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Workshop
September 20, 2017

Tuberculosis 2017



Global summit on

TUBERCULOSIS AND LUNG DISEASE

September 20-21, 2017 Philadelphia, USA

Joan-Miquel Balada
Ohio State University, USA

Shu-Hua Wang
Ohio State University, USA

The role of the laboratorian and clinician in the diagnosis and management of tuberculosis in the US and developing countries

Early diagnosis and treatment initiation of tuberculosis (TB) is critical for patient survival, and infection control. The session will cover patient management, clinical epidemiology of TB, current laboratory tests used for TB diagnosis, and the barriers of implementing rapid testing in resource-limited areas through clinical research trials experience. Co-infection with HIV and the rise of multi-drug resistant TB (MDR-TB) are two major issues for tuberculosis management. Consequently, rapid diagnostic testing is essential to identify infected individuals to initiate therapeutic regimens. While novel, rapid methods may be available in developed countries, there are barriers for implementation in resource-limited settings. Management strategies between the United States and developing countries, by highlighting experiences in laboratory-focused clinical trials in developing countries, where low cost tests using urine are being assessed, will be also discussed. This session will provide an opportunity to learn more about current and leading-edge technologies available for TB testing both here and abroad, and patient management.

Speaker Biography

Joan-Miquel Balada is the Director of Immunology and Associate Director of the Clinical Microbiology at the Ohio State University Wexner Medical Center and an Associate Professor of Pathology at the Ohio State University. He also directs the Mycobacteriology Laboratory. His major research and clinical interest focus on the implementation of rapid laboratory tests for the diagnosis of infectious diseases and its resistance pattern with special interest of low cost tests for use in areas of limited resources. He is working on antimicrobial resistance and tuberculosis global health initiatives in Central America, Ethiopia and India.

Dr Wang is an Associate Professor of Internal Medicine in the Division of Infectious Diseases at Ohio state University. She is the Medical Director of the Ben Franklin Tuberculosis Control Program, which reports and investigates all tuberculosis cases for Franklin County, Ohio. Currently, she is also the Ohio Department of Health State Medical TB Consultant as well as Medical TB Consultant for the CDC Regional Training and Medical Consultation Center. Dr Wang's clinical interest is in tuberculosis and tropical medicine. Her major research interest has been molecular epidemiology and diagnosis of tuberculosis. She also has overseas experience with TB in China and Guatemala. She is a member of the Infectious Diseases Society of America.

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Mycobacterium fortuitum as a rare etiology of red breast syndrome: A case report and review of literature

Benjamin O Lawson and **Laura Schroeder**
Honor Health Medical Center, USA

Background: Based on the 2015 plastic surgery statistics report, 106,338 females underwent breast reconstructive surgery in the United States. Infection following breast reconstruction with tissue expanders and implants remains a concern, with a reported incidence that ranges from 1 to 6 percent. We present a case of patient who developed red breast syndrome after undergoing breast reconstructive surgery involving a tissue expander placement without an acellular dermal matrix product.

Case Presentation: A 54-year-old otherwise healthy female underwent a left modified radical mastectomy and right prophylactic simple mastectomy for inflammatory breast cancer. Pathology returned as Grade III invasive ductal carcinoma with 1/7 positive lymph nodes in left breast and lobular carcinoma *in situ* in right breast. Five years later, she underwent bilateral breast reconstruction with tissue expanders. Two and a half months later, the patient noticed a small area of redness. She was diagnosed with mastitis and IV vancomycin and ceftriaxone were initiated. The patient returned to the operating room two days later where an exchange of right breast tissue expander with another expander and debridement within the breast pocket with lateral and inferior pole capsulotomies was performed. During that procedure, cultures were taken and subsequently grew *M. fortuitum*. She was discharged home with IV amikacin and cefoxitin through PICC line, and changed to oral ciprofloxacin and clarithromycin based on sensitivities. Her infection cleared shortly thereafter.

