Iatrogenic acid suppression is associated with an increased risk of *Clostridium difficile* colitis.

**Background:** Numerous studies have shown that the incidence and severity of *Clostridium difficile* colitis has been increasing. It has been suggested that the increasingly widespread use of acid-suppressive medications may be associated with *C difficile* infection, but data are controversial.

**Objective:** To determine if receipt of acid-suppressive medication is associated with *C difficile* colitis.

**Design:** Pharmacoepidemiologic cohort study of prospectively collected data on 101,796 discharges over a 5-year period at a tertiary care medical center in New England.

**Methods:** The primary outcome was *C difficile* colitis. The primary exposure was acid-suppressive therapy, which was classified as none, histamine-2-receptor antagonist (H2RA), daily proton pump inhibitor (PPI), or PPI more frequently than daily. A propensity score was developed to adjust for potential selection bias among patients receiving acid-suppressive therapy.

**Results:** A total of 665 nosocomial cases of *C difficile* colitis were identified. By unadjusted analysis, the risk of *C difficile* colitis significantly increased along with increasing intensity of acid-suppression (0.3% for no acid-suppression to 1.4% for maximal acid suppression). As expected, the risk of *C difficile* colitis also increased with antibiotic exposure. After adjusting for comorbid conditions and receipt of antibiotics, the association of *C difficile* colitis with acid-suppressive therapy persisted, increasing from 1.00 (reference) to 1.53 for H2RA use, to 1.74 for daily PPI, to 2.36 for maximal PPI. A nested case-control study using different statistical methods arrived at similar conclusions.

**Conclusions:** Increasing levels of pharmacologic acid suppression are associated with an increasing risk of *C difficile* colitis. The dose-response nature of the relationship supports the causal nature of the relationship.

**Reviewer's Comments:** Over the past decade, it has become increasingly common for patients to receive acid-suppressive medications in the hospital, despite a paucity of data supporting such widespread use. This article serves as another example of the "nothing comes for free" maxim of medicine. Through rigorous statistical analysis, the authors make a strong case that acid-suppressive therapy results in an increased risk of *C difficile* colitis, a common nosocomial infection that causes significant morbidity and mortality. These data are supported by animal studies, and another article from the same journal issue demonstrates that acid-suppressive medications are associated with increased rates of *C difficile* recurrence. Together with recently published data regarding increased rates of hospital-acquired pneumonia among patients receiving acid-suppressive medications, these data should raise serious concerns regarding our complacent approach to use of acid suppression among hospitalized patients. (Reviewer-Samuel Shelburne, MD).

**Keywords:** *Clostridium difficile*, Acid Suppression, Risk Factors

**Print Tag:** Refer to original journal article
Polymorphisms in the cytokine-inducible SRC homology 2 domain protein are associated with increased susceptibility to common infections.

**Background:** The interleukin (IL)-2–mediated response is known to be critical for combating infectious agents. The suppressor of cytokine signaling (SOCS) family proteins, which includes the cytokine-inducible SRC homology 2 domain protein (CISH), is important for controlling cytokine signaling.

**Objective:** To determine if CISH polymorphisms are associated with susceptibility to bacteremia, tuberculosis, and severe malaria.

**Design:** Case-control design using blood samples collected from 8402 persons in Gambia, Hong Kong, Malawi, and Vietnam.

**Methods:** CISH polymorphisms were determined using standard genotyping. Gene expression from peripheral blood mononuclear cells (PBMCs) was assayed following stimulation with IL-2 and -3.

**Results:** In this pilot study, 8 single nucleotide polymorphisms (SNPs) were identified in the CISH gene. Four SNPs (at positions –639, –292, –163, and +3415) showed evidence of association with bacteremia, 3 SNPs (–292, +1320, +3415) were associated with tuberculosis, and 4 SNPs (–639, –292, +1320, +3415) were associated with severe malaria. On pooled analysis, CISH alleles at –639, –292, –163, +1320, and +3415 were associated with an increased susceptibility to the infectious diseases studied, with –292 accounting for most of the association. There was a strong association between increasing numbers of SNPs and increasing susceptibility to 1 of the infections studied. The overall risk of a single CISH “risk” allele was 18%, but this increased to 81% among persons with ≥4 risk alleles. PBMCs isolated from patients who were homozygous for CISH –292TT has significantly lower CISH RNA levels at 30, 60, and 120 minutes following stimulation with IL-2.

**Conclusions:** SNPs in the CISH gene were associated with increased susceptibility to major infectious diseases and a decreased functional response to IL-2 stimulation.

