



MGH Transplant Infectious Disease and Compromised Host Program

I. Background and Goals.

The Transplantation Infectious Disease and Compromised Host Program developed as a part of the comprehensive and life-long care provided to transplant recipients and other immunocompromised individuals with unique susceptibility to infection. The program in Transplantation Infectious Disease is also an integral part of the MGH Transplant Center and facilitates the evaluation, prevention, and treatment of infectious disease in Liver, Kidney, Pancreas, Heart, Lung and hematopoietic stem cell (HSCT) recipients. Over 200 solid organ transplants were performed at MGH in 2014. This group manages infections in many acute leukemia and lymphoma patients. In addition to providing clinical care on a longitudinal basis for this unique “at risk” population, this service also provides an educational opportunity for Infectious Disease Fellows and other trainees in infectious disease management of immunocompromised individuals. This program has trained many of the leaders in this field internationally – a list of trainees is appended. In general, there is one fellow per year in this track at MGH.

The Compromised Host Program allows the rapid communication of clinical recommendations to the primary care medical and surgical teams on a continuous basis. As participants in the primary care of these patients, we are afforded a unique opportunity to participate in the development of antimicrobial and immunosuppressive protocols on the clinical service. This provides a valuable venue for clinical research. There is an ongoing relationship with basic research scientists studying models of transplantation (in the Infectious Disease Division, Transplant Unit and Center for Transplantation Science), with particular interests in preclinical models of tolerance induction and control of the immune response for clinical applications.

II. Clinical Activities – Fellowship Description

This Fellowship Program is open only to those trainees who have successfully completed an approved first year Infectious Disease Fellowship Program and completed Internal Medicine Training. The **Fellow in Infectious Disease Transplant Medicine** carries progressively greater responsibility for the clinical care of complex immunocompromised hosts as well as for the education of residents and Fellows in earlier years of training and for presentation of the biomedical literature in related fields at weekly journal clubs and clinical rounds. The Fellow will also develop and complete a research study (targeting publication) that will be developed with one or more of the staff of the program.

An optional second year of training is available in clinical or basic research and is designed to allow the Fellow greater independence as a Clinical or Basic investigator. Such opportunities are dependent upon the availability of research funding to support full PGY salary



scale and acceptance by a specific mentor for that experience. In the second year the clinical track includes a Program in Clinical Effectiveness at the Harvard School of Public Health (2 summers) and progressive responsibility for a clinical research project in outcomes research with the Program faculty. In the second year in basic science, the Fellow will assist in the design and performance of a bench research project in the general field of Transplantation Immunology and Infectious Disease with one of the faculty of the Transplant Infectious Disease Program or the faculty of the Transplantation Research Programs at MGH. The fellow will gain independence as a clinician in the weekly outpatient clinic if desired as a component of these programs.

One attending physician and one first year Infectious Disease Fellow and a second year **Fellow in Transplant Infectious Disease** staff the inpatient Transplant ID Service, with physicians from outside institutions participating on the service by special arrangement. Transplantation Infectious Disease participates in the pre-transplant evaluations of ambulatory patients and inpatients. The Fellows and Attending round with the Transplant team each morning. The Transplant ID Fellow will participate in the outpatient care of Transplant recipients (see below). ***The goals of the Fellowship in Transplant Infectious Disease have been endorsed by the Infectious Disease Society of America (written by Drs. Fishman and Robin Avery).*** A formal fellowship program has been in existence since 1997. Fellows are active members of both the Infectious Disease Division of the MGH and of the MGH Transplant Center.

This program is designed for those fellows completing their first, clinical year in Infectious Diseases and desiring an expanded exposure to patient management in the area of Immunocompromised Hosts. **Applicants will have completed an ACGME-certified clinical Infectious Disease fellowship or the equivalent by the time they start Transplant ID training at MGH.** Individualized academic programs are developed for trainees upon acceptance into the program. Each Fellow will complete one clinical year of advanced training under the direct supervision of the faculty. Full-time research in Transplantation and Immunocompromised Host biology is also available with a commitment of at least 1-2 years for training.

