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Importance of Neurovirology Diagnostic Laboratory at Referral Neuroscience Hospital in Bangladesh

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Neurovirological diseases are prevalent worldwide. There is a huge burden of these diseases in Bangladesh as well. The neurovirology is a major discipline over the last 30 years. This subject covers areas including virology, neurosciences and clinical neurology, molecular biology, and immunology as well[1]. This subject also covers a wide range of virology-related topics and these are pathogenesis and pathophysiology of viral infections related to the nervous system which includes both in human and experimental animal models, in vitro studies of the effects of viruses on defined neural cell types known as cytopathic effects, the application of live attenuated viruses as research tools in the field of neuroanatomical and developmental studies, and the use of genetically engineered viruses as vectors to deliver therapeutic genes into the human central nervous system (CNS)[2]. It also includes the laboratory diagnosis and clinical-epidemiology of viral infections of the CNS. Furthermore, the development of specific antiviral agents to treat the disease is also a part of neurovirology. For example, the antiviral drug, acyclovir, is a very good and effective treatment of herpes simplex encephalitis[3]. Therefore, it is a discipline of both clinical as well as biological subjects' area and has much importance to both human disease as well as many aspects of neuroscience. However, clinical studies and the basic knowledge of neurovirology give complementary information in many aspects.

There are many neurovirological diseases. However, most of the neurovirological research works have mainly focused on herpes simplex virus types 1 and 2 especially herpes simplex encephalitis and herpes virus latency, varicella-zoster virus, human immunodeficiency virus (HIV) in both basic and clinical aspects, human T cell leukaemia virus, JC virus causing progressive multifocal leucoencephalopathy in humans, measles virus, poliovirus, rabies virus, Borna disease virus. There are some animal models of neurotropic viruses related to a demyelinating disease such as Theiler's virus, Semliki Forest virus, coronaviruses, and visna-maedi virus[4]. However, the SARS CoV2 causes a worldwide pandemic killing more than thousands of people in Bangladesh. Furthermore, some viruses have emerged and these situations create much interest among researchers and these emerging viral infections of the nervous system are also found in Bangladesh such as the Nipah virus[5-6]. The immune responses toward human hosts' defense by CNS viral infections are also very much important in the field of neurovirology. Molecular neurovirology works associated with apoptosis, cytokines, and chemokines are also progressing[7-8].

HIV infection frequently involves the nervous system and about 10.0% AIDS patients are presented with neurological features. Furthermore, over 80.0% cases are found neurologically affected at necropsy[7]. Clinicians are currently dealing with the challenge of a changing neurological disease profile of HIV infection with the introduction of highly active retroviral therapy. There are also various common viruses that affect the CNS, such as influenza, where the neuropathogenesis is still not properly well-understood. In addition, the immunosuppression accompanies more effective antibacterial treatment and it has in turn led to increased interest in the better treatment of neurovirological disease. However, more widespread international air travel causes more chances of viral infections[9]. Thus both host and viral factors may be contributing to the changing pattern of neurovirological diseases.

There are several specific laboratory methods. Among these few are classical techniques which are applied from many years. Tissue culture of the nervous system has been applied in different research and diagnostic purposes. Isolation of viruses from human tissues and body fluids is a classical method of establishing the viral aetiology of a neurological condition[5]. Electron microscopy is available in Bangladesh. This technique has been useful in identifying various viruses in

neurological conditions. Serological analyses is an important classical method of detection of viruses. A significantly rising viral antibody titre in paired serum or cerebrospinal fluid (CSF) samples provides convincing evidence of a current virus infection as the cause of a neurological illness. Identification of viral antigens in tissues and body fluids of patients provides strong evidence of the involvement of a virus in an illness. The techniques used include enzyme linked immunosorbent assays (ELISA), western blotting for viral proteins, immunofluorescence, and immunocytochemistry[1]. Double label immunofluorescence or immunocytochemistry are techniques whereby two viral antigens can be colocalised within the same tissue region or cell. Polymerase chain reaction has revolutionised both CNS viral diagnosis and pathogenic studies. PCR can identify a single viral genome in a tissue specimen containing many thousands of cells[8]. A further advantage of this technique is that reverse transcription PCR (RT-PCR) can be used to detect viral RNA, which can be quantitated; this allows the measurement of viral load-for example, in patients with HIV infection[10]. A recently developed and extremely sensitive technique known as real time PCR and digital droplet PCR uses a special PCR system to quantitate viral DNA or RNA in terms of viral copies[9]. Molecular hybridisation studies like southern and northern blots which detect DNA and RNA, respectively. In situ hybridisation (ISH) is one of the most useful techniques currently available in studies of viral pathogenesis. ISH is more sensitive than Southern and northern blotting[10]. PCR in situ amplification is a recently developed technique that combines the exquisite sensitivity of PCR with the cell localising ability of ISH. RT-PCR in situ amplification to detect RNA in specific tissue areas are avaliable. Combined ISH and immunocytochemistry is another useful but technically difficult technique in which tissues or cells under test are first labelled immunocytochemically with specific antibodies against. The advent of gene microarrays for analysing thousands of different genes simultaneously represents one of the most exciting and promising advances in basic and applied molecular biology in recent years. The two main types of microarray are oligonucleotide arrays and DNA microarrays[11]. Molecular analysis of viral isolates are also available.

Bangladesh is densely populated country. There are several suspected neurovirological diseases prevalent in this country. The laboratory diagnosis is very much important to confirm the disease. In this regards the establishment of diagnostic laboratory is now a burning issue. National institute of Neurosciences and Hospital, Dhaka is the only referral neuroscience hospital in Bangladesh. Neurological patients of all aspects are referred to this hospital. Many suspected cases of virological diseases are treated without confirmation in the laboratory. Clinicians are very much aware of it. Therefore it is now a time to establish a neurovirology laboratory in this referral institute. This laboratory can give a huge diagnostic support to the neurologists for the confirmation of neurovirological diseases.

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