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ISID NEWS

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The 11th International Congress: A Recap

by Tim Brewer MD, MPH • ISID Program Director

Over two thousand participants from more than 90 countries convened in Cancun for the 11th International Congress on Infectious Diseases from March 4–7, 2004. Prof. Dennis Kasper, President of the 11th ICID, set the tone for the Congress in his welcoming remarks as he highlighted both the depth and breadth of the scientific contributions to be discussed during the meeting. Dr. Samuel Ponce de León, Chairman of the Local Organizing Committee and Dr. Dagoberto Garcia Garcia, Health Secretary of the State of Quintana Roo, also added their welcomes. The Society was honored to have Dr. Roberto Tapia Conyer, Undersecretary of Health, Prevention of Disease and Health Promotion for Mexico address the delegates. Following the opening remarks and the presentation of the awards for outstanding abstracts submitted to the ICID, dancers demonstrating a variety of popular Mexican dancing styles entertained delegates with their skillful performance and colorful costumes. The Caribbean Sea, lush palm trees and a moonlit night provided a spectacular setting for the Opening Ceremony reception that followed.

Despite the attraction of the sun, surf and sand, delegates packed the lecture halls to participate in what all agreed was an outstanding, eclectic scientific program. Dr. Paul Farmer of the United States gave the Edward Kass Lecture on community-based therapy for Acquired Immunodeficiency Syndrome (AIDS) and drug resistant tuberculosis in low resource settings. Dr. Farmer challenged delegates to think how public health officials, scientists and health care workers can use arguments about cost-effectiveness of interventions to promote or prevent treatment for the world's poor, and the need for physicians to be at the forefront of advocating for high-quality medical care for everyone regardless of where they live. He discussed efforts by he and his colleagues to build and maintain programs that provide sustainable, exceptional care for AIDS and tuberculosis patients in the poorest of settings in Haiti and Peru.

Prof. Adrian Hill from the United Kingdom gave the second plenary lecture of the Congress. Like Dr. Farmer, Prof. Hill's work addresses some of the most crucial infectious disease pathogens of our times, including tuberculosis, malaria and pneumococcal disease. In understanding the impact of genetic determinants of susceptibility to infectious diseases, Prof. Hill shared with attendees not only his impressive contributions to our understanding of this field, but also some of the challenges that lay ahead for scientists hoping to exploit the potential of the human genome project.

The potential of genetic information to revolutionize the control, diagnosis and treatment of infectious diseases recurred throughout the ICID, both in symposia and in Prof. Rino Rappuoli's plenary presentation on using genetic information to develop new vaccines. Prof. Rappuoli of Italy is one of the world's pioneers in reverse vaccinology, the method by which a pathogen's genome may be used to develop candidate vaccine targets. He described the impressive efforts to develop rapidly candidate targets for a meningococcal B vaccine using this approach. Unlike vaccines for meningococcal types A and C that rely on the capsular polysaccharide as the vaccine target, type B required a new approach because its capsular polysaccharide is a self-antigen. Knowledge of the meningococcal genome made this new approach possible.

Dr. Jaime Sepulveda of Mexico fascinated delegates with the history of pandemic cholera, including the

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The 11th International Congress: A Recap *continued from page 1*

impact this disease continues to have on global public health. Dr. Sepulveda demonstrated how epidemic control efforts could have important benefits for improving public health systems with subsequent improvements in health. The role of the illegal drug trade in spreading cholera in Latin America and a video of patients suffering from cholera brought home the challenges of dealing with global pandemics.

The first retrovirus discovered to cause disease in humans is Human T-Cell Lymphotropic Virus Type I (HTLV-1) in 1980. Prof. Eduardo Gotuzzo of Peru, an internationally recognized expert on HTLV-1, advanced participants' knowledge of the epidemiology and pathophysiology of this infection through his presentation of work done with HTLV-1 patients in Latin America. Leukemias, lymphomas, autoimmune disorders and neurological diseases have been conclusively demonstrated to be caused by this retrovirus. Prof. Gotuzzo and colleagues have convincingly shown that, in Peru, this viral infection contributes to an increased burden of parasitic diseases and morbidity from HIV.

Most practicing physicians probably spend little time thinking about toll-like receptors and their role in host defense. However, their function is essential for host survival. Innate immunity is often considered as a non-specific defense to pathogen invasion, but as Prof. Shizuo Akira of Japan eloquently described in his plenary lecture, toll-like receptors are both specific for the substrates they recognize and for their activation of T-cell immune responses. Prof. Akira's contributions have been essential to understanding how toll-like receptor signaling works. His presentation guided the audience through this complex but fascinating journey of molecular biochemistry.

