Division of LGM Laboratory & Genomic Medicine

Newsletter

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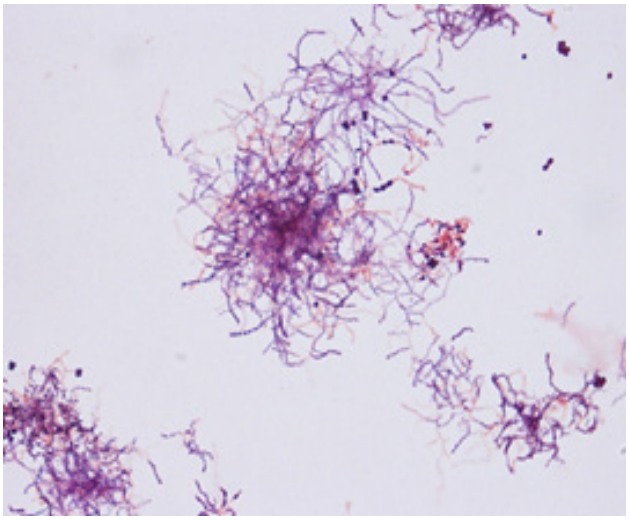
Expedited Identification of *Nocardia* spp. Recovered from Clinical Specimens

by: Melanie Yarbrough, Ph.D. and Carey-Ann Burnham, Ph.D.

Nocardia are medically important aerobic actinomycetes that are ubiquitous in soil & decaying plant matter. Members of the genus *Nocardia* can cause pulmonary infection, most commonly in immunosuppressed patients. *Nocardia* also causes cutaneous infection through direct inoculation, in addition to bacteremia and disseminated disease (such as central nervous system infection). Species-level identification of *Nocardia* can inform empiric antimicrobial therapy, as it is well established that different species have predictable antimicrobial susceptibility patterns.

Previously, isolates were sent to a reference laboratory for species-level identification. Because *Nocardia* spp. are slowing growing organisms, this process required approximately three weeks to complete. As of September 2016, the BJH Microbiology lab transitioned to the use of matrix-assisted laser desorption ionization- time of flight mass spectrometry (MALDI-TOF MS) for identification of *Nocardia*. This method is already in routine use at BJH for the identification of bacteria, yeast, and mycobacteria. Using MALDI-TOF MS, the microbiology laboratory can identify eight of the most common *Nocardia* spp. to species level directly from a bacterial colony. Therefore, for the species encountered most frequently in clinical practice, the use of MALDI-TOF MS will reduce the time to reporting of species-level identification by two to three weeks. Of note, all *Nocardia* species are sent to a reference lab for antimicrobial susceptibility testing.



For questions regarding identification of *Nocardia*, please contact:

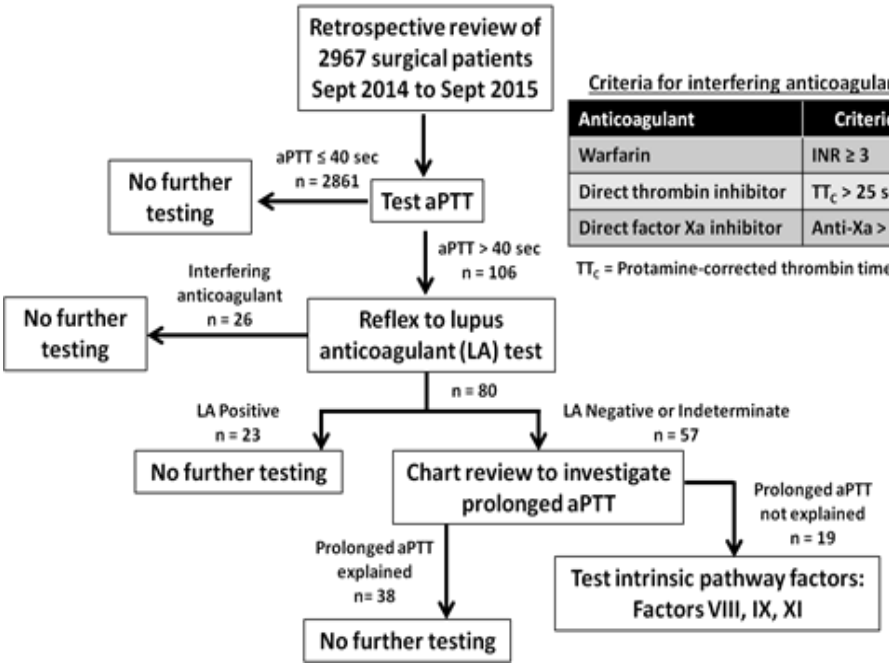
Carey-Ann Burnham, PhD, Medical Director of Clinical Microbiology, BJH Laboratories (cburnham@wustl.edu) or the Microbiology Fellow at 314-801-3108.

