THERAPEUTIC SERUM CONCENTRATIONS AND SAMPLING GUIDELINES

Drug	Usual Sample Time	Therapeutic Serum Concentration	Physicians' Routine Inpatient Orders	Comments
Amikacin	Pre: 0-30 min. prior to next dose	2.5-10 mg/L	**Initial:** Pre and Post with third regular dose. **Maintenance:** Pre and Post: Once weekly.	- Half-life (t½) will be prolonged in patients with renal dysfunction. - Levels are sent off-site for analysis; allow time for results.
	Post: 30 min. after end of infusion	20-35 mg/L		
Carbamazepine (Tegretol^{R})	Pre: 0-60 min. prior to next dose	20-50 microMol/L	**Initial:** Pre: 3-7 days after final dosing alteration. **Maintenance:** Pre: Only if patient still has seizures. If toxicity is suspected, take sample at time of symptoms, or 3 hours after the dose.	- Enzyme auto-induction occurs so that t½ during chronic dosing may be much shorter than after first dose. - Dose should be increased at 5-7 day intervals over a 4-6 week period and the first serum level measured at 5 weeks.
Chloramphenicol	Post: 30 min. after end of IV flush or 1 hr and 2 hr after PO admin-istration	15-25 microMol/L	**Initial:** Post on Day 2 of therapy. **Maintenance:** Post: Once weekly.	- Pharmacokinetics in pediatric patients are highly variable and unpredictable. - Clinical microbiologists will determine if therapeutic drug monitoring is necessary. - Levels are sent off-site for analysis; allow time for results

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Cyclosporine	Pre: 0-60 min. prior to next dose Renal Graft Rejection: Liver Graft rejection: GVHD Prophylaxis in BMT Early Phase: Maintenance Phase: Aplastic Anemia (IST) (first month)	 Time Post-transplant: 0-30 days: 280-360 µg/L 31-60 days:200-280 µg/L 61-90 days:120-200 µg/L > 91 days: 80-200 µg/L Time post transplant: <3 months: 240-320 µg/L 3-6 moths: 160-240 µg/L > 6 months: 80-160 µg/L 240-320 µg/L 160-240 µg/L 240-320 µg/L	**Initial:** Pre: Day 3 of therapy. **Maintenance:** Pre: Three times weekly during first 2-3 weeks, then twice weekly x 2-3 weeks then monthly.	- Ranges have been adjusted (downwards by 20%) to reflect the method change to tandem mass spectrometry (VGH laboratory) in August 2010. This method measures parent drug and is free from metabolite interference. Methods susceptible to metabolite interference may give higher results. - Monitoring is necessary to avoid extremely high or low levels which may precipitate nephrotoxicity or therapeutic failure, respectively. - See “Practical Guidelines for Cyclosporine Use” on page 297 for information on AUC and dose adjustments - Monitoring may be less frequent if patient is stable.
Digoxin	Pre: 0-60 min. prior to next dose (Must be AT LEAST 8 hours postdose)	1.3-2.7 nmol/L	Pre levels should be drawn only if risk factors are present. Risk factors include: • suspicion of toxicity • renal or hepatic impairment • poor response • drug interactions • non-compliance • prematurity • hypokalemia	- The correlation between serum levels and therapeutic effect is not clearly defined. - Digoxin serum levels are useful when toxicity is suspected. - Digoxin therapy should be monitored by clinical effect rather than serum levels. - Digoxin serum levels are meaningless after Digibind^{R}.

Drug	Usual Sample Time	Therapeutic Serum Concentration	Physicians' Routine Inpatient Orders	Comments
Gentamicin **Extended Interval**	Pre: 18–24 hr after 2nd dose No peak level required	≤ 1 mg/L	**Initial:** pre level 18–24 hr after 2nd dose **Maintenance:** Pre: once weekly. Administer over 30 minutes	- If therapy is anticipated > 72 hours: ▪ Trough level prior to 3rd dose (18– 24 hrs after 2nd dose) ▪ Administer 3rd dose ▪ Before giving 4th dose: - if level ≤ 1 mg/L: Administer next dose - if level > 1 mg/L: DO NOT administer next dose until pharmacy is consulted - For therapy beyond 7 days: ▪ Trough level once weekly
Gentamicin **Traditional dosing**	Pre: 0-30 min. prior to next dose	0.6-2 mg/L	**Initial:** Pre & post with 3rd dose. (See Comments.) **Maintenance:** Pre: Once weekly in stable patients. Pre & Post: As required in patients with unstable renal function.	- No monitoring required for (patients with normal renal function): • uncomplicated UTIs • surgery prophylaxis < 72 hr. • empiric therapy < 72 hr. - t½ will be prolonged in patients with renal impairment.
	Post: 30 min. after end of infusion	5-10 mg/L		
Phenobarbital	Pre: 0-60 min. prior to next dose	65-170 µmol/L	**Initial:** Pre: After 10-14 days, unless toxicity is suspected or patient still has seizures.	- Some patients may tolerate and benefit with levels that are significantly higher than the recommended maximum limit.

