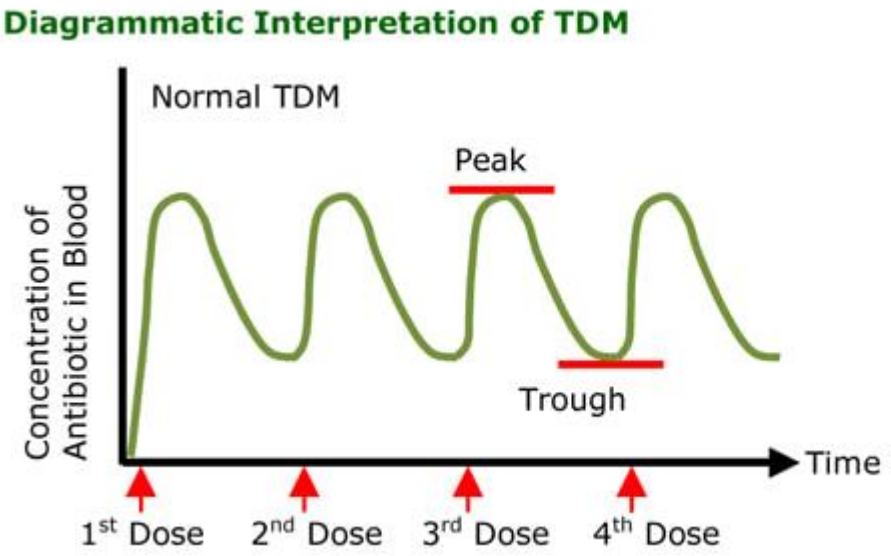
To minimize the time period needed for dosage adjustment.

To identify poisons and to assess the severity of poisoning on an emergency basis in a poisoned patient.

To assist dose adjustment in various disease states where individual variations in drug ADME is important.

SAMPLING

Sample should be drawn at TROUGH LEVEL [after steady state concentration is reached (at least 4-half lives after a dose adjustment)and just before the next dose]



TDM REQUEST FORM

Therapeutic Drug Monitoring Request

Patient's name _____ Date _____

Age: _____ Sex : M ☐ F ☐ Wt: _____kg

Hospital : _____ Ward or clinic: _____

PLEASE INDICATE WHEN RESULT IS NEEDED

Within 24 Hrs ☐ Within 2–4 Hrs ☐ Immediately ☐

REASON FOR REQUEST

Suspected toxicity ☐ Possible drug interaction ☐

Therapeutic confirmation ☐ Lack of therapeutic response ☐

Other (please specify) .....

