

Neuropathology through the ages

My life between neurology and neuropathology

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Introduction

When the editors of Free Neuropathology, Werner and Tibor, approached me about writing an autobiography for the journal, similar in scope to Sam Ludwin's excellent piece two years ago [1], I confess that I had reservations about writing an autobiography, because I never wanted to talk about myself. However, after a lengthy hesitation and eager discussions with my wife and my former scholar and friend, Hans Lassmann, I realized with a certain degree of doubt that, on the threshold of age 90 years, I could perhaps provide some thoughts about the bridges between clinical neurology and neuropathology for those who might be interested in the experiences of an old neuroscientist.

Thus, in lieu of concentrating on my career as neuropathologist, I wish to instead write about my life in the context of unifying these intrinsically linked but disparate areas within the rapidly progressing scientific world: neurology and neuropathology. This long, and not always easy, path through the wide field of practical and theoretical neuroscience, as well as other interests, was influ-

enced by my late mother, my beloved wife Elisabeth, colleagues, patients, friends, and students whom I met during my professional and private life.

This essay is intended to encourage young colleagues to not concentrate exclusively on experimental neuropathology without also considering the practical part of the neurosciences since there is an urgent need to inspire young neurologists to pursue a double career as both a clinician and neuroscientist in order to promote progress in the neurosciences.

Why the appeal of clinical neurology and neuropathology?

There are three principal reasons to try to unify these two closely connected fields of neuroscience. First and foremost is the aim to help patients suffering from disorders of the nervous system by trying to make an early diagnosis, provide effective treatment, and promote preventive measures. Second, is the ongoing need to apply ever-evolving basic scientific approaches to diseases of the nervous system in order to support the clinical neurolo-

gist in elucidating the pathogenesis of disorders afflicting their patients. Neuropathology should be pursued not just for its own sake but to aid the clinician with the mutual goal to improve diagnoses and enable successful therapeutic strategies for many hitherto incurable disorders. Lastly, there is inherent fascination and fulfillment in using our knowledge to elucidate the structure and function of the nervous system in the healthy and diseased human individual.

Based on this knowledge, the neuropathologist is able to elucidate much of the background of disorders of the nervous system using immunohistochemical, molecular, biological, and ultrastructural methods not only in autopsy material but also tissues from living patients, including biopsies, cerebrospinal fluid, and blood. Often, these images are comparable to modern art (Fig. 1). The selective and interdisciplinary application of these methods may enable the neuropathologist to not only make a reasonable diagnosis of many, though not all, disorders of the nervous system but may also provide insight into the complex pathogenetic cascades that are responsible for the onset and progression of such disorders. In this respect, the neuropathologist is privileged to act as both a physician and a basic scientist.

This retrospective will consider highlights and drawbacks in my 63 years of life between clinical neurology, neuropathology, and private activities. Given my many years of work and limited space herein, may my friends, scholars, colleagues, and co-workers excuse that I regrettably could not consider all of them in this review.

Early life and schooling

I was born May 28, 1931 in Vienna, as the only child to Rosa and Alois Jellinger, both with roots from Upper Austria and Moravia (near Olomouc). My father was an official in the government of Lower Austria; my mother, a trained dressmaker, was a housewife. In the prewar years, I had a wonderful and well-kept childhood filled with summer vacations in the beautiful surroundings of Vienna and in the idyllic countryside, while in the city there were increasing tensions, poverty, and changes in the political atmosphere. I remember Kurt Schuschnigg's radio speech of March 11, 1938, with his concluding sentence "May God protect Austria," after which my father commented, "This will be the beginning of the end."

After Austria's "Anschluss" to the German Reich, I attended a public primary school in Vienna and later, during World War II, a public secondary school (Realgymnasium, also in Vienna), where I received basic education in languages, natural sciences, geography, and history. In 1943, to escape from air raids on the city, many children were sent to live with farmers in the Batschka, then southern Hungary, now Serbia. Once there, we had a wonderful and peaceful time, though the atrocity of witnessing the pogroms of Jewish people was never far from sight or mind.

On our way home we passed the then peaceful city of Budapest, which I would see again during the Hungarian revolution in 1956. Once returned to Vienna, in 1944, we had to change school buildings due to bombing damages. Air raids were still so frequent that I often did not make it home in the evenings but had to instead seek shelter along the way.

In September of 1944, we lost our home due to an air raid and had to wait for a new flat. Around this time, I attended one of the last performances of Schiller's Wallenstein trilogy of plays featuring the famous actor Werner Krauss in the Vienna Burgtheater. Soon afterwards, all theaters were closed. On April 13, 1945, during the battle between German and Russian armies in the city of Vienna, I had my first medical "experience" by cleaning up brain tissue of Russian soldiers who were killed by the projectile from a German tank. After my father died in a Russian POW camp in 1947, my mother and I were left alone to overcome the difficult times after the end of the war. She worked in her former profession as a dressmaker and I became tutor of children.

In 1949, I graduated high school summa cum laude. In that final year, our class contained 18 boys and, when we had our final exams, I got excellent marks (Fig. 2). After graduation, our class, led by our Latin teacher, traveled to Rome and Naples, where we enjoyed arts, cuisine, and life in Italy. To this day, I remain grateful to my many teachers who encouraged me to liberally approach history and natural sciences. Years later, one of my favorite high school teachers became a patient in my clinic with myasthenia gravis, which we treated with success. Over the years, my classmates and I met several times at reunions to remember and discuss previous experiences. The last meeting was 2009 to celebrate the 50th anniversary of our graduation.

