The prevalence of chronic *Chlamydia pneumoniae* infection as detected by polymerase chain reaction in pharyngeal samples from patients with ischaemic heart disease

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**Aims** Cross-sectional serological studies have suggested an association between ischaemic heart disease and infections from *Chlamydia pneumoniae* and *Helicobacter pylori*. We therefore sought to find out if patients with ischaemic heart disease had an increased prevalence of *C. pneumoniae* in the pharynx. As the course of the *C. pneumoniae* infection remains unclear, both acute and follow-up samples were taken and compared with antibody levels.

**Methods and Results** We studied 282 patients with ischaemic heart disease. One hundred and two subjects without history or symptoms of ischaemic heart disease served as controls. Pharyngeal specimens for polymerase chain reaction detection of *C. pneumoniae*, and blood samples for *C. pneumoniae* and *H. pylori* antibody detection, were collected. In patients with positive polymerase chain reaction or *C. pneumoniae* IgA titres §32, indicating current infection, convalescent samples were taken at least 6 weeks later. An immunofluorescent antigen detection test was used to confirm the presence of *C. pneumoniae* elementary bodies in specimens found to be polymerase chain reaction positive. The prevalence of positive polymerase chain reaction tests was 36% among patients and 22% among controls (P <0.05). Forty-seven percent of patients with positive polymerase chain reaction remained positive in the convalescent test. Elevated *C. pneumoniae* IgG titres ≥512 were found in 39% of patients and 26% of the controls (P <0.05). IgA titres ≥32 were found in 46% of the patients and 44% of the controls (ns). Antibody titres remained largely unchanged at convalescent testing. Two patients and none of the controls had IgM titres >16. There was no link between positive *H. pylori* serology and positive *C. pneumoniae* polymerase chain reaction tests.

**Conclusions** The high prevalence and persistence of positive pharyngeal *C. pneumoniae* polymerase chain reaction and elevated antibody titres in patients with ischaemic heart disease indicate a chronic infection. The pharyngeal presence of *C. pneumoniae* might contribute to a low grade inflammatory activation or be a source for further spread of the bacteria to atherosclerotic vessels. (Eur Heart J 1998; 19: 1321–1327)

**Key Words:** Cardiovascular diseases, coronary disease, *Chlamydia pneumoniae*, *Helicobacter pylori*, polymerase chain reaction.

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**Introduction**

Data obtained from several seroepidemiological studies have given rise to the hypothesis that an infection can initiate or maintain the arteriosclerotic process. Pathophysiological mechanisms by which this may occur have been described in experimental studies [1,2] and involve, among others, effects on lipid metabolism, leukocyte-endothelial cell interaction and platelet activation. Both bacterial and viral agents have been implicated. Of the former, infections caused by *Chlamydia pneumoniae* and *Helicobacter pylori* have been postulated to be of interest. Both organisms are widely spread and have a tendency to cause chronic low grade infections [3–5]. Recent studies have indicated a link between *C. pneumoniae*, a Gram-negative obligate intracellular bacterium with a unique growth cycle, with arteriosclerosis and ischaemic heart disease. Saikku and co-workers [6] were the first to publish results indicating a link between...
C. pneumoniae infection and ischaemic heart disease in a serological study of patients with chronic coronary heart disease and acute myocardial infarction. Later, a serological study by Thom and co-workers\(^{[17]}\) reported an increased prevalence of specific C. pneumoniae IgG antibodies in patients with angiographically confirmed coronary heart disease. The prognostic importance of C. pneumoniae infection was highlighted in study by Saikku et al.\(^{[8]}\) where elevated IgA and immune complex titres constituted a significant risk factor for the development of coronary heart disease. Further studies, using immunochemical and polymerase chain reaction techniques, have demonstrated the presence of C. pneumoniae in arteriosclerotic lesions of the coronary\(^{[9]}\) and carotid arteries\(^{[10]}\).

H. pylori causes an infection of the stomach believed to be acquired during childhood. The organism has a high prevalence and has been shown to be important for the development of duodenal ulcer, as well as gastric cancer. Seroepidemiological studies\(^{[11,12]}\) have indicated association between H. pylori and coronary heart disease.