Co-morbidities or other clinical comments

Name of drug to be assayed _____

Dose _____ Frequency _____ Dosage form _____

Route of administration (please circle): IV IM PO SC

Duration of therapy _____

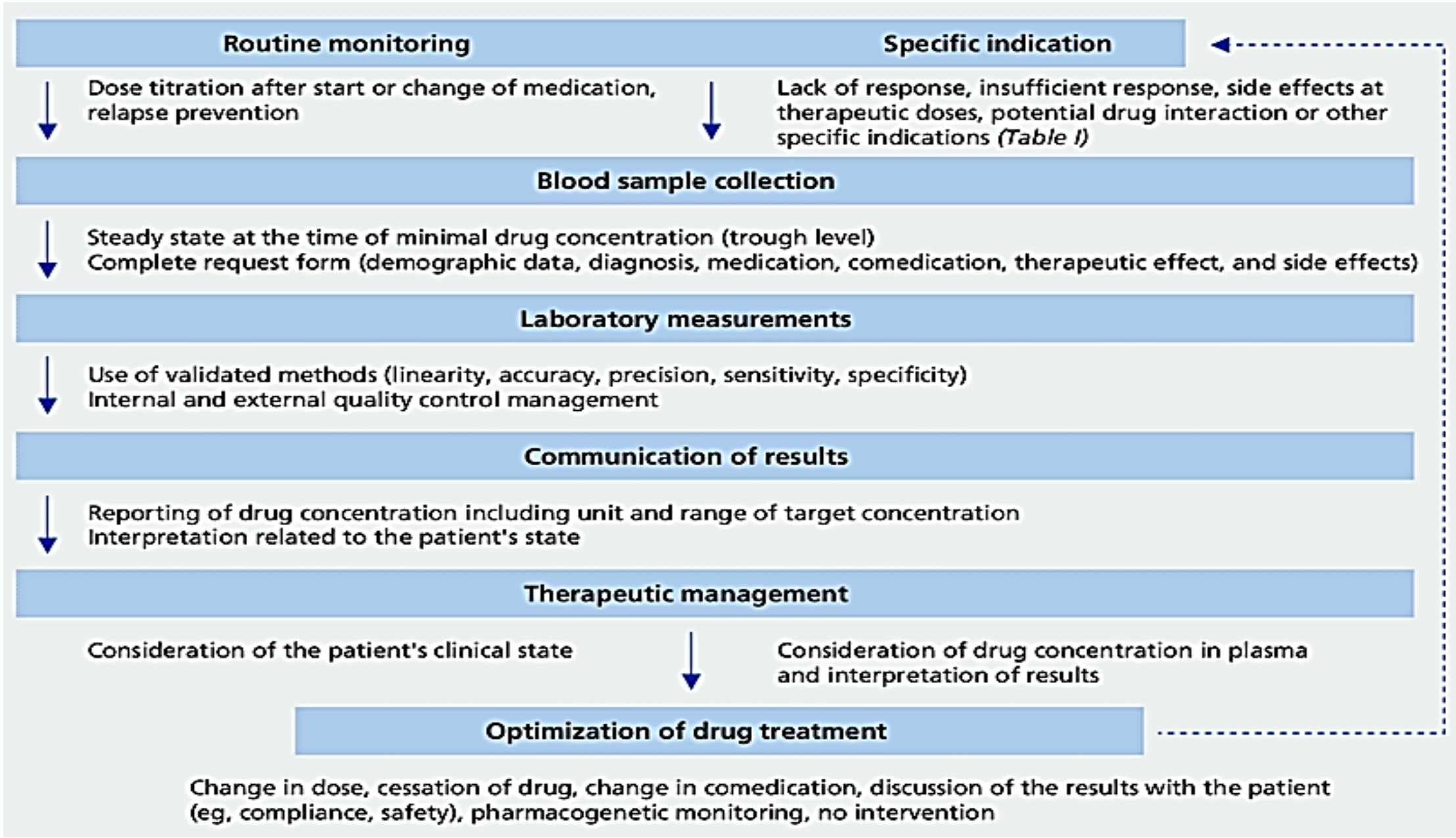
Time and date of last dose _____

Time and date when sample was drawn _____

Doctor's signature _____ Date _____

Contact details for urgent results _____

TDM PROCESS


Routine monitoring
Specific indication
Dose titration after start or change of medication, relapse prevention
Lack of response, insufficient response, side effects at therapeutic doses, potential drug interaction or other specific indications (Table I)
Blood sample collection
Steady state at the time of minimal drug concentration (trough level)
Complete request form (demographic data, diagnosis, medication, comedication, therapeutic effect, and side effects)
Laboratory measurements
Use of validated methods (linearity, accuracy, precision, sensitivity, specificity)
Internal and external quality control management
Communication of results
Reporting of drug concentration including unit and range of target concentration
Interpretation related to the patient's state
Therapeutic management
Consideration of the patient's clinical state
Consideration of drug concentration in plasma and interpretation of results
Optimization of drug treatment
Change in dose, cessation of drug, change in comedication, discussion of the results with the patient (eg, compliance, safety), pharmacogenetic monitoring, no intervention

EXAMPLES OF DRUGS INDICATED FOR TDM

Bronchodilators: Theophylline

Antibiotics

- Aminoglycosides - Gentamicin, Amikacin
- Others - Vancomycin

Immunosuppressants: Cyclosporine

Anticancers: Methotrexate

Antiepileptics: Phenobarbital, Phenytoin, Valproate

Cardiac Drugs : Digoxin, Procainamide, Lidocaine

Psychoactive Drugs: Lithium, TCA

INDIAN SCENARIO FOR THERAPEUTIC DRUG MONITORING

Therapeutic Drug Monitoring (TDM) was introduced in India in the mid and late 1980s.

