Evaluation of C-Reactive Protein, an Inflammatory Marker, and Infectious Serology as Risk Factors for Coronary Artery Disease and Myocardial Infarction

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Coronary artery disease (CAD), which frequently becomes manifest as myocardial infarction (MI), continues to exact an enormous toll in Western society. Despite progress in its prevention, detection and treatment, it continues to be the leading cause of death (1). Several risk factors for coronary heart disease have been well documented, including hyperlipidemia, hypertension, smoking, diabetes, a positive family history, obesity and inactivity (2). However, these factors explain only part of attributable cardiovascular disease. It is clear that other and unknown factors are involved (2,3).

A growing body of evidence supports the concept that local and systemic inflammation play a role in the initiation and progression of atherosclerosis and its complications (4–7). C-reactive protein (CRP) is an acute-phase reactant marker for underlying systemic inflammation. CRP has been reported to be elevated in patients with acute ischemia (8) and MI (9,10). CRP was subsequently shown to predict risk of recurrent ischemia in patients with unstable angina (11,12), subsequent MI in patients with angina (12,13) and coronary death in smokers (14). Recently, CRP was shown to be a risk predictor for future MI or stroke over a period of at least 6 years in apparently healthy men in a case-control substudy of the Physicians’ Health Study (15).

The inflammatory signals driving immunologic activity in CAD are unknown. They may be nonantigenic or antigenic but of noninfectious origin. Oxidized low density lipoprotein (LDL) and hypertension represent proposed noninfectious stimuli. Finally, they may include an infectious, antigenic source. A distant infection might generate circulating cytokines, or persistent local infectious (as well as noninfectious) sources within plaque may provide the ongoing stimulus. Chlamydia pneumoniae (16–23) and cytomegalovirus (CMV) (24–26) are intracellular pathogens that might serve as a source of chronic local or systemic infection. Helicobacter pylori, demonstrated to be etiologic in peptic ulcer disease, is a candidate organism that might be a chronic source of distant inflammation (27,28).
Systemic antibody titers demonstrating previous exposure to infectious pathogens with persistently positive serology represent candidate markers for chronic, persistent infection. Saikku et al. (16) reported serologic evidence of an association of Chlamydia pneumoniae with chronic coronary heart disease and acute MI in 1988 (16). Since then, over a dozen serologic studies have been undertaken, with variable but generally positive results. CMV infection also has been associated with CAD risk (24,25). An association between anti-CMV titer positivity and angiographic coronary restenosis has been reported (26). H. pylori seropositivity has been associated with coronary heart disease in some reports (27,28). No studies to date have attempted to correlate markers of inflammation (e.g., CRP) with candidate infectious serology. Thus, the objective of the present study was to test whether CRP correlates with angiographic CAD as well as clinical MI and whether serologic evidence of infection correlates with CRP and also predicts CAD and MI.

Methods

Study hypotheses. Our objectives were to test 1) whether patients defined by angiographic CAD as well as those defined by a previous clinical history of MI would have elevated serum CRP levels; 2) whether these same patients would have a greater prevalence of seropositivity for C. pneumoniae, CMV and H. pylori than control patients with no disease; and 3) whether seropositivity to these agents would correlate with elevated CRP levels.

Patients. The study sample included consecutive clinically stable, consenting patients undergoing coronary angiography because of either symptoms of suspected CAD or unrelated conditions requiring angiographic evaluation (e.g., valvular disease, cardiomyopathy). Subjects were of unrestricted age and gender who gave written informed consent for blood to be drawn at angiography for use in confidential “blood bank” studies approved by the hospital's institutional review board (29). In general, subjects were residents of Utah, southwestern Idaho or southeastern Wyoming, a population that is ethnically primarily of Northern European (Anglo-Scandinavian) descent (30).

