“Considering how much attention has been paid to diseases of the heart during the past twenty years, their history and causes might by most persons be regarded as nearly complete”

—George Burrows, FRSA
February 23, 1847

A century and a half after the proclamation of Burrows, the search for a marker of coronary heart disease continues; more than 60% of those who develop coronary events have only one, or even none of the traditional risk factors, and more than half have either normal or mildly increased lipid values. Because of the unexpected early termination and recent release of the positive findings of the Justification for the Use of Statins in Primary Prevention: an Intervention Trial Evaluating Rosuvastatin (JUPITER\(^3\); ClinicalTrials.gov number NCT00239681), this issue of Clinical Chemistry is devoted to C-reactive protein (CRP) research. We believe that JUPITER is a landmark trial in preventive cardiology and one of the most significant developments in this field since the inception of the National Cholesterol Education Program. The JUPITER findings will most likely lead to changes in clinical practice and in the clinical assessment of cardiovascular disease risk.

We have chosen for this issue reports of studies that reflect all aspects of CRP research, including basic science and clinical, epidemiological, and analytical investigations. Furthermore, because we are aware that the utility of this marker in cardiovascular disease is not universally embraced, the opposing point of view is also represented. In addition, Reflection and Perspective articles have been included that are meant to highlight the evolution of the utility of high-sensitivity CRP (hsCRP) in cardiovascular disease risk prediction and the clinical implications of JUPITER, as well as editorials and reviews by world-renowned scientists. A preamble describing the recommendations of the National Academy of Clinical Biochemistry’s Laboratory Medicine Practice Guidelines for the utility of emerging biomarkers in cardiovascular disease is also included.

With the increased interest in the utility of hsCRP in cardiovascular disease risk assessment, the number of hsCRP measurements performed in laboratories in the US has been rising over the past few years (Fig. 1). As a result of the findings from JUPITER, we anticipate an even greater increase in hsCRP testing in the US and elsewhere. On November 9, 2008, the day the data from JUPITER were presented and the findings from 2 pivotal hsCRP studies from the Physicians’ Health Study and the Framingham Heart Offspring Study were published, Elizabeth G. Nabel, director of the National Heart, Lung and Blood Institute, released a statement on the role of inflammation and hsCRP in cardiovascular disease.

Nabel concluded that “Together, these studies show great promise in helping clinicians better identify and treat individuals at risk for cardiovascular disease—potentially saving millions more lives.” These developments create a larger role for clinical chemists in this endeavor, through implementing appropriate methods, providing correct interpretations, and supporting clinicians. Unfortunately, 2 common problems in the measurement of hsCRP and the reporting of its results remain to be addressed.

1. As shown in Fig. 1, the number of CRP tests performed by using traditional methods for the detection and monitoring of active infection and inflammation was almost constant between 1997 and 1999. Since that time infectious disease clinical protocols have undergone no important changes related to the utility of CRP that justify or explain the increase in CRP measurement in the following years. The exponential rise seen since 1998 in CRP testing by use of both the high-sensitivity and traditional assays suggests that laboratories may have been using both assays for assessing cardiovascular disease risk. The traditional method is useless in this regard because it cannot detect values below 3 mg/L, and most values measured in apparently healthy individuals will be reported to the clinician as below the detection limit. Clinical chemists must provide the correct method of testing and work with clinicians to identify the appropriate mechanism and protocols for ordering the test. Failure to do so will serve only to frustrate and discourage clinicians and potentially harm the patients they are trying to serve.

2. The American Heart Association and the CDC have issued guidelines for the utility of hsCRP in cardiovascular disease risk assessment; values below 1 mg/L are associated with low risk, between 1 and 3

\(^3\) Nonstandard abbreviations: JUPITER, Justification for the Use of Statins in Primary Prevention: an Intervention Trial Evaluating Rosuvastatin; CRP, C-reactive protein; hsCRP, -sensitivity CRP.
mg/L with moderate risk, and above 3 mg/L with high risk. Data from the College of American Pathologists surveys have repeatedly suggested that substantial numbers of laboratories still report their hsCRP results in milligrams per deciliter. Such a practice is inconsistent with national guidelines, confusing to physicians, and potentially harmful to the patient. Laboratories should follow current recommendations to report hsCRP values only in milligrams per liter.

Close collaboration between physicians and clinical chemists will be required to correctly implement hsCRP testing for cardiovascular disease risk assessment and to fully realize the benefits of hsCRP testing for patient care. We sincerely hope that the articles in this issue will encourage clinical chemists to take a leadership role in this worthwhile endeavor.

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