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## Association of *Chlamydia pneumoniae* with Chronic Human Diseases

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### Introduction

*Chlamydia pneumoniae* was initially recognized as a cause of acute lower respiratory tract infections such as pneumonia and bronchitis in both adults and children (1-7), hence the species name "*pneumoniae*." Moreover, *C. pneumoniae* was noted in some individuals to cause a persistent respiratory tract infection following an acute infection (8), which is entirely consistent with the known chronic nature of chlamydial infections (9,10). In addition, *C. pneumoniae* has been shown to establish a subclinical asymptomatic respiratory tract infection (11).

### Pathogenesis of Chronic Chlamydial Infections

Establishment of persistent low-grade infections in the lung by *C. pneumoniae* creates an important factor for the pathogenesis of this microorganism. The ability of *C. pneumoniae* to infect a wide variety of human cells, including epithelial, endothelial, and smooth muscle cells as well as macrophages and monocytes, is well documented (12-20). The infection of macrophages, in particular, allows *C. pneumoniae* to enter the circulation from pulmonary tissues and cause systemic dissemination. The tendency for *C. pneumoniae* to disseminate from the initial site of infection in the lung has been described in the murine model of infection (21,22). Similar dissemination is presumed to occur in humans. Indeed, the presence

of *C. pneumoniae* DNA in peripheral blood mononuclear cells (PBMCs) has been well documented (23-29). Moreover, the viability of *C. pneumoniae* in circulating PBMCs has recently been established (30). The ability of *C. pneumoniae* to cause persistent infections combined with its ability to disseminate via the vascular system has raised questions as to the role of this pathogen in a number of chronic human diseases (31-33). Viable *C. pneumoniae* circulating in PBMCs may reach various human tissues after an inflammatory trigger event occurs in the tissue and then cause chronic infection in the tissue. This might create or worsen a chronic disease process. The purpose of this article is to review the association of *C. pneumoniae* with chronic human diseases.

### Chronic Lung Diseases

The predilection of *C. pneumoniae* to cause acute respiratory tract infections combined with its persistent nature suggests that it might play a role in chronic lung diseases (34). Chronic obstructive pulmonary disease (COPD) is a slowly developing irreversible and generally progressive chronic lung disease in which three disorders are commonly included: chronic bronchitis, peripheral airway disease, and emphysema. Indeed, *C. pneumoniae* has been found to be a frequent cause of acute exacerbations of COPD (35). Accordingly, it has been suggested that *C. pneumoniae* may have a role in the pathogenesis of COPD (36). Immunohistochemical staining for *C. pneumoniae* is increased in lung tissue from

subjects with COPD, suggesting that persistent infection with this organism is common (37). In addition, morphological findings by electron microscopy in pulmonary emphysema reveal aberrant chlamydiae that are identical to those seen in atherosclerosis (38). Persistent low-grade infection of the lung by *C. pneumoniae* is thus likely to contribute to chronic lung disease and, in some instances, may even be causal.

### Chronic Otolaryngeal Diseases

Otolaryngeal infections include sinusitis, otitis media, pharyngitis, tonsillitis, and laryngitis. These infections may be acute, recurrent, or chronic. The seroprevalence of antibodies to *C. pneumoniae* suggests that this microorganism is an important and common pathogen of otolaryngeal disease (39). *C. pneumoniae* has been isolated from both acute and chronic otitis media (40,41), and polymerase chain reaction (PCR) studies have confirmed and extended these early observations (42,43). Isolation of *C. pneumoniae* from the maxillary sinus has been described in one case report (44), but additional studies evaluating the role of *C. pneumoniae* in sinusitis have not been done. *C. pneumoniae* has been isolated from pharyngeal tissue biopsies as well as demonstrated by

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immunohistochemical methods in patients with chronic pharyngitis (45). Similarly, immunohistochemical analysis and PCR have demonstrated *C. pneumoniae* in adenoid tissue from children undergoing adenoidectomy for hyperplastic adenoids (46,47). Clearly *C. pneumoniae* is present in otolaryngeal tissues and plays a role in both acute and chronic infections as well as a possible role in a hyperplastic response.

### Asthma

Infection has long been thought to play a role in asthma (48). For example, respiratory tract infections are thought to precipitate wheezing in many asthmatic patients. The recent use of PCR to diagnose viral infections of the respiratory tract has documented the role of rhinovirus and respiratory syncytial virus in acute exacerbations of asthma (49). As *C. pneumoniae* is a pathogen causing acute and chronic respiratory tract infections, it may play a similar role in asthma. One of the first studies to investigate this possibility found that there is an association of *C. pneumoniae* infection with wheezing, asthmatic bronchitis, and adult-onset asthma (50). Not only did *C. pneumoniae* appear to exacerbate asthma, it seemed in some patients to initiate asthma. The authors concluded that repeated or prolonged exposure to *C. pneumoniae* may have a causal association with wheezing, asthmatic bronchitis, and asthma. Other investigators have confirmed the association of *C. pneumoniae* with acute exacerbations of asthma in both adults and children (51-58). Several studies suggest that antimicrobial therapy against *C. pneumoniae* is beneficial in the course of reactive airway disease (59-61). Whether or not *C. pneumoniae* plays a causal role in addition to its role in exacerbations of asthma remains to be determined.

