

Lab Updates

October 2008

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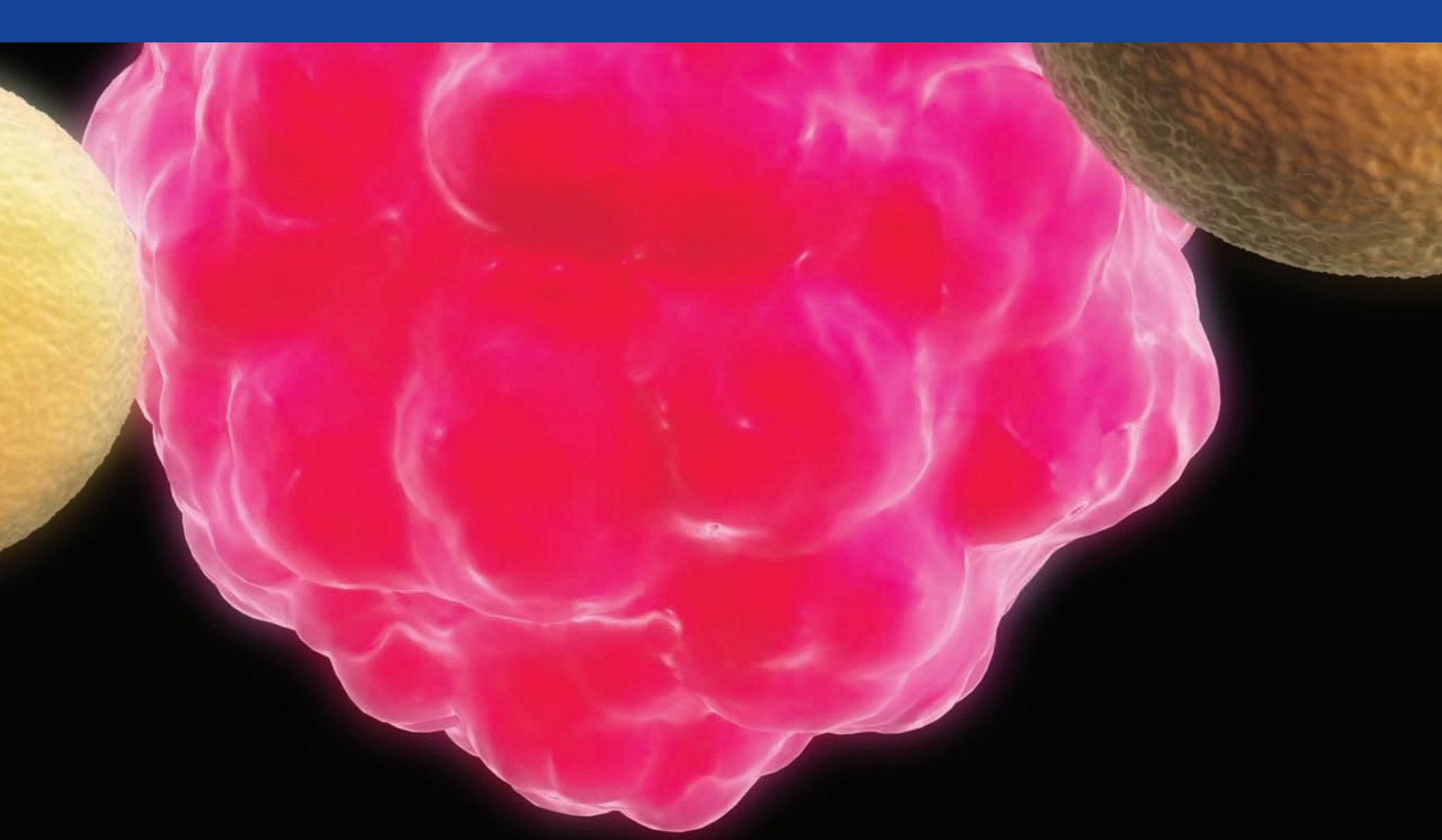
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New Immunoassay Based Fecal Occult Blood Test (FIT)

UMass Memorial Medical Center Laboratories

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IN THE UNITED STATES, **COLORECTAL CANCER (CRC)** is the third most common cancer diagnosed among men and women and the second leading cause of death from cancer. CRC largely can be prevented by the detection and removal of adenomatous polyps, and survival is significantly better when CRC is diagnosed while still localized.

