**36** Lack of Association between Genetically Mediated Hypercoagulable States (HCS) and Infection of Intravenous Catheters (IVC)

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Bacteria adhere to mammalian proteins on the surfaces of IVC. Genetic defects that predispose to a HCS include mutations in factor V (factor V Leiden, FVL), prothrombin (FII) 20210G→A, methylenetetrahydrofolate reductase (MTHFR) 677C→T and cystathionine beta-synthase (CBS) 844ins68. We hypothesized that a disproportionate number of persons who develop IVC infection may have one of these mutations, leading to a HCS. We identified 50 consecutive patients whose IVC, once removed, was found to have >100 bacterial cfu by the roll-plate method. We obtained uncoagulated blood from patients and from random control patients in our hospital; controls were excluded if, by chance, they had a positive catheter culture. A molecular probe sought R506Q as a marker for FVL, FII 20210A, and MTHFR 677T. Results for CBS 844ins68 are pending. Table shows numbers of subjects (%) homo/heterozygous for normal (N) or mutant (M); numbers of subjects vary based on the capacity to amplify. This study shows clearly that mutations in factors V or II, or in MTHFR associated with HCS are not increased in patients who develop bacterial infection around an IVC.

| | | Patients | Controls |
|---|---|---|---|
| R506Q | N/N | 37/38 (97) | 43/43 (100) |
| | N/M | 1/38 (3) | 0/43 (0) |
| | M/M | 0/38 (0) | 0/43 (0) |
| 20210A | N/N | 23/25 (92) | 26/29 (90) |
| | N/M | 1/25 (4) | 3/29 (10) |
| | M/M | 1/25 (4) | 0/29 (0) |
| 677T | N/N | 28/42 (67) | 32/48 (67) |
| | N/M | 13/42 (31) | 16/48 (33) |
| | M/M | 1/42 (2) | 0/48 (0) |

**37** Role of *Chlamydia pneumoniae* in the Diagnosis of Temporal Arteritis

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Temporal arteritis (TA), a medium and large-vessel arteritis, is the most common primary systemic vasculitis. There have been reports of *C. pneumoniae*, detected by polymerase chain reaction (PCR) in temporal artery biopsy specimens from patients with TA. To examine the reported correlation between *C. pneumoniae* in temporal artery biopsy specimens and the diagnosis of TA, we performed a case-control study to document the prevalence of *C. pneumoniae* in all biopsy-proven TA cases diagnosed over a 32-year period at our institution. We reviewed all cases of TA identified by biopsy between 1968 and 2000 (n=90). Of the temporal artery biopsies, 79 (88%) demonstrated giant cells and 11 (12%) had other histopathological features compatible with TA. Through chart review, we confirmed that all 90 cases met the 1990 American College of Rheumatology classification criteria for TA. Controls were chosen from the individuals who had negative temporal artery biopsies during the same time period. Charts of the potential controls were also reviewed to ensure that their post-biopsy courses were not compatible with TA. One control was matched to each case on: gender, age (within 10 years), and year of biopsy. The biopsies of all cases and controls were re-evaluated in a masked fashion by an ocular pathologist to confirm the original readings. Following de-paraffinization and DNA extraction from the biopsy specimens, PCR analysis was performed for *C. pneumoniae* on the 180 samples. A primer set targeting the *ompA* gene (CP1-CP2/CPC-CPD) was used to perform a nested PCR. Positive and negative controls were used, as well as controls made from infected and non-infected Hep-2 cells, suspended in a formalin-fixed, paraffin-embedded matrix. From the 90 cases of biopsy proven TA, 1 (1.1%) had a positive PCR. Of the 90 controls, 1 (1.1%) had a positive PCR. Confirmation of these findings are being performed using primers targeting the 16S rRNA gene in a touchdown enzyme time-released PCR (CPN90/CPN91). This comprehensive study of a large number of biopsy-proven cases of TA and matched controls, using sensitive and specific PCR analyses, does not support an association of *C. pneumoniae* in the pathogenesis of TA.