Discussion: *M. fortuitum* is classified as nontuberculous *Mycobacterium* that is described as rapidly growing mycobacteria as they usually grow in subculture within one week. *M. fortuitum* is considered the most common rapidly growing *Mycobacterium* (RGM) from non-respiratory specimens (11). If there is high suspicion for nontuberculous mycobacterial infection, then it is recommended empiric therapy to include intravenous amikacin plus intravenous Cefoxitin and total treatment for a minimum of 3-6 months. To our knowledge and after literature search, this is the first report of *M. fortuitum* cultured status post breast reconstructive surgery with tissue expanders, not implants and without acellular dermal matrix.

Speaker Biography

Benjamin O Lawson has attended medical school at the Universidad Autónoma de Guadalajara in Guadalajara, Mexico where he has graduated valedictorian of his class in 2015. He completed undergraduate studies at the University of Arizona with a Bachelor of Science degree in Ecology and Evolutionary Biology with a minor in Business Administration. From 2015-2016, he completed an internship year in General Surgery at Banner University Medical Center in Phoenix, AZ. He is currently, practicing medicine as an Internal Medicine Resident at Honor Health Medical Center in Scottsdale, AZ. His research interests are in quality improvement, rare infections, and Eosinophilic Esophagitis.

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Notes:

Molecular epidemiology in Chile: First confirmed study of cross-contamination of *Mycobacterium tuberculosis* through MIRU-VNTR15 in a regional laboratory

Karla Kohan-Ivani, Álvaro Díaz B, Tamara Leiva C, Jaime Lagos B, Marcos Gallardo M, Jorge Fernández Ó and **Fabiola Arias M**
Instituto de Salud Pública, Chile

Tuberculosis is one of the main causes of mortality of infectious disease in the world. Chile is considered a low incidence country and maintains an active surveillance through the National Tuberculosis Control Program (NTCP). The tuberculosis diagnosis in clinical laboratories requires qualified equipment and personnel in microbiology techniques. The increase of performed samples, in certain periods of time, might exceed the capacity of some laboratories, added to, due to bad microbiological practices, may produce false positive results by cross-contamination cases. This study details the confirmation process of a cross-contamination case detected in a regional laboratory in Chile. A group of 31 strains identified as *Mycobacterium tuberculosis* by line probe assay (LPA), from patients' samples with negative baciloscopy and positive culture, which had a low count of colonies, were studied. Those samples were processed in the same period by the same operator in a regional laboratory. The study included cultures with (+) to (+++) bacilloscopic results, since they could correspond to a contamination source. The suspicious strains were sent to the Chilean Tuberculosis Reference Laboratory and analyzed by MIRU-VNTR15. The MIRU-VNTR15 assay showed 4 different genetic patterns among the 31 strains. Two pairs of patients were related to each other, while the rest of them had not epidemiological connection. MIRU-types results, including the patients' epidemiological backgrounds analysis, allowed the first confirmation case of cross-contamination in the country. A direct supervision to the regional laboratory was needed to train and implement corrective actions to the laboratory staff. In this way, the molecular and epidemiological analysis as well as the direct supervision enabled the definition and implementation of a surveillance strategy to detect an early, suspicious, cross-contamination case in the country, furthermore determine the follow-up actions to the clinic and epidemiological control of the involved patients.

Speaker Biography

Karla Kohan-Ivani has completed her PhD from Universidad de Chile, Chile. She is a part of the professional staff of the Chilean Tuberculosis Reference Laboratory as the Molecular Epidemiology Laboratory's Manager.

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Notes:

Role of imaging in management of tuberculosis

Arun Nachiappan
University of Pennsylvania, USA

Imaging plays an important role in management of Tuberculosis. Primary tuberculosis may manifest as lymphadenopathy, pulmonary consolidation, and pleural effusion. Postprimary tuberculosis may manifest as cavities, consolidations, and centrilobular nodules. Miliary tuberculosis manifests with miliary lung nodules and multiorgan involvement. Imaging findings, particularly the presence of cavitation, can affect treatment decisions, such as the duration of therapy. In patients who are suspected of having latent tuberculosis, chest radiographs are used to stratify for risk and to assess for asymptomatic active disease. Sequelae of previous tuberculosis that is now inactive manifest characteristically as fibronodular opacities in the apical and upper lung zones. Stability of radiographic findings for 6 months distinguishes inactive from active disease. Nontuberculous mycobacterial disease can sometimes mimic the findings of active tuberculosis. Familiarity with the imaging of tuberculosis is important for diagnosis and management.

