

Profile

Alois Alzheimer, Neuroscientist (1864–1915)

Gayatri Devi and *Wolfgang Quitschke

*Gertrude H. Sergievsky Center, Taub Alzheimer Disease Research Center, and the Department of Neurology,
Columbia University College of Physicians and Surgeons, New York, New York, U.S.A.;
and *Department of Psychiatry and Behavioral Science,
State University of New York at Stony Brook, Stony Brook, New York, U.S.A.*

Summary: Little is known about the person behind the eponymous dementia, Alois Alzheimer. We wished to study his life and contributions to the field of neuroscience. All cited articles about Alzheimer by his contemporaries and selected correspondence by him was translated from German. Additional personal information was obtained from his granddaughter. Alois Alzheimer made seminal contributions to the field of neuroscience, not only through his own research but also through the numerous scientists and physicians whom he taught. His contributions made a lasting impact not only in the area of Alzheimer disease but also other aspects of brain disease. In addition, he emerges as a complex person who coped successfully with numerous personal and career-related dilemmas that remain relevant in the academic environment today. **Key Words:** Alois Alzheimer—Biography—Neuroscience—History.

In an era of subspecialization, related disciplines such as neurology, psychiatry, and neuropathology have evolved into separate fields. Yet, in the field of Alzheimer disease (AD), all three disciplines collaborate routinely to help understand this fascinating illness. Organizations such as the Committee to Establish a Registry for Alzheimer's Disease (CERAD), the Alzheimer's Disease Research Centers (ADRCs), and the Alzheimer's Disease Cooperative Studies group (ADCS) have championed a multispecialty approach to investigating this dementia. As we near the centennial of the first description of this disease, a look back illustrates how such an interdisciplinary approach by Alois Alzheimer yielded so much early in the history of this illness. We also present a short biography of his life, with special emphasis on his qualities as a teacher and mentor.

More than nine decades ago, Alois Alzheimer reported on the case of a 55-year-old woman whom he had admitted and followed (Alzheimer, 1907). He noted her paranoia, agitation, apraxia, aphasia, memory impairment, and progressive motor failure. His postmortem finding of plaques and tangles in the brain continue, along with his clinical description, to be the clinical and pathological hallmarks of AD (Alzheimer, 1907; Bick et al., 1987; Bick and Amaducci, 1989). He appeared to be an accomplished psychiatrist, neurologist, and pathologist. A study of the collaborative environment of those times hints at the excitement during those times for neuroscience, reminiscent of the atmosphere in the field today.

METHODS

All articles about Alzheimer by his contemporaries and some of his correspondence cited in this paper were translated from German. Historical articles by Amaducci, Bick, Hippus, Hoff, and others were reviewed. Personal history was provided by his granddaughter.

Received April 1, 1998. Revised October 30, 1998. Accepted January 5, 1999.

Address correspondence and reprint requests to Gayatri Devi, M.D., Gertrude H. Sergievsky Center, Columbia University College of Physicians and Surgeons, 630 West 168th Street, New York, NY 10032, U.S.A.

EARLY TRAINING

Alzheimer's year of training after medical school prepared him well for the career that lay ahead. In the first half of that year, the 70-year-old von Kolliker, an eminent physiologist and colleague of Virchow, oversaw Alzheimer's thesis examination of the tracts of cerumen producing glands from four newborns, three children, and six adults (Alzheimer, 1888; Hoff and Hippus, 1989; Hippus, 1990; Hoff, 1991). In the second half of the year, he was caretaker to a mentally ill woman (Hoff, 1991). Thus, early in his career, he was exposed to both clinical and basic research.

THE FRANKFURT YEARS (1888–1902)

Alzheimer's first and longest appointment was with Emil Sioli at the Municipal Asylum at Frankfurt. Sioli fostered a richly academic and bustling clinical department where Franz Nissl, Alois Alzheimer, Ludwig Edinger, and Carl Weigert were physicians (Hippus, 1990; Nissl, 1916). Sioli pioneered the friendly and humane treatment of psychiatric patients and eliminated restraints, practices Alzheimer embraced (Nissl, 1916; Kraepelin, 1987). Very busy at the bedside, Alzheimer in time became an outstanding clinician wishing "to help psychiatry through the microscope" (Spielmeyer, 1916).

