Guidelines for Monitoring Patients on Anticoagulation: It starts with a good sample

A Good Sample: All the tests discussed require blood in a blue top tube. These tubes contain a specific amount of sodium citrate for the designated amount of blood (1.8 cc or 2.7 cc) to give a ratio of 9:1 anticoagulant to blood. The larger tube is required for more than a simple PT/PTT. The vacuum of the tubes will aspirate the correct amount of blood. If the top is removed (not recommended) fill the tube to the level of the blue line. Underfilling the tube will make the results invalid. Overfilling may result in clotting. Citrate binds calcium in plasma. If the hematocrit is > 55%, the amount of plasma will not be appropriate. Ask the laboratory for a tube with the amount of citrate adjusted for the higher hematocrit. Venipuncture, with a needle no smaller then 23 gauge, is the recommended draw method. When drawing multiple tubes, the blue top tube should not be the first tube drawn. “Tissue factor,” released by a traumatic stick, activates coagulation. This problem is minimized in later tubes. If a winged collection set is used, the first tube drawn may be under-filled. Drawing through a heparinized line is the biggest problem. Heparin inhibits multiple coagulation factors resulting in a markedly elevated PTT. In high concentrations, heparin can even prolong the PT. It helps to “waste” some blood before drawing the specimen but this measure is seldom completely effective in eliminating the heparin effect. For two assays, PTT and Standard Heparin, the order screen asks how the specimen was obtained (line versus venipuncture) and if the patient is on heparin drip therapy. If the specimen was obtained from a line and the patient is not on heparin drip therapy, the laboratory will inactivate the heparin if the PTT is elevated and repeat the test.

Monitoring Coumadin (Warfarin): Coumadin inhibits vitamin K, a cofactor in the synthesis of coagulation factors II, VII, IX, and X, as well as proteins C and S. The net result is a prolonged PT. Coumadin is monitored with the INR, which is calculated from the PT in a manner that normalizes the result from lab to lab so that it is independent of the particular PT test reagent used: INR= (Patient PT/Mean normal PT)ISI. The international sensitivity index (ISI) is a measure of the sensitivity of a particular PT reagent and is calculated for each test reagent. The INR should fall from 2.5 to 3.5, depending on the patient’s diagnosis.

Monitoring Standard Heparin: Heparin inhibits coagulation factors II, IX, X, XI, XII, and probably VII. Its mechanism is to enhance the activity of antithrombin III. Therapeutic levels of heparin prolong the PTT. A value 1.5 to 2 times the upper limit of normal for the age of the patient is thought to be adequate. If the patient is not responding as expected, check the level of antithrombin III and/or directly measure standard heparin. This latter test is sent to St. Luke’s Hospital.

Monitoring Low Molecular Weight Heparin (LMWH). LMWH predominately inhibits factor Xa and does not significantly prolong the PTT. Laboratory monitoring may not be needed. However, if desired, monitoring is with anti-factor Xa assay with a therapeutic range of 0.5-1.0 IU/ml when drawn at four hours (peak level) after twice daily dosing.
News from the Toxicology Laboratory
by Uttam Garg, PhD

Drug Screens Offered in the CMH Toxicology Laboratory

For clinical use, Children’s Mercy Hospital’s Toxicology Laboratory offers various panels for screening drugs. Hopefully, the discussion below will help you to pick the right one.

Comprehensive Urine Drug Screen: This drug screen detects a large number of drugs (>200 drugs) and is useful in overdose situations when a history of drug ingestion is not known. The methods used include immunoassays, spot tests, thin layer chromatography, and gas chromatography-mass spectrometry. A partial list of drugs includes the following (some of the drugs may be detected only in an overdose): Acetaminophen, Alprazolam, Amantadine, Amitriptyline, Amobarbital, Anoxapine, Amphetamine, Benztropine, Bupivacaine, Bupropion, Butabarbital, Butalbital, Cannabinoids, Carbamazepine, Carisoprodol, Chlor Diazepam, Chlorpheniramine, Chlorpromazine, Clonazepam, Clomipramine, Cocaine, Codeine, Cyclobenzaprine, Desipramine, Dextromethorphan, Diazepam, Diphenhydramine, Disopyramide, Doxepin, Doxylamine, Egonine Methyl Ester, Ethotoxin, Fenfluramine, Flecainide, Fluoxetine, Flurazepam, Glutethimide, Guanafenesin, Hydrocodone, Imipramine, Ibuprofen, Ketamine, Lidocaine, Maprotiline, MDA, MDMA, Medazepam, Meperidine, Mephenytoin, Meprobamate, Methadone, Methamphetamine, Methaqualone, Methohexitol, Methsuximide, Methylphenidate, Methyprylon, Metoclopramide, Midazolam, Mirtazapine, Morphine, Nordiazepam, Norfluoxetine, Normeperidine, Norpropoxyphene, Nor triptyline, Olanzapine, Orphenadrine, Oxazepam, Oxycodone, Papaverine, Paroxetine, Pentazocine, Pentobarbital, Phencyclidine, Phenobarbital, Phensuximide, Phenyltoloxamine, Phenylpropanolamine, Procainamide, Propyclidine, Promethazine, Propoxyphene, Propranolol, Profenamine, Pseudoephedrine, Pyrilamine, Quinidine, Quinidine, Salicylates, Secobarbital, Sertraline, Temazepam, Theophylline, Thiopental, Timolol, Trimadol, Trazadone, Trimeprinone, Trimipramine, Triprolidine, Valproic Acid, Venlafaxine, Verapamil, and Warfarin.

Blood Drug Screen: The laboratory uses the same methodology for a blood drug screen as for a urine drug screen. Generally, concentrations of the drugs are much higher in urine than blood. In addition, the methods are better suited for urine. For example, benzodiazepine and opiates immunoassays are more sensitive to conjugated/glucuronide drugs in urine as compared to free drugs in blood. Therefore, the urine drug screen picks up more drugs than the blood drug screen. However, when quantitation of a particular drug is needed, such as Acetaminophen or Salicylates, blood is the sample of choice due to a better correlation between drug levels and toxicity.

Urine Drug of Abuse Screen: This screen includes Amphetamine/Methamphetamine, Barbiturates, Benzodiazepines, Cannabinoids (Marijuana), Cocaine/Cocaine Metabolites, Ethanol, Opiates, Phencyclidine, and Propoxyphene. Drug of abuse screening is done by immunoassays. It is important to keep in mind for drugs of abuse that the results by immunoassays are presumptive only. Due to cross-reactivity with other drugs, results may be falsely positive. For faster turnaround time and for rapid clinical intervention, the laboratory releases these presumptive results as soon as possible. Confirmation of these drugs by gas chromatography-mass spectrometry takes several hours to days. Therefore, before talking to a patient or parent about drug abuse, it is important to confirm the drug in question or to discuss the limitations of the methodology. On the other hand, the immunoassays for a group of drugs, such as benzodiazepines and opiates, are sensitive to some drugs in the group and insensitive to others. In addition, depending on the dose and metabolism, concentrations of two drugs in urine may be quite different. For example, Diazepam dose may be 10 times higher than Clonazepam. Opiate assays are more sensitive to Morphine and Codeine than to Oxycodone and Hydrocodone. This can produce falsely negative results. Call the Toxicology Laboratory (816-234-3295) if you have a question about a particular drug.