

Division of Infectious Diseases



Adolf W. Karchmer, MD,
Chief



Peter F. Weller, MD,
Co-Chief

● *Overview*

The Division of Infectious Diseases, recognized nationally and internationally for excellence in clinical care and teaching and a broad research agenda, is composed of 24 physicians who are clinician-scientists, 2 physicians whose activities are restricted to research, 1 physician based in the Division of AIDS, Harvard Medical School, and 3 physicians with part-time clinical appointments.

● *Clinical Activities*

The Division annually provides consultative services to approximately 1,500 patients hospitalized at BIDMC and to outpatients in the Infectious Disease Clinic. This clinic, with approximately 7,200 visits annually, also provides primary care for approximately 500 human immunodeficiency virus (HIV)-infected patients. Embedded within the Clinic is the multi-disciplinary Anal Screening Clinic, which is focused on prevention and treatment of anal papilloma and cancer in gay males. The Travel Clinic annually provides preventive care to 3,250 patients who plan international travel. Special clinics have been established to provide the recently licensed Zostavax, a live virus vaccine to prevent shingles, to eligible adults. Infectious disease consultative services at the Manchester Veterans Administration Hospital in Manchester, New Hampshire and at the Hebrew Senior Life Center in Brookline, Massachusetts, are provided by Drs. Howard Gold and Erika D'Agata, respectively. Drs. Wendy Stead, Elisa Choi and two infectious disease fellows assist in the staffing of the HIV Evaluation and Consultation Clinic in Healthcare Associates, bringing subspecialty expertise to the 500 HIV-infected patients who receive care in the General Medical Clinic. Drs. Christopher Rowley and Rachel Baden have developed a highly regarded weekly HIV Clinic

at Outer Cape Health Services in Provincetown, MA. Dr. Lori Panther provides Anal Screening Clinic services on site at Outer Cape Health and the Fenway Community Health Center. Dr. Michael Wong continues to provide HIV care at Dimock Community Health Center.

● *Quality Improvement*

In collaboration with the Department of Medicine's Quality Assurance and Improvement Program, Dr. Sigall Bell directs the Division's QA initiative. Dr. Bell, working with Dr. Christine Kerr, a senior infectious disease fellow, and the Information Systems team, developed a comprehensive, continuously updated database with information drawn from the BIDMC electronic medical record. This ongoing system allows analysis of aggregate institutional and provider-specific care for HIV patients and compliance with guidelines for the care of HIV-infected patients as published by the Department of Health and Human Services. The measures monitored include appropriate timing of initiation of antiretroviral therapy, appropriate prophylaxis of opportunistic infections, baseline serologic surveillance and immunizations, monitoring of immune function and HIV suppression, and screening and treatment of co-morbid conditions (diabetes, lipid abnormalities). Notably, rates for prophylaxis for specific opportunistic infections, where indicated, ranged from 91 to 96% and the initiation rate of appropriate antiretroviral therapy was 97%. Areas identified for improvement include cholesterol and glucose surveillance. The system is a powerful tool for assurance of quality in HIV care.

The Travel Clinic and the Zoster Vaccine Clinic's records have been transitioned to the BIDMC online medical record (OMR). This insures that administered immunizations are documented, that immunization information is readily available to primary care physicians, and that neither

vaccine nor drug incompatibilities arise from patient encounters in these clinics. Dr. Howard Gold, in collaboration with Christopher McCoy, Pharm.D. of the Pharmacy Department, directs the hospital-wide antibiotic stewardship program which seeks to insure appropriate usage of antimicrobials throughout the hospital.

● *Educational Programs*

The educational activities of the Division are focused on Harvard Medical School students, medical residents, fellows, and practicing physicians. Drs. George Eliopoulos (Tullis Firm), John Doweiko (Kurland Firm), and Elisa Choi (Robinson Firm) continue in leadership roles in the house staff Firm System. Dr. Clyde Crumpacker directs the Harvard-MIT Health Science and Technology "Mechanisms of Microbial Pathogenesis" course (HST 040) for second year students. Drs. Peter Weller, Sonia Nagy Chimienti and Lori Panther direct a highly rated annual postgraduate course, HIV Update, through the HMS Department of Continuing Education and Dr. Adolf Karchmer co-directs the long-standing Winter Course in Infectious Diseases with faculty from non-Harvard institutions. Electives for medical residents and HMS students built around the clinical consulting services and the Infectious Disease Clinic are offered. A new elective in Travel Medicine has been designed and is now available to medicine residents.

