STANFORD UNIVERSITY MEDICAL CENTER

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LAB letter

SUMMER 2009

PATHOLOGY & LABORATORY MEDICINE NEWSLETTER

NEWS YOU CAN USE

Dr. Jim Faix explains the difference between calculated & direct LDL cholesterol (see page 1). Drs. Ellen Jo Baron & Ben Pinsky detail Stanford's response to the recent H1N1 pandemic (see page 2).

New Administrative Director

Fe Araceli (Celli) Frost is the new Administrative Director of Anatomic Pathology and Clinical Laboratory Services. Celli comes to us from Kaiser Permanente, South San Francisco/Daly City where she served as the Administrative Director for Laboratory and Pathology. She is a licensed Clinical Laboratory Scientist with a Master's degree in Health Care Administration from San Francisco State University. Her many accomplishments include serving as President of the Golden Gate Chapter of the Clinical Laboratory Management Association.

Joint Commission Survey of SHC

The Point-of-Care Testing program at SHC was recently surveyed by the Joint Commission. Inspectors praised both the nursing staff who perform the tests and the laboratory staff who provide coordination and support.

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READ MY LIPIDS:

LDL Cholesterol: Calculated vs. Direct

Jim Faix MD - *Director, Clinical Chemistry & Immunology*

Last month we changed the names of the commonly ordered lipid panels to clarify the difference between *calculated and direct* LDL cholesterol, the primary target for lipid-lowering therapy

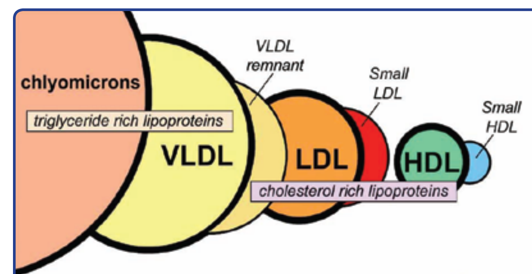
Traditionally, LDL could not be measured and had to be calculated, using the Friedewald equation introduced in 1972: total cholesterol minus HDL cholesterol minus VLDL cholesterol. Total and HDL cholesterol are measured; VLDL cholesterol is estimated by dividing the triglyceride level by 5.

For the past decade, however, we have been able to measure LDL cholesterol directly, in ways which are similar to the direct measurement of HDL cholesterol. (Selective detergents release cholesterol only from specific lipoprotein fractions.) The advantage of direct methods is that they are not influenced by chylomicrons, the triglyceride-rich fraction present after meals. The Friedewald calculation underestimates LDL in non-fasting specimens because it assumes that all of the triglycerides are VLDL.

At Stanford, there are two "lipid profiles". One is the traditional one in which LDL is calculated using the Friedewald equation and requires a fasting specimen. The other includes the components needed to calculate LDL (total cholesterol, HDL cholesterol, and triglycerides) but also measures LDL cholesterol directly. This order was originally introduced to be used when the patient was not fasting.

Some experts recommend that cardiovascular risk assessment be performed on a fasting specimen using the calculated LDL cholesterol. Others believe that non-fasting specimens better represent the patient's lipid status. When following patients, it is also possible to order the direct LDL cholesterol alone. Both calculated and direct cholesterol results correlate with the reference method (ultracentrifugation) but there is a bias between the two; at Stanford, the direct LDL is approximately 10 mg/dl higher than the calculated LDL on fasting specimens.

New guidelines being developed by the National Cholesterol Education Program may eventually replace LDL with "non-HDL cholesterol" (total cholesterol minus HDL cholesterol). This change would eliminate the confusion and also allow potentially dangerous lipoprotein remnants, not currently included in the LDL result, to be taken into consideration. In the meantime, note that there are two choices for "lipid profile" and consider which one is appropriate for your patient.



LDL (low density lipoprotein cholesterol) is currently the primary target for lipid-lowering therapy. It may be calculated by subtracting the cholesterol in HDL (high density lipoprotein) and VLDL (very low density lipoprotein) from the total cholesterol. Alternatively, it may be measured directly.

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NEWS YOU CAN USE (CONT.)

Brief Updates

HCV Viral Load - Quantitative HCV testing has moved to a new platform which automates the extraction process and streamlines amplification. The new test extends the upper limit of the reportable range ten-fold but requires a higher volume of sample than our previous method. Only serum samples are accepted for HCV viral load testing.

