APPROPRIATE TIMING OF SERUM DRUG SAMPLING

1. **Digoxin.** Wait 5-7 days to reach steady state. Drug concentrations should be drawn during the post-absorptive, post-distributive phase of drug elimination, i.e. during the 6-24 hour interval following the previous dose. Trough level should be drawn within 1 hour of dose. Repeat level every 5-7 days, or as dictated by a change in concurrent disease state/drug therapy, lack of response to previously adequate dose, or occurrence of adverse effects.[1,2]

2. **Carbamazepine.** Do not draw levels during the first 2 weeks of therapy because autoinduction of the drug is taking place and steady state concentrations are not achieved. During the third week of therapy, wait 3-5 days before drawing level. A trough level drawn just before the morning dose is **most** appropriate for the evaluation of efficacy. [1,2,5]

3. **Aminoglycosides: (gentamicin/tobramycin/amikacin) Conventional dosing.** Draw peak and trough levels when the drug is at steady state, which is at least the third dose. Peaks should be drawn 30 minutes after a 30 minute infusion and troughs may be drawn 30 minutes before the next dose, but ideally should be drawn **immediately** prior to the next dose.

	Gentamicin/Tobramycin	**Amikacin**
C_{trough} (mg/ml)	**0.5 – 2**	**4 - 10**

Once daily aminoglycoside dosing for gentamicin and tobramycin. This term refers to a method of dosing that is different from conventional dosing. Do not draw peaks and troughs. A random level should be drawn between hour 6-14, after start of the infusion (10 hours is preferred) and applied to the appropriate nomogram to confirm the dosing interval. [1,2,4,6]

4. **Phenytoin.** Levels are not necessary prior to reaching steady-state (7-28 days).
   Indications for drawing plasma phenytoin levels:
   1. Recurrence of seizures
   2. Uncontrolled seizures
   3. Following loading dose or rebolus dose
   4. Following change of dosage form
   5. Following dosage adjustment
   6. Addition/discontinuation of interacting drug
   7. Signs and symptoms of toxicity

   A single phenytoin level may be drawn:
   1. No sooner than 2 hours after IV loading dose or IV rebolus
   2. No sooner than 6 hours after completion of an oral loading dose or oral rebolus dose.
   3. 3-5 days after a change of dosage form. Draw prior to morning dose.
   4. 3-5 days after initiating of changing maintenance dose. Draw prior morning dose
   5. 3-5 days after adding/discontinuing a metabolism altering drug. Draw prior to morning dose
   6. 1-2 days after adding/discontinuing a phenytoin displacing drug. Draw prior to morning dose.
   7. Signs and symptoms of toxicity; Stat and q 2-3 days

   Trough levels should be drawn. Free phenytoin levels may be drawn if a patient exhibits signs of toxicity or continues to have seizure activity with a therapeutic total serum level (Free phenytoin serum concentration = 1-2 mcg/ml). [1,2,5]

5. **Phenobarbital.** Obtain level after 3-5 half-lives (20-30 days). Trough level is suggested, but timing of level is not critical. Phenobarbital's half-life is so long, daily fluctuations in serum concentrations are minor. If administering the drug IV, wait at least one hour after infusion to avoid distribution phase. Primidone is metabolized to phenobarbital and phenylethylmalonamide (PEMA). [1,2,4]

6. **Theophylline.** Sampling times for the various age groups, along with the reasons for the timing, are listed below (Murphy):
   Neonates: (1) Two hours after the first loading dose to calculate the volume of distribution (Vd). (2) Every 4-7 days to calculate clearance and dosage adjustment.
   Infants: (1) 30 min after the first loading dose, if administered intravenously, to calculate the Vd and additional loading doses (2) 12 -24 hours after initiation of maintenance dose to determine if adequate concentrations are being maintained or if the drug is accumulating rapidly. (3) 72 hours after initial dosing and then every 24 hours as needed to calculate clearance and dosage adjustment. (4) Every 4-7 days once hospitalized patient is stabilized, unless otherwise indicated, to calculate clearance and dosage adjustment.
   Children: (1) 30 mins after the first loading dose, if administered intravenously, to calculate the volume of distribution and additional loading doses. (2) 4-6 hours after initiation of maintenance dose to determine if adequate concentrations are being maintained or if the drug is accumulating rapidly. (3) 12-24 hours after initial dosing and then every 24 hours as needed to calculate clearance and dosage adjustment. (4) 72 hours after initial dosing and then every 24 hours as needed to calculate clearance and dosage adjustment. (5) Every 4-7 days once hospitalized patient is stabilized, unless otherwise indicated, to calculate clearance and dosage adjustment.
   Adults and geriatrics: (1) 30 minutes after the first loading dose, if administered IV, to calculate the volume of distribution and additional loading doses (2) Eight hours after initiation of maintenance dose to determine if adequate concentrations are being maintained dose to determine if adequate concentrations are being maintained or if the drug is accumulating rapidly (3) 12-24 hours after initial dosing to determine further dosage adjustments (4) 72 hours after initial dosing to determine further dosage adjustments (5) Every 4-7 days once hospitalized patient is stabilized, unless otherwise indicated, to calculate clearance and dosage adjustment.[1,2,3]

7. **Vancomycin.** Draw trough level 5 – 30 minutes prior to 4th dose when the drug is at steady state (4-5 half lives). Monitoring vancomycin serum levels is a controversial practice because serum concentrations do not correlate well with efficacy or toxicity of the drug. Peaks are rarely drawn. Troughs should be drawn 5 - 30 minutes before the dose. The desired trough level depends on the site of infection. Infections that are difficult to penetrate (pneumonia, osteomylitis, endocardits, and meningitis) require higher trough levels between 15 – 20 mcg/ml. [1,2,3,4]

8. **Valproic Acid.** Draw levels after steady state has been achieved (2-4 days) (Murphy). Troughs should be drawn prior to the am dose. When dose is changed, wait at least 2-4 days (to get to steady state) before rechecking serum level. [1,2]

9. **Lithium.** Draw levels after steady state has been achieved (4-5 days) (Lexi-Comp). Trough levels should be drawn prior to next dose (8-12 hours post previous dose). If dose is changed re-draw trough levels after 4-5 days to again reach steady state. Therapeutic levels 0.6-1.2 mEq/l. Toxic level >1.5mEq/l. Monitoring: draw levels twice weekly until patient is stable, and then draw levels every 1-3 months. [1,3]

10. **Cyclosporine.** Draw levels at steady state (5 t½'s = 90-200 hours) after initiation of therapy or a change in any dose. The level is drawn just prior to the next dose. Due to the wide variation in absorption, serum levels are necessary when switching for IV to PO or vice versa. Desired serum concentration depends on type of transplant, type of sample, and method of assay. For example, the desired concentration measured by HPLC on whole blood for renal transplant patients is 100-200 ng/ml.[1,2,4]

11. **Tacrolimus.** Draw whole blood trough level on 3rd day of therapy. Trough levels are most variable during 1st week post-transplant. Measure daily to every three days until level stabilizes (2-4 weeks, depending on patient).

    Recheck whole blood trough level with:

    1. Change in hepatic or renal function
    2. Signs of tacrolimus toxicity
    3. Signs of graft rejection
    4. Change in tacrolimus dose or route of administration (IV « PO)
    5. Addition, deletion or dose change of potentially interacting drug
    6. Severe illness affecting drug absorption/elimination (i.e. severe immune reaction or sepsis)
    7. Suspect noncompliance [1,2,3]

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