New Laboratory Algorithm for Preoperative Hemostasis Testing

by: Stephen Persaud, M.D., Ph.D. and Ronald Jackups, M.D., Ph.D.

Numerous studies have demonstrated that preoperative coagulation screening tests should be reserved for patients with clinical evidence of a bleeding disorder. Despite this, routine ordering of these tests remains common practice. At our institution, there has been particular interest in screening patients using the activated partial thromboplastin time (aPTT). Abnormal results prompt additional workup, including return visits, repeat blood draws, and procedure delays. To address this, we initiated a testing algorithm in the Barnes-Jewish core laboratory designed to expeditiously investigate prolonged aPTT results during the preoperative evaluation. The algorithm begins by testing aPTT of patients who are either 1) undergoing procedures with high bleeding risk (e.g., neurosurgery) or require intraoperative anticoagulation, or 2) whose clinical evaluation suggests a coagulopathy. Patients with aPTT > 40s not taking an interfering anticoagulant undergo lupus anticoagulant (LA) testing and chart review to explain the prolonged aPTT. If these cannot explain the prolonged aPTT, activities of intrinsic coagulation pathway factors VIII, IX, and XI are obtained.

In collaboration with Drs. Troy Wildes and Broc Burke in the Department of Anesthesiology, we studied the utility of this algorithm in revealing causes for a prolonged aPTT in order to identify patients at risk for intraoperative bleeding. 2,967 patients presenting to the Center for Preoperative Assessment and Planning (CPAP) for presurgical evaluation were retrospectively analyzed, of whom 80 (2.7%) had aPTT > 40 sec and were not taking an interfering anticoagulant. In most of these patients (61/80, 76%), the prolonged aPTT could be explained by either a positive lupus anticoagulant (23/80) or in the charted history (38/80). In the remaining 19 cases, no clinically significant factor deficiencies or intraoperative hemostatic complications were identified. These findings bolster the argument that indiscriminate preoperative coagulation testing is of low utility in asymptomatic patients.



Criteria for interfering anticoagulant

Anticoagulant	Criterion
Warfarin	INR ≥ 3
Direct thrombin inhibitor	TT_c > 25 sec
Direct factor Xa inhibitor	Anti-Xa > 0.05

TT_c = Protamine-corrected thrombin time

Did You Know??

Barnes Hospital has been a leader in laboratory automation for over 50 years!

Barnes Hospital Is a Leader in the Field of

LABORATORY AUTOMATION

THIS AUTOANALYZER, "Felix," was installed to do protein bound iodine tests. In the past several months, Miss White and an associate have used the machine for endocrine analyses. Here, Bill Price, a graduate of Technicon in New York, inserts a sample into the circular tray.

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An article from the Barnes Hospital Bulletin July 1966.

Jacqueline Payton Receives Distinguished Investigator Award

On February 15, 2017, Jacqueline Payton, MD, PhD, Assistant Professor of Pathology and Immunology, will be honored with the WUSM 2017 Distinguished Investigator Award. Payton's research focuses on epigenetics--phenotypic trait variations that are caused by external or environmental factors that switch genes on and off. One of the broad goals of her work is development of novel precision medicine approaches with application to many cancer types. In addition to her research, Payton is the Medical Director of the BJH Molecular Diagnostics Laboratory. She is also actively involved in Resident education in molecular diagnostics.

New Hemoglobin/Hematocrit and Platelet Count Testing

by: Ronald Jackups, M.D., Ph.D.

Beginning January 16, 2017, the BJH Hematology Lab and Siteman Cancer Center South County Lab will being offering individual testing for "Platelet Count" (Plt Ct) and "Hemoglobin/Hematocrit" (Hgb/Hct). These tests will be available in all electronic ordering systems. These tests are recommended when only one component of the CBC is desired, and will result in shorter turn-around times compared to "CBC With Differential".

