Therapeutic Drug Monitoring in Adults at NUH

Nottingham University Hospitals NHS
NHS Trust

The aim of TDM is to provide information that assists in achieving rapid, optimum treatment. In general, routine measurements are not required (exceptions: lithium, ciclosporin, IV aminophylline and some antibiotics – see below), but rather taken to resolve a specific clinical problem, e.g. inadequate response, signs of toxicity.

Appropriate and documented specimen collection time is vital

When taking a level, the following must be considered to avoid misleading results:

1. For dosage adjustment guidance, sampling at 'steady-state' is essential (unless confirming toxicity) and thus at least four elimination half-lives must have elapsed since the last change of maintenance dose
2. Samples must be taken at an appropriate time during a dose interval.
Interpretation of most results is made in relation to the therapeutic range but clinical decisions should not be based on drug concentrations alone. The range is only a guideline derived from a normal population and some patients will respond or exhibit toxicity outside the expected ranges. Concentrations can be affected by factors such as age, drug interactions, protein binding and drug metabolism. Also, liver and/or renal impairment may reduce clearance and increase the risk of toxicity, especially after a dose increase.

The following provides a guide to the most requested drug assays provided by the Department of Clinical Pathology. Drugs analysed daily at NCH & QMC are: lithium, digoxin, theophylline, carbamazepine and phenytoin. Ciclosporin and tacrolimus are analysed at NCH every weekday; to arrange analysis on Saturday contact the NCH Duty Biochemist on ext 59729. Lamotrigine and clozapine are analysed at QMC 1-2 times per week. If results for any drug are required urgently please telephone the laboratory first: QMC 63312, NCH 59729, out of hours bleep via switchboard.

Drug	Therapeutic range	Number of days before steady state	Optimum sampling time	Common signs and symptoms of toxicity	Type of sample required
Lithium	0.6 - 1.3 mmol/L	5	12 hours after evening dose (for once daily dosing; otherwise, please discuss)	Tremor, ataxia, dysarthria, nystagmus	5mL SST
Digoxin	0.8 – 2.0µg/L	5	At least 6 hours after oral dose. A trough measurement before a dose is preferred	Anorexia, vomiting, diarrhoea, visual disturbances	5mL plain (not SST)
Aminophylline Infusion	10 - 20mg/L	1	Sampling time not critical	Nausea, vomiting, tachycardia, anorexia, arrhythmias	5mL plain (not SST)
Theophylline Tablets	10 - 20mg/L	2	Trough measurement before a dose	Nausea, vomiting, tachycardia, anorexia, arrhythmias	5mL plain (not SST)
Carbamazepine	4 - 12mg/L	8 after first dose 4 after a dose change	Trough measurement before a dose	Nausea, vomiting, dizziness, visual disturbances	5mL plain (not SST)
Phenytoin	10 - 20mg/L	7	PO: Sampling time not critical due to slow absorption time. IV: trough measurement	Ataxia, slurred speech, nystagmus, blurred vision	5mL plain (not SST)
Tacrolimus	5 - 15 µg/L	4	Trough measurement before a dose	See data sheets/BNF Note, many drug interactions	5mL EDTA
Ciclosporin	Contact lab. Varies with indication	4	For renal transplant patients, use pre-dose (trough) or 2 hour post dose measurements (label clearly). For all other oral uses, take trough level. IV anytime.	See data sheets/BNF Note, many drug interactions	5mL EDTA
Lamotrigine	2-15mg/L	5	Trough measurement before a dose	Nystagmus, ataxia, impaired consciousness	5mL plain (not SST)
Clozapine	350-1000mg/L	2	Trough measurement before a dose	Drowsiness, lethargy, areflexia, coma, confusion, hallucinations	5mL plain (not SST)

SST: Serum Separator Tube – yellow top ; Not SST: Plain Tube – red top tube

Antibiotics analysed daily by Microbiology at QMC are: gentamicin, vancomycin and tobramycin. The following summarises optimum sampling times for antibiotics:

