

## New assays detect MRSA, enterovirus in CSF and more



*Patricia Ferrieri, M.D.*

### PROFESSOR HONORED FOR APPOINTMENT

**Patricia Ferrieri, M.D.**, professor, Department of Laboratory Medicine and Pathology, was honored at a reception this summer for her 2006 appointment to the newly established Chairman's Fund Endowed Professorship in the Department of Laboratory Medicine and Pathology. Ferrieri was selected for her years of leadership within the department and the university. In 2005, she received the President's Award for Outstanding Service from University of Minnesota for her dedication to clinical medicine through her responsibilities in pediatric infectious diseases at University of Minnesota Medical Center, Fairview.

### New assay detects *Clostridium difficile* toxins A and B

A new enzyme immunoassay that detects both toxins A (enterotoxin) and B (cytotoxin) in fecal specimens has been optimized for a new automated ELISA instrument. The ability to detect both toxins will enhance patient care. In contrast to the previous toxin A assay, the new assay also detects toxin B. Nationally, approximately 3 percent of *Clostridium difficile* isolates express only toxin B. Since the assay does not distinguish the toxins separately for reporting, the report will indicate positive for toxins A and/or B or negative for toxins A and B. The laboratory will continue to culture for *C. difficile* according to national guidelines. The lab performs the assay twice a day.

### MRSA by real-time PCR

Some U.S. hospitals are using real-time polymerase chain reaction (PCR) detection of methicillin-resistant *Staphylococcus aureus* (MRSA) for newly admitted patients upon request. This assay, using MRSA colonized from swabs of patients' anterior nares, is based on amplification of a sequence of the staphylococcal chromosome cassette *mecA* gene that mediates methicillin resistance. In contrast to microbiologic culture, real-time PCR provides a rapid turn-around time.

The Centers for Disease Control and the Minnesota Department of Health are finalizing recommendations for determining which high-risk patients should be screened at hospital entry for MRSA (either by real-time PCR or culture). High-risk groups include surgical patients, those admitted to medical or surgical intensive care units, infants in neonatal intensive care units, pregnant women admitted in labor and nursing home patients. Hospitals screening high-risk patients report a dramatic decline in hospital-associated MRSA infections—resulting in shortened hospital stays and financial savings. Experts recommend patients blow or clear their noses before the sampling to prevent mucus interference with the assay. Other body site samples will not be tested, since the assay is FDA-approved only for anterior nares. The laboratory will perform the assay in batches twice daily.

### Assay detects enterovirus in CSF

Using reverse transcription-PCR (RT-PCR) in real-time, the laboratory will start testing cerebrospinal fluid (CSF) only for this RNA virus. The test amplifies and detects the untranslated region (UTR) between nucleotides 452-596 of the enterovirus genome. The assay permits detection of

all enteroviruses, including polioviruses, coxsackie A and B viruses, echoviruses and the more newly designated, numbered enteroviruses. This test offers particular value during epidemic enterovirus meningitis/meningoencephalitis in the summer and fall, as well as during episodic infections that occur off-season. The assay is FDA-approved only for CSF samples. The laboratory performs the assay daily, upon request.

### Laboratory offers emergency rapid screening for malaria

For emergency purposes only, the laboratory is offering a malaria screening assay for the qualitative detection of *Plasmodium falciparum* and pan-malarial antigens (common to *P. vivax*, *P. ovale*, and *P. malariae* species). This immunochromatographic assay is expensive and has been released only to those laboratories prepared to correlate the result with precise identification of malaria species microscopically, with quantitation. Giemsa-stained thin and thick blood smears, the current test, will serve as quality control of the assay. The new assay is not a stand-alone test, nor does it convey the level of parasitemia

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# Special Coagulation Laboratory to offer PAI-1 test

**P**lasminogen activator inhibitor 1 (PAI-1) is a regulatory protein of the fibrinolytic system, regulating fibrinolysis by decreasing the production of plasmin.

