

Barry Blackwell: Thudichum: “Father of Neurochemistry”

Collated by Olaf Fjetland

This collated document is comprised of Barry Blackwell's essay, posted on July 30, 2015, and the exchange that followed between Edward Shorter and Blackwell after the posting of this essay.

This collated document is now open to all INHN members for final comment.

Barry Blackwell	July 30, 2015	essay
Edward Shorter	September 17, 2015	comment
Barry Blackwell	October 8, 2015	reply to Shorter

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BARRY BLACKWELL: THUDICHUM: “FATHER of NEUROCHEMISTRY”

Our Fathers

“The poets and philosophers before me have discovered the unconscious; I have discovered the scientific method with which the unconscious can be studied.”

FREUD, Father of Psychotherapy

“Many forms of insanity are unquestionably the external manifestations of the effects upon the brain substance of poisons fermented within the body”

THUDICHUM, Father of Neurochemistry

She wakes me up in early morning doubt.
Crazed eyes and alien name, Luz Medino;
both fuel the need in me to know about

her persona, gene pool, Puerto Rico.

Sour culture and unruly cells enslave
her brain in bitter juice. It can't go free,
slumped sad inside its melancholy cave,
bound by its own unraveled chemistry.

The day they cut her breast away she wept,
her hardwood face dissolved in acid tears.
Except for dream-infested nights she kept
slammed shut that angry door to all her fears.

She doesn't rage against her fate. So sure
she is a devil who deserves to die
that words or drugs have not produced a cure
and Freud or Thudichum can't tell me why.

Twenty one years ago I composed and published this poem dedicated to "Our Fathers" (Blackwell, 1994). As befits the topic, it is in a classical form with four stanzas, each of four lines with 10 syllables and alternating end rhymes.

The poem portrays the frustration we all feel when our best therapeutic attempts and all our tools fail to benefit the patient. When it was penned all I knew about Thudichum was his paternal eponym as "father of neurochemistry." Then Tom Ban suggested I write a biography of Joel Elkes, born only 12 years after Thudichum's death in 1901 and described by Jean Paykel as the "father of neuropsychopharmacology" (Paykel, 2003, cited by Shorter, 2011).

To accomplish the task, I needed to learn more about Thudichum and was surprised to discover a copy of his only biography (Drabkin, 1958) on Amazon for the bargain price of \$3.50. It was a second hand copy in pristine condition, its former owner identified by a rubber stamp on the fly leaf.

Donald B. Tower M.D.

National Institute of Neurological Disease and Blindness

Bethesda, Maryland.

Knowing more about the book's former owner might enlighten my understanding of Thudichum. Donald Tower's own autobiography was available in Volume 3 of the series *The History of Neuroscience in Autobiography*" (Squire, 2001).

A medical graduate of Harvard (1944) with a Ph.D. in neuroscience from McGill (1951), Towers trained in wartime as a physician and post-war began neurological and neurosurgery training under Wilder Penfield at the Montreal Neurological Institute where both clinical care and laboratory research were mandatory. This involved neurosurgery on the foci of seizures and bench work on the excitatory role of acetylcholine in epilepsy. After graduation he chose to pursue the research track with work in humans and animal species from rats to whales and elephants.

At the outbreak of the Korean War Towers satisfied his reserve military obligation in an assignment to the National Institute of Health's Institute of Neurological Diseases and Blindness (1953) where he moved up the ladder to become Director of Neurological Diseases and Stroke (1974-1981). Like Thudichum, he engaged in both clinical and chemical work on the brain, on the manifestations of disease and its putative origins.

Following retirement from the NIH, Donald Towers pursued his hobby and delved into the history of neurochemistry. From the German edition of Thudichum's monograph on the *Chemical Composition of the Brain* (1901), David learned of the 17th century career and contributions of Johann Hensing who, like Thudichum and Tower, was both a clinician and neurochemist. Tower obtained a photocopy of the only known text of Hensing's monograph on cerebral chemistry that included the discovery of phosphorous, the first specific chemical substance to be isolated from the brain. Tower published his own monograph of Hensing (Tower, 1983) which received an Award of Distinguished History from a German University.

