Association Between Infection With Helicobacter pylori and Chlamydia pneumoniae and Risk of Ischemic Stroke Subtypes

Results From a Population-Based Case-Control Study

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Background and Purpose—Helicobacter pylori and Chlamydia pneumoniae have been associated epidemiologically and pathogenetically with coronary atherosclerosis. However, population-based data on chronic infection and stroke are lacking. Therefore, we investigated the association of both bacterial pathogens and ischemic stroke subtypes in a population-based case-control study.

Methods—Patients with first ischemic stroke in the population-based Erlangen Stroke Project were collected as cases. Neighborhood controls were drawn from the study population, matched for age, sex, and place of residence. IgG antibodies to H pylori were measured by enzyme immunoassay, and IgG antibodies to C pneumoniae were measured by microimmunofluorescence technique. Conditional logistic regression was used. Analyses were stratified for etiologic stroke subtypes according to Trial of Org 10172 in Acute Stroke Treatment (TOAST) criteria.

Results—A total of 145 case and 260 control subjects were included. Chronic H pylori infection was associated with a higher risk of stroke caused by small-artery occlusion (adjusted odds ratio, 3.31; 95% CI, 1.15 to 9.56) and a lower risk of cardioembolic stroke (adjusted odds ratio, 0.21; 95% CI, 0.06 to 0.71). Overall, elevated H pylori as well as elevated C pneumoniae antibodies were not associated with ischemic stroke.

Conclusions—Our population-based study does not provide evidence of any strong association between the immune response to C pneumoniae as a marker of prior infection and ischemic stroke. Further studies are required to reveal the role of chronic H pylori infection as an independent risk factor for the subgroup small-artery occlusion. (Stroke. 2001; 32:2253-2258.)

Key Words: Chlamydia pneumoniae ■ Helicobacter pylori ■ seroepidemiologic studies ■ stroke

Helicobacter pylori and Chlamydia pneumoniae are notorious for causing chronic infections and have been seroepidemiologically linked to coronary heart disease and atherosclerosis.\(^1,2\) In addition, C pneumoniae has been directly recovered from atheromatous plaques.\(^3\)

Ischemic stroke is a heterogeneous mixture of different stroke subtypes caused by atherosclerotic as well as nonatherosclerotic mechanisms.\(^4\) Although stroke is thus pathogenetically related to coronary atherosclerosis, data on chronic infection in cerebrovascular disease are limited.\(^5-10\) For a valid and reliable evaluation of the risk factor chronic infection in cerebrovascular disease, the underlying pathomechanisms of ischemic stroke must be considered by stratifying the analyses for different etiologic subtypes. Because direct detection methods for H pylori and C pneumoniae depend on cerebrovascular wall samples retrieved in vivo, which are obviously not available, surrogate markers such as antibody levels must be used to describe the association between stroke and previous infection in an indirect manner.

Therefore, we have investigated, in a population-based case-control sample, whether serological evidence of H pylori or C pneumoniae infection is an independent risk factor in different etiologic subtypes of ischemic stroke.

Subjects and Methods

The Erlangen Stroke Project (ESPro) is an ongoing, prospective, population-based stroke registry in Germany, monitoring a study population of 100 330 inhabitants (December 31, 1997). The methods for case detection and the characteristic of the study area were described in detail elsewhere.\(^11\)

Selection of Cases

First-ever stroke patients in the ESPro were enrolled in the study if they met the following criteria: (1) first ischemic stroke, (2) stroke...
mg/L were defined\(^{13}\) by use of a high-sensitivity assay (N High Sensitivity CRP, Dade Behring Marburg GmbH).

Ischemic stroke was classified according to the Trial of Org 10172 in Acute Stroke Treatment (TOAST) criteria\(^{4}\) into large-artery atherosclerosis, cardioembolism, small-artery occlusion, other determined etiology, and undefined cause. The TOAST classification was performed by 2 neurologists on the basis of a clinical examination as well as the results of standardized diagnostic tests including CT scan or MRI, vascular imaging, and ECG or echocardiography. The overall interrater reliability for the classification was good (unweighted kappa = 0.65). Because of small numbers (n = 2), subgroup analyses were performed without the stroke subtype of other determined etiology.

