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FALL 2017

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### From the Chair

Welcome to the Fall 2017 issue of Neurotransmissions, the UW Department of Neurology's newsletter for colleagues, alumni and friends. I am proud to share the latest exciting developments in our department, including news on research, clinical resources, and education.

In this issue we spotlight the UW Headache Clinic, the only academic headache center in the WWAMI region, and a unique clinical asset. The Headache Clinic is led by Drs. Natalia Murinova and Jenna Kanter. They are bringing innovative practices to the stubborn problem of refractory migraine and cluster headache, including shared visits with allied practitioners focused on lifestyle modification to improve headache control. This holistic approach has won rave reviews from their patients, and clinical volumes are booming, especially at the Eastside Specialty Center. Head to our feature on page two to learn more about this unique resource within UW Neurology.

On the research front, Professor and Vice Chair for Academic Affairs Christina Marra, MD runs a highly successful program into the surprisingly common problem of neurosyphilis. Dr. Marra

### **INSIDE THIS ISSUE**







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**Headache Clinic** 



Bruce R. Ransom, MD, PhD

NEUROTRANSMISSIONS

the context of HIV infection, and why its clinical manifestations are more severe in that setting. Her work has garnered abundant funding from the NIH, and she has become an internationally recognized expert in this disorder.

Finally, do not miss the latest installment of Phil Swanson's History of Neurology. In this issue, he describes the growth of the Division beginning in 1967 when Phil took over as Chief at the "tender age of 34." Neurology at that time had five faculty members aside from Phil, and believe it or not, no full-time faculty at Harborview. Over the next several years, a number of new faculty joined the Division, and you will recognize their names as storied contributors to our neurological past. You will see them in their youthful glory ca. 1970 when you turn to page four.

Neurology Division in 1970

### The UW Headache Clinic: innovative treatments for a vexing disorder

Migraine is one of the leading causes of disability worldwide. It disproportionately affects patients in young adulthood and middle age, and results in billions of dollars of lost productivity annually in the US alone. While many effective treatments are available for migraine and other headache disorders, many patients continue to struggle with pain and disability due to delays in diagnosis and lack of appropriate treatment.

The UW Headache Clinic is currently the only university-based clinic specializing in headache disorders in the Pacific Northwest and the entire WWAMI region. The clinic is proud to offer multimodal headache management, and emphasizes patient education and empowerment as integral components of the treatment plan. In addition to migraine, the Headache Clinic also specializes in less common headache disorders such as cluster headache.

Patients who are referred to the clinic are asked to fill out a comprehensive online questionnaire reviewing their preferences for treatment, headache history, and other aspects of their medical and social history. Having this information in advance allows the providers to tailor the initial consultation to the individual patient's needs. Additional questionnaires are sent before each follow-up visit, promoting efficient clinical care and also allowing outcomes to be tracked over time. New patients are typically seen by a team of a neurologist and a nurse practitioner to review their headache history and establish an accurate diagnosis and preliminary treatment plan. Next, patients with a diagnosis of migraine attend a shared medical visit



Members of the UW Headache Clinic team, from left to right: Natalia Murinova, MD; Mui Chan-Goh, ARNP; Jenna Kanter, MD; Melissa Schorn, DNP; Debbie Nesbitt, ARNP.

led by Natalia Murinova, MD, Clinical Associate Professor of Neurology, and Melissa Schorn, DNP, where they learn more about the pathophysiology of migraine and the spectrum of treatments available at the Headache Clinic. A similar shared visit led by Jenna Kanter, MD, Clinical Assistant Professor of Neurology, and Mui Chan-Goh, ARNP is offered for patients with cluster headache.

Lifestyle factors including sleep, exercise, and diet are crucial for successful headache management. Due to time constraints, however, these issues are often deprioritized in the traditional model of one-on-one patient care. The Headache Clinic under the leadership of Dr. Murinova is pioneering the use of shared medical visits to provide more comprehensive patient education and motivation to address lifestyle factors: Melissa Schorn leads shared medical visits devoted to nutrition, while **Flavia Consens, MD**, Associate Professor of Neurology, and Mui Chan-Goh lead shared visits focused on sleep hygiene. The Headache Clinic plans to develop additional sessions devoted to other topics such as physical activity. Early feedback on these visits has been overwhelmingly positive: patients value the in-depth education provided, as well as the opportunity to learn from the perspectives and questions of their peers.

