

Alzheimer's 100th anniversary of death and his contribution to a better understanding of Senile dementia

O 100º aniversário de morte de Alzheimer e sua contribuição para uma melhor compreensão da Demência senil

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ABSTRACT

Initially the trajectory of the historical forerunners and conceptions of senile dementia are briefly presented, being highlighted the name of Alois Alzheimer who provided clinical and neuropathological indicators to differentiate a group of patients with Senile dementia. Alzheimer's examination of Auguste D's case, studied by him with Bielschowsky's silver impregnation technique, permitted to identify a pathological marker, the intraneuronal neurofibrillary tangles, characterizing a new disease later named after him by Kraepelin – Alzheimer's disease. Over the time this disorder became one of the most important degenerative dementing disease, reaching nowadays a status that may be considered as epidemic.

Keywords: dementia, Senile dementia, history of medicine, Alzheimer, Alzheimer's disease.

RESUMO

Inicialmente é apresentada brevemente a trajetória histórica dos precursores e dos conceitos da demência senil, sendo destacado o nome de Alois Alzheimer que forneceu indicadores clínicos e neuropatológicos para diferenciar um grupo de pacientes com Demência senil. O exame de Alzheimer do caso de Auguste D, estudado por ele com a técnica de impregnação argêntica de Bielschowsky, permitiu identificar um marcador patológico, os emaranhados neurofibrilares intraneuronais, caracterizando uma nova doença, mais tarde denominada com seu nome por Kraepelin – doença de Alzheimer. Com o passar do tempo esta desordem tornou-se uma das mais importantes doenças demenciante degenerativa, alcançando, na atualidade, um status que pode ser considerado como epidêmico.

Palavras-chave: demência, Demência senil, história da medicina, Alzheimer, doença de Alzheimer.

Alzheimer's 100th anniversary of death raises an opportunity to remember his contributions to the study of senile dementia and allied disorders. Senile dementia has a very long history. Greek philosophers such as Plato and Aristotle were imbued with the conviction that old age is inseparable from mental failure. This belief was further elaborated, as by Cicero, who suggested that an active mental life could prevent or at least postpone mental decline¹. In the 18th century, Senile dementia was recognized by Cullen as a "decay of perception and memory, in old age (Amentia senilis)" (*apud*¹). Later, Philippe Pinel's asylum reforms gave the ground to the widespread clinical and pathological observations on mental disorders, including Senile dementia. In the 19th century, numerous famous names were engaged in the study of dementing illnesses, and among them, Alzheimer¹.

ALZHEIMER: LIFE, PARTNERSHIPS AND ACHIEVEMENTS

Aloysius "Alois" Alzheimer (June, 14th, 1864-December, 19th, 1915) (Figure 1), German psychiatrist and pathologist, was born in the Bavarian town of Marktbreit. He obtained his medical degree at the Würzburg University (1887), and within months began working at the Hospital for the Mentally Ill and Epileptics, in Frankfurt^{2,3,4}. He married a banker's widow, Cecile Geisenheimer, but after seven years she died, leaving him alone with three children^{2,4}. Alzheimer died relatively young, as described by Kraepelin, due to an "infective angina associated with nephritis and inflammation of the articulations..." that led to severe renal and respiratory failure (*apud*⁵).

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Figure 1. Alois Alzheimer.

Alzheimer worked as psychiatrist and pathologist in Frankfurt (1888-1902), at the Municipal asylum; Heidelberg (by 1902), where Franz Nissl assumed the chair of psychiatry previously occupied by Emil Kraepelin; Munich (1903-1912), at the Royal psychiatric hospital, under Kraepelin's direction; and Breslau (1912-1915), as assistant professor of psychiatry at the Neurological and Psychiatric Clinic of the Friedrich-Wilhelm University⁵. Besides the professional relationship, he entertained a solid companionship with Nissl, which lasted a quarter-century, and an enduring friendship with Kraepelin. He held successfully positions that matched clinical practice and pathology. His pathological knowledge was solid, which he considered essential for the psychiatric study. He was also praised as a teacher and colleague^{2,4}.