Common scenarios in which individual test results may be useful include: determining eligibility for invasive procedures, establishing transfusion requirements, and monitoring response to transfusion. In particular, "Hemoglobin/Hematocrit" is recommended following a one-unit packed red blood cell transfusion in stable patients before deciding whether a second unit is necessary. Likewise, "Platelet Count" is recommended within 5-60 minutes following a platelet transfusion if transfusion refractoriness is suspected, so that the count increment can be compared to the expected increment.

White blood cell differentials are of limited utility in most clinical situations and add unnecessary time and expense to blood count evaluations. "CBC Without Differential", "Hemoglobin/Hematocrit", and "Platelet Count" provide valuable information on blood counts without performing a differential. Consider ordering "CBC With Differential" only for evaluation of fever or for situations in which specific white blood cell defects, such as leukemia or neutropenia, are suspected.

Have You Noticed the Faster Turnaround Time??

by: Mitchell Scott, Ph.D.

The BJH core laboratory, which includes clinical chemistry, hematology, coagulation, urinalysis, immunology, and flow cytometry moved into the new 40,000 square foot facility on the 4th floor of the BJC IOH building in April 2016. Many colleagues have commented to us about the improvement in lab services and the faster turnaround time for many tests. Therefore, we thought we would briefly share the lab testing process.

The Laboratory Testing Process: High volume tests are performed on a fully automated system which is one of the largest, if not the largest, hospital installation of its kind in the U.S. Upon arrival, samples are placed on the automation line in a first-in, first-on basis (except STAT samples) and from that point all barcode reading, sample processing (centrifugation, aliquots, mixing) and analytical testing are performed without a technologist touching the samples. Once testing is performed results go directly to the laboratory information system (LIS) where they are checked against a series of hundreds of rules (examples Table 1). If these rules are "passed" the result is transmitted directly to downstream systems such as Compass, Clinical Desktop, TouchWorks, etc. If all rules are not "passed" technologists must intervene to investigate problems with either the sample or the testing process before manually verifying or cancelling results. In the core lab approximately 75% of chemistry results and 85% of hematology pass all rules and "autoverify" without technologist intervention.

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Have You Noticed the Faster Turnaround Time?? (Cont'd from page 3)

In addition to rules such as these, patient results are also prevented from verification if the results from our Quality Control (QC) samples are not within acceptable range. These frequent QC samples check the analyzers for accuracy.

After testing is completed and the results are verified, tubes are transferred to a short-term storage area within the automation system where they remain for 4 hours. From this area samples can be rapidly placed back on the automation line for any additional "add-on" testing without human intervention. After 4 hrs in this area samples are automatically moved into a large, storage refrigerator for five days (chemistry) or 24 hrs (hematology) after which they are automatically disposed of by the system.

Table 1. Examples of US Rules

	What it does	What it detects	Why?
Delta Check	Compares current value to previous value from same patient. Changes beyond normal variability are flagged for review.	Mislabeled samples and contaminated samples (usually IV fluid or wrong tube type).	Prevents incorrect results from being reported.
Indices Check	Examines red and yellow color and turbidity of sample.	Hemolyzed, icteric and lipemic samples.	Prevents tests that are spectrally interfered with from being reported. Prevents falsely high K values from being reported.
Linearity Check	Examines results above the reportable range of a method.	Samples that require dilution to report accurate values.	Prevents incorrect results from being reported.
Feasibility Check	Examines results that do not seem feasible in any setting.	Samples with insufficient quantity, clotted samples or contaminated samples.	Prevents results such as albumin < 1 g/dL or Ca < 3 mg/dL from being reported.
Abnormal White Cells	identifies results that may suggest blast cells.	Previously unknown abnormal cells.	Requires manual differential.
Critical Alert Values	Examines results with "alert" values.	Alert values. Prompts call to care provider regarding lab result.	Prevents critical alert values from being unnoticed.

