Chlamydia pneumoniae IgG seropositivity and risk of deep-vein thrombosis

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In a population-based case-control study of 474 patients with a first episode of deep-vein thrombosis and 474 age-matched and sex-matched controls, we found no effect of *Chlamydia pneumoniae* infection on the occurrence of deep-vein thrombosis.

Deep-vein thrombosis is a common disease with an annual incidence in the general population of about 1 per 1000. Numerous acquired and inherited risk factors have been identified, but many thrombotic episodes occur in the absence of these predisposing conditions. High titres of IgG antibodies against *Chlamydia pneumoniae* have been associated[1] with an overall increased risk of venous thromboembolism of between six-fold and seven-fold;[1] in that study, patients with the highest IgG titres (≥1:1024 in 14% of all patients) had the most pronounced risk (odds ratio 32). Chronic chlamydia infections may lead to increased concentrations of clotting-factor VIII, which is also a strong risk factor for venous thrombosis.[2] However, the mechanism by which high concentrations of this clotting factor leads to thrombosis is still unknown. Research also suggests that markers of inflammation, such as C-reactive protein, are increased in patients with venous thrombosis.[3] We compared IgG titres against *C pneumoniae* among 474 unselected outpatients with a first, objectively confirmed episode of deep-vein thrombosis and 474 age-matched and sex-matched healthy controls. We also looked for a possible relation between IgG titres and concentrations of clotting-factor VIII and other markers of the acute-phase reaction.

The selection procedures for patients and controls have been described in detail previously.[4] Briefly, we included 474 consecutive outpatients, younger than 70 years of age, who were referred for monitoring of anticoagulant treatment after a first, objectively confimed episode of deep-vein thrombosis that occurred between Jan 1, 1988, and Dec 31, 1992. Patients with a known malignant disease were excluded. 90% of eligible patients were willing to take part in the study. For each patient, we enrolled one healthy age-matched and sex-matched control (53% were friends, 47% were partners of other patients). The controls and cases were inhabitants of the same geographical area and had on average the same level of education. The median time between the occurrence of deep-vein thrombosis and venepuncture for this study was 19 months (range 6–68). *C pneumoniae* serological status was measured with a qualitative ELISA (Savyon SeroCP-IgG kit. Ashdod, Israel). A test was regarded as positive when the cut-off index was greater than 1·1. Technicians were unaware of whether samples were from patients or controls. We calculated odds ratios with 95% CIs as estimates of the relative risk by simple cross tabulation. Since concentrations of IgG against *C pneumoniae* have a continuum of values instead of binary outcomes, we also calculated odds ratios over several strata of antibody responses.

Reactivity of ELISA	Patients	Controls	Odds ratio (95% CI)
≤1·1	94	103	1·0*
1·1–1·8	124	114	1·1 (0·8–1·5)
1·8–2·5	123	118	1·1 (0·8–1·4)
2·5–3 2	95	98	1·0 (0·8–1·4)
>3·2	38	41	1·0 (0 7–1·5)

*Reference category; adjustment for level of education, and concentration of fibrinogen clotting-factor VIII, and C-reactive protein did not alter the results.

Thrombosis risk for several concentrations of IgG against *C pneumoniae*

The mean age of patients and controls was 45 years (range 15–69 for patients, 15–72 for controls). 57% of patients and controls were women. Positive *C pneumoniae* serology was detected in 380 (80%) of the 474 patients, and 371 (78%) of controls (odds ratio 1·1 [95% CI 0·9–1·4]). The high prevalence of exposure to *C pneumoniae* is in agreement with the reported prevalences in other published reports.[5] The table presents the thrombosis risk for several categories of IgG responses against *C pneumoniae*. Patients and controls were equally distributed over the strata of IgG concentrations. Among patients and controls there was a poor correlation between concentrations of IgG against chlamydia and concentrations of factor VIII:C, C-reactive protein, and fibrinogen (Pearson's correlation coefficients −0·07, −0·07, and 0·04, respectively).

The finding of a similarly high prevalence of IgG seropositivity to *C pneumoniae* in 474 outpatients with a first, objectively diagnosed episode of venous thrombosis, and in 474 healthy age-matched and sex-matched controls suggests that IgG seropositivity to *C pneumoniae* is not associated with an increased risk of deep-vein thrombosis, and thus that prior *C pneumoniae* infection does not increase the risk of venous thrombosis. We also found no evidence of an association between IgG seropositivity and clotting factor VIII and other markers of the acute-phase reaction.

Our findings are in contrast with those reported by Lozinguez and colleagues,[1] who found that significantly more patients than controls had high IgG titres (≥1:256) against *C pneumoniae* (54% *vs* 16%). We suggest that the findings of Lozinguez and colleagues may have been biased by the probable higher socioeconomic status of the controls, who were recruited from a health-care centre to which they had been referred for a routine check-up. The role of prior infection with *C pneumoniae* in the occurrence of deep-vein thrombosis remains a disputed issue.

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