Thus, we have a four-century chain of distinguished clinician-scientists through Hensing, Thudichum, Tower and Elkes from a single simple chemical substance in the 17th century to the elegant but baffling complexity of contemporary 21st century neuroscience.

The origin of Drabkin's interest in Thudichum appears to date from 1925 when their paths crossed over an unlikely scientific problem they shared in common concerning the color of urine and its biochemical significance. When Drabkin became interested in this topic (Drabkin, 1927) an intensive search of the literature turned up Thudichum's early "Treatise on the Pathology of Urine" (Thudichum, 1858) and his later discovery of urochrome (Thudichum, 1868). While Drabkin was developing his own paper (1925-1927), he sought further information about Thudichum and received a message from Irvine Page, Research Director of the Cleveland Clinic Foundation, making him aware that Dr. Otto Rosenheim, an outstanding steroid chemist, had collected a substantial amount of archival information about Thudichum. Rosenheim's interest was stimulated by his own early research when he found proof in defense of Thudichum's controversial view that Liebreich's "Protagon" was not a discrete chemical entity but a combination of two others (Rosenheim and Tebb, 1910). This debate had sparked a contentious dispute, described later, that tarnished Thudichum's reputation and career.

In his biography of Thudichum, Drabkin devotes an entire appendix to Rosenheim's distinguished career (he discovered ergosterol, precursor to Vitamin D) and acknowledging the material about Thudichum he provided. He also dedicates the biography to Rosenheim noting that "With characteristic generosity he put at my disposal many salient facts he gathered on Thudichum's life." We do know that Drabkin and Rosenheim corresponded with one another beginning in 1929 and Drabkin promised that in return he would produce a biography on Thudichum in the future. Eighteen years later he published a brief historical synopsis in two chapters for a history of biochemistry (Drabkin, 1947) and in 1954 he gave two unpublished lectures in Chicago on "Thudichum a Neglected Genius of the Nineteenth Century: His Times and Contemporaries."

In the prologue to the biography, Drabkin berates himself for the dilatory implementation of his promise to Rosenheim made a quarter century earlier.

He then relates how this "writer's block" is overcome after a meeting with another scientist enthused about Thudichum. Drabkin's friend Harold Himwich introduces him to Percival Bailey, a neurosurgeon who served as research consultant to the State of Illinois. Together they are planning a ceremony to name the new Laboratory of the Galesburg State Research Center in honor of Thudichum. Bailey invites Drabkin to give the opening lecture,

acknowledging “You are the man who knows more about Thudichum than anyone” and then relates the origins of his own interest which are retold in his introduction to Thudichum’s biography.

It began 40 years earlier in 1913 when Bailey attended a course in biochemistry at the University of Chicago and the lecturer, Fred Conrad Koch, made frequent reference to Thudichum. This knowledge lay dormant for several years until Percival married into a family of grape growers in California. Becoming an oenophile he browsed second hand book stores in search of texts about wine making and came upon an author named Thudichum (Thudichum, 1894). Sensing this might be the same man, he began a search for Thudichum’s classic monograph, *“The Chemical Composition of the Brain”* (Thudichum, 1884). A prominent London bookseller had a dozen requests on a waiting list, but a copy had not been found in as many years. Quite by chance, in a pile of catalogues he was about to discard, he noticed a copy selling for \$4.50. This began his own search for historical material.

After telling his own story, Bailey unveils a strategy designed to enable Drabkin to fulfill his promise to Rosenheim. “You must get rid of your guilt complex; I shall arrange it.” Within weeks Drabkin receives “the following guilt purging program.” It outlines a four-lecture series incorporating the two he has already given on “The Neglected Genius” with a lecture to be written for the naming ceremony on “His Works” to be followed by a final named lecture at the University of Illinois on “Thudichum: Chemist of the Brain.”

