REX HEALTHCARE

Laboratory Bulletin...

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Reporting Susceptibility Test Results -- Are We Really Communicating?

"Reporting Susceptibility Test Results -- Are We Really Communicating with Physicians?" is the title of an article from the December 1, 1996 issue of the *Clinical Microbiology Newsletter*.[1] Susceptibility testing of bacterial isolates and the interpretation of these tests is not an exact science and is becoming more complex as we discover more problems with developing resistance, often through mechanisms that cannot be reliably detected using standard laboratory procedures.

Antibiotics are often initially administered "empirically" based on the clinical presentation. Antibiotics are selected to provide coverage for the most likely infecting organisms based on the site and type of infection. Current broad spectrum antibiotics generally mean that empiric therapy works well in most cases. When empiric therapy fails or because of the need to target therapy, the isolation of the infecting bacteria and susceptibility testing may be warranted.

The need to detect resistance in bacterial isolates has led to a complex testing scheme involving many different laboratory methods. Rex uses the beta lactamase test, standard disk susceptibility tests, a new variation on the disk test called the E test, agar dilution tests and our automated Vitek susceptibility test. These tests generally produce some type of semi-quantitative result as measured in zone sizes or in MIC (minimal inhibitory concentrations). These results are then "interpreted" using standards based on the pharmacokinetics of the specific antibiotic into interpretive categories, "Susceptible", "Intermediate" and "Resistant".

There is an evolving and continually changing proliferation of rules, exceptions and special circumstances that should be evaluated in the final selection of antibiotics to assure proper patient management. The laboratory is developing and implementing new systems to assist the clinician in antibiotic selection. Because of resistance which may be difficult to detect, some antibiotics or groups of antibiotics should not be used for certain types of infections as listed in the table below (from the cited reference) and will no longer be routinely reported at Rex.

Examples of inappropriate reporting of susceptibility to antimicrobial agents[1]
(these bacteria/drug combinations will no longer be reported at Rex)

Enterococcus spp.	Sulfamethoxazone-trimethoprim[1]
Enterococcus spp.	Cephalosporins
Enterococcus spp.	Clindamycin
Streptococcus spp.	Erythromycin, Tetracycline[2]
Staphylococcus spp.	Cephalosporins[3]
Erysipelothrix sp.	Vancomycin
Listeria sp.	Cephalosporins
Salmonella & *Shigella* spp.	Aminoglycosides
Salmonella & *Shigella* spp.	1st & 2nd generation cephalosporins
Stenotrophomonas sp.	Imipenem
Pseudomonas aeruginosa	3rd generation cephalosporins[4]
Klebsiella spp.	1st generation cephalosporins[5]

[1]Despite in vitro results, resistance is thought to be intrinsic.

[2]If infection is systemic, do not report results for oral agents.
[3]If resistant to methicillin.
[4]Except ceftazidime and cefoperazone.
[5]If resistant to any 3rd generation cephalosporins.

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On the other hand, because some organisms are uniformly susceptible to certain antibiotics, it is not necessary or desirable to test these bacteria. These are listed below and these susceptibilities will not be routinely performed at Rex.

Predictable organism-drug susceptibility[1]
(susceptibilities for these bacteria no longer performed at Rex)

Organism	Drug or Drug Group
Staphylococcus spp.	1st generation cephalosporins (if susceptible to methicillin)
Groups A,C,G, Streptococcus	Penicillin
Group B Streptococcus	Ampicillin
Listeria spp.	Ampicillin
Nocardia spp.	Sulfamethoxazone-trimethoprim
Neisseria gonorrhoeae	3rd generation cephalosporins
Haemophilus spp.	3rd generation cephalosporins

To aid clinicians in the selection of antibiotics for therapy, in addition to published recommendations, Rex Service Lines are developing guidelines and recommendations for empiric therapy. The Rex Antibiotic Utilization Committee will also be working with the laboratory to provide better laboratory reports that will utilize computerized logic to conditionally report antibiotics based on current recommendations. One of the options under consideration is the "blocking" of reports for antibiotics not on the Rex formulary. If you have any comments or concerns about any of these issues, please notify the laboratory.

Karl T. Kleeman, Ph.D.

[1]"Reporting Susceptibility Test Results - Are We Really Communicating with Physicians?", Mary K. York, *Clinical Microbiology Newsletter*, Vol 18, No. 23, December 1, 1996.

