

November 2016

Flu Season Near

As of November 19, influenza activity remains at low levels in the United States. Missouri and Kansas are reporting sporadic influenza cases only. Surveillance data collected thus far indicate that influenza A H3N2 is predominant, followed closely by influenza B.

Saint Luke's Laboratories offer three different tests for detection of influenza. Rapid antigen testing is performed by all testing sites. It detects both influenza A and influenza B. The major disadvantage of rapid antigen testing is low sensitivity of 60-80%. Sensitivity of the rapid antigen tests is variable from season to season, depending on the predominant strain.

Specimens can also be sent to the central Microbiology laboratory at Saint Luke's Hospital for respiratory PCR panel testing. The panel detects influenza A, influenza B, and differentiates A subtypes H1 & H3. Additional pathogens detected by the panel include coronavirus (not MERS co-V), human metapneumovirus, rhinovirus, parainfluenza, RSV, adenovirus, *Bordetella pertussis*, *Mycoplasma pneumoniae*, and *Chlamydia pneumoniae*. Respiratory panel testing can be performed on bronchoscopy specimens in addition to nasal swabs or washes.

The Microbiology laboratory also performs PCR testing for influenza viruses only. In addition to influenza B, the flu A/B PCR detects influenza A H1 and H3 subtypes and differentiates 2009 H1N1. Sensitivity averages 90% with specificity near 100%. During seasons when rapid antigen sensitivity is low, influenza PCR testing is recommended for patients needing hospitalization for respiratory illness, at the time of admission. Nasopharyngeal or nasal swabs submitted in viral transport media or nasal washes are the only acceptable specimen types for flu A/B PCR.

Prevention of Transfusion-Transmitted Cytomegalovirus Infection

Cytomegalovirus (CMV) is a DNA virus in the *Herpesviridae* family. The primary infection is often subclinical and resolves with emergence of antibodies. During latent phase CMV resides within white blood cells. Primary and reactivation infections can lead to severe, disseminated and fatal disease in very low birth weight neonates, fetuses requiring intrauterine transfusion, pregnant women, patients with primary immunodeficiencies, transplant recipients, and patients receiving chemotherapy or transplantation for malignant disease. The risk of transfusion-transmitted cytomegalovirus (TTCMV) infection is between 1-3%. However, breakthrough TTCMV infection has not been reported recently with current mitigation methods. The methods used in blood bank to prevent TTCMV infection includes; 1) Leukocyte-reduction of cellular blood products and, 2) Collection from CMV-seronegative donors.

Convincing randomized control trial data comparing the efficacy of these methods alone or in combination is lacking. But various observational studies have shown leukocyte-reduction to be as effective as collection from CMV-seronegative donors in prevention of TTCMV. Theoretically, both methods are unable to prevent TTCMV infection if a blood product is collected during the "window period". A recent AABB (American Association of Blood Banking) committee report (Heddle, N.M., *Transfusion* 2016;6(6):1581-1587) listed the problems with providing definitive guidelines due to lack of good quality data. But more recently an editorial (Strauss, R.G., *Transfusion* 2016;56(8):1921-1924) suggested that leukocyte-reduction alone is the recommended method to prevent TTCMV. In Saint Luke's Health System we provide leukocyte-reduced cellular blood products (Red blood cells and platelets) to prevent TTCMV.

Is Vitamin D Deficiency Widespread?

A recent article published in *New England Journal of Medicine* (Manson J.E., 2016;375(19):1817-1820), raises an important question regarding appropriate interpretation of serum vitamin D (25-

hydroxyvitamin D [25(OH)D]) reference ranges. Most of the studies concluding a wide spread existence of vitamin D deficiency use serum vitamin D value cut-off of 20 ng/mL (50 nmol/L) or failure to achieve a serum level of 20 ng/mL in adults on 600-800 IU supplementation, which is the IOM (Institute of Medicine) Recommended Dietary Allowance (RDA). Consequently, blood testing for vitamin D levels has soared. It is now reportedly Medicare's fifth most common test after cholesterol levels and ahead of blood glucose levels with approximately 8.7 million tests performed last year (83-fold increase in vitamin D blood testing observed from 2000-2010).

While developing the reference ranges, referred to as Dietary Reference Intakes (DRIs), IOM considers the reality of individual variability in the biological need of a nutrient, generally present in a normal distribution pattern across the population. Based on the variability, two DRI values are published, namely, an Estimated Average Requirement (EAR), and RDA. EAR represents the median value of the normal distribution, in contrast to RDA, which is the estimated nutrient requirement for people at the highest end of the distribution. Therefore, most likely for the majority of people (at least 97.5%, or 2 SD of the median), the nutrient requirement is below RDA. Of note, EAR and RDA values published assume minimal to no sun exposure.

Since vitamin D plays an important role in bone health, the EAR is set at 400 IU per day for 1 to 70 years of age and 600 IU per day for adults over 70 years, which corresponds to a serum level of 16 ng/mL (40 nmol/L). Unfortunately, the utility of parathyroid hormone (PTH) levels in identification of optimal serum vitamin D levels has been controversial due to inconsistencies. Additionally, the impact of lower circulating serum vitamin D levels observed in people with greater adiposity, and consequent dietary supplementation with vitamin D on bone health is inconclusive and not well established. If correctly interpreted, data from National Health and Nutritional Examination Survey (NHANES) from 2007 through 2010 shows that approximately 13% of Americans between 1-70 years of age are "at risk" of vitamin D deficiency. Furthermore, approximately <6% are deficient in vitamin D levels (less than 12.5 ng/mL).

The NEJM article has raised important questions regarding routine screening for vitamin D levels and recommended vitamin D intake. At present, the

majority of medical organizations do not recommend routine screening for vitamin D levels. Further, the relationship of vitamin D levels and risk of cancer, heart disease, stroke, memory loss, depression, diabetes, bone loss, or other problems are currently under investigation with results expected in 2018. It will be interesting to see what conclusions can be drawn regarding health improvement in relation to vitamin D levels.

Below are graphs of the distribution of vitamin D levels tested at Saint Luke's Hospital laboratory over two weeks in the months of April and September, 2016. Although the sample size is not large (n=900-1000 for each month), it appears our patients' median vitamin D levels are higher as indicated by the shift in columns as compared to the normal distribution. Whether this distribution is attributed to supplementation of vitamin D is not clear.