The outstanding Infectious Disease Fellowship, under the leadership of Dr. Sonia Nagy Chimienti and Dr. George Eliopoulos, admits five fellows annually, each of whom typically spends a minimum three years in clinical and research training. The program offers three tracks: (1) clinician-teacher, (2) clinical investigation, and (3) laboratory investigation. The clinical investigation pathway offers participation in the Clinical Effectiveness summer curriculum of the Harvard School of Public Health. Laboratory research training is offered by laboratories in the Division and by the Laboratory of Viral Pathogenesis under the direction of Dr. Norman Letvin. The Division participates in three NIH-funded T32 Harvard-wide infectious diseases training grants. Graduates from

the Fellowship Program have been recruited to excellent faculty and leadership positions at major U.S. and international academic centers.

● *Research Activities*

<i>Research Funding • AY'07</i>	
Federal Direct	1,114,965
Federal Indirect	532,227
Other Direct	549,116
Other Indirect	39,678

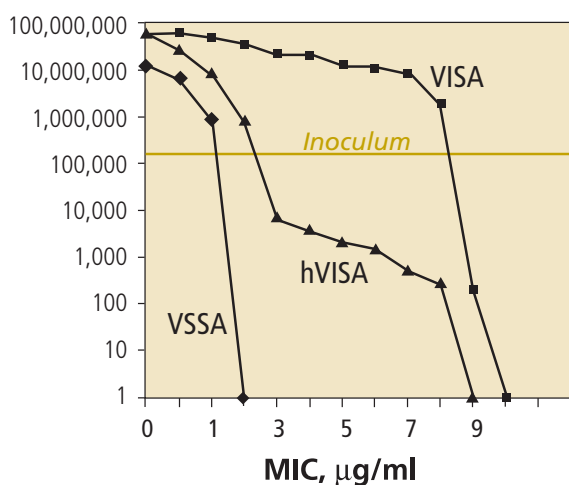
The research programs of the Division cover a broad range of important epidemiologic, clinical, translational, and basic science areas.

External funding for research projects of Division faculty, fellows and post-doctoral research associates (exclusive of that for Drs. Peter Weller and Anne Nicholson-Weller which is listed in the Allergy Division) received during the year totals about \$2,400,000 (direct and indirect) of which \$1,900,000 represents NIH and Centers for Disease Control awards.

Clinical research efforts are focused on HIV/AIDS, the epidemiology of antibiotic resistant bacteria, nosocomial infections, studies of new anti-infective agents, and travel medicine. Dr. Mary Albrecht leads the BIDMC site of the NIH-funded Harvard AIDS Clinical Trials Group (ACTG). She and Dr. Clyde Crumpacker direct industry-funded trials with newly developed antiretroviral agents and HIV vaccine candidates. Dr. Lori Panther studies the role of human papilloma virus (HPV) anal infection and its treatment. Dr. Sigall Kassutto studies immunologic events of primary HIV infection as related to disease expression.

Drs. Adolf Karchmer and Michael Wong conduct studies of epidemiology and treatment of invasive fungal infections as well as treatment trials with experimental antifungal agents and new antibacterial agents. Dr. Wong participates in studies of solid organ transplantation in HIV infected persons. Drs. Erika D'Agata and Sharon Wright pursue studies directed at the epidemiology of nosocomial infection

and the spread of resistant organisms in the hospital environment, in long term care facilities, in hemodialysis units, and in ambulatory HIV infected persons. Dr. Karchmer also directs Centers for Disease Control-funded studies in travel medicine. Dr. Roger Shapiro conducts NIH-funded research efforts in Botswana on the prevention of maternal to infant transmission of HIV and the impact of breast feeding on infants born to HIV positive women.



