



History

Professor Alois Alzheimer (1864–1915): Lest we forget



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ABSTRACT

December 19th 2015 marks the centennial anniversary of the death of the great Bavarian psychiatrist and neuropathologist, Alois Alzheimer (1864–1915), a man immortalised by the still incurable dementing process described by him in 1906 and firmly established in his name. Notwithstanding the great wealth of research into the history of Alzheimer's disease and legacy, the life of this exemplary clinician remains less than widely appreciated today, and it is the purpose of this brief reminiscence to retell the story of the pioneering neuropsychiatrist in this centenary year of his passing.

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1. Introduction

"During the night from Saturday to Sunday Prof. Alois Alzheimer passed away after many weeks of illness. We lose in him not only our highly esteemed teacher, who will always remain a shining example to us in our scientific work and in the loyal fulfilment of our medical duties, but also and above all a truly fatherly friend whose memory we will never forget." [1]

[The Breslau Psychiatry Clinic, December 21st 1915]

By the end of his life, Professor Alois Alzheimer (1864–1915) had established himself as a well-rounded clinical psychiatrist and leading authority on the histopathology of the cerebral cortex [2] (Fig. 1). Today he is most widely known through the time honoured medical eponym named for him – *Alzheimer's disease* – but his legacy as one of Germany's premiere scientific psychiatrists stretches far more than commonly meets the eye. Alzheimer's untimely death from subacute infective endocarditis at the relatively young age of 51 was cause for much bereavement to his close associates and assistants, and the great losses suffered by the Royal Psychiatry Clinic in Breslau shortly after his passing are emotionally captured in the contemporary newspaper announcement reproduced above. A century onwards, the Professor's life story will help to put these sentiments into perspective.

2. Born in Bavaria

Born into a devout Catholic family in the small Bavarian town of Marktbreit, it was in the early hours of Tuesday June 14th 1864,

that Alois Alzheimer, second child of the Royal Notary Eduard Alzheimer (1830–1891) and his new wife Barbara Theresia Busch (1840–1882), first drew breath. Raised care-free in a well-educated and supportive household, the young Alzheimer was expected to succeed. He completed his early education at a local Catholic school in Marktbreit, but owing to the lofty expectations of his father, was sent off on his own in 1874 to board at the *Royal Humanistic Gymnasium* (now the *Kronberg-Gymnasium*) in Aschaffenburg, where both his father and uncle Karl George—then a Catholic Priest in Grosswallstadt—had once studied. Alzheimer's family moved down to Aschaffenburg in 1878, and his four brothers thereafter joined him at the Gymnasium. Despite losing his mother in 1882, the adolescent Alois excelled in many school activities and passed his final examinations with some distinction in July of 1883. His report card recorded how the enterprising student: *"displayed outstanding knowledge of the natural sciences ... behaved with decency, and evidenced a cast of mind turned positively to the good"* [3].

3. Breaking with family traditions

Alzheimer was the first in his family to embark on a medical career. His father Eduard supported him in this decision and encouraged him to pursue studies in Berlin, then the Mecca of international scientific medicine. Following his father's advice, Alzheimer enrolled in medicine at the Friedrich Wilhelm University on October 15th 1883. He learnt his anatomy from Waldeyer and was influenced by Westphal; Virchow and Koch were in their prime. But even the great medical minds of Berlin were not enough to keep the country boy for long, and within less than five months of commencing his studies, he received his leaving certificate to

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Fig. 1. Professor Alois Alzheimer (1863–1915), the namesake for Alzheimer's disease, passed away a century ago. Courtesy of the National Library of Medicine.

allow for his transfer to Würzburg. Alzheimer clearly favoured the calmer Franconian city to the bustling academic life of Berlin, and so on April 23rd 1884, he officially enrolled at the University of Würzburg where he would continue his medical degree. He was now closer to his family in Aschaffenburg, and knew the town well from his childhood visits there. Alzheimer's older half-brother, Karl Eduard Sebastian (1862–1924), was well established in Würzburg at this stage, and headed the local Franconian Corps Fraternity. Karl recruited Alois to the fraternity in July of 1884, and before long, the supposed-to-be studious medical student was engaging in all manner of extracurricular activities, not surprisingly at the expense of his academic duties. A fencing injury to the left side of his face temporarily cost him his good looks, and a poodle based prank he later pulled on his father made him a laughing stock in Aschaffenburg.