Today there is a range of options for CRC screening in the average-risk population, with current technology falling into 2 general categories:

- **Stool tests**, which include tests for occult blood or exfoliated DNA; and
- **Structural exams**, which include flexible sigmoidoscopy (FSIG), colonoscopy, double-contrast barium enema (DCBE), and computed tomographic colonography (CTC).

Stool tests are best suited for the detection of cancer, although they also will deliver positive findings for some advanced adenomas, while the **structural exams** can achieve the dual goals of detecting adenocarcinoma as well as identifying adenomatous polyps. These tests may be used alone or in combination to improve sensitivity or, in some instances, to ensure a complete examination of the colon if the initial test cannot be completed.

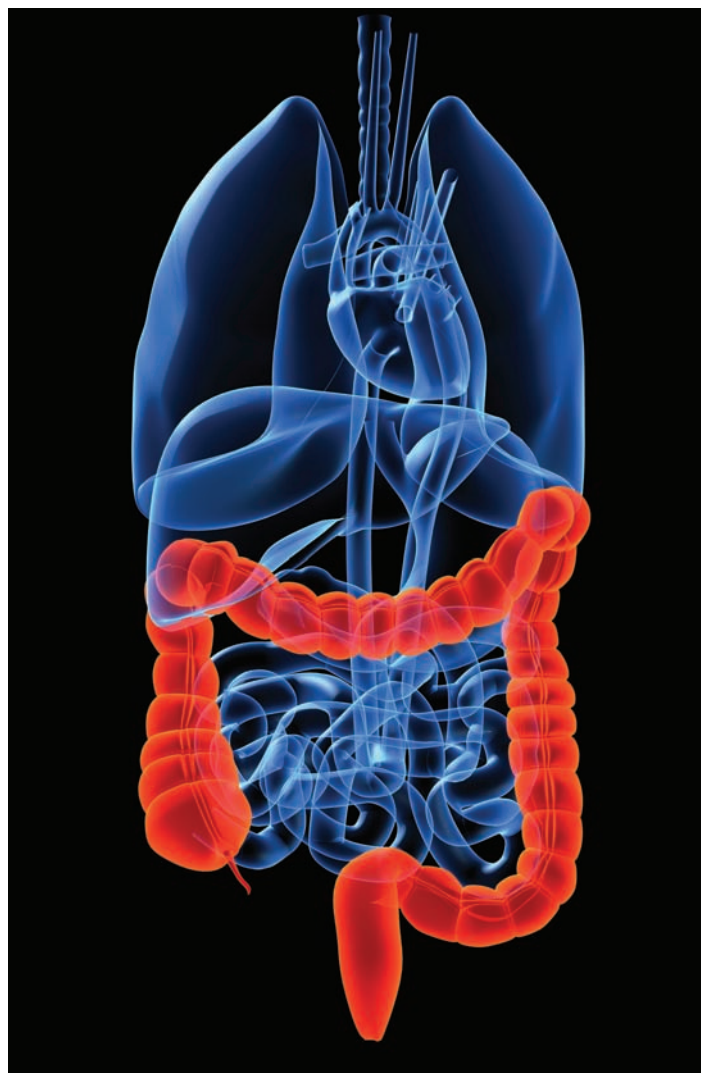
Guidelines for screening and surveillance for the early detection of adenomatous polyps and CRC in average risk adults have been updated in a consensus process that included American Cancer Society (ACS), US Multi-Society Task Force (USMSTF) on CRC and American College of Radiology¹. In this update of guidelines, the expert panel concluded that a screening test must be able to detect the majority of prevalent or incident cancers at the time of testing. It is the strong opinion of this expert panel that *colon cancer prevention* should be the primary goal of CRC screening. Tests that are designed to detect both early cancer and adenomatous polyps should be encouraged if resources are available and patients are willing to undergo an invasive test.