Studies have found a high prevalence of mental health comorbidities such as anxiety and depression in patients with migraine, and these comorbidities are also known to be associated with higher levels of migraine-related disability and a higher risk of progression to chronic migraine. Stress is the most common trigger identified by patients with migraine. Behavioral approaches to headache management are safe and effective, however access to these methods in the community is limited, especially for patients with public insurance or limited financial means. Because of this unmet need, the Headache

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### Two Decades of Research on Syphilis and HIV

#### By Christina Marra, MD, Professor and Vice Chair of Neurology

After my Neurology residency at UW, I began a fellowship in Infectious Diseases at UW. One of my tasks was to attend in the STD Clinic at Harborview, which increased my interest in sexually transmitted diseases. I went to graduate school before medical school, and I never thought that I would work in the lab again. But under the mentorship of Sheila Lukehart, PhD, in Infectious Diseases, I began laboratory-based studies of syphilis and neurosyphilis. While many think of syphilis as a disease of purely historical interest, this is far from the truth. For example, between 2000 and 2016, the rate of infectious syphilis in the US has increased more than 300%; similar increases have been seen worldwide. In the US, about half of those with syphilis are also infected with the human immunodeficiency virus (HIV).

Early in the HIV epidemic, reports of increased risk of neurosyphilis and poorer serological response to syphilis treatment in HIV-infected compared to HIVuninfected individuals piqued my interest. Between 1996 and 2014, my research group conducted an NIH-funded observational study of syphilis and neurosyphilis. Overall, we enrolled 760 HIV-infected and 220 HIV-uninfected individuals with syphilis who underwent a structured medical history and neurological examination, blood draw and lumbar puncture for collection of cerebrospinal fluid (CSF). Over 120 participants re-enrolled in our study with one or more repeat episodes of syphilis.

We identified risk factors for neurosyphilis in HIV-infected and HIV-uninfected individuals, and we showed that HIV- infected individuals with neurosyphilis had poorer treatment responses than their HIV-uninfected counterparts. The syphilis bacterium (*Treponema pallidum* subspecies *pallidum* or *T. pallidum*) is cleared from sites of infection by macrophages that ingest and kill it when it is coated with opsonic antibody. We showed that, compared to HIV-uninfected individuals with syphilis, HIV-infected persons with syphilis have reduced *T. pallidum* opsonic antibody activity in serum. This finding may provide a mechanism to explain differences in the clinical course of syphilis in HIV-infected individuals.

In a separate group of HIV-infected individuals, we found that those with previous syphilis performed more poorly on neuropsychological tests than individuals who had never had syphilis. This finding is important because it suggests that an inflammatory insult may worsen current HIV-associated cognitive impairment. With Dr. Emily Ho, we



recently added support to this hypothesis using our syphilis cohort. We showed that HIV-infected individuals with neurosyphilis have increased CSF concentrations of CXCL10 and CCL2, two chemokines that are associated with HIV-related cognitive impairment.

We currently have two ongoing NIHfunded studies. One addresses the best clinical practice for evaluation of patients with syphilis. Specifically, we hope to determine whether lumbar puncture, with treatment based on CSF findings, improves serological, cognitive and functional outcomes in patients with syphilis. The other study is more laboratory-based, and investigates the impact of differences in the innate and acquired immune response on risk of neurosyphilis.

In 2014, I received the Achievement Award from the American Sexually Transmitted Diseases Association for our body of work on syphilis and neurosyphilis. The efforts

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Front from left to right: Shelia Dunaway, Haley Mendoza, Christina Marra Back from left to right: Sher Story, Arielle Davis, Lauren Tantalo, Sharon Sahi