Drug	Usual Sample Time	Therapeutic Serum Concentration	Physicians' Routine Inpatient Orders	Comments
Phenytoin (Dilantin®)	Pre: 0-60 min. prior to next dose	40-80 µmol/L "free" phenytoin: 4-8 µmol/L	**Initial:** 1 hr. post IV load. Wait 7 days after each oral dosing change to measure pre level. In acute management of seizures, where patient continues to seize, measure serum levels (pre) 1 or 2 times daily. **Maintenance:** Pre: Only if patient still has seizures. If toxicity is suspected, take level at time of symptoms. **Fosphenytoin**: 2 hr. post IV load or 4 hr. post IM load	- Phenytoin exhibits dose dependent pharmacokinetics: plasma drug concentration may change disproportionately with dosage changes. - Phenytoin is highly protein bound. - Free phenytoin levels may be useful in monitoring patients with chronic renal failure (hypoalbuminemia), or who are receiving drugs that displace phenytoin from protein (e.g. valproic acid) or in disease states that may displace phenytoin from plasma protein (e.g. hyperbilirubinemia). - Free phenytoin levels are sent to VGH with turn around time approximately 8 hours. For ongoing monitoring in stable patients, free phenytoin can be calculated from total phenytoin by using percentage free phenytoin from a previous result.
Salicylate (ASA)	JIA : Pre: 0-60 min. prior to next dose	1.1-2.2 mmol/L	**Initial:** Pre on Day 3. **Maintenance:** Pre: Once weekly.	- For overdose, see Resident's Handbook or Poison Manual.
Sirolimus	Pre : 0-60 min. prior to next dose	6-12 mcg/L	**Initial:** 2-3 x weekly **Maintenance:** Q 2-4 weeks	- samples are sent to VGH; allow time for results.
Tacrolimus **(Prograf, FK506)**	Pre: 0-60 min. prior to morning dose	Renal transplant: Trough level: 4-12 mcg/L	Renal Transplant: **Initial:** 2 – 3 x weekly **Maintenance:** Q 2-4 weeks; depends on many factors	- For renal transplant, the therapeutic range is patient-specific and varies according to the time post transplant - Different trough concentrations may apply to organ transplants other than kidneys

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				- Samples are sent to VGH; allow time for results.

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Theophylline	Timing depends on route of administration and dosage form.	55-110 µmol/L		- See page 296 for more details on theophylline. - Samples are sent to VGH. Turn around time for STAT request is 2 hours. Please notify labe is stat levels will be required.
Tobramycin **(Extended interval)**	Pre: 18 – 24 hr after 2nd dose No peak level required	≤ 1 mg/L	**Initial:** pre level 18 – 24 hr after 2nd dose **Maintenance:** Pre: once weekly. Administer over 30 minutes	- If therapy is anticipated > 72 hours: ▪ Trough level prior to 3rd dose (18 – 24 hrs after 2nd dose) ▪ Administer 3rd dose ▪ Before giving 4th dose: - if level ≤ 1 mg/L: Administer next dose - if level > 1 mg/L: DO NOT administer next dose until pharmacy is consulted - For therapy beyond 7 days: ▪ Trough level weekly
Tobramycin **(Traditional dosing)**	Pre: 0-30 min. prior to next dose	0.6-2 mg/L	**Initial:** Pre & post with 3rd dose. (See Comments.) Maintenance: **Pre:** Once weekly in stable patients. **Pre & Post:** As required in patients with unstable renal function.	- No monitoring required for (patients with normal renal function): • uncomplicated UTIs • surgery prophylaxis < 72 hr • empiric therapy < 72 hr. - Half-life will be prolonged in patients with renal impairment.
	Post: 30 min. after end of infusion	5-10 mg/L		
	Cystic Fibrosis	10-15 mg/L		
Valproic Acid **(Depakene)**	Pre: 0-60 min. prior to next dose	350-700 µmol/L	**Maintenance:** Pre: Only if patient still has seizures. If toxicity is suspected, take sample at time of symptoms.	- t½ may be longer in patients with hepatic disease and may be shorter in patients receiving other anticonvulsant drugs. - Some patients may tolerate higher levels (>1000).

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Vancomycin	Pre: 0-30 min. prior to next dose	8-15 mg/L	**Initial:** Pre with 3rd dose (except in suspected renal impairment when pre & post would be helpful). Maintenance: **Pre:** Once weekly in stable patients. **Pre & Post:** As required in patients with unstable renal function. Consult with a clinical pharmacist	- Pre-level of 15-20 mg/L may be warranted for serious infections (eg meningitis, endocarditis, osteomyelitis, pneumonia) or when the infection is caused by an organism with a high MIC. - No monitoring required for (patients with normal renal function): •surgery prophylaxis < 72 hrs. •empiric therapy < 72 hrs. - t½ will be longer in patients with renal impairment. - In complete renal failure, patient may only need one dose per week.
	Post: 60 min. after end of infusion	20-40 mg/L		