**Reviewer’s Comments:** One of the holy grails of infectious diseases research is identification of genetic susceptibilities to infectious diseases that are common in the population. The marked expansion of genetic data has begun to make such identification possible, although application of such technologies is certainly just beginning. This was an ambitious study that investigated a wide range of infectious diseases among diverse genetic populations. As such, it provides new information regarding the role of SOCS family members in the genetic susceptibility to important infectious agents. There are numerous limitations to such studies, and it will be important to see if future studies are able to replicate these findings. If so, then it may be possible to consider targeting SOCS pathways as part of the development of novel therapeutics. (Reviewer-Samuel Shelburne, MD).

**Keywords:** Genetic Predisposition, Disease Polymorphism, Single Nucleotide Suppressor, Cytokine Signaling Proteins

**Print Tag:** Refer to original journal article
Widespread use of linezolid appears to be associated with an outbreak of linezolid-resistant Staphylococcus aureus.

**Background:** Staphylococcus aureus strains resistant to linezolid are very uncommon, but reports of linezolid-resistant staphylococci have been increasing.

**Objective:** To describe an outbreak of linezolid-resistant *S aureus* (LRSA) in an intensive care department.

**Design/Participants:** Outbreak study of consecutive, critically ill patients who were either colonized or infected with LRSA at a tertiary-care teaching hospital in Madrid, Spain. **Outcome Measures:** Clinical data from LRSA-colonized or infected patients and linezolid use data were collected. Pulsed-field gel electrophoresis and polymerase chain reaction were used to determine genetic-relationships among the isolates. **Infection Control Measures:** During the outbreak, patients were isolated and cohorted. Intensive environmental cleaning and sampling were performed, and linezolid use indications were reviewed.

**Results:** Between April 13 and June 26 of 2008, there were 12 patients with LRSA identified among 3 distinct ICUs) Eleven patients had been receiving linezolid prior to LRSA isolation for a median of 7.5 days. Six patients had ventilator-associated pneumonia, 3 had bacteremia, and 3 were colonized. All isolates remained susceptible to vancomycin, daptomycin, and tigecycline. Patients were treated with either vancomycin or tigecycline. One patient was thought to have died from complications of LRSA infection. The same LRSA clone was identified from 11 of these 12 patients. All LRSA isolates contained the *cfr* gene as the mechanism of linezolid resistance. LRSA was isolated from 1 environmental sample. Linezolid use decreased by 90% over the course of the study. Over the next 20 months, no new cases of LRSA were identified.

**Reviewer's Comments:** As I detailed in a review earlier this year, linezolid resistance is becoming increasingly common among staphylococci. Concerning aspects of this outbreak are presence of the genetically transferable *cfr* gene and the polyclonal nature of the outbreak. This suggests that *S aureus* isolates that carry the *cfr* gene may not have significantly reduced in vivo fitness, as appears to be the case for *S aureus* that carry ribosomal mutations mediating linezolid resistance. Thus, *cfr*-containing staphylococci may be able to spread in the nosocomial setting similar to what has been observed for methicillin-resistant *S aureus*. This outbreak, and others, should be a wakeup call that continued widespread use of linezolid is likely to result in reduced efficacy. Fortunately, marked reductions in linezolid use and increased infection control measures appear to have stemmed the outbreak, at least for now. Note also that these same authors recently detailed this same outbreak in *Clinical Infectious Diseases*. (Reviewer-Samuel Shelburne, MD).

**Keywords:** Staphylococcus aureus, Disease Outbreaks, Antimicrobial Stewardship

**Print Tag:** Refer to original journal article
A positive sputum smear or culture at 2 months during treatment of tuberculosis has a poor sensitivity and modest specificity at predicting treatment failure or relapse.

**Background:** The World Health Organization (WHO) has previously recommended that patients who are newly diagnosed with tuberculosis (TB) and are on treatment receive a sputum smear evaluation at 2 months. If the smear evaluation is positive, the intensive treatment phase should be continued for an additional month before switching to the continuation phase. However, there is a dearth of data on the sensitivity and specificity of sputum examination at 2 months to predict outcome.

**Objective:** To estimate the sensitivity and specificity of a positive sputum smear or culture for *Mycobacterium tuberculosis* (MTB) at 2 months into a standardized anti-tuberculosis treatment regimen that contains rifampin.

