REMEMBERING EMILE KRAEPLIN AND CALLING UP A PARADIGM SHIFT ON THE EVE OF THE FIRST CENTURY OF ALZHEIMER’S DISEASE

In 1901, Dr. Alois Alzheimer (1864–1915), a German psychiatrist, examined a patient named Mrs. August Deter. She was 51 years old and had been suffering from amnestic disorder. She died in April 1906. Dr. Alzheimer performed post-mortem examination of the macroscopic and microscopic morphology of her brain. On November 3, 1906, he presented the case of presenile dementia of Mrs. August Deter in front of the 37th Assembly of Southwest Psychiatrists and highlighted the marked changes he observed in her brain, namely reduction and smoothening of cerebral cortex, and presence of amyloid plaques and neurofibrillar tangles in brain sections, the latter two considered as the hallmark of the disease. He provided further details in the following year. Alzheimer’s second case was a 56-year old man who was examined in September 1907 and showed behavioural anomalies very similar to that of Mrs. August Deter. The patient died on October 3, 1910 and revealed similar changes in the brain on anatomical and histopathological examination. Dr. Alzheimer presented the case in the following year. Dr. Gaetano Perusini, an Italian physician, also published four more similar cases in 1910. As a result, the syndrome-based identity of the condition was indexed under Alzheimer’s disease first by Professor Emile Kraepelin in his textbook, and very soon the name of the disease was well established among the specialists by 1911.

Emile Kraepelin (1856–1926) played a major role in creating the momentum of understanding psychiatric disorders in biological terms. He was a German psychiatrist and much less renowned than another contemporary psychiatrist Sigmund Freud. They both were born in 1856, only three months and three hundred miles apart. Sigmund Freud was born in Freiberg in the Austrian Empire on May 6, 1856. Emile Kraepelin was born on February 15, 1856 in Neustrelitz, Prussia. Both studied medicine and eventually became two great founder-pillars of modern psychiatry that started its new journey a hundred year ago. However, these two great psychiatrists had so different approaches to psychiatry: Freud’s approach was psychological and Kraepelin’s was somatic. Kraepelin postulated that there is

1Also see the Guest Editorial ‘Remembering Sigmund Freud on his 150th Birth Anniversary’ on page 4 in the this issue of IJPP.
In November 2006, that is after a hundred year of the first scientific report on Alzheimer's disease, a search of the Pubmed Medline database retrieves about 42,000 entries and a Google search yields about 44,900,000 hits, and Yahoo search yields 26,500,000 hits on 'Alzheimer' alone. Still, our knowledge about the pathophysiological basis of this disorder is alarmingly thin, while Alzheimer's disease is one of the major public health challenges today. As a result, frustration among medical practitioners is very high. This human problem shall eventually take a gigantic shape in future unless scientists, science managers, different related agencies and industries take a profound stance with true interest towards understanding the biology of this disorder.

One thing is however evident even today. Alzheimer's disease takes place through a complex process. It involves a plethora of molecular and cellular effectors towards its persistence and propagation, and it involves interactions among hormonal, nutritional, immunological, environmental and genetic factors. Thus this behavioural disorder appears to be a multimodal networks-based process involving polygenic polymorphic epiphenomena on the background of multiple risk factors in the environment and lifestyle. Several biologists have placed a common conjecture in recent time that such a complex process can only be approached using hypothesis-free through-put data mining and construction of functional networks among biological modules. Interestingly, modern genomic and proteomic tools coupled with bioinformatics and new mathematical and computational
approaches now provide efficacious strategy towards elucidating such a complex process. Therefore, the call of the hour is to undertake multi-centered, multiparametric study on populations systematically derived from different ethnic-anthropological, socio-economic and geographical backgrounds inflicted with Alzheimer’s disease condition as identified under standard clinical norm and sequel towards compiling demographical and clinical data along with high throughput genomic and expressionnal data profiling and bioinformatics based data analysis to unravel biological interaction networks functionally relevant for pathophysiology of Alzheimer’s disease. It is possible that a clinically meaningful molecular classification protocol may evolve through such endeavour. It will be possible to resolute the clinical panorama of heterogeneity of Alzheimer’s disease condition into certain genomic-proteomic clusters and signatures (potential biomarkers) linked with clinical specificity, morphological characteristics, severity and therapeutic sensitivity. This will also offer possible screening for genes and products for diagnostic purposes, targeted drug discovery and disease prognosis. We believe such a high throughput study, data mining and elegant modeling and effective heuristics will not only provide improvement in the basic understanding about the pathophysiology of Alzheimer’s disease, but also its diagnosis, management and treatment, thereby improving the quality of life to patients and providing a substantial relief from economic, aesthetical, cultural, social and human loss.

Charles Best and Normal Taylor wrote in 1936 in the preface to first edition of their magnum opus ‘The Physiological Basis of Medical Practice’ that physiology tends to give to the medical practitioner a vantage point to gain a rational view of pathological processes. The new paradigm of systems physiology approach, as outlined above, to understand and deal with complexities of physiological order and disorder, albeit appears to be unfathomable gigantic job today, holds keys to open in future many black boxes including Alzheimer’s disease. It is therefore essential that all those who are involved in understanding Alzheimer’s and similarly complex clinical entities from all possible angles embrace without further delay the ‘daddy long-legs’: the new paradigm of systems physiology.