From over 1000 abstracts received, six hundred and ninety were accepted for poster presentation at the 11th ICID. After much deliberation given the high quality of abstracts received, 5 abstracts were recognized for their outstanding contributions. The Society was delighted to once again present the Chiron Awards for Epidemiology of Infectious Diseases, the Aventis Pasteur Awards, and the ISID New Investigator Award during the Opening Ceremony of the Congress. Sponsored by through the generous support of Chiron Vaccines, two Chiron Awards were given for outstanding abstracts in the epidemiology of infectious diseases from the Latin American region. Dr. Roberto Debbag of Argentina and Dr. Maria Eugenia Jimenez-Corona of Mexico won these prestigious awards. Abstracts in any field of infectious diseases submitted to the ICID are eligible for the coveted Aventis Pasteur Awards, which were made possible through the generous support of Aventis Pasteur. Dr. Awo Osafo-Addo of Ghana and Dr. Alexandre Alcais of France each received an Aventis Pasteur Award for their superb abstracts. Individuals from low resource areas who have not previously had an abstract accepted for presentation at an international meeting are eligible for the ISID New Investigator Award. For the 11th ICID, this important award was given to Dr. Sunil Lal of India.

Thirty-six symposia, 8 satellite symposia and 4 meet-the-expert sessions rounded out the scientific program for the 11th ICID. Topics ran the gamut from polio eradication to studies demonstrating the ability of bacteriophages to eliminate pathogen colonization in mice. Organizational and Societal partners that contributed symposia for the Congress included the European Society of Microbiology and Infectious Diseases (ESCMID), the International Society for Anaerobic Bacteria (ISAB), the Japanese Association for Infectious Diseases, the Pan-American Association of Infectious Diseases (API), UNAIDS, the World Bank Group, and the World Health Organization.

International meetings such as the ICID are not possible without industry support, and the Society appreciated the active involvement of its industry partners in the scientific program, satellite sessions, and the exhibits. Aventis Pasteur, Eli Lilly & Company, GlaxoSmithKline, Merck Sharpe & Dohme, Pfizer Global Pharmaceuticals and Wyeth supported symposia within the scientific program, and enabled the Congress to cover a range of important topics that would not have been possible without this crucial support. Satellite symposia from Baxter BioScience, Bayer HealthCare, Chiron Vaccines, Daiichi Pharmaceuticals, Inc., GlaxoSmithKline, Merck Sharpe & Dohme, Pfizer Global Pharmaceuticals, and Wyeth also provided delegates with opportunities to learn about developments in infectious disease prevention and treatment outside of the official program. Numerous other partners contributed to the success of the meeting, either by partial support for symposia, or involvement in the exhibits.

With a faculty that included speakers from almost 40 different countries and participants from an additional 50 more, the 11th ICID was truly a meeting of the global infectious disease scientific community. From the latest developments in genomic research to challenges in disease control at the global level, the scientific program shared advances, obstacles and variety that make infectious diseases such a fascinating field to work in. Though it will be difficult to match the exciting program presented in Cancun, the Scientific Committee for the 12th International Congress on Infectious Diseases is looking forward to building on the success of the recent Congress for the next meeting to be held in Lisbon, Portugal, from June 15–18, 2006. ❖

Keryn Christiansen, M.D.

A Letter from the President

I feel very fortunate to become the President of the International Society for Infectious Diseases. I was initially attracted to the ISID because I saw that it was fulfilling a need not met by other Societies. It is truly an international society with a broad membership that encompasses all individuals interested in infectious diseases. It is therefore very much inclusive rather than exclusive. The collegiate spirit is welcoming and the biennial meetings a wonderful environment for the exchange of information. The meetings have always been informative with a high standard of speakers and the topics are of major relevance, some of which provide added insight into the difficulties experienced by those countries less endowed with resources. The Society has many other activities. The funds of the Society are used to run programs that enable the transfer of expertise, both clinical and research, to practitioners in low resource countries. Also of international importance is the ProMED-mail program for monitoring emerging infectious diseases. This outstanding program provides a service to nearly 32,000 users around the world at no cost to the subscriber. It is informative at many levels extending from government agencies charged with policy decision right down to the clinicians managing outbreaks locally.