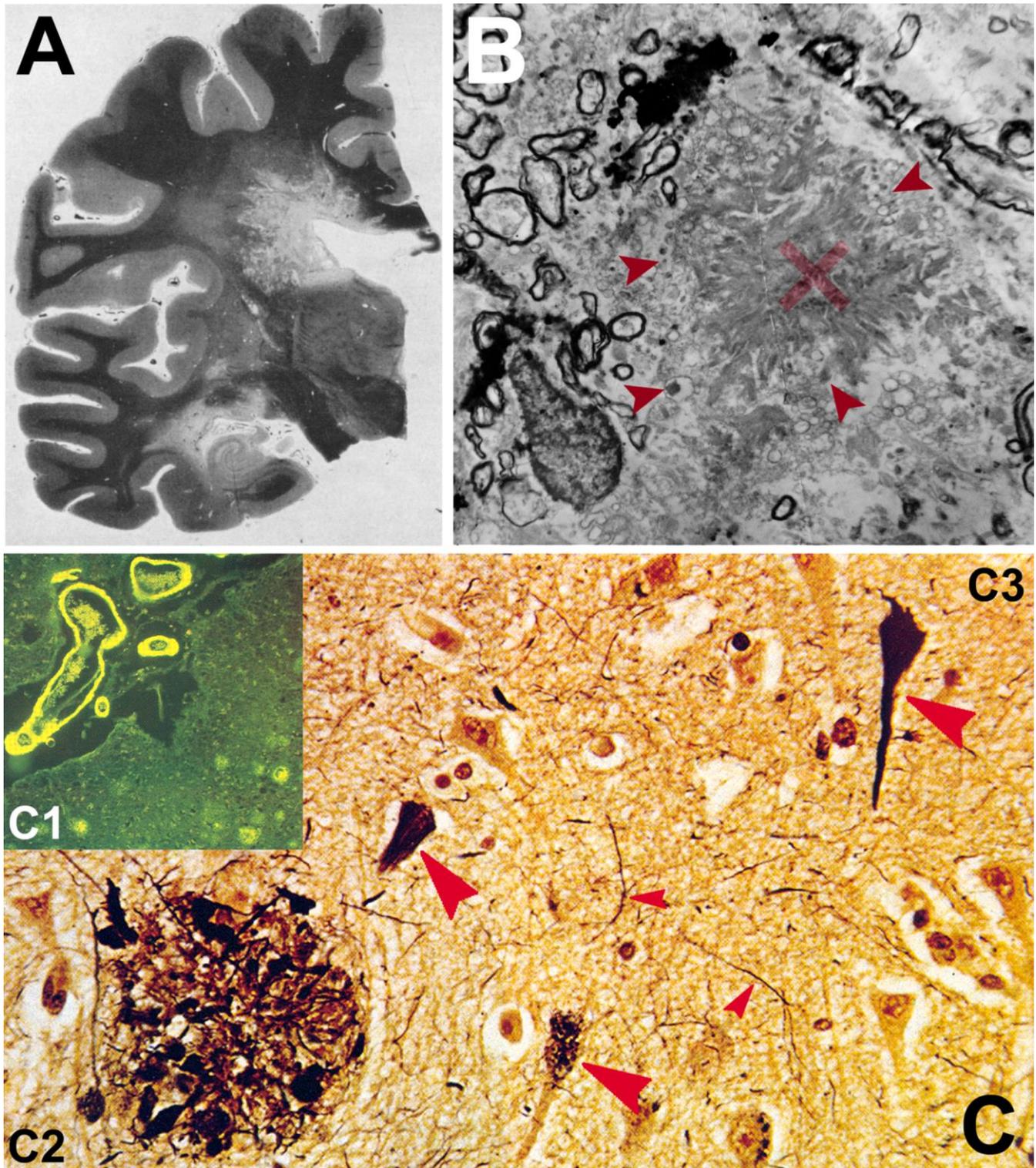


Fig. 1. (A) MS-like autoimmune encephalitis after repeated subcutaneous injections of lyophilized calf brain cells in male aged 51 years with hemi-Parkinson syndrome. Left hemisphere with prominent periventricular demyelinated lesion and multiple demyelinated plaques in cortex and subcortical nuclei. From [2] (B) EM image of focal (core) plaque in hippocampus showing dense accumulation of thick amyloid fiber bundles, surrounded by dystrophic neuritic endings and hyperintense structure of myelinated axon. (x 4000). Photo: K.A. Jellinger. (C) Major histopathological changes in Alzheimer's disease. (C1) Amyloid deposits in the neuropil (plaques) and vasculature (CAA) (congo red stain). (C2) Neuritic plaque with dystrophic neurites (Bodian stain). (C3) Neurofibrillary tangles (large arrows) and neuropil threads (small arrows) (Bodian stain). From [3].

Medical school and beyond

In 1949, I entered the Medical Faculty of the University of Vienna, where the circumstances of medical education were made far more difficult due to the sequelae of the war. For example, we worked in the anatomy theater in winter with glassless windows and without warm water. Despite this, and with eight of us were working on a corpse, we succeeded thanks to the influence of our professor, Alfred Gisel, a wonderful teacher and enthusiastic anatomist, who, in addition, was medical chief of the Austrian Red Cross.

The curriculum had basic subjects like anatomy, chemistry, physics, and physiology for 2 years, followed by 3 years of theoretical and practical training, beginning with pathological anatomy, physiology, pharmacology, and clinical specialties. Most of our teachers were outstanding, some of them scientists of high reputation, such as: Prof. H. Tuppy, chemistry (Nobel Prize candidate); Prof. F.T. Brücke, pharmacology; Prof. G. Schubert, physiology; and Prof. H. Chiari, head of pathological anatomy. During my studies, and despite regular grants, I supported myself with work as a paramedic for physically disabled people, as a tutor for children and students, and as a writer of short stories for newspapers and magazines.

Our clinical teachers were very dedicated and regularly organized seminars and clinical practicums, but the majority of teaching was much less practical but more formal and didactic than in the new curricula. In December 1955, I finished my medical studies, but had to wait for my graduation due to administrative delay since mine was the first

“Promotio sub auspiciis Praesidentis rei publicae,” the highest possible distinction for academic achievements in Austria, in medicine since the end of World War II. In the meantime, I worked as guest doctor without salary in the Franz Josef Hospital in Vienna, within the department of Internal Medicine and Surgery, directed by Prof. Herbert Kraus, later chairman of the first Department of Neurosurgery of Vienna Medical School. On April 14, 1956, I was promoted to Doctor of Medicine “sub auspiciis praesidentis rei publicae,” which I received in the uniform of an officer of the Austrian Red Cross (Fig. 3).

Hospital years and first experiences

In 1956, once the Soviet army left Budapest subsequent to the bloody uprising of the Hungarian people, I went with a Red Cross convoy to deliver medical supplies and blood bottles to the liberated citizens of Budapest. We were lucky to return to Vienna before the Russian army reconquered Budapest.

I enjoyed clinical medicine but my major interest was neuropathology. On January 5, 1957, I began as a postdoctoral fellow (wissenschaftliche Hilfskraft) at the Neurological Institute (NI) a.k.a. Obersteiner Institute of the Vienna Medical School headed by Hans Hoff, who was also chairman of the neuropsychiatric clinic. Founded by Heinrich Obersteiner in 1882 as a box that was subsequently expanded by Obersteiner's personal expenses, the NI became the first interdisciplinary institute of neurosciences and was visited by many scientists from Japan, the USA, and other countries.



Fig. 2. Our graduation class 1949 together with H.R. Klieba, principal of the Realgymnasium Wien VIII, and Dr. Seifert, our class teacher. KJ second left in the first row.



Fig. 3. Promotion to Doctor of Medicine 1956 in the uniform of a Red Cross officer, with Dr. Heinrich Drimmel, Federal Minister of Education and Science.

Obersteiner edited a series of publications under the title “Arbeiten aus dem Obersteinerschen Institut” and books about basic neuroanatomy and pathology. Together with the Edinger Institute in Frankfurt, the NI became one of the leading centers of neurosciences in the world until the beginning of World War II, when it was directed by Oskar Gagel, an experienced neurooncologist. The NI, together with the Institute of Histology, occupied the first floor in a building of preclinical institutes, next to the general hospital of the Vienna Medical School (Allgemeines Krankenhaus/AKH). Parts of this area had been bomb-damaged during the war.

My first venture into neuropathology was to save and reorganize the large collection of slides that included material from major brain diseases. It was through this work that I learned the basics of neuroanatomy and neuropathology. The NI had a huge library, originally compiled by Obersteiner himself, which was a treasure trove of rare and antique books, including an original edition of Thomas Willis' “*Circulus arteriosus cerebri*,” one of the first descriptions of brain vasculature. In 1958, Prof. Franz Seitelberger became director of the NI (Fig. 4). In the same year, I met and immediately fell in love with Elisabeth, a beautiful and clever girl aged 21 years, born in Brno (then CSSR), who studied English, Russian, and history of arts. We attended theaters, operas, concerts, and frequently met in the university library. Elisabeth and I married on August 17, 1960.

Training progress

During the following years, I was trained by Franz Seitelberger, an internationally renowned neuropathologist with particular interest in metabolic and neurodegenerative diseases of the nervous system, who later became dean and rector of the University of Vienna. I was in charge of brain autopsies (600 to 1000 per year) and diagnostic workup of neurosurgical biopsies.

My early scientific work concerned acute demyelinating encephalitis following injections of lyophilized calf brain cells in a patient suffering from Parkinson's disease (PD) [2] (Fig. 1a). This particular case, which closely resembled those of patients who received rabies vaccinations in Japan, was later re-published as acute autoimmune demyelinating encephalitis [4]. Other projects included studying the neuropathological side effects of the 1958 influenza epidemic and the neuropathology of Spring-Summer (tick-borne) encephalitis in Austria, which we described in detail.

In parallel to my work at the NI, I underwent specialization in neurology and psychiatry as a guest doctor at the University Clinic of Neurology and Psychiatry in Vienna, headed by Hans Hoff, between January 1958 and December 1963. Among my tutors were Klara Weingarten, an excellent clinical neurologist, and Franz Gerstenbrand, later chairman of the Clinic of Neurology, Medical University Innsbruck. We examined patients, both clinically and neuropathologically, with chronic coma or apallic syndrome (now unresponsive wakefulness syndrome) following head injury and those who suffered hypoxic brain damage and found a close relationship between the pattern of brainstem lesions due to intracranial pressure, the state of consciousness, and clinical outcome.

In addition to hospital work, I was assistant to Prof. Hoff's lectures in neurology, which was often difficult since he wanted the patients' histories and clinical statuses to be in exact accordance with his neurology book. I also heard lectures by Prof. Herbert Reisner, an excellent neurologist and psychiatrist, who later became chairman of the Clinic of Neurology of the University of Vienna. After training in neurology, I worked in the Division of Psychiatry, where I got experience in all kinds of psychiatric disorders. On free weekends, I worked as a voluntary health officer with the Red Cross.

