REX HEALTHCARE

Laboratory Bulletin...

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New CDC Guidelines for Prevention of Perinatal Group B Streptococcal Disease

In the August 16th edition of *Morbidity and Mortality Weekly Report*, the CDC provides an update on Group B streptococcus (GBS). The revision of the 1996 guidelines contains several changes. Most of the new recommendations relate directly to the treating physicians, but several affect laboratories.

Background

In the 1970's GBS emerged as the leading infectious cause of perinatal morbidity and mortality in the United States. Mortality rates approached 50% at that time. GBS remains a major cause of disease in infants. Early-onset disease, defined as within the first week of life, and late-onset infections have both been linked to GBS genitourinary colonization in mothers. Colonization rates are estimated between 10-30% in pregnant women in the vagina or rectum. Since 1990 there has been a fall in the rate of invasive GBS infections in infants and an estimate that intrapartum antibiotics have prevented 4,500 early-onset cases and 225 deaths per year. The current mortality rate has been reduced to about 5% thanks to improvements in perinatal care.

Collection and Culture

Collection of cultures is recommended between 35 and 37 weeks gestation. Swabs are collected from the rectum and vagina and placed in a single broth medium to reduce cost. In the lab the swabs are inoculated into an enrichment broth, which reduces interfering bacteria and promotes the growth of GBS, and directly plated on a sheep blood agar plate. The broth is then subcultured to another sheep blood agar plate. Standard identification procedures are used to identify GBS. If penicillin allergy was not noted, the result is reported as GBS, with a comment that penicillin is the treatment of choice. Negative cultures are discarded and all cultures with growth are retained in the lab for an additional four days.

Recommendations for antibiotics and susceptibility testing of GBS

The following table is adapted from the CDC report:

Recommended	Penicillin G, 5 million units IV initial dose, then 2.5 million units IV every 4 hours until delivery
Alternative	Ampicillin, 2 g IV initial dose, then 1 g every 4 hours until delivery
If penicillin allergic but not at high risk for anaphylaxis	Cefazolin, 2 g IV initial dose, then 1 g IV every 8 hours until delivery
If penicillin allergic and high risk for anaphylaxis with GBS susceptible to clindamycin and erythromycin	Clindamycin, 900 mg IV every 8 hours until delivery **OR** Erythromycin, 500 mg IV every 6 hours until delivery
If penicillin allergic and high risk for anaphylaxis with GBS resistant to clindamycin or erythromycin, or susceptibility unknown	Vancomycin, 1 g IV every 12 hours until delivery

Resistance in GBS

GBS remains susceptible to penicillin and no reports of resistance have been made. Rates of resistance to clindamycin and erythromycin have increased since the prior set of recommendations in 1996. Figures range from 7% to 25% resistance for erythromycin and 3% to 15% for clindamycin. Cefazolin, a first generation cephalosporin, is still considered efficacious in all case of GBS.

If the patient is noted to be penicillin allergic and a vaginal/rectal Group B strep screen is received in the lab, susceptibilities for clindamycin and erythromycin will be performed on GBS isolates. It is important to note the allergy on the requisition at the time of sending the culture. If this is forgotten, or the history of penicillin allergy was not available at the time of culture, please call the lab **immediately (784-3051)** and request the susceptibility testing. This testing is not performed unless the history of penicillin allergy is noted. Plates are kept 4 days after reporting a positive culture and can thus be still used for testing during this period.

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Reference:

Prevention of Perinatal Group B Streptococcal Disease, Revised Guidelines from CDC. Morbidity and Mortality Weekly Report. Centers for Disease Control and Prevention. August 16, 2002. Volume 51. No. RR-11/

Laboratory Diagnosis of Urinary Tract Infections

Urinary tract infections (UTIs) are among the most common infections in women. Approximately 8 million office visits per year in the United States are related to UTIs. In addition, 1 million hospitalizations involve UTIs. Approximately one half of all women will have at least one episode of a UTI during their lifetime. These figures represent a significant morbidity to the individual patient as well as a large financial burden on society, with estimates in excess of $1 billion dollars per year. Fortunately, most UTIs are uncomplicated and can be treated in an outpatient setting with low cost antibiotics.

The two major laboratory tools in diagnosing and managing UTIs are urinalysis and urine culture. A large pool of literature exists concerning when to do one or both of these tests. Most authors break down UTIs into acute uncomplicated cystitis in young women and several categories of “complicated” UTIs including recurrent cases, cases in men, pregnant women, children, and those associated with catheters. Patients in the first category generally submit urine for an office dipstick urinalysis. Empiric treatment is based on a positive result for leukocyte esterase (LE) or nitrite, which are surrogate markers for pyuria and bacteriuria respectively. Because the pathogens causing acute uncomplicated cystitis have remained relatively constant (80%-90% E. coli, 10%-20% S. saprophyticus, and 5% other Enterobacteriaceae or enterococci) with predictable sensitivities, this practice has been successful, with trimethoprim-sulfamethaxazole being the most widely used treatment. All other patients not fitting into this group have a urinalysis and a urine culture with treatment modified based on the culture results.