All was not lost however, and towards the end of 1884, Alzheimer began to more seriously commit himself to his studies. Drawing on his childhood love of the natural sciences, he enrolled himself in physics, physiology, zoology and botany courses, but it was his exposure to the art of microscopy in Albert von Kolliker's (1817–1905) laboratory that invigorated him most. Breezily passing his preliminary *Physikum* examinations in 1885, the young medical student embarked on his clinical semester with great passion. He spent the better part of a year learning how to auscultate and percuss, and also attended lectures in pathology, toxicology, and another favourite subject of his, forensic psychiatry. Having exhausted his opportunities in Würzburg at this stage, he opted to complete his seventh semester in medicine in the historical academic Swabian town of Tübingen. Arriving in November of 1886, the promising young Franconian enrolled in Tübingen's Eberhard

Karl University with the financial support of his well to do father. He completed eight courses in only a few months, but made equally vigorous attempts to establish himself socially. It was in Tübingen that Alzheimer personally traversed the freezing Main River in winter after losing a bet to his fellow students, and to this day, a historical record remains in the university archives showing that he was fined three marks for "improper disturbance of the peace in front of the police station" [4]. In his bravado and self-assuring spirit, the physically imposing Alzheimer (he stood at six feet tall) would have won many hearts in Tübingen (Fig. 2), but his stay in the university town was only short lived, and after completing his winter semester there in 1887, he moved back to Würzburg to finish his medical degree.

On returning to Würzburg, Alzheimer commenced embryology lessons under his former microscopy teacher Albert von Kolliker. Alongside Würzburg anatomist Philip Stohr (1849–1911), Kolliker supervised Alzheimer's doctoral thesis 'On the earwax glands'—*Über die Ohrenschmalzdrüsen*— which outlined the early development and histological appearances of the ceruminous glands and their secretions [5]. The import of this 17-page thesis in laying down the foundations for the author's future works in neuropathology can be appreciated by inspecting the expertly executed histological figures, all of which were hand-drawn by Alzheimer himself (Fig. 3). With his medical doctorate under his belt, Alzheimer passed his final examinations with ease, and on June 4th 1888, just



Fig. 2. Alzheimer's massive build and occasional boisterousness earned him the nicknames 'big brute' and 'enormous fellow' in his student days. This photo from around 1884 shows him after his induction into the Würzburg Franconian Corps. Image from Maurer's biography [1].

