

WHAT'S NEW?

We are pleased to announce the appointment of Drs. Amy Heerema-McKenney and Ann Folkins to new positions in pediatric laboratory services.

Dr. McKenney, the current Director of Perinatal Pathology, will become the Interim Associate Director of Clinical Laboratories for Pediatrics and Interim Chief of Pathology at Lucile Packard Children's Hospital.

Dr. Folkins will become the Medical Director for LPCH Point of Care Testing (POCT), one of four current POCT licenses serving LPCH and its affiliated services.

Cynthia V. Samson has been appointed interim administrative director for Anatomic Pathology and Clinical Laboratories.



LABORATORY SEND-OUT TESTING: A PROPOSAL FOR IMPROVED UTILIZATION

ANN FOLKINS, M.D. – CLINICAL INSTRUCTOR, DEPARTMENT OF PATHOLOGY

In an era of increasing healthcare costs and exponential growth in the availability and utility of specialized tests, organization of the laboratory send-out department is becoming an important topic for most hospitals. The need for oversight of testing sent to non-Stanford laboratories (so called send-out testing) stems not only from a desire to work within budgetary constraints but also to provide the best quality of care for each patient by offering direction and practice standards for ordering esoteric tests.

There are unique challenges involved in creating a streamlined and effective send-out department. Because the send-out department coordinates tests in every field of medicine, it needs to also seek input from ordering physicians and pathologists from all specialties. Depending on the institution, pathologists are not always intimately involved in or aware of the specific tests being ordered and sent elsewhere, even though selecting and monitoring all reference laboratories for quality of service is part of the definition of being a medical director, is required by the agencies that accredit our laboratories and hospitals, and is expected of the laboratory by both SHC and LPCH. Choosing a reference laboratory involves evaluating a number of criteria, including test performance; comprehensiveness of the test menu, especially molecular testing; special patient populations (pediatrics, transplant patients, etc.); courier services; turnaround time; accessibility of test information (website); availability of consultative pathologists; laboratory information system interfaces; and potential for third party billing (Blum RA et al. Choosing a reference laboratory? MLO. 2004; 36(8):30-33).

There is a small but growing literature on management of reference testing. Some of the methods used by other laboratories include pathologist review of expensive tests (gatekeeper model); encouraging ordering expensive tests as outpatient rather than inpatient when it does not affect clinical care; development of practice guidelines as a coordinated effort between the laboratory and the ordering clinicians; pop-up windows to guide ordering of appropriate tests; development of a laboratory reference test formulary similar to a pharmacy formulary; and negotiating third-party billing with reference lab vendors of choice (Malone B. The send-out testing boom. Clinical Laboratory News. November 2010; 36(11)).

We would like to announce our evolving plan to improve our processes for send-out testing. Currently, we have approximately 850 defined send-out tests available in our system. Each month, however, we continue to send about 300 various undefined ("lab unlisted") tests in addition to the defined tests. Our average total expense per month for send-out testing is approximately \$550,000 (SHC and LPCH combined). The State of California does not allow us to "mark up" or charge a handling fee for such send outs, and these charges often cannot be billed back to the patient when they are ordered on inpatients. We are aware of numerous areas that need improvement in our system; our individual goals and corresponding action plans are outlined at <http://www.stanfordlab.com/pages/sendoutplan.html>. We are looking forward to improving the interaction between the send-out department and the clinical faculty/staff. Please feel free to contact me with any questions or concerns.

NEW TEST ANNOUNCEMENTS

Heavy Metals Screen, Blood
(test code: LABHMET)

HPV 16/18 PCR on paraffin
embedded tissue
(test code: LABHPVPCR)

HPV 6/11 PCR on paraffin
embedded tissue
(test code: LABHPV6PC)

Enterovirus by PCR, CSF
(test code: LABEVPCR)

Lamotrigine Level
(test code: LABLAMOL)

Levetiracetam Level
(test code: LABLEVETL)

Lactate, Whole Blood
(test code: LABLACWB)

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John Christopher was promoted to Director of Laboratory Finance and Business Operations. John moved to laboratory administration in July 2007 where he was placed in charge of all budget and contracting services activities for the division and will now oversee laboratory billing and business development functions of Anatomic Pathology and Clinical Laboratory departments.