After clot formation, endothelial cells release tissue type plasminogen activator (tPA) or urokinase-like plasminogen activator (uPA). Both tPA and uPA convert plasminogen to its active form, plasmin. Plasmin dissolves clots and maintains vessel patency. PAI-1 is the primary physiological inhibitor of tPA and uPA *in vivo*, promoting the formation of stable thrombi.

PAI-1 is produced primarily in the liver, but adipose tissue, endothelial cells and platelets also contribute significantly to plasma concentration. PAI-1 is an acute-phase reactant; levels rise after severe trauma or sepsis, during pregnancy and in inflammatory diseases or DIC secondary to cytokines and hormones (e.g., IL-1, TNF- $\alpha$ , TGF- $\beta$  and insulin).

PAI-1 promotes cell migration and is involved in tissue remodeling, neointima formation and deposition of extracellular matrix. PAI-1 may have a pathogenic role in the development of atherosclerosis. Numerous studies also have

shown that low fibrinolytic activity precedes cardiovascular disease. High tissue PAI-1 levels indicate a poor prognosis in various types of cancers.

Patients with PAI-1 deficiency tend to bleed after trauma, surgical procedures or dental extraction. Patients with <3 AU/mL results should repeat the test with a new fasting, early morning sample. If the PAI-1 level remains <3 AU/mL in the second sample, then elevated t-PA activity can confirm clinically significant PAI-1 deficiency.

Normal ranges: 3-37 AU/ml

Collecting samples: fasting, early morning plasma can be assayed for two hours after

collection if kept at 2-8 °C, or for one month if kept at -20 °C.

#### References:

1. Thrombosis Haemostasis 2004; 91;425-37
2. Thrombosis Haemostasis 2005; 93;631-40
3. British Journal of Haematology 2004; 125:12-23

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*Clinical Microbiology from cover* provided by the traditional Giemsa-stained smears.

The assay's sensitivity is highest at very high levels of parasitemia, and is much lower for low levels of parasitemia with *Plasmodium falciparum*. The sensitivity and specificity for *Plasmodium vivax* is lower than that for *Plasmodium falciparum*. Experts recommend that the test be used only by laboratories that can acquire blood samples containing *Plasmodium falciparum* to use as a positive control. To perform the assay, the laboratory needs to receive venous blood in an EDTA tube, as well as three unstained thin and three unstained thick blood smears, as soon as possible after collection. The laboratory will monitor the rationale for requesting the emergency test.

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## Microalbumin vs. albumin, and more

- The terms **microalbumin** and **albumin** are sometimes used interchangeably in the literature, causing confusion about what assays are measuring. While assays for microalbumin and albumin both measure albumin, those for microalbumin are more sensitive. The term microalbumin was introduced with testing that could measure very small amounts of albumin in urine. Current recommendations from the American Diabetes Association define cut-off values for random urine albumin-to-creatinine ratio for microalbuminuria and

albuminuria as 30 mg/g and 300 mg/g, respectively, without regard to gender. Fairview laboratories currently are flagging all results greater than 20 mg/g as abnormal. According to the National Kidney Foundation's K/DOQI Clinical Practice Guidelines, the prevalence of microalbuminuria and albuminuria is approximately 30 percent in adults at age  $\geq$  70 years—26.6 percent with microalbuminuria and 3.7 percent with albuminuria. At all ages, the prevalence is higher among individuals with diabetes. At age  $\geq$  70 years, the prevalence among adults with a history of diabetes is 43.2 percent and 8.4 percent, respectively.

- **Patient charges for laboratory tests** now are available on the Fairview intranet. Click on Laboratory Services in the left menu box and type in the desired test name. Look for pricing information and CPT code at the bottom of the page.
- **The Riverside campus's Acute Care Laboratory** is providing supplies and sample testing for a new free clinic now open in the Phillips Neighborhood. Medical residents staff the operation, which is funded by the University of Minnesota, Department of Medicine. At the start of their shifts, residents pick up phlebotomy supplies for point of care testing, and drop off samples at the laboratory at the end of their shifts.