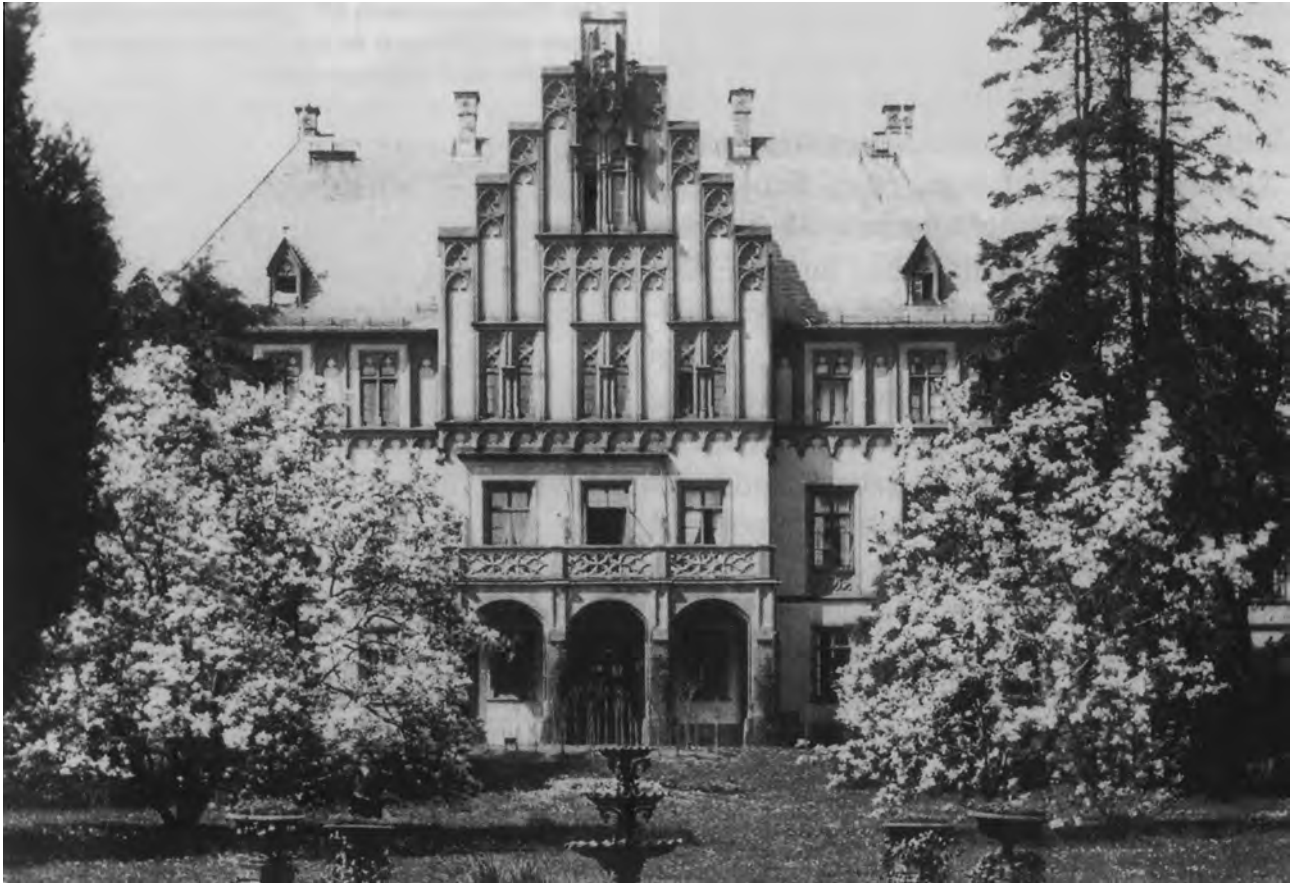


Fig. 4. Alzheimer worked for some 14 years at the *The Municipal Asylum for the Insane and Epileptic* in Frankfurt am Main—the so called ‘Castle of the Insane’—which he helped to renovate and modernise with the assistance of his close colleagues Franz Nissl and Professor Emil Sioli. Image from Maurer’s biography [1].

and encouraging patient freedoms. Duration balneotherapy was instituted to keep patients calm, and Alzheimer became a particularly strong proponent of this method of therapy – ‘*The introduction of permanent bathing proved to be an uncommonly beneficial practice*’ [7], he once stated.

The versatility of Alzheimer’s researches in Frankfurt is marked by the wide array of topics he covered in this period; spinal muscular atrophy, cerebral arteriosclerosis, Binswanger’s disease, hereditary psychosis, epilepsy, senile dementia, and general paralysis—each came under the intensive concern of the budding neuropsychiatrist. Alzheimer’s investigations into general paralysis were at the forefront of his researches. He had prepared some 200 brain tissue slides for his future habilitation thesis on the subject, and was to become widely known as a leading authority on all aspects of both juvenile and adult onset forms of the disease. Alongside the widespread reputation he earned for his meticulous research into this horrid disease, Alzheimer’s interests in general paralysis would also have other rather unforeseen consequences.