LABletter

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REVISED INTERPRETIVE CRITERIA FOR β -LACTAMS AND ENTEROBACTERIACEAE

NIAZ BANAEI, M.D. - DIRECTOR, MICROBIOLOGY SECTION

In 2010 the Clinical and Laboratory Standards Institute (CLSI) revised the interpretive criteria (breakpoints) for some cephalosporins, aztreonam, and all carbapenems for members of the Enterobacteriaceae. Table 1 shows the old and new breakpoints.

TABLE 1. COMPARISON OF OLD AND NEW CLSI BREAKPOINTS FOR ENTEROBACTERIACEAE AND SELECT β -LACTAM AGENTS

Antimicrobial Agent	Old Breakpoints (CLSI and/or FDA) $\mu\text{g/mL}$			New/Revised Breakpoints (CLSI) $\mu\text{g/mL}$		
	S	I	R	S	I	R
Cefazolin	≤ 8	16	≥ 32	≤ 2	4	≥ 8
Cefotaxime	≤ 8	16-32	≥ 64	≤ 1	2	≥ 4
Ceftriaxone	≤ 8	16-32	≥ 64	≤ 1	2	≥ 4
Ceftazidime	≤ 8	16	≥ 32	≤ 4	8	≥ 16
Aztreonam	≤ 8	16	≥ 32	≤ 4	8	≥ 16
Cefuroxime	≤ 8	16	≥ 32	no change	no change	no change
Cefepime	≤ 8	16	≥ 32	no change	no change	no change
Ertapenem	≤ 2	4	≥ 8	≤ 0.25	0.5	≥ 1
Imipenem	≤ 4	8	≥ 16	≤ 1	2	≥ 4
Meropenem	≤ 4	8	≥ 16	≤ 1	2	≥ 4
Doripenem	≤ 0.5	-	-	≤ 1	2	≥ 4

Why change the Breakpoints? There are several reasons for revising the breakpoints: (i) The original breakpoints for many of the β -lactams were established several decades ago, prior to the emergence of plasmid-encoded resistance mechanisms seen today. Consequently, this required the microbiology laboratory to do screening and confirmatory testing by looking for the resistance mechanism. The lowered breakpoints detect resistance to cephalosporins and carbapenems in greater majority of enteric isolates that have known mechanism of resistance to β -lactams. (ii) The new breakpoints take into account pharmacokinetic/pharmacodynamic (PK/PD) profiles for each antibiotic. Simulation was used to predict whether serum drug levels above the in vitro breakpoint concentration would be achieved in vivo with the appropriate antibiotic dosing based on the FDA-approved dosages (See Table 2 for dosing). (iii) The CLSI also reviewed limited clinical data for deriving the new breakpoints.

How will this affect the clinician? The new CLSI breakpoint criteria will simplify reporting of antibiotic susceptibility results for enteric gram negative rods. The clinician will no longer see the terminology ESBL, non-ESBL or carbapenemase which refer to the mechanism of resistance. Instead,

organisms will be reported as sensitive, intermediate, or resistant for each cephalosporin, aztreonam, or carbapenem. When a third generation cephalosporin (cefotaxime, ceftriaxone, or ceftazidime) or aztreonam or a carbapenem tests intermediate or resistant, the lab report will recommend Infectious Diseases consultation because in these cases, a β -lactam antibiotic that is reported as sensitive could be used for treatment, as long as the appropriate dosing regimen is used (See Table 2).

TABLE 2. ANTIBIOTIC DOSING REGIMEN UPON WHICH THE REVISED BREAKPOINTS ARE BASED.

New Interpretive criteria were based on the following dosage regimen:

Cefazolin: 1 g every 8 h	Aztreonam: 1 g every 8 h
Cefotaxime: 1 g every 8 h	Cefuroxime: 1.5 g every 8 h
Ceftriaxone: 1 g every 24 h	Cefepime: 1 g every 8 h or 2 g every 12h
Ceftazidime: 1 g every 8 h	
Ertapenem: 1 g every 24 h	Imipenem: 500mg every 6 h or 1 g every 8 h
Meropenem: 1 g every 8 h	Doripenem: 500 mg every 8 h

In summary: The updated CLSI breakpoints are predicated on the best available scientific evidence, and obviate the need for screening and confirmatory testing. The new breakpoints will provide improved information for directing patient care.