

Annual Report
Division of Infectious Diseases
Department of Medicine - Jewish General Hospital
April 1, 2011 – December 31, 2011

I HIGHLIGHTS

Infectious Diseases continue to be a major threat to health and economic development throughout the world, including Canada. The annual reappearance of influenza and other viral infections; the resurgence of measles and whooping cough due to unfounded fears of vaccines; the appearance and spread of “super-bugs” in hospitals and the community; the continued onslaught of diarrheal disease, tuberculosis, malaria and other parasitic infections and HIV in the developing world; all of these issues plus many others, are adversaries against which we continue to find solutions. It is not surprising that the Division of Infectious Diseases continues to be one of the busiest clinical services at the JGH, a direct reflection of the ongoing and important role of infectious diseases in our local, national, and international communities. Building on a strong tradition of clinical service, research, and teaching, the Division continues to expand its activities in the following fields:

- Clostridium difficile infection (CDI)
- refugee and immigrant health
- vaccine-preventable diseases
- tuberculosis
- emerging infections and “super-bugs” (e.g. MRSA, VRE, CRO)
- new vaccines (i.e. hepatitis B virus and varicella-zoster virus)
- novel antibiotics and immune system modifiers for the treatment of infectious diseases

Members of the Division continue to perform ground-breaking research in the field of Clostridium difficile infections (CDI). This infection remains responsible for widespread and highly-lethal outbreaks in Quebec, Ontario, the United States, and Western Europe. Studies have been completed and are ongoing in order to investigate better diagnostic tests, improved therapies, the ability of this pathogen to spread among patients, and the genetics of these bacteria. The CDI genetics research by Drs. Oughton and Dascal (in collaboration with Dr. Ken Dewar of the McGill University and Genome Quebec Innovation Centre) may provide the basis for a possible preventive vaccine. Dr. Miller continues to lead the Canadian group which performs annual surveillance for CDI, as part of a joint effort with the Public Health Agency of Canada. At least five CDI clinical studies have been undertaken in 2010 in order to improve our understanding of this infection and to test improved therapies.

Large grants were received from public sources for the continued studies into vaccine-preventable diseases in the Canadian foreign-born population of immigrants and refugees. Dr. Greenaway has continued these projects as part of a high-profile multidisciplinary team at McGill. She has been appointed a primary author of the new Canadian guidelines on the screening, prevention and treatment of diseases in newly-arrived immigrants and refugees.

The division has maintained an extremely active and high-profile clinical research unit, with new studies related to infectious disease vaccines (VZV), over-whelming sepsis (“SIRS”), prevention of tuberculosis, and ultra-rapid diagnostic methods for “super-bugs” such as VRE, MRSA, C. difficile, and CRO. Therapeutic studies of C. difficile-associated disease remain a high priority, as well. The

JGH was one of the principal sites which investigated the novel antibiotic, Fidaxomicin, for the treatment of CDI – a drug now licensed in the USA and under review in Europe and in Canada. The JGH continues its pivotal participation in the current trials of other novel antibiotics, non-toxicogenic C.difficile and anti-toxin monoclonal antibodies as improved therapies for this infection.

The Division is continuing its “Multicultural Communication” project in order to increase the understanding of “Infectious Diseases” and “Infection Prevention & Control” among our ethnically and linguistically diverse patient population. Twenty patient information pamphlets have been translated into 20 diverse languages spoken by our clientele, as a means of encouraging their full participation in their healthcare. A language survey of JGH patients has been conducted and analyzed, which will be the cornerstone for the introduction of a multicultural resource center to improve the quality of care of our patients with language barriers.

Dr. Portnoy continues to serve the Hospital in the capacity of Director of Professional Services and his dedication has been recognized with a special award.

Dr. Miller has been the Chairman of the Infection Prevention and Control Committee (IPC) at the JGH for the past 20 years and is the head of the IPC Unit mandated to protect patients, personnel, and visitors from healthcare-associated infections.

Associate members (Dr. Tim Brewer, Dr. David Portnoy, Dr. Martin Teltscher, and Dr. Karl Weiss) who are busy as full-time clinicians at other Montreal hospitals, contribute their time and expertise to the JGH for the high-quality clinical care which we give to our patients. All Division members serve as teachers and examiners for medical students, and also serve on various Hospital committees. Residents and fellows are supervised all year round on the ID consultation service and in the ID outpatient clinic.