At Frankfurt, Alzheimer and Nissl began their long and productive collaboration that culminated with the publication of the six-volume *Histologic and Histopathologic Studies of the Cerebral Cortex* (1904–1918). Emil Kraepelin clearly felt that the collaboration between the two was critical to Alzheimer's success as a researcher. He wrote that the meeting between Nissl and Alzheimer "was pivotal to his [Alzheimer's] scientific development . . . the two friends received extensive guidance from Weigert who was working on completing his glial stain . . . Alzheimer now embarked on investigating a large number of brains in all sections with the new myelin, glial and cell stains. In this way he gained an extraordinary repertoire of knowledge which he would later draw from" (Kraepelin, 1921).

Nissl found working with Alzheimer to be exciting and intellectually invigorating.

During the day we had our hands full at the ward and at night we sat in front of the microtome, the stain buckets and the microscope smoking one cigar after another. . . . It was a *Sturm und Drang* period. What didn't we do back then? Wherever we looked every preparation stared back at us, filled with the enigmatic and unintelligible. Only the goal was clear . . . the pathological process in our mentally ill patients was to be uncovered. . . . How did we argue through

the nights about a single preparation: then followed weeks of fruitless work where each of us chased after a different problem. We sometimes reveled in the joy of discovery . . . nobody fearfully guarded their thoughts or plans; to speak of a teacher–student relationship . . . [is] utterly ridiculous. (Nissl, 1916)

Later, however, he stated, "Indeed, I could not be more proud than to have the honor to be called his teacher" (Nissl, 1916).

Alzheimer acknowledged his debt to Nissl and reciprocated the feeling of good will, stating "my friendship with him and our scientific interactions . . . have contributed to so many diverse impulses . . . anything in the following presentations that may advance our knowledge has not emerged without his direct or indirect influence" (Spielmeyer, 1916). Thus Alzheimer and Nissl viewed their collaboration as important to the furthering of both of their scientific careers.

THE ROYAL PSYCHIATRIC HOSPITAL OF THE UNIVERSITY OF MUNICH (1903–1912)

By 1902, at the age of 38, after 14 happy years at the Frankfurt Asylum, Alzheimer may have reached a personal and professional nadir. His beloved wife died suddenly, leaving him with three young children under the age of 6. His close friend and colleague, Franz Nissl, had left to work with Emil Kraepelin at Heidelberg. "Only after being rejected for a position as head of a clinic" (Kraepelin, 1921) did Alzheimer later accept an offer from Kraepelin. However, after a few months at Heidelberg, Alzheimer left with Kraepelin for Munich and Nissl assumed Kraepelin's position as chairman of psychiatry at Heidelberg (Nissl, 1916; Hoff and Hippus, 1989; Hippus, 1990; Hoff, 1991).

The forerunner of the German Research Institute for Psychiatry (later the Max Planck Institute), the directory of the Royal Psychiatric Hospital at Munich eventually read like a Who's Who in neuroscience. Under Kraepelin's adept leadership, Alois Alzheimer, Korbinian Brodmann, and Franz Nissl headed laboratories here. Walther Spielmeyer, Frederick Lewey, Gaetano Perusini, Alfons Jakob, Hans Creutzfeldt, were all students in Alzheimer's laboratory. Korbinian Brodmann had studied under Alzheimer in Frankfurt. Although all were clinical psychiatrists, their contributions to neurology and neuropathology are undeniable.

At the hospital, Alzheimer reached the heights of his professional productivity, with Kraepelin as his mentor. Meyer noted that at the hospital,

neuropathologic research was applied science in the service of clinical psychiatry. Alzheimer immediate-

ly found his echo in the goals of Kraepelin's clinic . . . probably no psychiatrist at that time clearly recognized the importance of pathological anatomy for the systematic study of psychiatric diseases as Kraepelin did. (Meyer, 1961)

During this time, Alzheimer published his landmark paper, entitled the "Clinical and Pathologic Study on Syphilis," making general paresis the classical model of a psychosis (Meyer, 1961). He had also done seminal work on arteriosclerotic brain atrophy, epilepsy, senile dementia, spinal muscular atrophy, and named the dementia for Otto Binswanger (Spielmeyer, 1916; Hippus, 1990; Hoff, 1991).

