

Infectious Diseases 2017



3rd Annual Congress on

INFECTIOUS DISEASES

August 21-23, 2017 San Francisco, USA

Keynote Forum

Day 1

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Michael T Brady

Nationwide Children's Hospital, USA

Maternal immunizations: Protects mother, fetus and newborn infant

Many infectious diseases can adversely affect the health of pregnant women; adversely impact the fetus directly during gestation and cause infectious illnesses in newborn infants who are too young to receive benefit from available vaccines. Globally, 10-50% of still births are due to maternal/fetal infections; 600,000-800,000- neonatal deaths are due to infections. Maternal immunizations with vaccines targeting influenza, pertussis and tetanus have already provided improved maternal health during pregnancy, fewer adverse fetal events and reduced illness in young infants. Infections in young infants frequently result in illness and the need for medical care; while some result in morbidity and even mortality. Some of these infections are due to vaccine-preventable conditions which are acquired at an age prior to completion of an effective vaccine series, e.g. influenza, meningococcal group B, pertussis. Other infections are caused by infections for which there is no currently available vaccine, e.g. group B streptococcus and respiratory syncytial virus (RSV). Utilizing vaccines more effectively during pregnancy could result in better health outcomes for the mother, her off-spring or both. Future candidates for maternal immunizations include: Group B streptococcus vaccine, respiratory syncytial virus vaccine, meningococcal group B vaccine, meningococcal conjugate vaccine (MenACWY) and pneumococcal conjugate vaccine. Considerations that will impact successful utilization of a maternal immunization strategy include: Vaccine safety during pregnancy: Mother and fetus, vaccine efficacy for mother, fetus and infant, increasing capacity and acceptance of vaccine administration by obstetric providers and cost.

Biography

Michael T Brady is an Emeritus Professor of Pediatrics at The Ohio State University. He is a Pediatric Infectious Diseases Clinician and Researcher. He is an Associate Editor of the 2015 and 2018 *American Academy of Pediatrics Committee on Infectious Diseases Red Book*. He has made presentations on Maternal Immunizations nationally and internationally.

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Stef Stienstra

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Cooperation in public health to fight infectious diseases in developing countries is good for the global economy

Public health systems are not always prepared for outbreaks of infectious diseases. Although in the past several public health institutes, like the French 'Institut Pasteur' and the Dutch 'Tropeninstituut', were prominent surveyors of infectious diseases, the investments in worldwide public health have decreased. Now more attention is given to curative healthcare compared to preventive healthcare. The recent Ebola Virus Disease outbreak in West Africa initiated a new wave of interest to invest in Worldwide Public Health to prevent outbreaks of highly contagious diseases. Zoonotic diseases are threatening as the population does not have natural nor artificial (from vaccination) immune response to new diseases like in the Ebola Virus Disease outbreak in 2014. The new strain of the Ebola Virus in West Africa was slightly less lethal, compared to other Ebola Virus strains, but the threat of spreading was far bigger as it had a longer incubation time. Most public health systems are not trained well enough to mitigate highly infectious and deadly disease outbreaks. NGO's helping to fight the outbreak are often better trained in curative treatments and have less experience with biological (bioweapon) threats for which the military are trained for. The UNMEER mission was unique in this. It was a setting in which military and civilian actors cooperate in fighting a biological threat. Protection is essential for health workers. Smart systems have to be developed to prevent further spreading of the disease, but it is not only the biosafety, which has to be considered, but also the biosecurity, as misuse of extremely dangerous strains of microorganisms cannot be excluded. Several zoonotic infectious diseases, like anthrax, smallpox and haemorrhagic fevers are listed as potential bioweapons. Therefore both biosafety and biosecurity have to be implemented in all measures to fight outbreaks of highly infectious diseases.

Biography

Stef Stienstra works internationally for several medical and biotech companies as Scientific Advisory Board Member and is also an active Reserve-Officer of the Royal Dutch Navy in his rank as Commander (OF4). For the Dutch Armed Forces, he is CBRNe Specialist with focus on (micro) biological and chemical threats and Medical- And Environmental Functional Specialist within the 1st CMI (Civil Military Interaction) Battalion of the Dutch Armed Forces. For Expertise France, he is now managing an EU CBRN CoE public health project in West Africa. In his civilian position, he is at this moment developing with MT-Derm in Berlin (Germany) a novel interdermal vaccination technology as well as a new therapy for cutaneous leishmaniasis for which he has won a Canadian Grand Challenge grant. With Hemanua in Dublin (Ireland), he has developed an innovative blood separation unit, which is also suitable to produce convalescent plasma for Ebola virus disease therapy. He has finished both his studies in Medicine and in Biochemistry in the Netherlands with a Doctorate and has extensive practical experience in cell biology, immuno-haematology, infectious diseases, biodefense and transfusion medicine.