At angiography, key demographic characteristics were captured on computerized data forms, including age, gender, present diagnosis and past history of MI. Assessment of CAD was made by review of angiograms by the patient's cardiologist and entered into the computer database in a format modified after the Coronary Artery Surgery Study (CASS) protocol (29). Patients were designated as having CAD (n = 219) if they had >60% stenosis of at least one coronary artery or its major branch and no CAD (control subjects, n = 126) if <10% stenosis was present in all vessels. Patients with mild CAD (10% to 60% stenosis) were designated as having “intermediate” CAD status and were excluded from further comparison. Assessment of CAD was performed in blinded manner with regard to results of blood testing for inflammatory and serologic markers. Patients with MI (n = 112) (current hospital admission, n = 71; previous admission, n = 41) were compared with control patients (n = 197) presenting for catheterization with chest pain but normal coronary arteries (n = 118), valvular heart disease (n = 27), cardiomyopathy (n = 2), a combination of these (n = 19) or other reasons (n = 31), except an acute coronary syndrome.

Determination of CRP. CRP determinations were done by an automated nephelometric immunoassay using a Beckman Array multitest immunoassay system. The detection range for CRP by this method is ≤0.4 to 12.0 mg/dl. (The range can be extended to 72 mg/dl by dilution of the sample.) The test is standardized to the International Federation of Clinical Chemistry (IFCC) International Reference Preparation for Plasma Proteins. The within-run coefficient of variation for a 1.78-mg/dl standard is 3.68%; for an upper range standard (7.94 mg/dl), it is 1.13%. Between-run coefficients of variation vary from 3.89% for a 0.74-mg/dl standard to 3.03% for a 9.08-mg/dl standard.

Testing for infectious serology. Commercial ELISA assays were used to measure IgG antibody to CMV (Wampole Laboratories) and to H. pylori (Meridian Diagnostics). Serum dilutions and ELISA procedures followed the protocols supplied by the respective manufacturers. Detection of IgG antibody to C. pneumoniae was done by a microimmunofluorescence assay (MIF) obtained from MRL Diagnostics. Sera were screened at a 1:16 dilution against C. pneumoniae, Chlamydia psittaci and Chlamydia trachomatis; a serum was considered positive only when species-specific antibody was observed.

Statistical considerations. On the basis of previous regional studies of C. pneumoniae (18,19), we estimated conservatively that control prevalence of seropositivity would be 40%, and the relative risk of a positive IgG titer would be ~2 for MI or CAD. To discover an increase in relative risk of 2 for patients compared with control subjects with a power of 80% and an alpha value of 0.05 requires a sample of ~133 subjects/group (GB-stat for Windows). Accordingly, we performed serologic titers in overlapping subgroups among 363 subjects: 60% had severe CAD, and 31% had a history of MI. Similar power assumptions were made for the organisms of secondary interest (CMV and H. pylori).

Mean values or proportions for baseline risk factors were calculated for patients and control subjects. A difference in mean values was tested with the Student t test (with p values based on unequal variances when suggested by Levene’s test), except that nonparametric testing (Mann-Whitney) was used for nonnormally distributed variables (i.e., CRP). Variance is
expressed as standard deviation (SD), unless otherwise indicated (i.e., SE for CRP). Differences in proportions were tested by the Pearson chi-square statistic. Two-tailed p values are presented, with 0.05 designated as nominally significant. No correction for multiple comparisons was made.

**Results**

**Patient groups.** A total of 363 subjects were studied (mean 62.5 years, range 17 to 89; 70% men); 219 (60%) had advanced CAD, and 112 (31%) had a history of MI. Subgroups of the total group were tested for CRP and each of the infectious serologies. Key patient characteristics are summarized for patients grouped by disease category in Table 1. Patients with CAD were more likely to be male and to have diabetes than were control subjects. Patients with MI more frequently were male and smoked. Other demographics were generally similar between the CAD and respective control groups.

**CRP in patients with MI or CAD.** In our cohort, plasma CRP was more frequently elevated in patients with MI than in control subjects with no MI (mean CRP: 2.05 mg/dl [SE 0.36, median 0.50], n = 47 vs. 0.54 mg/dl [SE 0.08, median 0.40], n = 133, respectively, p = 0.0002) (Fig. 1). Most of the elevation in CRP was accounted for by an acute or recent (same admission) MI (CRP 2.33 mg/dl [SE 0.52], n = 28) rather than a remote MI (CRP 0.86 mg/dl [SE 0.36], n = 16, p = 0.009).

Angiographic evaluations allowed assessment of CRP as a predictor of CAD: CRP was found to be more frequently increased in patients with CAD (>60% stenosis, n = 80) than in control subjects without CAD (<10% stenosis, n = 109): mean CRP 1.32 mg/dl [SE 0.22, median 0.4] versus 0.58 mg/dl [SE 0.11, median 0.33], p = 0.004 (Fig. 1).