The discipline of infectious diseases is interesting and challenging. It constantly brings challenges of new and emerging diseases such as SARS, avian influenza, Nipah & Hendra viruses, Hantavirus and vCJD to name but a few. Continuing challenges exist for the established diseases, tuberculosis, respiratory infections, diarrhoeal illnesses, HIV infection, dengue, and malaria. In addition antimicrobial resistance is a problem facing all practitioners in every part of the world. The ISID provides a forum and a collegiate network to discuss these challenges and by working with other agencies can assist in formulating control strategies. I look forward to the next two years and hope to help shape the response of the Society to many of these issues.

This is an exciting, progressive Society and I urge all readers to work with us to achieve our objectives. An excellent way of participating is by taking up Society membership. There are wonderful opportunities to become involved in working parties addressing specific areas such as education, emerging diseases and infection control, to have a voice in the planning of the Society's programs by being nominated for the council and to make long lasting friendships and collaborative relationships around the world. Membership will provide access to the Society journal, the *International Journal of Infectious Diseases* and I encourage you to submit your research for publication in this excellent journal. As the strength of any Society is dependent on the level of participation of its members we welcome your input, your enthusiasm and your contribution. In 2006 the International Congress of Infectious Diseases will be in Lisbon, Portugal. This will mark the 20th anniversary of the ISID. I invite you to join me at the meeting and more importantly join me in becoming part of this stimulating Society.

Keryn Christiansen, M.D.
President
International Society for Infectious Diseases

Swiss Society for Infectious Diseases (SSI)/ISID Infectious Diseases Research Fellowship Program Final Report

by Dr. Li Dongmei, MD, MSc
Division des Maladies Infectieuses, Hôpital Cantonal Universitaire de Genève • Switzerland

I have been working under the direction of Dr. Pierre Vaudaux and Prof. Daniel Lew on my doctoral thesis, entitled 'Impact of antimicrobials and resistance determinants on the expression and molecular control of virulence factors in nosocomial strains of *Staphylococcus aureus*' using phenotypic and molecular assays (e.g. adhesion assays, flow cytometry, real-time PCR, northern blotting). Portions of this work have been presented at the 10th International Symposium on Staphylococci and Staphylococcal Infections in Japan (October 2002) and the 13th European Congress of Clinical Microbiology and Infectious Diseases in Glasgow, Scotland (May 2003). Now I am completing the writing of my doctoral thesis and also plan to submit a peer-reviewed manuscript in the next few weeks. I also contributed to other completed or ongoing projects of Dr. Pierre Vaudaux' group evaluating *in vivo* activities of antibiotics (daptomycin, oritavancin, vancomycin) in the therapy of experimental foreign body infection due to *S. aureus*. Other completed projects in which I participated include the modulation of fibronectin adhesins and other virulence factors in a teicoplanin derivative of methicillin-resistant *S. aureus*, and the ciprofloxacin-induced fibronectin binding in *S. aureus* mediated by a RecA-LexA-dependent pathway. Along with these projects, I have read more than 100 papers in international journals on molecular genetics of bacteria and molecular cloning, and have participated in the weekly group meetings and journal club sessions. I also participated in training courses on clinical infectious diseases given by SSD at Bern, which greatly broadened my knowledge of clinical infectious diseases.

My training experience in the laboratory of the University Hospitals of Geneva has been enjoyable and challenging. I will always appreciate this opportunity. I feel confident that what I have learned here will have a very positive impact on my future research and bring benefits to my home country, China.

I am very grateful to the ISID/SSD Review Committee for this unique and invaluable opportunity to study and work in the Division of Infectious Diseases at the University Hospitals of Geneva, where I have been learning from internationally recognized scientists and highly motivated younger researchers as well as benefiting from the sort of well-equipped facilities not currently available in China. ❖

Dr. Li Dongmei, MD, MSc

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Before moving to Geneva, Dr. Li was the Assistant Director of the Clinical Laboratory at the Shantou Central Hospital in Shantou, Guangdong Province, China. Dr. Li received her Medical Degree from the Lanzhou Medical College in Lanzhou, Gansu Province, China. She also has a Masters degree in Medical Microbiology from Dalian Medical College in Dalian, Liaoning Province, China.

The ISID and the Swiss Society for Infectious Diseases (SSI) jointly sponsor the SSI/ISID Infectious Diseases Research Fellowship Program.

The purpose of this Fellowship Program is to support infectious disease physicians and scientists from developing countries through multidisciplinary clinical and laboratory training at select biomedical institutions in Switzerland. The objectives of the Fellowship Program are:

- to train promising young physicians and scientists from developing countries for clinical and research positions in infectious diseases,
- to foster partnerships between Fellows and infectious disease leaders in Switzerland, and
- to increase scientific research capacity in low income/high disease burden countries.

