

EPILEPSY AND EEGs IN BOSTON, BEGINNING AT BOSTON CITY HOSPITAL

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Early Neurology at Harvard Medical School:

*In the 1920s and 1930s: Neurology and Psychiatry were largely one field.
“All practitioners of the specialty [Neurology] were neuropsychiatrists”
-- Merritt: History of Neurology (1975)*

- 1923: David Edsall, first full-time Dean at Harvard Medical School “creates a Department of Neurology to build on the fame of James Jackson Putnam” [1]
- 1928: Harvard, Penn, and Montefiore-Columbia were the only Neurology departments in the US.
- 1930: The Harvard Medical School Neurology service at Boston City Hospital, one of the first training centers in the US, founded by Stanley Cobb
- 1935: American Board of Psychiatry and Neurology
- 1936: “There were only 16 hospitals listed in the United States a having approved training for residency in Neurology.” [1]
- 1947: There are 32 Neurology residency positions in the US
- 1948: Founding of the American Academy of Neurology

Stanley Cobb (1887 – 1968)

- 1887: Brahmin, born in Boston. Speech impediment.
 - 1914: Harvard Medical School grad, after Harvard College
Studied Physiology at Hopkins
 - 1919: Physiology research with Walter B Cannon and Alexander Forbes at Harvard
 - 1925: Appointed Bullard Professor of Neuropathology at Harvard Medical School
{Successors: Raymond Adams, E Pierson Richardson, Joseph Martin}
- Interested in Neurology and Psychiatry, and particularly, epilepsy and its relation to cerebral blood flow
- 1925: Starts the Neurology program at Boston City Hospital (with financial support from Abraham Flexner)
Faculty include: Harold Wolff (headaches; cerebral circulation; founder of Cornell Neurology Department), Paul Yakovlev, Sam Epstein
Cobb’s Neuropathology group at the HMS medical school campus includes William Lennox
 - 1928: Cobb hires Tracy Putnam for a research position in the Neurosurgery division; Houston Merritt arrives as a resident

1934: With interest in Psychiatry >> Neurology, Cobb leaves Boston City Hospital to become Chief of Psychiatry at MGH.
First Department of Psychiatry in a general hospital.
Founder of Biological Psychiatry in the US

Putnam is appointed his successor.

Boston City Hospital:

“During the 1930’s the Boston City Hospital dominated the evolution of Neurology.”

“Boston City Hospital (1938) was the premier training program among the few centers actively turning out new neurologists.”

-- Rowland in Chapter: “Boston City Hospital: the Cradle of Modern Neurology in the United States”

Chairmen, then and later:

Tracy Putnam	Chairman, BCH, HMS, later Columbia
Houston Merritt	Professor, HMS, BCH, later Columbia
Frank Forster	Chaired: Georgetown, Wisconsin
Carle Aring	“ UCSF, later Cincinnati
Harold Wolff	Cornell
Joseph Foley	Cleveland (Metropolitan)
Raymond Adams	MGH
Milton Rosenbaum	Einstein (Psychiatry)
Robert Aird	UCSF
Adolph Sahs	U Iowa

Tracy Putnam (1894 – 1975)

Also a Boston Brahmin.

Forebears: Josiah Quincy(s) (4 men with the same name) include Boston mayors, President of Harvard University

James Jackson, the first Hersey Professor of Physick at Harvard Medical School

George Minot, Professor of Medicine at HMS and 1934 Nobel laureate (pernicious anemia research at Boston City Hospital)

Putnam’s uncle, James Jackson Putnam, first Professor of Neurological Disease at HMS; founder and president of the American Neurological Association

James Jackson Putnam Professorship: the first endowed chair in Neurology in the US
[subsequently, Norman Geschwind and Clif Saper, at Beth Israel Deaconess]

1916: Harvard College
1920: Harvard Medical School
1920: Resident in Pathology at Hopkins (met his wife, a psychiatrist analyzed by Freud)
1921: Surgery residency at MGH
1923: Trained in Neurosurgery at PBrigham with Harvey Cushing
1924: Studied with Brouwer in Amsterdam
1925-28: Resident with Harvey Cushing. Published with Cushing on SDH
1930: Research in both Neurology and Neurosurgery
1930: joins Cobb at Boston City Hospital
1934: succeeds Cobb as Chief of Neurology at Boston City Hospital

1935-55: Editor in chief, Archives of Neurology and Psychiatry
1939: leaves to become chief of Neurology and Neurosurgery at Columbia

Advanced basic neuroscience research at BCH / HMS, and at Columbia
President of American Association of Neurological Surgeons

Putnam at Columbia:

Endless political problems [e.g., heading both Neurology and Neurosurgery; liberal in a very conservative environment; refusing to fire Jewish MDs]

1945: Job “re-defined.” No colleagues stood up for him.
1946: on leave in California
1947: resignation from HMS and BCH

Private practice in California; saw very few epilepsy patients.
Neurosurgery at (now) Cedars-Sinai in LA (very few surgical cases)