**Infectious seropositivity and risk of MI or CAD.** Infectious serology was frequently positive both in patients with MI or CAD and in the respective control groups (Table 2). Odds ratios are shown in Figure 2.

*Chlamydia pneumoniae* titers were positive in 43 (75%) of 57 patients with MI tested compared with (94) (66%) of 143 without a history of MI (odds ratio [OR] 1.6, p = 0.18). The prevalence of seropositivity was similar in those with and without angiographic CAD (68% [84 of 124] vs. 65% [63 of 97]).

For CMV, high but essentially equivalent seropositivity (range 74% to 77%) was noted for patients with MI and their control subjects as well as for patients with CAD and control subjects (Table 2).

*Helicobacter pylori* seropositivity was present in just over 50% of patients with MI and in 50% without MI (Table 2). A trend to somewhat increased prevalence of seropositivity in patients with CAD was not significant (58% vs. 46%, OR 1.6, p = 0.07).

Despite the negative results for individual agents, seropositivity to an increasing number of agents (from 0 to 3) was associated with an increasing risk of CAD of borderline significance (Table 2).

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**Table 1. Demographics of Patient and Control Groups**

<table>
<thead>
<tr>
<th></th>
<th>CAD (n = 219)</th>
<th>No CAD (n = 126)</th>
<th>p Value</th>
<th>MI (n = 112)</th>
<th>No MI (n = 197)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age (yr)</strong></td>
<td>63 ± 11</td>
<td>62 ± 11</td>
<td>0.87</td>
<td>63 ± 11</td>
<td>62 ± 11</td>
<td>0.71</td>
</tr>
<tr>
<td><strong>Men</strong></td>
<td>81%</td>
<td>52%</td>
<td>&lt; 0.001</td>
<td>85%</td>
<td>60%</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td><strong>Smoker</strong></td>
<td>28%</td>
<td>24%</td>
<td>0.41</td>
<td>38%</td>
<td>21%</td>
<td>0.001</td>
</tr>
<tr>
<td><strong>Diabetes</strong></td>
<td>20%</td>
<td>11%</td>
<td>0.04</td>
<td>16%</td>
<td>15%</td>
<td>0.75</td>
</tr>
<tr>
<td><strong>Hypertension</strong></td>
<td>49%</td>
<td>38%</td>
<td>0.04</td>
<td>47%</td>
<td>43%</td>
<td>0.48</td>
</tr>
<tr>
<td><strong>BP (mm Hg)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Systolic</strong></td>
<td>136 ± 22</td>
<td>141 ± 24</td>
<td>0.41</td>
<td>134 ± 24</td>
<td>140 ± 23</td>
<td>0.90</td>
</tr>
<tr>
<td><strong>Diastolic</strong></td>
<td>73 ± 10</td>
<td>73 ± 9</td>
<td>0.99</td>
<td>72 ± 9</td>
<td>73 ± 10</td>
<td>0.34</td>
</tr>
</tbody>
</table>

Data presented are mean value ± SD or percent of patients. BP = blood pressure; CAD = coronary artery disease; MI = myocardial infarction.
significance (p = 0.05, Mantel-Haenszel test for linear association). Risk was especially evident for the combined presence of seropositivity to *C. pneumoniae* and *H. pylori* compared with seronegativity to both (OR 2.6, p = 0.02 for CAD; OR 2.0, p = 0.15 for MI) (Table 2, Fig. 2). Dual seropositivity remained a significant predictor of CAD risk (adjusted OR 3.2, p = 0.015), together with diabetes and gender, in conditional logistic regression modeling that simultaneously considered five other baseline factors (age, gender, smoking, diabetes, hypertension).

Correlation of CRP with positive serology. Table 3 shows the average CRP concentrations in patients with or without seropositivity for any single agent. However, patients seropositive for both *C. pneumoniae* and *H. pylori* did have higher CRP levels (mean 1.07 mg/dl) than patients negative for both (0.53 mg/dl), which bordered on significance (p = 0.06).

Figure 3 shows CRP by the proportion of positive serologies in patients in whom all three were measured simultaneously. A linear, increasing trend was seen, with increasing proportions positive, although variances were large, and significance was not achieved.