### Swanson's History of Neurology The Bronze Age of UW Neurology: Part 3. 1967-1974

#### **By Phillip D. Swanson, MD, PhD,** Professor of Neurology

In 1967, I became the fourth Division Head of Neurology at UW which consisted of five other faculty members at the time: August (Gus) Swanson, then Associate Dean for Academic Affairs who continued some clinical activities; Henry Leffman, a clinical neurologist at the VA; Coldevin (Coley) Carlson, head of Child Neurology, then based at the University Hospital; John (Tim) Chapman, a pediatric neurologist at Children's Hospital who had a clinical appointment, and John R. Green, a junior faculty member who had finished his residency in 1965 and showed an interest in epilepsy. There was no full-time neurologist at the busiest hospital, King County Hospital (now Harborview Medical Center). Two additional neurologists who would play key roles in developing UW Neurology were S. Mark Sumi, trained as both a neurologist and neuropathologist, and Wayne E. Crill, a neurologist and superb basic neurophysiologist. Mark Sumi had returned to Seattle in 1966 after two years studying neuropathology at the Max Planck Institute in Munich, Germany. He had dual appointments in Pathology and Neurology, but needed to take a Washington licensing examination before he could practice clinical neurology. Wayne Crill, a UW medical school graduate, had returned to Seattle after neurology residency under Fred Plum at Cornell. Wayne began a research fellowship in the Department of Physiology and Biophysics chaired by Harry Patton, PhD. Wayne's initial research, in collaboration with Dr.

Thelma Kennedy, was to investigate the physiology of cerebellar climbing fibers. He began seeing patients in the Neurology outpatient clinic at UWMC.

In 1967, the residency program was largely financed by a Clinical Neurology Training Grant from the NIH. This grant program began in the early 1950s and was designed to encourage medical schools to develop programs for training academic neurologists by contributing support to faculty and stipends for neurology trainees for whom previously there had been little hospital support. Training grants now became available for neurology, neurosurgery, neuropathology, and neuroradiology. There was no national matching program for neurology residency positions, though medicine internships were distributed through the National Matching Program.

#### Neurology research programs.

Research activities at University Hospital (now UWMC) and the Seattle VA were primarily in the area of neurochemistry. William Stahl, PhD, a biochemist with expertise in Neurochemistry from his post-doctoral work in Henry McIlwain's laboratories in London, followed by two years in the NIH Laboratory of Neurochemistry under Eberhard Trams, joined us that year. His primary laboratory was newly established at the Seattle VA, and was supported by VA research funding. He collaborated with my laboratory at the University Hospital in exploration of energy-utilizing processes in the CNS, especially cation

transport. We also collaborated with researchers in Neuropathology such as Dr. E.C. (Buster) Alvord Jr, and Dr. Sumi. We were the first to show that the post-mortem human brain could be divided into subcellular fractions such as microsomes and mitochondria. We applied these techniques to the brains of patients with Huntington's Disease and cerebro-tendinous xanthomatosis, the latter found to be a leukoencephalopathy associated with storage of dihydrocholesterol (cholestanol). Donald F. Farrell joined the Division in 1971. After his neurology residency at Stanford, Don completed a fellowship at Johns Hopkins, developing an interest in studying lipid storage disorders such as Krabbe disease.

Neurology clinical services. Even though we were a Division within the Department of Medicine, we had autonomy on the inpatient and outpatient services. Residents rotated at HMC, UH, Children's, Seattle VA, and the USPHS hospital. Rotations were usually for three-month blocks. Outpatients were seen in clinics at the hospital to which the resident was assigned. There was no continuity clinic, but residents did have continuity with discharged inpatients. Non-clinical rotations included neuropathology for six months, and electrophysiology with an emphasis on EEG. Pediatric neurology was a three-month block rotation for adult residents, who were paired with a senior pediatric neurology fellow. The number of residents was usually three or four at each level of training.



Division of Neurology faculty in 1970. Shown are faculty from left to right, beginning with Top row: Luke Kao, Jim Coatsworth, Herb Goldston, Bill Bozarth, Mike Copass, Dick Matthews. Middle row: Bill Stahl, Bob Wilkus, Bob Gotshall, Bill Kuhn, Vicki Boyd. Bottom row: John Green, Mark Sumi, Wayne Crill, Phil Swanson, Henry Leffman, Gil Frank