**Laboratory Methods**

Blood samples were labeled with a serial number immediately after blood was taken. Thus, all investigators were blind to case-control status during the laboratory tests. Samples of case and control subjects were prepared, centrifuged, and stored in 2-ml aliquots within the first 2 hours after the blood sample was drawn. Sera were kept frozen at −80°C until the analyses. Immunoglobulin G (IgG) antibody titers to *C pneumoniae* were analyzed with a microimmunofluorescence test (MIKRO-IFT, Labsystems OY). The resulting antibody titers were classified into titers ≤ 1:32, 1:32, 1:64, 1:128, 1:256, 1:512, and 1:1024 on the basis of their serial dilution. A priori, we agreed on classifying *C pneumoniae* antibodies ≤ 1:32 as negative or low positive. High-positive titers (≥ 1:64) were used as cutoff because they were rated most appropriate for seroepidemiological purposes.\(^{16}\)

To investigate the reliability of the microimmunofluorescence test, the analyses were repeated in 45 randomly selected specimens. The agreement of the classification was good (quadratic weighted kappa = 0.70). IgG antibodies to *H pylori* were analyzed with a commercial enzyme immunoassay (Pyloriset, BAG). The manufacturer’s recommended cutoff was chosen to indicate *H pylori* seropositivity. To study the influence of both infectious agents together on an individual’s risk of stroke,\(^{17}\) we further classified cases and controls as having 0, 1, or 2 positive IgG antibody titers to *H pylori* and/or *C pneumoniae*. Because of the small number of subjects with no serological evidence of any infection (13 case and 21 control subjects), data from these participants and from participants with 1 positive IgG antibody titer were analyzed together.

**Statistical Analyses**

Statistical analyses were performed with the SAS 8.0 software (SAS Institute). The t test was used to test differences in continuous variables, and the χ² test was used to test differences in proportions. The sample size of the study was powered to detect an odds ratio (OR) of ≥ 2-fold with 80% power at a 5% level of significance for all ischemic strokes, on the basis of previous findings.\(^{5,6,10,16}\)

To estimate the OR and the resulting 95% CI for the matched case-control pairs, conditional logistic regression was performed. The OR was calculated before and after adjustment for potential confounders. Possible interaction between elevated antibody titers and the other covariates in the model was controlled by adding terms of interaction to the regression model and testing the statistical significance of the resulting coefficient. Subgroup analyses were performed by running different regression models for each stroke subtype. All tests were 2-tailed; statistical significance was determined at an α level of 0.05.

**Ethics**

The design of the study was approved by the Ethics Committee (No. 1041/1998) and the Data Protection Committee of the University of Erlangen-Nuremberg. All case and control subjects gave their written informed consent to take part in the study. The participants who were not able to consent for themselves because of severe illness or unconsciousness had given consent through their next of kin or guardian.
The mean age of the 145 ischemic stroke cases was 74.6 years (SD 10.4), and 77 (53%) were females. Characteristics of case and control subjects are demonstrated in Table 1. Table 2 shows the prevalence rates of seropositivity to *H pylori*, *C pneumoniae*, and a concomitant infection with *H pylori* and *C pneumoniae*.

In conditional logistic regression (Table 3), elevated IgG antibodies to *H pylori* were significantly associated with a higher risk of stroke due to small-artery occlusion (adjusted OR, 3.31; 95% CI, 1.15 to 9.56). *H pylori* seropositivity demonstrated a positive but nonsignificant risk of stroke due to large-artery atherosclerosis (adjusted OR, 6.18; 95% CI, 0.48 to 80.42) on the basis of the small number of cases and controls in this subtype. An inverse, significant relation was found between elevated *H pylori* IgG antibodies and cardioembolic stroke (adjusted OR, 0.21; 95% CI, 0.06 to 0.71). Because of these differential associations in stroke subtypes, chronic *H pylori* infection was overall not associated with ischemic stroke (all subtypes combined). Tests for interaction between *H pylori* seropositivity and the other examined risk factors revealed no significant terms of interaction.