By the end of their training, they will understand:

- Multidisciplinary approaches to complex patients with organ failure, malignancy, and immunosuppression.
- The pre- and post-transplantation assessment of critically ill patients and the timeline of infection after transplantation (See, e.g., Fishman JA, NEJM, 2007, 357, 25:59-72.)
- The optimal deployment of diagnostic techniques in clinical management including radiological and molecular diagnostic tools
- Development of individualized prophylactic strategies including immunizations
- Important aspects of basic science relevant to transplantation immunology and infectious disease. They will participate in a clinical/basic science research project and



will contribute to peer-reviewed publications. Additional research training is available for interested fellows.

Inpatient Clinical time: The expectation is 7-8 months total, with the possibility of 3-4 weeks at the BWH/Dana Farber Cancer Institute on the which can be planned in second half of year. Research time is developed over the course of the first few months of the fellowship training.

Outpatient Clinic: Weekly on Wednesday mornings with attending backup for inpatient service when TXID fellow is in clinic

Emergently as needed if not required on inpatient service

ID continuity: HIV clinic 2x month, HIV pts only (for prior MGH ID fellows only)

No clinic when at DFCI, or on other clinical rotations (will have clinic during research periods)

Transplant ID Rounds and Journal club (Tuesday 8:00 am in ID Division Library): Present carefully reviewed papers on immunocompromised host as suggested and reviewed with attending physician. Will include basic and clinical papers preferably from major journals.

Clinical Protocol development: The TXID Program is responsible for developing many of the hospital-wide protocols for immunocompromised hosts including deployment of new antimicrobial agents and microbiological assays, infection control, antimicrobial stewardship – with the appropriate stakeholders.

Antimicrobial stewardship: Partake in antifungal and other stewardship activities as they pertain to Transplant ID (may intersect with protocol development)

Employment Search: Important component of year – to discuss with Dr. Fishman

Research project (Coordination and approval for all by Drs. Jay Fishman and Camille Kotton) – may participate in multiple projects through year. (Develop project by September with mentor)

Meetings and funding: AST Fellows meeting (funded by AST) in the Fall of each year. Others by arrangement.

Vacation: Same time allotment as first year fellows (not taken from research time)

III. Clinical Activities - Transplantation

The Abdominal Transplant team is responsible for renal, liver, pancreas, and bowel transplants as well as ancillary surgical procedures (dialysis access, general surgery) in solid organ transplant recipients. This team generally includes the Transplant Surgery Attending, 2-3 Surgical Residents, a rotating first year Infectious Disease Fellow from the combined Partners Infectious Disease Program, a Nephrology Fellow and Nephrology Attending, an Attending Gastroenterologist and Fellow, and participation of representatives from Nursing, Pharmacy and Social Service. Consultations on patients on the Cardiac (Heart Failure and Transplant),



Pulmonary, Bone Marrow Transplantation and Leukemia and Lymphoma services are also seen in consultation on a routine basis. Visiting fellows who have generally completed Infectious Disease training elsewhere may apply to attend this program as observers.

Weekly activities include:

- Friday morning (8 AM) conference on clinically related topics in solid organ transplantation and Morbidity and Mortality Conference monthly
- Tuesday morning ‘Compromised Host Conference’ (ID Library, 8:00-9:00) to discuss ID issues from active patients and present journal articles weekly
- Wednesday morning Transplant “Chief’s Rounds (8:30 AM, Blake 6) and Transplant Center Grand Rounds (quarterly, 7:30 or 8:00 AM in Bigelow Amphitheater)
- Wednesday Bone Marrow Rounds: 12:00 noon Cox 8
- Special Transplant Immunology (noon Friday) and Immunology (Thursday noon, CNY)
- Special lectures and Visiting Faculty.

Outpatient Experience

A variety of patients are seen in the Transplant Infectious Disease and Immunocompromised Host outpatient clinic:

- Pre-transplant evaluation for all patients undergoing kidney, liver, pancreas, heart, and lung transplantation
- Follow-up after inpatient stays (or emergency room/observation) for active infectious disease issues
- Urgent access for transplant recipients with acute issues appropriate for outpatient evaluation
- Monitoring via OPAT (Outpatient Antibiotic Therapy) is performed on transplant patients per year to ensure safety and enhance therapeutic efficacy
- “Travel after Transplant Clinic” provides focused travel advice and care for solid organ and bone marrow transplant recipients

Infectious disease fellows in the out-patient clinic enhance knowledge of:

- Pre-immunosuppression evaluation
- Acute evaluation of illness in immunocompromised hosts
- Routine follow-up of inpatients with active infectious disease issues
- Vaccines in immunocompromised hosts
- Mitigation of risk of side effects from antibiotic therapy
- Enhancing lifestyle safety after transplant, including travel medicine
- Patient educational tools regarding transplant infectious diseases topics (including vaccines, pets, food safety, arboviral avoidance).