**Design:** Systematic review and meta-analysis of the English-language medical literature.

**Methods:** The authors included randomized controlled studies, cohorts, and case-control studies that evaluated smear-positive or culture-positive pulmonary TB patients who underwent treatment with a standardized, rifampicin-including regimen and had sputum evaluation during treatment. Treatment failure or relapse was measured as an outcome. Treatment failure was defined as detection of MTB at 5 months or later during treatment, and treatment relapse was defined as detection of MTB after successful completion of a course of TB treatment.

**Results:** The final analysis included 28 studies from 15 publications. Most studies were done in developing countries and did not assess patients for coinfection with HIV. Two studies excluded HIV-coinfected patients. A positive sputum culture at 2 months had a sensitivity of 40% and a specificity of 85% at predicting relapse. A positive sputum smear at 2 months had a sensitivity of 24% and a specificity of 83% at predicting relapse. Low sensitivity and modest specificity were also found when the outcome measured was treatment failure. A positive smear or culture at 2 months had a low positive-predictive value (9% to 18%) and a strong negative-predictive value (93%) at predicting failure or relapse.

**Conclusions:** A positive sputum smear or culture at 2 months into treatment of pulmonary TB is a poor predictor of treatment outcome.

**Reviewer's Comments:** It is surprising to realize that the historic practice of making a treatment decision based on the result of the sputum evaluation at 2 months was largely unjustified. Accordingly, the WHO new guidelines no longer carry this recommendation, in part as a result of this meta-analysis. The study has limitations: heterogeneity of the studies, lack of documentation of HIV serostatus, lack of differentiation between re-infection and relapse, and exclusion of non-English publications. (Reviewer-Hana El Sahly, MD).

**Keywords:** Tuberculosis, Treatment, Sputum Monitoring
Contamination of food can be a cause of large outbreaks of Chagas disease in urban, affluent areas.

**Background:** In the past decade, there has been a campaign to eradicate the vector responsible for transmission of *Trypanosoma cruzi* in various American countries, with variable success. However, there are other reported modes of disease transmission: transfusion-related, transplant-related, congenital, and oral. In Venezuela, there have been some epidemiologic data that suggest an increase in Chagas disease. Recently, a large outbreak of orally acquired Chagas disease has been reported in Caracas, Venezuela.

**Objective:** To describe the epidemiology and clinical features of orally acquired Chagas disease. Case Report: A 9-year-old boy presented with fever of unknown origin (FUO) and was found to have acute Chagas disease. Multiple similar illnesses and high absenteeism were reported from the boy's school. This prompted researchers to conduct a nested, case-control study involving all school attendees and those related to them. The study involved collection of blood samples for smear evaluation, culture, and serologic studies. In addition, a questionnaire that collects clinical and epidemiologic variables was administered to the study population. A confirmed case was any suspected case patient or symptomatic person with the epidemiological link and blood parasites or specific anti-*T. cruzi* antibodies by 2 different serological techniques. A suspected case was any person with an epidemiological link to the institution involved who developed FUO of 15 days' duration and other clinical manifestations.

**Results:** Of 1000 individuals tested, there were 103 cases of confirmed acute Chagas disease, including 1 death in a 5-year-old boy. There were 2 variables that were significantly associated with Chagas disease: attending school in the morning shift (vs afternoon shift) and consumption of guava juice. Guava juice was prepared in a poor neighborhood at the edge of the city. The woman in charge of preparing the juice was also infected. Fever, arthralgias, skin lesions (including erythema nodosum), and cardiac abnormalities were the most common findings. The majority of patients (75%) were symptomatic.

**Conclusions:** Oral acquisition of Chagas disease can cause large outbreaks in urban centers and may be underestimated as a route of transmission.

**Reviewer's Comments:** The authors describe the largest outbreak of Chagas disease secondary to food contamination. Contamination of food with the trypomastigotes is a frequently overlooked etiology of the disease but may be of rising importance. Also, the urban affluent location of the outbreak is unusual. However, given the increasing size of the poverty belts that are in proximity to forests on one end and the city on the other end, a shift in the epidemiology of the disease could be underway. Clinicians and public health authorities need to be aware of this evolving epidemiology. (Reviewer-Hana El Sahly, MD).

Keywords: Chagas Disease, Epidemiology

Print Tag: Refer to original journal article
Objective: To determine the prevalence of fungi in the deep tissues of diabetic lower-limb wounds, and to define the spectrum of the isolated fungi.

Participants: 518 consecutive patients at 1 hospital center in India who had type 2 diabetes and required hospitalization for surgical management of lower-limb wounds.

