



BIOGRAPHY OF ALOIS ALZHEIMER (1864-1915)

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Alzheimer's disease is a neurodegenerative disorder. It is characterized clinically by a progressive decline of several cognitive functions and it is the most common cause of dementia. The prevalence of this disease is expected to increase during the next decades because of the increasing of the human age population. It is one of the greatest burdens in modern medicine.

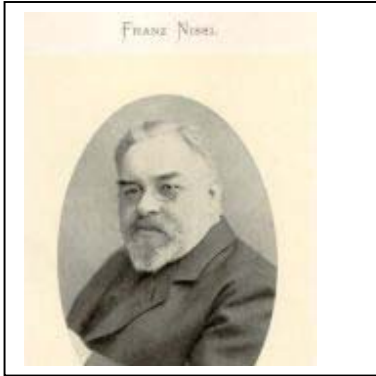
The symptoms of Alzheimer's disease were first described in the early 1900s by Emil Kraepelin, a German psychiatrist. The neuropathological features were later described by Alois Alzheimer, another German psychiatrist, who worked in Kraepelin's laboratory. The description of this disease is his most known contribution to Neuroscience. However, the research on this disease represents only a small part of Alzheimer's interests, which also included the histopathology of the cerebral cortex in the mentally ill.

Who is Alois Alzheimer and what were the main stages of his carrier?



Alois Alzheimer was born on the 14th of June 1864 in Markbreit a small Bavarian village, Southern Germany where his father was notary. Excelling in science at school he studied medicine in Berlin, Tubingen and Wurzburg where he wrote his doctoral theses on ceruminal glands and graduated with a medical degree in 1887.

In December 1888 he began his medical career as a resident at the Hospital for the Mentally ill and Epileptics in Frankfurt am Main where he stayed for seven years and was subsequently promoted to senior physician. Later Alzheimer worked seven more years as an assistant physician at the Municipal Hospital for Lunatics and Epileptics also called Asylum in Frankfurt headed by Emil Sioli. Here he made his education in psychiatry and devoted himself to his main interest, neuropathology. He became interested in research of the human brain cortex. He found himself in a unique position and was able to contribute to the development of a modern clinical service and to create a scientific patient database. He set up an archive of autopsy cases which would prove to be useful to him during his career. One year after Alzheimer started to work in the Asylum, the neurologist Franz Nissl joined the team. Nissl was known for his revoutionary "Nissl staining" method for nerve cells which is still used in routine and experimental neurohistology laboratories around the world. A close friendship arose between the two scientists, working with the patient during the day and spending evenings discussing findings over the microscope. They worked together on an extensive investigation of the pathology of the nervous system. They studied more particularly the normal and pathological anatomy of the cerebral cortex and presented their result in a major six volume work entitled "Histologic and Histopathologic Studies of the Cerebral Cortex" published between 1906 and 1918. Alzheimer's efforts were



more concentrated on the patient material while Nissl worked on experimental studies of the reaction of nerve cells after sectioning axons. Nissl's strong influence on his work was acknowledged by Alzheimer in the following beautiful manner: *"I shall mention Nissl's name as often as scientific works by him on the topic under discussion are known to me. However, Nissl's share in these studies does not end with that. The amicable scientific interactions which I was allowed to entertain with him over the last 15 years have given me so much stimulation that I must*

concede – to give but one example – that none of the following ideas that might enhance our knowledge has been conceived without his direct or indirect participation." Alzheimer was known for his great capacity of description of his microscopical observation.

In April 1894, Alzheimer married a banker's widow Ceacilia Geiseinheimer and they had three children. This marriage made him financially independent so he became able to support his own research. Ceacilia died in 1901 after seven years of marriage.



In 1895 Nissl moved to Heidelberg to work with the most important German psychiatrist of that time Emil Kraepelin. Later, he succeeded him as director of the clinic there. The same year Alzheimer became the director of the Asylum in Frankfurt. His studies included a wide range of subjects such as clinical studies of manic depression and schizophrenia.

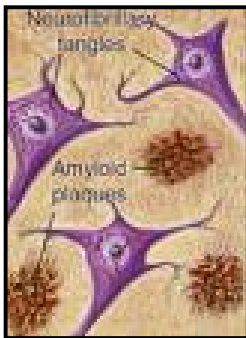
During his stay in Frankfurt, Alzheimer met a 51-year-old woman, Auguste Deter who had been admitted in 1901. She was suffering of disorientation, impaired memory and troubles in reading and writing. The symptoms increased to hallucinations and to loss of higher mental functions. Deter died in 1906 four years after Alzheimer had left Frankfurt, but her brain and all the records he had made were sent to him to Munich. This woman is known as the first described case of Alzheimer's disease.



Auguste Deter

In 1902 Kraepelin invited Alzheimer to work with him in Heidelberg. One year later they moved together to the university psychiatric clinic in Munich where his life as a scientist reached its peak. In 1904 he published his habilitation

thesis on the histopathology of the general paralysis of the insane based on 170 clinically typical cases. Alzheimer showed how the histological diagnosis can be used to answer clinical questions. Importantly, in this study Alzheimer noticed that the degenerative process that underlies this illness takes place independently from the inflammatory reactions. However, the exact nature of the disease process has remained enigmatic. Very little of Alzheimer's teachings had to be revised and, though 100 years old today, they have not been corrected or amended but only confirmed.