5. The diamond dealer’s widow

On the insistence of fellow German neurologist Wilhelm Heinrich Erb (1840–1921), Alzheimer left for Algeria in 1892 to attend to Otto Geisenheimer, a wealthy diamond merchant and personal patient of Erb’s who was thought to be suffering from general paralysis and neurasthenia. When he arrived in North Africa, it was decided that Alzheimer should escort Erb’s prominent patient back to Germany, and although he proved a careful and supportive physician along the journey, nothing could be done for

Mr. Geisenheimer who passed away in Saint Raphael on the way home. Alzheimer accompanied Geisenheimer’s grieving widow—Cecile Wallerstein (1860–1901)—all the way back to Frankfurt, and remained a supportive friend to her over the coming months. The two developed a close friendship and eventually, on the courageous instigation of Miss Wallerstein herself, the psychiatrist and wealthy widow were to become engaged. The couple were legally wedded in April of 1894, but it wasn’t until further arrangements could be made—including Cecile’s conversion from Judaism to Christianity—that a full Church ceremony could be enacted. Having been delayed for some nine months, Cecile was already heavily pregnant with her first child when the formal wedding finally took place in February of the following year.

Through his marriage to Geisenheimer’s well-off widow, Alzheimer became financially independent and fathered three children. His daughter Gertrud (1895–1980) was born less than a month after the wedding, and his only son Hans Eduard (1896–1981) was delivered some 17 months later. The couple’s third child Maria (1900–1977) was born in 1900 and with her arrival the family was completed (Fig. 5). Sadly, Cecile Alzheimer, the matron and sustainer of a happy and vibrant household, grew increasing ill shortly after Maria’s birth and died in February of 1901. Alzheimer’s sister Elisabeth (1872–1968) took over the role of mothering Cecile’s children, but her widowed husband never married again. From what his biographers have collated, we find that Alzheimer was a loving and nurturing father to his three children. In all he inculcated a love for the natural world, and with Hans he shared a special interest in lepidopterozoology. Alzheimer made significant sacrifices for his children and relished family life. In December of 1904, he bought them a summer home in Wessling for Christmas,



Fig. 5. The Alzheimer family, c1900; Cecile and Dr. Alzheimer with their three children Hans, Maria, and Gertrude. Image from Maurer's biography [1].

and it is a testament to his still cheerful nature that he can be seen skipping rope in front of that house in a well preserved photograph taken from that time (Fig. 6). The street outside the house—'Alzheimergassl'—was later named in his memory.

6. Meeting Auguste Deter

In the same year as his marriage to Cecile (1895), the appointment of Chief Physician at the Frankfurt Asylum was made vacant when Franz Nissl opted to leave for Heidelberg to pursue scientific work in the laboratories of Emil Kraepelin (1856–1926). With full support from his superiors, Alzheimer was given the position in July of the following year. Alzheimer kept in close touch with Nissl over this period and made regular visits to Heidelberg where he was introduced to the techniques of microphotography that were being popularised by Kraepelin at the time. He would have enjoyed catching up with his old friend over neuropathology research, but it was back in Frankfurt that he would soon consult the case of his career.

Admitted on November 25th 1901, Auguste Deter (1850–1906), the wife of local railway clerk Mr. Carl Deter, was referred to the Frankfurt Asylum by her family doctor with concerns relating to her long term *weakness of memory, persecution mania, sleeplessness, and restlessness* [8]. She was carefully assessed by Alzheimer the following day when he recorded a meticulous mental state examination of her, and took special note of Auguste's hometown of Cas-sel, where Alzheimer's own grandfather Johann (1797–1882) had once been a teacher. Over the proceeding four days, Alzheimer visited and documented his conversations with Auguste D. He made a preliminary diagnosis of '*arteriosclerotic brain atrophy*' and prescribed regular warm baths as a means to soothe her agitation.