The specificity of this strategy, building on previous work and defining two future distinguished lectures, produced the desired results and became a framework for the long awaited biography which was finished within a year.

In January 1955 Drabkin set sail for England on the Queen Mary to deliver his completed text (not yet published) to whom it was dedicated and long ago promised. Sadly, Max Rosenheim was too sick to receive visitors, so David placed the document in the hands of his mother. The next day she telephoned to report that Max was “excited that the work was completed and very much moved by the dedication.” David Drabkin returned to America where four months later he received a letter reporting that Max Rosenheim had died peacefully in his sleep.

With the provenance of the biography unveiled by this voyage of discovery, its form and content will be reviewed for the main purpose of familiarizing the reader with the source of my brief biographical synopsis of the character, career and accomplishments of “The Father of Neurochemistry.”

“Thudichum: Chemist of the Brain” (Drabkin, 1958)

No source of information compares with Drabkin’s biography of Thudichum. It is scrupulous in design and encompassing in its scope. The text is 309 pages, including a Forward by Percival Bailey, an author’s Prologue and Epilogue and five Appendices; **I**: An annotated bibliography of Thudichum’s 213 publications (1846-1901); **II**: A chronological Outline of Thudichum’s Life; **III**: ‘Belated Honors’ documenting efforts in England and America to raise resources to support his bereft family, as well as founding the kind of research institutions Thudichum envisaged, such as at NIH and Galesburg, Illinois; **IV**: Transcriptions of letters in his native language to colleagues and critics; and **V**: A brief memoir of Otto Rosenheim documenting a career-long devotion to collecting information and memorabilia about Thudichum that forms a foundation for Drabkin’s Biography.

The main text (pp. 29-183) is divided into three chapters: “The Man,” “His Time and Contemporaries,” and “His Works.” The first of these includes 15 pages of memorabilia including photographs of Thudichum at different ages, the spectroscope he used, instruments given him by Liebig, drawings from his texts, title pages of his books, lecture notes, letters, his degree Diploma, the title page, in German, of his classic monograph “*Chemical Composition of the Brain*,” pictures of his homes in London, pencil drawings made while a surgeon in the Danish war, a poem to his favorite daughter Lottie on her birthday and photo reproductions of his unpublished books: “*History of Beer and Ale*” and “*Cape of Good Hope Wines*.”

Dobkin’s literary style is impressionistic, reflecting thoughts, feelings and events as they occur during his excavation of Thudichum’s life. Reconstructing this treasure trove in a coherent, chronological sequence was challenging, an invitation for a synopsis to become plagiarism. So this text makes liberal use of quotation marks to preserve the flavor and provenance of the original biography.

Ludwig: The Man

Ludwig Thudichum was the progeny of forbears who toiled with their hands, traced back to the 17th century, including a cloth maker, cooper and coppersmith. The original family name was Dudichum, a condensation of three German words, *du dich um* which translates roughly to “bestir yourself,” “get to work,” a “wonderful admonition and motto” for a man who once wrote to his friend and mentor, Liebig, proudly proclaiming he had “done the work of three men.”

In the early 18th century the family changed its name to Thudichum and began to climb the social ladder moving from handicrafts to intellectual pursuits. Ludwig’s father, Georg, was a minister in the Reformed Lutheran Church, Principal of the local Gymnasium (high school) and Doctor of Philosophy, an authority on the epic verse and prose of ancient Greece. He would sire three sons and three daughters. Ludwig was the eldest son, another would become Vice President of a German University and the other founded a famous boys’ school.