Is the Glucose Tolerance Test Obsolete?[1]

A recent review article and meta-analysis[2] adds to the growing literature[1,3-7, 13] questioning the utility of the oral glucose tolerance test (OGTT) in the diagnosis of nongestational diabetes mellitus. Current diagnostic standards for nongestational diabetes are one of the following:

a) "classic symptoms of diabetes" (polydipsia, polyphagia, polyuria, and weight loss) accompanied by a plasma glucose greater than 200 mg/dL,
b) fasting plasma glucose greater than 140 mg/dL on two occasions, or
c) an OGTT with results interpretable as diabetes when performed twice.
The 2 most common criteria for glucose tolerance interpretation were devised by the World Health Organization (WHO) and the National Diabetes Data Group (NDDG) to be used following 3 days of unrestricted diet, an 8 - 16 hour fast, and administration of a 75g glucose load in the morning to a healthy outpatient. The WHO protocol measures only a fasting and 2 hr. post glucose load blood specimen, while the NDDG protocol includes values obtained between 0 and 2 hours. Some prefer the WHO classification because it avoids the problem of "nondiagnostic" OGTT's.[2,3]

Interpretation of Glucose Tolerance in Non-pregnant Adults[3]

	NDDG Criteria Plasma Glucose (mg/dL)	WHO Criteria Plasma Glucose (mg/dL)
Normal		
Fasting	<115	<115
2 hr.	<140	<140
Any value between 0-2 hr.	<200	Not Applicable
Impaired Glucose Tolerance		
Fasting	<140	<140
2 hr.	140-199	140-199
Any value between 0-2 hr.	200 or above	Not Applicable
Diabetes (either fasting or 2 hr. criteria suffices)		
Fasting	140 or above	140 or above
2 hr.	200 or above	200 or above
Any value between 0-2 hr.	200 or above	Not Applicable

[3] Modified from Davidson, Peters & Schriger
Criticisms of the OGTT include: patient inconvenience, the nonphysiologic nature of the glucose

load, external variables affecting the test (diet, exercise, drugs, smoking), the arbitrary nature of the glucose values used to separate interpretive categories (since glucose intolerance is a continuum), poor reproducibility, and the ability of fasting glucose and glycosylated hemoglobin (glycohemoglobin, hemoglobin A1c , or HbA1c) to define populations at risk for the microvascular complications of diabetes.[1-7]

Peters et al performed a meta-analysis involving 18 different studies where HbA1c was measured in conjunction with an OGTT(modified WHO interpretive criteria).[2] A total of 8984 subjects were included in the study. After massaging the data, an HbA1c cutpoint was identified that resulted in concordance with OGTT defined diabetes mellitus cases 89% of the time. Of the remaining 11% of cases with HbA1c above the cutpoint, 7% had "impaired glucose tolerance" and 4% were "normal" by OGTT.

The authors discussed limitations of their study - including the lack of standardization of HbA1c assays, the possible mathematical errors resulting from the data massage, and data from other studies which could not be incorporated. Nevertheless they concluded (and the accompanying editorial concurred[8]) that the combination of fasting plasma glucose "...followed by selective measurement of HbA1c level may be the most clinically relevant method for diagnosing pharmacological treatment-requiring diabetes."[2] This study and others suggest that HbA1c may ultimately prove to be the single most efficient test for the diagnosis of diabetes.[8] While work towards standardization of glycosylated hemoglobin assays progresses, it has been suggested that the values equal to or greater than 1% of the upper limit of normal for a given assay be considered to have crossed the threshold for diabetes.[2,3] (For the assay used at Rex, the upper limit of normal is 7.8% and 1% of the upper limit of normal is 7.9%.)

The comments above pertain to the diagnosis of nongestational diabetes mellitus in adults. Recommended screening for gestational diabetes remains a 50g glucose load followed by a 1 hour plasma glucose (O' Sullivan test) administered between weeks 24 - 28 of the pregnancy. If the 1 hour glucose exceeds 140 mg/dL, a 3 hour OGTT using a 100g glucose load is indicated.[9] However, another recent study suggested that the 3 hour OGTT may be omitted in some, if not all, obstetrical patients.[13] Landy et al retrospectively reviewed 514 singleton pregnancies with a glucose screen value of 140 mg/dL or greater. Women with screens greater than 185 mg/dL behaved like diabetic patients (with regard to fetal macrosomia and neonatal hypoglycemia) regardless of the OGTT results. They concluded that "...patients with 1-hour glucose screens greater than 185 mg/dL have a high probability of gestational diabetes mellitus and the diagnosis can be made without the GTT. Using this approach could allow prompt initiation of therapy without the inconvenience and discomfort of the GTT."[13]