Speaker Biography

Arun Nachiappan has completed his MD at Rutgers New Jersey Medical School, USA. He is an Associate Professor of Clinical Radiology at the University of Pennsylvania, USA. He specializes in thoracic radiology and has a clinical interest in tuberculosis. He is also the Director of Medical Student Education for the Department of Radiology at the University of Pennsylvania.

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Suppressor cell-targeted immunotherapy with denileukin diftitox improves tuberculosis treatment

Shashank Gupta
Brown University, USA

Current therapies for tuberculosis (TB) are problematic due to emerging drug resistance, toxicity, and the need for prolonged treatment. Host-directed therapies that augment host immune effector mechanisms may serve as important adjunctive therapies for tuberculosis treatment. Regulatory T cells and myeloid derived suppressor cells are important populations of cells that are induced during TB infection and can suppress the effector T cell response. We evaluated a recombinant fusion protein toxin, denileukin difititox (DD), as a host-directed immunotherapy in an acute mouse model of TB infection and analyzed the cellular composition and bacterial burden in lungs and spleens. The *in vivo* studies in Balb/c mice indicate that DD administration results in reduced bacterial proliferation during lung infection and augments the effect of standard TB drugs in the mouse model. This beneficial effect is likely due to its activity in depleting regulatory T cells and other cells that express high levels of CD25 during TB infection. Our results indicate that denileukin diftitox and other suppressor cell–depleting therapies may be useful adjunctive, host-directed therapies for TB.

Speaker Biography

Shashank Gupta is currently working in Brown University, USA and he has previously worked on tuberculosis in Johns Hopkins Medicine.

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Notes:

Mycobacterium tuberculosis toxin; antitoxin genes: Modulators of growth and fibromyalgia

Shaleen B Korch[1], Vandana Malhotra[2], Heidi Contrerasand Chronic[3], Josephine E Clark[3] and **Pain-Curtiss[4]**
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One aspect of Mtb's (*Mycobacterium tuberculosis*) pathogenic success is undoubtedly its ability to adapt to adverse environments encountered during infection of human macrophages. By mechanisms not fully understood, Mtb is able to transition from active growth to dormancy and can persist for extensive periods of time, with the potential of causing reactivation disease. Remarkably, Mtb encodes 90+ TA modules belonging to TA families relBE, vapBC, parDE, higBA and mazEF, suggesting involvement of toxin: antitoxin genes in Mtb pathogenesis. This talk will focus on the role of TA modules as regulators of cell growth and potential effectors of mycobacterial persistence, with an emphasis on the relBE family. We have established that the mycobacterial RelEMtb toxin negatively impacts growth and the structural integrity of the mycobacterial envelope in the absence of its cognate RelBMtb antitoxin, generating cells with aberrant forms that are prone to extensive aggregation. At a time coincident with growth defects, RelEMtb mediates mRNA degradation *in vivo* resulting in significant changes to the proteome. We establish that relMtb modules are stress responsive, as all three operons are transcriptionally activated following mycobacterial exposure to specific adverse environments. Overall, analysis reveals that the relMtb toxin: antitoxin family is stress-responsive and, through the degradation of mRNA, the RelEMtb toxin influences the growth, proteome and morphology of mycobacterial cells.

Speaker Biography

Shaleen B Korch has received her PhD in Microbiology and Immunology from the University of North Dakota (USA) in 2005. After completing her PhD, she did a Post-doctoral fellowship at the Bio design Institute at Arizona State University (USA) which is focused on characterizing the first toxin: antitoxin modules in *Mycobacterium tuberculosis*. Currently, she is an Associate Professor of Pharmacology at Midwestern University, with research interests in *M. tuberculosis* pathogenicity and the role of toxin: antitoxin modules in *M. tuberculosis* persistence. In addition, she evaluates novel, synthetic man-made proteins as potential antimicrobial chemotherapeutics and biological tools.