Urinalysis and Urine Culture

At Rex Hospital, the IRIS Urinalysis Workstation performs the three parts of a routine urinalysis: specific gravity, reagent strip chemistries, and microscopic examination. The optimal specimen is 6.0 ml, with a minimum of 1.5 ml for testing. Specimens are tested within 4 hours of receipt in the lab. Those that are more than 2 hours post-collection are refrigerated. Rapid testing is performed to avoid deterioration of unstable compounds, limit the effects of bacteria on glucose and pH, and of course, to provide timely information to the ordering clinician. Urine cannot be tested if it is greater than 24 hours from collection or is visibly contaminated by fecal material.

Urine cultures can be obtained in many different ways. Microbiologic processing of urine cultures at Rex separates those obtained by sterile technique (suprapubic aspirate or cystoscopy) and all others. For the sterile samples any growth is reported and all organisms are identified with appropriate sensitivity testing. The

remaining urines follow an algorithm that initially divides them into those with 3 or more isolates versus those with only 1 or 2. They are further subdivided based on type of specimen (catheterized or not), number of organisms, and potential pathogenicity of the isolates.

Can Urinalysis Substitute for Urine Culture?

Since dipstick urinalysis is such a simple, rapid, and inexpensive test, clinicians often use it as an initial decision point for treatment of UTIs. To answer the proposed question one must investigate the sensitivity and specificity of this test. The results of studies vary depending on the cutoff for a "positive" culture result. Using the LE result as a marker for infection has shown 75% -90% sensitivity while that of a positive nitrite has been found to be closer to 50%. Specificity is higher for the nitrite result, while more false positives occur for LE. Positive and negative predictive values depend, of course, on the prevalence in the group tested. A recent study calculated the negative predictive value of the leukocyte esterase test to be 86%, and thus 14% of infected women by culture were not detected by urinalysis. They did not find increased detection by combining the nitrite result. These two factors were the only results to be statistically significant along with the presence of bacteria on microscopic examination. Some labs have even tested to see if they could reduce costs by selecting which cases to culture by eliminating those with a negative urinalysis. This resulted in a 27% positive predictive value and a 81% negative predictive value and a conclusion that the low cost of a negative urine culture did not justify looking for a way to avoid setting them up.

Experience at Rex

To see if these observations held true at Rex, Dr. John Sorge analyzed a month's data from June 1998. When a culture result greater than 50,000 organisms per ml was used as a cutoff, 90% of cases had at least one abnormality in the urinalysis (WBC> 2, positive LE, positive nitrite). This left 10% of cases with a pathogenic organism on culture in numbers > 50,000 per ml with negative urinalysis results. When there were between 10,000 to 50,000 pathogenic organisms per ml, the urinalysis was more likely than not to be negative (table 1). Review of October 2002 data showed similar findings.

Table 1: Urinalysis and urine culture data from June 1998.

	<10,000 Pathogen	10-50,000 Pathogen*	>50,000 Pathogen**	>50,000 Commensal***
# of isolates	2	18	80	11
LE +	1	6	56 true positive	9
LE -	1	11	12 false negative	2
Nitrate +	0	0	32 true positive	1
Nitrate -	2	18	45 false negative	10
WBC > 14	0	3	46 true positive	7
WBC > 2	0	4	65	8
WBC </= 2	2	14	12 false negative	3
At least 1 of the above positive	1	5	72	9
% with at least 1 of above positive	50%	28%	90%	82%

*Data includes only cultures with organisms identified. 11 were mixed with more than one organism
** 1 case of Corynebacterium urealyticum-D2 with a negative urinalysis
*** Candida albicans, non-saprophyticus coagulase negative Staph., Candida tropicalis

Conclusions

Urinalysis can be done in a clinician's office or in a central laboratory. Centralized urinalysis provides the advantage of microscopic examination, which has been shown to increase the accuracy of reagent strip chemistries. All of the non-culture methods for diagnosing UTIs have shown significant false positives and false negative results, which cause some patients to receive antibiotics unnecessarily and some to miss appropriate

treatment. The one scenario where it is considered standard practice to not culture the urine is in the case of a non-elderly woman with classic symptoms of an uncomplicated UTI. This may change with alterations in susceptibility patterns of the major uropathogens. All other cases benefit from a urine culture and appropriate sensitivity testing.

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MRI Contrast Agents Interfere with Calcium Measurement

We recently became aware that gadolinium complexes used for contrast-enhanced magnetic resonance imaging (MRI) may interfere with either serum total calcium or ionized calcium measurements, depending on the specific contrast agent used. Gadiodamide (Omniscan®) may produce artifactual hypocalcemia for 12-24 hours when a colorimetric method is used to measure total serum calcium. This effect is particularly pronounced in patients with renal insufficiency. Gadopentetate demglumine (Magnevist®) may artifactually decrease *ionized calcium* levels, but appears to have less of an effect of colorimetric serum calcium levels. The Rex Radiology Department currently uses Magnevist® for inpatient MRIs, and Omniscan® for outpatients. If routine calcium measurement is planned for patients undergoing MRIs, blood should be collected prior to administration of contrast agent or wait 12-24 hours after the MRI. If "stat" calcium determinations are necessary on a patient who has undergone outpatient MRI study, an ionized calcium level is recommended. In contrast, if "stat" calcium determination is needed on an inpatient, total serum calcium is recommended, but the results should be interpreted with caution.

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