On January 1st, 1960, I was promoted from assistant to consultant (Oberarzt) at the NI. I studied encephalitis and myelitis following poliomyelitis vaccination and movement disorders (progressive pallidum atrophy and striatonigral degeneration) with Erwin Neumeier, who unfortunately died early. In 1961, Elisabeth and I attended the International Congress of Neuropathology in Munich where we met all the top scientists in this field. In 1962, after a lecture on chronic vascular myelopathy at the 25th Reunion Neurologique in Paris, I became Membre associé à titre étranger (associate foreign member) of the French Neurology Association. During that time, many excellent neuroscientists visited the NI and lectured there, such as Hugo Spatz, Hans Jacob, Wilhelm Krücke, chief of the Max Planck Institute of Brain Research in Frankfurt, Webb Haymaker, chief of the Armed Forces Institute of Pathology (AFIP), and Ludo van Bogaert of Bunge Institute in Antwerp, Belgium, for whom I had the honor of translating his lectures. A number of postdocs and research fellows, particularly from Japan, were trained in the NI, such as Mansori Tomonaga, Professor at Tokyo University (his charming wife was a wonderful soprano singer), Riki Okeda (who counted cells in the pons during the night while listening to classical music), and many others (see [5]). It was an exciting time in the international neuroscience community!

Between February and August 1963, I worked part-time as guest at the Institute of Pathology,

Vienna Medical University, chaired by Hans Chiari, where I performed general autopsies and brain cutting. I detected the first case of clinically-suspected Creutzfeldt-Jakob disease (CJD), which I “stole” in order to study it histologically, with the consequence that I was dismissed from the morgue. This was the end of my training in general pathology, but the relations with this department remained excellent. Between 1963 and 1974, I additionally worked two afternoons each week as chief of the outpatient service of the Anton Proksch Institute, a therapy facility for alcoholism and addiction, in order to supplement my low salary as a university assistant. With Wichard Kryspin-Exner, later chairman of the Department of Psychiatry, Medical University of Innsbruck, a number of papers about the course and prevention of alcoholism were published.

Full-time neuropathology

In the following years, in addition to routine postmortem neuropathology and diagnostic biopsy work, I examined vascular spinal cord pathology and commented on Zülch's vascular “borderline zones.” Other subjects included spinal cord injuries, in particular, cervical hyperextension trauma with vascular complications. In January 1963, I earned board certification as specialist (Facharzt) in neurology and psychiatry and returned as a full-time consultant to the NI.



Fig. 4. Briefing with Prof. F. Seitelberger (left) and Dr. H. Hoff (right) in the Neurological Institute, 1958.

In 1965, a postmortem study of a series of anoxic-vascular brain lesions resulting from complications of open heart surgery caused quite an outcry in the surgical community, but, as a consequence, the incidence of complications was reduced due to changed modalities and techniques in cardiac and vascular surgery. At the International Congress of Neuropathology in Zurich, I gave a lecture on the neuropathology of coma and postcomatose encephalopathies. Then, I began experimental studies of spinal cord vasculature in cats and other animals, working together with the neurosurgeon Heinrich Brenner in the experimental laboratory of the department of surgery. These studies, together with large human postmortem material, were the basis for my PhD thesis "Zur Onkologie und Pathologie der Rückenmarksdurchblutung" ("On the oncology and pathology of spinal cord blood circulation"), published in 1966 by Springer Verlag Wien. On January 19, 1966, I was granted the *Venia Legendi* (Dozentur, lecturer) in neurology, neuroanatomy, and neuropathology, and became chief of the Division of Neuropathology of the NI Vienna. In addition to routine diagnostic work, I lectured about general and specific neuropathology, and performed regular brain cutting sessions for students and colleagues who were interested in neuropathology (Fig. 5). In the same year I received the Kardinal Innitzer Award for Promotion of Medical Research.

Atypical encephalitides and spinal cord circulation disorders were presented at the 1st meeting of the CSSR Neuropathology meeting in Prague in September 1966, where Prof. Bednar, chairman of the Institute of Pathology of Prague Medical School, was a charming host. 1967, with W. Sturm, a series of radiation injuries of the cervical spinal cord with relation to the applied radiation doses was published. At that time of progressing international congresses, publications and oral presentations were increasingly presented in English, and I published many articles in *Acta Neuropathologica*, founded in 1961 by Franz Seitelberger, who was editor-in-chief until 1987.

The focus of clinical work and research were brain tumors, which were discussed in weekly clinico-pathological conferences with the Department of Neurosurgery. Tumor cell imprints for rapid diagnosis were introduced, which were confirmed by histology with up to 95% concordance.



Fig. 5. Brain Cutting with (left to right) Hans Lassmann, Gernot Wöber (neurosurgeon), KJ, and Georg Spiel (later pediatric neurologist) in the Neurological Institute, 1966. Note the numerous fixed brains in the glass jars in the back.

In 1970, invited by M. Mossakowski, head of the Polish Academy of Sciences, I lectured about various neuropathological subjects in Warsaw, Poznań, and Kraków, and was impressed by the lifestyle of the political upper class. At the 6th International Congress of Neuropathology in Paris, where I spoke about delayed radiation lesions of the spinal cord, Elisabeth and I were overwhelmed by the charm of France's capital. In Verona, the neuropathology of the "apallic syndrome" after head trauma was presented. In the same year, Seitelberger and Igor Klatzo, from the NIH, Bethesda, USA, organized an international symposium on axons and axonal flow, where I discussed neuroaxonal dystrophy in humans.

In October 1971 Herbert Budka joined us and became my assistant for more than three years. We shared routine diagnostic neuropathology. Herbert recently described the situation and further fate of the NI, and became director of the Clinical Institute of Neurology, the successor of the NI after its transfer to the Allgemeine Krankenhaus (see [5]). In 1972, I lectured in Baltimore, Kansas City (J.J. Kepes' invitation), and New York.

Heinz Regele, later chief of pathology in Linz, and I observed peculiar things that were described later by others. This included, in patients with brain death, finding cerebellar material around the cervical and thoracic spinal cord, which dropped down as sequelae of cerebellar incarceration due to increased intracerebral pressure, later reported as a

characteristic finding in brain death (*vita reducta*). With Lothar Kucsko, a highly experienced pathologist and heavy smoker, a postmortem transorbital puncture of the brain in a patient with clinically-suspected CJD was performed. Under the electron microscope, I saw ruptured cell membranes, which I initially interpreted as postmortem artifact, but Peter Lampert from the AFIP published these findings as typical lesions in CJD [6] - so we were too late!

In the course of routine examination of brain tumor biopsies, I detected a large B cell lymphoma in the parietal lobe of a famous conductor. Erwin Deutsch, chairman of the Department of Internal Medicine, did not believe in my diagnosis, since whole body examination did not show any malignancy. So I sent slides to Harry Zimmerman, chairman of neuropathology at Montefiore Hospital in New York, one of the world's best neuropathologists and mentor to generations of neuropathologists, who confirmed my diagnosis. This patient survived for more than 12 years. Autopsy revealed a generalized immunocytoma, but no tumor residual in the brain. Together with Harry and Seitelberger, in 1974, an international symposium on malignant lymphomas of the central nervous system (CNS) in Vienna was organized, where experts discussed the classification of primary lymphomas of the CNS.

In 1972, traumatic vascular diseases of the spinal cord were reviewed for the Handbook of Clinical Neurology. With T. Radzskiewicz, an excellent expert in lymphomas who unfortunately died too soon, a large collection of primary and secondary lymphomas of the CNS was published. In 1973, Hanno Bernheimer, Oleh Hornykiewicz (who died May 26, 2020), Walther Birkmayer, Franz Seitelberger, and I published a highly-cited paper (currently 3,005 citations) about dopamine in the syndromes of Parkinson and Huntington. It was one of the first studies that correlated the neuropathological findings in the striatonigral system (semiquantitative assessment of neuronal loss in substantia nigra) and the biochemical data (dopamine and its metabolites) in a large number of autopsy cases [7].

During my time at the NI and afterwards, I extended brain autopsy service to several institutions outside of Vienna, including the neurological hospital in Linz. Since I had no car, I traveled by train. Once, on the return trip to Vienna, while transporting sacks with freshly-dissected brains soaked with

formalin to be examined in the NI, an acute train stop resulted some brains falling out of the sacks. I was almost arrested as a suspected mass murderer but the awful smell of formalin explained the reality.

Later career

In 1973, I was offered the position of chairman of the Division of Neuropathology at the Institute of Pathology in Zürich, but as I was number two on the list, Reinhard Friede was instead appointed. In February 1974, I was offered the position of professor and chairman of the Department of Neuropathology at the Medical University Düsseldorf, Germany, which after 2 years of unsuccessful negotiations and for family reasons, I had to decline. Wolfgang Wechsler, then at the Max Planck Institute at Cologne, got this position which he held until his retirement in 1998.

In 1975, in collaboration with Andras Guseo, a young neurologist from Székesfehérvár, Hungary and guest in the NI, the patterns of inflammatory perivascular infiltrates and their impact on the type and prognosis of multiple sclerosis were published. This was the beginning of a fruitful cooperation with the group of Hans Lassmann, then chief of the Neuroimmunology Division of the Austrian Academy of Sciences and later of the Department of Neuroimmunology at the Institute for Brain Research in Vienna. In the same year, together with Felicia Slowik, a young neurooncologist from Budapest and guest in the NI, a large collection of biopsy and autopsy-proven meningiomas was examined with impact on the histological specificities and prognostic relevance of various subtypes.