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Eugénie Bergogne Bérézin

Bichat-Claude Bernard Hospital-Paris University, France

Digestive tract diseases and infections

Human digestive tract (DT) is one of the most vulnerable organs to microbial aggressions. A natural bacterial flora in the DT is a source of maturation of immune systems: *Lactobacilli*, *Bifidobacterium lactis* contribute to children growth. Normal adult intestinal flora includes Enterobacteriaceae, *Escherichia coli*, *Proteus spp.*, and anaerobes, as contributors to digestive tract functions. In adults who suffered of recurrent gastric pain, the discovery of *Helicobacter pylori*, Gram negative micro-aerophilic, helix-shaped organism, has been shown as responsible for gastric ulcer, Malt lymphoma, adeno-carcinoma: living in acidic areas, (upper digestive tract, 50% of elderly), treatment omeprazole+ clarithromycin has proven efficacy. Lower intestinal tract can be invaded by species responsible for diarrhea, contagious, of variable severity: *Shigella*, *Salmonella spp.*, *Vibrio cholerae*: in countries with poor hygiene, cholera epidemics often occur. *Yersinia enterocolitica*, *Y.pseudotuberculosis* carried by pigs and contaminant to humans, determine sporadic acute gastro-enteritis, (contact with animals, contaminated food). Intestinal infections should not be treated with antibiotics systematically, as in some cases they result in aggravation, emergence of *Clostridium difficile*. The presence in intestinal flora of *Escherichia coli* resistant to β -lactams is a threat for treatment failure. *E. coli* resistant to β -lactams and carriage of genes of resistance became international problems. In ICU patients, disorganized flora occurs whatever treatment used: pathogenic MDR are often isolated. To re-establish equilibrium with a "normal" flora, the development of "Fecal Microbiota Transplant" becomes extensively used (in pills or tablets). Another option has been successful using living organisms ("probiotics") such as fungi (*Saccharomyces spp.*, *S.bouardii sp.*) can control ICU diarrhea

Biography

Eugénie Bergogne-Bérézin is Professor of Clinical Microbiology at the University Paris 7. She is Doctor in Medicine (MD and PhD), specialized in Microbiology-Infectious Diseases. She has developed several fields of Research: 1-*Acinetobacter spp* as a nosocomial pathogen (epidemiology, resistance, infections); 2-Pharmacology of antibiotics tissue and body fluid distribution Pharmacodynamics of Antibiotics -3 Intestinal microbial Ecology, jejunal flora, bacterial adhesion to intestinal mucosa, impact of antibiotic therapy on intestinal flora. She has published ~200 International Articles, 6 Medical Books, she contributed to Chapters in recent International Books of Infectious Diseases (Mosby), Pneumology (Respiratory Infection, James Pennington Ed, Raven Press), Antimicrobial Therapy (Victor Yu). She continues to work on *Acinetobacter* at an International level.

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Chris Whiteley

National Taiwan University Science & Technology, Taiwan

Docking of HIV aspartic protease to gold nanoparticles: Molecular dynamics simulations

Statement of the Problem: There is an increasing need for the development of new drug protocols against human immunodeficiency virus (HIV) and HIV protease (HIVPR) is identified as a promising biomedical target in this regard.

Methodology: The interaction of gold nanoparticles (AuNP) with HIVPR is modelled using a molecular dynamics simulation computer programme (Colores) from the Situs suite package.

Findings: The simulation of the 'docking', first as a rigid-body docked complex, and eventually through flexible-fit analysis, creates 36 different complexes from four initial orientations of the nanoparticle strategically positioned around the surface of the enzyme [Fig A]. The rigid-body docked complex is conformationally flexible to accommodate the AuNP that orientates itself within the 'docking' site until a more stable structure is formed at convergence. Normalization of the data, for these AuNP-HIVPR complexes, is obtained from changes to interactive binding energy profiles, RMSD, B-factors, dihedral angles [ϕ , $\Delta\phi$; ψ , $\Delta\psi$; χ , $\Delta\chi$], size, volume occupied by $C\alpha$ [$\Delta V_{C\alpha}$], secondary structural elements (α -helix, β -strands, random coil), number of contact residues, their hydrophobicities and surface electrostatic potentials.

Conclusion & Significance: From a molecular dynamic simulation perspective it is possible to provide insights into the 'best' most probable AuNP-HIVPR complex formed no matter which biophysical technique is monitored.