For more information please see http://www.isid.org

ISID Small Grants Program Final Report

by Dr. Pablo C. Baldi • Argentina

Characterization of virulence factors secreted by *Brucella* species: amino acid sequence, triggering stimuli, cellular effects, and recognition by the immune system of the host.

Background and objectives

Brucella is a facultative intracellular bacterium that can survive inside professional and non-professional phagocytes by evading the endocytic pathway. It has been shown that *Brucella* possesses a homologue of the type IV secretion system (TFSS) encoded by the *virB* operon found in *Agrobacterim tumefaciens* that mediates transference of molecules to the external milieu. *Brucella* mutants lacking the *virB* operon cannot evade the endocytic pathway and are killed. Other studies have shown that live *Brucella*, but not killed bacteria, somehow modify the phagosome to prevent its fusion with the lysosome. These and other findings strongly suggest that *Brucella* secretes virulence factors, but these factors have not been identified until now.

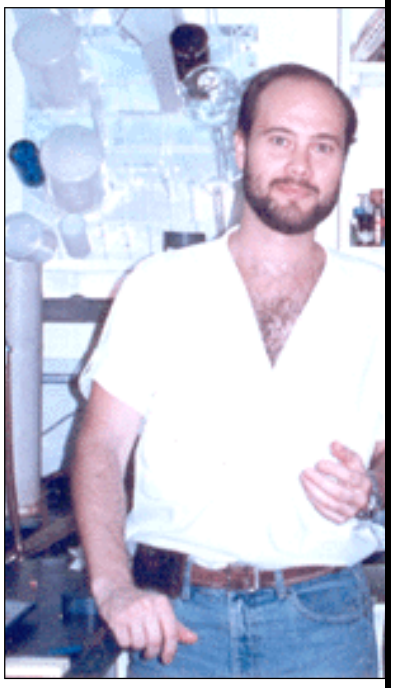
The goals of our ISID-funded project were to identify TFSS-secreted proteins in culture supernatants of *Brucella*. Our approach was to grow wild-type *Brucella abortus* 2308 and isogenic mutants with deletions in the *virB*10 gene. Culture supernatants were concentrated and analyzed by MALDI-TOF.

Our first task was to design a culture medium that could support the growth of *Brucella* with a minimum of other proteins. After several attempts, a medium based on RPMI, yeast extract, and inorganic salts was developed. Supernatants from *Brucella* cultures were concentrated 500X to 1000X and were subjected to 2D electrophoresis (isoelectric focusing in the first dimension, SDS-PAGE in the second dimension). The 2D gels were stained with SYPRO Ruby. Some spots seen with the supernatants of the wild-type strain were absent from the supernatants of the *virB* mutants. We focused our attention on these "differential spots," which were likely to correspond to TFSS-secreted proteins. Differential spots were excised from the gel and subjected to trypsin digestion. Tryptic peptides were analyzed by MALDI-TOF, and peptide mass fingerprints were searched against the ORFs of the *B. suis* 1330 genome.

Sixteen spots from the *B. abortus* wild-type strain were missing from supernatants of *virB*10 polar and non-polar mutants. Protein mass and MALDI-TOF spectrum were sufficient to confirm the identity of five and to assign tentative identification to six other spots. We have just obtained two of these proteins in recombinant form, and we plan to assess their biochemical and immunomodulatory properties.

Other experiments were carried out in our laboratory to study the effect of substances present in *Brucella* supernatants on macrophage functions. The human monocytic cell line THP-1 was incubated for 1 hour with supernatants of *B. abortus* 2308 or with supernatants of a *virB*10 polar mutant (or with unconcentrated culture medium) before being infected with *B. suis* 1330. After 1 hour of infection, cells were washed and treated with gentamicin to eliminate non-phagocytized bacteria. At different times post-infection (p.i.) cells were lysed in order to count colony-forming units (CFU), and supernatants were harvested for measuring of TNF alpha and nitrites. At 16 and 48 hours p.i., there were significantly more CFUs in cells pretreated with supernatants of wild-type *B. abortus* than in those pretreated with control medium or with supernatant of the *virB*10 mutant. At the same time points, levels of TNF-alpha and nitrites were significantly lower in the supernatants of infected cells pretreated with culture supernatants of wild-type *B. abortus* than in cells pretreated with control medium or with supernatants of the *virB*10 mutant. These results suggest that factors produced by the type IV secretion system of *Brucella* (*virB* operon) modulate functions of human macrophages, facilitating the infection of these cells by *Brucella suis* and/or the intramacrophagic survival of the bacterium. We hope to identify such factors among the "differential spots" detected in *Brucella* supernatants. (Results presented in the 50th Meeting of the Argentine Society for Immunology, Mar del Plata, Argentina, November 2002).