For elevated *C pneumoniae* antibodies, no significant association with subtypes of ischemic stroke was observed. The risk for first ischemic stroke (all subtypes combined) was also not associated with prior *C pneumoniae* infection (Table 3). No significant interaction could be found for *C pneumoniae* antibodies and risk factors. As a secondary analysis, a possible association between *C pneumoniae* antibodies and risk for ischemic stroke was evaluated for higher cutoff titers ($\geq 1:128$; $\geq 1:256$; $\geq 1:512$). Varying the titer cutoffs also resulted in no significant association between elevated *C pneumoniae* antibodies and ischemic stroke (data not shown).

A simultaneous immune response to *H pylori* and *C pneumoniae* was associated with an increased risk of stroke due to small-artery occlusion (adjusted OR, 2.88; 95% CI, 1.03 to 8.09) and a decreased risk for cardioembolic stroke (adjusted OR, 0.28; 95% CI, 0.08 to 0.91).

In response to the possibility that controlling for elevated C-reactive protein levels might result in an overadjustment for chronic inflammatory response, all multiple analyses were repeated without adjustment for C-reactive protein. Removal of C-reactive protein from the model did not alter any of the results considerably.

### Results

The mean age of the 145 ischemic stroke cases was 74.6 years (SD ± 10.4), and 77 (53%) were females. Characteristics of case and control subjects are demonstrated in Table 1. Table 2 shows the prevalence rates of seropositivity to *H pylori*, *C pneumoniae*, and a concomitant infection with *H pylori* and *C pneumoniae*.

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In response to the possibility that controlling for elevated C-reactive protein levels might result in an overadjustment for chronic inflammatory response, all multiple analyses were repeated without adjustment for C-reactive protein. Removal of C-reactive protein from the model did not alter any of the results considerably.

### Table 1. Characteristics of Case and Control Subjects

<table>
<thead>
<tr>
<th></th>
<th>Controls (n=260)</th>
<th>Cases (n=145)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension</td>
<td>113 (43)</td>
<td>95 (66)</td>
<td>0.0001</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>31 (12)</td>
<td>36 (25)</td>
<td>0.0008</td>
</tr>
<tr>
<td>Hypercholesterolemia</td>
<td>62 (24)</td>
<td>26 (18)</td>
<td>0.16</td>
</tr>
<tr>
<td>Previous myocardial infarction</td>
<td>23 (9)</td>
<td>21 (14)</td>
<td>0.08</td>
</tr>
<tr>
<td>Current smokers</td>
<td>17 (7)</td>
<td>23 (16)</td>
<td>0.003</td>
</tr>
<tr>
<td>Elevated C-reactive protein</td>
<td>86 (33)</td>
<td>96 (66)</td>
<td>0.0001</td>
</tr>
<tr>
<td>High school graduation</td>
<td>86 (33)</td>
<td>20 (14)</td>
<td>0.001</td>
</tr>
</tbody>
</table>

### Stroke subtype

- **Large-artery atherosclerosis**
- **Cardioembolism**
- **Small-artery occlusion**
- **Undefined cause**
- **Other cause**

Values are number (percentage).

### Table 2. Crude Prevalence of Elevated IgG Antibodies to Chronic Infectious Agents Among Cases and Controls

<table>
<thead>
<tr>
<th></th>
<th>Cases (n=145)</th>
<th>Controls (n=260)</th>
<th>Cases (n=145)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>117/257 (46)</td>
<td>67/145 (46)</td>
<td>216/260 (83)</td>
</tr>
</tbody>
</table>

#### Age group, y

- **<65**
  - Controls: 11/48 (23) Cases: 9/22 (41)
  - Controls: 38/48 (79) Cases: 19/22 (86)
  - Controls: 8/48 (17) Cases: 8/22 (36)

- **65–74**
  - Controls: 47/104 (45) Cases: 19/40 (48)
  - Controls: 88/105 (84) Cases: 35/40 (88)
  - Controls: 37/104 (36) Cases: 16/40 (40)

- **75–84**
  - Controls: 48/87 (55) Cases: 27/61 (44)
  - Controls: 76/89 (85) Cases: 49/61 (80)
  - Controls: 42/87 (48) Cases: 22/61 (36)

- **>84**
  - Controls: 11/18 (61) Cases: 12/22 (55)
  - Controls: 14/18 (78) Cases: 19/22 (86)
  - Controls: 8/18 (44) Cases: 11/22 (50)