Despite the aforementioned studies, it remains unclear whether C. pneumoniae infection is merely associated with arteriosclerosis or if it is of pathogenic importance. Since the serological diagnostic criteria for C. pneumoniae infection are controversial\(^{[13,14]}\), serological cross-sectional studies are open to interpretation of whether the results indicate a previous or an ongoing infection, either acute or chronic. Furthermore, a design to study the dynamics of C. pneumoniae and H. pylori infection in patients with ischaemic heart disease over a period of time has been lacking in previous studies. The polymerase chain reaction method for detection of C. pneumoniae has recently become available and is an important addition to the diagnostic arsenal, having a high degree of sensitivity and specificity\(^{[15]}\).

The present study was designed to investigate a large population of patients with various clinical manifestations of ischaemic heart disease and to determine the presence of C. pneumoniae. This was done using polymerase chain reaction on pharyngeal swabs and by determining specific C. pneumoniae antibodies of the IgA, IgG and IgM classes in acute and convalescent sera. Verification of polymerase chain reaction results was by a direct antigen test, which visualized C. pneumoniae elementary bodies in specimens. In addition, specific antibodies to H. pylori were determined in all patients allowing further study of the possible association between H. pylori infection and ischaemic heart disease, and possible interrelationships with C. pneumoniae infection.

**Methods**

Subjects and procedures

Consecutive patients admitted to the Department of Cardiology, Huddinge University Hospital, Stockholm, Sweden with various manifestations of ischaemic heart disease were included in the study. The inclusion period was from February to August of 1995. A total of 136 patients with acute myocardial infarction and 146 patients with angina pectoris were studied. Of the angina pectoris patients, 129 underwent a scheduled coronary angiogram, following which 24 underwent percutaneous transluminal angioplasty (PTCA), and 17 were treated for unstable angina. In patients undergoing a coronary angiogram, only those with coronary arteriosclerosis were included. In patients with acute myocardial infarction and unstable angina pectoris, pharyngeal specimens for polymerase chain reaction detection of C. pneumoniae carriage and venous blood samples were taken within 6 days after the diagnosis had been established (mean 2 ± 2 days after admission). Samples were taken on admission prior to the procedure in patients undergoing a planned coronary angiography. Four patients with acute myocardial infarction and three patients with angina pectoris did not consent to the collection of pharyngeal specimens.

The control group consisted of 68 healthy health care and administrative personnel at our hospital, and 34 patients admitted to the hospital without any history or symptoms of arteriosclerotic cardiovascular disease, lung disease or ongoing infection.

Patients with positive polymerase chain reaction tests or with specific C. pneumoniae IgA titres of ≥32, thought to be an indication of current infection\(^{[8]}\), were followed-up by a second pharyngeal sample for polymerase chain reaction and serology at least 6 weeks after the initial test (mean 104 ± 35 days). The second specimen was done in order to discriminate between acute or chronic/persistent infection. Convalescent tests were obtained from 146 patients out of a possible 183.

All patients participating in the study gave their informed consent after receiving oral and written information. The study was approved by the Ethics Committee at Huddinge University hospital.

**Serology**

Blood was obtained for serological investigation at admission. All sera were kept frozen at −20°C until analysed.

**Chlamydia antibodies**

Serological analysis was by microimmunofluorescence according to previously described methodology\(^{[16]}\). Antigens used in the microimmunofluorescence test were C. psittaci (IOL-395), C. pneumoniae (IOL-207) and pooled C. trachomatis serovars D-K (I.O. International Ltd., London, U.K.).

The technique used for antibody determinations has been standardized within the laboratory and both high and low titre control sera included on every testing...
occasions. Deviations of ± one serum dilution were allowed in control sera for acceptence of test performances. Control sera, including high titre IgG and IgA, low titre IgG and IgA and an IgM positive were sent to two independent laboratories for verification of titre values. The method used in this study, overnight incubation of serum dilutions with antigen substrate, has been found to significantly increase the sensitivity of detection of specific C. pneumoniae antibodies.

A acute convalescent sera from the same individual were titrated and tested on the same antigen-containing slide for comparison of titres. Serum dilutions of 1:32 were used to screen for humoral antibodies of IgG, IgM and IgA classes. All sera demonstrating IgG antibodies were titrated using twofold dilutions; all sera with IgM or IgA antibodies in the screening test were first absorbed with Culsorb (Gull Laboratories, Ltd., U.S.A.) to remove IgG[17], then titrated and retested. Serum dilutions were incubated with antigen for 16–18 h at +4–+8 °C. Secondary antibody conjugates were incubated for 30 min at 30 °C. All tests were read by the same investigator using a Zeiss UV microscope with a 40 × oil immersion lens (total magnification 400 ×), and antibody titres were expressed as reciprocal titres.

