Saint Luke's REGIONAL LABORATORIES

Clinical Laboratory News

September/October 2015

Urine Reflex Cultures: New Process, Improved Clinical Utility

Appropriate antibiotic therapy for urinary tract infection can be delayed in the time period between receipt of an abnormal urinalysis result by a clinician, and ordering of a urine culture. Likewise, unnecessary urine cultures may be requested based on symptoms and prior to receipt of a normal urinalysis result. For these reasons, the 'UA reflex' order which allows the lab to only perform urine culture if criteria suggestive of infection is found on the urinalysis, has been available to physicians for several years.

A review of SLHS data revealed many contaminated urine samples were still set up for culture, using the original UA reflex criteria. Based on a literature search, and analysis of SLHS data, the laboratory has modified criteria for urine specimens reflexed to culture to include the following:

UA Reflex criteria that trigger a culture
Nitrite = Positive
WBC $\geq$ 11
WBC = 6-10 **and** Protein $\geq$ 30

Of note, the use of leukocyte esterase as reflex criterion was found to be non-specific. Urine culture testing based on the microscopic WBC count, along with the other parameters, resulted in elimination of 43% of contaminated urine cultures, and 20% of urine cultures overall without missing any true positive urine cultures.

Urinalysis findings that will result in a microscopic exam are unchanged, and include:

Urinalysis criteria that trigger a microscopic exam
Hemoglobin ≥ small
Protein $\geq$ 100
Leukocyte Esterase = Positive
Nitrite = Positive

Physicians are encouraged to use the urine reflex order for most patients in which a urinary tract infection is being considered. For patients on whom a urine culture result is essential regardless of urinalysis results, such as renal transplant, urologic or obstetric patients, the current stand-alone urine culture order is still available for use. Please note that if a urine culture has already been ordered within a 72 hour period, a second UA reflex order will not reflex another culture.

Inpatient GI Panel Testing

Testing for community-acquired gastrointestinal pathogens, such as Salmonella and Giardia, on patients who develop diarrhea while hospitalized has not been recommended for many years. The likelihood is higher that those patients may have Clostridium difficile-associated diarrhea. Since 1999, Microbiology has not performed cultures or parasite testing on stool samples submitted from patients hospitalized longer than 3 days. Likewise, the Gastrointestinal Pathogen Panel PCR is not performed on inpatients hospitalized for longer than 3 days. Clostridium difficile toxin gene PCR is the test of choice in this circumstance. Stool samples are held for 7 days, in the event that further testing is warranted, such as for patients who are immunocompromised or who were symptomatic prior to admission.

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Molecular Testing in Hematological Malignancies

With the advent of sequencing, newer mutations are being identified and added to the ever growing list of genetic/molecular lesions associated with malignancy. These lesions may be actionable and a target for new drug discovery or may have a prognostic/diagnostic role. Many of these lesions can be identified by chromosome analysis or karyotype. In suspected hematological malignancies, peripheral blood or preferably bone marrow aspirate should be submitted for testing. Genetic lesions, if present, are identified and reported. Over the years genetic lesions pathognomic of certain cancers/neoplasm have been identified. Following are examples of such lesions:

1. *PML/RARA* t(15;17): is a protein generated as a result of fusion of retinoid acid receptor alpha gene on chromosome 17 (RARAα) with transcriptional factor gene on chromosome 15 (PML). RARAα protein is normally involved in the regulation of protein transcription, especially those involved in differentiation and maturation beyond promyelocyte stage in myelopoiesis. PML protein, on the other hand, is a known tumor suppressor that regulates uncontrolled or rapid growth of a cell. The fusion protein generated interferes with normal functioning in the neoplastic cell and is detectable in almost 100% of acute promyelocytic leukemia (APL).
2. *BCR/ABL1* t(9;22): is a balanced reciprocal translocation generating chimeric BCR-ABL1 oncogene (also known as Philadelphia chromosome {Ph+}) with constitutive kinase activity. By definition, demonstration of *BCR/ABL1* translocation is required for diagnosis of chronic myeloid leukemia (CML). Depending upon the breakpoints on chromosome 9, three different transcripts can be detected- p210 mRNA, most commonly identified in CML, p190 mRNA, most commonly seen in B cell lymphoblastic lymphoma/leukemia, and p230 mRNA, which can also be identified in CML.
3. *CCND1/IGH* t(11;14): is a translocation which juxtaposes the *CCND1* gene encoding cyclin D1 to an enhancer of the immunoglobulin heavy (*IgH)* gene resulting in over expression of cyclin D1. Virtually all mantle cell lymphomas harbor this translocation, the demonstration of which is required for diagnosis. In contrast, *CCND1/IGH* translocation has also been reported in 40% of multiple myeloma or plasma cell disorders, where it portends favorable prognosis.

The majority of genetic lesions however, are non-specific, can be present in either myeloid or lymphoid malignancies and are not required for definite diagnosis. For example deletion 5q, 7q, and TP53, and trisomy 8 and trisomy 21 are seen in myeloid neoplasms including myelodysplastic syndrome and myeloproliferative neoplasm, but are not specific. 7q deletion,most commonly seen in myelodysplastic syndrome, has also been reported in approximately 30% of splenic marginal zone lymphomas. Similarly, TP53 deletion has been reported in numerous malignancies including solid tumors, and is usually associated with poor prognosis.

The final diagnosis of malignancy therefore is mainly based on morphology. The genetic abnormalities either confirm the diagnosis or are used in patient stratification. FISH or chromosome testing in hematological malignancies are performed on cells isolated from the specimen and cultured *in vitro* for 48-72 hours. These cultures can be stimulated with addition of mitogens to promote proliferation of neoplastic cells, if morphological information or a working diagnosis is available. For known myeloid and undiagnosed malignancies, however, the cultures set up are mostly unstimulated. Accurate identity of these cells post culture, especially in unknown malignancies, cannot be determined. Therefore, a definite diagnosis cannot be rendered solely based on the genetic abnormalities reported. Such findings should be interpreted in the context of finalized histological/morphological diagnosis.