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Notes:

Pharmacological therapy of asthma during pregnancy

Iram A
National University Hospital Rigshospitalet Glostrup, Denmark

Asthma is one of the most frequent chronic diseases that complicate pregnancy. Well-controlled asthma during pregnancy reduces the risk for an exacerbation during pregnancy. Pharmacological asthma therapy in pregnant women is a challenge due to suboptimal adherence with controller therapy, pregnant women's and professional health care's concerns about harmful effects of medication on the fetus. These aspects make it necessary to evaluate the harmful effects of pharmacological asthma therapy and poor asthma control during pregnancy. The aim for my presentation is to provide an update on safety of asthma medication during pregnancy, based on recent clinical studies and International Guidelines.

Speaker Biography

Iram A has completed her Master's degree from Copenhagen University, Denmark. She is a Resident and Researcher with asthma among pregnant women as field of interest. She has published one article and is going to publish her second article.

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Notes:

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Timing of Pott's disease for proper surgical treatment: Traditional open surgery and minimally invasive, anterior and posterior approach

Stefano Rigotti and **C Zorzi**
Ospedale Sacro Cuore Don Calabria, Italy

The physiopathology of tuberculosis has several phases, initially by infection, with activation of T CD4+ CD8+ specific for tuberculous antibodies, followed by an activation and enhancement of macrophages from INF-gamma, IL-2 and TNF-alpha that originate from a tuberculous granuloma, formed in the core by macrophages and from the infectious tissue that is easily aspirated or drained. Subsequently, the macrophages that form the granuloma wall (Giant Cells of Langerhans) are bound to death and together with the necrotic fluid tissue within the granuloma form an amorphous mass, and begins the caseosophageal phase, which has adherent properties on the adjacent tissues and more difficult to remove surgically, following the activation of fibroblasts around the casein granulomatous mass with collagen production and fibrotic tissue. These phases with their timing (between 2 and 4 weeks) are well-known and identifiable at the pulmonary level, less in bone and vertebral bone. Spongy bone tissue for trabecular anatomy allows a rapid evolution of the Colliquin process. The cortical component of the vertebral body, more rigid and compact, facilitates the blocking phase of Langerhans cell granuloma. When the infection also involves the vertebral walls, the vertebral collapse causes skeletal instability, and aggravation of the pain. At this point there is the evolution of infection from the next phase, caseosa. Magnetic resonance, especially if with contrast medium, is a valid examination that can detect the infected tissue but does not have any valid information about tissue texture and metabolic activity. A useful diagnostic evaluation is TC-PET that can provide us with information about the metabolic activity of the affected tissue, allowing to interpret the physiopathological phase. The timing of tuberculous pathophysiology of vertebral bone tissue should be considered of primary importance, as well as the risk of fracture and nervous involvement in the choice of the surgical solution. Specifically, a combined approach (abscess drainage and possibly bone grafting) and back (stabilization with peduncle screws) in a patient with vertebral collapse and nerve involvement is considered useful within the first weeks of the onset of the disease when the colliquin phase is still present; in these patients that have spent more time and already evolved the caseosa-fibrotic phase infection, a single back approach (peduncle stabilization open or minimally invasive and channel decompression) is preferable.

Speaker Biography

Stefano Rigotti is a Medical Specialist in Orthopedics and Traumatology, Spine Surgery in Dolomiti Sport Clinic.

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Notes:

25 cases with pulmonary tuberculosis sequelae due to surgical procedures; Experience in Japan