Biography

Chris Whiteley is an Emeritus Professor of Biochemistry at Rhodes University, Grahamstown, South Africa and distinguished Research Professor at National Taiwan University Science & Technology, Visiting International Professor in Enzymology at School of Bioscience & BioEngineering of South China University Technology, Guangzhou, PRC. He served as Visiting Research Scientist at the Department of Chemical Engineering, National Taiwan University, Taipei, Taiwan in 2004 and as Visiting Professor of Biochemistry at Institute of Biomedical Technology, Veterans General Hospital, Yang Ming University, Taipei, Taiwan. He also worked as Visiting Professor of Enzymology & Organic Synthesis at Oregon State University, Corvallis, Oregon, USA and Visiting Professor of Organic Synthesis at University British Columbia, Vancouver, Canada. He is the Executive Member of Royal Chemical Society (London), MRSC (C. Chem), South African Chemical Institute (SACI). He has published 6 chapters in books and has 110 peer-reviewed papers on Biomedical Enzymology and Nanomaterials.

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Stef Stienstra

Royal Dutch Armed Forces, Netherlands

Managing bio-threat information under the WHO international health regulations of biosecurity

Sharing security threat information is a challenge for governments and their agencies. Especially in biotechnology and microbiology the agencies do not know how to classify or to disclose collected information on potential bio-threats. There is vague border between man-made and natural biological threats. An example is the several month delay of the publication of research on the transmissibility of H5N1 avian influenza virus in the leading scientific journal Science by researchers of the Erasmus Medical Centre in Rotterdam, The Netherlands. The publication was delayed in 2012 by several months due to the fact that various organizations first wanted to investigate whether the details could be misused by malicious individuals. In the study the researchers show that only a small number of mutations were necessary to change the H5N1 virus so that it can spread through the respiratory system between mammals. This implies that the risk of a H5N1 pandemic cannot be ruled out. On the other hand, this information can be used to develop new therapies and/or vaccines for influenza. It gives also insight into the disease mechanism, which helps in the prevention. The same arguments are valid for therapeutic antibodies, like the antibodies, which are developed to treat anthrax. They have an extreme high affinity for the lethal factors of the bacterium and stop the disease, but the same antibodies could be misused to select the most pathogenic strains. Micro-organisms have from nature itself the capacity to reorganise and change their pathogenicity, which could lead to a pandemic spread of a disease. But if the disease is too infectious and too deadly, like some stains of Ebola Virus are, the lethality will be locally limited. But if the incubation time is longer in a certain strain of an Ebola virus, the risks on epidemics and even a pandemic is much higher. The knowledge of these natural mutation mechanisms could be misused to weaponize micro-organisms. It enables the engineering of the lethality like it is done with some anthrax strains. Are these laboratory techniques considered as public science or should it be classified? Academics want to publish and to share information for the progress of science and to find useful applications. The Rotterdam scientists were really annoyed when their research was blocked for publication and feared that other groups would be first in publishing a part of their obtained experimental results. Biosafety is already common practice in microbiology, but biosecurity is often still questionable. A 'Code of Conduct', like the Dutch Academy of Science has developed, would help; especially for the so-called insider risk. Educational programs for the identification and assessment of risks and threats to security have to be developed to give scientists bio-threat awareness and for government officials to rationalize the real threat, without damaging the progress of science.

Biography

Stef Stienstra works internationally for several medical and biotech companies as Scientific Advisory Board Member and is also an active Reserve-Officer of the Royal Dutch Navy in his rank as Commander (OF4). For the Dutch Armed Forces, he is CBRNe Specialist with focus on (micro) biological and chemical threats and Medical- And Environmental Functional Specialist within the 1st CMI (Civil Military Interaction) Battalion of the Dutch Armed Forces. For Expertise France, he is now managing an EU CBRN CoE public health project in West Africa. In his civilian position, he is at this moment developing with MT-Derm in Berlin (Germany) a novel interdermal vaccination technology as well as a new therapy for cutaneous leishmaniasis for which he has won a Canadian Grand Challenge grant. With Hemanua in Dublin (Ireland), he has developed an innovative blood separation unit, which is also suitable to produce convalescent plasma for Ebola virus disease therapy. He has finished both his studies in Medicine and in Biochemistry in the Netherlands with a Doctorate and has extensive practical experience in cell biology, immuno-haematology, infectious diseases, biodefense and transfusion medicine.

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Michael D Geschwind

University of California, USA

The spectrum of human prion diseases

Statement of the Problem: Diagnosis of human prion diseases can be difficult as they can present similar to many other conditions, and many other conditions can clinically mimic prion disease. Correct diagnosis of prion disease is important in order to prevent accidental transmission of the prions, to prevent further unnecessary diagnostic testing and to provide a realistic prognosis to the patient and family.

