

Therapeutic Drug Level Collection Guidelines

Anti-epileptic drugs (carbamazepine, phenobarbital, phenytoin, primidone, valproic acid)

- Consider collecting after steady state conditions are reached, i.e. after 4-5 half-lives on unchanged dose regimen
- Consider collecting samples following oral dosing immediately prior to next dose for drugs with short half lives. For drugs with long half-lives, ≥ 24 hours, draw time is less critical.
- If suspecting altered pharmacokinetics, consider obtaining samples following IV dosing of phenytoin at 1-4 hours post dose.
- If fosphenytoin are ordered, collect specimens 2 hours post IV or 4 hours post IM dose.
- May consider collecting drug levels within 6 hours after a seizure in previously controlled patient

Antibiotic Drugs (aminoglycosides, vancomycin)

- Obtain a baseline creatinine and repeat at 1-3 day intervals, or as clinically indicated.
- Begin monitoring after steady state is achieved (usually 3-4 doses).
- Consider monitoring at least one peak for aminoglycosides (60-90 min after IM or 30-60 min IV) and one trough (within 30 min of next dose) for vancomycin if therapy is intended for 3 or more days of therapy.
- Consider repeating trough measurements at 3-4 day intervals or sooner if warranted by clinical status
- Base frequency of monitoring on changes in dose and patient symptoms
- If proximal tubular dysfunction is suspected, consider perform urinalysis and repeat as necessary

Random levels are available for any patient on these medications that is not receiving recurrent doses. For example, if a patient is on dialysis or has acute renal failure and receives one dose at a time, checking a random level to decide if another dose is to be given is reasonable. More specifically, in the following patients:

Vancomycin

- Acutely declining renal function
- Unknown renal function (especially in ICU with unstable hemodynamics)
- Dialysis
- Suspected supratherapeutic doses with doses being held
- Some others

Aminoglycosides

- As with vancomycin

- Extended interval dosing- drawn 10-14 hours post dose.

For other antibiotics, consider the following monitoring:

- Linezolid - weekly CBC
- Daptomycin - weekly CPK

Antiarrhythmic Drugs (procainamide/NAPA, quinidine, lidocaine, disopyramide, flecainide)

- Both procainamide and NAPA should be monitored after steady state is achieved
- The acetylation status of patients in whom renal dysfunction has been ruled out should be established
 - Obtain blood sample 3 hours after administration of last dose of procainamide
 - Measure both procainamide and its metabolite, NAPA
 - If the concentration of NAPA is \geq procainamide, the patient is considered a fast acetylator and at lower risk for developing lupus-like toxicity.
- Consider monitoring quinidine, disopyramide and flecainide after steady state is achieved
- Monitoring of lidocaine is only recommended when propranolol is co-administered or toxicity is suspected.

Cardiac Glycoside Drugs: (digoxin, and digitoxin)

- Consider monitor after patient reaches steady state and at least 8 hours after last dose and/or as clinically indicated. The serum concentration does not correlate with pharmacologic activity until the post distribution period (at least 8-12 hours after last dose).

Immunosuppressant Drugs (cyclosporine, tacrolimus)

- Consider monitoring levels in the immediate peri-transplant period during hospitalization: every 24-48 hrs
- First 3-6 months following transplant until patient stabilizes: 2-3 times per week with frequency gradually decreasing as clinically indicated.
- Stable patients 6 months post transplant: every 6 months, or as clinically indicated

Thymoleptic Drugs:

- Lithium: At the start of therapy, the consider monitoring as follows:
 - First 2 weeks: consider monitoring every 3-4 days
 - 20 weeks: consider monitoring weekly, adjusting dose as needed
 - 6 weeks to 3 months: monitor monthly
 - >3 months: consider monitoring every 3-6 months once patient is well stabilized on given regimen
- Clozapine - monitor according to clozapine REMS.

Analgesic Drug Monitoring

- The following frequency for acetaminophen overdose is recommended:
 - Following acute overdose of regular formulation acetaminophen, obtain one stat level at 4 hours after ingestion, if the exact time of ingestion is known.
 - Follow initial level by one additional level every 2 hours until a peak concentration has been reached.
 - Following acute overdose of sustained release acetaminophen, measure acetaminophen concentration at both four and eight hours following ingestion. Plot both concentrations on the Rumack nomogram.
 - Obtain one additional level at completion of antidote therapy to assure the acetaminophen concentrations are nondetectable prior to stopping N-acetylcysteine.
- The following frequency for salicylate overdose is recommended:
 - Measure initial serum concentration at time of presentation
 - Perform additional measurements every 2 hours until a peak concentration has been reached
 - Measure serum concentrations every 4 hours thereafter until values are less than 200 ug/ml (assuming normal acid-base and mental status).