In between, I was offered the position of head of the division of Neuropathology at Miami School of Medicine, FL. On this occasion, Elisabeth and I toured through the USA and I lectured at various universities. We got a deep impression about the way of living in the USA, which differed considerably from ours. A few months later I was offered the position of head of the Division of Neuropathology at Case Western Medical School of Medicine, Cleveland, OH (successorship of R. Friede). However, due to personal and family reasons, I declined all these positions.

Since it was impossible to get an independent position in Vienna,, I finally decided to accept the position as Head of the Department of Neurology

at Lainz Hospital, one of the oldest municipal and teaching hospitals in Vienna. It was built between 1908 and 1913 together with a large geriatric centre on the occasion of the 60th anniversary of Emperor Franz Josef's regency and was equipped with all facilities of modern medicine. During Julius Tandler's time, a famous anatomist and counselor of health of the City of Vienna, Lainz Hospital became "a second university." In 2006 it was fused with the nearby Neurological Hospital Rosenhügel as a neurological center and is currently named Clinic Hietzing.

On October 12, 1976, I was appointed chief of the department of Neurology and became director of the Ludwig Boltzmann Institute of Clinical Neurobiology in January 1977, as successor of Walter Birkmayer, one of the "fathers" of research in PD. The Ludwig Boltzmann Society, named after the Austrian physicist Ludwig Boltzmann, was founded 1960 as an Austrian network of specialized research institutes in the fields of medicine, humanities, and social sciences, all of which were sponsored by the City of Vienna and the Austrian government. In 2002, the society was reorganized and the number of institutes greatly reduced.

So, one career ended and a new area of neuroscience began, although many within the Vienna neurological community reacted with skepticism whether a neuropathologist would be able to manage a new clinical department. And, indeed, the beginning was difficult. The department had 75 beds, part of them still occupied by geriatric patients, a waterbed ward, two trained nurses, and some auxiliary personnel but only a minimum of technical equipment. I had to find coworkers, some of whom needed a training position, which was not easy to organize. In addition to the clinical department, which occupied the ground floor of the building, the histological and neurochemical labs on the second floor had to be equipped and prepared for functioning.

My first coworkers from the previous neurogeriatric department were M. Podiwinisky, an elderly neuropsychiatrist, and Roda Weiss, a young Armenian doctor born in Odessa and married to a Viennese lawyer. Soon afterwards, Herbert Flament and Hannes Schmidt, two young neurologists in training from the nearby Rosenhügel hospital, and two specialists, Peter Kothbauer, nephew of the former Minister of Health, Ingrid Leodolter, and Edith Sunder-Plassmann, wife of a neurosurgeon,

completed my first crew. Kothbauer later had to leave the department. Within a few years, I finally gathered a crew of 12 neurologists, most of them becoming excellent clinicians. For the neuropathological lab, Mrs. Veronika Rappelsberger followed me from the NI. Without her help, I would never have been able to do my routine work and research in neuropathology. I had to perform brain autopsies and biopsies for the whole hospital and geriatric center and biopsies for a large neurosurgical department. Since I received no funding from the city, I had to pay my lab assistant from my own pocket. The chief of the neurochemistry lab was Peter Riederer, an experienced neurochemist who had graduated from the Technical University Vienna and, since 1971, had worked together with Walter Birkmayer in the Ludwig Boltzmann Institute (LBI) of Neurochemistry, the predecessor to the LBI of Clinical Neurobiology. Later, a number of students and postdocs joined us.

In addition to my new double functions, in 1976, I was appointed editor-in-chief of *Acta Neuropathologica*, after having acted as supplementary editor for several years. Between 1976 and 1981 I also edited the series "Current Topics in Neuropathology" with selected papers from meetings of the Austrian Society of Neuropathology. In total, I edited or co-edited 10 books.

With Peter Riederer, Wolf-Dieter Rausch, a dedicated post-doc who is currently Professor of Neurochemistry at the Veterinary University of Vienna, Paul Kruzik, and others, we examined the biochemistry of hepatic encephalopathy and the mode of action of L-deprenyl in the human CNS. Peter left Vienna in 1986 and became Professor of Neurochemistry and head of Clinical Neurochemistry at the Psychiatric Clinic of Würzburg Medical University until his retirement in 2008. We had a successful scientific cooperation and became close friends with him and his wife, Inge. Graduate engineer Ildiko Wichart, a young neurochemist from Budapest, also joined our group and worked with us for many years even after her retirement.

In addition to clinical service, with 1,700 to 2,000 in-patients and an outpatient service with more than 15,000 consultancies per year, our department had to perform the neurological and psychiatric consultant service for the whole hospital complex. The clinical crew published about brain tumors, intramedullary metastases, and lymphomas; while the neurochemistry group wrote about

neurotransmitters in metabolic encephalopathies, hepatic coma, brain infarcts, and deprenyl in the human brain. In June 1976, I gave lectures about CNS involvement by malignant lymphomas/leukemias and radiation-induced lesions of the CNS in New York, Philadelphia, and Baltimore. In 1977, I received the award of the Vienna University Foundation, and in 1979 the Award of the Medical Scientific Foundation of the City of Vienna.

We organized the first neurooncology group in Vienna, in which the preoperative examinations were done by my department, neurosurgery by the Hospital Rudolfstiftung (head H. Brenner), biopsy diagnosis, combined radiation, and polychemotherapy according to the COMT scheme, and post-operative care by our department. We introduced modern CSF cytology, and studied cytological changes of gliomas caused by chemotherapy. The clinical crew was organized in a way that everyone had their own specialty: clinical neurology (Edith Sunder-Plassmann, Herbert Flament, Roda Weiss, Andrea Vass, Maria Grisold, Dieter Volc); and neurophysiology (Rembert Vollmer, Wolfgang Grisold). With Alexander Meng, son of a Chinese professor of pediatrics and a Viennese mother, and a specialist in acupuncture and Traditional Chinese Medicine (TCM), a successful multidisciplinary pain clinic was organized.

Later, we performed the first biomarker screenings (total tau and β -amyloid-42) in CSF for the early diagnosis of Alzheimer disease (AD). The department got the first transmission Zeiss EM 9 microscope in a city hospital, transferred from the LBI of Hematology (chief Alois Stacher, both an experienced hematologist and dedicated politician).

In 1978, our neurochemistry group studied the activity of tyrosine hydroxylase (TH), the key enzyme of the dopaminergic system in the brain and adrenal medulla. We found that the TH activity was not only reduced in the striatonigral system by up to 90% but also in the adrenal medulla by about 74% [8], a fact that questioned later research about transplantation of adrenal glands in patients with PD and would go on to save billions of dollars.

In the background of this research, a laboratory for muscle diseases and electromyography was opened with Wolfgang Grisold, one of the best clinical neurologists and neurophysiologists. He later became chief of the Neurology Department of Franz Josef Hospital, the LBI for Neurooncology,

and is currently secretary of the World Federation of Neurology.

Between 1975 and 1980, I wrote the chapter of pathology of the nervous system for several editions of the working book of pathology, edited by J.H. Holzner, successor of M. Chiari as chief of pathology of the Vienna Medical University. In 1978, reviews about vascular tumors and malformations were published, and lectures were given in New York, Bethesda, and Washington (International Congress of Neuropathology). Again in collaboration with Peter Riederer, the first Austrian-German brain bank was organized and we collected a host of neurodegenerative diseases, AD, PD, and normal controls, all of which was later transferred to Peter's lab in Würzburg. In 1980, with Filippo Gullotta, first chairman of the Department of Neuropathology at Münster Medical School, Germany, and Mirosław Mossakowski from Warsaw, the First European Congress of Neuropathology in Vienna was organized, bringing together many neuropathologists in our city.

In the following years, many new associates joined our group. Christian Bancher was active in both clinical and neuropathological research, with a focus on neurodegenerative and senile brain diseases, and Werner Paulus, a postdoc from Germany, worked on brain tumors, lymphomas, and iron and ferritin in PD brains. He later became chairman of the Department of Neuropathology at Münster Medical School and editor-in-chief of *Acta Neuropathologica* until 2019, and is the current editor-in-chief of *Free Neuropathology* since 2020.