#### Sex

- **Male**
  - Controls: 70/136 (52) Cases: 34/68 (50)
  - Controls: 125/136 (92) Cases: 61/68 (90)
  - Controls: 63/136 (46) Cases: 28/68 (41)

- **Female**
  - Controls: 47/121 (39) Cases: 33/77 (43)
  - Controls: 91/124 (73) Cases: 61/77 (79)
  - Controls: 32/121 (27) Cases: 29/77 (38)

#### Stroke subtype

- **Large-artery atherosclerosis**
  - Controls: 9/14 (64) Cases: 10/14 (71)
  - Controls: 10/14 (71) Cases: 6/14 (43)

- **Cardioembolism**
  - Controls: 11/39 (28) Cases: 33/39 (85)

- **Small-artery occlusion**
  - Controls: 29/48 (60) Cases: 43/48 (90)
  - Controls: 29/48 (60) Cases: 25/48 (52)

- **Undefined cause**
  - Controls: 16/42 (38) Cases: 34/42 (81)
  - Controls: 16/42 (38) Cases: 13/42 (31)

Values are prevalence/total (percentage).

*Measurement for *H pylori* IgG antibody titers failed in 3 controls.
Discussion

In our population-based study, IgG antibody responses in *H pylori* and in parallel infection with *H pylori* and *C pneumoniae* were associated with an increased risk of stroke in the subtype of small-artery occlusion and a decreased risk of stroke caused by cardioembolism. However, no evidence was found for any strong association between elevated IgG antibodies to *H pylori* and *C pneumoniae* and the overall risk of stroke.

### *H pylori* Infection and Stroke Risk

Data on chronic infection and stroke are limited. Our findings were consistent with the results of the only study that addressed the relation between chronic *H pylori* infection and ischemic stroke. Markus and Mendall 10 reported elevated IgG antibodies to *H pylori* in the subgroup of lacunar stroke, which is comparable to the subtype of small-artery occlusion and a decreased risk of stroke caused by cardioembolism. However, no evidence was found for any strong association between elevated IgG antibodies to *H pylori* and *C pneumoniae* and the overall risk of stroke.

#### Table 3. ORs for Association of IgG Antibodies With Chronic Infectious Agents and Ischemic Stroke Subtypes

<table>
<thead>
<tr>
<th></th>
<th>Unadjusted OR*</th>
<th>Adjusted OR†</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>OR 95% CI P</td>
<td>OR 95% CI P</td>
</tr>
<tr>
<td><strong>H pylori</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>0.99 0.65–1.51 0.97</td>
<td>0.87 0.52–1.46 0.59</td>
</tr>
<tr>
<td>Stroke subtype</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Large-artery atherosclerosis</td>
<td>3.31 0.61–17.95 0.16</td>
<td>6.18 0.48–80.42 0.16</td>
</tr>
<tr>
<td>Cardioembolism</td>
<td>0.34 0.14–0.83 0.02</td>
<td>0.21 0.06–0.71 0.02</td>
</tr>
<tr>
<td>Small-artery occlusion</td>
<td>2.75 1.14–6.64 0.02</td>
<td>3.31 1.15–9.56 0.03</td>
</tr>
<tr>
<td>Undefined cause</td>
<td>0.64 0.29–1.42 0.27</td>
<td>0.58 0.21–1.62 0.30</td>
</tr>
<tr>
<td><strong>C pneumoniae</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>1.11 0.63–1.97 0.71</td>
<td>0.86 0.44–1.67 0.65</td>
</tr>
<tr>
<td>Stroke subtype</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Large-artery atherosclerosis</td>
<td>0.28 0.05–1.57 0.15</td>
<td>0.32 0.04–2.25 0.25</td>
</tr>
<tr>
<td>Cardioembolism</td>
<td>1.61 0.52–4.98 0.41</td>
<td>0.93 0.21–4.07 0.92</td>
</tr>
<tr>
<td>Small-artery occlusion</td>
<td>1.57 0.52–4.74 0.42</td>
<td>1.58 0.44–5.73 0.49</td>
</tr>
<tr>
<td>Undefined cause</td>
<td>0.95 0.35–2.56 0.92</td>
<td>0.70 0.21–2.34 0.56</td>
</tr>
<tr>
<td><strong>H pylori and C pneumoniae</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>1.08 0.69–1.69 0.73</td>
<td>0.85 0.49–1.46 0.56</td>
</tr>
<tr>
<td>Stroke subtype</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Large-artery atherosclerosis</td>
<td>1.43 0.27–7.48 0.67</td>
<td>0.97 0.05–19.94 0.98</td>
</tr>
<tr>
<td>Cardioembolism</td>
<td>0.53 0.22–1.26 0.15</td>
<td>0.28 0.08–0.91 0.04</td>
</tr>
<tr>
<td>Small-artery occlusion</td>
<td>2.85 1.16–6.97 0.02</td>
<td>2.88 1.03–8.09 0.04</td>
</tr>
<tr>
<td>Undefined cause</td>
<td>0.64 0.26–1.53 0.31</td>
<td>0.50 0.16–1.55 0.23</td>
</tr>
</tbody>
</table>