The panel recognized that some patients will not want to undergo an invasive test that requires a bowel preparation, may prefer to have screening in the privacy of their home, or may not have access to the invasive tests due to lack of coverage or local resources. Collection of fecal samples for blood or DNA testing can be performed at home, without bowel preparation. However, providers and patients should understand the limitations and requirements of noninvasive tests:

Stool Blood Tests

Stool blood tests are conventionally known as fecal occult blood tests (FOBT) because they are designed to detect the presence of occult blood in stool. FOBT fall into 2 primary categories based on the detected analyte: **Guaiaic based (gFOBT)** and **Immunoassay based (FIT)**.

The **gFOBT** are the most common stool blood tests in use for CRC screening and they detect blood in the stool through the pseudoperoxidase activity of heme or hemoglobin, while immunochemical-based tests react to human globin. Prior to testing with a sensitive guaiac-based test, individuals usually will be instructed to avoid aspirin and other nonsteroidal anti-inflammatory drugs, vitamin C, red meat, poultry, fish, and some raw vegetables because of diet-test interactions that can increase the risk of both false-positive and false-negative (specifically, vitamin C) results. The sensitivity and specificity of a gFOBT has been shown to be highly variable and varies based on the brand or variant of the test; specimen collection technique; number of samples collected per test; whether or not the stool specimen is rehydrated and variations in interpretation, screening interval, and other factors. This test must be performed properly with 3 stool samples obtained at home. A single-stool sample FOBT collected after digital rectal exam in the office is not an acceptable screening test, and it is not recommended.



FIT (Immunoassay based) has several technological advantages when compared with gFOBT. **FIT** detects hemoglobin, thus is more specific for human blood than guaiac-based tests, which rely on detection of peroxidase in human blood and also react to the peroxidase that is present in dietary constituents such as rare red meat, cruciferous vegetables, and some fruits. Further, unlike gFOBT, FIT is not subject to false-negative results in the presence of high-dose vitamin C supplements, which block the peroxidase reaction. In addition, because globin is degraded by digestive enzymes in the upper gastrointestinal tract, FIT also are more specific for lower gastrointestinal bleeding, thus improving their specificity for CRC. Finally, the sample collection for some variants of FIT are less demanding of patients than gFOBT, requiring fewer samples or less direct handling of stool.

At this time, the optimal number of FIT stool samples is not established, but 2 samples may be superior to one. Annual screening with FIT that have been shown in the published, peer-reviewed literature to detect a majority of prevalent CRC in an asymptomatic population at the time of testing is an acceptable option for CRC screening in average-risk adults aged 50 years and older. Any positive test should be followed up with colonoscopy. Adults should be informed that annual testing is necessary to achieve the fullest potential of this test and that they will need follow-up colonoscopy if test results are positive.

This immunoassay based test offers several benefits over card based tests, which includes,

- No dietary or medication restrictions required.
- Easy single sample collection (Each single use kit contains easy to understand instructions and patient friendly collection device.
- Improved patient compliance.
- Fewer false positive results.

Effective October 20, 2008, UMass Memorial Laboratories will be performing this automated immunoassay based fecal occult blood test (FIT). This procedure will replace our existing guaiac card methodology performed in the laboratory. Please

submit a single sample from one stool specimen collected in the sampling bottle provided in the kit. Samples may be obtained during routine physical exam or by use of personal pack for home collection provided by the laboratory. The transportation of the sample to the laboratory can be by routine courier pick up for the physician office/site or via US mail in the provided mailer. Once collected the specimen is stable up to 14 days refrigerated or 7 days at room temperature. Testing will be performed routinely in the hospital labs on a daily basis.