### Atherosclerosis

Despite significant advances in our understanding of the various risk factors involved in atherosclerosis, there are significant gaps in the elucidation of the etiology of vascular injury and atherogenesis. Chronic infection of vascular tissue has received considerable attention recently as an inducer of vascular injury and subsequent development of atherosclerosis. Although infection with a variety of infectious agents such as cytomegalovirus has been implicated in atherogenesis, the best evidence to date links the presence of *C. pneumoniae* with the pathogenesis of atherosclerosis. Saikku et al. (62,63) first reported an association between anti-*C. pneumoniae* antibody titers and coronary artery disease. In a 1999 review, Wong, Gallagher, and Ward (64) reported that 21 of 27 studies showed "some sort of positive serological association between positive anti-*C. pneumoniae* titers and atherosclerosis." Similar results have been reported in cerebrovascular accidents with a number of studies showing a positive correlation with anti-*C. pneumoniae* antibodies (65-67). Direct evidence of *C. pneumoniae* infection of blood vessels is provided by studies using electron microscopy (68,69,74), PCR (69,71-78,82), immunohistochemistry (68,70-75,80,82), reverse transcriptase PCR (79), and cultures (75,77,80,81). Finally, animal models support a role for *C. pneumoniae* in the pathogenesis of atherosclerosis (83-85).

### Neurological Diseases

The serologic association of *C. pneumoniae* infections with neurological diseases began with several individual case reports that linked this microorganism with Guillain-Barre syndrome (86) and lumbosacral meningoradiculi-

tis (87). These observations were followed by additional reports associating *C. pneumoniae* with meningitis (88,89). The association of chlamydial infections with neurological syndromes has been strengthened by a large serological survey of patients with neurological disease (90). These observations suggest that *C. pneumoniae* may be more prevalent as an associated agent in central nervous system (CNS) diseases than appreciated (90) and that chlamydial infections should be included in the differential diagnosis of neurological syndromes (91). The first direct evidence that *C. pneumoniae* infection may be risk factor for a chronic neurological disease was a study that demonstrated that *C. pneumoniae* is present, viable, and transcriptionally active in areas of neuropathy in the Alzheimer's disease brain (92). This was followed by a report of a case in which *C. pneumoniae* was isolated from the cerebrospinal fluid (CSF) of a patient with multiple sclerosis (MS) (93). Anti-chlamydial therapy markedly improved the course of MS in this patient. A more extensive study by the same investigators demonstrated that infection of the CNS is a frequent occurrence in MS patients (94). Other investigators have confirmed the presence of *C. pneumoniae* in CSF from MS patients (95,96) as well as in CSF from patients with other types of neurological disease (97). Additional case reports for meningoencephalitis and encephalomyelitis (98,99) suggest that *C. pneumoniae* is a neurotrophic pathogen and thus may play a role in a variety of chronic neurological diseases.

### Chronic Rheumatological Diseases

Rheumatological diseases include those diseases that involve the connective tissues. Joints and related structures of

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the skeleton are considered the principal connective tissues and vary widely in structure and function as well as in predisposition to disease. Many connective tissue diseases in humans are chronic and involve inflammation. The most common is rheumatoid arthritis (RA). RA is a chronic connective tissue disease of unknown etiology which has been considered by some to be the result of a chronic inflammatory synovial response to an unrecognized antigen, such as that from infectious agent(s). Vasculitis is a recognized component of many chronic rheumatological diseases (100) including RA (101). Vasculitis has been associated with a number of infectious agents (102). The recognition that *C. pneumoniae* may induce isolated and systemic vasculitis in small and large blood vessels (103) has therefore raised questions as to its role in chronic rheumatological diseases. Moreover, *Chlamydia* species are known to cause polyarthritis in calves and sheep (104-107). Thus, it is not surprising to find that *C. trachomatis* is now recognized as a cause of reactive arthritis (108-112). Similarly, *C. pneumoniae* also has been associated with reactive arthritis (113-118). It is possible that *C. pneumoniae* could also play a role in RA. Such a role may be secondary infection of inflamed joints, or it may be causal. The observations that antimicrobial therapy with tetracyclines, agents active against *Chlamydia* species, is beneficial for some patients with rheumatoid arthritis (119-122) suggests that chlamydial infection may be a factor.

In addition, *C. pneumoniae* has been associated with other chronic rheumatological diseases. One case report has found an association of *C. pneumoniae* with systemic lupus erythematosus in which the patient was cured by a combination of clarithromycin, prednisolone, and cyclophosphamide (123). More intriguing is the association of *C. pneumoniae* with temporal arteritis. Temporal arteritis is a clinical manifestation of giant-cell arteritis. Giant-cell arteritis is a vasculitis of unknown etiology that predominantly affects medium- and large-sized arteries (124). Giant-cell arteritis and a closely related clinical syndrome, polymyalgia rheumatica, affect the elderly and often involve an acute onset with flu-like upper respira-

tory tract symptoms. For this reason, an infectious process has been proposed as a trigger mechanism (125). An initial case in which *C. pneumoniae* DNA was detected in an artery specimen has been reported (126). A more extensive investigation found that *C. pneumoniae* was present in temporal artery specimens from most patients with giant cell arteritis (127). This study detected *C. pneumoniae* by both immunohistochemistry and PCR and noted that the dendritic cells in the adventitial layer of the arteries may represent the antigen-presenting cells. This work further supports the association of *C. pneumoniae* with chronic rheumatological diseases.

### Cancer

Chronic infections are known to predispose to malignant growth. As *C. pneumoniae* may cause chronic infections, it may predispose to cancer. There is serological evidence of an association between *C. pneumoniae* infection and lung cancer. In one study, chronic *C. pneumoniae* infection was positively associated with the incidence of lung cancer and was especially increased in men younger than 60 years (128). This has been corroborated by a second study showing that chronic *C. pneumoniae* infection is common in patients with lung cancer (129). Another serological study found evidence of an association between chronic *C. pneumoniae* infections and malignant lymphoma (130). In cutaneous T-cell lymphoma, there is a protein that has been identified and found to be stimulatory for malignant Sezary T cells. This protein has been termed Sezary T-cell activating factor and is often present in the skin of patients with mycosis fungoides, the predominant form of cutaneous T-cell lymphoma. This Sezary T-cell activating factor has been found to be a *C. pneumoniae*-associated protein (131). Therefore, it is possible that *C. pneumoniae* may play a role in the pathogenesis of cutaneous T-cell lymphoma.