Methods: Consecutive diabetic patients hospitalized for surgical management of lower-limb wounds were enrolled. Wounds were classified according to the University of Texas Wound Classification System. Data collected on each patient included HbA1C level, ankle brachial index, vibration perception threshold, and transcutaneous oxygen tension. Superficial necrotic tissue was removed from the wounds, followed by a saline wash. Then, a deep-tissue specimen 0.5 x 0.5 cm in size was removed from the wound bed and cultured in Sabouraud's agar. Antifungal susceptibility testing was done with ATB Fungus-3 strips against fluconazole, voriconazole, flucytosine, itraconazole, and amphotericin B. Simultaneous specimens were cultured for bacteria in thioglycolate medium, 5% sheep's blood, and MacConkey agar.

Results: 518 patients were enrolled (382 [73.7%] males and 136 [26.3%] females). Of patients, 141 (27.2%) had fungi isolated from their wounds. *Candida* species accounted for 108 of 141 (76.6%) isolated fungi, the most common of which were *C. parapsilosis* (36 isolates) and *C. tropicalis* (32 isolates). Of 141 isolated fungi, 18 (12.8%) were *Trichosporon asahii*, 12 (8.5%) were filamentous fungi, and 3 (2.1%) were other yeasts. A total of 18 different fungal species were identified in the 141 isolates. A total of 130 isolates were available for susceptibility testing; resistance was present in 2 (1.5%) against flucytosine, 5 (3.9%) against fluconazole, 9 (6.9%) against voriconazole, 9 (6.9%) against amphotericin B, and 23 (17.7%) for itraconazole. Of 518 patients, 30 (5.8%) had only fungi isolated from their wounds, 302 (58.3%) had only bacteria, 75 (14.5%) had neither bacteria nor fungi, and 111 (21.4%) had both bacteria and fungi isolated together. Bacteria were present in 79.7% of wounds with an average of 1.5 species from each specimen. Of bacteria, 55.3% were Gram-negative and 44.7% were Gram-positive. There was no correlation between frequency of fungal isolation and depth of wound. Fungal isolation was significantly related to HbA1C level ($P=0.04$), but not with age, sex, duration of diabetes mellitus, duration of the foot lesion, ankle brachial index values, vibration perception threshold, or transcutaneous oxygen tension.

Conclusions: There is a high prevalence and wide spectrum of fungal isolation from deep tissues of lower-extremity wounds in type 2 diabetic patients. The prevalence of fungal isolation is significantly correlated with HbA1C levels.

Reviewer's Comments: The data from this study are provocative; however, in the absence of quantitative fungal cultures or confirmatory histopathological analysis, it is virtually impossible to judge the significance of this finding. (Reviewer-Richard J. Hamill, MD).

Keywords: Type 2 Diabetes, Lower-Limb Wounds, Fungi

Print Tag: Refer to original journal article
Alternative Tx for Early Syphilis Using Azithromycin

A Phase III Equivalence Trial of Azithromycin Versus Benzathine Penicillin for Treatment of Early Syphilis.

Hook EW III, Behets F, et al:

J Infect Dis 2010; 201 (June 1): 1729-1735

In a phase III equivalence trial, 2.0 g of azithromycin via oral administration can be potentially useful for treating early syphilis in penicillin-allergic patients.

Background: Syphilis is a common sexually transmitted disease that has been on the rise since 2000. According to the Centers for Disease Control and Prevention, rates have increased from 2.6 to 5.7 in the last 10 years. For years, the main treatment has been benzathine penicillin G for early syphilis. If the patient has an allergy to penicillin, there are very few alternative antibiotics, with the most common being doxycycline. Doxycycline’s main drawback is its variable adherence and side effects. Azithromycin is being proposed as an alternative treatment for early syphilis.

Objective: To determine whether azithromycin treatment is non-inferior to penicillin treatment by measuring cure rates.

Design: Open-label, randomized, controlled multicenter trial.

Participants: 517 patients aged 18 to 55 years who were HIV-uninfected, nonpregnant, and having early syphilis (primary, secondary, or early latent).

Methods: Patients were enrolled during June 2000 through March 2007. Patients were randomized to received 2.0 g azithromycin or 2.4 million units of benzathine penicillin.

Results: Of 517 patients, 255 received azithromycin and 262 received penicillin G. Response to treatment for azithromycin was similar to that for benzathine penicillin G. Cure rates at 6 months were 77.5% for the azithromycin group and 78.9% for the penicillin group. The 1-sided 95% CI lower bound was −7.9%, thus indicating non-inferiority of azithromycin when compared to penicillin. Also, only 2.8% of the azithromycin group experience severe adverse effects compared to 3.5% in the penicillin group.