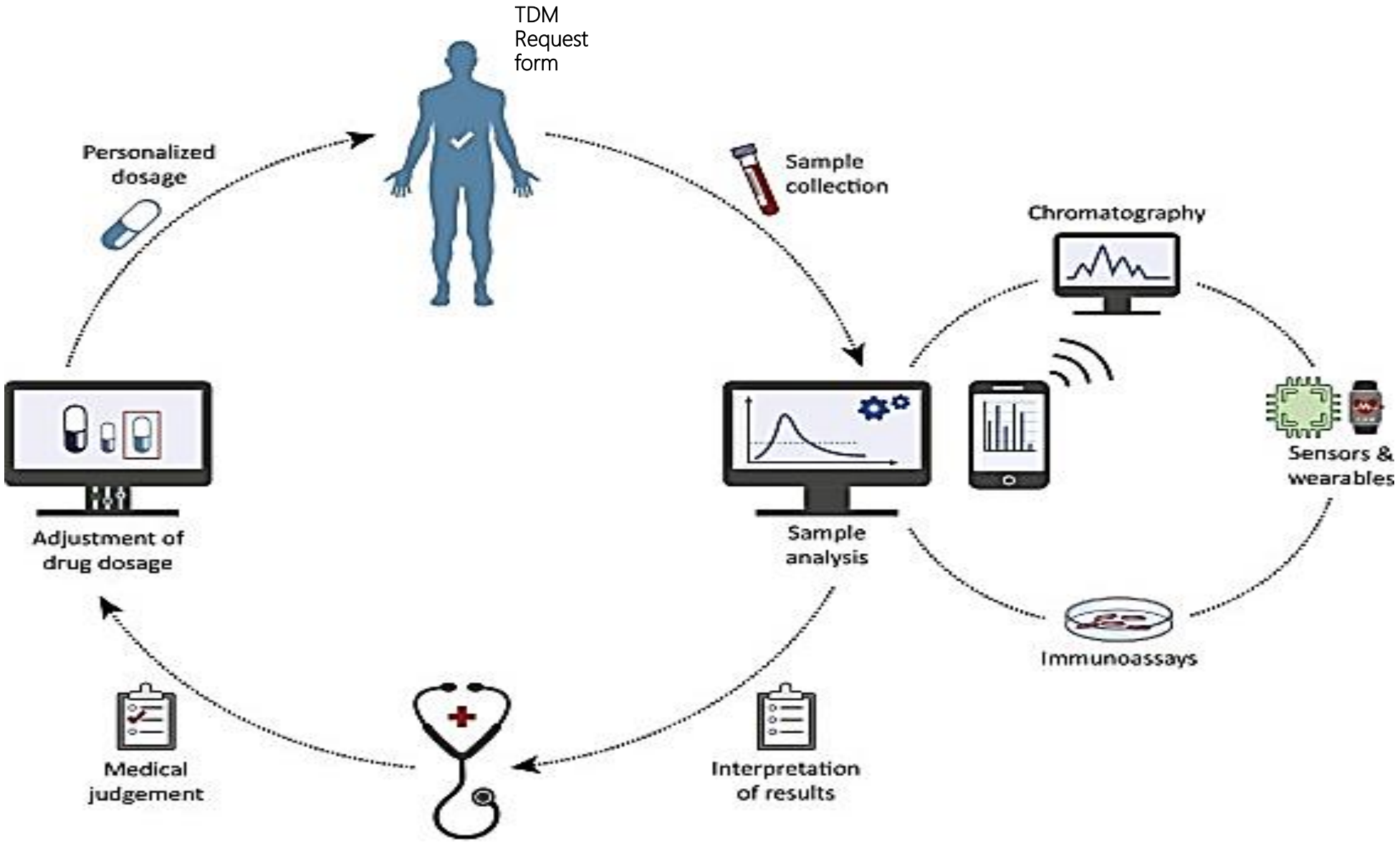
The TDM service in the country is broadly of two types:

- in large teaching hospitals where the service is available through departments of Clinical Pharmacology, (e.g. King Edward Memorial Hospital, Mumbai), **Public sector tertiary care hospitals** and
- in the private sector, where drug estimations are done by clinical biochemistry departments with minimal interpretation (e.g. Apollo Hospital, New Delhi). **Private owned health care Institutions**

- Began in a small way in 1988 with a single high performance liquid chromatograph (H.P.L.C.) and one research assistant in a tiny laboratory tucked away in a corner of an 1800 bed teaching public hospital.
- In 1992, India reported experiences in the management of epilepsy in a developing country
- TDM service started with the monitoring of three anticonvulsants—phenytoin, phenobarbitone and carbamazepine as an adjunct to the epilepsy clinic run by the Neurology Department.
- In 10 years the laboratory has grown to a fully fledged department of Clinical Pharmacology with a total staff of 30, three H.P.L.C.s, and an automated immunoassay laboratory.

CHALLENGES FOR TDM IN INDIA

1. To prove the cost-effectiveness and cost-utility of TDM service.
2. To establish the population (ethnicity) specific therapeutic ranges for various drugs.
3. Infrastructure and trained manpower
4. Minimal turnaround time is a challenge when the workforce is limited.
5. Need for standardization of the laboratories (accreditation) providing TDM services.
6. Need for National Proficiency Testing Programs to ensure external quality assurance.


TDM
Request
form
Sample
collection
Chromatography
Sensors &
wearables
Sample
analysis
Immunoassays
Interpretation
of results
Medical
judgement
Adjustment of
drug dosage
Personalized
dosage