1 Bernard Levin et al. "Screening and Surveillance for the Early Detection of Colorectal Cancer and Adenomatous Polyps, 2008:" *A Joint Guideline from the American Cancer Society, the US Multi-Society Task Force on Colorectal Cancer, and the American College of Radiology. CA Cancer J Clin*, May 2008; 58: 130-160.

If you have questions, comments or suggestions, please contact:

Dr. L.V. Rao, Director at 508-334-7593 or via email at Raol@ummhc.org

Ms. Judy Rennell, Manager at 508-334-3803 or via email at Rennellj@ummhc.org



Sample Preparation for Uric Acid Testing in Patients Receiving Rasburicase (ELITEK) Therapy

Rasburicase (ELITEK) is a recombinant urate oxidase enzyme, indicated for the initial management of plasma uric acid levels in pediatric patients with leukemia, lymphoma, and solid tumor malignancies who are receiving anticancer therapy expected to result in tumor lysis and subsequent elevation of plasma uric acid.

ELITEK will cause enzymatic degradation of uric acid within blood samples left at room temperature resulting in spuriously low uric acid levels. To ensure accurate measurements in patients who have received rasburicase, blood must be collected into pre-chilled tubes containing heparin anticoagulant and immediately immersed and maintained in an ice bath; plasma samples must be assayed within 4 hrs of sample collection. Please call the lab in advance to alert, when the sample needs to be tested.

If you have questions, comments or suggestions, please contact:

Dr. L.V. Rao, Director at 508-334-7593 or via email at Raol@ummhc.org

Ms. Judy Rennell, Manager at 508-334-3803 or via email at Rennellj@ummhc.org



New IgG Based ELISA Assay for Diagnosis of Heparin-Induced Thrombocytopenia (HIT)

Heparin induced thrombocytopenia (HIT) is a frequently suspected diagnosis, especially in the setting of hospitalized patients anticoagulated with heparin. It is primarily a clinical diagnosis. The diagnostic interpretation of laboratory tests must be made in the context of the clinical estimation of the pretest probability of HIT¹. A high probability of HIT exists when Warkentin's 4 Ts criteria are present:

1. a fall in platelet count by 50%,
2. the fall takes place between days 5 and 14 (inclusive) after initiating heparin therapy,
3. new thrombosis, and
4. no other cause for the drop in platelet counts.

The presently available assays are sensitive in detecting HIT antibodies, but none is completely specific for the HIT syndrome, i.e. negative tests have a very low likelihood ratio for the presence of HIT. The HIT assay (PIFA) that our lab offers presently has a good negative predictive value; unfortunately its specificity is low, hence the positive results have to be retested by the serotonin release assay (SRA). The SRA is a test with a TAT of 7-10 days hence not very useful in clinical situations where decisions are made based on the HIT results. **The physician who orders the SRA should understand that it is not a STAT test.**

We have validated a new ELISA HIT assay. This assay is specific for IgG HIT antibodies and has very high negative and positive predictive values (the ELISA has a 99.5% negative predictive value according to the manufacturer). The results will be reported in **optical density (OD)** units. The ELISA will be performed in the Hematology lab three times a week: Mondays-Wednesdays-Fridays (except holidays). All negative ELISA results will be reported on the day of their performance. The positive results however will need a confirmatory test using excess heparin, thus delaying the report until further batches of ELISAs are done. Turnaround time for a **positive** ELISA assay is 5-7 days. Negative results will be reported the same day the assay is performed.

The OD cut off for negative results will be <0.4 OD, i.e. all results <0.4 will be interpreted as **negative**. OD results between **0.4-1.4** should be interpreted as **positive**, and those >1.4 as **strongly positive**. The ELISA assay will go live on **September 29, 2008**.



Whenever an HIT assay is ordered, the lab will:

1. Perform PIFA (done Monday through Friday from 7am to 11pm, except holidays); if negative, **HIT is excluded**; no additional testing is recommended.
2. If PIFA is positive the result will be reported as "pending ELISA" and the new ELISA HIT assay will be performed without the need of reordering it. **Negative ELISA results exclude the diagnosis of HIT** in the vast majority of cases.
3. If the ELISA is positive, especially with a high OD and a high clinical suspicion, a serotonin release assay may be ordered if clinically indicated.