My working day was full and split. Often, in the mornings, I went to pick up fresh brains from the nearby mortuary and carried them over the yard to the laboratory to dissect them for the brain bank, with one half being deep frozen for neurochemistry and the other fixed in formalin for histological examination. The first part of the day was dedicated to clinical work and, after the morning conference with my coworkers, I went on clinical rounds twice a week and every Saturday. In between, I saw patients in the outpatient department or had conferences with other clinicians or neuroscientists. Meals were eaten together with doctors and nurses in the kitchen of the ward. The afternoons were dedicated to neuropathology, brain cutting, and sign out (about 700 brains per year), or research in the EM lab (Fig. 1b). In addition, I prepared a catalogue of all in-patients and their diag-

noses on cards intended to be computerized later, which unfortunately was not possible at that time. I routinely read the letters of dismissal (discharge) of patients, since all of my associates had to prepare these letters spontaneously – “trust is good but control is better.” This usually lasted until night. Besides the clinic and the institute, I ran a small private praxis once or twice a week, together with Elisabeth, who was an ideal and helpful companion, loved by most of our patients. In addition, I served as court-certified expert witness for insurance companies or courts. So, my clinical duties were as broad as my scientific interests, which suited me very well and was tolerated by Elisabeth with great patience.

International activities: the roaring eighths

In 1980, I was invited to speak by Prof. Hoshino, chairman of the Department of Neurosurgery, Teikyo University, Tokyo, one of the founders of high dose irradiation of brain tumors. In addition to lecturing, I reclassified the tumor collection of this department. During my 3-week stay in Japan, I got deep insights into the Japanese lifestyle, culture, and cuisine, not only in big cities but also in the countryside. Also around this time, I presented holoprosencephaly and agenesis of the corpus callosum at the meeting of the American Association of Neuropathology in Vancouver, Canada.

In 1982, together with F. Seitelberger, and H. Lassmann, the 9th International Congress of Neuropathology in Vienna was organized, one of the most important meetings of this specialty in Vienna that was visited by about 700 specialists from all over the world. At a meeting about advances in neurotraumatology in Milan, October 1982, I presented brain stem involvement in blunt head injuries and Elisabeth and I were welcomed by our Italian colleagues and we thoroughly enjoyed their hospitality and the flair of the city.

Again with Peter Riederer, metabolic brain diseases, Dopa and tryptamine binding, selegiline effects, and lisuride in the treatment of PD were studied, thus broadening my experience beyond neuropathology. At a 1984 symposium on Parkinsonism in Bermuda, I was impressed by this wonderful island. Between clinical work, congresses, routine neuropathology, and publishing scientific papers, my editorial work for *Acta Neuropathologica* occupied much of my private time. Since we had

no computers or internet and I often read articles and proofs during bathing in our home, the journal caused some tension in our private life.

Many of the clinical and clinicopathological presentations were performed together with members of my team, in particular with Wolfgang Grisold, one of the best neurologists I ever met, Dieter Volc, later chief of the Parkinson service in a private clinic, and Mrs. Elisabeth Kienzl, student of the Technical University Vienna and one of my best assistants in the laboratory. With Andreas Rett, an experienced neuropediatricist, a large number of brain malformations were studied. Franz Seitelberger, Dawna Armstrong, an outstanding pediatric neuropathologist from Houston, Texas, and I were among the first to extensively study the morphology and neurochemistry of Rett syndrome. In 1985, I attended workshops in Baltimore and Bethesda, and was regularly invited to the annual meeting of the British Neuropathological Society. In addition to neurodegenerative disorders, the morphology and biochemistry of schizophrenia was studied with my cousin Eberhart Gabriel, director of the Vienna Psychiatric Otto Wagner Hospital and renowned historian in psychiatry.

In 1986, I edited the book “Therapy of Malignant Brain Tumours” (Springer Verlag, Vienna), in which international experts reviewed pathology, imaging, neurosurgery, radiation, and chemotherapy of brain neoplasms. Between 1986 and 1999, I published chapters about neurodegenerative diseases, brain tumors, and spinal circulation disorders in the book series “Neurology in Clinic and Practice” and, in 1987, about pallidal degeneration in the “Handbook of Neurology.” In September 1986, Elisabeth and I visited Stockholm for the 10th International Congress of Neuropathology, where I presented Rett syndrome and changes of subcortical nuclei in AD and PD. We were overwhelmed by this charming city and the hospitality of its citizens. In September 1986 I attended the workshop “Histological Classification of Tumors of the Nervous System” in Houston, Texas, which initiated a new classification of brain neoplasms (Fig. 6). In May 1988, I participated in the preparation of the 11th International Congress of Neuropathology 1990 in Kyoto and gave lectures in Tokyo, Sendai, and Niigata, where Elisabeth and I were hosted by Professor Iikuta, head of the Institute of Brain Research in Niigata and his wonderful wife, who spoke perfect English. Here, we saw the other side of the Japanese island (Figs. 7 and 8).



Fig. 6. Brain Tumor meeting in Houston, Texas, 1988, with (left to right) Lucien Rubinstein, KJ, Lucy Rosko and Paul Kleihues.

In March 1989, we had a wonderful Austrian Neuroscience Winter Meeting at Kitzbühel, and in April 1989 I discussed Lewy bodies at a Parkinson symposium in Chicago. The pathology of Parkinson syndrome was published in the Handbook of Experimental Pharmacology, edited by Donald Calne, a pioneer of PD research. Between 1989 and 1991, Felicia Slowik, a highly experienced neurooncologist in Budapest worked with me on hemangiopericytomas, the ultrastructure of malignant lymphomas, and cerebral sarcomas. With Werner Paulus, the neuropathological basis of different clinical subgroups of PD and their clinical relevance were studied. In 1991, I received the City of Vienna Prize for Medical Sciences. The next year, together with E. Kienzl and Emin Sofic, now professor of pharmacology, Faculty of Sciences, University of Sarajevo, selective increase of iron in the SN of PD and changes in the iron-melanin complex in the SN of PD brains with X-ray microanalysis were studied and presented at the Meeting of the Canadian Association of Neuropathology, September 1992 in Toronto, Canada.



Fig. 7. Visit to Yashiko Shrine Hiigata, May 1988 with Prof. Kreutzberg and Prof. Ikuta.

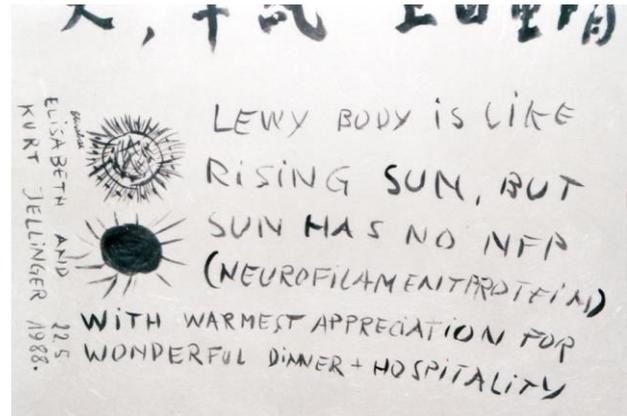


Fig. 8. Neuropathology and hospitality in Niigata, 1988.

More work, more congresses

In April 1990, I participated in The WHO Meeting on Histological Classification of Tumors of the CNS, organized by my friend Paul Kleihues, chairman of neuropathology in Zürich and later director of the WHO International Agency for Research on Cancer in Lyon, France. Werner Paulus and I, together with 25 other distinguished brain tumor experts, participated in the meeting of the Blue Book's Classification of Brain Tumours. The 2nd edition followed in 1993, the 3rd edition in 1997, and another in 2000, following a meeting in Lyon in 1997, where I also participated. In its update, retitled "Pathology and Genetics of Tumours of the Nervous System," edited by P. Kleihues and W. Cavane, with Werner Paulus, malignant lymphomas, histiocytic tumors, and melanotic lesions were reviewed. In August 1990, I presented primary cerebral lymphomas at the International Cancer Congress in Hamburg, and in September 1990, Elisabeth and I visited the 12th International Congress of Neuropathology in Kyoto, where we were hosted by Prof. Yonezawa, who is not only an excellent neuropathologist but also a gourmet and friend of the good life. Further highlights were the 5th World Congress of Biological Psychiatry in Florence in June 1991, where I presented pathomorphological aspects of schizophrenia, and the 10th International Symposium of Parkinson's Disease in Tokyo in October 1991. At the Paneuropean Congress of Neurology in Vienna, December 1991, the results of the Vienna Longitudinal Study of Dementia were presented, which showed correlations between cognitive impairment and quantitative Alzheimer pathology.