I thank the ISID for supporting this project. I especially appreciate this Small Grant, since it was awarded in a moment of serious economic troubles in Argentina. The project would have been impossible without the ISID's support. ❖



Dr. Pablo C. Baldi

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Dr. Pablo C. Baldi received his PhD from the School of Pharmacy and Biochemistry at the University of Buenos Aires in 1996. He is currently an Associate Researcher at the National Research Council (CONICET), and Associate Professor in the Department of Immunology, School of Pharmacy and Biochemistry at the University of Buenos Aires. His research is focused on the evaluation of *Brucella* proteins of potential interest for the improvement of diagnosis and vaccination in human and animal Brucellosis.

ISID Small Grants Program Final Report

by Niyaz Ahmed • India

AmpliBASE - Pathogen Barcodes:® A project aimed at analyzing the complex interaction between infection dynamics and evolutionary biology of *Mycobacterium tuberculosis*.

Human infectious diseases have always challenged public health workers, due to the complexities of tracing the origins of infection and identifying factors that govern the nature and extent of infection in communities. Tuberculosis is one such disease that afflicts millions of people worldwide with a spectrum of epidemiological features, the product of a complex interaction between infection dynamics and genetics of both the bacillus and the host. Mapping the human genome has begun to reveal the molecular events that shape the population biology of today's TB bacillus, in close association with its host and the environment.

Changes in the bacterial gene pool accumulate through gene acquisition and abrogation on a genome-wide and evolutionary time scale. For many human pathogens, such changes can be ascribed to rigorous selection against the host's defenses and adaptation to different ecological niches. Such genomic lesions, in combination with differences in molecular clocks, form a unique tool with which to analyze and reconstruct the complex evolutionary history of pathogens in a given endemic zone. We have coined the term *geographic genomics* to describe the analysis of epidemics based on genetic sequencing as well as the biological, geographic, and climatic history of both the pathogen and its human or animal host.

We have applied the concept of *geographic genomics* to tuberculosis with the aid of markers derived from genomic sequencing of more than 2000 bacterial strains from across the world, representing almost every epidemiologic setting (such as pediatric, geriatric, HIV, zoonotic, aquatic, hyper-endemic, multidrug-resistant, etc.). Our analyses revealed interesting results in terms of origin and spread of different genotypes in India and elsewhere [Ahmed *et al.*, 2003. J. Clin. Microbiol. 41: 1712-1716; Ahmed *et al.*, 2004. J. Clin. Microbiol. (In Press)].

AmpliBASE-Pathogen Barcodes® is the epidemiology program developed under the auspices of the *M. tuberculosis* evolutionary genomics interest group co-ordinated by Dr Seyed Hasnain, Director of the Centre for DNA Fingerprinting and Diagnostics (CDFD) in Hyderabad, India.

With the help of two ISID grants, we have constructed a detailed map of evolutionarily significant alterations in the genome of *M. tuberculosis* isolates recovered from hundreds of patients. Fluorescent amplified fragment length polymorphism techniques (FAFLP) have been employed to construct a model of the global phylogeny of the present-day TB bacillus and its evolutionary status in some TB-endemic countries of the world including India. Based on our observations and the information so far collected, we have implemented a web-based portal called *AmpliBASE*-MT® (http://www.cdfd.org.in/amplibase) [Majeed *et al.*, 2004. Bioinformatics 20: 989-992].

AmpliBASE-MT® is essentially an online databank of high-resolution DNA fingerprints representing FAFLP profiles or *amplitypes* developed for *M. tuberculosis* complex strains from 48 different countries. It is based on an SQL database system hyperlinked to visualize genotypic data in the form of DNA fingerprint images for individual strains. A flexible search system based on systematic comparisons of fragment sizes in base pairs allows inter-laboratory comparison of strains. The database displays previously published data on IS6110 profiles, spoligotypes, MIRU-VNTRs, and large sequence polymorphisms, along with the FAFLP records and overall comparisons. Another database called *miniBASE* MT has been developed for fast strain comparisons based on genomic signatures corresponding to copy numbers at 21 minisatellite-like loci (MIRU-VNTR loci) in the *M. tuberculosis* genome. Genomic signatures based on MIRU-VNTR loci can be obtained via automated analysis of PCR products using Genotyper software (which uses standard conventions for estimation of copy numbers). *miniBASE*-MT has been developed on a MySQL format with a simplified search engine that provides for a faster inter-laboratory exchange of data via the internet. Both databases are extremely user-friendly, freely accessible, and are expected to strengthen the concept of geographic genomics. The *AmpliBASE*® portal has been hosted from our dedicated server (Compaq ProLiant ML 370 G2) and supported in part by the ISID. This portal is expected to enable epidemiologists not only to identify circulating clones, but also to compare and contrast genotypes against existing and emerging genotypes throughout the world on a multi-platform identification system.