**38** *Chlamydia pneumoniae* PCR and Markers of Abnormal Fibrinolysis as Predictors of Progression of Heart Transplant Accelerated Graft Arteriosclerosis

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Background: In cardiac transplants, accelerated graft arteriosclerosis (AGA) is the leading cause of allograft failure and mortality after the first post-operative year. Infectious agents such as CMV have been implicated in this process. Heart transplant recipients have high C. pneumoniae antibody titers, and the organism has been recovered from the coronary arteries of both donors and recipients. This study seeks to evaluate association between C. pneumoniae infection and abnormalities of the coagulation and fibrinolytic system and examines these factors as predictors of AGA development. Methods: We measured plasma C. pneumoniae IgG, d-dimer, prothrombin fragment 1.2, p-selectin, thrombomodulin, and fibrinogen, and processed buffy coat specimens for PCR detection of C. pneumoniae DNA in a cohort of heart transplant patients at Johns Hopkins Hospital. Annual follow-up coronary arteriography was obtained over a 2-year period. Progressive disease was defined prospectively as > 2 new lesions, progression of stenosis in > 2 lesions, new type B disease, or clinical evidence of cardiac ischemia. CMV IgG and traditional cardiac risk factors were evaluated as covariates in statistical analysis. Results: 44% of patients developed progressive AGA over a 2 year period. 47% were CMV IgG +. Geometric mean C. pneumoniae IgG did not vary between progressors and nonprogressors, though 50% of progressors had +PCR detection of C. pneumoniae DNA compared to 20% of nonprogressors (OR=4.3, p=0.1). The level of d-dimers was significantly ($p<0.001$) lower in the progressors (median 71 ng/dL) than in nonprogressors (median 165 ng/dL). There was no statistically significant difference between the groups in the levels of the other markers. Conclusions: Chronic endovascular infectious agents and impaired fibrinolysis may be important cofactors in development of AGA. Further study of the impact of C. pneumoniae and CMV infection on the coagulation and fibrinolytic system will help to shed light on the underlying pathophysiology of AGA.

**39** Levofloxacin Kills *Chlamydia pneumoniae* and Modulates Interleukin 6 (IL-6) Production by HEp-2 Cells

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This study addresses the anti-chlamydial effect of levofloxacin (LE) and its role in modulation of IL-6 (a pro-inflammatory cytokine) production in uninfected and infected HEp-2 cells. *Chlamydia pneumoniae* (*Cpn*) strain AR-39 (ATCC 53592) inocula were prepared from 3-day-old infected cultures of HEp-2 cells. Cells were disrupted, vortexed, filtered (0.45 $\mu$m pore-size), and frozen in aliquots in liquid $N_2$. Three-day-old HEp-2 cell monolayers were infected with $10^3$ inclusion-forming units (IFU)/ml of *Cpn*. The infected cells were treated with 0.05, 3, or 8 $\mu$g/ml of LE at 0, 4, or 24 h after infection. Aliquots were examined at 24, 48, 72, and 96 h after infection by (a) counting inclusions stained with fluorescently labeled anti-chlamydial monoclonal antibody, (b) determining the titers (in IFU/ml) of *Cpn*, and (c) measuring cytokine production using ELISA assays. Results: 1) LE at 3 and 8 $\mu$g/ml prevented infection of HEp-2 cells when given immediately or 4 h after exposure; 2) when LE was given 24 h after exposure, infection progressed for from 48 to 72 h, but resulted in very low inclusion counts and *Cpn* titers; at 96 h, 85% of the HEp-2 cells were uninfected; 3) LE modulated IL-6 production in uninfected and infected HEp-2 cells; 4) HEp-2 cells infected with *Cpn* and treated with LE produced more IL-6 than untreated HEp-2 cell controls; 5) IL-6 production by HEp-2 cells infected with *Cpn* and treated with LE was higher at 48 and 72 h than in untreated controls; however, IL-6 production was lower at 96 h when LE-treated cells were cleared of infection; 6) results from infected HEp-2 cells treated with 0.05 $\mu$g/ml of LE and untreated control cells were similar; 7) HEp-2 cells did not produce TNF-$\alpha$, INF-$\gamma$, or IL-8. Conclusions: 1) LE at serum-attainable concentrations (3 and 8 $\mu$g/ml) is effective in eliminating *Cpn* from infected HEp-2 cells; 2) LE modulates IL-6 production by uninfected HEp-2 cells and HEp-2 cells infected with *Cpn*.