The family lived in Budigen, a small medieval town unspoiled and idyllic, “with narrow cobbled streets and inner court yards glimpsed through stone archways, its castle and hilly vineyard.” Thirty miles north is the “University town of Giessen where the great Liebig founded a chemical dynasty.” Ludwig’s birth on August 27, 1829, and his subsequent baptism, is recorded in documents dating from 1630. He was named Johann Ludwig Wilhelm, later anglicized to John Lewis William, alternatives he “abhorred.” His close friends in England and Germany all called him Ludwig.

Ludwig led a charmed childhood. He was talented in amateur theatricals and his writing skills at age 17 earned him an offer to edit the town weekly newsletter. He belonged to a coterie of talented children, two of whom also became physicians and in whose company he became an excellent swimmer in the local river during the summer and a fine figure skater on its ice in winter.

The family dwelt in a large house, beautifully situated in a lovely park, leading life “on a modestly elegant scale.” Parents and children toiled together to turn a plot of land behind the house into a terraced garden growing fruit and nut trees along with grape vines that yielded a wine “as good as any on the Rhenish slopes,” as well as a garden “to rival any in England.” Clearly these endeavors were the seedbed for Ludwig’s lifelong interest in viniculture and horticulture.

Inside the house his father's study was a shrine to his own scholarly accomplishments, translating Greek poetry and tragedies, playing a piano with a "noble tone" alongside his guitar with a compilation of 100 lieder songs. "In this room the Classic and Romantic, song and wine, were wed, a marriage proclaimed by three busts of Zeus, Goethe and Schiller. These symbols were for the children ingredients of the growing up process, much as the garden was."

The climate of the Thudichum household must have resembled that of the European "Salons" of that era: popular intellectual and social gathering spaces. "The important medical and scientific achievements in Germany in this period were co-linked with the extraordinary liberalism of its great universities." A prevailing sentiment was Goethe's view that "conflict of opinion does not determine truth but states the problem to be solved." Ludwig absorbed this truism in a life devoted to problem solving, although the debates that ensued were often mired in controversy

Ludwig was the most apt of the six children in absorbing the fruits of the environment in which they lived. He became a gifted pianist and singer with vocal training from a famous Italian tenor that equipped him to sing in an amateur opera. Georg Thudichum's "scholarship and broad interests brought distinguished people to his door." Among them was the renowned chemist Justus von Liebig. "Georg, the Greek savant attended some of his lectures at Giessen." In his diary Ludwig's father recorded his admiration and critical analysis of Liebig's lectures: "*Without doubt chemistry will bring new light to agriculture and to physiology. Perhaps also to medicine? At the best, if the true principles of life were known, the ancient diseases which have plagued man could be prevented.*"

Impressed with Liebig's talents, Georg consulted him about an analysis of mineral waters from a newly discovered spring on his property to determine if they justified building a spa. Liebig advised otherwise, but visited the Thudichum property when Ludwig was 18-years-old, preparing for university. Little did any of them realize that Liebig would become Ludwig's mentor and Ludwig would become Liebig's torch bearer, seeking the fruits of chemistry to illuminate the diseases of body and brain just as his father had imagined might be possible.

At 18 Ludwig graduated from the Gymnasium and embarked on medical school. At the time it was quite usual in Germany to obtain training at more than one university; Ludwig opted to go first to Heidelberg and then Giessen. In Heidelberg, from 1847 to 1851, he was taught by

Wilhelm Bunsen, the inventor of the spectrograph, and in Giessen he was mentored by Liebig in novel methods of chemical analysis, techniques he employed in his life's work. In Heidelberg he wrote a prize winning essay on "Urea in Amniotic Fluid" (Thudichum, 1850), but his M.D. thesis in Giessen was on "Fractures of the Upper End of the Humerus" (Thudichum, 1851).

At age 19, during his first year as a medical student, Ludwig visited the Dupre family in Frankfurt and met his third cousins, two boys and a girl, Charlotte: "small and warm, with dark hair, French-like." In two weeks they bonded, but six years would elapse before they married in London (1854). "But from the first this small woman became the refuge of the big man."

