



On the cover: "Detail of The Triumph of Death," c. 1350 (fresco) by Master of the Triumph of Death (fl.1360–1380), Museo delle Sinopie, Camposanto, Pisa, Italy. Alinari/The Bridgeman Art Library. Reproduced with permission.

The location of this fresco is the Camposanto (literally "holy field"), or cemetery, which was begun in Pisa in the 12th century and completed in the 15th century. On an oblong cloister in the cemetery, frescoes were painted in the 14th and 15th centuries. After World War II bombing damaged the roof of the cloister, the frescoes were detached and moved to a gallery for conservation. As the title of the fresco would suggest, *The Triumph of Death* emphasizes the evanescence of earthly life, featuring piles of corpses, cripples, beggars—and, in the detail shown, persons afflicted with leprosy. The white-bearded man is a blinded leper, with flesh falling from his arm, and both hands are missing from his outstretched arms, which beseech for death to come. Death, however, is depicted as capricious, intent on killing two lovers pictured in a grove shown elsewhere in the same fresco. (Mary and Michael Grizzard, cover-art editors)

i 15 March News

iii In the Literature

## ARTICLES AND COMMENTARIES

### 797 **Blastomycosis of the Central Nervous System: A Multicenter Review of Diagnosis and Treatment in the Modern Era**

J. Ryan Bariola, Paul Perry, Peter G. Pappas, Laurie Proia, Wesley Shealey, Patty W. Wright, James M. Sizemore, Matthew Robinson, and Robert W. Bradsher, Jr

This review of central nervous system infections with *Blastomyces dermatitidis* provides an update on this relatively rare manifestation and focuses on clinical presentations, diagnostic options, therapeutic strategies, and outcomes in the modern era of fungal therapies.

### 805 **Increasing Incidence of Empyema Complicating Childhood Community-Acquired Pneumonia in the United States**

Carlos G. Grijalva, J. Pekka Nuorti, Yuwei Zhu, and Marie R. Griffin

Decreases in childhood pneumonia hospitalizations following 7-valent pneumococcal conjugate vaccine introduction were sustained through 2007. Although empyema complicated only a small fraction of pneumonia hospitalizations, the incidence of childhood empyema increased substantially. This increase was due to several pathogens and warrants close monitoring.

### 814 **Etiology of Illness in Patients with Severe Sepsis Admitted to the Hospital from the Emergency Department**

Alan C. Heffner, James M. Horton, Michael R. Marchick, and Alan E. Jones

Sepsis is often diagnosed on the basis of presumed infection. Some noninfectious conditions have presentations similar to those of sepsis. This study found that ~50% of subjects with sepsis at hospital admission had negative culture results and that 18% had a noninfectious diagnosis that mimicked sepsis.

### 821 **Resistance to Linezolid Is Mediated by the *cfz* Gene in the First Report of an Outbreak of Linezolid-Resistant *Staphylococcus aureus***

Gracia Morales, Juan J. Picazo, Elvira Baos, Francisco J. Candel, Ana Arribi, Beatriz Peláez, Raquel Andrade, María-Ángeles de la Torre, José Fereres, and Miguel Sánchez-García

The first report of resistance to linezolid in an outbreak of methicillin-resistant *Staphylococcus aureus* was investigated. Molecular analysis revealed the presence of the *cfz* gene, whereas G2576T or other resistance mutations were absent. We conclude that the *cfz* gene is the underlying mechanism of resistance.

### 826 **Sex and Gender Differences in Travel-Associated Disease**

Patricia Schlagenhauf, Lin H. Chen, Mary E. Wilson, David O. Freedman, David Tcheng, Eli Schwartz, Prativa Pandey, Rainer Weber, David Nadal, Christoph Berger, Frank von Sonnenburg, Jay Keystone, and Karin Leder, for the GeoSentinel Surveillance Network

Men and women present with different travel-related disease profiles. Preventive travel medicine and future travel medicine research need to address sex- and gender-specific intervention strategies and differential susceptibility to disease.

### 833 **Safety of 3 Different Reintroduction Regimens of Antituberculosis Drugs after Development of Antituberculosis Treatment-Induced Hepatotoxicity**

Surendra K. Sharma, Rohit Singla, Pawan Sarda, Alladi Mohan, Govind Makharia, Arvind Jayaswal, Vishnubhatla Sreenivas, and Sarman Singh

Little empirical evidence exists comparing different reintroduction regimens of antituberculosis drugs. This study provides evidence supporting the safety of introducing isoniazid, rifampicin, and pyrazinamide simultaneously at full doseage, which is a finding that may enable timely therapy for patients with severe disease and limit ongoing disease transmission.



**840 Editorial Commentary: Challenges in Reintroducing Tuberculosis Medications after Hepatotoxicity**

Jussi Saukkonen

**843 Outbreak of Leptospirosis among Adventure Race Participants in Florida, 2005**

Eric J. Stern, Renee Galloway, Sean V. Shadomy, Kathleen Wannemuehler, David Atrubin, Carina Blackmore, Taylor Wofford, Patricia P. Wilkins, Mary D. Ari, Lazenya Harris, and Thomas A. Clark

An outbreak of leptospirosis occurred during a 2005 endurance-length swamp adventure race that took place in a flooded national park outside Tampa, Florida. Fourteen ill racers had laboratory-confirmed infection. *Leptospira* organisms isolated from one of the racers may represent a novel serovar.