- Population analysis of a *Staphylococcus aureus* isolate. The horizontal line at 100,000 colony-forming units represents the limit of detection of the standard broth microdilution MIC reference method. The curve on the left side of the figure represents a vancomycin-susceptible organism. The curve on the right represents a vancomycin-intermediate *S. aureus* (VISA) strain. The middle curve is a vancomycin-heteroresistant *S. aureus* (hVISA) isolate that demonstrates the presence of a subpopulation of cells for which the vancomycin MICs are 3–8 µg/mL.

Laboratory research conducted by Division faculty and their associates is focused on antibiotic resistance, herpes viruses, human immunodeficiency virus, hepatitis C virus, and inflammation. Drs. Robert Moellering, George Eliopoulos, Satish Pillai, Howard Gold, and Claudie Thauvin-Eliopoulos in the laboratory of Antibiotic Resistance study mechanism of action and resistance of antimicrobials with particular emphasis on resistance in enterococci and the genetic events in methicillin-resistant *S. aureus* (MRSA) that are responsible for the increasingly recognized ability of MRSA to evade vancomycin therapy. (see Figure)

Dr. Joyce Fingerroth studies viruses that are causally associated with human cancer at the basic and translational levels, including characterization of cell surface receptors for the Epstein-Barr virus (EBV), and the Kaposi sarcoma virus (KSHV, also called human herpes virus 8). Translational studies focus on characterizing targets for antiviral therapy of EBV and KSHV.

Drs. Clyde Crumpacker and Jie Lin Zhang study HIV, focusing on the mechanisms by which viral DNA is integrated into the human genome and the potential for newer therapies to eliminate integrated viral genetic material from human monocytes.

Dr. Margaret Koziel investigates host cellular immune response against hepatitis C virus and the pathogenesis of hepatitis C.

Dr. Nira Pollock, who received a K23 Award from the NIH, is investigating techniques to diagnose *Mycobacterium tuberculosis* infection including the development of a test to detect *M. tuberculosis* antigen in urine.

Dr. Christopher Rowley investigates antiretroviral resistance in HIV isolation in women from Botswana who have received antiretroviral therapy to prevent HIV transmission to their newborn.

Dr. Elisa Choi investigates immune responses to HIV infection and HIV vaccine development in the laboratories of the Division of Viral Pathogenesis.

Dr. Jose Trevejo completed fellowship training and became a member of the Division faculty and Instructor at Harvard Medical School. He will continue his research on the use of volatile bacterial products as targets for the diagnosis of infection, especially tuberculosis.

Dr. Chen (Sabrina) Tan completed fellowship training and became a member of the Division faculty and Instructor at Harvard Medical School. She will continue her studies of viral infections of the central nervous system, focused on JC virus, in the laboratory of Dr. Igor Koralnik in the Division of Viral Pathogenesis.

The laboratories directed by Dr. Peter Weller and Dr. Anne Nicholson-Weller are described under the Allergy Division.

● Awards and Honors

Members of the Division have leadership roles in state, national, and international professional organizations. Dr. Peter Weller co-edited a major new textbook entitled *Tropical Infectious Diseases – Principles, Pathogens, and Practice* (W.B. Saunders). Dr. George Eliopoulos is co-editor of the *Sanford Guide to Antimicrobial Therapy*, Editor-in-Chief of *Antimicrobial Agents and Chemotherapy*, and a member of the Clinical Laboratory Standards Institute, which establishes benchmark test systems and criteria for antimicrobial susceptibility testing in clinical laboratories nationally. Dr. Karchmer is the President of the International Society of Cardiovascular Infectious Diseases, a member of the Harvard Medical School Alumni Council, and an Associate Editor of *Clinical Infectious Diseases*. Dr. Margaret Koziel is Chair of the Hepatitis Research Committee, AIDS Clinical Trials Group (NIH). Dr. Robert Moellering is Editor-in-Chief (consulting editor) of *Infectious Disease Clinics of North America* and a Co-Editor of *The Sanford Guide to Antimicrobial Therapy*. Dr. Michael Wong serves on the Massachusetts Public Health Council. Additionally, Drs. Eliopoulos, Karchmer, Moellering and Weller were selected as “Best Doctors in America.” Dr. Nira Pollock received the Maxwell Finland Award of the Massachusetts Infectious Diseases Society for excellence in research.