Helicobacter pylori antibodies

Antibodies to H. pylori were measured using an in-house enzyme immunoassay[18]. The enzyme immunoassay test has been shown to have a sensitivity of 0·99, a specificity of 1·00, and positive and negative predictive values of 0·96 and 1·00, respectively, when used parallel to culture and histology on specimens from patients with duodenal ulcer[19]. A absorbance values of <0·500 were interpreted as negative, values of ≥0·700 were interpreted as positive and values between as inconclusive.

Polymerase chain reaction

Specimens were taken from the back of the throat by scraping with CTA swabs (Chlamydia trachomatis aluminium, BiOHopital AB, K opparberg, Sweden), which were then immediately immersed in 25P (Sucrose-phosphate buffer) and then frozen at −70 °C to await transportation to the laboratory. On arrival at the laboratory, the specimens were prepared for polymerase chain reaction according to Gnarpe and Eriksson[20]. Polymerase chain reaction followed the method of Campbell et al.[15] using a primer pair that resulted in a 437 bp product. All polymerase chain reaction products were visualized in agarose gel (International Biotechnologies Inc., New Haven, Connecticut, U.S.A.) with added ethidium bromide on an ultraviolet transilluminator. All specimens were prepared for polymerase chain reaction using stringent precautions in a sterile bench. Negative controls consisting of specimen preparation reagents were included in each preparation batch. All specimens positive for polymerase chain reaction were re-run, with negative controls flanking most specimens. No contamination was observed. This polymerase chain reaction technique has been standardized for use in the laboratory in collaboration with another independent laboratory in Sweden. No reactions have been found with other microorganisms or cell types found in the pharynx. The detection level is 20 elementary bodies.

Verification of C. pneumoniae polymerase chain reaction-positive specimens

C. pneumoniae-positive throat specimens were verified by staining 5 μl aliquots of the polymerase chain reaction specimen preparations applied to Syva Mikrotrak Specimen slides (Syva, Palo Alto, CA) with C. pneumoniae FITC Research Reagent (DAKO Diagnostics Limited, Denmark). One slide was used for each test sample and fixation was accomplished by adding acetone to the air-dried sample drop. Twenty-five microlitres of the FITC conjugated monoclonal antibody suspension was layered on the fixed specimens and incubated at +37 °C for 15 min in a moist chamber. Slides were rinsed phosphate buffered saline pH 7·4 for 5 min by repeated applications of phosphate buffered saline on individual slides to avoid possible cross-contamination. Positive and negative controls used for polymerase chain reaction were used as controls for antigen-detection tests. Slides were air dried and coverslips mounted. All tests were read at 40 × (total magnification 400 ×), using a Zeiss UV microscope with an oil immersion lens; when suspected elementary bodies were found, morphology was verified using the 100 × oil immersion lens (total magnification 1000 ×).

Statistical analysis

As no differences were found between the acute myocardial infarction and angina pectoris groups, they were considered as one entity for the statistical analysis. All values are given as mean ± SD or as number of subjects and percentages if not otherwise stated. Student’s t-test for unpaired observations was used for statistical evaluation of age, cholesterol and triglyceride levels. All other statistical comparisons were done by use of chi-square analysis. P-values are two-tailed and values of less than 0·05 were considered to indicate statistical significance.

Results

Characteristics of patient and control groups are described in Table 1. The mean age was somewhat higher in the patient groups compared to the control group (P <0·001). There were also more men in the patient groups than in the control group (P <0·001). Smoking
habits did not differ between the groups, nor did they differ between patients with positive as compared to those with negative C. pneumoniae polymerase chain reaction, or H. pylori serology (ns).

Positive C. pneumoniae polymerase chain reaction was more common in the patient groups than in controls; 36% in both the acute myocardial infarction and angina pectoris groups were positive as compared to 22% of the controls (P < 0.05) (Table 2, Fig. 1). All C. pneumoniae polymerase chain reaction-positive specimens were verified using the immunofluorescent monoclonal antibody. The frequency of positive polymerase chain reaction tests was as high in patients below the median age as in those above (Table 2). Fifty percent of positive polymerase chain reaction tests in the acute myocardial infarction group and 44% in the angina pectoris group remained positive in the convalescent test. Seventeen percent of patients from the acute myocardial infarction group with a negative polymerase chain reaction and 21% in the angina pectoris group were found to be positive in the convalescent sample. These patients had been called for convalescent sampling on the basis of elevated IgA titres in the initial serological investigation.