Despite having trained under powerful mentors, Ludwig's career did not prosper following graduation principally because he became politically compromised after volunteering for military service on the revolutionary side of the 1848 movement that attempted to establish a democracy in Germany. When he was denied a post in the Pathology Department at Giessen University in 1853 he knew the reason. "The impetuous young and older men associated with it (the revolution) were destined to pay the price for non-conformity. Many, like Thudichum, found the aftermath unpropitious and migrated to other lands." For Ludwig, this meant London.

Thudichum's Time and Contemporaries

Of Thudichum's 72 years on earth, 50 were spent in Queen Victoria's England until she died, just eight months before he did in 1901. Within 10 years of arriving, he had established himself as a prominent physician, surgeon and scientist. Regarded by some as England's leading biochemist (there were not many), his reputation was cemented by winning the prestigious Hasting's Gold Medal for work on urochrome, also leading to appointment as the Honorary Lettsomian Professorship. "It was the heyday of Thudichum's life."

Dobkin provides an itinerary of Thudichum's dwelling places in London (1853-1901) and vignettes of his life in them. The principal and final of these was an elegant house in Pembroke Gardens (from 1876). Adjoining it was a converted greenhouse where Ludwig housed his private laboratory stocked with analytical equipment (some of it from Liebig's own lab) and where he did much of his research.

Thudichum became a British citizen six years after his arrival (1859), but "frequently made trips to Germany for scientific meetings and particularly to visit loved ones." At home he

preserved a climate “of good things, music, gardens (the best dahlias in London) and subtle family customs. This is the real Thudichum, a man of love and fun.” He sired six daughters and two sons, all proficient pianists with fine singing voices. Strongly built and athletic, he was an expert duelist and a fine horseman who owned two steeds he rode daily in Hyde Park.

Thudichum “was a prodigious worker and maintained a strict routine.” An early riser, he made time for his dogs, horses and garden before patients arrived at 11, followed by two hours in the laboratory. After lunch he took 10 minutes rest before returning to research. He read the literature late at night, rarely went to bed before two, and slept for only four hours – all he needed. Overall, “he was somewhat of an eccentric and epicure. But he was also an indulgent father and had a lusty, boyish humor.” Ludwig smoked three carefully selected Havana cigars a day, an indulgence he viewed as “an ambrosial offering to Apollo ... to compose my shattered nervous system.” He was also a lifelong oenophile for whom “wine was truly God’s gift to man.”

Thudichum’s capacity to unite work with pleasure is reflected in an occasion when, as the first Professor of Clinical Pathology at Saint Thomas’ Hospital, he designed a study of the conversion of alcohol to energy “in the course of wining and dining a large group of medical students in the garden. There were 33 in number, including myself. We drank from two in the afternoon till seven in the evening, 44 bottles of wine consisting of white and red, Hungarian, Burgundy and Sauterne – the alcoholic contents were an aggregate of 4,000 grammes of acute alcohol. All the urine passed from two in the afternoon till six next morning was collected and distilled – only 10 grammes of alcohol were collected. The rest was burned in the system” (Thudichum, 1866-67).

Ironically, all the London homes Thudichum lived in were destroyed by German bombs during the Blitz of World War II. His children survived and the last to die was his favorite daughter Lottie, on September 30, 1947, at age 85.

During his first decade in London, Thudichum made friends and enemies. First among the former was John Simon (later Sir John). Like Liebig in Germany, Simon became Thudichum’s major support in England, funding and sponsoring his research with the Royal Society of London. Sir John was also Chief Medical Officer for the Medical Department of the Privy Council (later the Medical Research Council). It was to him Thudichum dedicated the second edition of his book, “*A Treatise on the Pathology of Urine*” (Thudichum, 1877), “as a

small tribute of admiration for his many and eminent public services in improving the health of the people.” It was this relationship between a leading and innovative public health administrator and a talented physician-biochemist that led to Thudichum’s “*Further Reports on Research Intended to Promote and Improve Chemical Identification of Diseases*” (Thudichum, 1867). These reports covered fundamental contributions to the chemistry of pigments in gallstones, bile and blood (the "luteins").