● Selected Publications

D’Agata EMC, Horn MA, Webb G. Quantifying the impact of bacterial fitness and repeated antimicrobial exposure on the emergence of multidrug-resistant gram-negative bacilli. *Math Mod Nat Phen* 2007; 2;115-24.

D’Agata E, Mitchell S. Antimicrobial utilization patterns among nursing home residents with advanced dementia. *Arch Int Med* 2008; 168;357-62.

Rowley CF, Boutwell CL, Lockman S, Essex M. Improvement in allele-specific PCR assay with the use of polymorphism-specific primers for the analysis of minor variant drug resistance

in HIV-1 subtype C. *J Virol Methods* 2008; 149:69-75.

Tenover FC, Moellering RC Jr. The rationale for revising the clinical and laboratory standards institute vancomycin minimal inhibitory concentration interpretive criteria for *Staphylococcus aureus*. *Clin Infect Dis* 2007; 44:1208-1215.



● Infectious Disease team

Sakoulas G, Rose W, Rybak MJ, Pillai S, Alder J, Moellering RC Jr, Eliopoulos GM. Evaluation of methicillin-susceptible *Staphylococcus aureus* endocarditis developing nonsusceptibility to daptomycin. *J Clin Microbiol* 2008; 46:220-224.

Pollock N, Campos-Neto A, Kashino S, Napolitano D, Behar S, Shin D, Sloutsky A, Joshi S, Guillet J, Wong M, Nardell E. Discordant quantiferon-gold results among US hospital workers with increased risk of latent tuberculosis infection – A problem or its solution? *Infect Control Hosp Epidemiol* 2008; 29:878-886.

Shapiro RL, Lockman S, Kim S, Smeaton L, Rahkola JT, Thior I, Wester C, Moffat C, Arimi P, Ndase P, Asmelash A, Stevens L, Montano M, Makhema J, Essex M, and Janoff EN.

Infant morbidity, mortality, and breast milk immunologic profiles among breastfeeding HIV-infected and HIV-uninfected women in Botswana. *J Infect Dis* 2007; 196:562-9.

Lockman S, Shapiro RL, Smeaton LM, Wester C, Thior I, Stevens L, Chand F, Makhema J, Moffat C, Asmelash A, Ndase P, Arimi P, van Widenfelt E, Mazhani L, Novitsky V, Lagakos S, Essex M. Response to antiretroviral therapy after a single, peripartum dose of nevirapine. *N Engl J Med* 2007; 356:135-47.

Ishii S, Koziel MJ. Immune responses during acute and chronic infection with hepatitis C virus. *Clin Immunol* 2008; 128:133-47.

Markowitz M, Nguyen BY, Gotuzzo E, Mendo F, Ratanasuwan W, Kovacs C, Prada G, Morales-Ramirez JO, Crumpacker CS, et al. Rapid and durable antiretroviral effect of the HIV-1 integrase inhibitor raltegravir as part of combination therapy in treatment-naive patients with HIV-1 Infection: Results of a 48-week controlled study. *J Acquir Immune Defic Syndr* 2007; 46:125-33.

● Faculty

Mary Albrecht, MD	George Eliopoulos, MD	Anne Nicholson-Weller, MD	Claudie Thauvin-Eliopoulos, MD
Rachel Baden, MD	Joyce Fingerth, MD	Lori Panther, MD, MPH	Jose Trejejo, MD, PhD
Sigall Kassutto Bell, MD	Howard Gold, MD	Satish Pillai, MD	Peter Weller, MD
Barbra Blair, MD	Camilla Graham, MD	Nira Pollock, MD, PhD	Michael Wong, MD
Elisa Choi, MD	Lisa Hirschhorn, MD	Christopher Rowley, MD	Sharon Wright, MD
Clyde Crumpacker, MD	Adolf W. Karchmer, MD	Roger Shapiro, MD	Dori Zaleznik, MD
Erika D'Agata, MD, MPH	Margaret Koziel, MD	Chen Sabrina Tan, MD	Jie Lin Zhang, MD
John Doweiko, MD	Robert C. Moellering, Jr., MD		