Alzheimer's dedication to his field went beyond the routine as, initially, the hospital was short on funds, labor, and facilities. Kraepelin wrote evocatively of the difficulties of this time:

[I had to] pay attention to beds, all kinds of furniture, linen, kitchen and table cutlery. . . . I was forced to work laboriously for several months, supported conscientiously and steadfastly by Alzheimer to choose each individual object according to type, size, quality, and price. . . . Alzheimer initially worked without being paid, as I had no position for him and he wanted to be able to spend his time as he wished. In order to integrate him into the clinic, I created the class of scientific assistants. This consisted of researchers, who were free to use the scientific facilities. (Kraepelin, 1987, pp. 116–8)

Alzheimer's marriage had left him wealthy enough to be able to do so and to afford the then luxury of illustrating his articles (Hippus, 1990; Hoff, 1991).

ALZHEIMER, THE TEACHER AND COLLEAGUE

As a teacher, Alzheimer was universally respected and liked. He seems to have been unflinchingly positive in his outlook for the future of science, trying to convey his philosophy that

whoever labors on a difficult task can easily become despaired and discouraged if they only look ahead and see new obstacles that stand in the way of progress. One has to occasionally glance backward to view the distance already traveled. . . . This in turn will benefit our future work. Because not excessive doubt and immobilizing despair help science move forward but instead a healthy optimism and great confidence in the search for new ways to find knowledge since they will certainly be found. (Alzheimer, 1913; Spielmeyer, 1916)

Spielmeyer (1916) wrote of Alzheimer's ability to explain clearly otherwise tedious concepts:

I believe that many people like myself had problems finding their way in the difficulties of modern cortical pathology that was introduced by Nissl. But in Alzheimer's descriptions and illustrations, the "where and how" became apparent . . . this . . . contributed greatly to the stimulation of additional work on the subject. . . .

Thus, in addition to his own contributions to neuroscience, through his ability to mentor and inspire others, Alzheimer's influence was far reaching.

Alzheimer went to great lengths to make each student feel comfortable and was an "affable advisor, who could not be dissuaded even by abuse of his kindness" (Kraepelin, 1921). Meyer (1961) wrote:

His large lab was filled with students from all over the world . . . he taught . . . with enthusiasm and consideration, individually and without letting them know he was overextended. Each morning and afternoon, then later, he came into the lab and went from work table to work table and taught each to recognize details in the microscope and to draw conclusions. . . .

A chain smoker, he would put down his cigar, his pincez dangling on its string, and expound on a topic. Moving on to the next workbench, he would light up again, so that, by the end of the day, each desk would have a cigar butt next to it (Lewey, 1970). Thus, he regularly mentored a large body of students with tremendous enthusiasm.

Among the personal traits that endeared him to his colleagues and students alike was his unflinching modesty (Nissl, 1916; Kraepelin, 1921), which is evident in this excerpt¹ from an unpublished letter (Alzheimer, 1912) to a Dr. William Maloney of New York, a professor of psychiatry who had trained at Munich.

Munich, 12 January, 1912

Dear esteemed colleague,

Your friendly invitation for a psychiatry course in the fall of this year in New York honors me. I thought about it a lot in order to come to a decision on whether to accept this honor. . . .

But I have to finish a lot of work I have started. . . . Please don't be angry with me if I decline . . . I would gladly come . . . later . . . if you still want me. For now,

¹Courtesy of The New York Academy of Medicine Library

I am of the opinion that I have to advance my science rather than to present the little I have at this time. . . .

(signed) Alois Alzheimer

His colleagues respected his precision in his field as well as his personal warmth.