### Miscellaneous Chronic Diseases

*C. pneumoniae* has been associated with a number of other chronic diseases. It is not surprising that *C. pneumoniae* has been reported as a treatable cause of chronic fatigue syndrome (132). It is likely that many chronic infections would result in patients experiencing

chronic fatigue; thus, a chronic chlamydial infection would be expected to do the same. Fibromyalgia and other myalgia of unknown cause have been described in patients with chronic fatigue syndrome; *C. pneumoniae* antibodies have been linked with myalgia of unknown cause, including fibromyalgia (133). An interesting association of *C. pneumoniae* infections with diabetic nephropathy has been noted (134). This is interesting because of the possible relationship between glucose metabolism and chlamydial infection. For years, it has been speculated that chlamydiae are energy parasites that are totally dependent on their host cells for ATP and other high-energy intermediates (135), although this concept has been questioned recently due to the complete sequencing of genes from *C. trachomatis* and *C. pneumoniae*. Analysis of these chlamydial genes suggests that chlamydiae have some functional capacity to produce their own ATP and reducing power (136). Nonetheless, it is clear that infection of eukaryotic cells with chlamydiae results in an increase in the rate of glycolysis and that this increase is not caused by chlamydial metabolic activity but instead is a host cell response to the infection (137,138). This might offer an advantage for chlamydial replication in a host with diabetes and increased levels of glucose. If this were the case, chlamydial infection might be the source of the accelerated atherosclerosis known to occur in diabetics. An association of *C. pneumoniae* infection with pyoderma gangrenosum/skin ulcers in diabetic patients has been described (139,140). *C. pneumoniae* therefore might be an important pathogen in diabetic patients. Finally, an association of *C. pneumoniae* and interstitial cystitis has recently been described (141). Interstitial cystitis (IC) is a chronic inflammatory disease occurring primarily in females. IC is considered a sterile bladder condition characterized by symptoms of urgency, frequency, and pain. The etiology of IC is unknown, but autoimmune mechanisms have been thought to play a role. Analysis of urine samples of IC patients by PCR revealed that 71% of patients with IC were positive for *C. pneumoniae* (141). Therefore, bladder biopsies were done for culture of this pathogen. Of those patients with IC, 82% (14/17)

had tissue cultures positive for *C. pneumoniae* (141). Control patients were limited to those patients without a history of irritative voiding symptoms, transitional cell carcinoma, or recurrent urinary tract infection. In these control patients, 16% (1/6) had tissue cultures positive for *C. pneumoniae*. This difference was statistically significant ( $P = 0.004$ ). Thus, *C. pneumoniae* may have a role in the pathogenesis of IC.

## Summary

It is apparent from this review that *C. pneumoniae* has been implicated in many chronic diseases of humans. Whether the role is that of innocent bystander, cause, or perhaps something in between remains to be determined. Regardless of the role of *C. pneumoniae* in these or other chronic diseases, this microorganism is becoming a major health concern. Considerable resources will be needed to determine its role in human disease. If *C. pneumoniae* proves to play an important role in any or all of these chronic diseases, its eventual control or eradication may do much to improve the health of countless persons.

