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Biochemistry III

**Monitoring of drug metabolism in patient.**

It has been said that if a drug has no side effects, then it is unlikely to work. Drug therapy labours under the fundamental problem that usually every single cell in the body has to be treated just to exert a beneﬁcial effect on a small group of cells, perhaps in one tissue. Although drug-targeting technology is improving rapidly. So all drug treatment is a compromise between positive and negative effects in the patient. Drugs vary enormously in their toxicity and the concentrations at which one drug might cause potentially lethal effects might be 10 or 100 times lower than a much less toxic drug. A convenient measure for this is the ‘therapeutic index’. This has been deﬁned as the ratio between the lethal or toxic dose and the effective dose which shows the normal range of pharmacological effect. Because of imbalance of drug in the body, it is necessary to monitor the metabolism of a patient when it is been administered.

**Therapeutic drug monitoring in patient.**

Monitoring of drug metabolism in patient is mostly reefed clinically as Therapeutic drug monitoring (TDM). Therapeutic drug monitoring (TDM) is a branch of [clinical chemistry](https://en.wikipedia.org/wiki/Clinical_chemistry) and [clinical pharmacology](https://en.wikipedia.org/wiki/Clinical_pharmacology) that specializes in the measurement of [medication](https://en.wikipedia.org/wiki/Medication) concentrations in [blood](https://en.wikipedia.org/wiki/Blood). Its main focus is on drugs with a narrow [therapeutic window](https://en.wikipedia.org/wiki/Therapeutic_index#Therapeutic_window), i.e. drugs that can easily be under- or overdosed.[[1]](https://en.wikipedia.org/wiki/Therapeutic_drug_monitoring#cite_note-Clinical_Chemistry-1) TDM aims at improving patient care by individually adjusting the dose of drugs for which clinical experience or clinical trials have shown it improved outcome in the general or special populations. It can be based on a priori pharmacogenetic, demographic and clinical information, and/or on the a posteriori measurement of blood concentrations of drugs (pharmacokinetic monitoring) or biological surrogate or end-point markers of effect (pharmacodynamic monitoring).

Therapeutic drug monitoring is the measurement of specific drugs at timed intervals in order to maintain a relatively constant concentration of the medication in the bloodstream. Monitored drugs tend to have a narrow "therapeutic index," a ratio between the toxic and therapeutic doses of medications. For some drugs, maintaining this steady state is not as simple as giving a standard dose of medication. Each person will absorb, metabolize, utilize, and eliminate drugs at different rates based upon their age, general state of health, genetic makeup, and the interference of other medications that they are taking. These rates may change over time and vary from day to day. Changes in the rate may also occur in various disease states or through interaction with other medications.

Not all medications require therapeutic monitoring. Most drugs have a wide therapeutic index and can be prescribed based upon pre-established dosing schedules. The effectiveness of these treatments has been evaluated, but monitoring the concentration of the drug in the bloodstream is not required for dosing. Examples of drugs that do not require monitoring include high blood pressure ([hypertension](https://labtestsonline.org/understanding/conditions/hypertension/)) medications and many of the antibiotics given to treat [bacterial](https://labtestsonline.org/glossary/bacterium/) infections. If an infection resolves with a given antibiotic or if blood pressure is lowered with the prescribed blood pressure medication, then the treatments have been effective.

There are numerous variables that influence the interpretation of drug concentration data: time, route and dose of drug given, time of blood sampling, handling and storage conditions, precision and accuracy of the analytical method, validity of pharmacokinetic models and assumptions, co-medications and clinical status of the patient (i.e. disease, renal/hepatic status, biologic tolerance to drug therapy, etc.).

Many different professionals ([physicians](https://en.wikipedia.org/wiki/Physicians), [clinical pharmacologists](https://en.wikipedia.org/wiki/Clinical_Pharmacology), [clinical pharmacists](https://en.wikipedia.org/wiki/Clinical_pharmacists), [nurses](https://en.wikipedia.org/wiki/Nurses), [medical laboratory scientists](https://en.wikipedia.org/wiki/Medical_Laboratory_Scientist), etc.) are involved with the various elements of drug concentration monitoring, which is a truly multidisciplinary process. Because failure to properly carry out any one of the components can severely affect the usefulness of using drug concentrations to optimize therapy, an organized approach to the overall process is critical.