**40** A Prospective Multicenter Study of Community-Acquired Pneumonia in Korea

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Background: To compare the etiologic agents and antimicrobial resistance rates of community-acquired pneumonia in Korea and Western countries, the causative pathogens were prospectively investigated in patients requiring hospitalization. Method: A prospective multicenter (9 university hospitals) study of community-acquired pneumonia in Korea was carried out between May 1997 and April 2000. The microbiologic diagnosis was based on the results of sputum culture and blood culture. We utilized specialized tests for respiratory viruses and *Legionella* species including culture and indirect immunofluorescence test of nasal aspirates. We used the PCR of nasal aspirates for *Legionella* spp, *Chlamydia pneumoniae*, *Mycoplasma pneumoniae* and the passive hemagglutination of serum for Leptangamushi. Results: Five hundred eighty five cases of community-acquired pneumonia admitted to the hospitals. The mean age was 60.1 and 368 (62.9%) had underlying illness. The etiologic agents were identified in 40.0% and the list of individual agents (number), in decreasing order, was *Streptococcus pneumoniae* (59), *Klebsiella pneumoniae* (40), *Pseudomonas aeruginosa* (26), *Staphylococcus aureus* (25), *C. pneumoniae* (13), *Haemophilus influenzae* (11), *Enterobacter cloacae* (11), *M. pneumoniae* (10), influenza virus (9), parainfluenza virus (7), *Orientia tsutsugamushi* (6), *Legionella* spp (5). The rates of admission to the intensive care unit was 10.3%. The motality was 7.0%. Susceptible rates of *S. pneumoniae* to penicillin was 42.9%. *S. pneumoniae* showed multidrug resistance including erythromycin, chloramphenicol, doxycycline. Thirty six percents of *S. aureus* were methicillin-resistant *S. aureus*. *K. pneumoniae* were susceptible to cefuroxime (92.5%) and quinolone (96.4%). Conclusion: In Korea, *S. pneumoniae* is the most important etiologic agent of community-acquired pneumonia. But, when compared with that of Western countries, gram negative bacteria such as *K. pneumoniae*, *P. aeruginosa* showed high incidence. Most of them had history of recurrent hospitalization and underlying diseases including bronchiectasis and chronic obstructive pulmonary diseases.

**41** Legionnaires' Disease Outbreak in an Automobile Engine Manufacturing Plant, Ohio, 2001

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Background: Outbreaks of legionellosis have occurred in industrial settings. In March 2001, 4 cases of Legionnaires' disease (LD) were reported among workers at the same automotive plant; all were diagnosed by Legionella urine antigen testing. We sought to identify new cases and sources of Legionella transmission. Methods: A confirmed case of LD was defined as X-ray-confirmed pneumonia plus a positive urine antigen test or isolation of Legionella from respiratory secretions or lung tissue in a plant worker. We collected clinical specimens, established active surveillance for LD, and reviewed hospital and employee absentee records. An environmental investigation was conducted to look for aerosol-producing water sources. We conducted a case-control study to determine risk factors for exposure to Legionella. Cases included confirmed LD or possible cases of legionellosis, i.e., respiratory symptoms and a titer of anti-Legionella IgG antibody >=1:1024. Controls were randomly selected workers with fewer than 2 symptoms and IgG antibody < =1:64. Results: No additional cases occurred. L. pneumophila serogroup 1 (LP1) was isolated from 1 patient. Legionella was isolated from 18 (9%) of 197 environmental samples; 3 were LP1 but none matched the case isolate by monoclonal antibody testing. Of 484 (57% of 855) workers who agreed to participate in the case-control study, 9 met case criteria (4 confirmed, 5 possible) and 89 met criteria for controls. Visiting one specific finishing line (OR=11.83; CI=2.20-63.61), working in the finishing region of the plant (OR=3.53; CI=0.87,14.30), being a smoker (OR=4.22; CI=0.78,22.55) and having heart disease (OR=5.13; CI=1.21,21.85) were associated with disease. Conclusions: A particular finishing line in the automotive plant was the likely source of exposure. Clinicians should consider LD when treating persons from industrial settings for pneumonia, and plants should do routine maintenance designed to reduce transmission of Legionella.