Discussion

As our knowledge of the atherosclerotic process has improved in recent years, evidence suggests that inflammation plays a significant role in the development of this disease. With inflammation receiving increased research interest, a variety of markers of inflammation have also been evaluated as potential indicators for predicting the risk of coronary events. As a consequence of the expanding interest in inflammation and the relation to cardiovascular disease (CVD), a variety of commercial assays for inflammatory markers have been developed. As would be expected, this interest in inflammation has also resulted in an increase in the number of inflammatory marker tests ordered by clinicians for evaluating CVD risk. Unfortunately, unlike cholesterol, there has been no consensus among professionals as to which markers may be most suitable for use in clinical practice as indicators of inflammation.

The Centers for Disease Control and Prevention (CDC) in collaboration with the American Heart Association (AHA) convened a workshop in Atlanta on March 14 and 15, 2002 titled, "CDC/AHA Workshop on Inflammatory Markers and Cardiovascular Disease: Applications to Clinical and Public Health Practice" intended to address issues concerning the appropriate selection and use of inflammatory markers to predict CVD risk (*Circulation* 2003;107:499-511). The workshop consisted of 1½ days of presentations and discussions of topics relevant to inflammatory markers and CVD. Three concurrent discussion groups on issues related to laboratory science, clinical science, and population science were held.

The goals of the workshop were to determine which of the currently available tests should be used; what results should be used to define high risk; which patients should be tested; and the indications for which the tests would be most helpful.

The major recommendations from the workshop are:

1. Measurement of hsCRP is an independent marker of risk and in those judged at intermediate risk by global risk assessment, at the discretion of the physician, may help direct further evaluation and therapy in the primary prevention of CVD.

This recommendation assumes the assessment of traditional cardiovascular risk factors and the calculation of an absolute risk score before measurement of hsCRP. The workshop experts discouraged the use of hsCRP as an alternative to the major risk factors for risk assessment. Treatment of patients with elevated hsCRP on the basis of the hsCRP alone has limited data to support it at the present time.

2. Patients with persistently unexplained, marked elevation of hsCRP (>10 mg/L) after repeated testing should be evaluated for noncardiovascular etiologies.

3. Measurement of hsCRP may also be useful in the estimation of prognosis in patients who need secondary preventive care, such as those with stable coronary disease or acute coronary syndromes and those who have undergone percutaneous coronary intervention (PCI).

4. Application of secondary prevention measures should not depend on hsCRP determination.

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5. Application of management guidelines for acute coronary syndromes should not be dependent on hsCRP levels.

6. Serial testing of hsCRP should not be used to monitor effects of treatment.

7. Widespread public screening of the adult population for hsCRP for purposes of cardiovascular risk assessment should not be done.

8. Other inflammatory markers (cytokines, other acute-phase reactants) should not be measured for the determination of coronary risk in addition to hsCRP.

9. Measurement of hsCRP should be done twice (averaging results), optimally two weeks apart, fasting or nonfasting in metabolically stable patients.

10. hsCRP results should be expressed as mg/L only and reported to one decimal place.

11. Risk categorization of patients expressed as tertiles is as follows:

< 1.0 mg/L	low risk
1.0 to 3.0 mg/L	average risk
> 3.0 mg/L	high risk

These recommendations should not be interpreted to mean that the scientific evidence is fully adequate. The currently available evidence was assessed in the development of these recommendations. The workshop experts developed a list of recommendations for research reflecting the need for clarification on a number of issues.

A review of the results from the 2004-A mailing of the Cardiac Risk Survey for hsCRP indicates continued reporting errors. Similar to the previous mailing, the data have been left in their raw form without any outliers removed to help illustrate these findings.

For all three specimens, hsCRP-01, hsCRP-02 and hsCRP-03, the median values for each of the methods best represent the expected results. Since the misreporting of results in the wrong unit of measure influences the overall mean, participants will likely find it more useful to compare their result with the median value. To help illustrate the misreported results, one can see for specimen hsCRP-02 that the "low values" reported for most methods is one-tenth the median value, strongly indicating that participants are incorrectly reporting values in mg/dL. Similar reporting errors can be seen for the other two specimens, hsCRP-01 and hsCRP-03, where the low values are one-tenth the median value and the high values are ten times greater than the median value.

Again, the correct units for reporting hsCRP results for the Cardiac Risk Survey are **mg/L**. Some assays express hsCRP results as mg/L, while others express results as mg/dL. Participants are strongly advised to carefully check the assay vendor's product insert to determine the default reporting units for the particular assay in use. If the default units are in mg/dL than simply multiply by 10 to convert mg/dL to mg/L. Care must be taken to determine the correct units reported for a specific assay.