To the degree possible, all Infectious Disease Fellows including the Fellow in Infectious Disease Transplant Medicine participate in the teaching activities of the Infectious Disease



Division during their participation on the Transplant Service. All Transplant I.D. Attending physicians also participate in the Clinical and Teaching activities of the M.G.H. Infectious Disease Division. Activities include Management Conference (Monday A.M.), Intercity Rounds with the ID physicians of other Boston Centers (Wednesday AM), and a didactic seminar series. There are additional clinical conferences and journal clubs that are available for those with special interests in the field.

III. General Strategies in the Care of Transplant Patients

Drug therapy in transplantation revolves around an immunosuppressive regimen that entails multiple drugs with frequent interactions in terms of toxicities as well as immunosuppressive effects. Therapy is individualized for each patient based on clinical data and unique risk factors. The basic principle of antimicrobial therapy in this population is that established infection is poorly tolerated -- requiring that emphasis be placed on prevention whenever possible. The preventative antimicrobial strategies are linked to the immunosuppressive regimens required to control rejection or graft-vs-host- disease (GvHD).

In general, the use of empiric antimicrobials for immunocompromised patients with infectious “syndromes” is routine; the spectrum must be narrowed based on microbiologic data as soon as is possible.

Transplant Infectious Disease Attending Physicians:



Dr. Jay A. Fishman, Director

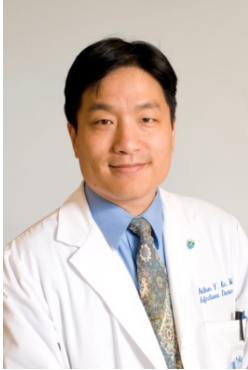
Jay A. Fishman, M.D. is a Professor of Medicine at Harvard Medical School, Director of the Transplant Infectious Diseases and Compromised Host Program at the Massachusetts General Hospital (MGH), and Associate Director of the MGH Transplant Center. Dr. Fishman is an internationally recognized expert in infectious diseases in individuals with abnormal immune systems including organ transplant recipients and has trained many of the leaders in this field. His research laboratory is investigating infections related to the development of swine as organ donors for humans (xenotransplantation) and the molecular biology of viruses in transplantation. He has a special interest in molecular diagnostics and biotechnology, transplant virology, and in medical education.



Camille Nelson Kotton MD, FIDSA, FAST is the clinical director of the Transplant Infectious Disease and Immunocompromised Host Program at the Massachusetts General Hospital. She is the current chair of The Infectious Disease Community of Practice of The American Society of Transplantation. From 2007-2013 she was the president of The Transplant Infectious Disease Section of The Transplantation Society. Highlights of her time as president include the development and subsequent update of international guidelines on CMV management after solid organ transplant, published in *Transplantation* (2010 and 2013). Her clinical interests include cytomegalovirus, donor-derived infections, zoonoses, and travel and tropical medicine in the transplant setting.



Joseph El Khoury, M.D., Ph. D., is an immunologist with an interest in host-pathogen interactions and neuroimmunology. His lab studies the role of innate immune cells such as monocytes, macrophages and dendritic cells in the pathogenesis of fungal infections observed in immunocompromised transplant recipients, such as *Cryptococcus neoformans*, and have identified macrophage receptors for this organism. He is also working on innate host determinants of latency and reactivation of cytomegalovirus infection in solid organ transplant recipients.



Arthur Kim, M.D. is the Director of the Viral Hepatitis Clinic in the Division of Infectious Diseases at Massachusetts General Hospital and Assistant Professor of Medicine at Harvard Medical School. He received his medical degree at Harvard Medical School and trained in internal medicine at MGH and infectious diseases at MGH/Brigham and Women's Hospital. He expresses a longstanding interest in those living with HCV, especially in special populations such as acute infection, prisoners, post-transplantation, and HIV co-infection.



Alyssa Letourneau M.D. 's research interests include clinically based research related to antimicrobial use in immunocompromised hosts and the appropriate use of prophylaxis. In her role as Assistant Director of the Antimicrobial Stewardship Program, she assists in developing antimicrobial use policies and managing the program.