IgG titres $\geq 512$, reflecting prior exposure to C. pneumoniae, were found in 81% of the acute myocardial infarction patients, 84% of the angina pectoris patients and 74% of the controls (Table 3). If an IgG titre of $\geq 512$ is an indicator of current infection, as suggested by Kuo et al. [21], 39% of patients in both the acute myocardial infarction and angina pectoris groups had significant titres, as compared to 26% of the controls (P < 0.05) (Table 3, Fig. 1). Similar differences between patient and control groups were found for IgG titres $\geq 256$ and $\geq 1024$ (Table 3). Elevated IgG titres of $\geq 32$ were found in 49% of the acute myocardial infarction patients, 44% of the angina pectoris patients and 44% of the controls (ns) (Table 3, Fig. 1). The IgG and IgA titres remained unchanged for the majority of the

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**Table 1 Characteristic of the study groups**

<table>
<thead>
<tr>
<th></th>
<th>n</th>
<th>Age mean (range)</th>
<th>Gender male/female</th>
<th>Smokers* (%)</th>
<th>Cholesterol** (mmol · l$^{-1}$) mean ± SD</th>
<th>Triglycerides** (mmol · l$^{-1}$) mean ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>AM I</td>
<td>136</td>
<td>67 (37–89)</td>
<td>96/38</td>
<td>34</td>
<td>5.87 ± 1.40</td>
<td>2.10 ± 0.92</td>
</tr>
<tr>
<td>AP</td>
<td>146</td>
<td>63 (34–81)</td>
<td>116/30</td>
<td>15</td>
<td>6.01 ± 1.19</td>
<td>2.11 ± 1.13</td>
</tr>
<tr>
<td>C</td>
<td>102</td>
<td>53 (34–93)</td>
<td>33/69</td>
<td>29</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>


*Data on smoking habits was gathered from the patients medical record and was not available in all subjects. For AM I: n=110; for AP: n=139; for C: n=88.

**Lipid levels were not determined in all subjects. For cholesterol: n=223; for triglycerides: n=110.

**Table 2 C. pneumoniae polymerase chain reaction and H. pylori serology in patients and controls**

<table>
<thead>
<tr>
<th></th>
<th>Pos C. pneumoniae polymerase chain reaction</th>
<th>Pos H. pylori serology</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Total</td>
<td>Male</td>
</tr>
<tr>
<td>AM I</td>
<td>36</td>
<td>38</td>
</tr>
<tr>
<td>AP</td>
<td>36</td>
<td>36</td>
</tr>
<tr>
<td>C</td>
<td>22</td>
<td>16</td>
</tr>
</tbody>
</table>


Figure 1 Left bars: prevalence of positive C. pneumoniae polymerase chain reaction; middle bars: Prevalence of C. pneumoniae IgG titres $\geq 512$; right bars: Prevalence of C. pneumoniae IgA titres $\geq 32$. ■ = patients with acute myocardial infarction; □ = patients with angina pectoris. △ = control subjects.
patients in the convalescent tests, only 6% of the patients had a titre change of \( \geq 2 \) dilutions. No correlation was found between elevated IgA titres \( \geq 32 \) or IgG titres \( \geq 512 \) and positive C. pneumoniae polymerase chain reaction tests, as the prevalence of these titre levels was similar among patients with positive and negative C. pneumoniae polymerase chain reaction. Only two patients and none of the controls had detectable IgM titres to C. pneumoniae.

Ten patients lacking serological evidence of prior or ongoing C. pneumoniae infection had positive polymerase chain reaction tests. Five of these remained positive in the second polymerase chain reaction test despite a continued lack of antibody response. Similar cholesterol levels were found in polymerase chain reaction-positive and in polymerase chain reaction-negative patients (5.98 \( \pm \) 1.41 vs 5.92 \( \pm \) 1.23 mmol \( \cdot \) l\(^{-1}\), ns). Triglyceride levels did not differ between patients with positive and negative polymerase chain reaction (2.11 \( \pm \) 0.92 vs 2.05 \( \pm \) 1.14 mmol \( \cdot \) l\(^{-1}\), ns).

The prevalence of positive H. pylori serology was 52% in ischaemic heart disease patients as compared to 38% in controls (P < 0.05). Twenty-eight patients had inconclusive H. pylori serology (see Methods) and were therefore not included in further comparisons. The prevalence of positive H. pylori serology in patients with positive C. pneumoniae polymerase chain reaction was 54%. The prevalence of positive H. pylori serology was similar in patients with positive and negative C. pneumoniae polymerase chain reaction. The results of H. pylori serology in relation to positive or negative polymerase chain reaction tests are shown in Table 4.