It was at the age of 40 (1869) that Thudichum, supported by Sir John Simon and government funding, began his seminal work on the chemistry of the brain, resulting in a series of reports called “Parliamentary Blue Books” beginning five years later, by which time he had studied 1,000 brains. It was this work that led eventually to “*The Chemical Composition of the Brain.*” (Thudichum, 1884), translated promptly into Russian, but not into German until just prior to his death (Thudichum, 1901).

During this epoch, seeds of enmity had been sewn among his less talented detractors irked by “his non-conformity, individuality and obvious virtuosity.” His work on the brain was vigorously attacked and “at fifty five Thudichum was a discredited man” -- he lost his government funding and although he was able to continue research in his private well-equipped laboratory, he was forced to spend more time on income generating medical practice and less on research. Although this was the nadir of his reputation, opposition to Thudichum’s original ideas and challenging personality began much earlier, within a few years of winning the Hasting’s Gold Medal. “Vilification by powerful members of the biochemical fraternity would be his lot; he would have to wage a ceaseless bitter struggle to maintain his place in the sun.”

In 1868 Hoppe-Seyler, Germany’s leading biochemist, published a slanderous review of Thudichum’s discovery of “cruentine” (hematoporphyrin) in a German journal, accusing him of falsifying his results (Hoppe-Seyler, 1868). Thudichun appealed to the journal editor, Virchow, requesting a public retraction. This produced a letter of apology for “possibly one-sided and too categorical a judgement” coupled with promise of a future report which never appeared. Fearful his reputation was in jeopardy, Thudichum wrote to Sir John complaining that his position as Professor of Chemical Pathology at St.Thomas was inadequate to support the expense of his research (which he carefully itemized). The result was a generous increase in government research, given although “he was under a cloud.”

Although the results of Thudichum's research were appearing in Government reports and Blue Books, they were being "effectively buried" by "garbled re-abstraction or willful misinterpretation." In a "valiant attempt," Thudichum founded his own biomedical journal, "*Annals of Chemical Medicine*," which foundered after only two issues (1879 and 1881) largely because the contents were made up almost exclusively by Thudichum's own research, inviting virulent rebuttals from his European detractors, Hoppe-Seyler, Stadelers and Maly.

The dispute with Maly was typical of those which plagued Thudichum. Maly, the influential editor of a German journal, critiqued Thudichum's finding that bromo-bilirubin was a bromine substitution product of bile pigment. Maly maintained it was an oxidation product (Maly, 1877). Thudichum's correct analysis was based on use of the spectroscope, an instrument with which Maly was not familiar.

Disparagement of Thudichum's research also took the form of "re-discovering" the substances he found and re-naming them in a different journal. Dobkin gives several examples and names the scientific miscreants, Salomon, Abderhalden, Geheimrat and Otto Von Furth, all tucked away in German journals safe from English eyes.

Not everyone in Germany was a detractor. Liebig, Thudichum's lifelong friend and mentor continued to lavish praise: "it is hard to understand how you find time for these difficult investigations" and "you are remarkably active in fields in which work is extremely difficult."

Thudichum also had powerful enemies in England. Chief among them was Arthur Gamgee, the country's first physiological chemist, who "came to loathe him with unreasonable and self-damaging fury." Dobkin makes an effort to uncover the source of this "Thudichumphobia" and attributes it to twin sources: Gamgee's unstable mental temperament and controversy over his discovery in the brain of a compound he named "protogon" which Thudichum considered inaccurate. "The verbal fireworks on both sides became ill-mannered and intemperate." Gamgee criticized Thudichum in his Textbook which Thudichum destructively reviewed for a journal titled, "Modern Textbooks as Impediments to Animal Chemistry." This contentious debate stirred up "new and powerful enemies."