#### King County Hospital (Harborview

Medical Center). Even though King County Hospital had the busiest clinical service, there were no full-time Neurology (or Neurosurgery) faculty located on-site. In 1969, Dr. Sumi agreed to assume the role of Chief of the Neurology Service. At that time, much of the attending at HMC was done by community neurologists such as William Sata, Bob Rankin, Bob Aigner, and Bob Colfelt. These volunteer faculty usually made rounds on Tuesdays and Thursdays. Dr. Sumi increased attending rounds to three or more times per week. At about the same time, during the Presidency of Lyndon B. Johnson, the Regional Medical Program (RMP) was created with the goal of improving care for people with cancer, heart disease, and stroke. We obtained an RMP contract to improve stroke education and treatment in the Northwest including Alaska. Dr. Gilbert Frank, a neurologist who had come from Iowa to join the EEG unit, changed direction to develop a stroke program at HMC. He created teaching materials and undertook trips to southeast Alaska to consult on stroke-related issues. We obtained office space for the stroke program

and for the Neurology Division on the fifth floor of Harborview Hall. When Mike Copass completed his residency and a neuropathology fellowship in 1973, he joined HMC Neurology and became heavily involved in developing the Medic One program for early intervention in outside hospital resuscitation protocols. The present two neurology inpatient services are named the Sumi and Copass services to honor these two pioneers.

**U.S. Public Health Service Hospital** (**USPHS**). In 1966, Robert Gotshall came to Seattle to join the Internal Medicine program at the US Public Health Service Hospital (now Pacific Medical Center) on Beacon Hill. Bob decided to train as a neurologist and then he joined our faculty. He, too, developed a special interest in stroke. He participated in multicenter studies on TIA and was a strong contributor to the residency teaching program before moving to the Group Health system in 1982.

# **The Seattle Veterans Hospital.** This hospital was constructed in 1951. Henry Leffman, an Army neurologist stationed at Fort Lewis near Tacoma became the VA neurologist and

remained there until his retirement in 1969. Dr. Leffman was a wonderful teacher of residents and students, though he saw only a limited number of the neurology inpatients and there were no outpatient clinics there until 1972. Dr. Leffman was said to have read every article in the journal *Brain*. He did little research, but made important contributions to studies on periodic lateralized epileptiform discharges (PLEDs), and other clinical studies.

Pediatric neurology. In the 1950s and early 60s, the Department of Pediatrics maintained inpatient and outpatient services at the University Hospital. Children's Hospital was affiliated. Dr. John T. Chapman was trained in Pediatric Neurology and was employed by Children's Hospital until he left for private practice in 1970. In 1964, when August Swanson became Head of the Division of Neurology, he recruited Coldevin Carlson to head Pediatric Neurology. Dr. Carlson was initially based at the University Hospital, but when it became clear that there was greater potential for pediatric neurology at Children's, Dr. Carlson moved there. A pediatric neurology clinic continued at the University Hospital, with Don Farrell and I attending.

#### Clinical neurophysiology and epilepsy.

Dr. Gian-Emilio Chatrian became the Director of EEG. Dr. Chatrian was trained in neurology in Italy, and came to Seattle from the Mayo Clinic. Dr. Chatrian developed an outstanding laboratory, and taught all neurology residents, who rotated usually for three months. In 1969, when the School of Medicine combined UWMC and HMC laboratories into a new Department of Laboratory Medicine, Dr. Chatrian chose that department for his primary academic appointment. He trained Dr.

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# Update from the Division of Pediatric Neurology

#### **By Russell Saneto, PhD, DO** Acting Division Head of Pediatric Neurology

The coolness of fall reminds us of the changing of seasons. Part of our lives revolves around changes, and within our group, there have been some significant changes. Dr. Sid Gospe has stepped down as Division Head, as of March 1, 2017. We will miss Sid greatly. He expanded child neurology from four to over 22 members. The child neurology residents increased from one to three per year. We have become one of the premier programs in the nation under Sid's leadership. For all that you have done Sid, thank you. Sid will now become a doting grandfather to his first grandson in North Carolina. Soon, his daughter Jessica will give the Gospes a

second round of grandchildren: Jessica is pregnant with twins.

The coming of spring gives us the anticipation of new potential growth. We welcome our second class of three residents who have entered their pediatrics years. This outstanding group of new interns are: Angad Kochar, MD; Laurel Persa, MD; and Brittany Sprigg, MD. Our current residents just beginning their N1 year are Jeremy Chan, MD, and Michelle Kerr, MD (pictured below). And our newest division addition is Dr. Mark Wainwright from Lurie Children's Hospital in Chicago. Mark will become our new Division Head beginning in December. Mark has been on the forefront of developing pediatric neurocritical care. He has developed a nationally respected Neurocritical Care fellowship at Lurie Children's Hospital. He is also involved in outcomes research. More details to follow in the Spring 2018 Newsletter!