Testing Turn-Around-Time. A major goal of the new automation system was to decrease in-laboratory turn-around-time (TAT). The part of the total testing process that the laboratory has complete control over is the time from sample arrival in the laboratory to result verification. Time from ordering to collection and collection to receipt are not under direct laboratory oversight but use of the positive patient identification system, pneumatic tubes and a constantly circulating team of couriers are in place to optimize these aspects of the total testing process. When the core laboratory first moved in April there was a steep learning curve for both the laboratory and for the manufacturer of the automation. As many may recall there were some significant bumps in the road for the core lab during the first several months of operation. In July, the manufacturer performed a major rewrite of the automation software that corrected errors in sample workflow within the system. Since August, the system has performed excellently and we are now seeing significant decreases in within-lab TAT (Table 2).

Table 2. Examples of Test TATs before and after the move of the Core Lab

% of Results	50th percentile (Median)		90th percentile		97.5th percentile
Month	Jan 2016	Oct 2016	Jan 2016	Oct 2016	Oct 2016
BMP	45 min	28 min	71 min	47 min	81 min
CMP	46 min	30 min	75 min	55 min	93 min
Troponin	43 min	37 min	65 min	58 min	81 min
CBC	13 min	10 min	49 min	44 min	88 min

Continued on page 5

Have You Noticed the Faster Turnaround Time?? (Cont'd from page 4)

We perform about 45,000 BMPs, 14,000 CMPs, 4500 troponins and 36,000 CBCs a month and we track the median (50th percentile) and 90th percentile times for in-lab TAT for these and other high volume tests. The times shown in Table 2 represent the time from lab-in to result verification for 50% and 90% of the samples received for that test, e.g., in October 2016 50% of our CBCs were verified within 10 min of lab-in and 90% were verified within 44 min. CBC times are generally faster than chemistry or immunochemistry testing as they bypass the automated centrifuge on the automation system. In addition to the data for all samples that is shown in Table 2 we also track TAT for subcategories including certain locations, STAT orders and by shifts. Recently, we have begun tracking the 97.5th% to track the "tails" of our TAT distribution to help investigate causes for samples with delayed TAT and generally found that these represent samples that do not autoverify, require repeat testing or testing following a dilution of the sample. In the near future we will be installing software that should further improve the percent of samples that can autoverify without technologist intervention and we hope to see the time for these "tails" decrease as well.

The BJH clinical laboratories are dedicated to providing accurate and rapid test results and we hope that you have noticed the improvements resulting from our new core lab. As always, feel free to contact us if you have any problems or call to arrange a tour of the new facilities which we think you would find quite interesting. Please contact Nick Hardy at 314-362-2998 to set up a visit.

Changes in Male Estradiol Reference Interval

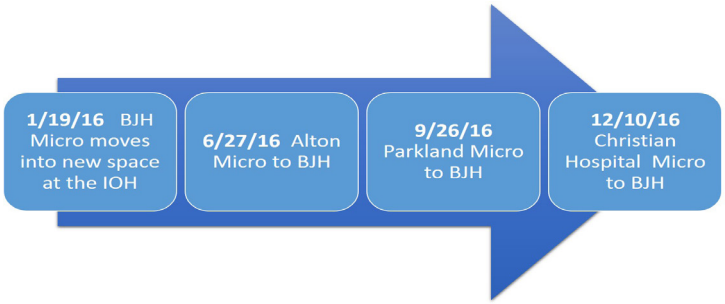
by: Ann Gronowski, Ph.D.

Effective February 1, 2017 the reference interval for Estradiol in healthy men has changed to 11-43 pg/mL (previous reference interval 25-60 pg/mL).

The manufacturer of the assay, Roche Diagnostics, informed us that many of their customers questioned the range as their populations reflected a lower reference interval. In response, Roche initiated a new reference study. The new reference interval is more in line with customer observations.

If you have questions, please contact Jennifer Hayes at 314-362-5009 or contact the chemistry laboratory medicine resident/fellow at beeper 747-1320, opt. 2.

Clinical Microbiology Update



2016 was a year of many changes and growth for the clinical microbiology laboratory. In January, the microbiology laboratory relocated to its new home in the IOH building. Subsequently, the laboratory prepared for relocation of microbiology services from some of the other BJC hospital laboratories to the IOH laboratory. In June of 2016, microbiology from Alton Memorial Hospital was relocated to the IOH, followed by Parkland Health Center in September, and then Christian Northwest and Christian Northeast in December of 2016. We look forward to continuing to work with our colleagues at these other hospitals as we navigate this transition.

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