The foremost criterion of Alzheimer's personality was the impression of absolute trustworthiness and reliability, qualities that also kept him in demand as an expert witness . . . clear thinking, hardworking, industrious, and scientifically truthful. . . . His powerful appearance and straight posture, normally reminiscent of a ranking officer . . . his innermost feelings remained locked to others, even to his closest acquaintances. (Kraepelin, 1921)

His colleague Gaupp's observations of his "warmhearted interest in people . . . [Alzheimer] tried to bring joy to soften suffering" (Gaupp, 1916) was echoed by his friend Nissl (1916): "[Alzheimer] had soul . . . [and was] friendly, helpful, selfless. . . ." He loved hiking and nature but "did not understand music . . . did not care about the rest of the arts . . . philosophy was alien to him and he rejected politics . . . [Alzheimer was a] born mediator. . . . He was open to jest and humor . . . [and] refrained from large scale social functions" (Kraepelin, 1924). Alzheimer emerges as a person who, although well liked and sociable, preferred more tranquil and solitary pursuits.

ALZHEIMER'S PERSONAL LIFE

Details regarding his personal life are scarce and much of what follows is from his granddaughter (H. Koepfen, personal communication). The meeting between Alzheimer and his future wife was inadvertently arranged by his friend Wilhelm Erb (of the eponymous paralysis). Erb's patient, a wealthy banker, whom he had cured of syphilis, financed a scientific expedition in North Africa. The banker and his wife accompanied Erb on this trip, but on arrival in Algeria the banker suffered a nervous breakdown. As Erb wished to continue on, he prevailed on Alzheimer to come to Tunis and escort the couple back to Europe. The banker eventually died and Alzheimer married the banker's widow, Cecilia Gessenheimer, with Franz Nissl officiating as best man (Hippius, 1990; Hoff, 1991).

The happy union ended 7 years later with the untimely death of Mrs. Alzheimer in 1901. "Alzheimer was dealt a terrible blow" (Nissl, 1916). Alzheimer's daughters were 1 and 6 years old, his son 5. Alzheimer was 37 at the time and he never remarried. Alzheimer's granddaughter states that his wife's death was the "greatest agony of his life. . . . [Only] concern about

his children and his work . . . helped him in restoring a meaning to his life" (H. Koepfen, personal communication).

For Alzheimer, who "perceived changes as disturbing and uncomfortable" (Kraepelin, 1921), this was a time of many changes at home and at work. Fortunately, his sister, "a marvelous woman who was adored by the children and grandchildren" moved in to care for the children (H. Koepfen, personal communication).

In 1907, Alzheimer presented his children with a house at Christmas. It has remained for generations "the center of [family] life" (H. Koepfen, personal communication). His eldest granddaughter now lives there, the street renamed Alzheimer Gasse (alley). Her mother, Gertrud, Alzheimer's eldest daughter, was 20 when he died of rheumatic endocarditis. Prior to Alzheimer's death, Gertrud married his assistant, Professor Stertz. Gertrud's daughter, Hildegard married an assistant to Professor Stertz, a neurologist and psychiatrist (H. Koepfen, personal communication).

Alzheimer's son Hans became a farmer at the age of 19 and "endured a harsh destiny in the third Reich" because he was half Jewish from his mother's side (H. Koepfen, personal communication). His youngest, Maria, was 14 when he died. She went on to become a children's nurse and married a professor of cartography.

THE BRESLAU YEARS (1912–1915)

In Munich, Alzheimer achieved worldwide recognition as a scientist and teacher but he left to become chair of psychiatry at Breslau. A puzzled Kraepelin noted, "the very best he had to offer our science would be lost in such a position . . . [however] his new position seemed to satisfy him" (Kraepelin, 1987, p. 149) because "he felt uneasiness that his public station did not match his intellectual significance . . . it filled him with satisfaction that he was awarded proper recognition through his appointment at Breslau" (Kraepelin, 1921).

It is not clear why Alzheimer would leave his scientific position to become an administrative head. Perhaps he felt he would be best able to accomplish much more in such a role, as he had observed in his mentors, Sioli and Kraepelin. He had at one point observed "in reality there is no reason why the better institute director should not be the one who, in addition to performing his professional duties, attempts to advance the cause of psychiatry" (Nissl, 1916). Although his goal was finally realized, it was short lived as he became ill and died shortly thereafter. In Alzheimer's obituary, Gaupp (1916) stated, "If his scientific talents had not made him a researcher, he would certainly have become an excellent institution chief."