Drug/Dosing Schedule	Optimum sampling time(s)	Dose adjustments	Target Range/Points to note	Sample Required
Once Daily Gentamicin + Tobramycin Dosing	Trough level **18-24 hours** after the first dose	If patient is <65yrs with good renal function + urine output, give second dose without awaiting result If patient is >65yrs or abnormal renal function await result and advice from medical microbiologist	The ideal pre-dose (trough) level is <1.0mg/L. It is not necessary to do a post-dose level. Further monitoring is usually twice weekly pre-dose (trough) levels if no dose-change and normal renal function +urine output. A medical microbiologist will give advice on dosage and the need for further assays if abnormal results	5mL plain (not SST)
Conventional Gentamicin Dosing	Pre-dose (trough) level just before the **third** or **fourth dose** and post-dose (peak) level **one hour** after administration.	Patients with impaired renal function should have a loading dose, but subsequent dosing and monitoring should be discussed with a microbiologist	Ideal levels: Pre-dose (trough) <2mg/L Post-dose (peak) 5-10mg/L(endocarditis 3-5mg/L) Further monitoring is usually twice weekly trough levels, if no dose changes and normal renal function +urine output. A medical microbiologist will give advice on dosage and the need for further assays if abnormal results	5mL plain (not SST)
Conventional Tobramycin Dosing	Pre-dose (trough) level just before the **third** or **fourth dose** and post-dose (peak) level **one hour** after administration.	Advice on dosing and dose adjustments in renal impairment and subsequent monitoring should be discussed with a medical microbiologist.	Ideal levels: Pre-dose (trough) <2mg/L Post-dose (peak) 5-10mg/L Further monitoring is usually twice weekly pre-dose levels if no dose changes and normal renal function +urine output. A medical microbiologist will give advice on dosage and the need for further assays if abnormal results	5mL plain (not SST)
Vancomycin	Pre-dose (trough) level just before the **third or fourth dose**. A level should be taken and the dose administered	The normal dose is 1g bd, adjust dose to 1g od if patient is >65 yrs or has mild renal impairment	The ideal level is 5-15mg/L (10-15mg/L for deep-seated infections – e.g. endocarditis, pneumonia, bone/joint etc.) Further monitoring is usually twice weekly pre-dose (trough) levels if no dose-change and normal renal function +urine output. A medical microbiologist will give advice on dosage and the need for further assays if abnormal results	5mL plain (not SST)
Amikacin	Pre-dose (trough) level and post-dose (peak) level **one hour** after administration. Samples should be taken after 24hrs	Usual dose is 15mg/kg/day in two divided doses. Advice on dosing and dose adjustments in renal impairment and subsequent monitoring should be discussed with a medical microbiologist.	Weekdays only. Processed off-site, results available next day. Ideal levels: Pre-dose (trough) <10mg/L Post-dose (peak) >20mg/L Further monitoring is usually twice weekly pre-dose levels if no dose change and normal renal function +urine output A medical microbiologist will give advice on dosage and the need for further assays if abnormal results	5mL plain (not SST)

Information needed on the request card: Time of last dose, dosage regimen and level taken (Pre/Post), indication for treatment, body weight and other antibiotics: see Antibiotics website for more details.

Timing of doses: Doses should ideally be timed for convenience eg. 10.00am. For pre-dose levels, a sample should be taken and the dose administered. For example, if the dose is 1g bd, and the 3rd dose is at 6pm, then take levels before the 4th dose the following morning.

- **Teicoplanin and aciclovir**, monitoring is not normally required, but can be monitored after discussion with microbiology in renal impairment or when treating severe infections.
- Monitoring for **5-Flucytosine** should be arranged with microbiology who will advise what levels are required.
- For **streptomycin,** levels should be arranged with microbiology and taken pre and (1 hour) post the fourth dose (sent by microbiology to reference laboratory).

Opening times: antibiotic assays are performed in the QMC microbiology laboratory, for same-day results samples should arrive at the pathology receptions (NCH/QMC) by:
Mon – Fri: 0900 – 1530 (NCH), 1630 (QMC) for routine specimens Sat-Sun: 0900 – 1000 (NCH), 1030 (QMC) Out of hours antibiotic assays are performed and processed the following morning.

For further information or advice on therapeutic drug monitoring, or how to manage toxic or sub-therapeutic levels, please contact:
Pharmacy, Medicines Information 64185 or 61200 out of hours contact the **On-call Pharmacist** via switchboard
Microbiology, blood culture/assay duty medic ext. 64941
Clinical Pathology, QMC 63059, NCH 55084 out of hours contact the **On-call Clinical Chemist** via switchboard

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