

EXPERIMENTAL *CHLAMYDIA PNEUMONIAE* INFECTION MODEL: EFFECTS OF REPEATED INOCULATIONS AND TREATMENT

ABSTRACT

Objectives. *Chlamydia pneumoniae* is a common human pathogen worldwide, which causes both upper and lower respiratory tract infections. In addition, *C. pneumoniae* infections have been associated with atherosclerosis and other chronic diseases, and successful treatment and eradication of the organism from tissues would therefore be desirable. The purpose of the study was to assess the effects of *C. pneumoniae* inoculations on the development of chronic infection and atherosclerotic changes in normocholesterolemic, wild-type mice. Another aim was to elucidate the effects of antibiotic and other treatments on the eradication of chlamydia and on the reduction of the pathologic sequelae induced by these infections.

Study design. Female C57BL/6J mice were fed either normal chow when assessing the effects of acute infection, or a diet supplemented with 0.2% cholesterol when evaluating the atherosclerotic changes. Primary or repeated inoculations with *C. pneumoniae* isolate K7 were given to the mice intranasally, and the effects of treatments with telithromycin, levofloxacin and erythromycin antimicrobial agents and with the phenolic compounds quercetin, luteolin and octyl gallate were evaluated.

Methods. The following methods were used to measure infection and treatment effects and the presence of chlamydia in tissue: chlamydia culture, PCR and RT-PCR methods, histology of lung, heart and aortic tissue, serologic methods and measurements of aortic contractility responses.

Results. Repeated *C. pneumoniae* inoculations induced persistent chlamydial DNA and inflammation in lung tissue and development of mouse Hsp60 autoantibodies. Infection was shown to influence aortic endothelial function, and repeated inoculations significantly increased subendothelial lipid accumulation in the aortic sinus area. A flavonoid, luteolin, was shown to effectively decrease the chlamydial load and



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inflammatory reactions in lung tissue. All antimicrobial agents eradicated the presence of viable chlamydia effectively; however, PCR positivity persisted in lung tissue despite the treatments. Only immediate treatment after each inoculation was able to decrease aortic sinus lipid accumulation.

Conclusions. These data support the role of *C. pneumoniae* in promoting atherosclerotic development via autoimmune responses and also via direct effects on aortic tissue. Conventional antimicrobial treatments may not effectively eradicate persistent infection, and further studies are warranted to seek for alternative treatment options.

Keywords: antibacterial agents, atherosclerosis, C57BL mice, *Chlamydia pneumoniae*, flavonoids, persistent infection

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