Criticism of Thudichum survived into the early 20th century, gradually reversing after Rosenheim's research proved Thudichum correct about "protogon" while his interest and

admiration grew (Drabkin, 1958, Appendix V). Furth's "glowing tribute" also served to further restore his reputation and credibility in Germany (Furth, 1928).

Ludwig Thudichum's Diverse Interests and Philosophy of Science

Drabkin's synonym for Thudichum is "Multiple Man." This seems paradoxical since he points out that Ludwig was accused of "dilettantism by his detractors, the Brahmins of his day, (Hoppe-Seyler, Maly and Gamgee and Co.)." Thudichum, in his own words, says in a lecture to the Medical Society of London titled, "*Rise of Specialism Limited*" (Thudichum, 1864): "Do not spread yourself too thin; do not dissipate your energies in breadth." Drabkin resolves this paradox by noting, "Thudichum plumbed deeply and yet allowed himself the broadest latitude in casting his lines." Metaphorically, wherever Ludwig cast he caught big fish. Only by shrinking his catch to minnows did ignorance and envy enable detractors to call him a dilettante.

To make his point, Drabkin lists Thudichum's accomplishments across the oceans he fished and furrows he ploughed: "Thudichum and Public Health, Thudichum the Physician (Thudichum's test for creatinine), Thudichum the Surgeon (Thudichum's speculum for nasal polyps), Scientist, Chemical Pathologist and Physiological Chemist, Thudichum the Historian, Thudichum Chemist of the Brain, Thudichum the Humanist, Poet and Musician." And Drabkin's list does not include viticulture and horticulture. This is the repertoire not of a dilettante but a polymath. No wonder he infuriated lesser mortals!

Drabkin illustrates each of these domains in detail for which the reader of this brief biography must consult the original. Suffice for this biography and its home at the International Neuropsychopharmacology History Network (INHN) to note Drabkin's comments on Ludwig Thudichum's views as an historian: "To him it was a most necessary phase in which the current literature not only is casually scanned, as is usual, his was a deep approach from the very roots – a critical sifting of past errors from adequately established fact, which in the long run saved valuable time by avoiding unprofitable pathways. His appraisals and opinions were never based upon the past evaluations of others. He read the contributions in their original and weighed them carefully, whatever may have been the contemporary opinion of their merits."

Drabkin concludes that "Thudichum's introductions to his various treatises are truly masterful historical contributions... although this aspect of his work has received no notice

whatsoever.” The introduction to the German edition of his classical monograph, *Thudichum* (1901) expresses a philosophy of science linking medicine to chemistry.

“My medical soul hangs, expressed in poetical language, in ardent affection on the infallibility of the chemical method. It was for me a spiritual guide in the agitated sea of medical conjecture, on which one so often lacks that compass. The chemical method of investigating and managing disease, together with the development of etiology and diagnosis, has convinced me that the healing art, aside from its practice by men of genius and its sway over human minds, is capable of perfection into an exact science and of being applied with an almost astronomical precision. For this purpose, however, as in theology the falsification of the records, so also in medicine, to make use of an expression of Darwin, the 'false facts' must be rooted out and the scientific bases for judgement and all intelligences must be established.” This is translated into English and quoted by Percival Bailey in his Foreword to Drabkin’s biography.

Thus said, Ludwig Thudichum died a happy man. On May 24, 1901, his monograph on “The Chemistry of the Brain” was published in Germany 17 years after it was available in England and Russia. Three months later on August 23rd he received an Honorary Degree Diploma from Giessen University celebrating the 50th anniversary of his graduation. After he returned home, he celebrated his 72nd birthday on August 27th. On September 6th, walking with a colleague in the evening, he was noted to be “unusually elated” due to these recent events. The following day, September 7th, while dressing in the morning and preparing to tend his garden, he suffered a cerebral hemorrhage and died a few hours later. “Death came with kind swiftness” (Obituary, *West London Med. J.* 6 (1901), 297).