II EVALUATION OF THE PAST ACADEMIC YEAR

1. Teaching activities

Dr. T.F. Brewer

- Department of Epidemiology, Biostatistics and Occupational Health departmental lecture series. “Epidemic Intelligence: The Role for a Non-Governmental Reporting System” Lecturer for 30-40 McGill University Faculty and Graduate Students 20 hours of preparation; 1.0 hour lecture

-Tropical Diseases: A review of clinical and laboratory medicine Lecturer for McGill University Health Centre Continuing Medical Education Course
15 hours of preparation; 1.0 hour lecture

Dr. Andre Dascal

-Unit 7 (Infectious Diseases) teaching - McGill University Faculty of Medicine

Dr. Mark Miller

- Healthcare-associated infections and the legal system. McGill University Faculty of Law. 2 hours lecture.

-Unit 7 (Infectious Diseases) teaching - McGill University Faculty of Medicine

Topic: Medical mycology and antifungal therapies

Topic: Infection Prevention and Control for Medical Students

Dr. Christina Greenaway

-“Back to Basics” course (McGill University Faculty of Medicine): International Health and Tropical Medicine.

-Tropical Diseases: A review of clinical and laboratory medicine (McGill Centre for Tropical Diseases)

2. Research Activities

-Protocol # 06-072 - Miller, Dascal, Portnoy, Greenaway, and De Marchie - “ACCESS: A Controlled Comparison of Eritoran Tetrasodium and Placebo in Patient with Severe Sepsis.” Approved 2006 – completed 2011

-Optimer 08-035 - Miller, Dascal, Portnoy, Greenaway, Zaharatos - A Multinational-Multicenter, Double-Blind, Randomized, Parallel Group Study To Compare The Safety And Efficacy Of 200 Mg Par-101 Taken Q12h With 125 Mg Vancomycin Taken Q6h For Ten Days In Subjects With Clostridium Difficile-Associated Diarrhea Protocol 101.1.C.004. Approved 2008 completed 2010

-Merck Covance Protocol 08-118 - Miller - Prospective Observational Study of Nosocomial Clostridium difficile Toxin Antibody Concentrations, Incidence, and Recurrence. Approved 2008 completed 2011

-Protocol 08-118A - Miller, Manges - Altered intestinal microbial flora and Clostridium difficile colonization, infection and disease. Approved 2009 - completed 2010

-Protocol # 08-131 BioMerieux - Miller - Immunologic markers of Clostridium difficile infection. Approved 2008 completed 2010

-Protocol # 08-131 BioMerieux – Miller - Immunologic markers of Clostridium difficile infection negative and positive patients. Approved 2008 completed 2010

-Protocol# 09-122 - Miller, Dascal, Portnoy, Greenaway , Zaharatos, Oughton - A phase 3, Open Label, Randomized Study of the Antiviral Activity, Safety and Tolerability of Intravenous Peramivir in Adult and Adolescent Hospitalized Subjects with Confirmed or Suspected Influenza Infection (H1N1). Approved 2009 - completed 2010

-Protocol # 10-156 - Miller, Greenaway, Zaharatos and Oughton - Actelion “A multi-center, double-blind, randomized, active reference, parallel group study to evaluate the efficacy, safety

and tolerability of a 10-day twice daily oral administration of 3 doses of ACT-179811 in subjects with Clostridium. Approved 2010 - ongoing

-Protocol #10-001 – Zaharatos, Miller, Lipman - An Observer-Blinded, Randomized Study Comparing the Safety and Immunogenicity of HEPLISAV™ to Licensed Vaccine (Engerix-B®) among Adults (18 to 70 Years of Age) with Chronic Kidney Disease (CKD) DV2-HBV-17. Approved 2010 completed 2011.

-Protocol 10-008 - Zaharatos, Miller - An Observer-Blinded, Randomized, Parallel-Group, Multi-Center Study Comparing the Safety and Immunogenicity of HEPLISAV™ to Licensed Vaccine (Engerix-B®) among Healthy Subjects 40 to 70 Years of Age DV2-HBV-16. Approved 2010 completed 2011

-Protocol #10-050 - Miller, Manges, Leung - “Fecal Transplantation for Treating Clostridium Difficile.” Approved 2010 - ongoing

3. Clinical Activities

The walk-in Infectious Diseases Clinic operates on a daily basis (Monday to Friday) in the mornings (08h30-11h00). The clinic is staffed on rotation by Infectious Diseases specialists (i.e. Dr. Jack Mendelson, Dr. Mark Miller, Dr. David Portnoy, Dr. A. Dascal, and Dr. K. Weiss). The clinic also provides teaching to residents who request this clinic as an elective.