Mizu Nonaka, Hitomi Goto, Rie Shigemasa, Yuika Sasatani, Naoki Arai, Kai Yazaki, Hiroaki Ishikawa, Kentaro Hyodo, Kenji Nemoto, Yukiko Miura, Takio Takaku, Shuji Oishi, Kenji Hayashihara and **Takefumi Saito**
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Surgery was one of the main treatment options for tuberculosis before the introduction of effective anti-tuberculosis medicines. Early surgical therapies consisted of a variety of collapse therapies including thoracoplasty, ball plombage, artificial pneumothorax and phrenicotomy and the first report of pulmonary resection was in 1891. Although surgery played a prominent role in tuberculosis management during the early twentieth century, it was largely abandoned with the introduction of modern anti-tuberculosis chemotherapy and chemotherapy has been the main treatment method for tuberculosis until the present day. However, the global emergence of drug-resistant TB including multidrug resistant (MDR) and extensively drug-resistant (XDR) disease has led to the re-examination of surgery as an adjunctive treatment for highly drug-resistant TB and there are few reports of long-term prognosis. We have carried out a retrospective analysis on 25 pulmonary tuberculosis sequelae cases due to surgical procedures. The analysis was based on the medical records of tuberculosis sequelae cases who visited Ibarakihigashi National Hospital from 2012 to 2016. They include 10 thoracoplasty cases, 6 pneumonectomy cases, 6 upper lobe resection cases, 2 artificial pneumothorax cases and 1 phrenicotomy case. Although 16 of 18 cases with spirometry data available had restrictive ventilatory defect after a median time of 60 years from surgical procedures, 25 cases survived for a media time of 56 years from surgery, though 7 cases needed long-term oxygen therapy and 5 cases did non-invasive positive pressure ventilation. Most cases of pulmonary tuberculosis sequelae due to surgical procedures survived for a long time after surgery. This study suggests that surgical procedures may be an important element of successful therapy for non-tuberculous mycobacteria, MDR-TB or XDR-TB with limited therapeutic options.

Speaker Biography

Mizu Nonaka has completed his MD from University of Tsukuba, Japan. He belongs to Department of Respiratory Medicine, Ibarakihigashi National Hospital.

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Strong association of tuberculosis and bronchial anthracofibrosis

Majid Mirsadraee
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Bronchial anthracofibrosis (BAF) is the black discoloration of bronchial mucosa associated obliteration of large and small airways and clinical manifestation resembling COPD but albeit without smoking. Chung et al introduced BAF first in modern era to the world and he believed that tuberculosis (TB) as the main cause of BAF. Later many studies in Korea, Turkey and Iran reported frequency of tuberculosis in BAF. Among the eight studies on anthracofibrosis, six studies showed a significantly higher frequency of TB (32.3%) in comparison to the control groups. The cumulated Odds Ratio of TB in all studies of anthracosis was 3.16 (95% CI = 2.49 – 6.85). Laboratory techniques used in these studies were mainly acid fast bacilli staining, Löwenstein-Jensen, and Middlebrook culture and histopathology. Histopathology usually revealed granuloma formation and macrophage containing anthracotic nodules. Two new studies used molecular technique and PCR for better evaluation of tuberculosis. They reported positive results in 37-40% which are the highest frequency of tuberculosis reported in BAF. PCR and finger print method was also used for evaluating the origin of mycobacterium tuberculosis. Spoligotyping of M. tuberculosis showed four distinct patterns: East-African-Indian (11, 47.8%) and Central-Asian (7, 30.4%), Haarlem I (4, 17.4%) and T-1 (1, 4.3%) which were similar to their community in Iran and middle east. Therefore we can conclude that BAF is susceptible to tuberculosis due malfunctioning to alveolar macrophage occupied by anthracotic nodule and there are not a cause and effect relationship between tuberculosis and BAF.

Speaker Biography

Majid Mirsadraee is Professor in Department of Internal Medicine, Islamic Azad University- Mashhad branch. He has completed his sub-specialty in pulmonary medicine in Mashhad University of Medical Sciences, Iran. His expertise in pulmonary medicine are endobronchial ultrasonography, tuberculosis, fungal and lophomonas infection of lung and severe asthma. His interests in research are anthracosis of lung and triazole therapy for severe asthma. He has over 50 publications that have been cited over 180 times, and his/her publication H-index is 7. He is Editor in Chief in Medical Journal of Islamic Azad University and Member of Editorial Board in *Journal of Cardio-Thoracic Medicine*.