Conclusions: This study shows strong evidence for using azithromycin at 2.0 g given as a single dose for treatment of early syphilis. By being an oral, single agent, it can help enhance treatment for syphilis and for its control.

Reviewer's Comments: Penicillin is the recommended treatment for early syphilis; this clinical phase III trial shows us an alternative for those patients who are penicillin-allergic and HIV-uninfected with this disease. Azithromycin is a good alternative in resource-limited countries where refrigeration is a problem. In addition, it can provide treatment not just for early syphilis but also for other sexually transmitted diseases such as chancroid, chlamydia, and gonorrhea. The limitation in using this medication is the acquired resistance to macrolide by the Treponema pallidum. (Reviewer-Laila Woc-Colburn, MD).

Keywords: Syphilis, Azithromycin vs Benzathine Penicillin

Print Tag: Refer to original journal article
Using urinary antigen for detecting pneumococcal pneumonia in HIV-infected patients is a reliable and fast diagnostic tool.

**Background:** HIV-infected individuals are affected more with bacterial infections due to impaired cell-mediated and humoral immunity. The most common bacterial infection in this population is *Streptococcus pneumoniae* and it is associated with a high morbidity and mortality. *S pneumoniae* is the leading cause for community-acquired pneumonia (CAP). There is no gold standard for diagnosing the etiology of CAP. For *S pneumoniae*, the use of urinary antigen has been proposed as a rapid and reliable test in identifying this causative agent.

**Objective:** To determine whether use of urinary antigen for *S pneumoniae* in emergency care is a diagnostic, fast, and reliable test in diagnosing CAP in HIV-infected patients.

**Design:** Prospective noninterventional study.

**Methods:** The study was conducted in Barcelona, Spain, from January 2007 to December 2008. All HIV-infected patients who presented to emergency care and were admitted to the hospital with respiratory symptoms were included in the study. Patients had urinary antigen determination for pneumococcus, blood culture, and sputum culture.

**Results:** The study recruited 150 HIV-infected patients with the diagnosis of CAP, and 88 met eligibility criteria. Twenty-four patients were excluded due to poor samples in the sputum. Of 64 remaining patients, 31 (48%) had positive urinary antigens, 21 (33%) had positive sputum cultures, and 12 (19%) had positive blood cultures. These results were independent of CD4 count, HIV viral load, and antiretroviral treatment.

**Conclusions:** Use of pneumococcal urinary antigen in HIV-infected patients in the emergency department is a useful tool for diagnosis and treating CAP.

**Reviewer's Comments:** Diagnosing pneumococcal pneumoniae using urinary antigens has not been used frequently due to its poor sensitivity. In recent years, better urinary antigens have been developed. As this study shows, urinary antigen has better sensitivity and specificity than sputum and blood cultures when diagnosing pneumococcal pneumoniae. This will help in the diagnosis of CAP in HIV-infected patients since they have a higher incidence of acquisition. One limitation for this study is its size. It would be helpful to do a larger trial to prove the usefulness of the pneumococcal urinary antigen in identifying the cause of CAP. (Reviewer-Laila Woc-Colburn, MD).

Keywords: Pneumococcal Pneumoniae, Urinary Antigen, HIV

Print Tag: Refer to original journal article
Does Early PCR Offer Any Benefit in Empiric-Tx-Resistant Fever?

*Diagnostic Value of PCR Analysis of Bacteria and Fungi From Blood in Empiric-Therapy-Resistant Febrile Neutropenia.*

Nakamura A, Sugimoto Y, et al:

*J Clin Microbiol 2010; 48 (June): 2030-2036*

Polymerase chain reaction may improve outcome of neutropenic fever when there are pathogens that are particularly difficult to treat or grow.

**Background:** Bacterial and fungal infections cause significant morbidity and mortality in patients with prolonged neutropenia. Specific pathogens are frequently not found by standard culture techniques. It is unclear whether polymerase chain reaction (PCR) of blood for bacterial and fungal pathogens would improve outcomes.

**Objective:** To conduct periodic analyses of blood from patients following intensive chemotherapy using a PCR system able to detect a broad range of bacteria and fungi.

**Design:** Prospective pilot study.

**Methods:** PCR was used to detect DNA from both bacteria and fungi. A pilot study was performed in 7 patients with weekly PCR during neutropenia or during fever. Blood was obtained for culture and fungal antigen testing. A second phase of the study involved sporadic PCR during febrile neutropenia.