SENILE DEMENTIA UNFOLDINGS

Alzheimer provided numerous contributions to neuropathology, as on acute alcoholic delirium, pseudo-sclerosis of Westphal-Strümpell, early dementia, brain tumors, progressive paralysis of young, epilepsy, encephalitis, chorea of Huntington, General paresis, arteriosclerotic brain disorders, among others, besides developing neurohistological stains. With Nissl he published histologic and histopathological studies of the cerebral cortex. He described for the first time, in hepatic encephalopathy, a specific cell type – Alzheimer's type II cell¹. Alzheimer and Binswanger may be recognized as pioneers in the study of vascular brain diseases, and Alzheimer (among others) established pathological distinction among them and from syphilis, one of his objectives⁶.

Alzheimer interacted clinically with a 51 years old demented patient, Auguste D (Deter) (Figure 2), in 1901. Her ailment

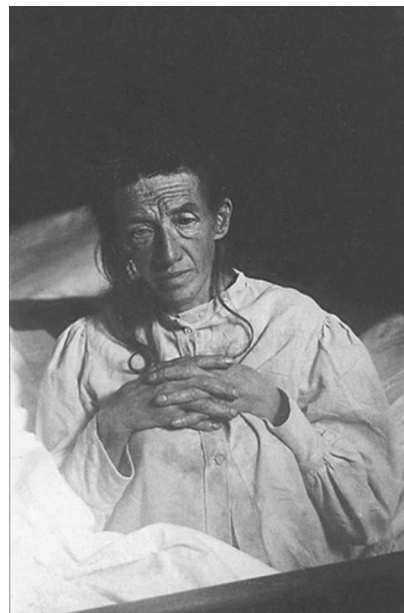


Figure 2. Auguste Deter.

initiated with jealousy towards her husband, followed by memory impairment, disorientation, aphasia, apraxia, agnosia, paraphrasing, and persecutory delusions. Alzheimer examined her during five months, when he left the institution, but made frequent inquiries about her state, which deteriorated considerably in the last years, until her death, in 1906, at the age of 55 years⁷. Meanwhile, Alzheimer was working on vascular diseases of the brain, and has already identified, among the senile dementia patients, one case with primary [cortical] ganglion degeneration (1898)⁶. With the notice of Auguste D's death, Alzheimer requested from his friend Dr. Sioli, director of the Frankfurt Institution, her medical records and brain. When he received the material, Bielschowsky has already published, in 1903, a silver impregnation method that revealed the neurofibrils^{1,2}. In the occasion, among others, he counted in his laboratory with two Italian disciples, Francesco Bonfiglio and Gaetano Perusini, who collaborated in the analysis and discussion of the case. The microscopic examination of the histological preparations revealed, stained in sharp definition with Bielschowsky's technique, a novel feature – the presence of thick bundles of neurofibrils within the cytoplasm of cortical neurons. He also found, dispersed in the cortex, miliari foci of a peculiar substance, a feature already known. This case was object of Alzheimer's seminal presentation of his findings at the 37th Meeting of South-west German Psychiatrists held in Tübingen, Germany, in 1906, under the title *Über eine eigenartige Erkrankung der Hirnrinde* (About a peculiar disease of the cerebral cortex)², quickly published, in 1907, in the *Allgemeine Zeitschrift für Psychiatrie und psychisch-gerichtliche Medizin*⁷(Box). This was the first documented case of a new presenile dementia subtype, soon named after him, Alzheimer's disease, by Kraepelin, as described in the eighth edition of his