One cannot help wondering what Ludwig Thudichum might think and feel if were alive today, 114 years after his death, at that time a happy, contented chemist, physician and scientist. He would find his expectation that neurochemistry could achieve “almost astronomical precision” in the treatment of diseases of the mind was tragically unfulfilled. Instead our generation is engaged in rooting out “false facts” while attempting to find better “scientific bases” for judgement. Aware of all this, Ludwig, the skilled physician and occasional poet, might empathize with Luz Medino and her frustrated doctors, impotent to find a cure for her psychotic melancholia brought about in an unknown manner by upbringing, persona, culture, genes, gender and mutilating surgery. Thudichum knew chemistry had shone light on the brain’s structure, but

how that organ orchestrated its miracles and misfortunes remains a mystery. Much work remains to be done.

Du Dich Um

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July 30, 2015

Edward Shorter's comment

I've now had a chance to read your very interesting and learned essay on Thudichum, who seems to have been a bit of an odd duck, and it's apparent that you see yourself more as a "Drabkinite" than a Thudichumite, to coin a horrible term. Is Thudichum the "father of brain chemistry?" A couple of points:

1. The belief that psychiatric illness stemmed from biological disorders of the brain was common in his day and not at all an original idea of his.
2. He did undertake a number of studies of brain chemistry, although it is not clear from your account exactly what he found out. My recollection is that, by boiling a number of brains, he found that some had more phosphorus (or whatever) than others. I don't mean to be flippant, but here I am stuck in Madrid, with no library access, and no resource other than my memory to what Thudichum actually discovered. However, if you intend to keep his memory alive, maybe you should tell us.
3. More importantly, he did not have a "school" and his work evidently had zero impact. My belief is that the era of brain chemistry truly originates with Bernard Brody and his lab at NIH, in the 1950s, made possible with the discovery of the fluorospectroscope. Before that, the main

discoveries were in the PNS, and brain chemistry itself lay largely fallow. Certainly Thudichum had no impact on any of this as no one had ever heard of him.

4. T Thudichum's main interests seem to have been general biochemistry rather than the brain itself, and I suppose one might call him "an influential early biochemist," but not really much more than that. Hoppe-Seyler was a big name, and that he considered Thudichum a fool or a charlatan should set alarm bells ringing. WTF, as we say.

September 17, 2015

Barry Blackwell's reply

Thanks so much for your cogent and critical analysis of the Thudichum paper. The point you make about the lack of any substantive findings relevant to how the brain works or how to treat it are, I believe accurate. All of what he did was strictly chemical. Like Freud, he believed in a biology of the brain, but had no tools adequate to explore that. His hypotheses were in advance of evidence. But I began this biography, not so much to support the posthumous title others bestowed on him, but simply to better understand who he was and what he did. The poem with which I start the biography says that in so many words. Neither Freud nor Thudichum were helpful in understanding or treating a difficult patient. For all that, he was an energetic, determined and courageous searcher after truth with the means available at the time. That he did not found a "school," speaks not so much of what he accomplished, but of the enmity and rivalry he (unwittingly?) aroused. The German school did its best (sans Liebig) to bury or refute his findings. He was posthumously revived by biochemists, far more knowledgeable than I, to assess his accomplishments (Drabkin, Himwich and Rosenheim). I skimmed the surface of the area you rightly question, but in my own defence, my goal was to enlighten others who, like me, had cited a title he never bestowed on himself, but who knew nothing of him. If you read my memoir, you will discover that I flunked organic chemistry three times and would never have become a physician if my Cambridge tutor had not turned a blind eye to the fact that my name

was falsely placed in the "pass" column. "Blackwell, I know you failed but I shall say nothing. I think you will make a good doctor!" A year later, he died at a young age from a cerebral hemorrhage, taking my secret to the grave with him. Who am I to adjudicate the validity of claims made for Thudichum by my betters?!

October 8, 2015

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