ALZHEIMER'S LEGACY

In 1909, Alzheimer co-founded the *Journal for the Entire Field of Neurology and Psychiatry* with M. Ledanowsky. The Royal Psychiatric Hospital in Munich was thriving, with Kraepelin at the helm. Kraepelin viewed psychiatry as a field best served by a strong foundation in pathology and neurology. In his introductory lectures to psychiatry, he noted ". . . it is the disturbances in *physical foundation* of mental life which should occupy most of our attention . . ." (Kraepelin, 1910, emphasis is Kraepelin's). He became annoyed with medical students of his time whom he noted had "an extensive lack of neurological knowledge, which should unite neurological with psychiatric training" (Kraepelin, 1987, p. 130). For example, his course in psychiatry for students emphasized training in epilepsy and movement disorders as well as slide preparations of various of these and other illnesses. His 3-week training courses for colleagues "who wished to improve their psychiatric knowledge" consisted of clinical demonstrations, review of the pathological anatomy of psychoses (Alzheimer), topographical histology of the cortex (Brodmann), problems of localization (Liepmann and von Monakow), genetics (Ruedin), serology (Plaut), metabolism (Allers), neurological problems with regard to psychiatric treatment (Katwinke), and, finally, "a short summary" on experimental psychology (Kraepelin) (Kraepelin, 1987, p. 129).

Although he felt that both fields of psychiatry and neurology "cannot be adequately represented by the same scholar," he was just as clear that psychiatric study could not be made in the absence of a strong neurological and pathological foundation (Kraepelin, 1987, p. 68).

Alzheimer embraced these views of Kraepelin, as noted in his statements that the study of clinical psychiatry needs to be explained by the study of pathology and anatomy of the cortex. Meyer (1961) noted that one of Alzheimer's key accomplishments was the integration of neurosciences:

It is to a large degree [Alzheimer's] legacy that . . . neuropathology occupied a central place in the psychiatric sciences. . . . [He] and later the teachers and students at the German Research Institute for Psychiatry, while looking for the physical causes of psychiatric diseases, as a byproduct, established a considerable portion of the morphological basis of neurological disease has, without doubt contributed to the situation that neurology and psychiatry have not developed into separate disciplines [in Germany].

However, Kraepelin's vision of an integrated approach to the study of brain diseases, resting on a foundation of

neurology, pathology, and psychiatry, was set back by an unlikely source, Sigmund Freud (Torack, 1979). Freud, an accomplished neurologist who was introduced to hypnosis by none other than Charcot, was gaining the public and scientific community's attention with his theories on the unconscious as an etiology of mental illness.

Although early on, Freud's theories were dismissed as "a scientific fairy tale" by the chairman of the elite Society of Psychiatry and Neurology in Vienna, they were soon being applauded vigorously by learned audiences that included the Harvard Professor of Neuropathology, James Putnam (Torack, 1978). Previously acknowledged as "the king of psychiatry," Kraepelin relinquished this honor to Freud in 1909 (Thomas and Isaac, 1987). Much of psychiatry embraced psychoanalysis, beginning a schism between the disciplines of neurology and psychiatry.

In addition, there was competition between Kraepelin and the Prague group headed by Arnold Pick (Hoff, 1991). One controversial speculation was that Kraepelin named the disease process described in his laboratory for Alzheimer to gain further recognition for the Munich group (Hoff, 1991; Bick, 1994). Soon after, Kraepelin obtained half a million dollars from a wealthy American to start what was later to become the renowned Max Planck Institute, where research on a unified neuroscience would continue (Kraepelin, 1987, p. 176).

However, within a period of 5 years, three of Kraepelin's major collaborators, Nissl, Brodmann, and Alzheimer, were dead. Kraepelin noted,

When we mention the names Alzheimer (1915), Brodmann (1918), and Nissl (1919), the size of this loss becomes clear with painful clarity. Three researchers of outstanding intellect have died, each one in his own right irreplaceable, all three pioneers [in] . . . the important work . . . [of laying] . . . the physical foundation for mental disturbance. (Kraepelin, 1920)

And of Alzheimer in particular, he noted, "the excellent man and scientist succumbed . . . without having shown us the pathological anatomy of mental disorders, although he was better qualified than anyone else" (Kraepelin, 1987, p. 149).