I thank ISID for the sponsorship of our research through 2 small grants. This program support was a timely help for a young researcher to attract other funding sources adequate to run an international program like *ampliBASE*-Pathogen Barcodes. ❖

Niyaz Ahmed

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Niyaz Ahmed is a Staff Scientist and currently leads the Pathogen Evolution Program at the Centre for DNA Fingerprinting and Diagnostics (CDFD), Hyderabad, India. He is a member of the National Academy of Sciences of India. His group analyzes pathogen behavior through analysis of genomic and proteomic diversity in gene content, gene order, and gene regulation, especially in relation to evolution of "fittest" genotypes in response to changes in host niches and the environment. He is currently studying the geographical genomics of two important pathogens, *M. tuberculosis* and *Helicobacter pylori*.

http://www.cdfd.org.in/~niyaz

Dr. Nico C. Gey van Pittius

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Nico Gey van Pittius was awarded an ISID Small Grant in 2002 for research into multiple infection by Mycobacterium tuberculosis. He conducted his investigations at the US/MRC Centre for Molecular and Cellular Biology at the University of Stellenbosch in South Africa. He is currently a South African Medical Research Council (MRC) Postdoctoral Fellow, working on the mycobacterial genetics and the molecular epidemiology of tuberculosis under the supervision of Dr. Robin M. Warren, an MRC Chief Specialist Scientist in the Centre.

ISID Small Grants Program Final Report

by Dr. Nico C. Gey van Pittius • South Africa

A molecular and epidemiological investigation into the factors contributing to the prevalence of reinfection and the paucity of dual infections in a community with a high incidence of tuberculosis.

The dogma that a cured single-agent infection is followed by lifelong protective immunity has been refuted over the years by data indicating that a number of tuberculosis patients from high-incidence communities present with postprimary tuberculosis after curative treatment. These episodes of disease are almost invariably passed off as relapse with the same strain that caused the primary infection, with reinfection by a different strain considered rare. Thus, the original infecting strain of *M. tuberculosis* is considered to be responsible for tuberculosis disease at all anatomic sites and during recrudescence of disease after curative treatment. Though this is frequently the case, molecular techniques using RFLP genotyping analyses of the bacterial genomic DNA have shown that the strain causing the second episode is frequently totally distinct from the organism causing the first episode. This points to two possible mechanisms: either endogenous reactivation of a second latent strain that formed part of an initial (dual/multiple) infection, or exogenous reinfection at a later stage by a different organism. Both possibilities have serious implications with regard to current tuberculosis vaccine development, as the mechanisms by which the organism causing the second infection evades the so-called "host-acquired immunity" are largely unknown. The prevalence of endogenous reactivation of dual infection as a cause for postprimary disease—as opposed to exogenous reinfection after curative treatment—has been a matter of debate for a number of years, as reinfection in tuberculosis is not well-understood and is difficult to prove. However, our group published a study indicating that exogenous reinfection is the major cause of postprimary tuberculosis in the high-incidence communities of Ravensmead and Uitsig, South Africa. This was further supported by a mathematical model developed in our Centre demonstrating that in a high-incidence community, the burden of disease from reinfections is likely to be considerable, given the high annual risk of infection. Initially, our data indicated a paucity of sputum isolates that contain more than one clinical strain of *M. tuberculosis*. This was confirmed by RFLP genotyping analyses of samples collected from Ravensmead and Uitsig over a space of more than five years. The resulting genotype database of clinical isolates contains specimens from over 900 patients and represents the molecular epidemiology of disease in this community.

Subsequently, it was shown by others that patients may become infected by more than one strain of *M. tuberculosis*, although it was suggested that the strains are situated in different parts of the patient's lungs. This result contradicted the RFLP data from this high-incidence community, in which only a single strain genotype was detected in the vast majority of cases. Cases in which two different strains were isolated on different occasions were always assumed to reflect laboratory error. Given the likelihood of reinfection, we hypothesized that either the RFLP technique is insufficiently sensitive to identify dual infections or that certain strains of *M. tuberculosis* are specifically adapted for secondary infection.