## References

- Saikku P, Wang SP, Kleemola M, et al. An epidemic of mild pneumonia due to an unusual strain of *Chlamydia psittaci*. *J Infect Dis* 1985; 151:832-839.
- Grayston JT, Kuo C-C, Wang S-P, Altman J. A new *Chlamydia psittaci* strain, TWAR isolated in acute respiratory tract infections. *N Engl J Med* 1986; 315:161-168.
- Grayston JT, Campbell LA, Kuo C-C, et al. A new respiratory tract pathogen: *Chlamydia pneumoniae* strain TWAR. *J Infect Dis* 1990; 161:618-625.
- Grayston JT, Aldous MB, Easton A, et al. Evidence that *Chlamydia pneumoniae* causes pneumonia and bronchitis. *J Infect Dis* 1993; 168:1231-1235.
- Falk G, Heyman L, Gnarpe J, Gnarpe H. *Chlamydia pneumoniae* (TWAR): a common agent in acute bronchitis. *Scand J Infect Dis* 1994; 26:179-187.
- Jantos CA, Wienpahl B, Schiefer HG, Wagner F, Hagemann JH. Infections with *Chlamydia pneumoniae* in infants and children with acute lower respiratory tract disease. *Pediatr Infect Dis J* 1995; 14:117-122.
- Kauppinen M, Saikku P. Pneumonia due to *Chlamydia pneumoniae*: prevalence, clinical features, diagnosis, and treatment. *Clin Infect Dis* 1995; 21(Suppl 3):S244-S252.
- Hammerschlag MR, Chirgwin K, Roblin PM, et al. Persistent infection with *Chlamydia pneumoniae* following acute respiratory illness. *Clin Infect Dis* 1992; 14:178-182.
- Beatty WL, Morrison RP, Byrne GI. Persistent chlamydiae, from cell culture to a paradigm for chlamydial pathogenesis. *Microbiol Rev* 1994; 58:686-699.
- Beatty WL, Byrne GI, Morrison RP. Repeated and persistent infection with *Chlamydia* and the development of chronic inflammation and disease. *Trends Microbiol* 1994; 2:94-98.
- Hyman CL, Augenbraum MH, Robin PM, Schachter J, Hammerschlag MR. Asymptomatic respiratory tract infection with *Chlamydia pneumoniae* TWAR. *J Clin Microbiol* 1991; 29:2082-2083.
- Kaukoranta-Tolvanen S-S, Laitinen K, Saikku P, Leinonen M. *Chlamydia pneumoniae* multiplies in human endothelial cells *in vitro*. *Microb Pathog* 1994; 16:313-319.
- Numazaki K, Suzuki K, Chiba S. Replication of *Chlamydia trachomatis* and *C. pneumoniae* in the human monocytic cell line U-937. *J Med Microbiol* 1995; 42:191-195.
- Godzik KL, O'Brien ER, Wang SK, Kuo CC. *In vitro* susceptibility of human vascular wall cells to infection with *Chlamydia pneumoniae*. *J Clin Microbiol* 1995; 33:2411-2414.
- Gaydos CA, Summersgill JT, Sahney NN, Ramirez JA, Quinn TC. Replication of *Chlamydia pneumoniae* *in vitro* in human macrophages, endothelial cells, and aortic smooth muscle cells. *Infect Immun* 1996; 64:1614-1620.
- Kaukoranta-Tolvanen SS, Teppo AM, Laitinen K, Saikku P, Linnavuori K, Leinonen K. Growth of *Chlamydia pneumoniae* in cultured human peripheral blood mononuclear cells and induction of a cytokine response. *Microb Pathog* 1996; 21:215-221.
- Knoebel E, Vijayagopal P, Figueroa JE, Martin DH. *In vitro* infection of smooth muscle cells by *Chlamydia pneumoniae*. *Infect Immun* 1997; 65:503-506.
- Fryer RH, Schwobe EP, Woods ML, Rodgers GM. *Chlamydia* species infect human vascular endothelial cells and induce procoagulant activity. *J Invest Med* 1997; 45:168-174.
- Redecke V, Dalhoff K, Bohnet S, Braun J, Maass M. Interaction of *Chlamydia pneumoniae* and human alveolar macrophages: infection and inflammatory response. *Am J Respir Cell Mol Biol* 1998; 19:721-727.
- Airenne S, Surcel HM, Alakarppa H, Laitinen K, et al. *Chlamydia pneumoniae* infection in human monocytes. *Infect Immun* 1999; 67:1445-1449.
- Yang Z, Kuo C, Grayston JT. Systemic dissemination of *Chlamydia pneumoniae* following intranasal inoculation in mice. *J Infect Dis* 1995; 171:736-738.
- Moazed TC, Kuo CC, Grayston JT, Campbell LA. Evidence of systemic dissemination of *Chlamydia pneumoniae* via macrophages in the mouse. *J Infect Dis* 1998; 177:1322-1325.
- Boman J, Soderberg S, Forsberg J, et al. High prevalence of *Chlamydia pneumoniae* DNA in peripheral mononuclear cells in patients with cardiovascular disease and in middle-aged blood donors. *J Infect Dis* 1998; 178:274-277.
- Wong YK, Dawkins KD, Ward ME. Circulating *Chlamydia pneumoniae* DNA as a predictor of coronary artery disease. *J Am Coll Cardiol* 1999; 34:1440-1442.
- Blasi F, Boman J, Esposito G, et al. *Chlamydia pneumoniae* DNA detection in peripheral blood mononuclear cells is predictive of vascular infection. *J Infect Dis* 1999; 180:2074-2076.
- Bodetti TJ, Timms P. Detection of *Chlamydia pneumoniae* DNA and antigen in the circulating mononuclear cell fractions of humans and koalas. *Infect Immun* 2000; 68:2744-2747.
- Maass M, Jahn J, Griefers J, Dalhoff K, Katus HA, Solbach W. Detection of *Chlamydia pneumoniae* within peripheral blood monocytes of patients with unstable angina or myocardial infarction. *J Infect Dis* 2000; 181(Suppl 3):S449-S451.
- Boman J, Gaydos CA. Polymerase chain reaction of *Chlamydia pneumoniae* in circulating white blood cells. *J Infect Dis* 2000; 181(Suppl 3):S452-S454.
- Iliescu EA, Fiebig MF, Morton AR, Sankar-Mistry P. *Chlamydia pneumoniae* in peripheral blood mononuclear cells in peritoneal dialysis patients. *Peritoneal Dialysis Int* 2000; 20:722-726.
- Gieffers J, Fullgraf H, Jahn J, et al. *Chlamydia pneumoniae* infection in circulating human monocytes is refractory to antibiotic treatment. *Circulation* 2001; 103:351-356.
- Leinonen M. Pathogenic mechanisms and epidemiology of *Chlamydia pneumoniae*. *Eur Heart J* 1993; 14(Suppl

