

CRITICAL VALUES FOR THERAPEUTIC DRUG LEVELS

The concept of critical values for drug levels was originally developed by the late Daniel M. Baer, MD, and first published in the April 1982 issue of *MLO*. This table is an expanded version of that publication and newly revised for 2011-2012 by Yashpal Agrawal, MD, PhD; associate professor of Clinical Pathology and Laboratory Medicine; director, Central Laboratory; director Point-of-Care Testing Services; Department of Pathology and Laboratory Medicine, New York Presbyterian Hospital-Cornell Campus, New York, NY.

Drug	Indication	Therapeutic range	Critical Value	Comments
Acetaminophen	Analgesic	5-20 µg/mL	>200 µg/mL *drawn 4 hours after ingestion	Determination if a concentration is toxic is dependent upon when it is drawn in relation to the time of ingestion of the dose. Multiple serum concentrations will be needed to monitor improvement and removal of drug.
Amikacin	Antimicrobial	Peak: 15-30 µg/mL Trough: 4-8 µg/mL	>10 µg/mL	Peak: 30 min. after end of infusion. Trough: before next dose.
Amiodarone	Antiarrhythmic	0.5-2 µg/mL	>2.5 µg/mL	Trough concentration. Serum amiodarone levels >2.5 µg/mL had a positive predictive value of 76% for adverse drug events.
Amitriptyline	Antidepressant/analgesic (neuropathic pain)	125-250 ng/mL	>500 ng/mL	Trough concentration. Life threatening cardiac toxicity and/or seizures with concentration >1000 ng/mL.
Carbamazepine	Antiepileptic/mood stabilizer	4-12 µg/mL	>20 µg/mL	Trough concentrations preferred. Correlate serum concentration with clinical presentation.
Cyclosporine	Immunosuppressant	100-400 µg/mL	>500 µg/mL	Specific goal concentration dependent upon clinical situation. For concentrations drawn with intravenous therapy, blood should be drawn from site other than that where drug is infusing. (Cyclosporine adheres to plastic). TDM levels are dependent on transplant type. Blood concentrations can be method (immunoassay or mass spectrometry) dependent.
Digoxin	Inotrope, AV node blocker	0.8- 1.2 ng/mL* (immunoassay)	>2.5 ng/mL	Concentrations should be drawn >8 hours after last dose. *Concentrations >1.5 in heart failure patients may be associated with higher mortality. Consult assay instructions for potential interfering factors.
Doxepin	Antidepressant	110-250 ng/mL	>500 ng/mL	Trough concentration
Ethosuximide	Antiepileptic	40-100 µg/mL	>200 µg/mL	Trough concentration
Flecainide	Antiarrhythmic	0.2-1.0 µg/mL	>1.0 µg/mL	Midpoint or trough concentration. Monitoring recommended when given concurrently with medications that may decrease metabolism (increase concentrations).
Flucytosine	Antifungal	25-50 µg/mL	>100-200 µg/mL	Concentration should be a peak drawn 2 hours post dose.
Gentamicin	Antimicrobial	Peak 5-10 µg/mL Trough < 2 µg/mL	Peak > 12 µg/mL Trough > 2 µg/mL	Monitoring of serum levels is suggested in patients with height and weight that are much different from normals. Peak: 1 hour after infusion. Trough: before next dose
Imipramine	Antidepressant	>180-240 ng/mL	(>500 ng/mL)	Concentration = imipramine + desipramine(metabolite).
Lamotrigine	Antiepileptic/mood stabilizer	1-4 µg/mL	>20 µg/mL	Trough concentration. High concentrations generally associated with increased somnolence/confusion.
Lidocaine	Antiarrhythmic	1.5-5 µg/mL	>6 µg/mL	Concentration can be drawn at any point (from separate IV line)
Lithium	Mood stabilizer	Acute: 1-1.6 mEq/L Chronic: 0.6-1.2 mEq/L	>2.0 mEq/L >5 mEq/L potentially fatal	Serum concentrations may increase in presence of hyponatremia. Concentration: 12 hours after dose.
Nortriptyline	Antidepressant/analgesic (neuropathic pain)	50-150 ng/mL	>500 ng/mL	Trough concentration.
Phenobarbital	Antiepileptic	15-40 µg/mL	>60 µg/mL	Trough or mid-interval concentration.
Phenytoin	Antiepileptic	10-20 µg/mL	>40 µg/mL	Toxic >20 µg/mL Toxicity may occur at lower concentrations in presence of hypoalbuminemia. Consider free phenytoin.
Primidone	Antiepileptic	5-12 µg/mL	>15 µg/mL	Metabolized to Phenobarbital.
Procainamide (PA) (metabolite: NAPA)	Antiarrhythmic	PA: 4-8 µg/mL (NAPA: 10-20 µg/mL)	>10 µg/mL (>40 µg/mL)	Mid-point or trough concentration. Procainamide monitoring is particularly important in patients who might be fast acetylators (60% to 70% of northern Europeans, and 50% of black and white Americans) and in patients with renal impairment. Procainamide and N-acetylprocainamide levels always should be measured on the same sample.
Protriptyline	Antidepressant	70-250 ng/mL	>500 ng/mL	Trough concentration.
Quinidine	Antiarrhythmic	2-5 µg/mL	>6 µg/mL	Midpoint or trough concentration.
Salicylate	Analgesic/anti-inflammatory	10-30 mg/dL	>40 mg/dL	Serum concentration should be used in conjunction with clinical presentation to make decision on therapy. Multiple serum concentrations will be necessary to monitor improvement and removal of drug.
Sirrolimus	Immunosuppressant	5-15 ng/mL	>20 µg/mL	Trough concentration. Whole blood samples. Therapeutic levels can be lower when used in combination with other immunosuppressants. Blood concentrations can be method (immunoassay or mass spectrometry) dependent).
Tacrolimus	Immunosuppressant	5-20 ng/mL	>25 ng/mL	Trough: 12 hours after given dose. Whole blood samples. Therapeutic levels can be lower when used in combination with other immunosuppressants.
Theophylline	Bronchodilator	5-20 µg/mL	>25 µg/mL	Pulmonary literature suggest that concentrations 5-15 mg/L may be as efficacious with less toxicity. Trough or mid-interval concentration depending upon drug formulation.
Tobramycin		Peaks 4-8 µg/mL – standard 8-12 µg/mL–once daily Trough <1.0 µg/mL – standard <0.5 µg/mL– once daily		Goal concentration (peak and trough) dependent upon dosing method. Peak: 1 hour after end of infusion. Trough: before next dose.
Valproic acid	Antiepileptic/mood stabilizer	50-125 µg/mL	>200 µg/mL	Toxicity may occur at lower concentrations in presence of hypoalbuminemia. Consider free valproic acid. Trough concentration preferred.
Vancomycin	Antimicrobial	Trough concentrations: General: 10-15 µg/mL Pneumonia: 15-20 µg/mL	Trough >30 µg/mL	Monitoring of peaks no longer recommended. Goal trough concentration dependent upon indication. Trough: before next dose
Voriconazole	Antifungal	>0.25-1000 µg/mL	>6 µg/mL	Trough concentration preferred. Steady state achieved after 7 days of therapy.

Ranges are approximate and may vary with laboratory and/or assay.

Proper interpretation of therapeutic drug concentrations requires that the specimen be drawn at an appropriate time in relation to drug administration.