**850 Delayed Clearance of Viral Load and Marked Cytokine Activation in Severe Cases of Pandemic H1N1 2009 Influenza Virus Infection**

Kelvin K. W. To, Ivan F. N. Hung, Iris W. S. Li, Kar-Lung Lee, Chi-Kwan Koo, Wing-Wa Yan, Raymond Liu, Ka-Ying Ho, Kwok-Hong Chu, Chi-Leung Watt, Wei-Kwang Luk, Kang-Yiu Lai, Fu-Loi Chow, Thomas Mok, Tom Buckley, Jasper F. W. Chan, Samson S. Y. Wong, Bojian Zheng, Honglin Chen, Candy C. Y. Lau, Herman Tse, Vincent C. C. Cheng, Kwok-Hung Chan, Kwok-Yung Yuen, and the Pandemic H1N1 Study Group

Viral load and immunodysregulation correlated with clinical severity of pandemic H1N1 2009 influenza virus infections and provided the basis for the treatment strategy for patients with severe disease.

**860 Impact of the Novel Influenza A (H1N1) during the 2009 Autumn-Winter Season in a Large Hospital Setting in Santiago, Chile**

Juan Pablo Torres, Miguel O'Ryan, Beatrice Herve, Ricardo Espinoza, Guillermo Acuña, Jaime Mañalich, and May Chomali

Emergency department visits for 10,048 patients (school-aged and adult individuals) who received a clinical diagnosis of influenza A (H1N1) resulted in a mild impact on the use of hospital beds. Early antiviral treatment may have played an important role in the low number of severe cases.

**869 Editorial Commentary: Containing the Novel Influenza A (H1N1) Virus**

W. Paul Glezen

**PHOTO QUIZ**

**871 A 79-Year-Old Man with Swelling and Crusted Cutaneous Ulceration of Both Hands**

(Answer on pages 933–934)

**INVITED ARTICLES**

**872 HIV/AIDS  
Clinical Implications of Genotypic Resistance to the Newer Antiretroviral Drugs in HIV-1-Infected Patients with Virological Failure**

Josep M. Llibre, Jonathan M. Schapiro, and Bonaventura Clotet

**882 FOOD SAFETY**

**The Global Burden of Nontyphoidal *Salmonella* Gastroenteritis**

Shannon E. Majowicz, Jennie Musto, Elaine Scallan, Frederick J. Angulo, Martyn Kirk, Sarah J. O'Brien, Timothy F. Jones, Aamir Fazil, and Robert M. Hoekstra, for the International Collaboration on Enteric Disease 'Burden of Illness' Studies

**HIV/AIDS**

**890 Protease Inhibitor–Based Antiretroviral Prophylaxis during Pregnancy and the Development of Drug Resistance**

Andrea Gingelmaier, Josef Eberle, Bernd P. Kost, Johannes R. Bogner, Joerg Hofmann, Tobias Weissenbacher, Ralph Kästner, Klaus Friese, and Katharina Weizsäcker

HIV-infected pregnant women received protease inhibitor–based antiretroviral prophylaxis for prevention of mother-to-child transmission of HIV. Genotypic resistance testing was performed before initiation of antiretroviral therapy and 4–8 weeks after delivery. No new clinically relevant resistance mutations were detected.

**895 Editorial Commentary: High Genetic Barrier Antiretroviral Drugs in Human Immunodeficiency Virus–Positive Pregnancy**

Maurizio Zazzi

**898 Efficacy and Safety of 1-Month Postpartum Zidovudine-Didanosine to Prevent HIV-Resistance Mutations after Intrapartum Single-Dose Nevirapine**

Marc Lallemand, Nicole Ngo-Giang-Huong, Gonzague Jourdain, Patrinee Traisaitit, Tim R. Cressey, Intira J. Collins, Tapnarong Jarupanich, Thammanoon Sukhumanant, Jullapong Achalapong, Prapan Sabsanong, Nantasak Chotivanich, Narong Winiyakul, Surabon Ariyadej, Annon Kanjanasing, Janyaporn Ratanakosol, Jittapol Hemvuttiphon, Karun Kengsakul, Wiroj Wannapira, Veerachai Sittipiyasakul, Witaya Pornkitprasarn, Prateung Liamongsabuddhi, Kenneth McIntosh, Russell B. Van Dyke, Lisa M. Frenkel, Suporn Koetsawang, Sophie Le Coeur, and Siripon Kanchana for the PHPT-4 Study Team

One-month postpartum treatment with zidovudine plus didanosine prevented selection of nonnucleoside reverse-transcriptase inhibitor resistance mutations in women receiving antepartum zidovudine and intrapartum nevirapine for prevention of mother-to-child transmission of HIV. No mutation was detected, after delivery, using consensus sequencing, and 1.8% of women had mutations detected using the more sensitive oligonucleotide ligation assay.