- K):S57-S61.
32. Ong G, Thomas BJ, Mansfield AO, Davidson BR, Taylor-Robinson. Detection and widespread distribution of *Chlamydia pneumoniae* in the vascular system and its possible implications. *J Clin Pathol* 1996; 49:102-106.
  33. Stille W, Dittmann R, Just-Nubling G. Atherosclerosis due to chronic arteritis caused by *Chlamydia pneumoniae*: a tentative hypothesis. *Infection* 1997; 25:281-285.
  34. Laurila AL, Von Hertzen L, Saikku P. *Chlamydia pneumoniae* and chronic lung diseases. *Scand J Infect Dis* 1997; 104(Suppl):34-36.
  35. Blasi F, Legnani D, Lombardo VM, et al. *Chlamydia pneumoniae* infection in acute exacerbations of COPD. *Eur Respir J* 1993; 6:19-22.
  36. von Hertzen LC. *Chlamydia pneumoniae* and its role in chronic obstructive pulmonary disease. *Ann Med* 1998; 30:27-37.
  37. Wu L, Skinner SJ, Lambie N, Vuletic JC, Blasi F, Black PM. Immunohistochemical staining for *Chlamydia pneumoniae* is increased in lung tissue from subjects with chronic obstructive pulmonary disease. *Am J Res Crit Care Med* 2000; 162:1148-1151.
  38. Theegarten D, Mogilevski G, Anhenn O, Stamatis G, Jaeschock R, Morgenroth K. The role of *Chlamydia* in the pathogenesis of pulmonary emphysema. Electron microscopy and immunofluorescence reveal corresponding findings as atherosclerosis. *Virchows Archiv* 2000; 437:190-193.
  39. Hashiguchi K, Ogawa H, Kazuyama Y. Seroprevalence of *Chlamydia pneumoniae* infections in otolaryngeal diseases. *J Laryngol Otol* 106: 208-210.
  40. Block SL, Hammerschlag MR, Hedrick J, et al. *Chlamydia pneumoniae* in acute otitis media. *Pediatr Infect Dis* 1997; 16:858-862.
  41. Ogawa H, Hashiguchi K, Kazuyama Y. Recovery of *Chlamydia pneumoniae* in six patients with otitis media with effusion. *J Laryngol Otol* 1992; 106:490-492.
  42. Storgaard M, Ostergaard L, Jensen JS, et al. *Chlamydia pneumoniae* in children with otitis media. *Clin Infect Dis* 1997; 25:1090-1093.
  43. Falk G, Engstrand I, Gnarpe J, Gnarpe H. Association of *Chlamydia pneumoniae* with otitis media in children. *Scand J Infect Dis* 1998; 30:377-380.
  44. Hashiguchi K, Ogawa H, Suzuki T, Kazuyama Y. Isolation of *Chlamydia pneumoniae* from the maxillary sinus of a patient with purulent sinusitis. *Clin Infect Dis* 1992; 15:570-571.
  45. Falk G, Engstrand I, Gad A, Gnarpe J, Gnarpe H, Laurila A. Demonstration of *Chlamydia pneumoniae* in patients with chronic pharyngitis. *Scand J Infect Dis* 1997; 29:585-589.
  46. Norman E, Gnarpe J, Naas J, Gnarpe H, Karlsson MG, Wettergren B. *Chlamydia pneumoniae* in children undergoing adenoidectomy. *Acta Paediatrica* 2001; 90:126-129.
  47. Engstrand I, Augustsson I, Bergemaim PO, Falck G, Gnarpe J, Gnarpe H. Demonstration of *Chlamydia pneumoniae* in the adenoid from children with and without secretory otitis media using immunohistochemistry and PCR. *Scand J Infect Dis* 2001; 33:132-136.
  48. Stenius-Aarniala B. The role of infection in asthma. *Chest* 1987; 91: 130-136.
  49. Johnston SL. Influence of viral and bacterial respiratory infections on exacerbations and symptom severity in childhood asthma. *Pediatr Pulmonol* 1997; 16(Suppl):S88-S89.
  50. Hahn DL, Dodge RW, Golubjatnikov R. Association of *Chlamydia pneumoniae* (strain TWAR) infection with wheezing, asthmatic bronchitis, and adult-onset asthma. *J Am Med Assoc* 1991; 266:225-230.
