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MICROBIOLOGY

***Klebsiella Pneumoniae* Carbepenemase (KPC) Organisms:** MCCG Microbiology Department has recently isolated its first KPC producing organisms. KPC is the acronym for *Klebsiella pneumoniae* carbapenemase. What is KPC? Carbapenemase is an enzyme first identified in Klebsiella pneumoniae isolates. Its gene is carried on a plasmid with a class A beta-lactamase, and the plasmid enhances transfer to organisms including Serratia spp, Enterobacter spp, E. coli, *Salmonella enterica* and even Pseudomonas sp. KPC organisms are resistant to all penicillins, cephalosporins, carbapenems, and aztreonam. Treating their infections is therefore very difficult with very few antibiotics effective. Who is at risk? Further studies are needed to confirm risk factors, but available data indicate patients receiving long courses of broad spectrum antibiotics and those with prolonged ICU stays. Previously at MCCG, if a KPC producing organism was suspected, an isolate was forwarded to the Centers for Disease Control for PCR confirmatory testing (~6 wks). The Microbiology Department is currently in the process of validating the modified Hodge test for in house KPC identification, which will decrease turn around time to <72 hours. The patient's physician and Infection Control are currently notified if a KPC infection is suspected as well as when confirmation is obtained.

References:
1. Quale, J. Global spread of Carbapenemase-producing Klebsiella pneumoniae. Microbe 3(11), 2008.
2. Hospital Epidemiology and Infection Control, The Johns Hopkins Hospital

HEMATOLOGY

Fondaparinux Assay: Effective June 15, 2009 the Laboratory will offer an Anti-Factor Xa activity assay for the assessment of fonduparinux (Arixtra®) levels in blood. This assay is similar to that used for assessment of low molecular weight heparin (LMWH) using fondaparinux sodium as calibrators expressed in mg/L. The detection limit is 0.10 mg/L. Laboratory therapeutic ranges are not well established at this time. Therefore PDR Guidelines will be provided. 1. Once daily prophylactic 2.5 mg injections provide an average peak plasma concentration at 3 hr post dose of 0.39 - 0.50

mg/L with a minimum of 0.14 – 0.19 mg/L. 2. Patients with symptomatic DVT and PE, receiving between 5 mg to 10 mg dependent on body weight, the observed mean peak plasma concentration is reported to be 1.20 – 1.26 mg/L with a minimum range of 0.46 to 0.62 mg/L. See Anticoagulation Guidelines below for additional information.

The assay will be performed once daily Monday – Sunday with a cut-off time of 1:00 p.m. for same day analysis.

Guidelines for Monitoring Anticoagulation Therapy:

Updated recommendations for monitoring anticoagulation therapy are available on the laboratory MCCG intranet site or from the Hematology section of the laboratory. Guidelines are as follows:

TESTS FOR ORAL ANTICOAGULANT THERAPY - WARFARIN (COUMADIN®)
PT/INR
The INR is a calculated index of the prothrombin time (PT) used to monitor oral anticoagulation. The following are recommended guidelines for oral anticoagulation use:

Indications	Recommended INR
Prophylaxis of venous thrombosis (high-risk surgery)	2..0 – 3.0
Treatment of venous thrombosis	2.0 – 3.0
Treatment of PE	2.0 – 3.0
Prevention of systemic embolism	2.0 – 3.0
Tissue heart valves	
AMI (to prevent systemic embolism)*	
Valvular heart disease	
Atrial fibrillation	
Bileaflet mechanical valve in aortic position	2.0 – 3.0
Mechanical prosthetic valves (high risk)	2.5 – 3.5

The recommended therapeutic target range for most patients and patients with Lupus inhibitor is an INR of 2.0 to 3.0.

*If oral anticoagulant therapy is elected to prevent recurrent MI, an INR of 2.5 to 3.5 is recommended, by the US Food and Drug Administration.