Fig. 6. Alzheimer was very much a family man; here the distinguished doctor jumps rope to entertain members of his family. Image from Maurer's biography [1].

Alzheimer's early interest in the case is marked by the fact that he ordered the clinical photographer at the Asylum (who was named Rudolf) to take pictures of Auguste D. for her file (Fig. 7), and that he personally intervened to avoid her being transferred to another asylum in August of 1902 when her husband could no longer support her stay in Frankfurt.

The re-discovery of Auguste D's original file in 1995 [9], and later neuropathology slides in 1997 [10,11], has given modern neurologists, neuropathologists, and psychiatrists unparalleled insights into the index case of Alzheimer's disease. It will interest Australian readers to know that Professor Manuel Graeber, who originally found Alzheimer's missing pathology slides when working at the University of Munich in the early 1990s, migrated to Australia in 2010, and is now seated in the Barnet-Cropper Chair of Brain Tumour Research at the University of Sydney, where he remains the custodian of some of Alzheimer's original case material (Fig. 8).

7. Leaving Frankfurt

About a year after his wife passed away, Alzheimer felt he should move on from Frankfurt. With some hesitation, he eventu-



Fig. 7. 'Touch with the slow finger of Time, the nutrition of that thin layer, and backward by slow degrees creep the intellectual faculties, back to childish simplicity, back to infantile silliness, back to the oblivion of the womb'—William Osler (1849–1919), May 21st 1894 [26]. Much the same could be said regarding the mental deterioration of Auguste Deter, pictured here in the famous November 1902 photograph found in her original file.

ally resigned from the institution in March of 1903, and transferred to Heidelberg to work with his friend Nissl and new boss Emil Kraepelin. Owing to poor research conditions in Heidelberg and a corresponding vacancy in Munich, Kraepelin soon left for the Bavarian Capital and took Alzheimer with him. The Royal Psychiatry Clinic of the Ludwig–Maximilian University in Munich was being refurbished when the duo arrived in October of 1903, and although Kraepelin was appointed to the directorship, there were no paid vacancies for Alzheimer initially. Tellingly, this did not deter the well-off widower in the slightest, and he proceeded to preside over and transform the fourth floor anatomical laboratory into a world class teaching facility (Fig. 9). Alzheimer greatly enjoyed the freedoms afforded by his new unpaid position, and within just over a month after settling in, he submitted his almost 300-page Habilitation thesis on '*Histological Studies of General Paresis*' to the medical faculty at the Ludwig–Maximilian University [12]. Based on researches initiated in Frankfurt, the work meticulously detailed the microscopic pathology of the cerebral cortex in general paresis, and importantly concluded that: '*pathological histology is a useful complimentary science to psychiatry*' [13]. The thesis was praised by Kraepelin as an '*extraordinary achievement*' and paved the way for Alzheimer's August 1904 appointment as *Privadozent* to the medical faculty at Munich. All the while, Alzheimer continued to direct and teach in his personally funded anatomical laboratory without reimbursement of any kind. He was very generous in his endowments, and even purchased his recently graduated brother Eduard (1867–1948) a new pharmacy in Schwabing to help kick-start his career. Alzheimer's charitable disposition and spirited influence on the clinic in Munich is handsomely related in the following anecdote once told by a granddaughter of his:

"It was Fashing [carnival] in the Nussbaumstrasse clinic in Munich. A poor peddler arrived, completely unexpectedly, with a sales tray full of toys hanging around his neck, offering his wares for sale. This didn't go over well: He was angrily prevented from plying his trade and threatened that Prof. Alzheimer would be brought in, and he would show him a thing or two. 'That is not necessary,' said the peddler mischievously and took off his disguise. Everyone had to laugh. The Professor as peddler! He distributed the toys to the young patients. Yes, gift-giving always gave him great joy." [14]

Alzheimer's perseverance was eventually rewarded, when, on the proposal of Emil Krapelin, he was promoted to Chief Physician at the Munich clinic in October of 1906. He lectured twice a week with his colleague Kraepelin to considerably large audiences and covered a broad range of psychiatric subjects. Certain neurological illnesses also caught the attention of the new chief, and subjects such as epilepsy and Tay-Sachs disease (or 'amaurotic idiocy' as it was then known) especially interested him. Perhaps one of the greatest burdens of Alzheimer's new position, was the expectation that he would regularly fill in for Krapelin when he was away on holiday or writing his famous psychiatry text books. So far as his modern legacy is concerned, however, Alzheimer's faithful assistance to his master in these years would prove something indispensable (*vide infra*).