**Discussion**

Summary of key findings. In our prospectively studied, angiographically defined cohort, we confirmed an association between the inflammatory marker CRP and a history of MI. The association was marked (fourfold elevation) and highly significant (p = 0.0002) but variable and mostly accounted for by a recent MI. In addition, we extended the association of

**Table 2. Seropositivity to Three Candidate Infectious Agents in Patient and Control Groups**

<table>
<thead>
<tr>
<th>Serologic Status</th>
<th>CAD</th>
<th>No CAD</th>
<th>p Value</th>
<th>MI</th>
<th>No MI</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>C pn+</td>
<td>84</td>
<td>63</td>
<td>0.06</td>
<td>43</td>
<td>75</td>
<td>0.018</td>
</tr>
<tr>
<td>C pn−</td>
<td>40</td>
<td>34</td>
<td>0.34</td>
<td>14</td>
<td>25</td>
<td>0.34</td>
</tr>
<tr>
<td>CMV+</td>
<td>166</td>
<td>71</td>
<td>0.53</td>
<td>82</td>
<td>75</td>
<td>0.65</td>
</tr>
<tr>
<td>CMV−</td>
<td>49</td>
<td>25</td>
<td>0.07</td>
<td>28</td>
<td>25</td>
<td>0.07</td>
</tr>
<tr>
<td>H pyl+</td>
<td>89</td>
<td>52</td>
<td>0.02</td>
<td>41</td>
<td>54</td>
<td>0.15</td>
</tr>
<tr>
<td>H pyl−</td>
<td>65</td>
<td>60</td>
<td>0.02</td>
<td>35</td>
<td>46</td>
<td>0.02</td>
</tr>
<tr>
<td>C pn+/H pyl+</td>
<td>54</td>
<td>30</td>
<td>0.02</td>
<td>27</td>
<td>79</td>
<td>0.02</td>
</tr>
<tr>
<td>C pn−/H pyl−</td>
<td>14</td>
<td>20</td>
<td>0.02</td>
<td>7</td>
<td>21</td>
<td>0.02</td>
</tr>
</tbody>
</table>

Data presented are number (%) of patients. CMV = cytomegalovirus; C pn = *Chlamydia pneumoniae*; H pyl = *Helicobacter pylori*; + = positive; − = negative; other abbreviations as in Table 1.

**Table 3. C-Reactive Protein Concentrations in Serologic Positive and Negative Groups**

<table>
<thead>
<tr>
<th>Serogroup</th>
<th>No. of Pts</th>
<th>CRP (mg/dl)</th>
<th>SE</th>
<th>p Value (+ vs. −)</th>
</tr>
</thead>
<tbody>
<tr>
<td>C pn+</td>
<td>88</td>
<td>0.79</td>
<td>0.16</td>
<td></td>
</tr>
<tr>
<td>C pn−</td>
<td>49</td>
<td>0.58</td>
<td>0.10</td>
<td>0.34</td>
</tr>
<tr>
<td>CMV+</td>
<td>128</td>
<td>0.89</td>
<td>0.14</td>
<td></td>
</tr>
<tr>
<td>CMV−</td>
<td>41</td>
<td>1.14</td>
<td>0.28</td>
<td></td>
</tr>
<tr>
<td>H pyl+</td>
<td>88</td>
<td>0.99</td>
<td>0.19</td>
<td></td>
</tr>
<tr>
<td>H pyl−</td>
<td>82</td>
<td>0.83</td>
<td>0.15</td>
<td>0.25</td>
</tr>
<tr>
<td>C pn+/H pyl+</td>
<td>49</td>
<td>1.07</td>
<td>0.26</td>
<td></td>
</tr>
<tr>
<td>C pn−/H pyl−</td>
<td>23</td>
<td>0.53</td>
<td>0.10</td>
<td>0.06</td>
</tr>
</tbody>
</table>

CRP = C-reactive protein; Pts = patients; other abbreviations and symbols as in Table 2.
CRP to coronary atherostenosis, where a substantial (more than twofold) and significant \((p = 0.004)\) correlation was observed.