TESTS FOR UNFRACTIONATED HEPARIN THERAPY

1. Activated Partial Thromboplastin Time (aPTT)
The laboratory's determined heparin therapeutic range for PTT reagent lot # 102005 is 70 – 116 seconds. This range corresponds with approximately 0.3 – 0.7 IU/ml of Xa.

2. Heparin Assay (Anti-Xa Assay)
Heparin Xa levels would be measured in situations such as but not limited to patients with heparin resistance, prolonged baseline aPTT due to lupus anticoagulants, factor deficiency or oral anticoagulant therapy. In these cases monitoring with an anti-Xa assay is appropriate and provides a better indication of plasma heparin levels.
The target therapeutic range for UFH is 0.30 – 0.70 IU/ml

TESTS FOR LOW MOLECULAR WEIGHT HEPARIN THERAPY (LOVENOX®)
Heparin Assay (Anti-Xa Assay)
Heparin Xa levels would be measured in situations such as but not limited to patients with renal insufficiency, women during pregnancy, children, newborn infants, patients being treated over a prolonged period, or patients who are markedly obese (>150 kg) or have low body weight.

The therapeutic range for LMWH is 0.50 – 1.00 IU/ml
The prophylactic range for LMWH is 0.10 – 0.30 IU/ml

TESTS FOR FONDAPARINUX THERAPY (ARIXTRA®)
Fondaparinux Assay (Anti-Xa Assay)
Plasma fondaparinux concentrations are monitored using the anti-Xa assay that has been calibrated using fondaparinux. The results are reported in gravimetric units (mg/L).

Clinical monitoring with plasma fondaparinux concentrations or anti-Xa activity is not necessary for most patients, due to low inter- and intra-subject variability in the pharmacokinetics of fondaparinux.

Heparin Xa levels would be measured in situations such as but not limited to patients with renal impairment. Fondaparinux elimination is prolonged in patients with renal impairment and fondaparinux is contraindicated in patients with severe renal dysfunction (CrCL <30mL/min). Such patients are at increased risk for major bleeding episodes. Also, total clearance of fondaparinux sodium is decreased by approximately 30% in patients weighing less than 50 kg and approximately 25% lower in patients over 75 years old as compared to patients less than 65 years old.

Peak plasma concentrations should be obtained at approximately 3 hours post-dosing.
The therapeutic range for fondaparinux (Arixtra®) is 0.62 – 1.26 mg/L
The prophylactic range for fondaparinux (Arixtra®) is 0.39 – 0.50 mg/L

TESTING FOR DIRECT THROMBIN INHIBITORS
Activated Partial Thromboplastin Time (aPTT)
The target range for anticoagulation with direct thrombin inhibitors is the laboratory's determined heparin therapeutic range for PTT (reagent lot # 102005) which is 70 – 116 seconds. This range corresponds with approximately 0.3 – 0.7 IU/ml of Xa.

EVALUATING VENOUS THROMBOEMBOLISM
D-Dimer
D-Dimer is a specific marker of the breakdown of a cross-linked fibrin clot (i.e., fibrinolysis) and an indirect marker of clot formation. D-Dimer levels will be elevated after clot formation and lysis in a wide variety of conditions known to be associated with the activation of coagulation such as surgery, trauma, hematoma, pregnancy, pre-DIC and DIC conditions, etc.

A cut-off value of 0.50 µg/mL FEU for the lab's D-Dimer method has been shown to provide a negative predictive value within the 95% to 100% range for deep vein thrombosis (DVT) and a negative predictive value within the 98% to 100% range for pulmonary embolism (PE).

References:
1. Chest**,** Hirsch et.al, American College of Chest Physicians,119:8-21, 2001.
2. Francis, C.W., Berkowitz, S.D., Consultative Hemostasis and Thrombosis. Philadelphia: W.B. Saunders Co., 2002; 378-379

3. Turpie AGG. Use of selective Factor Xa inhibitors in special populations. Am J Orthoped 2002;31(Suppl 11):1115.