ORs and 95% CI were calculated by use of conditional logistic regression analyses.

*Matched for age, sex, and place of residence.
†Matched for age, sex, and place of residence; adjusted for diabetes, hypertension, hypercholesterolemia, chronic inflammation, education; OR for *C pneumoniae* adjusted also for current smoking.

A similar trend was demonstrated for stroke caused by large-artery atherosclerosis in the study of Markus and Mendall 10 and our study (adjusted OR, 2.17; 95% CI, 1.11 to 4.21 and adjusted OR, 6.18; 95% CI, 0.48 to 80.42, respectively), even if no statistical significance could be achieved in our analyses because of the small number of cases in this stroke subtype. Comparisons between both studies about the role of *H pylori* in cardioembolic stroke could not be performed because the results of Markus and Mendall 10 were reported for the combined subtypes of cardioembolism and undefined cause. In our study *H pylori* infection was found to be associated with a 0.2-fold decreased risk of stroke by cardioembolism. Cardioembolic strokes are mainly caused by cardiac disorders, such as atrial fibrillation, that lead to a thromboembolic occlusion of cerebral arteries. Therefore, our findings are consistent with a positive association of chronic *H pylori* infection and ischemic stroke caused by an atherosclerotic mechanism of cerebral arteries. However, consideration of stroke as a nonhomogeneous condition and analysis of etiologic stroke subtypes separately result in small numbers among specific stroke subtypes. Therefore, the nonsignificant results in the subgroup of large-artery atherosclerosis need further investigations with larger sample sizes. Furthermore, it is possible that the results for *H pylori* were attributed to residual confounding, particularly by factors related to socioeconomic status, although we tried to control for them. This
might be of particular interest in regard to consideration of *H pylori* infection as a marker of lower socioeconomic status.\textsuperscript{20} which seems to be an independent risk factor of vascular disease.\textsuperscript{21} Childhood social class, which was not regarded in the present analyses, might also be an important confounder, since adjustment for markers of childhood socioeconomic status has recently been shown to weaken a potential association between *C pneumoniae* infection and coronary heart disease.\textsuperscript{22}