8. 'Alzheimer's disease'

In the same year as his promotion—on April 9th 1906—Alzheimer received a very important call from Frankfurt notifying him of the death of his former patient Auguste D. who had passed away in the evening a day earlier. True to his '*anatomic doctrine*' of mental disorders, Alzheimer asked for his former patient's brain and file to be sent down to Munich for inspection. He eagerly examined the contents of the file and read the preliminary autopsy report with

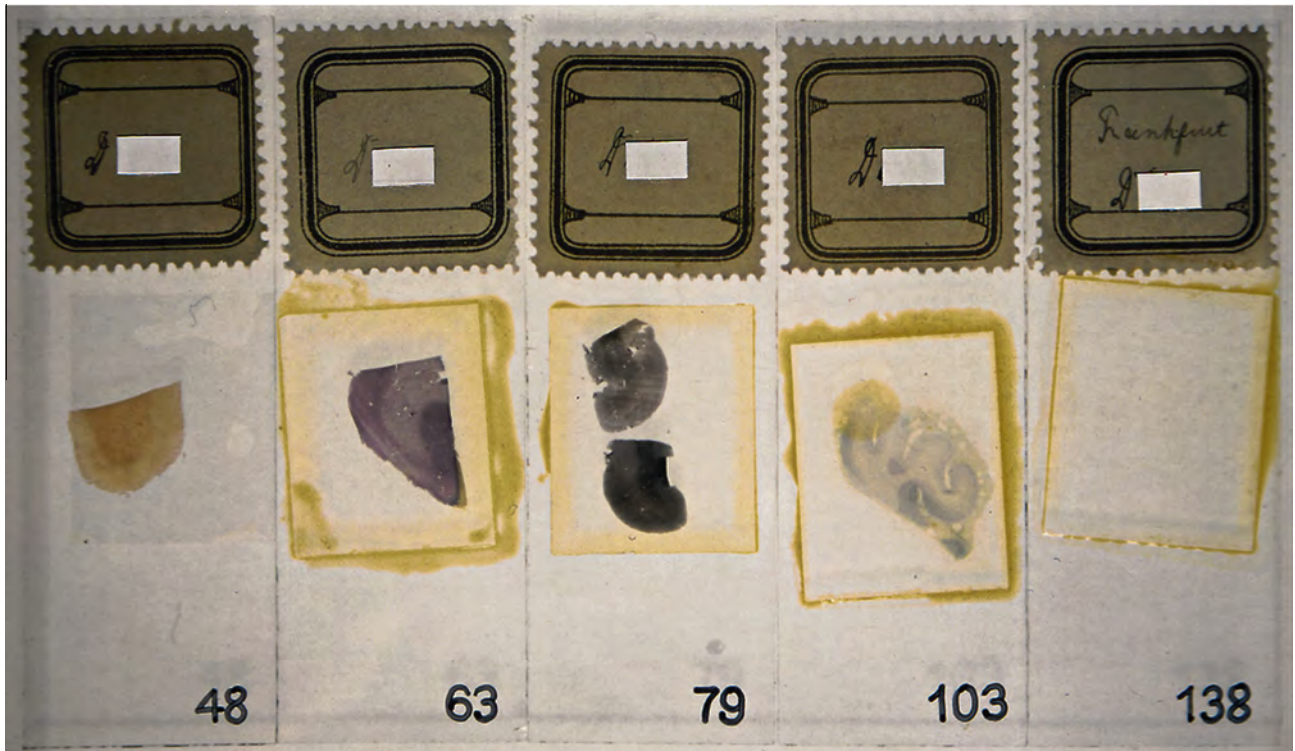


Fig. 8. With the instigation of Professor Kohshiro Fujisawa, mediation of Henry deF. Webster (1927–2012), and international collaboration of other colleagues [27], Auguste D's original neuropathology slides were rediscovered in Munich by Professor Manuel Graeber on September 21st 1997 (personal communication, November 2015). The slides were meticulously studied, stained, and genetically tested, thus dispelling any doubts around Auguste Deter's diagnosis of 'Alzheimer's disease'. A selection of the original slides remain under the custodianship of Professor Graeber in Sydney (including those shown here) and all will eventually be uploaded online. Image reproduced with kind permission from Professor Graeber.



Fig. 9. Many greats came out of Alzheimer's Munich laboratory. This popular 1910 picture alone for example, features Ugo Cerletti (1877–1963), the founder of electroconvulsive therapy (seated second from left), and Frederic Henry Lewy (1885–1950), who discovered the eponymous alpha-synuclein deposits named for him when working in Munich (he is standing on the far right). Alzheimer is standing third from the right, puffing on his trusty cigar.

great interest—*Cause of death: Septicæmia as a consequence of decubitus ulcer; . . . Atrophic cerebri; Arteriosclerosis of the smaller cortical vessels? Pneumonia of both lower lobes; nephritis* [15]. After familiarising himself with all 31 pages of the file, he drafted a summary of the case, and notified his former employer in Frankfurt—Professor Sioli—of his intention to present the case at the 37th Assembly of the Southwest German Psychiatrists in Tübingen in November of that year. On examining the 56-year-old brain themselves, Alzheimer and his colleagues in Munich were surprised to find advance changes of senile dementia.