The 5 hour glucose tolerance test is still used by some to evaluate reactive hypoglycemia, although many have questioned the validity of this approach.[8-12]

Conclusion: Although the OGTT may not yet be obsolete, the indications for its use appear to be decreasing. Glycosylated hemoglobin (HbA1c) holds promise as a useful marker for both the diagnosis and monitoring of nongestational diabetes mellitus. Using a cutpoint of 185 mg/dL for the O'Sullivan obstetrical glucose screening test may obviate the need for a glucose tolerance test in diagnosing gestational diabetes mellitus.

John D. Benson, M.D.

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12. Snorgaard O, Binder C. Monitoring of blood glucose concentration in subjects with hypoglycaemic symptoms during everyday life. Br Med J 300:16-18, 1990.
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Changes in the PT and PTT

In January 1997, Rex Hospital Lab will change to a new instrument and reagents for coagulation tests. Prothrombin times (PT) and activated partial thromboplastin times (PTT) are the most common tests ordered. Beginning at 10:00 AM on Monday, January 6, the new equipment will yield slightly longer PT and PTT values than previously. The new reagents are more sensitive to coagulation deficiencies, more economical, and make heparin and Coumadin therapy easier by widening the therapeutic range. All Coumadin therapy should be based on the international normalized ratio (INR). The therapeutic INR range of 2.0 to 3.0 will remain the same. Appropriate adjustments will be made in the preprinted standard heparin IV drip orders to account for the changes in the PTT. The PT and PTT normal ranges were determined by a study of Rex blood donors and Same Day Surgery patients. The numbers are summarized below and contrasted with the current normal and therapeutic values:

	Before January 6, 1997	After January 6, 1997
Normal Range:		
Prothrombin Time	10.5 to 12.4 sec.	12.1 to 14.5 sec.
PTT	22 to 32 sec.	29 to 37 sec.
Therapeutic Range:		
Prothrombin Time	INR 2.0 to 3.0 (17.0 to 20.0 sec.)	INR 2.0 to 3.0 (19.5 to 24.5 sec.)
PTT (0.2 to 0.4 u/ml of heparin)	39 to 54 sec.	50 to 77 sec.
Critical Values: (call physician)		
Prothrombin Time	INR greater than 7.3 (greater than 30 sec.)	INR greater than 7.3 (greater than 40 sec.)
PTT	greater than 85 sec.	greater than 100 sec.

The thrombin clotting time (TCT) and fibrinogen results will also change. The normal range studies for these tests are not completed at this time. These new normal ranges will be reported on the laboratory report below the test name and abnormal test results flagged appropriately.

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For further information, call the Laboratory (783-3040). Telephone extensions are: Dr. Benson (3059), Dr. Brainard (3056), Dr. Carter (3058), Dr. Chiavetta (3040), Dr. Kanich (3057), Dr. Kleeman (3063), Dr. Nance (3286), Dr. Sorge (3062), Barbara Wetherbee (Director 3055), Robin Ivosic (Core Lab Manager 3053), Linda Lompa (Blood Services Manager 781-0220), Kimberly Skelding (Customer Services Manager 3318), Rex Outreach (783-3040), Karen Sanderson (Lab Compliance Specialist 3396).

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1. Do you find the information in the Laboratory Bulletin to be...

   __Very helpful __Somewhat helpful __Needs improvement

2. Should the Laboratory Bulletin continue to be issued...

   __ Monthly __ Go to twice a month __ Change to quarterly

3. In general is the length of the articles...

   __ About right __ Too long __ Too short

4. Should the entire Bulletin be...

   __ One page, printed on both sides

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   __Other?

5. In general, have the topics covered been...

   __ Appropriate, additional suggestions are listed below

   __ Off the mark, please note suggestions below

Please list topics you would like to see covered in future issues of the Laboratory Bulletin...

PLEASE FAX YOUR RESPONSES TO 919-783-3363 OR RESPONSES MAY BE PICKED UP BY REX OUTREACH COURIERS OR MAILED TO:

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