Whether elevated CRP might be driven by infectious antigens was explored by measurement of serologic markers for the candidate infectious agents \(C. pneumoniae\), CMV and \(H. pylori\). Indeed, a high proportion of patients with disease were seropositive for these markers (54% to 77%). However, seropositivity also was highly prevalent among control subjects, and differences between control and CAD groups were not significant. Similarly, CRP was not significantly elevated in patients with positive serology for any single agent. Perhaps the poor predictive value of individual infectious serology is due to the high prevalence of exposure observed in control subjects and the inability to distinguish persistent from resolved infection. (Alternatively, other causes of inflammation, either non-infectious or infectious, may be operative.) However, we did note correlations between seropositivity to the combination of \(C. pneumoniae\) and \(H. pylori\) and CAD, MI and (trend) CRP levels, associations that should be prospectively reassessed.

Serology may be marking past exposure as well as persistent infection, so negative results do not exclude an infectious factor in CAD or MI. Nonetheless, seropositivity alone does not appear to be useful as a risk predictor for CAD or MI in individual patients. Additional studies to investigate the causes of elevated CRP, including infectious factors, are indicated.

**Inflammation and coronary heart disease.** Pathologically, atherosclerosis progression involves injury, inflammation, infiltration, degeneration and thrombosis (4–7). The roles of both the local inflammatory response in plaque (with macrophages and, to some extent, lymphocytes and other inflammatory cells) and systemic inflammation in patients at increased risk for coronary events have become increasingly recognized and documented (4–7). The stimuli for the inflammatory response are unknown, although experimental hypertension (causing vascular injury) and hyperlipidemia (i.e., oxidized LDL) are two of several possible candidates (7).

CRP as an acute phase reactant marker for systemic inflammation is reliably assayed and has been consistently found to be elevated in patients with coronary syndromes. Berk et al. (8) reported CRP to be elevated in patients with acute ischemia. Both de Beer et al. (9) and later Pietila et al. (10) reported elevations of CRP in patients with MI. The ability of CRP to predict future events was next demonstrated by Liuzzo et al. (11) who showed that elevated CRP in patients with unstable angina predicted recurrent ischemic events and Thompson et al. (12) who demonstrated that patients with unstable angina were at greater risk of subsequent MI if CRP was increased. A multicenter group (13) confirmed the predictive value of CRP for coronary events in both stable and unstable angina. Kuller et al. (14) reported an association between CRP and coronary death in smokers.

The independent and prospective value of CRP as a risk factor is most strongly supported by a report from the Physicians Health Study (15), which found that CRP in the highest quartile was associated with an increased relative risk (2.9) of future MI \((p < 0.001)\). Moreover, baseline CRP elevation was predictive of increased risk during each of 6 years of follow-up.
Therapy with aspirin reduced the excess risk. These observations suggest that CRP was marking a chronic, persistent inflammatory state rather than an acute, transient one. In the Physician’s Health Substudy (15), the relation of CRP with severity of CAD itself was not measured, nor was the cause of the inflammatory stimulus for elevated CRP determined.

The possibility that infectious agents may trigger a cascade of biological and biochemical reactions leading to inflammation, atherogenesis and vascular thrombotic events has recently been raised. For CAD, C. pneumoniae and CMV have received the most investigative attention and scientific support (16–26). However, causality has not been shown for any agent. The possibility that chronic inflammatory or degenerative diseases might have an infectious basis and potentially be treated with antibiotics is dramatically exemplified by the pathogenic role now demonstrated for H. pylori in peptic ulcer disease and its effective therapy with antibiotics (32,33). Indeed, H. pylori also has been variably associated with CAD (27,28). Other infectious (or noninfectious) causes of inflammation, such as chronic periodontal disease, also might be involved (5,34).

Evidence for an infectious association with CAD is currently most fully developed for C. pneumoniae (16–23). Although not yet demonstrated, C. pneumoniae involvement might begin with infection of alveolar macrophages during a respiratory illness. These macrophages might subsequently enter the circulation, then exit at sites of endothelial damage, lodging within the arterial wall in endothelial and smooth muscle cells (in which C. pneumoniae has proliferative potential) (35). Cytokine pathways, triggered by C. pneumoniae-infected macrophages, would provide a stimulus for smooth muscle cell proliferation and recruitment of additional inflammatory cells, resulting in plaque growth, ongoing inflammation and a prothrombotic state, favoring coronary occlusion (36–38). Activation of macrophages also could result in cell surface expression of the macrophage scavenger receptor, well known to result in phagocytosis of modified forms of LDL as well as microorganisms. The result would be the formation of foamy macrophages, a hallmark of the atherosclerotic plaque. T lymphocytes might also be activated. Indeed, T lymphocytes identified within the intima of fatty streaks respond to a family of heat shock proteins, at least one of which is expressed by C. pneumoniae during intracellular activity.