With Christian Bancher, the neuropathology of progressive supranuclear palsy (PSP) was reviewed in a book edited by Irene Litvan and Yves Agid. At this time, the clinical department was fully developed and successful, including a new laboratory for ultrasound examination of the cerebral vasculature. Upon the 80th anniversary of Lainz Hospital, a Festschrift was published in 1993 that documented the progress of our department. In April 1993, the neuropathology and classification of PSP was discussed in Bethesda, MD, and I received the Eloise Troxel Memorial Grant of the Society for Progressive Supranuclear Palsy, Baltimore, MD.

At meetings in Tokyo in April 1994, I lectured on new developments in AD and the pathogenesis of PD. A further highlight was the 12th International Congress of Neuropathology in Toronto in September 1994, where our group presented new data about cell death detected by DNA fragmentation and phospholipids in the Alzheimer brain. In 1994, together in a working group of Hans Lassmann, pathogenetic problems of multiple sclerosis were studied. That same year, with Werner Paulus, advances in the pathology of primary CNS lymphomas was also studied. A number of neurodegenerative disorders, like PSP, multiple system atrophy (MSA), and corticobasal degeneration (CBD) were studied in cooperation with an international group headed by Irene Litvan, now at University of California, San Diego, USA.

In 1995, Christian Bancher and I described the neurofibrillary predominant form of senile dementia, a rare subtype with low APOE ϵ 4 genotype, which recently was renamed primary age-related tauopathy (PART) [9]. In 1995, the pathology of AIDS encephalopathy and, together with Herbert's group, the neuropathology and diagnostic criteria of CJD and other spongiform prion diseases were studied. In October 1995, I attended the Workshop on Dementia with Lewy bodies (DLB) in Newcastle/Tyne, a dementing disorder hardly known at that time, and the guidelines for its diagnosis were published in the journal "Neurology" in 1996.

Organizations and committees

Through the years, I was elected to various national and international scientific organizations and committees. I served as vice president of the International Society of Neuropathology between 1981 and 1984; was chairman of the EU working group from 1996 to 1999; secretary of the European Soci-

ety of Psychopharmacology from 1994 to 2000; member of the FSN study group of neuropathology from 1987 to 2000; vice president of the Austrian Alzheimer Society from 1997 to 2002; president of the Viennese Association of Psychiatry and Neurology in 1986/87; and president of the Austrian Society of Neurology and Psychiatry from 1990-1992. From 1994 to 2000, I was a member of a committee reporting on neuroscience in Austria, on behalf of the Austrian Ministry of Sciences. Based on these data, a national program for neuroscientific research for Austria was prepared in 1966, coordinated by the LBI of Clinical Neurobiology as a basis for Austria's entry into the European Union.

With increasing age, I became member and honorary member of national and international scientific societies, including the American, British, German, Hungarian, and Austrian Societies of Neuropathology, the German Societies of Neurology and Pathology, the Austrian Neuroscience Association, honorary member of the Austrian and German Parkinson Societies, the Scientific Commission of the German Hirnliga, among many others. During these years, I reviewed articles for multiple national and international journals and became editor or member of the editorial board of many of them.

The great adventure: first Austrian neurologist in central China

In March 1996, a delegation from the Austrian Society of Neurology was invited by the Chinese Ministry of Health to visit medical institutions and hospitals in China. This included 6 persons: Hans and Jutta Lassmann, Alexander Meng, Christian Bancher, Barbara Zeman, and myself. The tour was organized and guided by Mrs. Zhou Quin, program officer of the Department of International Cooperation of the Chinese Ministry of Health (Fig. 9).

We visited China from March 31 to April 14, 1996. In Beijing, we were informed about the health organization in the People's Republic of China. During the weekend, we visited the Great Wall, the Ming graves, and the Imperial Palace. We then toured the neurological clinics of Beijing Hospital and of Capital Medical College, the two largest hospitals in the city, where Hans and I gave lectures about multiple sclerosis (MS) and PD. We flew to Chengdu, the capital of Sichuan, the largest province of China, where we visited the Medical College for Traditional Chinese Medicine, which consisted

of traditional and Westernized parts, the first specializing in acupuncture and other traditional methods.



Fig. 9. First delegation of Austrian neurologists in central China, with Hans Lassmann, KJ, Zhou Quin, Jutta Lassmann, Barbara Zeman, Christian Bancher (left to right).

We visited the largest herbal pharmacy of China and were invited to an herb dinner. On April 6, a Sino-Austrian Symposium on Neurosciences was organized in which lectures about MS, PD, and other topics were presented. By invitation of the Minister of Health of Sichuan, we visited the Min river and the Buddhist grove sanctuaries in Baodingshan and Beishan, which impressed us very much. After a short visit to Chongqing, a city with many respiratory diseases and lung cancers, we traveled by ship down the Jangtze River to Wuhan and visited the largest hospital of Hubei province, which had modern technical equipment and many German-trained professors. The journey on the Jangtse River, with the three gorges, was one of the most impressive adventures in our life.

We experienced China's culture, landscape, and people, and passed the largest hydroelectric power station in China spanning the Yangtse River, which at that time was in construction and considered one of the most impressive technical projects. For reasons of time, a visit to Shanghai was not possible, and we returned to Vienna. In conclusion, all of us were deeply impressed by the landscape, the historical relics, culture, health institutions, life in the countryside, and, in particular, by the friendly hospitality of our Chinese colleagues.

Difficult times and new challenges

In 1996, the Ludwig Boltzmann Society decided to dismiss Heinrich Gross, who had been in-

involved in the scandal about the euthanasia of handicapped children in the Vienna psychiatric institution "Am Spiegelgrund" during Nazi times, and I was asked to take over his LBI for the research of malformations of the CNS, located in the Psychiatric Hospital Baumgartner Höhe, which was now combined with the LBI of Clinical Neurobiology. While the formalin-fixed brains of these children were stored in the cellar of the Institute of Pathology of this hospital, blocks of those brains had been secretly stored somewhere in the premises of these former LBIs and I had the difficult task to find these materials from the archives so that they may be buried in a special memorial, which took place in 2002. This required much time to locate the specific material, to which I never had access before, while other specimens had been stored in the archives of the NI (see [5]). This affair was discussed in the popular media and had unforeseen political consequences, which hurt me, but I will not go into details.

In 1996, together with Norbert Rösler, a postdoc from Germany, the validity of CSF biomarkers (total tau and Amyloid- β -42) in the diagnosis of AD was studied. Christian Bancher and I visited an Alzheimer Congress in Osaka, Japan, and reported about the structural basis of dementia in AD and PD. The next year was of great importance for the department and myself, since I had reached the age of retirement from active service. However, my contract was prolonged for an extra year, during which we opened a stroke unit with 4 beds for surveillance and intensive treatment of patients with acute stroke. Furthermore, Christian Bancher got the lectureship (Dozentur) in neurology and neuropathology. In the years before, two other associates, Rembert Vollmer (neurology and neurophysiology) and Wolfgang Grisold (neurology) had got their Dozentur.

On September 30, 1997, I retired from my position as director of the department of Neurology at Lainz Hospital, but remained chief the LBI of Clinical Neurobiology, which was transferred to a building in the Psychiatric Otto Wagner Hospital. Together with my lab assistant, Mrs. Rappelsberger, I continued neuropathological routine work examining brains from a large psychiatric and geriatric hospital. Unfortunately, the archives of all the in-patients during the last 22 years, including the neuropathological protocols and brain material, was not available any more.

My successor was Dozent Manfred Schmidbauer, an excellent neurologist interested in neuropathology, book author, and painter. After the fusion of Lainz Hospital with the nearby Neurological Hospital Rosenhügel, Schmidbauer had to succeed the retired Gernot Schnabert as chief of both neurological departments. In addition, he continued routine neuropathology with focus on peripheral nerve biopsies. He retired in 2016 and became Professor of Neurodegenerative Diseases at the Sigmund Freud Private University in Vienna. He was succeeded by Christoph Baumgartner, a highly-qualified epileptologist. However, this marked the end of neuropathology, which I had initiated and continued for 22 years. But I overcame this blow and continued scientific work. In addition to a small private praxis, I worked as a court-certified expert and still write second opinion expertises about difficult neurological problems.

In October 1998, I presented data about movement disorders, malignant lymphomas, Lewy body disease, and tangle dementia in New York, Washington, Bethesda, and Montreal. At the 6th Conference on AD and related disorders, in Amsterdam in July 1998, I described vascular dementia and its relation with AD and received the Alzheimer Obelisk (Fig. 10).

