Correspondence

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Chlamydia pneumoniae, Antibiotic Treatment, and Early Atherosclerosis

To the Editor:

Sander et al.1 state that 30-day treatment with roxithromycin attenuates the thickening of carotid artery intima-media in Chlamydia pneumoniae (Cp)–seropositive patients aged >55 years. However, no benefit was observed in the combined incidence of stroke, myocardial infarction, and vascular death. Although the antibiotic therapy reduced C-reactive protein, no reduction in the Cp antibody titers was observed. The authors propose several explanations that might account for these discrepancies.

Another explanation is that Cp might simply have little impact on the arterial wall at this age. The multifactorial etiology of an acute event complicating an atherosclerotic plaque prevails in the elderly because of the potentially increased number of additional risk factors that accumulate with age and with which Cp may interact. We believe that a more effective approach to prevent the clinical manifestations of infection-related atherosclerotic disease is to address younger populations. The following arguments support our theory.

One fundamental issue is that atherosclerosis begins in childhood, and, as shown by serial angiographic studies,2 proceeds in steps, with episodes of vascular growth followed by incomplete healing. This emphasizes the causative role of the repeated acute inflammatory stimuli, eg, acute infection, reinfection, and/or reactivation of a chronic infection, in the early arterial disease. Indeed, such infectious phenotype is commonly encountered in childhood. This also holds true for Cp, herpes viruses, and Helicobacter pylori, which are primarily acquired in childhood. Of note, experimental studies have shown that the arterial injury—particularly in relation to Cp—is greater in younger animals and correlates with the number of repeated exposures.3 Earlier autopsy studies documented the association of acute infections with coronary intimal thickening demonstrable during the first weeks and months of life.4 Residual arterial thickening may persist beyond an acute infectious episode, as was recently demonstrated in a carotid ultrasonography study of children with acute systemic infections.5 Antibiotic treatment during the acute infection may lessen the postinfection thickening.6

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Response

We appreciate the interest of Liuba and colleagues in our work.1 They discussed the possibility that Chlamydia pneumoniae (Cp) might have little impact on the arterial wall in older patients and thus may explain the lack of effect of roxithromycin on clinical end points in our study. However, we recently demonstrated a significant enhanced progression of the common carotid intima to media thickness in Cp-positive patients over the age of 55 years.2 There are several other studies indicating the pronounced effect of Cp positivity on atherosclerosis formation, even in older subjects.3 On the basis of these findings, we believe that inflammation and infection play a role in atherosclerosis formation, even in older patients—particularly those with recent cardiovascular or cerebrovascular events, as in our study group.

We support Dr Liuba’s suggestion that it may be effective to address younger populations for prevention of clinical manifestations of infection-related atherosclerotic disease. This view was supported by recent investigations suggesting that antibiotic therapy is more effective if initiated early (within 1 week) after experimental Cp infection.4,5 However, we believe that it is difficult to measure the efficacy of such treatment regimens in younger individuals: First, the incidence of outcome events was rare in this population. Second, humans encounter Cp and other infectious agents commonly, with most individuals having several infections during their lifetime. Cp antibodies, unusual in children younger than 5 years of age, occur in up to 50% of individuals by age 20 years. To slow down this development, it may be necessary to prescribe repeated and regular antibiotic treatment. Third, there are no systematic investigations of the prognostic impact of coronary or carotid arterial thickening in early life.

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