At a meeting of the South-West German Society of Alienists in November 1906 in Tübingen, Alzheimer described “a peculiar disease of the cerebral cortex”, the clinical and neuropathological features of August Deter. The pathological and anatomical investigation for the brain showed a thinner cerebral cortex usually seen in elderly people. He noted two further abnormalities in the brain: neurofibrillary tangles which represent changes in the cytoskeleton of nerve cells which are often associated with cell death, and amyloid plaques which are extracellular deposits of a neurotoxic substance. In his presentation, Alzheimer made the assertion that her dementia was related to lesions in her brain. The speech was published the following year. The importance of this case lies in the fact that it marks the beginning of Alzheimer disease research. Today the neurofibrillary tangles first described in her brain represent an important topic of neuroscience research.

Alzheimer’s second case was a demented 56 years old man, Johann F. who was admitted to the university psychiatric clinic on September 12 1907. He died three years later. The autopsy of his brain showed changes similar to those of the first patient. E. Kraepelin proposed that the syndrome should be called “Alzheimer’s disease”.

In 1908, Alzheimer joined the staff of the Psychiatric Institute as associate professor and became the director of the clinic’s anatomical laboratory. He trained students from various countries. Alzheimer spent ample time with each one of them explaining things. Those who attended have described it as an unforgettable sight when Alzheimer with his large head bowed over the microscope with the pince nez dangling in a string around his neck, always with a cigar, which would be put down as he commenced his explanations. It is said that at the end of the day there would always be a cigar stump at every student's bench by the microscope, marking his tour in the laboratory.



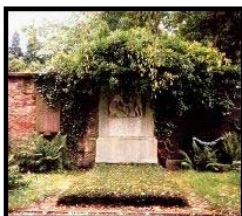
Alzheimer's laboratory



On July 1912 Wilhelm II of Prussia signed Alzheimer's certificate of appointment as full professor of psychiatry at the University of Breslau. On the train going there he felt ill and had to be hospitalized. His weak health prevented him of beginning his university duties as intended but he devoted

The last three years of his life were devoted to research and clinical work. During the later years of his career Alzheimer concentrated his efforts on the study of changes in glial cells in the diseases of the brain. His best-known works from this period were on Westphal-Strümpell pseudosclerosis of the brain, now assumed to be the same as Wilson's disease. In this work he distinguished between two forms of changes in the nucleus of the glial cells, termed Alzheimer's type I and II astrocytes. Alzheimer also realised that the neuroglia's responses depend on the type and intensity of the disease process.

During his carrier he also worked on general paralysis, cerebral atherosclerosis, damage caused by chronic alcoholism, acute syphilitic infections of the brain and anatomical basis of idiocy. Alzheimer further recognized the neoplastic nature of the tumourous "glial masse" in tuberous sclerosis. He also worked on the anatomical basis of Huntington's chorea and the choreatic movements in general. He described brain changes associated with arteriosclerosis and a loss of nerve cells, most pronounced in the striatum, in Huntington's disease. He also studied brain changes in epilepsy to define anatomical subtypes. He stated: *"If we aim to understand the nature of a disease, to predict its prognosis, to elucidate its course and finally treat it prophylactically or therapeutically, we must have clear, precisely defined disease entities before us. What we call epilepsy today, however, does not represent such an entity but apparently encompasses a whole group of different disorders"*. He noticed a loss of nerve cells in the hippocampus of many epileptic patients and suggested that the cellular loss might be caused by the attack itself. He showed the importance of studying the breakdown of nervous tissue and the types of neuroglial responses in epileptic brains.



He died at the age of 51 as a result of a serious infection of the heart. He was buried next to his wife in Frankfurt.

Alzheimer's research was characterized by a close interaction between the anatomical observation and the clinical experience. Difficulties simulated him to find new ways to explore the cases he was working on. He was meticulous and he never published before he was totally sure of his results and that he had something truly important to say. He was able to present his research work very clearly and to convince the scientists about the importance of his result and it seems that he never had to fight for the recognition for his work.

His colleagues had a high esteem for his work and also for his personality. Robert Gaupp, then head of psychiatry at Tübingen wrote: *“Alzheimer was a man with a clear head and unusual creative powers who took greatest pains over his work and had a strong sense for scientific truth. The right training provided, this combination of talents had to result in outstanding achievements in the field of science. This was complemented by his warmhearted interest in the fellow man, his mentality of a true physician, and the great enjoyment from combining science and medical practice. Although he mainly worked in a small, infinitely difficult specialist field, he always made sure that his research could not endanger the clinician and physician in him”*.



Through his early histopathological research in psychiatry, Alzheimer became one of the founding fathers of neuropathology, nurturing a unique brain research tradition in Germany that lasted for almost a century. Alzheimer always thought of himself as a physician and was able to combine his innovative research with the demanding clinical duties of a psychiatrist.

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