Methodology & Theoretical Orientation: Our center has evaluated more than 2500 cases of rapidly progressive dementia (RPD), including more than 600 cases of prion disease through our clinical research program. Most patients undergo a comprehensive evaluation including clinical history, cognitive testing, CSF analysis, research brain MRI protocol and other testing. These data are analyzed to identify measures that might improve diagnostic accuracy of prion disease compared to other non-prion RPDs.

Findings: The clinical presentation, including presenting symptoms, duration of disease, and laboratory findings are quite varied in prion disease. Brain MRI with diffusion sequences showed high diagnostic accuracy for human prion disease. Unfortunately, radiologists in the USA often miss the radiological diagnosis of prion disease, despite the MRIs showing classic features. A relatively new CSF test called RT-QuIC shows high specificity, although not as good sensitivity, for prion disease diagnosis.

Conclusion & Significance: Our ability to diagnosis prion disease has improved over the past few years to the point at which brain biopsies are rarely needed. Improved diagnosis will be important for future treatment trials and prevention of accidental transmission of these potentially infectious diseases.

Biography

Michael D Geschwind is a Professor of Neurology at the UCSF Memory and Aging Center who specializes in the assessment, treatment and management of rapidly progressive dementias, including prion diseases such as Jakob-Creutzfeldt disease (JCD) and autoimmune encephalopathies, and other cognitive/movement disorder syndromes. He helped to establish a program for the assessment of rapidly progressive dementias at UCSF Medical Center, the first of its kind in the country. He helped to run the first US treatment trial for sporadic disease, at UCSF. He has also helped to establish and co-direct a clinic for patients with autoimmune encephalopathy. He Co-directs the Huntington's Disease Society of America Center of Excellence (HDSA COE) and Ataxia Clinic at the UCSF Memory and Aging Center. His research interests include rapidly progressive dementias, cognitive dysfunction in movement disorders, such as Huntington's disease, spinocerebellar ataxia, corticobasal degeneration (CBD), progressive supranuclear palsy (PSP) and other Parkinsonian dementias.

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Harpal S Mangat

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Correlation of Lyme disease with immune dysfunction

Background: Lyme disease is caused by the bacterium *Borrelia burgdorferi*, transmitted to humans through the bite of infected blacklegged ticks. CD4/CD8 ratios in healthy adults vary across populations; in the US, a CD4/CD8 ratio ranging from 0.9 to 1.9 is considered to be normal in non-immunocompromised individuals. Lyme disease is diagnosed based on symptoms, physical findings (e.g. rash) and the possibility of exposure to infected ticks. Laboratory testing is helpful if used correctly and performed with validated methods. The US Center for Disease Control (CDC) diagnostic criteria requires the identification of five Western blot IgG bands for a positive diagnosis, although patients with less than five positive bands have been subsequently diagnosed with Lyme disease through urine PCR in Nanotrap testing.

Material & Methods: 183 patients at two medical centers were evaluated in Lyme endemic communities in Maryland, USA. Further investigation of 148 of these patients correlated their CD4/CD8 ratio with their Ig41 band, using one and two tail testing.

Results: The mean CD4/CD8 ratio in the 148 patients was 2.41 with a variance of 1.05 and a standard deviation of 1.025. Assuming a normal CD4/CD8 ratio of less than 2, with a 5% confidence interval, the p-value on both a one tailed and two tailed test was shown to be 0.00001. Two patients with an initial CD4/CD8 ratio of 2.7 and 2.8 who were IgG 41 positive were subsequently tested with the Nanotrap urine PCR and found to be positive for Lyme.

Conclusions: Increased CD4/CD8 ratio with a positive IgG 41 band appears to be a strong predictor of a subsequent diagnosis of Lyme disease despite current diagnostic guidelines. Further research should not only be directed towards investigating how *Borrelia burgdorferi* disrupts immune function, but also towards improving diagnostic guidelines in light of validated diagnostic methods.

Biography

Harpal S Mangat, MD, is an Assistant Professor at Howard University College of Medicine. He submitted recommendations to his US senator that got incorporated into the 2010 Affordable Health Care Act. He has four issued US patents and additional patents have been filed. He is a Graduate of the Royal College of Surgeons, Ireland, trained at Trinity College Dublin, Oxford University and London University in Family Practice and Ophthalmology. In the US, he trained at University of South Florida and Mercy Hospital Philadelphia in Ophthalmology and Internal Medicine. He is the Transport Physician for difficult cases returning to United Arab Emirates. His clinical interests include innovative new technologies, neuroprotection, diabetes, sleep apnea, Lyme disease, especially its neurological manifestations, as well as long distance air transport of seriously ill patients.

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