To investigate the prevalence of dual infection in the study community, the RFLP database containing genotype data on all clinical isolates from patients resident in the high-incidence communities were evaluated for the presence of underlying bands indicating dual infection (i.e. two different strains isolated from one patient). The results, presented at the 14th Conference of the International Union against Tuberculosis and Lung Disease (IUATLD) Africa Region (11-14th June 2002, Durban, South Africa), as well as at the 46th Academic Yearday of the Faculty of Health Sciences of the University of Stellenbosch, revealed that in most of the RFLP fingerprints analyzed, only a single *M. tuberculosis* strain was identifiable. This result supported previous observations but was surprising in a community with such a high incidence of tuberculosis, given the predictions of mathematical models. A total of 14 potential dual infection candidate isolates (representing only 1.4% of the patients) were identified. Of these isolates, only one patient was confirmed to be dually infected because multiple isolates were available, while for seven of the patients only a single isolate was taken (for which we were thus unable to confirm the observed dual infection in the first isolate). As the annual risk of infection in this study community is around 3.5%, it would be expected that an individual is exposed more than once within a period of 30 years. The fact that this study could detect dual infection in only 1.4% of patients suggests that the current methodology, with its reliance on the RFLP technique, underestimates the prevalence of dual infection due to insensitivity. Thus, more sensitive techniques needed to be developed to detect a ratio of dual infection of more than one in five.

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ISID Small Grants Program Final Report *continued from page 7*

by Dr. Nico C. Gey van Pittius • South Africa

This led to the development by our group (headed by Dr. Robin Warren as principal investigator) of a novel PCR method based on strain-specific deletions to specifically identify *M. tuberculosis* strains. This method was first used to identify strains belonging to the Beijing and non-Beijing evolutionary lineages. Application of the method to genotype *M. tuberculosis* in sputum cultures from patients in this high-incidence community showed that 57% of the patients infected with Beijing strain(s) were simultaneously co-infected with non-Beijing strain(s). This suggests that multiple infections play a significant role in active tuberculosis in this community. It also implies the presence of high reinfection rates and confirms the absence of an efficient protective immunity conferred by the initial infection. These findings will have important implications for the understanding of protective immunity and the development and testing of new vaccines and drugs for use in communities where the burden of disease is extremely high. Furthermore, it highlights the importance of preventing transmission to reduce the risk of exposure of "naïve" individuals and the re-exposure of patients to active sources of tuberculosis. This groundbreaking data was presented at the 2003 Keystone Symposium on Tuberculosis (Integrating Host and Pathogen Biology) at Taos, New Mexico, USA, the Poster Day of the Experimental Biology Group (EBG), and the 47th Academic Yearday of the Faculty of Health Sciences of the University of Stellenbosch. It was also published in AJRCC as: Warren, R.M., Victor, T.C., Streicher, E.M., Richardson, M., van Aardt, M., Beyers, N., Gey van Pittius, N.C., and van Helden, P.D., "Patients with active tuberculosis often have different *Mycobacterium tuberculosis* strains in the same sputum sample."

I would like to thank the ISID for the funding I received in 2002 and for supporting pilot research projects by young investigators in developing countries. The ISID gave me the opportunity to gain experience not only in my chosen field of research, but also in the writing of grant proposals, providing me with skills to obtain other grants to further this important study. I would also like to thank Dr. Rob Warren for allowing me to work under his very capable supervision. ❖

For more information on the ISID Small Grants Program please see http://www.isid.org

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The Small Grants Program is designed to fund pilot research projects by young investigators in developing countries. The goal is to support and foster the professional development of young individuals in the field of infectious diseases research by helping them to acquire additional skills and data to apply for other grants. Areas of interest include, but are not limited to investigations of the epidemiology, pathophysiology, diagnosis or treatment of infectious diseases, the epidemiology and control of hospital-acquired infections, and modeling of cost effective interventions.

