Indo-US Symposium on Viral Infections of the Nervous System

February 23-25, 2014

Meeting started with the welcome remarks by the Prof S. Sinha, The Director NBRC, India. Prof Sinha welcomed all the delegates from US and India and briefly noted the academic need of Indo-US symposium for exchanging ideas, knowledge, techniques and tool to broaden the research on neurovirology. With the opening remark Prof. NK Ganguly and Prof. M. Gouri Devi discussed about the perspectives of neurovirology in India and helped to set the stage for the three day meeting. With the first plenary talk, Prof. P. Satischandra, Director NIMHANS discussed perspectives of neurological opportunistic infections associated with HIV/AIDS in Indian populations and the type of neuroinfections that are common in India with emphasis on neuroAIDS. Dr. Donald H Gilden, Professor University of Colorado, Denver Medical College, USA discussed about the latent viral infection in the nervous system and how viral latency can be fatal and take the opportunity to replicate in the CNS and cause CNS infectious diseases. Challenges in the laboratory diagnosis of viral infection in the CNS were highlighted in his talk. The emerging global epidemiology of viral CNS infection was covered by a Scientist from CDC (Centers for Diseases control) laboratory, USA Dr. James Sejvar.

In the following, session we covered a series of scientific talks which mainly covered the most common viruses in India like Japanese encephalitis virus, HIV and Herpes virus infection. Several talks covered clinical aspects like lesions learned from encephalitis, viral encephalitis; changing scenario and emerging pathogens, their host pathogen interaction and several molecular pathways in JE infection. Mixed clinical and etiological presentations of acute encephalitis syndrome at Gorakhpur (encephalitis prone regions of India) were presented. There were several explicit talks regarding HIV infection, eradication from the brain, cognitive impairment in HIV/HCV co-infection, antiretroviral therapy and neurocognitive function in HIV Clade-C infected individuals, opoid modulations of gut-immune–brain axis in the contexts of HIV infection and microRNA and HIV neuropathogenesis from Invasion to inflammation.

Several scientists highlighted the importance and use of animal model to understand the mechanisms of viral induced neuropathogenesis. A large number of talks covered how the viral infection can directly cause lytic damage to neuron, astrocytes, oligodendrocytes and microglia and can cause the viral induced neuropathogenesis. In this session, people mainly covered the JC virus infection, mouse hepatitis virus infection and HIV/HCV co-infection and Varicella virus infection. Viral infection, viral latency and reactivation mediated neurological

disorders were discussed in details. Multiple sclerosis and other neurodegenerative diseases for long time were only believed to be due to either autoimmune T-cell activation of cell autonomous protein misfoldings. Cellular model of Prion diseases were also discussed in details.

In summary, scientific session covered most of the important neurotropic virus infection to most uncommon and rare viral infection in the CNS, their pathogenesis and the challenges how to get control over the viral load from the CNS to eradicate the viral induced neurological diseases.

(i) **New developments presented at the event**:
Advances in viral latency and reactivation in the CNS of an animal models and the role of astrocytes and microglia in the neuroinflammation mechanism of several viral infections was discussed in the meeting. New developments in viral diagnosis, antiretroviral therapy, viral latency and outbreak of several viruses like herpes virus, JE viruses, HIV, HIV/HCV coinfection and experimental mouse viruses like mouse hepatitis virus and Theiler's viruses were also discussed.

We also had a ***Panel discussion on Women in Neurovirology*** where all women delegates were attended the panel session and panel was moderated by several senior women scientists as well as junior Neurovirologists who openly discussed about the role of women in the field of Neurovirology and how to increase the number of women Neurovirologists. Two other panels were also part of the meeting on final day to highlight the developments of ***Emerging viral infections in the nervous system and how to challenge it together*** by Indian clinicians and basic researcher with US clinicians and basic researchers. The fourth panel discussed how drug developers challenges and handling the emerging CNS viral diseases both in India and US and how to improve the quality of therapy.

Two other panels (viz., ***Emerging viral infections of the nervous system. How to challenge it together?*** and ***Clinicians and Drug Developers – Challenges of Handling Emerging Diseases***) were also part of the meeting on the final day to discuss the current state of research and developments to understand the epidemiology, diagnostics and therapy to counter challenges the emerging viral infections in the nervous system***.*** The panelist consists of basic researchers, clinicians, and people from pharmaceuticals and biotechnology industries who are interested in drug discovery and vaccine research. The major focus of both the panel discussion emphasis on the fact that how drug developers face the challenges and handling the emerging CNS viral diseases both in India and US and how to improve the quality and cost effectiveness of therapy and diagnostic tools to detect viral infection.

In his opening remarks Prof P N Tandon mentioned about challenges in Neurovirology research in India and helped to set the stage for both the panel discussion. The first panel was moderated by Dr Shahid Jameel from India and Dr. Don Gilden from USA. Dr. Shahid Jameel started the discussion by stating the fact that the gap in undiagnosed cases is very large all over the world. In Indian scenario, although conventional methods have described newer methods have not been applied to a large extent. He also mentioned the inter-institutional as well as international cooperation in this.