In 1999 and 2000, the foci of my interests were PD and related disorders, in particular MSA, as well as mechanisms of neuronal cell death, including apoptosis. With Hallinah Baran, an experienced neurochemist, later at the Veterinarian University Vienna, we studied kynurenine metabolism in AD, and with Christine Stadelmann, then assistant in Lassmann's institute and now director of the Institute of Neuropathology, University Göttingen, we studied cell death mechanisms in neurodegenerative diseases.

At a traditional medicine symposium in Vienna, I discussed the basis and impact of acupuncture in neurology. The same year, I was invited as guest professor of neuropathology at the Medical University Innsbruck, where I gave block lectures and seminars for students and colleagues. Since the Innsbruck University had no neuropathology at that time, I examined a number of autopsy cases of rare movement disorders, such as MSA and PSP. The symposium was hosted by Prof. Werner Poewe, chairman of Neurology, and Gregor Wenning, later chief of the Division of Clinical Neurobiology, with

whom a long-lasting and fruitful cooperation and deep friendship began.

In 2000, I received the Burda Award of the Austrian Parkinson Society. In the same year, I was invited as guest professor at the Medical University of Graz, where I lectured about many subjects of clinical and theoretical neuropathology in the Clinic of Neurology under chairmen Erwin Ott and later Hans-Peter Hartung, now chairman of neurology in Düsseldorf, Germany. It was a wonderful time in the beautiful city of Graz and its surroundings, which I enjoyed very much. It was a leisure living compared to Vienna.

In 2000, we described cell death mechanisms in PD and, in 2001, AIDS-related pathologies before and after antiretroviral therapy. Since 2002, I helped the Pathological Bacteriological Institute of the Otto Wagner Hospital in the diagnostic workup of postmortem brains, mainly from elderly demented and non-demented individuals. I performed brain cuttings once a week, and instructed colleagues how to dissect brains, which were examined in the LBI. My trainee and friend Johannes Attems, then assistant at the local Institute of Pathology, examined the cases and we discussed them together between 2000 and 2008, thus giving him an excellent basis for his future career and a fruitful cooperation resulting in a number of shared publications. Since 2009, Johannes is Professor of Neuropathology and head of the brain bank at Newcastle University in England and, since recently, editor-in-chief of *Acta neuropathologica* as successor of Werner Paulus.

In 2002, I received the prestigious award for Meritorious Contribution to Neuropathology by the American Association of Neuropathology, together with S. Horoupian, Professor Emeritus at Stanford University in the USA and Fusahiro Ikuta, director of the Brain research center at Niigata University, Japan. The laudation of my award was written by Robert D. Terry, one of the most important neuropathologists of the 20th century and co-founder of US Alzheimer research (Addendum). We met on several occasions, including a visit to his home in California approximately one year before his death in May 2017.



Fig. 10. Presentation of the Alzheimer Obelisk with Dick Swab (left) and Henry Wisniewski (center) at the 6th Internat. Conference on AD, Amsterdam, July 1998.

End of an institution and a new beginning

In 2002, the LBI of Clinical Neurobiology was closed despite it being one of the most active scientific institutions outside the university with more than 1,400 publications until 2000. Since that year, we received no budget and I had to find other sponsors. The equipment was transferred to the new Institute of Clinical Neurobiology, which was run by the Society for the Support of Research in Experimental Neurology in Vienna, sponsored by donations and previous clinical trials. Since 1999, my assistant has been Dr. Erich Mitter-Ferstl, PhD, who studied at the Zurich Technical University and is an excellent computer specialist, without whom I hardly would have succeeded in this latest chapter of my career.

Time went on with both continuing examination of brain material at the Wagner-Jauregg Hospital, evaluating old material, and continuing research. In 2003, I wrote a chapter about the neuropathology of PD in the book "Neurodegeneration" (ISN Neuropath Press, Basel) edited by the International Society of Neuropathology and again for the 2nd edition, edited by D.W. Dickson and R.O. Weller in 2011. In 2007, a review of Lewy body disorders appeared in Abel Lajtha's book "Degen-

erative Diseases of the Nervous System" (Springer, Vienna) and since 2011, I continue to write the chapter on neuropathology of movement disorders in Youman's Neurological Surgery (Elsevier Saunders, Philadelphia, editor W.R. Winn), 6th edition, of which the 8th edition is currently in press. In 2014, I contributed the chapters on neuropathology and pathogenesis for the book "Multiple System Atrophy" (Springer, Wien) edited by G. Wenning and A. Fanciulli. Lastly, with Johannes Attems, the chapter on neuropathology for the "Textbook of Old Age Psychiatry," (Oxford Univ. Press, Oxford, UK) the 2nd edition of which is now in press.

We had a co-operation with the Vienna Transdanube Aging (VITA) study, a long-term inter-institutional clinical, neuropsychological, genetic, neuroimaging, and neuropathological assessment of a large group of individuals aged 75 years in the eastern part of Vienna, which was performed by the LBI of Aging under the direction of Hans Tragl. For this group, with Ildiko Wichart, who worked at the University of Veterinary Medicine, Vienna, A β -42 protein in plasma was studied and correlated as valid marker with many clinical and neuropsychological data, which resulted in a large number of publications and congress reports between 2005 and 2010. Unfortunately, the VITA study ended for financial reasons, although it had been the first

population-based long-term study about risks and development of cognitive changes in the oldest of old people.

In 2003, at the 3rd German Parkinson Congress in Dresden, Heiko Braak, an outstanding neuroscientist, who, among others, introduced the staging of PD and AD pathologies, and I received the Lundbeck Award for Parkinson Research (Fig. 11). In the same year, I received the Karl Maria Jakob Medal of the German Association of Neuropathology in Hamburg. The co-operation with Johannes Attems studying olfactory involvement and multimorbidity of the aging brain and with Gregor Wenning's team on Lewy body pathology was successfully continued. Furthermore, with Mrs. E. Kienzl and a research group of the Neurological Clinic of the Technical University of Dresden (chief Heinz Reichmann), the Alzheimer Associated (ALZAS) gene was studied as a possible marker for AD. In 2005, I received the István Környey Tarscosag award on the occasion of the 100th birthday celebration of this eminent Hungarian neurologist, for whom I had the honor to present the laudation. In the same year, I contributed the chapter on synucleinopathies for the Polish Mossakowski Memorial Book of Neuropathology (Wydawnictwo Czelej Sp. z o.o., Lublin, edited by P.D. Liberski and W. Papierz). Since 2006, I lecture on the neuropathology of stroke and vascular dementia at the Danube University in Krems.

The year 2006 was particularly busy. On the occasion of the 100th anniversary of Aloys Alzheimer's description of the disease, several books appeared. In one edited by George Perry, the clinicopathological results of a large series of demented elderly person were presented, and I published a book about the hallmarks of 100 years of scientific research on AD presenting the most important publications between 1938 and 1999 in German (translated by myself). In a book edited by H. Herholtz et al., I reviewed the early diagnosis of dementias from the neuropathological point of view based on 1,500 consecutive autopsy cases in comparison to the clinical diagnoses, where I emphasized the impact of multi-morbidity.

In October 2007, I lectured about Parkinson dementia in South Korea, vascular dementia in Budapest, and biological AD markers in Wroclaw, Poland. In 2008, together with Lassmann's group, the relations between MS and AD from the neuro-immunological point of view were examined, and,

at a Parkinson symposium in Tokyo, the formation and role of Lewy bodies were presented.

Between 2005 and 2008, the Kurt Jellinger Prize for outstanding scientific writing in neuropathology was sponsored by Acta Neuropathologica, for which I had served as executive editor for 29 years. The last recipient was Goran Simic (2008) from the Brain Research Institute in Zagreb, who had been guest scientist in my LBI a few years before. In 2008, I found myself among the 20 highly-cited scientists in Austria in the ISI Webb of Knowledge. Since Johannes Attems went to Newcastle uponTyne in Great Britain, I stopped lab work and concentrated on specific neuroscience problems, reviewing manuscripts, and writing invited review papers.

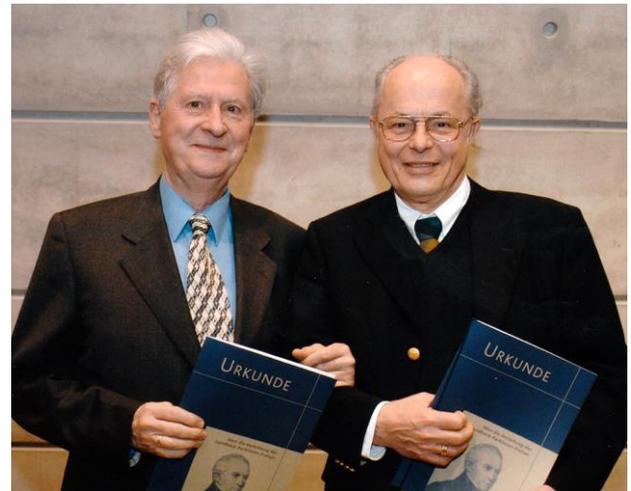


Fig. 11. With Heiko Braak receiving the Lundbeck Award for Parkinson Research at the German Parkinson Congress 2003 in Dresden.