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Notes:

Characterization of a probable GDSL lipase, *Rv1075c of Mycobacterium tuberculosis*

Jashandeep Kaur and **Jagdeep Kaur**
Panjab University, India

Tuberculosis is caused by *Mycobacterium tuberculosis*. Due to the emergence of multiple drug resistance organisms, research in this area is focused to identify new drug targets. In TB database, several genes have been annotated as hypothetical and needs characterization for assigning a role. *Rv1075c* has been annotated GDSL lipase. GDSL esterases/ lipases possess multi-functional properties due to broad substrate specificity, so some of them have thioesterase, protease, arylesterase, and lysophospholipase activity. In this study, we have cloned *Rv1075c* gene in pET28a vector, expressed in E. coli BL21 (DE3) pGro7 strain and protein was purified by Ni-NTA chromatography. Also, the active site mutants were created using site-directed mutagenesis technique. Based on biochemical characterization, it was found to posses' lipase activity toward mid-carbon chain length having pNP-laurate as its optimal substrate. Its optimum temperature and pH were 37˚C and 9˚C, respectively; and stable up to 60˚C and long pH range, pH5 to 11. It was also confirmed to be belonged to SGNH hydrolase subgroup of GDSL category of lipases by the activity analysis of active site mutants. The active site mutant's activity was found to be tampered as compared to wild-type protein.

Speaker Biography

Jashandeep Kaur is a PhD Scholar in the Department of Biotechnology, Panjab University, Chandigarh, India. She has been working on deciphering the role of lipases in the life-cycle of *Mycobacterium tuberculosis* under the supervision of Prof. Jagdeep Kaur. Her expertise is in Molecular Biology, Protein Biochemistry and Animal Tissue Culture.

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Notes:

Functional analysis of *Rv1900c* gene product from *Mycobacterium tuberculosis*

Bandana Kumari and **Jagdeep Kaur**
Panjab University, India

Tuberculosis is still a global threatened disease caused by intracellular pathogen *Mycobacterium tuberculosis (Mtb)*. India accounts for 60% new cases worldwide. The bacterium can outperform the host defense mechanism and can persist inside the body for decades in dormant stage. There are many factors that are known to play role during this stage of bacterium; storage of triacylglycerol (TAG) is one of them. The literature on *Mtb* is replete with strong evidence that TAGs play a critical role in the intracellular/ intraphagosomal survival of this pathogen in the host. *Mtb* genome contains about 4000 genes and 26 (LipA- lipZ) of them are annotated as putative lipases/esterases. *Rv1900c* of *Mtb* Lip family annotated as LipJ; conserved in all *Mycobacterium* species. It contains two domains, N- terminal α/β hydrolase domain and C- terminal cyclase homology domain. In this study we have cloned LipJ full length and N- Terminal lipolytic domain in pET28a vector, expressed in *E. coli* BL21 (DE3) host cells. Recombinant protein was purified using Ni-NTA affinity chromatography. Biochemical characterization of holoenzyme and its N-terminal revealed esterase activity towards pNP- caprate as their optimal substrate. Both the holoenzyme and N-terminal has 40°C as optimal temperature and is stable up to 60 °C, and their pH optima was found to be pH9 and stable from pH6 to 9. Hence, it is confirmed that the esterase activity of holoenzyme was just because of its N- terminal domain. Biophysical characterization confirms that it belongs to α/β hydrolase family.

Speaker Biography

Bandana Kumari is a PhD Scholar in Department of Biotechnology, Chandigarh, India. She has been working on mycobacterial lipases since last two years under the supervision of Prof. Jagdeep Kaur. Her expertise is in Molecular Biology, Protein Chemistry and Animal Tissue Culture.

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Video Presentations

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Nonquaternary diallylammonium polymers with different amine structure and their biocidal effect on *M. tuberculosis and M. smegmatis*