Alzheimer would have been well familiar with the town he had once studied in as a medical student, but this did not make his presentation at the psychiatry conference in Tübingen any easier. Presented in the afternoon session on November 3rd 1906, Alzheimer's talk 'On a peculiar, severe disease process of the cerebral cortex' was attended by some 88 prominent psychiatrists from all across the continent. The wide range of intelligentsia present would have made for an intimidating audience, but despite the full capacity of his listeners, none were to comment on the brief but epoch making delivery given before them:

"A woman 51 years of age showed jealous fantasies about her husband as a first sign of illness. Soon a rapidly increasing weakness of memory made itself noticeable . . . Her memory was most severely disturbed . . . Slide preparations made with the Bielschovsky silver method show remarkable changes in the neurofibrils. In the interior of a cell that otherwise still appears normal, one or a few fibrils stand out through their thickness and impregnability." [16]

The anxious period of silence following the presentation was only broken by the chairman directing Alzheimer to his seat: "So then, respected colleague Alzheimer, I thank you for your remarks; clearly there is no desire for discussion" [17]. But the seed had been planted, and what was initially deemed 'inappropriate for a brief report' in the conference proceedings was published in full the following year [16]. Alzheimer's works were further advanced by his close colleague and pupil Gaetano Perusini (1879–1915), an Italian aristocrat who shared his master's neuropathological interests. Perusini emphasised the neurofibrillary changes first described by Alzheimer and published a well-illustrated report of four such patients in his classical 1909 paper on the subject: 'On clinically and histologically peculiar mental illnesses in advanced age' [18]. Auguste D's case was reconsidered and the work was printed in a neuropathology text edited by Alzheimer and Nissl.