**909 Editorial Commentary: Another Milestone in Minimizing Risks to Mothers Exposed to Single-Dose Nevirapine for Prevention of Vertical Transmission of HIV-1 to Infants: What Next?**

Mark F. Cotton, Helena Rabie, and Gert U. van Zyl

**912 Short-Course Raltegravir Intensification Does Not Reduce Persistent Low-Level Viremia in Patients with HIV-1 Suppression during Receipt of Combination Antiretroviral Therapy**

D. McMahon, J. Jones, A. Wiegand, S. J. Gange, M. Kearney, S. Palmer, S. McNulty, J. A. Metcalf, E. Acosta, C. Rehm, J. M. Coffin, J. W. Mellors, and F. Maldarelli

Intensification of suppressive antiretroviral therapy by addition of raltegravir did not decrease persistent viremia in study participants. Low-level viremia is not derived from short-lived infected cells but more likely is derived from long-lived chronically infected cells. Eradication of HIV-1 from infected persons will require new therapeutic approaches.

**920 Does Choice of Combination Antiretroviral Therapy (cART) Alter Changes in Cerebral Function Testing after 48 Weeks in Treatment-Naive, HIV-1-Infected Individuals Commencing cART? A Randomized, Controlled Study**

Alan Winston, Chris Duncombe, Patrick C. K. Li, John M. Gill, Stephen J. Kerr, Rebekah Puls, Kathy Petoumenos, Simon D. Taylor-Robinson, Sean Emery, and David A. Cooper, for the Altair Study Group

In a prospective, randomized study, different changes are described in cerebral function testing parameters, including neurocognitive function, for treatment-naive, HIV-1-infected individuals commencing different combination antiretroviral regimens.

**930 Editorial Commentary: Benefit or Toxicity from Neurologically Targeted Antiretroviral Therapy?**

Bruce J. Brew

**CORRESPONDENCE**

**935 Pre-analytical Errors in Rapid Influenza Testing**  
Kemper Kelly

**935 When Is Rapid Testing for Influenza Useful?**  
Adam L. Hersh, Michael A. Kohn, and Thomas B. Newman

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Kamaljit Singh, Shawn Vasoo, and Jane Stevens

**937 Is Phenolic Glycolipid-I Really a Specific Antigen for Leprosy?**  
Roma Sinha, Ananya Sengupta, Nahid Ali, and Pratap Narayan Gupta

**938 Cover Image and Description for the 1 November 2009 Issue**  
Richard I. Frankel

**939 Reply to Frankel**  
Michael B. Grizzard and Mary F. Grizzard

**939 Rifampin and Posaconazole Coadministration Leads to Decreased Serum Posaconazole Concentrations**

Carina Hohmann, Elizabeth M. Kang, and Timothy Jancel

**BOOK REVIEWS**

**941 The Elusive Malaria Vaccine: Miracle or Mirage?**  
By Irwin W. Sherman  
Reviewed by Robert L. Atmar

**941 Practical Guide to Diagnostic Parasitology, 2nd Edition**  
By Lynne S. Garcia  
Reviewed by Aditya Reddy

**942 A Decade of HAART: The Development and Global Impact of Highly Active Antiretroviral Therapy**  
Edited by José M. Zúñiga, Alan Whiteside, Amin Ghaziani, and John G. Bartlett  
Reviewed by Olivia Keiser and Matthias Egger

**943 Books Received**

**ERRATUM**

**944 Berbari et al (Clin Infect Dis 2010; 50:8–16)**

**ELECTRONIC ARTICLES**

**Fulminant Infectious Mononucleosis and Recurrent Epstein-Barr Virus Reactivation in an Adolescent**

Jamie P. Nourse, Kimberley Jones, Ujjwal Dua, Naomi Runnegar, David Looke, Chris Schmidt, Siok-Keen Tey, Glen Kennedy, and Maher K. Gandhi

We describe a unique case of fulminant infectious mononucleosis and recurrent Epstein-Barr virus reactivation presenting in an adolescent. Detailed assays of Epstein-Barr virus-specific T cell immunity revealed defects in the patient's T cell receptor signaling pathway characterized by a lack of interleukin-2 and CD25 expression, which may have contributed to her clinical course. Allogeneic stem cell transplantation reversed the clinical and laboratory phenotype. [pp e34–e37]

**Intravenous and Inhalational Colistin-Induced Respiratory Failure**

Krista Wahby, Teena Chopra, and Pranatharthi Chandrasekar

The emergence of highly resistant gram-negative pathogens in hospitals around the world has placed emphasis on colistin, a seemingly ancient drug. Respiratory failure from colistin was reported in the years following its release; however, there are no recent reports of colistin-induced respiratory failure. We report a case of intravenous colistin- and, later, inhalational colistin-induced respiratory failure. [pp e38–e40]

The articles listed above are freely available in this issue of *Clinical Infectious Diseases online* (<http://www.journals.uchicago.edu/toc/cid/current>).