**Results:** Bacteria were detected by PCR in 11 of 23 febrile episodes by PCR compared with 3 of 23 detected by culture. No fungi were detected. Bacteria were discovered in 3 afebrile cases by PCR alone and 3 cases by culture alone. In the sporadic study, bacteria were detected by PCR in 13 of 15 cases with blood culture positive in 7 of 15. In all but 1 case, fever was treated successfully with empirical antibiotic therapy. PCR assisted in 2 refractory cases where the pathogens found were *Stenotrophomonas maltophilia* and *Pseudomonas aeruginosa*.

**Conclusions:** PCR may improve outcome of neutropenic fever when there are pathogens that are particularly difficult to treat or grow.

**Reviewer's Comments:** This was a small study but there are a couple of interesting points to mention. While detection of bacterial or fungal DNA is clearly more sensitive than standard culture techniques, this does not necessarily translate into improved outcomes. It appears that despite earlier detection by PCR, most pathogens were successfully treated with the empiric therapy that was chosen. However, there may be some situations where early detection of some pathogens might be helpful to dictate specific therapy such as in *Stenotrophomonas* or multi-drug resistant *Pseudomonas*. Larger studies will be needed to formally address whether outcomes can be improved. (Reviewer-David E. Greenberg, MD).

**Keywords:** Neutropenia, Fever, Polymerase Chain Reaction, Bacteremia, Fungemia

**Print Tag:** Refer to original journal article
Is Infection Control Out of Control in Nursing Homes?

Multidrug-Resistant Acinetobacter baumannii: An Emerging Pathogen Among Older Adults in Community Hospitals and Nursing Homes.

Sengstock DM, Thyagarajan R, et al:

Clin Infect Dis 2010; 50 (June 15): 1611-1616

The cycle of transmission of drug-resistant Acinetobacter between hospitals and nursing homes may be an area where infection control could be critical.

**Background:** Acinetobacter baumannii is becoming increasingly recognized as a pathogen in various health care settings throughout the world. A baumannii is associated with increased morbidity and mortality.

**Objective:** To determine the prevalence, resistance patterns, and outcomes of A baumannii in long-term care facilities and in older adults.

**Methods:** A baumannii epidemiology was tracked at 4 hospitals in Michigan. Demographic data were tracked, including where the patient came from (home vs hospital vs long-term care facility).

**Results:** During the 6-year study, 1441 patients had Acinetobacter recovered. In total, 32% were aged <60 years and 10% were admitted from other hospitals. Of those aged ≥60 years, 560 were admitted from home and 280 were admitted from nursing homes. In total, 56% of isolates were from respiratory secretions and 22% were from wounds. From 2003 to 2008, there was a 25% increase in Acinetobacter rates in older individuals. Antibiotic resistance also increased over time. There were 0 pan-resistant strains in 2003 to 2004 versus 40 cases in 2007. Fifty-five percent of nursing-home residents had Acinetobacter isolated within 2 days of admission. Adverse outcomes were related to the level of antibiotic resistance.

**Conclusions:** The prevalence and resistance of Acinetobacter species are increasing in the community. Patients with resistant isolates are selectively discharged to nursing homes and long-term acute-care facilities, introducing resistance to new facilities.

**Reviewer’s Comments:** This important study illustrates the increasing problem of Acinetobacter in various settings. Of particular concern is the increasing rate of antibiotic resistance. This study shows not only the increasing prevalence of Acinetobacter infections in patients in long-term care facilities, but also that there is a cycle of transmission between hospitalized patients and those in a nursing-home. The authors identify this as an important area to implement infection control practices to help control the spread of multi-drug resistant strains. (Reviewer-David E. Greenberg, MD).

Keywords: Acinetobacter, Nursing Home, Antibiotic Resistance, Bacterial Disease

Print Tag: Refer to original journal article
HAIs Are Significant Medical Problem Throughout the World

Hospital-Acquired Infections Due to Gram-Negative Bacteria.

Peleg AY, Hooper DC:


Hospital-acquired infections due to gram-negative pathogens remain a serious threat and increasing antibiotic resistance makes treating these infections difficult.

Background: Hospital-acquired infections (HAIs) remain a major public health problem. Gram-negative pathogens are responsible for >30% of HAIs.