In the decades after Alzheimer's death, the division between an "organic" neurology and a "functional" psychiatry deepened. However, an artificial segregation of the brain in this fashion does not conform to clinical reality. An outstanding clinician, Alzheimer taught that brain research must be guided by a unified view of the myriad neurologic and psychiatric manifestations of brain disease. The return at the end of this century to a more collaborative view of the various branches of neu-

rosience, especially in AD research, echoes the beliefs and practices of Alois Alzheimer and his colleagues at the beginning of this century and may be as rewarding.

REFERENCES

- Alzheimer, A. *Über die Ohrenschmalzdrüsen* [medical dissertation]. Würzburg, Germany: University of Würzburg, 1888.
- Alzheimer A. Über eine eigenartige Erkrankung der Hirnrinde. *Allgem Zeit Psychiatr Psych-Gerich Med* 1907;64:146–8.
- Alzheimer A. Unpublished correspondence. New York Academy of Medicine Library, 1912.
- Alzheimer A. 25 Jahre Psychiatrie. Ein Rückblick anlässlich des 25-jährigen Jubiläums von Prof. Dr. Emil Sioli als Direktor der Frankfurter Irrenstalt. *Psychiatr Nervenkrankh* 1913;52:853–66.
- Bick K, Amaducci L, eds. *Alzheimer's first case rediscovered*. Padua, Italy: Liviana Press, 1989.
- Bick K, Amaducci L, Pepeu G, eds. *The early story of Alzheimer's disease*. Padua, Italy: Liviana Press, 1987.
- Bick KL. The early story of Alzheimer's disease. In: Terry RD, Katzman R, Bick KL, eds. *Alzheimer disease*. New York: Raven Press, 1994:1–8.
- Gaupp R. Alois Alzheimer Obit. *Münch Med Wochenschr* 1916;63:195–6.
- Hippius H. Alois Alzheimer 14.06. 1864–19. 12. 1915. In: Maurer K, Riederer P, Beckmann H, eds. *Alzheimer's disease: epidemiology, neuropathology, neurochemistry, and clinics*. Vienna: Springer Verlag, 1990:XIII–XIX.
- Hoff P. Alzheimer and his time. In: Berrios GE, Freeman HL, eds. *Alzheimer and the dementias*. London: Royal Society of Medicine, 1991:29–56.
- Hoff P, Hippius H. Alois Alzheimer. Ein Überblick über Leben und Werk anlässlich seines 125. Geburtstages *Nervenarzt* 1989;60:332–7.
- Kraepelin E. *Psychiatrie: Ein Lehrbuch für Studierende und Ärzte. Klinische Psychiatrie, vol. 1*. Leipzig: Barth, 1910.
- Kraepelin E. Lebensschicksale deutscher Forscher (Alzheimer, Brodmann, Nissl). *Münch Med Wochenschr* 1920;67:75–8.
- Kraepelin E. Alois Alzheimer 1864–1915. In: Kirchoff A, ed. *Deutsche Irrenärzte, vol. 2*. Berlin: Springer-Verlag, 1924:299–307.
- Kraepelin E. Memoirs. In: Hippius H, Peters G, Ploog D, eds. *Memoirs*. Berlin: Springer-Verlag, 1987:116–8.
- Lewey FH. Alois Alzheimer (1864–1915). In: Haymaker W, Schiller F, eds. *Founders of neurology*. Springfield: CC Thomas, 1970:165–9.
- Meyer JE. Alois Alzheimer. In: Scholz W, ed. *50 Jahre Neuropathologie in Deutschland, 1885–1935*. Stuttgart, Germany: Thieme, 1961:67–78.
- Nissl F. Alois Alzheimer. *Dtsch Med Wochenschr* 1916;9:426–7.
- Spielmeyer W. Alzheimer's Lebenwerk. *Z Gesamte Neurol Psychiat* 1916;33:1–41.
- Thomas M, Isaac M. Alois Alzheimer: a memoir. *Trends Neurosci* 1987;10:306–7.
- Torack RM, ed. *Pathologic physiology of dementia: with indications for diagnosis and treatment*. Berlin: Springer-Verlag, 1978.
- Torack RM. Adult dementia: history, biopsy, pathology. *Neurosurgery* 1979;4:434–40.