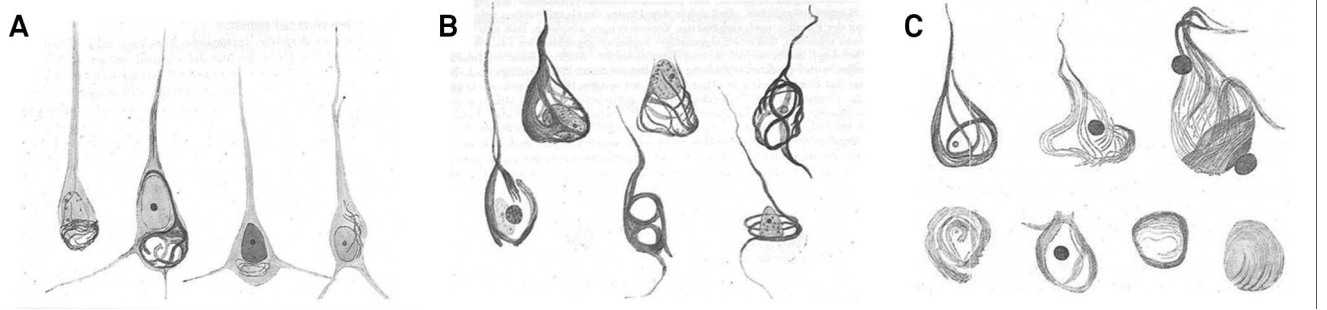


Figure 3. Drawings of histological preparations of Auguste D's material, stained by Bielschowsky's technique to demonstrate tangles, and their stages, from Alzheimer's 1911 paper⁹: (A) Beginning of the disease; (B) Advanced stage; and (C) Terminal state of the disease.

According to Alzheimer, "The examination of the brain showed an evenly atrophic aspect, without macroscopic foci. The larger cerebral vessels displayed arteriosclerotic changes". Further, Alzheimer described the histopathology of the tissue, in relation to the neurofibrils, as follows: "The histological preparations, stained with the Bielschowsky's silver method, show very striking changes of the neurofibrils (displayed in Figures 3A, 3B and 3C). Inside a cell which otherwise appears almost normal, one or several fibrils presenting special thickness and particular impregnability can be seen (A). In the further course, changed in the same way, many fibrils arranged close to each other can be noticed. Next, they assemble to constitute thick bundles, and appear gradually on the surface of the cell (B). Finally, the nucleus and the cell disintegrate, and only a tangled bundle of fibrils indicate the place where previously a neuron was located (C)"... "Approximately ¼ to ½ of all neurons of the cortex show such changes. Numerous neurons, especially in the upper cellular layers, have completely disappeared." He also described the senile plaques (as later named), in the following way: "Dispersed over the entire cortex, specially numerous in the upper layers, are found small miliary foci containing deposits of a peculiar material, limited to the cerebral cortex. This foci may already be observed without staining, however, they are very refractory to stains". Finally, Alzheimer states: "Summing up, we have here before us a peculiar disease process"...

He states: "Such observations suggest that we should not feel satisfied, in face of an unclear clinical case, and spend all efforts to accommodate it in one of the well-known disease groups. There are, doubtless, much more psychic ailments than those presented in our textbooks. Regarding some of such cases, a later histological examination will permit to determine the singularity of a given case". Concluding: "Then, we progressively will also reach a situation that will allow to separate single diseases clinically, amid the great disease groups of our textbooks, permitting a sharper medical definition".

Box. Excerpts from Alzheimer's 1907 paper, highlighting the histopathological findings of Auguste D's material⁷.

Textbook of Psychiatry (1910)^{2,3,8}. Thus, Alzheimer achieved another of his aims, the segregation of dementing disorders according to their causes, and was fortunate to reveal a new disease.

In 1911, Alzheimer published the paper *Über eigenartige Krankheitsfälle des späteren Alters* (About peculiar disease cases in the later age), where he displayed, for the first time, drawings of the intraneuronal tangles of Auguste D's material, classified in several stages (Figure 3). He also described in a detailed manner another case, Johann F, a 56-year-old male, hospitalized in Kraepelin's clinic, who suffered from presenile dementia⁹.

Auguste D's material remained unavailable for a long time, being rediscovered in the archives of the University of Frankfurt, confirming, almost a century later, Alzheimer's findings^{3,10}. This material was further studied, not only its histological aspects, but also the genetic ones¹⁰.

Over the time Alzheimer's disease, raised from the position of a infrequent disorder, to become one of the most important degenerative dementing disease, reaching nowadays what can be considered as an epidemic status.

FINAL REMARKS

Alzheimer gave the first steps to break apart the heterogeneous Senile dementia, in the late 19th and early 20th century. He was only able to reveal the identifying marker, the neurofibrillary tangles, thanks to the development of Bielschowsky's staining technique. These finding, the striking neurofibrillary pathology he identified, besides the already known "miliary foci" (senile plaques), were recognized afterward as markers of the disease that carries Alzheimer's name.

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