It was also mentioned that in public health perspective finding etiological agent responsible for outbreak is different than giving a diagnosis to each individual case and should be kept in mind. The view of panelists was also that as the cases arrive at the hospital chances of detecting the causative organism decreases, making NGS methods inconsequential. There was also an opinion that all of the existing diagnostic test kits are not of international quality and at times lead to erroneous results. There was also a need to evolve and develop antibody based tests that will give alternative methods for diagnosis. It was also mentioned that ICMR/DHR network of laboratories will decrease the existing gap of capability of modern diagnosis.

Dr. Milind Gore in his statement mentioned about neuroviral outbreak from Uttar Pradesh, and he further mentioned that so far no causative agent has been identified for several out breaks in the state. He has also shared his experience from Gorakhpur (in Uttar Pradesh), which is considered as an epicenter of neuro-viral out breaks in the country. Dr Sudhanshu Vrati has suggested to do mass scale viral metagenomics study to identify new viruses. Prof. Gourie-Devi emphasized on more sophisticated diagnostic laboratory in the medical colleges across the country. She has also mentioned that ICMR is planning to fund several sophisticated molecular biology laboratory in medical colleges across the country. These laboratories may be playing an instrumental role in viral detection. Dr. Anirban Basu suggested about vector controlling (as most of the emerging viral infections are vector borne) by remote sensing satellites. Dr. Sejvar suggested his experience from CDC's stand point. Dr. Cohr strongly recommended basic researcher to develop quick and cheap diagnostic tools which can easily identify the virus. At the end, Dr. Jameel and Dr. Gilden thanked all the panelists for their insights.

A mechanism of sharing information, samples and newer indigenous tests are also need of the hour. Furthermore, use of imaging techniques in diagnosis was also emphasized. A web based information exchange portal with experts on

radiology, clinical symptoms who can guide clinician to arrive at correct diagnosis needs to be developed and NBRC can take a lead in this.

The last panel discussion was moderated by Dr. Subrata Sinha from India and Dr. Lynn Pulliam from USA. Dr. Sinha initiated the discussion by mentioning the importance of repurposing of old drugs in new use. In his statement he has also mentioned about minocycline, which is currently going through a Phase III clinical trial in Japanese Encephalitis patients. Dr. Howard Lipton also commented about the using of old drugs for viral infections. Dr. Gilden suggested that US funding agency and Indian funding agency could identify some common area of interest in neuro virology research and together with the help from a private partner (Pharmaceutical and biotech industry) could develop a structure to generate newer vaccines and anti-virals. Dr. Lily Verma commented about her experience as clinicians and stated her experience in developing an anti-fungal agent. Dr. Dilip Upadhyay mentioned about the importance of animal model in drug discovery (for viral diseases). He has strongly urged the basic researchers to develop more and more relevant animal model for viral infections. Dr. Eugene Major commented that it is always possible to have an animal model to develop anti-virals. He gave several examples there people developed anti-virals based upon in vitro cell based studies. It was also mentioned that the need for drug or vaccine should be weighed case by case and efforts should be directed to more useful in terms of public health. Many drugs need to be explored and relicensed for newer use and there is need to develop vaccines for newly emerging diseases like West Nile that is taking roots in different parts of India. Dr. Sinha and Dr. Pulliam thanked all the panelists for their thoughtful insights.

A concentrated collaborative approach towards problem solving is necessary.

One of the unique session that was added in this meeting was the **Mentors meet** where a group of 6-7 students went around to 7 tables that had two to three senior faculties to interact both scientifically and socially to guide them over their careers in neurovirology which was very productive and appreciated by all the students and PDFs that attended the Mentors meet.

Advances of funding for neuroscience/Neurovirology were also discussed. In addition, to the scientific sessions, we had Panel discussion about the new developments on current funding scenario of Indian and US funding source by IUSSTF, ICMR and NIH representatives. It was a lively session where chiefs and heads of different funding programs discussed the new developments regarding the interaction between Indian and US scientist to expand the field of Neurovirology.

(ii) **Major recommendations of the event**:

This is the first Indo-US meet on Viral infection in the nervous system where we brought both clinicians and basic research and policy makers from funding bodies to discuss about the ongoing research on viral infections, how to challenge the viral infection in the nervous system and how to develop drugs to prevent CNS infectious diseases.

Major recommendations were -

1) The symposium was a unique opportunity for interaction between clinical and basic scientists from India and USA. This should be followed with exchange of ideas, technology and understanding the strength and weaknesses of different regions to improve our understanding or parthenogenesis and management of encephalitis.

2) Need to develop a platform for regular meetings (may be at alternate years) to keep the momentum and build upon scientific exchange focused on CNS infections. We must follow-up the findings and discussion on emerging cases of northern-India encephalitis outbreaks with closer interactions between NIV and CDC.

3) In future meetings, special topics like modern cutting edge neuroimaging techniques should be included to have better understanding of structural changes in brain following neuroinfections.

4) Identify outbreaks quickly and disseminate the information electronically. To get the Indian granting agencies involved in developing identification chips as well as grants to partner with pharma (like the NIH model).

5) Need to develop closer collaborations between neurovirologists in academic centers and the US for exchange of information, ideas, reagents etc to investigate and study the pathophysiology or viral encephalitis caused by known and unknown organisms.

6) Need to develop guidelines for diagnosis and management of viral infections that affect the brain.