The Division also has a weekly Tuberculosis (TB) Clinic (Thursday afternoons) which handles patients with active tuberculosis as well as a screening for potential TB. The clinic is involved with the Public Health Department for TB contact-tracing in the Montreal area. This clinic is staffed by Dr. C. Greenaway, Dr. Mark Palayew, Dr. Karl Weiss, Dr. Mark Miller, and Dr. Matthew Oughton. There were 18,646 patient visits in both Infectious Diseases Clinic and Tuberculosis and the GFT offices during the past year. Drs. Portnoy, Miller, Greenaway, and Dascal see patients in their clinical offices. There were over 6,000 in-patient consultations requested during the year.

4. Academic Staff

Full-time (GFT) members: Dr. Mark Miller (Chief), Dr. Andre Dascal, Dr. Christina Greenaway, Dr. Jack Mendelson, Dr. Matthew Oughton, Dr. Joseph Portnoy, Dr. G. Zaharatos. Part-time (associate) members: Dr. Timothy Brewer Dr. David Portnoy Dr. Karl Weiss

5) Consulting Activities: None reported

6) Honors, Awards and Prizes: None reported

7) Divisional Publications

Louie TG, Miller MA, Mullane KM, *et al.* Fidaxomicin versus vancomycin for Clostridium difficile infection. New Engl J Med 2011;364:422-31

Wilkinson K, Gravel D, Taylor G *et al* (including **Miller M**) and Canadian Nosocomial Infection Surveillance Program. Infection prevention and control practices related to *Clostridium difficile* infection (CDI) within Canadian acute and long-term care institutions. *Am J Infec Control* 2011;39:177-82

Oughton M, Dascal A, Laporta D, Charest H, Afilalo M, **Miller M**. Evidence of viremia in 2 cases of severe pandemic influenza A H1N1/09. *Diagn Micro Inf Dis* 70(2): 213-7 2011 Jun.

Forgetta V, Oughton MT, Marquis P, et al (including **Miller M**). A fourteen genome comparison of identifies DNA markers for severe disease-associated strains of *Clostridium difficile*. *Journal of Clinical Microbiology*, 49(6): 2230-8 2011 Jun.

Mullane KM, **Miller MA**, Weiss K *et al*. Efficacy of Fidaxomicin versus Vancomycin as therapy for *Clostridium difficile* infection in individuals taking concomitant antibiotics for other concurrent infections. *Clinical Infectious Diseases* 2011; 53(5): 440-447.

Forgetta V, Oughton MT, Marquis P et al (**including Miller MA**). Fourteen-Genome comparison identifies DNA markers for severe-disease-associated strains of *Clostridium difficile*. *J of Clin. Microbiol.* June 2011, p 2230-2238.

Miller Mark A, Blanchette R, Spigaglia P, Barbanti F, Mastrantonio P. Divergent Rifamycin susceptibilities of *Clostridium difficile* strains in Canada and Italy and predictive accuracy of Rifampin Etest for Rifamycin resistance. *J of Clin Microbiology*, Dec 2011, p 4310-4321.

Leung VL, **Miller M**. Detection of scabies: A systemic review of diagnostic methods. *J Assoc Med Microbio & Infect Dis Canada*, Winter 2011, 22(4), p 143-146.

Abstracts

Lefebvre B, Lamothe F, **Miller M**, Fortin C, Martin I, King Ng, L and Bourgault AM. Detection of prolyliminopeptidase-negative *Neisseria gonorrhoeae* strains in Québec. Presented at CACMID, Montreal, Canada, April 7-9, 2011

Sears P, Crook D, Louie T, **Miller M**, Weiss K. High fecal and low plasma levels of Fidaxomicin and metabolite OP-1118 in patients with CDI: combined results of two phase 3 trials. Presented at Digestive Diseases Week Conference, Chicago, IL, 2011 May 7-10.