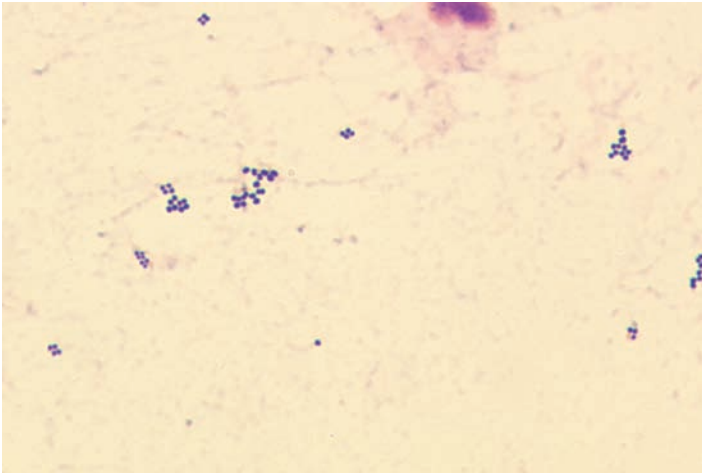
Please note that specimen requirements have not changed. Please obtain a red top tube (serum) spun and separated from red cells within one hour of drawing. The specimens must be received refrigerated

1. Warkentin et al. *Chest* 2008;133:340S-380S).

If you have questions, comments or suggestions, please contact:
Dr. Liberto Pechet, Directory of Hematology at 508-334-0265 or
via email at pechetl@umhmc.org



Methicillin-Resistant *Staphylococcus aureus* Detection—Two Choices



Detection of methicillin-resistant *Staphylococcus aureus* (MRSA) is critical for patient care. **There are two different types of MRSA detection in the laboratory:**

First, and most obviously, is for patients with an infected source. MRSA infections are diagnosed using routine bacterial cultures. MRSA strains are very robust and MRSA infections are efficiently diagnosed using routine bacterial cultures of wound, respiratory, tissue, urine, blood and other types of specimens. In routine bacterial cultures, the identification of any isolate that resembles SA is confirmed and, if positive, susceptibility testing is performed to rule-out MRSA. **Screening tests to rule-out MRSA need not be ordered to detect MRSA in infected tissues.**

The second role for MRSA detection is the identification of asymptomatic MRSA carriage in patients at risk for infection or who may be a source of MRSA transmission to others. MRSA carriage is diagnosed using Rule-out MRSA mnemonic = MRSACUL) test. The most common sites of MRSA carriage are the mucus membranes of the anterior nares. A single swab can be used to sample both the right and left anterior nasal membranes. The anterior nasal culture will be positive in ~95% of MRSA carriers. There may be a slight increase in the detection of MRSA by collecting cutaneous swab specimens of the axillae or groin/perineal sites.

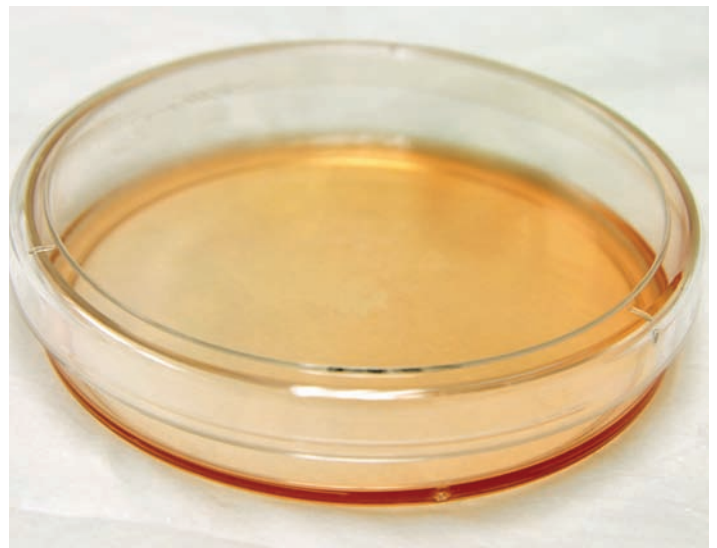
Patients with prior MRSA infection may become carriers in spite of successful therapy of the infection. Detection of MRSA carriage in these patients is also most effectively detected by sampling anterior nasal specimens. Submission of previously infected tissues for the test “Rule-out MRSA” does not significantly improve detection of carriage. If there is evidence of ongoing infection at the site of previous infection, routine bacterial cultures should be submitted.