  51. Allegra L, Blasi F, Centanni S, et al. Acute exacerbations of asthma in adults: role of *Chlamydia pneumoniae* infections. *Eur Resp J* 1994; 7:2165-2168.
  52. Hahn DL, Golubjatnikov R. Asthma and chlamydial infection: a case series. *J Fam Pract* 1994; 38:586-595.
  53. Bjornsson E, Hjelm E, Janson C, Fridell E, Boman G. Serology of *Chlamydia* in relation to asthma and bronchial hyperresponsiveness. *Scand J Infect Dis* 1996; 28:63-69.
  54. Miyashita N, Kubota Y, Nakajima M, Niki Y, Kawane H, Matsushima T. *Chlamydia pneumoniae* and exacerbations of asthma in adults. *Ann Allergy Asthma Immunol* 1998; 80:405-409.
  55. Cunningham AF, Johnston SL, Julious SA, Lampe FC, Ward ME. Chronic *Chlamydia pneumoniae* infection and asthma exacerbations in children. *Eur Respir J* 1998; 11:345-349.
  56. Hahn DL, Peeling RW, Dillon E, McDonald R, Saikku P. Serologic markers for *Chlamydia pneumoniae* in asthma. *Ann Allergy Asthma Immunol* 2000; 84:227-233.
  57. Gencay M, Rudiger JJ, Tamm M, Soler M, Perruchoud AP, Roth M. Increased frequency of *Chlamydia pneumoniae* antibodies in patients with asthma. *Am J Respir Crit Care Med* 2001; 163:1097-1100.
  58. Brinke A, Van Dissel JT, Sterk PJ, Zwinerman AH, Rabe KE, Bel EH. Persistent airflow limitation in adult-onset nonatopic asthma is associated with serologic evidence of *Chlamydia pneumoniae* infection. *J Allergy Clin Immunol* 2001; 107:449-454.
  59. Emre U, Roblin PM, Gelling M. The association of *Chlamydia pneumoniae* infection and reactive airway disease in children. *Arch Pediatr Adolesc Med* 1994; 148:727-732.
  60. Hahn DL. Treatment of *Chlamydia pneumoniae* infection in adult asthma: a before-after trial. *J Fam Pract* 1995; 41:345-351.
  61. Hahn DL, Bukstein D, Luskin A, Zeitz H. Evidence for *Chlamydia pneumoniae* infection in steroid-dependent asthma. *Ann Allergy Asthma Immunol* 1998; 80:45-49.
  62. Saikku P, Leinonen M, Matrila K, et al. Serological evidence of an association of a novel *Chlamydia*, TWAR, with chronic coronary heart disease and acute myocardial infarction. *Lancet* 1988; ii:983-985.
  63. Saikku P, Leinonen M, Tenkanen L, et al. Chronic *Chlamydia pneumoniae* infection as a risk factor for coronary heart disease in the Helsinki heart study. *Ann Intern Med* 1992; 116:273-278.
  64. Wong Y-K, Gallagher PJ, Ward ME. *Chlamydia pneumoniae* and atherosclerosis. *Heart* 1999; 81:232-238.
  65. Cook PJ, Honeybourne D, Lip GY, Beevers DG, Wise R, Davies P. *Chlamydia pneumoniae* antibody titers are significantly associated with acute stroke and transient cerebral ischemia: the West Birmingham Stroke Project. *Stroke* 1998; 29:404-410.
  66. Fagerberg B, Gnarpe J, Gnarpe H, Agewall S, Wikstrand J. *Chlamydia pneumoniae* but not cytomegalovirus antibodies are associated with future risk of stroke and cardiovascular disease: a prospective study in middle-aged to elderly men with treated hypertension. *Stroke* 1999; 30:299-305.
  67. Elkind MS, Lin IF, Grayston JT, Sacco RL. *Chlamydia pneumoniae* and the risk of first ischemic stroke: The Northern Manhattan Stroke Study. *Stroke* 2000; 31:1521-1525.
  68. Shor A, Kuo C-C, Patton DL. Detection of *Chlamydia pneumoniae* in coronary arterial fatty streaks and atheroscleromatous plaques. *South African Med J*