Mycophenolic acid - We recently brought mycophenolic acid (MPA) testing– which is one of our biggest send-out expenses – in-house using a tandem mass spectrometric method validated against that used at Mayo Clinic, our reference laboratory. The correlation is excellent for both MPA as well as MPA glucuronide and there is no change in the therapeutic range.

Sirolimus - We recently moved testing for sirolimus from a batch analyzer to the same automated analyzer we use for cyclosporine and tacrolimus. This change required a change to the therapeutic range however, from 5-20 ng/ml to 7-22 ng/ml.

Vancomycin - Complying with the new consensus guidelines for more aggressive therapy in order to prevent resistance, the recommended therapeutic range for trough vancomycin levels has changed from 5-15 to 10-20 microg/ml.

LAB*letter*
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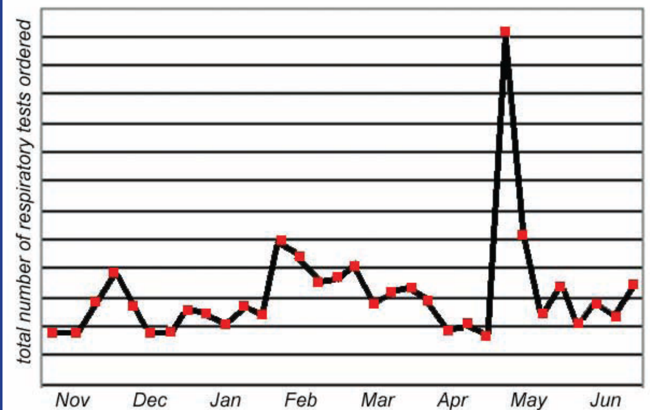
H1N1 PANDEMIC UPDATE

Ellen Jo Baron PhD - *Acting Director, Virology* & **Ben Pinsky MD PhD** - *Molecular Pathology Fellow*

In late April, the world learned of a new, highly contagious and virulent influenza outbreak in Mexico City. At Stanford, our Emerging Infectious Disease and Bioterrorism Subcommittee, directed by Dr. Eric A. Weiss, developed a plan to deal with this. When a woman in labor who had just returned from a visit to Mexico was wheeled through LPCH coughing and sneezing, the plan swung into action. Signs were placed at entrances; masks were pulled out of storage; employees were quickly updated; and the Command Center (under direction of Dr. Kevin Tabb), started holding daily briefings. The ED set up special respiratory screening protocols and a unit cleared of regular patients began to function as an influenza isolation ward.



Although requests for respiratory virus testing at Stanford and LPCH zoomed recently in response to the H1N1 pandemic, planning on the part of both hospitals and rapid action on the part of the Virology section allowed us to respond appropriately.

Stanford's laboratory had recently stopped performing rapid influenza antigen tests because their sensitivity was deemed too low (65%) to allow for effective physician decision-making. So, when requests for testing rose in the wake of the alert, the Virology section needed to gear up its performance of the more complex direct fluorescent antibody (DFA) test. This exam could accurately detect the presence of influenza A, but could not identify the new strain.

Two important proteins help influenza spread. Hemagglutinin (H) allows the virus to attach to the host and neuraminidase (N) helps new virus particles escape from the cell in which they are replicating. Strains are named based on the type of H and N antigens they express. Influenza A causes pandemics when it acquires new genetic material from other viruses, causing dramatic changes in these proteins and evading the immunological memory of the host. Previously circulating strains of influenza A in the US were H1N1 and H3N2. The new flu, also with H1N1 surface proteins, seemed to have jumped from pigs to humans, which is why it was originally called "swine flu".

During the first few weeks of the pandemic, we sent DFA-positive samples to the county laboratory for additional testing using PCR. At this time, the number of patients infected with influenza A is continuing to rise in our area, and we assume that nearly all of them are the new H1N1. Luckily, the disease produced by this swine-origin flu is usually mild.

Many parallels exist between this pandemic and the Spanish Influenza pandemic of 1918. Both involved H1N1 subtypes causing a first wave in the spring and summer, with a disproportionate amount of disease in otherwise healthy young adults. It is uncertain whether 2009 will see the severe disease that produced significant mortality in the winter of 1918. Genetic analysis suggests the current pandemic virus lacks virulence-associated mutations found in the 1918 strain. We also have the benefit of modern communication, advanced infection control practices, antiviral therapy, and antibiotics for potential secondary bacterial infections. Finally, pharmaceutical companies have recently announced successful manufacture of a vaccine using the new strain, making it likely that we will have sufficient supplies ready in time for the next respiratory season.

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