**Principle and method of monitoring drug metabolism in patient.**

The methods currently available for analyzing data obtained in drug disposition studies are enormous. The fundamental procedures necessary for the quantification of the drug in the body are

* recovery from body fluids
* tissues, and organs
* separation from the biological components,
* identification of the species concerned and finally quantification

**The analytical methodology employed should ideally:**

* Distinguish between compounds of similar structure – unchanged drug and metabolites.
* detect small amounts
* be simple enough to use as a routine assay and 4) be unaffected by other drugs administered simultaneously

**Methods of monitoring drug in patient.**

* FREE DRUG MONITORING
* THIN LAYER CHROMATOGRAPHY
* THE ASSAYS
* SERUM/BLOOD PLASMA

**Resources for Therapeutic Drug Monitoring Target Concentrations**

Most TDM-proposed target concentrations for ARVs focus on a minimum concentration (Cmin) (i.e., the plasma concentration at the end of a dosing interval before the next ARV dose). A summary of population average ARV Cmin can be found in a review on the role of ARV-related TDM.2 Population average Cmin for newer ARVs can be found in the Food and Drug Administration-approved product labels.

Guidelines for the collection of blood samples and other practical suggestions related to TDM can be found in a position paper by the Adult AIDS Clinical Trials Group Pharmacology Committee.4

Challenges and Considerations in Using Drug Concentrations to Guide Therapy

There are several challenges and considerations for implementation of TDM in the clinical setting. Use of TDM to monitor ARV concentrations in a patient requires the following:

* quantification of the concentration of the drug, usually in plasma or serum
* determination of the patient’s pharmacokinetic characteristics;
* integration of information on patient adherence;
* interpretation of the drug concentrations; and
* Adjustment of the drug dose to achieve concentrations within the therapeutic range, if necessary.

A final caveat to the use of measured drug concentrations in patient management is a general one—drug concentration information cannot be used alone; it must be integrated with other clinical information, including the patient’s ARV history and adherence before the TDM result. In addition, as knowledge of associations between ARV concentrations and virologic response evolves, clinicians who use a TDM strategy for patient management should evaluate the most up-to-date information regarding the exposure-response relationship of the tested ARV agent.

**Important of monitoring drug in patient.**

Many of the drugs that require therapeutic monitoring are taken for a lifetime. They must be maintained at steady concentrations year after year while the person ages and goes through life events that may alter that individual's therapeutic level, including pregnancies, temporary illnesses, infections, emotional and physical stresses, accidents, and surgeries. Over time, people may acquire other [chronic](https://labtestsonline.org/glossary/chronic) conditions that also require lifetime medication and that may affect the processing of their monitored drugs. Examples of these conditions include [cardiovascular disease](https://labtestsonline.org/understanding/conditions/cvd), [kidney disease](https://labtestsonline.org/understanding/conditions/kidney), [thyroid disease](https://labtestsonline.org/understanding/conditions/thyroid), [liver disease](https://labtestsonline.org/understanding/conditions/liver-disease), and [HIV/AIDS](https://labtestsonline.org/understanding/conditions/hiv).

Therapeutic drug monitoring follows these changes and accommodates them. It identifies patient noncompliance (when the person does not take the medication regularly as prescribed) and the effect of drug interactions, which may cause drug concentrations that are higher or lower than expected at a given dosage, and helps to personalize a dose to fit the specific needs of a patient. Along with tests such as [BUN](https://labtestsonline.org/understanding/analytes/bun), [creatinine](https://labtestsonline.org/understanding/analytes/creatinine), and [liver function tests](https://labtestsonline.org/understanding/analytes/liver-panel), monitoring can help identify decreases in the efficiency of and dysfunctions in the body's ability to metabolize and eliminate therapeutic drugs. Testing may also determine how a medication interacts with other necessary drugs.

Although immunoassays are most commonly used for therapeutic drug monitoring they suffer from many limitations, including interference from endogenous (high bilirubin, triglyceride, heterophilic antibody) and exogenous compounds (drug metabolite and other drugs with structural similarity with the drug being analyzed). Immunoassays are easy to operate and can be automated. However, analytical methods such as chromatography and chromatography combined with tandem mass spectrometry (LC-MS) are advantageous for drug monitoring because such techniques are less often affected by issues of interference. Unfortunately, interference can occur from ion suppression and insource transformation in LC-MS based methods. These techniques are also more sophisticated, and are not generally available in smaller community hospital laboratories.

**Reference**

aidsinfo.nih.gov

labestonline.org

en.wikipidia.org

Human Drug Metabolism. (Michael D. Coleman Aston University, Birmingham)