Objective: To review HAIs. Discussion: The most common life-threatening HAI is pneumonia, and many of these are associated with ventilators. In total, 10% to 20% of patients who are on ventilators for >48 hours will develop pneumonia. Gram-negatives predominate and the major pathogens include: Pseudomonas aeruginosa, Acinetobacter baumannii, and the Enterobacteriaceae. A baumannii is increasing in both prevalence and antibiotic resistance. Diagnosis remains challenging. A sample should be obtained from the lower respiratory tract. Bloodstream infections are usually due to the presence of a central vascular device. In the U.S., approximately 30% of bloodstream infections are due to gram-negatives including Klebsiella species, Escherichia coli, Enterobacter species, and Pseudomonas. Antibiotic resistance due to Klebsiella pneumoniae carbapenemase (KPC) is becoming an important resistance marker. Gram-negative pathogens are the predominant cause of urinary tract infections. Almost all are associated with urethral catheterization. Most are asymptomatic and the treatment is the removal of the catheter. Therapy for HAIs due to gram-negative pathogens should be based on local antibiotic susceptibility patterns.

Conclusions: HAIs due to gram-negative pathogens remain a serious threat and increasing antibiotic resistance makes treating these infections difficult.

Reviewer's Comments: This is a very thorough review that is worth reading by all practicing infectious diseases physicians who interact with hospitalized patients. It discusses in detail the epidemiology of various clinical infections, details regarding approaches to diagnosis, and current therapeutic approaches to various scenarios. It is a concise review, and I found it a current update of what is becoming an increasing problem in the U.S. and abroad. (Reviewer-David E. Greenberg, MD).

Keywords: Gram-Negative Bacteria, Iatrogenic, Ventilator-Associated Pneumonia

Print Tag: Refer to original journal article
Neuropathic pain and HIV-sensory neuropathy remain prevalent, causing substantial disability and reduced quality of life even with successful antiretroviral therapy.

**Background:** Although many neurological complications of HIV infection have declined with the widespread use of combined antiretroviral therapy (ART), peripheral nervous system complications continue to be reported. Little has been reported on the prevalence and clinical effects of HIV-associated sensory neuropathy (SN) and neuropathic pain during the past 10 years.

**Objective:** To report on the prevalence and adverse clinical impact of HIV-associated SN in the era of combination ART.

**Design/Participants:** Prospective observational study evaluating HIV-infected participants in the CNS HIV Anti-Retroviral Therapy Effects Research (CHARTER) study.

**Methods:** A standardized neurological examination was performed by trained physicians and nurses. Evidence of HIV-SN included the presence of ≥1 sign bilaterally. Neuropathic pain was classified as none, slight (occasional, fleeting), mild (frequent), moderate (frequent, disabling), and severe (constant, daily, disabling, requiring medication). Neurobehavioral and laboratory assessments included HIV viral load and CD4 counts, an instrument to define activities of daily living, Beck depression inventory, and the Medical Outcomes Study HIV Health Survey. A stepwise logistic regression was used.

**Results:** This cross-sectional analysis included >1500 HIV-infected individuals enrolled between 2003 and 2007. HIV-associated SN was detected in 57.2% of participants. These patients were older, had more frequent use of ART, and more frequent exposure to drugs like stavudine, didanosine, and zalcitabine. In total, 26.0% were hepatitis C virus-positive and 55.0% had a history of alcohol dependence or abuse; 14.6% were diagnosed with major depressive disorder and 19.0% reported dependence in instrumental activities of daily living. HIV-SN was more likely in those participants who started ART after CD4 counts had dropped to <350/μL than in those who started before CD4 counts fell below 350/μL.

**Conclusions:** In this cohort study, HIV-SN prevalence was not lower than seen in earlier reports. Neuropathic pain was associated with increased unemployment and disability. Peripheral nerve recovery is incomplete during ART.

**Reviewer’s Comments:** The authors discuss the fact that their study was not a random sample and there could have been selection bias. Nevertheless, the prospective nature, including multiple centers with well-trained study personnel, gives them reassurance that their results have validity. Although we do not understand the pathogenesis of this complication, newer treatment strategies need to be evaluated for this painful neuropathy. ART is not enough for recovery of this common complication. (Reviewer-Stephen B. Greenberg, MD).

Keywords: HIV, Neuropathy, Antiretroviral Therapy

Print Tag: Refer to original journal article
Local reactions to the herpes zoster vaccine occurred in approximately 1% of vaccine recipients.

**Background:** The results of a large randomized placebo-controlled trial of herpes zoster vaccine demonstrated significant protection in preventing herpes zoster and post-herpetic neuralgia in immunocompetent adults aged >60 years. This live-attenuated herpes zoster vaccine was approved for use, but the safety profile of this vaccine was not widely reported.