- 1992; 82:158-161.
69. Kuo CC, Shor A, Campbell LA, Fukushi H, Patton DL, Grayston JT. Demonstration of *Chlamydia pneumoniae* in atherosclerotic lesions of coronary arteries. *J Infect Dis* 1993; 167:841-849.
  70. Kuo C-C, Gown AM, Benditt EP, Grayston JT. Detection of *Chlamydia pneumoniae* in aortic lesions of atherosclerosis by immunocytochemical stain. *Arteriosclerosis Thrombosis* 1993; 13:1501-1504.
  71. Kuo C-C, Grayston JT, Campbell LA, Goo YA, Wissler RW, Benditt EP. *Chlamydia pneumoniae* (TWAR) in coronary arteries of young adults (15-34 years old). *Proc Natl Acad Sci USA*; 92:6911-6914.
  72. Grayston JT, Kuo C-C, Coulson AS, et al. *Chlamydia pneumoniae* (TWAR) in atherosclerosis of the carotid artery. *Circulation* 1995; 92:3397-3400.
  73. Blasi F, Denti F, Erba M, et al. Detection of *Chlamydia pneumoniae* but not *Helicobacter pylori* in atherosclerotic plaques of aortic aneurysms. *J Clin Microbiol* 1996; 34:2766-2769.
  74. Juvonen J, Juvonen T, Laurila A, et al. Demonstration of *Chlamydia pneumoniae* in the walls of abdominal aortic aneurysms. *J Vasc Surg* 1997; 25:499-505.
  75. Jackson LA, Campbell LA, Kuo C-C, Rodriguez DL, Lee A, Grayston JT. Isolation of *Chlamydia pneumoniae* from a carotid endarterectomy specimen. *J Infect Dis* 1997; 176:292-295.
  76. Maass M, Krause E, Engel PM, Kruger S. Endovascular presence of *Chlamydia pneumoniae* in patients with hemodynamically effective carotid artery stenosis. *Angiology* 1997; 48:699-706.
  77. Maass M, Bartels C, Engle PM, Mamat U, Sievers HH. Endovascular presence of viable *Chlamydia pneumoniae* is a common phenomenon in coronary artery disease. *J Am College Cardiol* 1998; 31:827-832.
  78. Petersen E, Boman J, Persson K, et al. *Chlamydia pneumoniae* in human abdominal aortic aneurysms. *Eur J Vasc Endovasc Surg* 1998; 15:138-142.
  79. Esposito G, Blasi F, Allegra L, et al. Demonstration of viable *Chlamydia pneumoniae* in atherosclerotic plaques of carotid arteries by reverse transcriptase polymerase chain reaction. *Ann Vasc Surg* 1999; 13:421-425.
  80. Karlsson L, Gnarpe J, Naas J, et al. Detection of viable *Chlamydia pneumoniae* in abdominal aortic aneurysms. *Eur J Vasc Endovasc Surg* 2000; 19:630-635.
  81. Apfalter P, Loidl M, Nadrchal R, et al. Isolation and continuous growth of *Chlamydia pneumoniae* from arterectomy specimens. *Eur J Clin Microbiol Infect Dis* 2000; 305-308.
  82. Jackson LA, Campbell LA, Schmidt RA, et al. Specificity of detection of *Chlamydia pneumoniae* in cardiovascular atheroma. *J Infect Dis* 2000; 181(Suppl 3):S447-S448.
  83. Moazed TC, Kuo C-C, Patton DL, et al. Experimental rabbit models of *Chlamydia pneumoniae* infection. *Am J Pathol* 1996; 148:667-676.
  84. Fong IW, Chiu B, Viina E, et al. Rabbit model for *Chlamydia pneumoniae* infection. *J Clin Microbiol* 1997; 35:48-52.
  85. Muhlestein JB, Anderson JL, Hammond EH, et al. Infection with *Chlamydia pneumoniae* accelerates the development of atherosclerosis and treatment with azithromycin prevents it in a rabbit model. *Circulation* 1998; 96:633-636.
  86. Haidl S, Ivarsson S, Bjerre I, Persson K. Guillain-Barre syndrome after *Chlamydia pneumoniae* infection. *N Engl J Med* 1992; 326:576-577.
  87. Michel D, Antoine JC, Pozzetto B, Gaudin OG, Lucht F. Lumbosacral meningoradiculitis associated with *Chlamydia pneumoniae* infection. *J Neurol Neurosurg Psychiatry* 1992; 55:511.
  88. Sundelof B, Gnarpe H, Gnarpe J. An unusual manifestation of *Chlamydia pneumoniae* infection: meningitis, hepatitis, iritis and atypical erythema nodosum. *Scand J Infect Dis* 1993; 25:259-261.
  89. Socan M, Beovic B, Kese D. *Chlamydia pneumoniae* and meningoencephalitis. *N Engl J Med* 1994; 331:406-407.
  90. Koskiniemi M, Gencay M, Salonen O. *Chlamydia pneumoniae* associated with central nervous system infections. *Eur Neurol* 1996; 36:160-163.
  91. Korman TM, Turnidge JD, Grayson ML. Neurological complications of chlamydial infections: case report and review. *Clin Infect Dis* 1997; 25:847-851.
  92. Balin BJ, Gerard HC, Arking EJ, et al. Identification and localization of *Chlamydia pneumoniae* in the Alzheimer's brain. *Med Microbiol Immunol* 1998; 187:23-42.
  93. Sriram S, Michell W, Stratton C. Multiple sclerosis associated with *Chlamydia pneumoniae* infection of the CNS. *Neurology* 1998; 50:571-572.
  94. Sriram S, Stratton CW, Yao S, et al. *Chlamydia pneumoniae* infection of the central nervous system in multiple sclerosis. *Ann Neurol* 1999; 46:6-14.
  95. Treib J, Haass A, Stille W, et al. Multiple sclerosis and *Chlamydia pneumoniae*. (Letter to the Editor) *Ann Neurol* 2000; 47:408.
  96. Layh-Schmitt G, Bendl C, Hildt U et al. Evidence for infection with *Chlamydia pneumoniae* in a subgroup of patients with multiple sclerosis. *Ann Neurol* 2000; 47:652-655.
  97. Gieffers J, Pohl D, Treib J, et al. Presence of *Chlamydia pneumoniae* DNA in the cerebral spinal fluid is a common phenomenon in a variety of neurological diseases and not restricted to multiple sclerosis. *Ann Neurol* (in press).
  98. Heick A, Skriver E. *Chlamydia pneumoniae*-associated ADEM. *Eur J Neurol* 2000; 7:435-438.
  99. Guglielminotti J, Lellouche N, Maury E, Alzieu M, Guidet B, Offenstadt G. Severe meningoencephalitis: an unusual manifestation of *Chlamydia pneumoniae* infection. *Clin Infect Dis* 2000; 30:209-210.
  100. Hunder GG. Vasculitis: diagnosis and therapy. *Am J Med* 1996; 100(Suppl 2A):S37-S45.
  101. Goronzy JJ, Weyand CM. Vasculitis in rheumatoid arthritis. *Curr Opin Rheumatol* 1994; 6:290-294.
  102. Lie JT. Vasculitis associated infectious agents. *Curr Opin Rheumatol* 1996; 8:26-29.
  103. Ljungstrom L, Franzen C, Schlaug M, Elowson S, Vidas U. Reinfection with *Chlamydia pneumoniae* may induce isolated and systemic vasculitis in small and large vessels. *Scand J Infect Dis* 1997; 104(Suppl):S37-S40.
  104. Storz J, Marriott ME, Smart RA, Davis RV. Polyarthritides of calves: isolation of psittacosis agents from affected joints. *Am J Vet Res* 1966; 27:633-641.
  105. Norton WL, Storz J. Observations on sheep with polyarthritides produced by an agent of the psittacosis-lymphogranuloma venereum-trachoma group. *Arthritis Rheum* 1967; 10:1-12.
  106. Eugster AK, Storz J. Pathogenic events in intestinal chlamydial infections leading to polyarthritides in calves. *J Infect Dis* 1971; 123:41-50.
  107. Cutlip RC, Ramsey FK. Ovine chlamydial polyarthritides: sequential development of articular lesions in lambs after intraarticular exposure. *Am J Vet Res* 1973; 34:71-75.