1962: Financial difficulties. Played an odd physician, in *The Slime People*, a sci-fi for which his son was the sound engineer.
1964: wrote that Lee Harvey Oswald and Jack Ruby could have had epilepsy ; (at Ruby’s trial; testimony ‘demolished’ by Frank Forster [1])

H Houston Merritt (1902 – 1979)

U North Carolina, then Vanderbilt

1926: MD from Hopkins, Internship in Medicine at Yale
1928: moves to Boston City Hospital as resident, to train in Neurology
Neuropathology research with Spielmeyer, Munich
1931-44: Faculty member at HMS and BCH, rising to Professor.
The master clinician to Putnam’s science
1939-41: Interim director of Neurology at BCH and Harvard Medical School when Putnam moved to Columbia.
1941: Assistant to Denny-Brown when he arrived

Merritt was assumed to be the heir to Putnam, but HMS selected Derek Denny-Brown, a New Zealander who had done research with Charles Sherrington, Nobel laureate.

Passed over as chief: too folksy?; a ‘commoner’?

Joseph Foley: “Cobb was also a Brahmin and disdained crudity in speech or manner – so he did not like Houston and made that clear.” [1]

1944: Merritt becomes chief at Montefiore, taking with him BCH resident Sidney Carter, later prominent Child Neurology chief.
1948: Chief of Neurology at the Neurological Institute at Columbia
1958-70: Dean of Columbia College of Physicians and Surgeons

Dilantin:

Putnam and Merritt tested and developed phenytoin (Dilantin) in the mid-1930s at Boston City Hospital

1928: Putnam (HMS Professor at 33) works with Neurology resident Merritt (26)
Earlier: just bromides and phenobarbital, sedating
1937-41: Putnam and Merritt publish 7 papers together
1937: 1st paper: determines seizure threshold of cats in electroshock model (no IRBs!)
Separates the sedative and anti-seizure effects of drugs
Began with 19 Parke Davis compounds with phenobarbital morphology

Phenytoin was the first drug studied!!

With the same sedating effect, DPH increased the seizure threshold >> PB, bro

Conclusion: [Dilantin had]... “the greatest anticonvulsant activity and the least hypnotic”

The other 18 had no anticonvulsant properties independent of the sedating effect.

1938: 2nd paper: compared anticonvulsant effects of drugs on seizure threshold in cats:

DPH > PB

1938: 3rd paper: the effects of DPH in humans, including side effects

Later, Putnam says Merritt played a minor role (likely untrue)

Significance of Merritt and Putnam’s Work: [per Rowland: “Dilantin: The Legacy”]

1. The electroshock model for testing anticonvulsant drugs
2. Results in cats predicted human response (first animal tests of ASDs)
3. Anticonvulsant and sedative effects could be separated
4. A given drug can be more effective in some seizure types than in others (implies different pathophysologies)
5. The clinical efficacy of phenytoin
6. A model for other drug development
7. Among the earliest “translational research:” from the lab to the patient [in 1 year!]

Hallowell Davis (1896 – 1992)

1922: begins research at Harvard Medical School and Boston City Hospital

Records the first EEG of normal brain rhythms in the US (on himself)

First to record a petit mal seizure. (Lennox the first to record absence status)

1930s: identifies Albert Grass, recent MIT grad, to build an EEG machine.

1946: leaves Harvard for Wash U after 24years without promotion from instructor

At Harvard and at Wash U: becomes the premier authority on the physiology of hearing

Frederick Gibbs (1903 – 1992)

1929: graduates from Johns Hopkins Medical School. Wants to study Epilepsy.

Gibbs: “the only place ... where epilepsy research was occurring was Harvard with Lennox and Cobb.”

Comes to Boston City Hospital to study Neuropathology with Stanley Cobb

[1928: Erna Leonhardt comes from Germany as a technologist for William Lennox]

Erna and Fred Gibbs, married in 1930, become prominent and prolific investigators of the use of EEG in Epilepsy.

Erna devises the thermocouple probe they use to record blood flow.

1930: using the probe, they do blood flow experiments on Lennox, who passes out

Trying to show that seizures start with vasoconstriction, they learn that blood flow increases during seizures.

Penfield comes from the Montreal Neurological Institute to lecture on vasoconstriction in epilepsy. Penfield asks Gibbs, “Fred, what did you think of it?”

Gibbs: “I thought you set these students’ knowledge of epilepsy back at least 30 years.”

1935: in Germany, the Gibbs visit Hans Berger, the inventor and developer of the EEG.

Berger, Jewish, had lost his university position under the Nazis.

(Later, depressed, he commits suicide in 1941)

1936: The Gibbs translate Berger’s publications (9, all with the same title, *Über das Elektrenkephalogramm des Menschen*) into English

~1937: They establish the first clinical EEG lab at Boston City Hospital

- 1941: Gibbs and Gibbs: (THE) Atlas of Electroencephalography [foto]
- 1944: Never likely to be promoted at HMS, the Gibbs move to U Illinois, Chicago, where they work with neurosurgeon Percival Bailey to develop surgery for (TLE) "psychomotor epilepsy"
- 1949: President, American Epilepsy Society
- 1951: The Gibbs and Lennox win Lasker Prize in Medicine for their work on epilepsy
Penfield writes the inscription for the Lasker award ['American Medical Nobel']
[Merritt and Putnam never nominated for the Nobel Prize]

Albert Grass:

MIT engineering graduate

- 1935: Gibbs asks Albert Grass, MIT grad to build a 3 channel EEG (all previously one channel). Done when they return from their summer in Europe

Grass' machine was also used to deliver the electroshock in Merritt and Putnam's electroshock model of seizures in cats.