Jeremy Chan, MD



Michelle Kerr, MD

## Neurology Residency Update

### By Patricia Oakes, MD, JD,

Co-director of Neurology Residency Program

We are happy to welcome the class of 2020 — our newest class of Neurology Residency N1's. The class includes two UW School of Medicine graduates, as well as five others from all around the country. They have already proven to be a dedicated, enthusiastic, and collegial group.



**George Banks, MD** Marshall University



David Ivanick, MD University of Rochester



**William Lou, MD** Cornell University



Alipi Naydenov, MD, PhD University of Washington



Valerie Olson, MD, PhD University of Washington



**Amita Singh, MD** Morehouse University



**Laudann Taravati, MD** University of Cincinnati

### Selected Recent Publications by Neurology Faculty

**Compiled by Nadine Waldmann,** Budget/fiscal analyst lead

Singh T, Peters SR, **Tirschwell DL, Creutzfeldt CJ.** Palliative Care for Hospitalized Patients With Stroke: Results From the 2010 to 2012 National Inpatient Sample. *Stroke* 2017.

Carter JC, **Wrede JE.** Overview of Sleep and Sleep Disorders in Infancy and Childhood. *Pediatr Ann* 2017.

McDonough A, Lee RV, Noor S, Lee C, Le T, Iorga M, Phillips JLH, Murphy S, Möller T, **Weinstein JR.** Ischemia/Reperfusion Induces Interferon-Stimulated Gene Expression in Microglia. J Neurosci 2017.

**Watson NF**, Martin JL, Wise MS, Carden KA, Kirsch DB, Kristo DA, Malhotra RK et al. Delaying Middle School and High School Start Times Promotes Student Health and Performance: An American Academy of Sleep Medicine Position Statement. J Clin Sleep Med 2017. Turk KW, Flanagan ME, Josephson S, Keene CD, **Jayadev S**, **Bird TD**. Psychosis in Spinocerebellar Ataxias: a Case Series and Study of Tyrosine Hydroxylase in Substantia Nigra, *Cerebellum* 2017.

Amos PJ, Fung S, Case A, Kifelew J, Osnis L, Smith CL, Green K, Naydenov A, Aloi M, Hubbard JJ, Ramakrishnan A, **Garden GA**, **Jayadev S.** Modulation of Hematopoietic Lineage Specification Impacts TREM2 Expression in Microglia-Like Cells Derived From Human Stem Cells. *ASN Neuro* 2017.

Zabetian CP, Mata IF; Latin American Research Consortium on the Genetics of PD (LARGE-PD). LARGE-PD: Examining the genetics of Parkinson's disease in Latin America. *Mov Disord* 2017. **Mata IF**, Johnson CO, Leverenz JB, Weintraub D, Trojanowski JQ, Van Deerlin VM, et al. Large-scale exploratory genetic analysis of cognitive impairment in Parkinson's disease. *Neurobiol Aging* 2017.

Wallace AS, Hudac CM, S**teinman KJ**, Peterson JL, DesChamps TD, Duyzend M, et al. Longitudinal Report of Child with *De Novo* 16p11.2 Triplication. *Clin Case Rep* [in press].

**Poolos NP**, Castagna CE, Williams S, Miller AB, Story TJ. Association between antiepileptic drug dose and long-term response in patients with refractory epilepsy. *Epilepsy Behav* 2017.

### Selected Recent Grant Awards to Neurology Faculty

GRANT TITLE	SPONSOR	PI
Stereotactic Laser Ablation for Temporal Lobe Epilepsy (SLATE)	MEDTRONIC	Miller
An Open Label, Multicenter, Safety and Pharmacokinetic Study of YKP3089 as Adjunctive Therapy in Subjects with Partial Onset Seizures	SK LIFE SCIENCE	Miller
AtRial Cardiopathy and Antithrombotic Drugs In prevention After cryptogenic stroke (ARCADIA)	COLUMBIA/ NIH U01	Tirschwell
A Phase 3, Open-Label Extension Study of Tirasemtiv for Patients with ALS	CYTOKINETICS	Weiss
Early Imaging Markers for Post-hemorrhagic Hydrocephalus	HYDROCEPHALUS ASSOCIATION	Tully
Navigating Patients and Families through the Neuro-ICU	NIH K23	Creutzfeldt
Integrated Cell-type Specific Biological Annotation of Genomic Variants in Alzheimer Disease	NIH R56	Jayadev
A Phase 3 Study in Subjects with Relapsing Remitting Multiple Sclerosis to Evaluate the Tolerability of ALKS 8700 and Dimethyl Fumarate	ALKERMES	Wundes
Genetic Movement Disorders: Etiologies and Pathogeneses	VA MERIT	Zabetian

