Antimicrobial Susceptibility Testing: Why We Do What We Do In Microbiology

The primary role of the clinical microbiology laboratory is to provide information with which physicians can diagnose and treat infectious disease. The most important issues are whether an infectious agent is present and which antimicrobial agents will provide adequate therapy.

The mechanisms of bacterial resistance are complex and not completely understood. Likewise, antimicrobial susceptibility testing has become more challenging with the continued emergence of unique resistance mechanisms. The goal of the microbiology laboratory in antibiotic susceptibility testing is to provide standardized in vitro susceptibility tests that can be reproduced from day to day and from laboratory to laboratory. Without reproducibility there is no scientific basis for therapy. Standardized guidelines for susceptibility testing are published and updated annually by the NCCLS (National Committee for Clinical Laboratory Standards). These guidelines provide susceptibility testing methods that have been validated as accurate, reproducible, clinically relevant and predictive of clinical efficacy based on pharmacokinetic and outcome data. Regulatory agencies, e.g. CLIA and CAP, expect microbiology laboratories to comply with the NCCLS guidelines for susceptibility testing.

Susceptibility testing of a presumed pathogen is indicated when its response to antimicrobial agents is not predictable. However, not all microbial pathogens and antimicrobial agents have been studied and validated by NCCLS, and hence, the Microbiology laboratory does not routinely provide susceptibility results for these organisms. The most common reasons that susceptibility tests are not performed include:

1. Antimicrobial-organism combination does not require testing because all strains are known to be either susceptible or resistant (e.g. group A strep vs. penicillin).

2. Pathogen is so rarely recovered that too few clinical studies exist to establish testing standards (e.g. Vibrio species).

3. Anitimicrobial-organism combination is found to give erroneous and misleading susceptibility results (e.g. Enterococcus vs. cephalosporins).

4. Organism does not grow well enough on standardized susceptibility media for testing to be performed.

5. Drug-organism combination does not have adequate clinical response data to define MIC breakpoints (e.g. Corynebacteria and Bacillus species).

6. Organisms recovered from culture represent normal human flora from the site of collection, or mixed flora from contamination of the collection site (e.g. skin flora from a wound swab or multiple gram-negative rods from a urine culture). Susceptibility testing is not indicated for normal flora or contaminating bacteria that are not the organisms responsible for the infection.

The most useful means for assessing the adequacy of antimicrobial treatment in many infections is the clinical response of the patient to therapy and, if needed, the demonstration by repeated culture that the infecting organism either has been eliminated or still persists. It is important to emphasize that antibiotic susceptibility tests are intended to be a guide for the clinician, not a guarantee that an antimicrobial agent will be effective in treatment. When therapy is indicated for organisms that cannot be tested according to NCCLS standards, consultation with an infectious disease specialist is recommended.

New Glucose Reference Range

The American Diabetes Association published new recommendations for diabetes screening in January 2004 (Diabetes Care 2004;27, Suppl 1:S11-14). Normoglycemia is now defined as a fasting plasma glucose level of less than 100 mg/dL. Fasting is defined as no consumption of...
food or beverage other than water for at least 8 hours before testing. Nondiabetic individuals with a fasting plasma glucose level of >100 but <126 mg/dL are considered to have impaired fasting glucose. Therefore, Saint Luke’s Regional Laboratories will change the reference range for fasting plasma glucose from 110 to 100 mg/dL.

**GFR Added to Renal Panel**

Glomerular filtration rate (GFR) is accepted to be the best overall index of kidney function in health and disease. The National Kidney Disease Education Program (NKDEP) of the National Institute of Diabetes and Diseases of the Kidney (NIDDK), National Kidney Foundation (NKF) and American Society of Nephrology (ASN) recommend estimating GFR from serum creatinine using the Modification of Diet in Renal Disease (MDRD) Study equation.

The MDRD Study equation has been validated to be more accurate than measured creatinine clearance from 24-hour urine collections. Limitations of serum creatinine and creatinine clearance as indicators of renal function were previously discussed in the November 2002 issue of the Clinical Laboratory Letter, which is available on the Saint Luke’s Health System web site.

The MDRD equation uses serum creatinine in combination with age, sex and race to estimate GFR. Pcr is the abbreviation for plasma creatinine.

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\text{GFR (mL/min/1.73 m}^2\text{)} = 186 \times (\text{Pcr})^{-1.154} \times (\text{Age})^{-0.203} \times (0.742 \text{ if female}) \times (1.210 \text{ if African American})
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Several aspects of this equation should be noted. The calculation does not require weight because GFR is normalized to 1.73 m² body surface area. The multiplier of 186 at the beginning of the equation has no physiologic significance and was derived empirically. The multipliers for female gender and African American race correct for differences in muscle mass and daily creatinine production. For any given age and creatinine combination, there can be more than a 1.5 fold range in estimated GFR depending on gender and race. Black men have the highest multiplier (1.210) and non-black women the lowest (0.742).

Most laboratories do not have access to a patient’s ethnic group. To overcome this limitation, NKDEP recommends that laboratories include estimated GFR values for both African American and non-African Americans in a single report. The clinician is then responsible for choosing the correct value for the patient in question.

The MDRD Study calculation has been validated for Caucasians and African Americans with nondiabetic kidney disease, diabetic kidney disease and kidney transplants. It has not been validated in children, pregnant women, elderly people >70 years, racial or ethnic subgroups other than Caucasians and African Americans, or in normal individuals. In acute renal failure, when serum creatinine is rising rapidly, calculated GFR overestimates true GFR.

Saint Luke’s Regional Laboratories will begin reporting GFR with every Renal Panel in August. Values for both African American and non-African American individuals will be reported for each patient. Values less than 60 mL/min/1.73 m² are consistent with chronic kidney disease and values less than 15 mL/min/1.73 m² are consistent with kidney failure.

**Inhibin Added to Maternal Serum Screening Program**

Maternal serum screening is used to identify pregnancies that may have an increased risk for birth defects such as neural tube defects, Down Syndrome and Trisomy 18. Since 1998, Saint Luke’s Regional Laboratories’ MSSP has tested for alpha fetoprotein (AFP), human chorionic gonadotrophin (hCG) and unconjugated estriol (uE3). A pattern of low AFP, high hCG and low uE3 is associated with an increased risk of fetal Down Syndrome.

Recent research has documented that prenatal detection of Down Syndrome can be improved by addition of inhibin A testing. Screening with four markers increases Down Syndrome detection rates without increasing the false positive rate above that encountered with 3 markers. At age 35 years of age, the risk that a woman is carrying a child with Down Syndrome during the second trimester is 1 in 270. Using this risk, four marker screening increases the detection rate for Down Syndrome from 60% with 3 markers to 75 to 80%.

Saint Luke’s Regional Laboratories began offering a Quad Screen on August 5, 2004. The Triple Screen will also remain available.