Lefebvre B, Lamothe F, **Miller M**, Fortin C, Martin I, Ng LK, Bourgault AM. Detection of prolyliminopeptidase-negative *Neisseria gonorrhoeae* strains in Quebec. Presented at AMMI Canada-CACMID annual conference, Montreal, April 2011.

Bauer MP, **Miller M**, Gerding DN, Kuijper EJ, Gorbach SL. Renal failure, fever, and leukocytosis all predict treatment failure in *Clostridium difficile* infection (CDI), but renal failure is the only predictor of recurrent CDI. Presented at 21st ECCMID, May 09, 2011, Milan, Italy.

Golan Y, Louie T, Weiss K, Mullane K, Kean Y, Lentnek A, Gorbach S, **Miller M**. Clostridium difficile recurrence, alcohol consumption, and the effect of fidaxomicin vs vancomycin. Presented at 21st ECCMID, May 09, 2011, Milan, Italy.

Golan Y, Mullane K, Louie T, **Miller M**, Weiss K, et al. Immunosuppression and the risk of death, cure rates and disease recurrence among patients with *Clostridium difficile* infection. Presented at 21st ECCMID, May 09, 2011, Milan, Italy.

Degrandpre G, Kyriazopoulos K, **Miller M**. Comparison of the Roche Amplicor and TaqMan Assays for detection of *M.tuberculosis* (Mtb) directly from clinical specimens and MGIT culture bottles. Presented at ICAAC, Sept. 17-20, 2011, Chicago, IL.

Jean A. Giannakakis A, Brukner I, **Miller M**, Dascal A. Enrichment for PCR for detection of Vancomycin Resistant Enterococci (VRE). Presented at ICAAC, Sept. 17-20, 2011, Chicago, IL.

Leung V, Levesque S, Domingo M, Bourgault A, **Miller M**. First Canadian Hospital outbreak of KPC – producing *Klebsiella pneumoniae*. Presented at ICAAC, Sept. 17-20, 2011, Chicago, IL.

Weiss K, Louie T, **Miller MA**, Mullane K, et al. Effect of proton pump inhibitors (PPI) and H2 reception antagonists (H2RA) on response to therapy with Fidaxomicin or Vancomycin in hospitalized patients with *Clostridium difficile* infection. Presented at Annual ACG meeting, Washington DC, 30 October 2011.

Minion J, Shenai S, Vadwai V, Tipnis T, Greenaway C, Menzies D, Ramsay A, Rodrigues C, Pai M. Fading of auramine-stained mycobacterial smears and implications for external quality assurance. J Clin Microbiol 2011;49:2024-2026 Epub 2011 Mar 23.

Greenaway C, Sandoe A, Vissandjee B, Kitai I, Gruner D, Wobeser W, Pottie K, Ueffing E, Menzies D, Schwartzman K. Tuberculosis: Evidence Review for Newly Arriving Immigrants and Refugees. Can. Med. Assoc. J. 2011 Sep 6; 183(12):E939-E951. (Epub 2010 Jul 15. DOI: 10.1503/cmaj.090302.)

Pottie K, Greenaway C, Feightner J, Welch V, Swinkels H, Rashid M, Narasiah L, Kirmayer L, Ueffing E, MacDonald N, Hassan G, McNally C, Kahn K, Burhmann R, Dunn S, Dominic A, McCarthy AE, Gagnon A, Rousseau C, Tugwell P and the Canadian Collaboration for Immigrant and Refugee Health. Review: Evidence-based clinical guidelines for immigrants and refugees. Can Med Assoc. J. 2011 Sep 6; 183(12):E824-E830. (Epub 2011 Jul 15. DOI: 10.1503/cmaj.090313.)

Greenaway C, Munoz M, Barnett E, Sandoe A, Ueffing E, Pottie K, Kunh S, Keystone J. Measles, Mumps, Rubella, Diphtheria, Pertussis, Tetanus & Polio: Evidence-based clinical guidelines for immigrants and refugees. Can Med Assoc. J. 2011 Sep 6; 183(12):E839-E842. (Epub 2011 Jul 15. DOI: 10.1503/cmaj.090313.)