Grass Co., becomes the largest maker of EEG machines in the US

William Lennox (1884 – 1949) [foto]

Son of a Colorado gold miner

Devout Methodist. Wanted to be a missionary in China, but could not get into Theology school without Latin and Greek; decides to study Medicine

- 1913: Harvard Medical School grad, MGH internship
- 1915-19: Works in China at Peking Union Medical College as MD, where the epilepsy of a friend's daughter piques his interest for life.
Children were too often ill. Returns to Boston to work with Stanley Cobb.
- 1944: Founder, the Seizure Unit at Childrens' Hospital
- 1946: Founder and first President of the American Epilepsy Society
- 1960: At the end of a gala retirement dinner, Lennox rises to speak, but can't.
First stroke.

One of the earliest investigators in the genetics of epilepsy.
Tried fasting (ketosis) for seizure control (used on self before patients)

Describes the different types of epilepsy, with different drugs for each
[William G. Lennox "Epilepsy and Related Disorders "]

Boston Neurology and Epilepsy in the later-20th and 21st Centuries

- 2017: 87 Neurology residencies in the US; > 50 Comprehensive Epilepsy Centers
- 1974: Harvard Neurology service leaves Boston City Hospital. Moves to Beth Israel Hospital, under Norman Geschwind, the James Jackson Putnam Professor

Beth Israel, Childrens' Hospital, and Brigham and Women's Hospital unite to form the Longwood Neurology Program
Raymond Adams' MGH Neurology Program gives Harvard Medical School 2 Neurology Programs

Cesare Lombroso (1917 – 2013)

- 1946: MD, University of Genoa
Grandfather was the founder of the field of Criminology in Italy
- 1960: Succeeds Lennox in the Childrens' Hospital Seizure Unit
The only Epilepsy fellowship in Boston until the 1980s
- 1987: President, American Epilepsy Society

Seizure Unit directors at Boston Childrens' Hospital:

William Lennox
Cesare Lombroso
Don Schomer
Greg Holmes
Blaise Bourgeois
Phil Pearl

Norman Geschwind (1926 – 1984)

- b. NYC. Harvard College, interrupted by US Army in WW II, 1944-46
- 1951: Harvard Medical School grad
- 1952-55: studies with Sir Charles Symonds at National Hospital Queen Square
- 1955: Neurology residency at Boston City Hospital with Derek Denny-Brown
- 1956-58: research in muscle disease (!?) at MIT
- 1966: "Disconnection Syndromes in Animals and Man" in *Brain*
- 1969: appointed James Jackson Putnam Professor of Neurology at HMS
- 1974: moves to Beth Israel Hospital, co-founder Longwood Neurology Residency
- 1984: untimely death at age 58

Father of American Behavioral Neurology

Colleagues and 'disciples' include: Drs Benson, Mesulam, Damasio, Heilman, Galaburda.

Explored temporolimbic epilepsy as a window into brain and behavior, and temporo-limbic dysfunction in interictal behavior problems

- 1979: to study epilepsy more thoroughly, recruits neurosurgeon Howard Blume and neurologist Don Schomer from the Montreal Neurological Institute, where they had worked with Jasper, Rasmussen, Gloor, and Andermann.

Don Schomer:

- 1980: establishes the first Comprehensive Epilepsy Center for adults in Boston, at Beth Israel Hospital, later Beth Israel Deaconess Medical Center
- 2004: President, American Clinical Neurophysiology Society (formerly the EEG Society, founded by Jasper, 1947)
[Among ≥ 8 Boston EEG-ers, incl. Gibbs, H Davis, Schwab, Lombroso, etc.]

Steve Schachter:

- 2009: President, American Epilepsy Society
[Most recent of ≥ 7 Boston epileptologists, incl. Lennox, Gibbs, Lombroso etc.]

Ed Bromfield (1951 – 2009):

- 1994: Comprehensive Epilepsy Center at **Brigham and Women's Hospital**
[former Peter Bent Brigham Hospital, home for (most) career, Harvey Cushing] Current director, Barbara Dworetzsky

Massachusetts General Hospital: Andrew Cole

Boston Medical Center (former Boston City Hospital): Georgia Montouris

Tufts Medical Center: Kimberly Parkerson

Reading:

1. Lewis P Rowland. The Legacy of Tracy Putnam and Houston Merritt. Oxford University Press, New York, 2009.
2. Berger H. Über das Elektrenkephalogramm des Menschen. Arch Psychiat Nerv Krankh 1929;87:527.
3. Gibbs F, Gibbs E. Atlas of Electroencephalography, 1941, second edition 1951.
4. Lennox WG. Epilepsy and Related Disorders, with Margaret Lennox (his daughter), Boston. Little, Brown & Company, 1960.