**Table 3** Percentage of subjects with regards to titre levels of C. pneumoniae IgG and IgA

<table>
<thead>
<tr>
<th>Titre</th>
<th>IgG (%)</th>
<th>IgA (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>AMI</td>
<td>AP</td>
<td>C</td>
</tr>
<tr>
<td>( \geq 32 )</td>
<td>86</td>
<td>89</td>
</tr>
<tr>
<td>( \geq 64 )</td>
<td>68</td>
<td>73</td>
</tr>
<tr>
<td>( \geq 128 )</td>
<td>53</td>
<td>58</td>
</tr>
<tr>
<td>( \geq 256 )</td>
<td>39</td>
<td>39</td>
</tr>
<tr>
<td>( \geq 512 )</td>
<td>18</td>
<td>22</td>
</tr>
</tbody>
</table>

AMI = patients with acute myocardial infarction. AP = patients with angina pectoris. C = control subjects.

different manifestations of the disease. This suggests that C. pneumoniae infection is associated with the underlying disease entity, i.e. the atherosclerotic process, rather than with one of its clinical manifestations. The high degree of persistence of positive polymerase chain reaction tests and elevated IgA and IgG titres, coupled with the very low prevalence of IgM antibodies, is suggestive of chronic or persistent C. pneumoniae infection as opposed to an acute or recent infection. The polymerase chain reaction results were similar in patients \( \leq 65 \) years, where mean age was in parity with that of the control group. The prevalence of positive polymerase chain reaction was similar in patients above or below median age, indicating that these findings were not age-related.

Very few of the patients and none of the controls had symptoms of ongoing respiratory tract infection. This is in accordance with earlier findings[22] indicating that most C. pneumoniae infections are asymptomatic. It is interesting that a few individuals showed pharyngeal carriage of C. pneumoniae by polymerase chain reaction without any signs of antibody response. This could indicate an acute infection where an antibody response is yet to occur; however, the convalescent tests revealed that five patients remained negative in antibody tests in spite of repeated positive pharyngeal polymerase chain reaction tests. This suggests that it is possible to be a carrier of C. pneumoniae for extended periods without production of an antibody response. This finding is of epidemiological interest and further complicates the interpretation of antibody titres and the role of the individual humoral immune response in this type of infection.

The detection of C. pneumoniae DNA by polymerase chain reaction does not reflect the viability of the organism. However, positive polymerase chain reaction findings in conjunction with persisting high specific antibody titres strongly suggest on ongoing infection. The polymerase chain reaction technique has, in previous studies, been shown to have a high sensitivity and specificity[15]. Our experience is that C. pneumoniae is difficult to culture. As C. pneumoniae is an obligate intracellular organism, the sampling procedure is very important. We have found that retropharyngeal sampling will give a higher rate of positive results than nasopharyngeal swabs[23]. Furthermore, the technique for pre-polymerase chain reaction preparation of the sample is important, and we have shown earlier that lysis of the tissue cells increases detection sensitivity[20]. This may explain the relatively high percentage of

**Discussion**

This is, to our knowledge, the first study demonstrating a higher prevalence of C. pneumoniae in the pharynx in patients with ischaemic heart disease. Both C. pneumoniae polymerase chain reaction tests and IgG titres were elevated in patients with ischaemic heart disease as compared to controls. No differences were found in the prevalence of positive polymerase chain reaction or increased IgG antibody titres between patients with
carriers in the patient as well as in the control group compared to previously published data\cite{24}.

We chose to verify the presence of \textit{C. pneumoniae} in polymerase chain reaction-positive specimens by using a direct antigen test rather than probe hybridization. The findings of elementary bodies in specimens prepared for polymerase chain reaction adds to the finding that \textit{C. pneumoniae} can be found in a high prevalence among patients with ischaemic heart disease.

We found higher antibody titres in both patients and controls compared to previously published data. Saikku et al.\cite{6} reported that 85% of patients with acute myocardial infarction and 87% of patients with angina pectoris enrolled for coronary angiography had IgG titres of $\geq 32$, as compared to 61% in the control group. In our study the prevalence of IgG titres $\geq 32$ was similar to this, but high titres $\geq 512$ were more prevalent among our patients and controls. The pattern is similar regarding IgA titres. In the study of Thom et al.\cite{25} of patients with angiographically demonstrated coronary artery disease, as many as 52% of the controls and 33% of the patients lacked measurable IgG titres ($<8$); in our study, only 16% in the control group, 14% in the acute myocardial infarction and 11% in the angina pectoris group lacked IgG antibodies ($<32$). These differences may be explained by the different epidemiological backgrounds at the time of sampling and by the different patient populations investigated. The studies of Saikku et al. and Thom et al. studies were limited to patients up to 50 and 55 years of age, respectively, whilst many of our patients were older.