# Neurology Faculty News

Jon Weinstein, MD, PhD, Associate Professor of Neurology, was honored last May with an Undergraduate Research Mentor Award at the annual UW Undergraduate Research Symposium. He was chosen from over 170 nominations from student researchers. Dr. Weinstein was cited as someone "who continuously exemplifies what a mentor should be. He always takes time out of his busy schedule, despite being both a physician and researcher, to happily sit down with his students to discuss their research and career aspirations. He makes sure that each of us are intellectually challenging ourselves through our research projects, and shows trust and respect in us as researchers. As a mentor, Dr. Weinstein

continually teaches his students the virtues of patience, perseverance, curiosity, and never-ending enthusiasm for scientific investigation."

Annette Wundes, MD, Associate Professor of Neurology, was recently selected by the National Multiple Sclerosis Society Volunteer Hall of Fame Selection Committee to receive the 2018 Health Professional award. She received the award in November at the MS Society National Leadership Conference in Denver, Colo. Patricia Shepherd-Barnes, President of the National MS Society, said "This is a big deal and no one in the country deserves it more." Congratulations, Annette!

#### NEUROLOGY FACULTY PROMOTIONS EFFECTIVE JULY 2017

#### TO ASSOCIATE PROFESSOR (WOT)

Sumie Jayadev, MD John Oakley, MD, PhD Kyle Steinman, MD Leo Wang, MD, PhD

TO PROFESSOR (WOT) Nicholas Poolos, MD, PhD

#### HAVE SOME NEWS TO SHARE?

A recent grant, publication, or award? Please send it along to Nadine Waldmann (dine33@uw.edu) so we may include it in the next issue of *Neurotransmissions*.

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Clinic staff includes **Debbie Nesbitt**, **ARNP**, a psychiatric nurse practitioner specializing in behavioral modalities such as biofeedback and hypnosis for pain and stress management. These techniques are taught in both shared and individual sessions.

The Headache Clinic offers procedures including Botox for migraine, and sphenopalatine ganglion blocks using the noninvasive Sphenocath device. The

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of many people have made this work possible, including Lauren Tantalo, Sharon Sahi and Jana Zahlan in my laboratory; Haley Mendoza, our study coordinator; **Dr. Arielle Davis**, Assistant Professor of Neurology; Dr. Shelia Dunaway and Sher Story, our study clinicians; Dr. Clare Maxwell, our statistician; and Dr. Sheila Lukehart, my ongoing mentor and our co-investigator. clinic also can prescribe neuromodulation therapy for suitable patients using the latest FDA-approved devices. When additional procedures such as nerve blocks or spinal injections are recommended, patients may be referred to the UW Center for Pain Relief, which is located upstairs from the Headache Clinic.

In addition to providing high quality clinical care, the Headache Clinic is developing a

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Robert Wilkus, who then directed the EEG lab at HMC. The program in clinical epilepsy expanded with the assistance of a contract from the NIH, with Arthur Ward, Chairman of Neurosurgery as the principal investigator. Initially, the epilepsy clinic was located at UWMC, but later moved to HMC when space became available for an inpatient unit that was separate from the Neurology and Neurosurgery Services. research program using the extraordinary volume of clinical information generated by the patient questionnaires. With patients' permission, the data from the online headache questionnaires is incorporated into a database. There are currently close to 3000 completed patient surveys in this database, a rich and growing source of information for research into headache disorders and treatments.

In 1974, with the exceptions of pediatric neurology, epilepsy and electroencephalography, there was little further specialization of Neurology clinical programs. The next segment will deal with the beginning of areas such as neuro-oncology, neurogenetics, movement disorders, as specialties within the field of neurology.