Not long after Perusini's work, came the new edition of Emil Kraepelin's widely influential *Handbook of Psychiatry* (1910), where, owing to his student's fastidious service over the years and ongoing support in difficult times, the term 'Alzheimer's disease' was originally inaugurated as a succinct title for the still uncertain disease process reportedly first alluded to by its namesake: "Alzheimer described a peculiar group of cases with very severe cellular changes. . . the clinical interpretation of Alzheimer's disease is still unclear" [19]. The readiness with which Alzheimer accepted the appellation is marked by his own passing reference to the eponym in his 1911 paper 'On certain peculiar diseases of old age' [20,21] where he describes another case of the dementing disease. As Graeber's research later pointed out, the original autopsy report of this patient—Johann Feigl—records the diagnosis of 'Alzheimer'sche Krankheit' ('Alzheimer's disease') in 'handwriting closely resembling that of Alois Alzheimer' [22]. The exact motivation behind Kraepelin's introduction of the eponym has been subjected to close scrutiny over the years; some accepting the simple novelty of Alzheimer's observations, others urging for more convoluted explanations [23]. Whatever Kraepelin's incentive was or may have been, it is clearly apparent that the eponym would come to be very

widely popularised, and 'Alzheimer's disease' is now one of the most famous disease names in all of medicine.

9. Final years

Owing to his longstanding interest in scientific psychiatry, and the lack of time available to him to pursue his research, Alzheimer relinquished his position as Chief Physician early in 1909. He was promoted to the rank of extraordinary Professor for the remainder of his term at Munich, and was appointed chief psychiatric editor to Kraepelin's new specialist *Journal of Complete Neurology and Psychiatry*—the *Zeitschrift für die gesamte Neurologie und Psychiatrie*. With these long overdue acknowledgements of his abilities, Dr. Alzheimer at last became a recognisable contender for a university chair in psychiatry. His life-long aspiration to occupy such a position was finally realised in June of 1912 when he was offered a full professorship in psychiatry at the Silesian Friedrich-Wilhelm University in Breslau. But Alzheimer's declining health over the coming months meant that his great achievement was only short lived. He was already unwell with heart failure on the way to Breslau, and although he persevered with his daily duties as Professor, he was eventually forced to take time out of work to seek treat-



Fig. 10. Professor Alzheimer was buried by his wife at the Main Cemetery in Frankfurt—the *Hauptfriedhof Frankfurt am Main*. His wife's relatives are buried in the Jewish section of the same cemetery, where the grave of the great German clinical scientist, Paul Ehrlich (1854–1915), can also be found. This picture of Alzheimer's grave was taken on the morning of Saturday 19th December 2015 (at 10 am) by Kate Miller, a professional Frankfurt based photographer. Centenary wreath and photograph commissioned by the author.

ment. In March of 1913 he checked in to the famous spa resort in Wiesbaden, but the benefits of balneotherapy were fleeting. It was in Wiesbaden that Alzheimer first heard that his chief physician George Stertz (1878–1959) had fallen for his daughter Gertrud, and despite his increasingly ailing health over the coming months, he lived to attend their wedding in May of 1915. But all went downhill for the Breslau Professor from then on. He became bed bound with renal failure in his final months and barely had the pleasure of meeting his son Hans one final time before losing his bearings. The title of Privy Councillor was conferred on him in these hours, but the honour fell on deaf ears. And then finally, in the early hours of Sunday December 19th 1915, the once lucid and lively character that was Professor Alois Alzheimer, quietly passed his final breath in the tender enclave of his loving family. Four days later, he was laid to rest by his wife at the Main Cemetery in Frankfurt (Fig. 10).

10. Conclusion

Professor Alois Alzheimer's death was deeply felt a century ago. Ever since that time, his memory has exerted a humanising influence on practitioners of medicine all over the western world. The centenary of his presentation on senile dementia was widely commemorated in 2006 [24], and it is only fitting that now, a decade onwards, we remember him once more for his hard-won contributions to modern neuropsychiatry. He was after all:

"A physician in the best and noblest sense of the word, a doctor and humanitarian who offered his patients not only his great experience and skill but also his heart." [25]

[Professor George Stertz (1878–1959)]

Conflicts of Interest/Disclosures

The authors declare that they have no financial or other conflicts of interest in relation to this research and its publication.

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