Although we cannot estimate the frequency of false-negative polymerase chain reaction results, these should have been equally distributed among patients and controls, resulting in an underestimation of the true prevalence of \textit{C. pneumoniae} in both patients and controls. Our control group could have reflected an overestimation of the occurrence of \textit{C. pneumoniae} in a healthy population since hospital-based workers are more likely to be exposed to individuals with respiratory tract infections. This is also corroborated by the higher prevalence of increased IgG and IgA antibody titres in our control group, compared to the titre levels observed among healthy blood donors. In a study comprising 123 men $\geq 35$ years during the same time period, IgG and IgA levels were significantly lower, with 20% having IgG titres $\geq 512$, and 14% IgA titres $\geq 32$ (unpublished results). Based on this epidemiological background, our results might have underestimated the degree of association between \textit{C. pneumoniae} and ischaemic heart disease. A high incidence of \textit{C. pneumoniae} in the background has been given as a possible explanation for a lack of confirmatory data in some earlier serological studies\cite{26}.

The prevalence of a positive polymerase chain reaction in the control group tended to be more common among women than men, 25% vs 16%. The number of subjects, is, however, too small for comparisons of subgroups. The relatively higher proportion of women in the control group compared to the patient group would, if anything, have diminished the observed difference in the subjects. Another factor that could also reduce differences between patients and controls is the possibility of asymptomatic coronary arteriosclerosis in the control group.

In the study of Mendall et al.\cite{11} of patients with angiographically confirmed coronary heart disease, 59% of the cases and 39% of the controls were seropositive for \textit{H. pylori}. Our results were of similar magnitude. However, in our study there was no significant difference between patients aged $\leq 65$ years (where the mean age was in parity with the total control group) and the controls. The observed differences with regards to \textit{H. pylori} serology between the patient and control groups in our study may therefore, at least in part, be age-related.

We found no correlation between positive \textit{H. pylori} serology and positive \textit{C. pneumoniae} polymerase chain reaction. Our results therefore do not suggest an increased overall susceptibility to infection per se or an interrelationship between \textit{H. pylori} and \textit{C. pneumoniae} infection.

The importance of smoking as a possible confounding factor in the association of \textit{C. pneumoniae} and \textit{H. pylori} infection with ischaemic heart disease has been addressed in previous studies\cite{12,27,28}. In our study we found no association between smoking and positive \textit{C. pneumoniae} polymerase chain reaction or \textit{H. pylori} serology.

Recent studies have demonstrated the presence of \textit{C. pneumoniae} in arteriosclerotic coronary vessels\cite{9,29}, yet it remains to be shown whether \textit{C. pneumoniae} is a causal agent for the arteriosclerotic process. Our findings suggest that a persistent \textit{C. pneumoniae} infection in the pharynx could contribute to low grade inflammatory activation with systemic effects. It could also serve as a source for intermittent spreading of the bacteria that could result in recurrent inflammatory responses in arteriosclerotic blood vessels.

Possible pathogenic mechanisms and pathways by which a chronic \textit{C. pneumoniae} infection might play a role in the arteriosclerotic process have been postulated. The infection could lead to an activation of cytokine pathways\cite{30} resulting in increased synthesis of acute phase proteins such as C-reactive protein and fibrinogen, previously described as prognostic risk factors in ischaemic heart disease\cite{31,32}. Cytokine activation could potentially influence the arteriosclerotic process by affecting leukocyte-endothelial cell interaction, T-cell activation and procoagulant activity of the endothelium\cite{33,34}. Bacterial lipopolysaccharide binding to lipoproteins could affect endothelial cell-lipids interaction\cite{35}.

In summary, the present results are the first evidence of increased and persistent pharyngeal carriage of \textit{C. pneumoniae} in patients with ischaemic heart disease. This could be the source of further spreading of the bacteria, or the maintenance of a low grade general inflammatory response. Further interventional studies are needed to assess the significance of these findings regarding the progression of the arteriosclerotic process and its clinical manifestations.
References