Background:

Staphylococcus aureus (SA) is an organism well armed with virulence factors that make it a potent human pathogen. SA causes a wide range of infections, from superficial skin infections to life-threatening systemic infections. SA strains can easily colonize the skin and mucus membranes of normal people without causing any symptoms. These strains can then be passed from person to person. Colonization is the usual first step in the progression to infection in susceptible individuals.

In the early 1960s, SA strains were isolated which were resistant to methicillin, and related antibiotics. Since then, MRSA has become firmly established as a major cause of nosocomial infections in health-care institutions. Recently, infections caused MRSA strains have been identified in patients who have had no significant exposure to health-care settings. These community-acquired strains seem to be genetically different than the usual MRSA strains associated with nosocomial infections, but they are detected using the same techniques.

Summary: Order routine bacterial cultures to detect the presence of MRSA and other pathogens for infected material. Order (ROMRSA) screening test to detect the presence of MRSA only.



If you have questions, comments or suggestions, please contact:

Brenda Torres, Manager at 508-334-3429 or via email at torresb@ummhc.org

Microbiology Laboratory at 508-334-2891 with questions related to MRSA detection.





Tips for a Successful Coagulation Blood Draw

Store empty blue coagulation tube between 39°-77° F.

Check your tubes. Never draw using expired tubes. The date of expiration is located on the label of the tube.

Always draw a discard tube when using a winged blood collection set (butterfly). Air will fill the tube if this is not done and the blood volume in the tube will be short.

Order of draw - blood culture tubes, coag tubes, serum tubes, heparin tubes, EDTA tubes, grey tubes

Gently invert all tubes 6-8 times.

Coag tubes must be filled to the black line on the side of the label. Inadequate filling of the tube causes inaccurate results. (see card).

If you have questions, please contact:

Diane Connor, Manager Hematology at 508-334-7153 or via email at connord@ummhc.org.

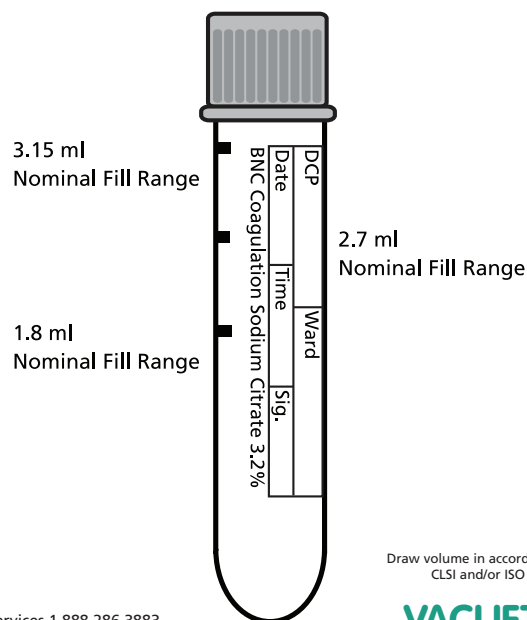


Coagulation Draw Volume Guide

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Take the Guesswork Out of It

Ensure that the correct blood to additive ratio is met by checking the draw volume against the nominal fill mark on the tube or by holding tube up to this guide.



Draw volume in accordance with CLSI and/or ISO Standards

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- To be one of the top ten academic medical center-based laboratories in the United States



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Dartmouth PSC is located at 72 State Rd., Dartmouth, MA.
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