Bronchodilator Drugs:

- The following is recommended for caffeine monitoring:
 - Monitor in patients who are clinically unresponsive following high doses of caffeine
 - Monitor in patients with evidence of toxicity
- The following is recommended for theophylline loading:
 - For theophylline loading dose in acute care, check baseline level to ensure no theophylline is present. Check theophylline again at 1 hour after IV loading to ensure dose is adequate.
 - Following scheduled IV administration, collect samples 1-4 hours post dose or when toxic symptoms are observed.
- The following is recommended for theophylline oral therapy:
 - Consider measuring concentration after 1-2 half lives to ensure therapeutic level has not been exceeded
 - Consider measuring concentrations after 5 half-lives to ensure steady state concentration is within desired therapeutic range
 - If applicable, wait 5 half-lives and recheck concentration after switching to oral dosing or making a dosage adjustment
 - If applicable, collect samples from patients receiving and oral formulation immediately before the next dose (trough) after steady state has been reached.

Anticoagulation Drugs:

- The following is recommended for **Warfarin (Coumadin®)** anticoagulant monitoring:
 - Monitor patients when treated for arterial and venous thrombosis to prevent clot propagation or for prevention of thromboembolic disease in thrombophilia, atrial fibrillation, mechanical heart valves, ACS, and high-risk surgery
 - Obtain baseline PT/INR, CBC, and liver function tests (ie. AST and/or ALT)
- Monitor using INR. The INR is calculated from the following formula:
$$\text{INR} = (\text{patient PT}/\text{mean normal PT})^{\text{ISI}}$$
 - Monitor patients at baseline and consider daily until INR is therapeutic twice at least 24 hours apart while inpatient, then as clinically indicated. May consider longer intervals between INRs for patients as clinically indicated (ie. Rehabilitation, psychiatric admissions, etc.)
 - Bassett Network Therapeutic Ranges:
 - Routine anticoagulation therapy: 2.0 – 3.0
 - Mechanical valve therapy: 2.5 – 3.5

The following is recommended for **Unfractionated Heparin** anticoagulant monitoring:

- Monitor patients when treated for arterial and venous thrombosis to prevent clot propagation or for prevention of thromboembolic disease in thrombophilia, atrial fibrillation, mechanical heart valves, and high-risk surgery
 - Monitor intravenous heparin therapy according to the Bassett Healthcare Network Heparin Protocol
 - Check CBC at baseline and every three days while on therapy, per the Heparin Protocol
 - Obtain baseline aPTT, CBC and CRTN prior to starting therapy
 - Check PLT at baseline and every 2-3 days to detect heparin induced thrombocytopenia (HIT). If count drops 50%, consider HIT, and treat as clinically appropriate.
- The following is recommended for **Low Molecular Weight (Enoxaparin or Lovenox®)** anticoagulant monitoring:
 - Check CBC at baseline and consider reassessment periodically (ie. every 3rd day while on acute therapy and periodically as clinically appropriate if on chronic therapy)
 - Obtain baseline CBC and CRTN prior to starting therapy
 - Anti-Factor Xa monitoring may be indicated for infants, children, obese (> 150kg) or underweight patients (Women < 45kg and Men < 57kg) or those with renal disease, long-term treatment, pregnancy, or unexpected bleeding or thrombosis
 - If obtaining anti-Factor Xa peak levels, draw at peak effect (4 to 6 hours after the dose) for maximum clinical usefulness

- Check PLT at baseline and every 2-3 days at therapy initiation to detect heparin induced thrombocytopenia (HIT). If count drops 50%, consider HIT, and treat as clinically appropriate.
- The following is recommended for **Direct Thrombin Inhibitors (Argatroban)** anticoagulant monitoring:
 - Substitute for heparin when HIT is suspected or confirmed. Even when HIT's only manifestation is thrombocytopenia and heparin is stopped, risk of thrombosis in subsequent 30 days approaches 50% unless alternative anticoagulant is used.
 - aPTT is used to prevent bleeding or thrombosis. Do not start in patients with aPTT longer than 2.5 x mean of reference interval.
 - Argatroban: collect blood two (2) hours after initial dosage, adjust dosage to aPTT 1.5-3.0 x mean of reference interval. Argatroban increases the INR more than heparin. Argatroban accumulates in liver failure, thus dose adjustments are recommended.