



Saint Luke's Regional Laboratories Clinical Laboratory Letter



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Non-HDL Cholesterol Added to Lipid Profile

Saint Luke's Regional Laboratories is adding a new parameter, non-HDL cholesterol (nonHDL-C), to its lipid profile. Non-HDL-C offers several advantages over LDL cholesterol (LDL-C). A practical advantage is that measurement of non-HDL-C does not require collection of a fasting sample. Laboratories use the Friedewald equation to calculate LDL-C:

$$\text{LDLC} = \text{TotalC} - \text{HDLC} - \text{Triglycerides}/5$$

This formula increasingly underestimates the true LDL-C value as triglyceride levels increase. This is why the laboratory does not report LDL levels when triglycerides are above 400 mg/dL. But the calculation is affected to some extent at all triglyceride levels above 100 mg/dL. A falsely low LDL-C level may give a patient and their physician a false sense of reassurance.

Patients with diabetic dyslipidemia and related conditions, such as the metabolic syndrome, often have elevated triglycerides, low HDL, and relatively normal calculated LDL values. Sustained hypertriglyceridemia eventuates in elevated levels of very low density lipoprotein (VLDL), intermediate density lipoprotein (IDL), and small dense atherogenic LDL particles. Non-HDL cholesterol provides a single index of all these apolipoprotein B-containing lipoproteins, essentially acting as a surrogate for direct apolipoprotein B determinations. The bottom line is that the measurement of LDL-C alone is not an adequate measure of atherogenic risk in hypertriglyceridemic patients.

Stated otherwise, non-HDL cholesterol is a stronger predictor of coronary risk than LDL or triglycerides in certain patient populations, since it reflects the sum of serum cholesterol carried by all of the potentially atherogenic lipoproteins including LDL, VLDL, IDL, and other remnant lipoproteins. Moreover, since it is calculated from

total cholesterol and HDL cholesterol, both of which are measured directly, it is not affected by the triglyceride level and does not require a fasting specimen.

A recent meta-analysis, which encompassed more than 300,000 patients and 10,000 major adverse events found that calculated LDL cholesterol is no more effective than using the non-HDL cholesterol level to predict the risk of vascular disease (Di Angelantonio E, et al. *JAMA*. 2009;302:1993-2000).

NCEP ATP III guidelines recommend lowering non-HDL cholesterol as a secondary goal when triglycerides are > 200 mg/dl. As can be seen in the following table, the target goal for non-HDL is always 30 mg/dl higher than the LDL target for each NCEP Risk Category.

Risk Category	LDL Goal	Non-HDL Goal
CHD & CHD Risk Equivalent	<100 mg/dL	<130 mg/dL
Multiple (2+) Risk Factors	<130 mg/dL	<160 mg/dL
0 – 1 Risk Factor	<160 mg/dL	<190 mg/dL

The concept of good and bad cholesterol is still correct. However, non-HDL cholesterol is becoming the new bad cholesterol.

Human Immune Response to Streptococcal Antigens

Two recent prospective studies provided important insight into the immune response to Streptococcal infection over an extended period of time (*Clin Infect Dis* 2010;50:481-90). One hundred and sixty randomly selected children between the ages of 6 and 15 years (mean 10 y) had monthly throat cultures and serum collections every 13 weeks for measurement of anti-streptolysin O (ASO) and anti-DNase B

(ADB) titers during an average observation period of 97 weeks. Each participant had an average of 21.8 throat cultures and 10.5 antibody titers during the study.

Approximately one third of patients with GAS infection demonstrated a positive throat culture and significant elevations of both ASO and ADB titers. In the remaining two thirds of cases, either ASO or ADB was elevated, but not both. Serological confirmation of infection would have been missed in 22% of cases if only one antibody had been ordered.

Demonstration of a rising ASO or ADB titer in 2 or more sequential samples over a 2 to 4 week period was the most accurate means of diagnosing a recent infection. Comparing the titer of a single ASO or ADB level to the upper limit of normal (ULN) proved to be unreliable for several reasons. In 60% of documented infections, titers rose in sequential samples but peaked below the ULN. Reliance on a single comparison to the ULN would have been incorrectly interpreted as a negative serological response. The second problem was that 40% of patients with an acute infection developed a significantly elevated ASO or ADB titer, which remained elevated for more than one year. Reliance on a single titer could not distinguish recent from remote infection. The third problem was that many asymptomatic GAS carriers have titers elevated above the ULN. A positive culture with a single elevated titer cannot distinguish the carrier state from active infection.

Group A, group C and group G streptococci all produce antigenically identical ASO and all three stimulate the same magnitude of ASO response. In contrast ADB is more specific for GAS infection. No ADB responses were seen following infection with group C or group G *Streptococcus*. Another interesting finding was that antibiotic treatment did not significantly affect ASO and ADB antibody responses even though bacteria were eradicated.

Dengue Virus

Dengue virus transmission has been increasing to epidemic levels in many parts of the tropics and subtropics where it had previously been absent or mild. Dengue-affected areas are widely distributed throughout Africa, Asia, Pacific, the

Americas and the Caribbean. With an extensive dengue outbreak occurring in Puerto Rico and evidence of continued transmission in Key West, Florida, travel to certain domestic locations may also pose a risk for travelers. Mosquitoes known to transmit dengue virus, *Aedes aegypti* and *Aedes albopictus*, are present throughout much of the southeastern United States and infected returning travelers may pose a risk for initiating local transmission.

Infection with dengue virus may manifest as either dengue fever (DF) or the more severe dengue hemorrhagic fever (DHF). DF is a self-limited febrile illness that is characterized by high fever, lasting 2 to 7 days, plus two or more of the following: headache, retro-orbital pain, joint pain, muscle or bone pain, rash, bleeding, and leukopenia. Because the incubation period for dengue infection ranges from 3 to 14 days, the patient may not present with illness until after returning from travel.

A small proportion of patients develop DHF, which is characterized by presence of recent fever, thrombocytopenia, bleeding and increased vascular permeability evidenced by hemo-concentration, hypoalbuminemia or hypo-proteinemia, ascites, or pleural effusion. DHF can result in circulatory instability or shock.

Specimens from patients with acute febrile illness who returned from dengue-affected areas within the past 14 days should be submitted for testing. Accuracy is increased when both acute and convalescent specimens are available for testing. Providers should submit acute specimens as soon as they are available and then submit the convalescent specimen later. The preferred specimen depends on the stage of the illness.

Specimen	Interval since Onset	Optimal Test
Acute	1-5 days	PCR
Convalescent	6 to 30 days	IgG & IgM

Both PCR and antibody testing for dengue virus are available through Saint Luke's Regional Laboratories.