**C pneumoniae** Infection and Stroke Risk

Five previous studies reported on the association between *C pneumoniae* infection and stroke risk. All of them,\textsuperscript{5–7,9} except 1,\textsuperscript{8} found a positive association between elevated *C pneumoniae* antibodies and stroke, varying from an OR of 1.71 (95% CI, 1.08 to 2.7)\textsuperscript{9} to 8.58 (95% CI, 1.07 to 68.82).\textsuperscript{7} However, a number of methodological aspects must be considered when these findings are interpreted. Previous studies analyzed ischemic strokes and transient ischemic attacks together,\textsuperscript{5,6} as well as first-ever and recurrent strokes.\textsuperscript{6} Some of them reported all strokes, including intracranial hemorrhages, subarachnoid hemorrhages, and undefined types,\textsuperscript{6,7} and 1 study excluded ischemic strokes of undefined cause.\textsuperscript{9} None of the former studies stratified for etiologic subtypes of ischemic stroke. Different case definitions, combination of incident and recurrent strokes, and analysis of all stroke subtypes together might influence a potential association in both directions. Additionally, most of the findings were based on case-control studies with small sample size,\textsuperscript{5,6,8,9} which might be prone to selection bias. Two studies chose hospital-based controls,\textsuperscript{5,6} which may not be representative of the study population or may lead to an overmatching of risk factors.\textsuperscript{23} One study used population-based controls, selected by random-digit dialing.\textsuperscript{9} No information was provided about the proportion of the study population with access to a telephone line, which might have caused an underestimation of lower social class in the control group. Differences were also found in measurement methods and definition of *C pneumoniae* infection. Even if all studies applied the microimmunofluorescence technique to diagnose chronic *C pneumoniae* infection, divergent antibody titers were used for defining seropositivity, ranging from IgA and IgG ≥1:16 as a cutoff titer\textsuperscript{9} to IgA ≥1:64 and IgG ≥1:512 as a combined cutoff point.\textsuperscript{7} If no “reference standard” for seropositivity to *C pneumoniae* is determined, varying cutoff points might be chosen after data exploration to report a maximal positive association between exposure and disease. Although the results of a microimmunofluorescence assay depend on the raters,\textsuperscript{24} no previous study checked interobserver agreement of the classification, and 1 did not report on blinding case-control status.\textsuperscript{9} A positive association between *C pneumoniae* antibodies and stroke was found only for elevated IgA\textsuperscript{5,9} or a combination of elevated IgA and IgG antibody titers.\textsuperscript{6,7} However, a *C pneumoniae* workshop group recently considered the actual data, which reported elevated IgA antibodies to *C pneumoniae* to be a marker of chronic infection, to be unconvincing.\textsuperscript{24} Thus, there is evidence that some of the positive associations between *C pneumoniae* seroprevalence and stroke risk reported in previous studies might be explained by selection bias, information bias, or residual confounding.

The presence of *C pneumoniae* in atherosclerotic plaques has been demonstrated in noncerebral vessels, and chronic infection and inflammation are becoming integral parts of the hypothesis of atherosclerosis.\textsuperscript{2} However, IgG as a serological marker for chronic *C pneumoniae* infection was not found to have any association with ischemic stroke in our study. In addition to methodological reasons, this result could be due to a different age distribution in our study. The mean age of case subjects was 75 years compared with 36.5 years\textsuperscript{5} to 68.5 years\textsuperscript{9} in previous studies. The prevalence of seropositivity to *C pneumoniae* increases with age.\textsuperscript{23} Therefore, the involvement of older cases might weaken a moderately positive association between *C pneumoniae* infection and stroke by higher prevalence rates in cases and controls. Our study was powered to detect an overall association of ≥2-fold between *C pneumoniae* seropositivity and ischemic stroke. Therefore, the number of case-control subjects within the subgroups was too small to detect a possible moderate association between elevated *C pneumoniae* antibodies and different etiologic stroke subtypes with a sufficient power. The low participation rate among control subjects might be caused by the older age distribution of our study. Potential controls from the general population within older age groups are more likely to be disabled or suffering from severe comorbidities. Therefore, they might be less willing to participate in any voluntary study than younger subjects, especially if they were not evaluated in their domestic surroundings. Thus, we cannot exclude that some of our findings might be caused by a potential selection of control subjects. As a result of the case-control design of our study, blood specimens were obtained from the cases during the acute hospitalization. Because the infection status of case subjects before stroke remains unknown, we cannot exclude that the disease condition itself might influence the antibody levels. However, we tried to minimize the possibility of changes in serology after stroke by restricting the study population to cases that were admitted within the first 72 hours after onset and by collecting the blood samples within the first 24 hours after admission. Additionally, it is known that serology correlates poorly with the presence of *C pneumoniae* in vascular specimens.\textsuperscript{24,26} Therefore, more reliable markers for the diagnosis of chronic *C pneumoniae* infections are required in epidemiological studies, for example, detection of infected peripheral blood mononuclear cells,\textsuperscript{24,27} before a potential causal relationship between *C pneumoniae* infection and stroke can be ascertained.

**Conclusion**

In summary, our study indicates no strong association between antibody response to *C pneumoniae* and first ischemic stroke in a population-based sample. This finding is in accordance with recently published epidemiological studies and meta-analyses on coronary artery disease.\textsuperscript{22,28–30} Further studies are required, however, to confirm whether chronic *H pylori* infection is an independent risk factor for strokes caused by an atherosclerotic mechanism.
Acknowledgments
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References
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