Michael Mansour M.D. PhD focuses on anti-fungal vaccine development and methods for predicting individual patient risk for invasive fungal infection. He has successfully competed for funding including National Institutes of Health (NIH) K08 grants and industry-sponsored support. Clinically, he serves on the consult staff as part of the general and transplant ID consult services.



Mark Poznansky M.B., Ch.B., Ph.D., is Associate Professor of Medicine at Harvard Medical School and Attending Physician in General and Transplant Infectious Diseases and Director of the Vaccine and Immunotherapy Center (VIC) at MGH. Dr. Poznansky is the discoverer of fugetaxis, the principle of immuno-repulsion that forms the basis of the Company's products. His laboratory defines molecular mechanisms for novel immune processes and explores the relevance of these mechanisms to novel approaches to vaccines and immunotherapies for cancer, infectious diseases and diabetes. Dr. Poznansky and his team at VIC have focused on the translation of novel vaccines and immunotherapies from discovery to first-in-human studies and is funded by the JDRF, NIH, DOD, The Trinity Foundation and philanthropy. He is the scientific founder of a number of spinoff biotech companies including Celtaxsys, VICapsys and ACTx. He is also a consultant to Cidara and was formerly a scientific consultant to Novelos and the St. Joseph's Translational Research Institute in Atlanta. Dr. Poznansky also serves on the Commercialization Council and Co-Chairs the Department of Medicine Innovation Taskforce at MGH.



Eric Rosenberg M.D. Is the Director of the Clinical Microbiology Laboratory and serves as the Microbiology Fellowship Program Director. Dr. Rosenberg is an Infectious Disease physician and member of the Infectious Disease Division and Department of Pathology. Dr. Rosenberg's research interests include HIV pathogenesis and diagnosis with a particular interest in acute HIV



infection. He has been a highly involved member of the transplant infectious disease team since 1998.

Current Fellow (2015–2016). C. Arianne Buchan

Past Trainees of MGH Fellowship in Infectious Disease Transplant Medicine

3 mo, 1997	Barbara Alexander / Chief, Transplant Infectious Disease, Professor, Duke University
1997-1998	Ban Hock Tan / Chief, Infectious Disease in Oncology, Singapore
1998-1999	Mun Sam Lam / Consultant, Transplant Infectious Disease, Singapore
2 mo, 1999	Atul Humar / Director of the UHN Multi-Organ Transplant Program and the University of Toronto Transplant Institute
4 mo, 2000	Dino Sgarabotto / Consultant, Transplant and Oncology ID, University of Padua
2 mo, 2001	Ana Maria Contreras / Infectious Disease Research: Hepatitis B, Guadalajara, Mexico
2001-2002	Albert Shaw / Associate Professor, Infectious Disease, Yale University, Basic Immunology Research
2001-2003	Costi Sifri / Associate Professor, Infectious Disease, University of Virginia
2002-2005	Nicholas Mueller / Associate Professor, Transplant Infectious Disease and HIV, University of Zurich
2003-2005	Camille Kotton / Associate Professor HMS, Clinical Director, Transplant Infectious Disease, M.G.H.
2003-2005	Stanley Martin / Transplant Infectious Disease, Assistant Professor, Ohio State University
2004-2005	Michael Ison / Director, Transplant Infectious Disease, Associate Professor, Northwestern University
2005-2006	Karen Doucette / Chair, Infectious Disease Division, Professor, University of Alberta
2007-2008	John Davis / Associate Professor, Transplant Infectious Diseases, Ohio State University
2007-2009	Nicolas Issa / Associate Professor, Transplant Infectious Disease, Univ South Florida, & Moffett Cancer Center
2008-2009	Alejandro Retrepo / Assistant Professor, Infectious Disease, MD Anderson Hospital, Texas
2009-2010	Anoma Nellore / Assistant Professor, University of Alabama Birmingham
2010-2011	Bettina Knoll / Assistant Professor, Brown University, Transplant Infectious Disease..
2011-2012	Paritosh Prasad, Assistant Professor Medicine, University of Rochester
2012-2014	Alissa Wright, Assistant Professor, University of British Columbia, Infectious Disease Pritha Sen, Instructor in Medicine, MGH and HMS Sarah Turbett, Fellow in Clinical Pathology, MGH
2014-2015	Tara Babu, Assistant Professor Medicine, University of Rochester