**Objective:** To describe the safety profile and local adverse effects of the live-attenuated herpes zoster vaccine in the original study group.

**Methods:** Of >38,000 adults aged ≥60 years, 6616 were enrolled in a substudy of adverse events of inoculation-site events and hospitalizations. All participants were asked to report serious adverse events and rashes during the first 6 weeks after inoculation. All deaths were reported for all participants.

**Results:** Among the approximately 21,000 participants aged 60 to 69 years, 2.1% of vaccine recipients died compared with 2.4% of placebo recipients. Among approximately 18,000 participants aged 70 years, 6.5% of vaccine recipients died compared with 6.2% of placebo recipients. These were not significantly different. In the 6616 participants who were enrolled in the sub-study, approximately 3500 were aged 60 to 69 years and approximately 3100 were aged 70 years. No significant differences were found in mortality rates in the 2 groups that received vaccine or placebo. Reported erythema, swelling, and pain/tenderness at the inoculation site were significantly more frequent in the vaccine recipients than in placebo recipients. Pruritus occurred more frequently in vaccine recipients than placebo recipients. The rate of serious adverse events was 1.6% during the first 6 weeks after inoculation.

**Conclusions:** Both short- and long-term follow-up showed similar rates of hospitalizations and death between vaccine and placebo recipients. Low rates of acute local reactions were observed in a closely monitored subgroup.

**Reviewer's Comments:** The local reactions observed in the herpes zoster vaccine recipients were transient and rarely severe. Since the participants in this study were ambulatory and non-institutionalized, this safety profile cannot be extrapolated to severely debilitated older adults or to individuals who may be immunosuppressed. Nevertheless, this post-study analysis provides additional assurance of safety for this newly recommended vaccine. Other studies have recently described the other potential barriers to the use of this live-attenuated herpes zoster vaccine (Hurley, et al: *Ann Intern Med* 2010; 152:555-560). (Reviewer-Stephen B. Greenberg, MD).

Keywords: Herpes Zoster, Immunization, Adverse Reactions

Print Tag: Refer to original journal article
Efforts to facilitate the financing of the herpes zoster vaccine could help increase its use.

**Background:** Based on recent national data, the approved herpes zoster vaccine has had low use. A survey performed prior to licensure found that physicians were more likely to recommend the herpes zoster vaccine if they thought herpes zoster and post herpetic neuralgia caused a significant clinical burden.

**Objective:** To assess vaccine practice, knowledge regarding reimbursement, and barriers to use among internists and family medicine physicians.

**Methods:** A mail- and internet-based survey was conducted nationally from July to September 2008. General, internists, and family medicine physicians were surveyed using a national network of primary care physicians. Likert-type responses were developed for questions regarding strength of recommendations and barriers to vaccine use. Respondents and non-respondents to the survey were compared based on all available characteristics. Since most responses to individual survey items were similar between internists and family medicine physicians, the results were combined.

**Results:** There was a 72% response rate to the survey. No significant differences were found by sex or age for respondents versus non-respondents. Overall, 39% of internists and 13% of family medicine physicians thought that over half their patients were eligible for this vaccine, and 93% of respondents offered ways for their patients to receive the vaccine. Less than half the respondents knew that herpes zoster vaccine is paid for through Medicare Part D. Few knew of eDispense Vaccine Manager, a web portal through which physicians are able to electronically submit Medicare part D claims for reimbursement. The complexity of the reimbursement process was seen as a major barrier by 43% of respondents. The 3 major perceived barriers to vaccination were cost concerns, reimbursement problems for the practice, and the up-front costs of purchasing the vaccine. The next most frequently reported barriers were the need to have the patient pick up the vaccine at the pharmacy and the need for freezer storage.

**Conclusions:** Physicians report several barriers to the increased use of the approved live-attenuated herpes zoster vaccine. The barriers are mainly financial and administrative processes.

**Reviewer’s Comments:** The authors discuss the potential limitations to their study. The sentinel physicians surveyed may not represent most of the physicians of the American College of Physicians and the American Academy of Family Physicians. Although there was a high response rate to the survey, non-respondents could have given different responses. External factors not explored in the survey may have also influenced the results. The results may have been different if physicians were observed directly in their practice rather than by self-reports. Nevertheless, I agree with the authors that financial issues have to be addressed if more widespread adoption of this vaccine is going to occur. (Reviewer-Stephen B. Greenberg, MD).

Keywords: Vaccine, Immunization, Herpes Zoster, Medicare

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