Calendar of Events

2004

June 27–30. Granada, Spain. *13th International Symposium on Infections in the Immunocompromised Host.* **Contact:** ICHS, 3224 Brooksong Way, Dacula, GA 30019 USA; e-mail, wsnow@ichs.org or cword@ichs.org; web, http://www.ichs.org

July 17–21. Annapolis, MD, USA. *7th Biennial Congress of the Anaerobe Society of the Americas (Anaerobe 2004)* **Contact:** ASA, P.O. Box 452058, Los Angeles, CA 90045-8526 USA; e-mail, asa@anaerobe.org; web, http://www.anaerobe.org

October 24–27. Charleston, SC, USA. *11th International Symposium on Staphylococci & Staphylococcal Infections.* **Contact:** John Nelson; e-mail, jnelson@ue4u.com; web, http://www.isssi.org

November 12–17. Boston, MA, USA. *2004 ACAAI Annual Meeting.* **Contact:** Dianne Kubis, American College of Allergy Asthma and Immunology, 85 W. Algonquin Road, Suite 550, Arlington Heights, IL 60005 USA; e-mail, diannekubis@acaai.org; web, http://www.acaai.org

November 25–28. Limasol, Cyprus. *14th Mediterranean Congress of Chemotherapy and 3rd Pancyprian Congress of Chemotherapy and Infectious Diseases.* **Contact:** George L. Petrikkos (Congress President), Laikon General Hospital, 17 Agiou Thoma St., Athens, Greece; e-mail, petrikos@hol.gr; web, http://www.medsocchem.org

December 1–3. Paris, France. *ECC & RICAI 2004, 6th European Congress of Chemotherapy and Infection, 24eme Réunion Interdisciplinaire de Chimiothérapie Anti-Infectieuse.* **Contact:** JCD Conseil, 4 Villa d'Orléans, 75014 Paris; web, http://www.ricai.org

2006

June 15-18. Lisbon, Portugal. *12th International Congress on Infectious Diseases.* **Contact:** ISID, 181 Longwood Ave., Boston, MA 02115, USA; tel, (617) 277-0551; fax, (617) 731-1541; e-mail, info@isid.org; web, http://www.isid.org/12th_ICID/

Update from ProMED-mail

by Larry Madoff, MD • Editor

The ProMED editorial staff had the exciting opportunity to meet face-to-face in conjunction with the 11th ICID this past March in Cancun, Mexico. With a staff of 20 individuals in 9 countries around the world, the ProMED team carries out its work via the Internet. However, there is no substitute for real dialogue, for the opportunity to put faces and personalities together and to allow for the give and take of lively discussion. Issues discussed at the two-day Editorial meeting ranged from policy topics to technical issues:

- Rumors of outbreaks—when and how to cover
- Endemic diseases –when are they noteworthy
- Information flow
- Management and reporting of corrections and errors
- New programs including our Russian language service being developed for the Newly Independent States of the former Soviet Union and the Mekong Basin region
- Fundraising efforts

We were treated to a preview of a new mapping system being developed in conjunction with the Health Protection Agency in the UK. This project promises a real-time visual representation of ProMED reports and will allow users to query the outbreak maps for temporal and geographical information.

In addition to the team of associate editors, Stuart Handysides, Don Kaye, Marjorie Pollack, and Jack Woodall, we had the opportunity to hear from each of the specialty moderators.

- **Animal Diseases and Zoonoses**
  – Tam Garland, Peter Cowen, and Arnon Shimshony
- **Epidemiology and Mekong Basin Disease Surveillance**
  – Marjorie Pollack
- **Viral Diseases**
  – Craig Pringle
- **Bacterial Diseases**
  – Larry Lutwick
- **Parasitic Diseases**
  – Eskild Petersen
- **Plant Diseases**
  – Dick Hamilton
- **ProMED-Port**
  Portuguese language service
  – Luiz Jacinta da Silva
- **ProMED-Esp**
  Spanish language service
  – Jaime Torres

ISID Executive Director Norm Stein, Program Director Tim Brewer, Program Coordinator Amy Galblum also had the chance to attend the meeting and share insights with the ProMED team.

Unable to attend the meeting were Nilufar Rachmanova, Russian moderator; Martin Hugh Jones, animal disease and zoonoses; Michael Service, medical entomology; Jorge Gonzalez-Mendoza, Spanish moderator; Dan Shapiro, associate editor; and Paul Guttry, copy editor.

In addition to attending the ProMED Editorial meeting, ProMED staff held interactive sessions with attendees at the 11th ICID and several were featured speakers or session chairs at the ICID. The Editorial meeting was sponsored in part by a grant from the Elsevier Foundation. ❖

ProMED-mail has continued to grow and now counts more than 32,000 subscribers in 160 countries.

Just wanted to thank you for the assistance and support that you have provided to us in the PMM postings on BSE in WA State. You have held to the science and dealt with the event factually and accurately. Your assessments and responses have been fair and balanced. Sincerest thanks and compliments.

Veterinarian
US Dept. of Agriculture
January 2004

Save the Date!

12th International Congress on Infectious Diseases

Lisbon, Portugal
June 15~18, 2006

Organized by the International Society for Infectious Diseases