108. Schachter J, Barnes MG, Jones JP, Engleman EP, Myer KF. Isolation of bedsoniae from the joints of patients with Reiter's syndrome. *Proc Soc Exp Biol Med* 1966; 122:283-285.
109. Keat A, Thomas B, Hughes R, Taylor-Robinson D. *Chlamydia trachomatis* in reactive arthritis. *Rheumatol Int* 1989; 9:197-200.
110. Hammer M, Nettelbreker E, Hopf S, Schmitz E, Porschke K, Zeidler H. Chlamydial rRNA in the joints of patients with *Chlamydia*-induced arthritis and undifferentiated arthritis. *Clin Exp Rheumatol* 1992; 10:63-66.
111. Raham MU, Cheema MA, Schumacher HR, Hudson AP. Molecular evidence for the presence of *Chlamydia* in the synovium of patients with Reiter's syndrome. *Arthritis Rheum* 1992; 35:521-529.
112. Schumacher HR Jr, Magge S, Chernian PV, et al. Light and electron microscopic studies on the synovial membrane in Reiter's syndrome; immunocytochemical identification of *Chlamydia* antigen in patients with early disease. *Arthritis Rheum* 1994; 37:710-717.
113. Gran JT, Hjetland R, Andreassen AH. Pneumonia, myocarditis and reactive arthritis due to *Chlamydia pneumoniae*. *Scand J Rheumatol* 1993; 22:43-44.
114. Saario R, Toivanen A. *Chlamydia pneumoniae* as a cause of reactive arthritis. *Br J Rheum* 1993; 32:1112.
115. Braun J, Laitko S, Trehanne J, et al. *Chlamydia pneumoniae* — a new causative agent of reactive arthritis and undifferentiated oligoarthritis. *Ann Rheum Dis* 1994; 53:100-105.
116. Melby KK, Kvien TK, Glennas A, Anestad G. *Chlamydia pneumoniae* as a trigger of reactive arthritis. *Scand J Infect Dis* 1999; 31:327-328.
117. Moling O, Pegoretti S, Rielli M, et al. *Chlamydia pneumoniae* — reactive arthritis and persistent infection. *Br J Rheumatol* 1996; 35:1189-1190.
118. Gerard HC, Schumacher HR, El-Gabalawy H, Goldbach-Mansky R, Hudson AP. *Chlamydia pneumoniae* present in the human synovium are viable and metabolically active. *Microb Pathog* 2000; 29:17-24.
119. Skinner M, Cathcart ES, Mills JA, Pinals RS. Tetracycline in the treatment of rheumatic arthritis: a double blind controlled study. *Arthritis Rheum* 1971; 14:727-732.
120. Kloppenburg M, Breedveld FC, Terwiel JP, Mallee C, Dijkman BA. Minocycline in active rheumatoid arthritis. A double-blind, placebo-controlled trial. *Arthritis Rheum* 1994; 37:626-636.
121. Tilley BC, Alarcon GS, Heyse SP, et al. Minocycline in rheumatoid arthritis. A 48-week, double-blind, placebo-controlled trial. MIRA Trial Group. *Ann Intern Med* 1995; 122:81-89.
122. O'Dell JR, Haire CE, Palmer W, Drymalski S, et al. Treatment of early rheumatoid arthritis with minocycline or placebo: results of a randomized, double-blind, placebo-controlled trial. *Arthritis Rheum* 1997; 122:81-89.
123. Takaki K, Tatu H, Shin H, et al. A case of *Chlamydia pneumoniae* and systemic lupus erythematosus (SLE) pleurisy. *Kansenshogaku Zasshi* 1999; 73:191-196.
124. Hunder GG, Bloch DA, Michel BA, et al. The American College of Rheumatology 1990 criteria for the classification of giant cell arteritis. *Arthritis Rheum* 1990; 33:1122-1128.
125. Russo MG, Waxman J, Abdoh AA, Serebro LH. Correlation between infection and the onset of the giant cell (temporal) arteritis syndrome: a trigger mechanism? *Arthritis Rheum* 1995; 38:123-192.
126. Rimenti G, Blasi F, Cosentini R, et al. Temporal arteritis associated with *Chlamydia pneumoniae* DNA detected in an artery specimen. *J Rheumatol* 2000; 27:2718-2720.
127. Wagner AD, Gerard HC, Fresemann T, et al. Detection of *Chlamydia pneumoniae* in giant cell vasculitis and correlation with the topographic arrangement of tissue-infiltrating dendritic cells. *Arthritis Rheum* 2000; 43:1543-1551.
128. Laurila AL, Anttila T, Laara E, et al. Serological evidence of an association between *Chlamydia pneumoniae* infection and lung cancer. *Int J Cancer* 1997; 74:31-34.
129. Koyi H, Branden E, Gnarpe J, Gnarpe H, Arnholm B, Hillerdal G. *Chlamydia pneumoniae* may be associated with lung cancer. Preliminary report on a seroepidemiological study. *APMIS* 1999; 107:828-832.
130. Anttila TI, Lehtinen T, Leinonen M, et al. Serologic evidence of an association between chlamydial infections and malignant lymphomas. *Br J Haematol* 1998; 103:150-156.
131. Abrams JT, Vonderheid EC, Kolbe S, Appelt DM, Arking EJ, Balin BJ. Sezary T-cell activating factor is a *Chlamydia pneumoniae*-associated protein. *Clin Diagn Lab Immunol* 1999; 6:895-905.
132. Chia JK, Chia LY. Chronic *Chlamydia pneumoniae* infection: a treatable cause of chronic fatigue syndrome. *Clin Infect Dis* 1999; 29:452-453.
133. Machtey I. *Chlamydia pneumoniae* antibodies in myalgia of unknown cause (including fibromyalgia) *Br J Rheumatol* 1997; 36:1134.
134. Kanauchi M, Kawano T, Dohi K. Association of *Chlamydia pneumoniae* infection with diabetic nephropathy. *Diabetes Res Clin Pract* 2000; 47:45-48.
135. Hatch TP. *Metabolism of Chlamydia*. CRC Press, Boca Raton, 1988.
136. Iliffe-Lee ER, McClarty G. Glucose metabolism in *Chlamydia trachomatis*: the "energy parasite" hypothesis revisited. *Mol Microbiol* 1999; 33:177-187.
137. Moulder JW. Glucose metabolism of L cell before and after infection with *Chlamydia*. 1970; *J Bacteriol* 104:1189-1196.
138. Ojcus DM, Degani H, Mispelter J, Dautry-Varsat A. Enhancement of ATP levels and glucose metabolism during an infection by *Chlamydia*. *J Biol Chem* 1998; 278:7052-7058.
139. Vannucci SA, Mitchell WM, Stratton CW, King LE. Pyoderma gangrenosum and *Chlamydia pneumoniae* infection in a diabetic man: pathogenic role or coincidence? *J Am Acad Dermatol* 2000; 42:295-297.
140. King LE Jr, Bushman T, Stratton CW, Mitchell WM. Diabetic foot ulcers and *Chlamydia pneumoniae*: innocent bystander or opportunistic pathogen? *Arch Dermatol* (in press).
141. Alberts GL, Stratton CW, Mitchell WM, Franke JJ. Potential role of *Chlamydia pneumoniae* in the pathogenesis or interstitial cystitis. Presented at the Annual Meeting of the Society for Urodynamics and Female Urology in Anaheim, CA, June 2001.

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The editors and the publisher of *Antimicrobics and Infectious Diseases Newsletter* invite you to contribute either a lead article or a case report. Of special interest are papers which discuss the appropriate use of antimicrobial agents. Case Reports should be concise papers and contain a) a brief clinical history of the illness; b) description of cultures or tests performed; c) antibiotics or antimicrobial agents administered; d) result of treatment. In addition, letters expressing opinions or offering insights on technical ideas and procedures will be considered for publication (subject to editing) providing they are signed by the authors and do not exceed two typewritten pages.

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