DIAGNOSTIC LABORATORY SERVICES, INC.

Laboratory Medicine Bulletin

C-reactive Protein (High Sensitivity) – Update

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On January 28, 2003 the Centers for Disease Control and Prevention (CDC) and the American Heart Association (AHA) published a scientific statement, "Markers of Inflammation and Cardiovascular Disease…", supporting high sensitivity C-reactive protein (hs-CRP) as an independent marker for cardiovascular disease risk assessment. This represents the first time a marker other than traditional lipid markers is being recommended by the CDC and AHA for assessing risk of future coronary artery disease. The following is a summary of the CDC/AHA opinions and recommendations, based on best evidence to date in the literature:

1. Measurement of hs-CRP is an independent marker of cardiovascular risk.
2. The entire adult population should not be screened for hs-CRP for the purposes of cardiovascular risk assessment.
3. In those patients judged to be at intermediate risk by global risk assessment (Framingham risk score of 10 – 20% risk of CHD per 10 years) hs-CRP levels might provide additional information to help direct further evaluation and therapy in the primary prevention of CVD.
4. hs-CRP may be used at the discretion of the physician as part of a global coronary risk assessment in adults without known CVD however the benefits of this strategy are uncertain.
5. Patients with persistent, unexplained, elevations of hs-CRP > 10 mg/L after repeated testing should be evaluated for non-cardiovascular etiologies of inflammation.
6. In patients with stable coronary artery disease or acute coronary syndrome (ACS), hs-CRP may be useful as an independent marker for prognosis for recurrent events, including death, MI, and restenosis after percutaneous coronary intervention.
7. The hs-CRP assay has test characteristics most conducive to use in clinical practice. Other inflammatory markers in addition to hs-CRP are not recommended.
8. hs-CRP should be measured twice (averaging results), optimally 2 weeks apart, fasting or non-fasting, in metabolically stable patients. If the level is > 10 mg/L the test should be repeated and the patient examined for sources of infection or inflammation.
9. hs-CRP should not replace other traditional risk factors and secondary prevention or application of management of ACS should not be dependent on hs-CRP levels alone. Serial testing of hs-CRP should also not be used at present to monitor the effects of treatment.

The CDC/AHA recommend the following hs-CRP cut points (tertiles) for CVD risk assessment:

hs-CRP Level (mg/L)	***Relative Risk***
< 1	Low
1.0 – 3.0	Average
< 3.0	High

(the high risk tertile has an approximate 2-fold increase in relative risk compared with the low-risk tertile)

Further investigation and research is needed to better elucidate the basic mechanisms by which inflammation leads to clinical disease, to determine if CRP is a risk factor or risk marker (i.e. does CRP participate in atherosclerosis directly), to standardize and improve hs-CRP methodologies, to look at combinations of various inflammatory markers, and to refine the cut points for hs-CRP in relation to absolute risk. Additional randomized clinical trials are needed and ongoing to further examine the hs-CRP-CVD relationship, the effect of pharmacologic/nonpharmacologic measures on hs-CRP levels and subsequent effects on CVD risk, and the cost-effectiveness hs-CRP in the medical care of patients. Finally, studies looking at hs-CRP levels as risk predictors in other ethnic subgroups as well as in children and young adults needs to be addressed.

Beginning May 1, 2003 DLS will be modifying its risk reportable ranges to conform to those recommended by the CDC/AHA. For additional information please refer to the CDC/AHA Scientific Statement in the issue of Circulation (2003; 107: 499 – 511).