

FAILURE OF FOUR AND SIX WEEKS OF TREATMENT TO ERADICATE
EVIDENCE OF *CHLAMYDIA PNEUMONIAE* FROM HUMAN LUNG AND
VASCULAR TISSUE: PATHOLOGY CASE REPORTS

D. Hahn,¹ L.A. Campbell,² C-C. Kuo²

¹ Dean Medical Center, Madison, Wisconsin USA;

² Dept. of Pathobiology, University of Washington, Seattle, Washington, USA

Objectives: Post-treatment persistence of *Chlamydia pneumoniae* (*Cpn*) has been reported after clinical resolution of acute *Cpn* respiratory illnesses treated with standard (7 to 10 day) courses of antimicrobial therapy (Harris *et al.* 1998 *Pediatr Infect Dis J* 17:865-871), suggesting that eradication of *Cpn* may be difficult. Studies are underway to assess the role of antimicrobials in atherosclerosis (Grayston *et al.* 1998 *Circulation* 97:1669-1670) and asthma (Hahn 1999 *Ann Allergy Asthma Immunol* 83:271-292), diseases that have been associated with chronic *Cpn* infection. It is unknown, however, whether chronic *Cpn* infection can be eradicated by treatment. We report two patients who received four to six weeks of antimicrobial therapy for presumptive chronic *Cpn* infections and for whom post-treatment vascular and/or lung tissues were available for testing.

Case reports: (1) A 76 year old male underwent elective resection of an abdominal aortic aneurysm in 1994. In March 1996 he began a 6 week course of azithromycin, 1000 milligrams once weekly, for a presumptive chronic *Cpn* infection (chronic asthmatic bronchitis) based on an IgG MIF serologic titer of 1:1024. In July 1996 he underwent a left carotid endarterectomy following a mild left carotid ischemic event, and later had a right carotid endarterectomy in December 1996. (2) A 77 year old male was treated with doxycycline, 100 milligrams twice daily for one month for a presumptive chronic *Cpn* infection (wheezing exacerbation of COPD) based on persistent IgG titers of 1:128. One month after beginning doxycycline he died of a ruptured aortic aneurysm.

Methods: Formalin-fixed, paraffin-embedded tissues were selected for (1) polymerase chain reaction (PCR) testing, using the HL-1 - HR-1 primer sets for *C. pneumoniae* with confirmation of presumptive positives by immunochemiluminescence and (2) immunocytochemistry (ICC) staining performed by the avidinbiotinylated enzyme complex method using the chlamydia genus-specific monoclonal antibody CF-2.

Results: Case (1): Pre-treatment aorta and post-treatment left carotid artery were PCR positive for *Cpn*; right carotid was negative. Case (2): Post-treatment lung was PCR positive and ICC positive, myocardium was PCR positive and atheroma was negative. ICC showed staining within Langhans giant cells (a monocyte/macrophage derivative) and peripheral alveolar epithelium.

Conclusions: It is not known how long nonviable DNA (PCR target) or protein antigen (ICC target) material may reside in tissues. Thus, neither PCR nor ICC can distinguish viable from dead organisms, so it cannot be concluded whether 4 weeks of doxycycline or 6 weeks of azithromycin resulted in eradication of viability of *Cpn* in vascular tissue, lung or heart. One possibility is that detection of *Cpn* DNA in carotid artery 3 months after treatment in Case 1 indicates that 6 weeks of antibiotic was insufficient to eradicate *Cpn*. This possibility supports the use of longer courses of antibiotic in attempts to eradicate *Cpn* from deep tissues. Since culture isolation in chronic infection is difficult, other methods such as reverse-transcriptase PCR should be investigated as a test for post-treatment viability of *Cpn*.