A similar sequence of events has been postulated for the putative role of CMV (26,39). Inflammation at distant sites (27,28,34) also might act as a general stimulant for atherosclerosis progression and a prothrombotic state through effects on circulating cytokines and prothrombotic factors (e.g., fibrinogen, tissue-type plasminogen activator, plasminogen activator inhibitor-1, platelets).

Implications and limitations of present study for infectious/inflammatory hypothesis of CAD/MI. Our data confirm the importance of CRP as a risk factor for MI and extend this to CAD. Our results also confirm a high prevalence of seropositivity for each of three agents postulated to play a potential role in CAD progression. Indeed, 50% to 75% of patients with CAD or MI have been exposed to these agents, according to serologic evidence, and potentially might be harboring a chronic infection. In this regard, our study is confirmatory of other serologic assessments (19). However, in our study, the prevalence of seropositivity also was high in control patients, without CAD or MI but of similar age.

Our results share the limitations of cross-sectional, observational studies. We evaluated associations, not prospective predictions or causation. Our study had the advantage of an angiographic cohort and could thus define the presence and extent of CAD better than with clinical history alone. Because even angiography may underestimate CAD, only those patients without any evidence of lumen irregularities formed our CAD control group. However, our angiographic control group (primarily patients with chest pain) might differ in unknown ways from free-living populations; thus, our conclusions are strictly applicable to subjects presenting for cardiologic evaluation.

Serology lacks the ability to distinguish persistent from resolved infection. Perhaps serologic markers other than IgG (i.e., IgM or IgA) might provide more informative data. The demonstration of infectious antigen in tissue (atherosclerotic plaque) would be a more compelling marker. Indeed, we have demonstrated (21) the presence of C. pneumoniae antigen in arterial wall samples in ~75% of atherectomy specimens tested from symptomatic patients with CAD. Antigen positivity was generally absent from autopsy specimens from control subjects without CAD or patients with CAD on an immunologic basis (transplant recipients). Other, novel approaches for determining active infection with these or other agents should be a high priority for future research. Antibiotic treatment studies might be undertaken and could focus on seropositive patients to enrich the treated population with those with potentially persistent infection (40). The response of inflammatory, serologic and prothrombotic markers, as well as clinical coronary events, to antibiotic therapy also might be enlightening (40). Preliminary laboratory- and clinic-based antibiotic studies point to a role for infection (40–42).

Despite these provocative observations (40–43), our findings also may be viewed as consistent with a more conventional view of atherosclerosis pathogenesis. The inflammatory stimulus may be nonantigenic or neoantigenic but primarily or entirely noninfectious in origin. Hemodynamic- (e.g., hypertension) and oxidation-sensitive stimuli (e.g., responding to oxidized LDL) have been recognized. In this context, it would not be surprising that elevated levels of CRP correlate with the extent of vascular disease rather than seropositivity.

Conclusions. The present study confirms the association of elevated CRP levels with a clinical history of MI and extends this association to patients with angiographically documented CAD versus angiographically normal coronary arteries. The association was highly statistically significant, although it showed substantial interindividual variability. The cause of this inflammation was explored by measuring infectious serology for three organisms proposed to play a possible role in atherosclerosis progression: C. pneumoniae, CMV and H. pylori. Seropositivity to each agent was extremely common in...
patients with CAD (54% to 77%) and also was highly prevalent in age-matched control subjects, indicating a high prevalence of population exposure. Exposure to two agents (i.e., C. pneumoniae and H. pylori) showed associations that deserve further exploration.

The poorer predictive value of individual infectious serologies than previously suggested might be due to an inability to distinguish persistent from resolved infection or because other causes of inflammation are primarily operative. Thus, additional studies investigating infectious factors in CAD and MI (43) and correlating CRP and other markers of inflammation with more specific markers of active infectious and noninfectious causes of inflammation are indicated.

References

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