Larisa M. Timofeeva
RC Biotechnology TIPS RAS, Russia

Statement of the Problem: Mycobacteria, especially *M. tuberculosis* is one of the most dangerous types of microorganisms to cause diseases and mortality. While specific resistance of *M. tuberculosis* to drug therapy is thought to be caused by antibiotics action, the general resistance is due to the known distinctive structure of mycobacterial cell wall (CW). Owing to the CW structure, mycobacteria are protected from the penetration of overwhelming number of soluble substances including majority of antibiotics and common chemical disinfectants and biocides. Methodology & Theoretical Orientation: In the presented work, protonated polydiallylamines (PDAAs) based on trifluoroacetic salts of the secondary and tertiary (with Me/Et N-substituents) diallylamines have been synthesized that may be defined as the representatives of a novel family of synthetic water-soluble cationic polyelectrolytes. The in vitro antimicrobial activity of PDAAs against *M. tuberculosis* and *M. smegmatis* including "nonculturable" dormant *M. tuberculosis* cells has been evaluated, as well of quaternary counterpart poly(diallyldimethylammonium chloride) (q-PDADMAC) and current antibiotics rifampicin and ciprofloxacin as control systems to compare activities at the similar conditions. Examination of *M. smegmatis* cells in presence of PDAAs/(rifampicin, isoniazid) under an optical microscope in the epifluorescence modes has been performed. Studies on electrophoretic mobility of *M. smegmatis* cells and some model liposomes have revealed a small negative charge of the cells outer surface and recharge in the presence of cationic PDAAs. Conclusion & Significance: The PDAAs possess high mycobactericidal activity including dormant *M. tuberculosis* cells at a variable time treatment (1.5-72 h) and cells concentration (105-107 CFU mL-1), unlike q-PDADMAC and the antibiotics which are significantly less efficient or inactive at all (at a maximal tested concentration of 500 □g mL-1). To all appearances, PDAAs' impact does not target specific metabolic processes, unlike antibiotics, and is related to disturbance of the integrity of mycobacterial outer bilayer followed by fatal damage of the inner membrane permeability of mycobacterial cells.

Speaker Biography

Larisa Timofeeva is an expert in the field of processes for preparing novel cationic polymers, including mechanism and kinetics of polymerization reactions in solutions and theory of monomers reactivity, as well as novel polyamines with antimicrobial activity. She has years of experience in scientific research work in Topchiev Institute of Petrochemical Synthesis of RAS. Last 15 years, her research activity was aimed at solving the known problem of polymerization of diallylammonium monomers. She has developed an approach which allowed to obtain protonated polyamines of poly(diallylammonium) series with relatively high molecular weight. It has been discovered that polymers of this novel family exert strong biocidal action on multiple clinically relevant pathogens including rare activity against mycobacteria *M. tuberculosis*.

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Notes:

Nutritional status during tuberculosis treatment in patients with or without HIV

Adriana Costa Bacelo
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Objective: assess the ability of unique dietary counseling recommended by the MoH in order to supply the nutritional demands caused by TB. As well as the factors that can affect adherence to dietary counseling. Methods: prospective observational study conducted in adults treated for TB, infected and not infected by HIV. These subjects were assessed through body composition, serum biomarkers and dietary recall, then we offered dietary counselling with subsequent self-reported in 180 days of study. Malnutrition was when at least one of the nutritional assessment results was outside the normal range. Data was analysed using the program R-project version 3.0.2 and considered as a significant difference p≤0.05. Results: 68 patients were included at the average age of 41.1 (± 13.4) years, predominantly presented pulmonary clinical form. All patients had some kind of malnutrition. Those with HIV (22 patients) had greater impairment of total proteins, hemoglobin and hematocrit. Only 25% were malnourished by BMI, 66.1% had anemia, 95.6% had protein malnutrition, 70.6% had energy malnutrition and 82.4% some degree or type of micronutrient disability. 34 completed the study protocol. The average of energy, zinc and protein consumption, during treatment, were close to the RDA recommended minimum, while for the other nutrients average consumption was generally lower than the recommended RDA. Only a small portion ingested at least once in the RDA counseling. Gastrointestinal disorders were the most prevalent reasons for a self-reported not adherence. Conclusion: dietary counseling alone did not reverse malnutrition during TB treatment, in patients with or without HIV.

Speaker Biography

Adriana Costa Bacelo has completed her PhD at the age of 42 years from National Institute of Infectious Diseases Evandro Chagas – Oswaldo Cruz Foundation. She is a Member of Nutrition Service of Oswaldo Cruz Foundation, Member of the Research Center for Micronutrients of Federal University of Rio de Janeiro and Member of Clinical Research Laboratory on Mycobacteria of Oswaldo Cruz Foundation.