In 2011, I received the G. Cotzias Award of the Movement Study Group of the Spanish Society of Neuropathology in Barcelona. In honor of my 80th birthday, four of my former scholars and now renowned neuroscientists, Hans Lassmann, Christian Bancher, Johannes Attems and Werner Paulus, dedicated a "Festschrift" of Acta Neuropathologica [10], for which I am very grateful to them. On the same occasion, my friends and former associates organized a festivity, which all of us enjoyed very much.

Together with Johannes Attems and A. Thomas, the correlations between cortical and subcortical tau pathologies and their relations with Braak tau stages were reviewed, in addition to the pathological correlates of behavioral disorders in demen-

tias with M.F. Casanova and S.E. Starkstein, and the problem of vascular depression with an international group. The role of α -synuclein in PD was presented in the book "Emerging Drugs and Targets for Parkinson's Disease," (The Royal Society of Chemistry, Cambridge, UK) edited by A. Martinez and C. Gil in 2013.

Invited in February 2013 by G. Logroscino, an US-trained Italian neurologist and neuroepidemiologist, I gave the *Lectio Magistralis* about the role of neuropathology in neurodegenerative diseases at the University of Bari, Italy. In June 2013, I discussed the role of α -synuclein as the gateway to neurodegeneration and demonstrated brain cutting to the members of the Division of Clinical Neurobiology (head Gregor Wenning), with whom we celebrated our cooperation since 1993, which still persists.

In March 2014, Elisabeth and I were invited to a series of lectures at the Department of Neurology at Seoul National University, where we were hosted by Prof. Beomseok Jeon, a wonderful neuroscientist, who had overcome serious injuries in an alpine accident with utmost energy. We were overwhelmed by the megacity of Seoul that had been completely destroyed during the Civil War, and were deeply impressed by the lifestyle and culture of the Korean people. We never had experienced such a warm-hearted hospitality before. After this tour, I was invited for the position of Pro-

fessor of Neuropathology at Seoul, but I had to decline for age reasons.

I like small and intimate meetings, such as those by the Society for Amelioration of the Quality of Life, organized by Stavros Baloyannis, chairman of Neurology at Thessaloniki Medical University, and sponsored by the Orthodox Church. These meetings occurred in Marseille 2008, Thessaloniki 2009, Delphi 2010, and Catania, Sicily, in 2009, where Franz, Mrs. Gerstenbrand and I climbed the Aetna mountain. Other favorite meetings were the "Neurology Spring" in the Austrian Waldviertel, organized by Christian Bancher, now chief of Neurology at Horn, and the World Congresses on Controversies in Neurology (CONy), organized by Amos Korczyn, Professor emeritus in Tel Aviv, where problems in neurology are discussed by international experts.

In May 2015, I presented the pathogenesis of MSA at the α -synuclein symposium in Innsbruck then once more at the Congress on Vascular Dementia in Ljubljana in October 2015. Postmortem assessment in vascular dementia, a consensus report on vascular depression, and the relations of diabetes mellitus and dementia were published in collaboration with international experts. Together with Amos Korczyn, an opinion paper discussing whether dementia with Lewy bodies and Parkinson dementia are the same disease was published in 2018.



Fig. 12. Workshop on neuropathological diagnosis of AD at the AD/PD Confernece in Lisbon, March 2019, with Johannes Attems, Irina Alafuzoff, KJ, Melissa Murray, Dieter Thal (left to right).

Together with Johannes Attems, Dietmar Thal, and Irina Alafuzoff, I helped lead a workshop on neuropathological diagnosis of AD, which was organized by Johannes at the AAIC Congresses in Copenhagen 2012, Washington 2015, and London 2017; and again at the AD/PD congress in Nice 2015 and Vienna 2017; and finally, with Johannes Attems, Irina Alafuzoff, Dietmar Thal, and Melissa Murray at the AD/PD conference in Lisbon, March 2019 (Fig. 12). My last congressional activities were the annual meeting of the Austrian Parkinson Society in Vienna in speaking about Parkinson dementia and dementia with Lewy bodies, and a biological definition of the Alzheimer spectrum at a course about CNS proteinopathies in Milan, Italy in November 29, 2019.

Now, at the age of 89, I still find it impossible to abandon my interest in neuropathology, and I try to continue scientific work as long and as well as I can. In the last year, I discussed whether Braak staging is valid for all types of PD, and, together with Gregor Wenning's group, protective therapies in MSA. After two extensive reviews about the neuropathology and pathogenesis of extrapyramidal disorders, the neuropathology of cognitive impairment in MSA and an update of MSA were published. Two reviews of the pathobiological definition of Alzheimer continuum, including the neuropathology of its pathobiological subtypes, are in press.

Life beyond neurology/ neuropathology

Although I "was married to neuropathology," together with Elisabeth, we had an intensive and happy private life, as busy as it has been. Before our wedding in August 1960, we rented a flat that took years to get completely refurnished. Elisabeth was a student, and I a poorly-paid university assistant. In summer 1958, she was an au pair with a family in London, while I was paramedic in a summer camp for students in Italy. In 1959, we spent a splendid summer vacation on the island of Maly Losinj at the Croatian coast, where I had helped to reestablish the school. In 1960, we spent our honeymoon in Lignano and Venice, and the next year we went to the Greek island of Mykonos, where we were among the very few tourists on this beautiful island, which later became a hotspot of elegant tourism. Elisabeth finished her studies in English with a thesis about the medieval Towneley plays,

which I typed. Later, she became administrator in the Institute of Immunology of Vienna Medical Faculty, run by my friend Prof. Martha Eibl. Afterwards, Elisabeth joined me in literature research and as an assistant in my private medical practice, where she was loved by all my patients.

In springtime, we traveled to southern countries, in particular Toscana, Umbria, the Marches, Romne, Gubbio, Urbino, Arezzo, Parma, Sicily, Corsica, Burgundy, Bretagne, and many other interesting regions, where we enjoyed the lifestyles, local gastronomy, cultures, and traditions. In summer we had regular vacations on many Greek islands, but also in Sicily, Mallorca, and Sardinia. In summer 1986, we spent our vacation in a beach house of my friend Nenad Grčević, an excellent Croatian neuropathologist, in Umag, a small town on the Istrian peninsula, when the "Prague Spring" was suppressed by the Soviet army. In 1996, after a peaceful stay at Syros, we escaped from the island, afraid of a possible war between Greece and Turkey, and had to wait in Athens for a flight home. Later, many summers were spent on the beautiful island of Chios, which is next to the Turkish border, in a small hotel run by a friendly Greek family, but during the last years we could not go there because of the refugee crisis and lack of direct flights.

At Christmas time and New Year, we used to spend some weeks in Paris, which we loved for its culture and way of life. Unfortunately, during this past year we could not go to our beloved Hotel De La Bretonnerie in the old Marais district because of the yellow jacket riots and the novel coronavirus pandemic.

During the rest of the year, we regularly attend the Vienna Opera and concerts. For years, we have had subscriptions to the Vienna Philharmonic Orchestra and many other chamber music presentations. In previous times, we regularly visited the Salzburg Festivals, where we met friends, many of them being members of the Vienna Philharmonic Orchestra. During leisure time, I regularly read historical books and try to inform myself about Austrian and international history. We like to walk in the idyllic landscape and, in order to exercise our brains, Elisabeth and I take regular Italian lessons with a nice Italian interpreter.

In 1969, my late father-in-law built a small house in Maierdorf, a small village at the foot of the Hohe Wand, a mountain of 1,200 meters, about 65 km south of Vienna, which we visited nearly

every weekend in summertime and around Christmas. Since March 13, 2020, and with few interruptions, we have lived in this house during the COVID-19 lockdown, and it is here, in the tranquil landscape and beautiful springtime, that I wrote the major part of this report.

Once the lockdown ends, we hope that “normal life” will resume, although this virus is still an enormous and expanding danger for the whole world. However, we don't agree with the slogan in a humorist Vienna journal in July 1918: “The Span-

ish Influenza finishes us all,” and, despite all warnings, we are looking optimistically to the future. We just celebrated the 60th anniversary of our wedding not on a Greek island but in our rural home.

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