Greenaway C, Rashid M, Barnett E, Munoz M, Sandoe A, Ueffing E, Pottie K, Swinkels H, Keystone J. Varicella: Evidence-based clinical guidelines for immigrants and refugees. Can Med Assoc. J. 2011 Sep 6; 183(12):E843-E846. (Epub 2011 Jul 15. DOI: 10.1503/cmaj.090313.)

Greenaway C, Narasiah L, Plourde P, Ueffing E, Deschenes M, Wong D, Kuhn S, Heathcote EJ. Hepatitis B: Evidence Review for Newly Arriving Immigrants and Refugees. *Can Med Assoc. J.* 2011 Sep 6; 183(12):E847-E851. (Epub 2011 Jul 15. DOI: 10.1503/cmaj.090313.)

Greenaway C, Wong D, Assayag D, Deschenes M, Hui C, Ueffing E, Pottie K, Sandoe A, Rashid M, Heathcote EJ. Hepatitis C: Evidence-based clinical guidelines for immigrants and refugees. *Can Med Assoc. J.* 2011 Sep 6; 183(12):E861-E864. (Epub 2011 Jul 15. DOI: 10.1503/cmaj.090313.)

Khan K, Heidebrecht C, Sears J, Chan A, Rashid M, Greenaway C, Stauffer W, Narasiah L, Pottie K. Intestinal Parasites: Strongyloides and Schistosoma: Evidence-based clinical guidelines for immigrants and refugees. *Can Med Assoc. J.* 2011 Sep 6; 183(12):E865-E868. (Epub 2011 Jul 15. DOI: 10.1503/cmaj.090313.)

Minion M, Pai M, Ramsay A, Menzies D, Greenaway C. Comparison of LED and conventional fluorescence microscopy for detection of acid fast bacilli in a low-incidence setting *PLoS ONE* 2011; 6(7) e22495. Epub 2011 Jul 21.

Boggild AK, Castelli F, Gautret P, Torresi J, von Sonnenburg F, Barnett ED, Greenaway C, Lim PL, Schwartz E, Wilder-Smith A, and Wilson ME for the GeoSentinel Surveillance Network.. Latitudinal Patterns of Travel Among Returned Travelers with Influenza: Results from the GeoSentinel Surveillance Network, 1997—2007. *Journal of Travel Medicine* (In Press)

Loo VG, Bourgault AM, Poirier L, Lamothe F, Michaud S, Turgeon N, Toye B, Beaudoin A, Frost EH, Gilca R, Brassard P, Dendukuri N, Beliveau C, Oughton M, Brukner I, Dascal A. Host and pathogen factors for *Clostridium difficile* infection and colonization. *New England Journal of Medicine.* 365(18):1693-703, 2011 Nov 3.

Forgetta V, Oughton MT, Marquis P, Brukner I, Blanchette R, Haub K, Magrini V, Mardis ER, Gerding DN, Loo VG, Miller MA, Mulvey MR, Rupnik M, Dascal A, Dewar K. Fourteen-genome comparison identifies DNA markers for severe-disease-associated strains of *Clostridium difficile*. *Journal of Clinical Microbiology.* 49(6):2230-8, 2011 Jun.

Oughton M, Dascal A, Laporta D, Charest H, Afilalo M, Miller M. Evidence of viremia in 2 cases of severe pandemic influenza A H1N1/09. *Diagnostic Microbiology & Infectious Disease.* 70(2):213-7, 2011 Jun.

Wainberg MA, Zaharatos GJ, Brenner BG. Development of antiretroviral drug resistance. *New England Journal of Medicine.* 365(7):637-46, 2011 Aug 18.

III OBJECTIVES AND PRIORITIES

The objectives of the Division of Infectious Diseases remain:

a) high-quality service to the outpatients and inpatients of the Hospital; b) continued research in the fields of new anti-infectives, novel vaccines, and cutting-edge diagnostic techniques; c) ongoing education in the vast field of Infectious Diseases for students, residents, fellows, nurses, other healthcare personnel, and

affiliated fields

The priorities of the Division of Infectious Diseases continue to be the expansion of our clinical and basic science research platforms. Since this Division has been in the forefront of *C. difficile* research for the past 3 years, we have prioritized this as an important continuing endeavor. We hope to expand our group to include new members with expertise in the analysis, typing, and control of *C. difficile*, while we maintain a high profile in our other areas of expertise.

Respectfully submitted,

Mark Miller, MD
Chief, Division of Infectious Diseases