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Notes:

Clinical features of Urogenital tuberculosis

Ekaterina Kulchavenya
Russia

Introduction: Urogenital tuberculosis (UGTB) is one of the most common forms of tuberculosis (TB) after pulmonary TB.

Material & Methods: With purpose to estimate clinical features of UGTB we analyzed history cases of 131 patients who were under supervision in Novosibirsk anti-TB dispensary in 2008-2011 years.

Results: Among 131 pts with UGTB 88 (67.2%) had isolated kidney TB (KTB): 10 pts (10.2%) – TB of parenchyma, 35 pts (39.8%) – papillitis, 22 pts (22.4%) - cavernous KTB, 21 pts (21.4%) - polycavernous KTB; in 10 pts alongside with polycavernous KTB male genital TB (MGTB) was diagnosed. In 33 pts (25.2) MGTB only was revealed: in 14 – orchiepidydidimitis, and in 19 – prostate TB. Main clinical features were pain (flank or perineal), dysuria, hematuria, hemospermia, toxicity, but their frequency varied from 0 till 60.0% in different groups. Among all cohort of UGTB asymptomatic course was in 12.2%, among kidney TB - in 15.9%. Every third patient complained of flank pain and dysuria (accordingly 35.2% and 39.8%), 17% presented toxicity symptoms, 9.1% - renal colic, 7.9% - gross-hematuria. MBT was found in 31.8% in isolated kidney TB as whole. Sterile pyuria was in 25%. The onset of TB orchiepidydydmitis was in 35.7%, hemospermia - in 7.1%, dysuria - in 35.7%. Most common complaints for prostate TB were perineal pain (31.6%), dysuria (also 31.6%), hemospermia (26.3%). MBT in prostate secretion / ejaculate was revealed in this group in 10.5%.

Conclusion: UGTB is multivariant disease, and standard unified approach is impossible. Join term "UGTB" has insufficient information in order to estimate therapy, surgery and prognosis – as well as to evaluate the epidemiology. Using clinical classification will improve the efficiency of the therapy of UGTB.

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Notes:

Clog-free pocket-size ultrasonic nebulizer using multiple fourier horns-driven faraday waves

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Drugs designed to treat lung diseases or for systemic absorption through the lung require optimum particle (aerosol) size (2 to 6μm) to target delivery. Current advanced commercial ultrasonic nebulizers for pulmonary drug delivery utilize piezoelectric disk together with an active vibrating mesh or a passive screening mesh to produce medicinal aerosols. These devices produce aerosols with uncontrolled sizes and broad (polydisperse) size distributions. Furthermore, these devices are prone to clogging due to the mesh component of the design and overheating due to the high drive power required which make them unsuitable for administration of expensive medications. In this paper the scientific and technological innovations of the patented Faraday waves-based meshless ultrasonic nebulizers capable of producing optimum aerosol sizes are introduced first. Realization of a fully integrated clog-free pocket-size (14 x 6 x 3 cm^3) nebulizer and applications to aerosolization of a variety of common pulmonary drugs and experimental drugs with desirable aerosol characteristics are then presented.

Speaker Biography

Chen S Tsai is a Chancellor's Professor of the University of California at Irvine (UCI), received his PhD in Electrical Engineering from Stanford University in 1965. He joined Carnegie-Mellon University as Assistant Professor (1969), and was awarded Endowed Chair Professorship (1979). He joined UCI in 1980, and served as the Founding Director of the Institute for Applied Science and Engineering of Academia Sinica in Taiwan (1999-2002). He published 190 journal papers, 450 conference papers, and 14 encyclopedia and book chapters; received the 2013 IEEE UFFC Society Achievement Award with award citation. For pioneering contributions to the science and technology of integrated acousto-optics, ultrasonic monodisperse micro droplet generation, acoustic microscopy, and guided-wave magneto-optics and International Micro-Optics Award. He is Fellow Member of IEEE, OSA, AAAS, SPIE, Russian Popov Society, Academician of Academia Sinica, and a Foreign Member of Russian Academy of Applied Sciences.

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