Collated

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BARRY BLACKWELL: JOEL ELKES

Collated Document

Thomas A. Ban

This collated document includes Barry Blackwell's biography of Joel Elkes, his In Memoriam after Joel Elkes passed away and the exchange that followed.

Eight participants exchanged a total of 15 postings, including five postings by Barry Blackwell, three postings by Ross J. Baldessarini, two postings by Samuel Gershon and one posting each by Robert Belmaker, William Bunney, Reid Finlayson, Paul Grof and James Harris.

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

Barry Blackwell	August 20, 2015	Joel Elkes An Integrative Life
Barry Blackwell	November 12, 2015	In Memoriam. Personal recollection
Samuel Gershon	January 7, 2016	Comment
Paul Grof	January 28, 2016	Comment
Barry Blackwell	April 14, 2016	Reply to Grof
Robert H. Belmaker	February 4, 2016	Comment
Ross J. Baldessarini	March 10, 2016	Comment on Barry Blackwell's biography. Recollections of [OK1]Joel Elkes from the 1960s
Samuel Gershon	March 17, 2016	Comment on Barry Blackwell's biography and Ross Baldessarini's comment
Barry Blackwell	May 2, 2016	Reply to Baldessarini
Baldessarini	August 11, 2016	Response to Blackwell's reply

Barry Blackwell	August 18, 2016	Response to Baldessarini's response
Samuel Gershon	March 17, 2016	Comment
Reid Finlayson	March 31, 2016	Comment
William E. Bunney, Jr	April 21, 2016	Comment
James Harris	August 4, 2016	Comment Joel Elkes at Johns Hopkins

Barry Blackwell: Joel Elkes An Integrative Life

This brief biography and review of Joel Elkes' scientific, literary, artistic and other accomplishments is in three parts. First, a synopsis of Elkes' singular and pre-eminent historical role as the first modern neuropsychopharmacologist. Then a chronological account of his early life, followed by the three epochs of a professional career, in Birmingham, U.K., the National Institute of Mental health at St. Elizabeth's Hospital in Washington D.C. and Johns Hopkins University. Finally, a review of Joel's later life activities including his literary and artistic accomplishments.

Historical Role and Singular Accomplishments

Joel Elkes is now in his one hundred and second year of a distinguished life and is the oldest living pioneer in our field, recognized as the "father of modern neuropsychopharmacology" (Paykel, 2003; Shorter, 2011); a worthy successor to Thudichum, the acknowledged founder of neuroscience and first "Chemist of the Brain." Both men are polymaths with wide ranging interests, Thudichum, dubbed by his biographer as "The Multiple Man," who "lived broadly and deeply" (Drabkin, 1958) akin to Elkes' integrative life portrayed here.

Joel was born in 1913, twelve years after the death of Thudichum. Elkes' early research on the molecular structure of myelin (Elkes and Finean, 1949) is an echo of Thudichum's work in "The Chemical Composition of the Brain" (Thudichum, 1884).

Joel Elkes' designation as "the father" of modern neuropsychopharmacology is bolstered by many "firsts" in the field.

In 1951 he established a Department of Experimental Psychiatry in Birmingham, the first in the world. (See The Oral History of Neuropsychopharmacology (OHP), Vol.1: Starting Up, Series editor, Tom Ban, Volume Editor, Edward Shorter). With his wife Charmian he conducted the earliest controlled trial of chlorpromazine in overactive states (Elkes and Elkes, 1954), an early empirical approach, "one of the first in any medical specialty" (Silverstone, 1998).

Later in life (Elkes, 2011a), Joel describes the wisdom derived from this seminal controlled study: " The research instrument in a trial of this sort being a group of people, and its conduct being inseparable from the individual use of words, we were impressed by the necessity for a 'blind' and self-controlled design, and independent multiple documentation. Furthermore, we were equally impressed by the false picture apt to be conveyed if undue reliance was placed on the interview alone, as conducted in the clinic room. The patients' behavior in the ward was apt to be very different. For that reason the Day and Night Nursing staff became indispensable and valued members of the observer's team. We were warmed and encouraged by the energy and care with which they did what was requested of them, provided this was clearly set out at the beginning. A chronic 'back' ward thus became a rather interesting place to work in. There may well be a case for training senior nursing staff in elementary research method and in medical documentation. This would make for increased interest, increased attention to, and respect for detail and the availability of a fund of information, all too often lost because it has not been asked for."

Not only is this an early endorsement of controlled trial methodology which would henceforward become the gold standard but it is a prescient statement of what would be helpful as the State Hospitals and VA became the seed bed for early trials of future psychotropic drugs.

Another innovation, before the foundation of the CINP or ACNP, and in the wake of the chlorpromazine discovery, was Joel's role in initiating the First International Neurochemical Symposium representing 11 countries held at Oxford in 1954 (Elkes 2011a). It was attended by Seymour Kety, Heinrich Welsh, Louis Flexer and Jordi Folch-Pi from the USA, with Geoffrey Harris, Derek Richter and Joel Elkes from the UK.

After moving to the USA the scope of Joel's interests and influence expanded and in 1957, as a consultant, he convened the first World Health Organization (WHO) group on psychotropic drugs that issued its report in the following year (Elkes, 1958).

As the science of neuropsychopharmacology grew its pioneers coalesced into collegial organizations. Joel Elkes became the first President of the American College of Neuropsychopharmacology(ACNP) in 1962 and when the history of the Collegium Neuro-Psychopharmacologicum (CINP) was written the first chapter was by Joel Elkes titled "Towards Footings of a Science: Personal Beginnings in Psychopharmacology in the Forties and Fifties" (Elkes, 1998). At a later meeting in Glasgow he was awarded the CINP Pioneer award for his help and guidance at the organization's inception (Bradley, 2001). The Department at Hopkins he inherited from Adolf Meyer and John Whitehorn was named by Joel as the first Department of Psychiatry and Behavioral Science, a title often emulated elsewhere.

When the pioneer discoverers of all the first generation psychotropic drugs were convened to honor them in 1970 (Ayd and Blackwell, 1971) Joel Elkes, then aged 53, delivered the opening paper titled, "Psychopharmacology: On beginning in a New Science" (Elkes, 1971). He described his early approach to a discipline as "resting on the assumption that the various manifestations of gross mental disorder and milder dysfunction have their counterpart in the disturbed physiology of the brain, and that the study of the chemistry, cellular constitution and the electrical activity of the brain may contribute to an understanding of its functions as the highest integrating organ."

Joel was a founding member of two editorial boards, The Journal of Psychiatric Research and Psychopharmacologia (now Psychopharmacology). In addition he was also a founding Council member of the International College of Psychopharmacology and of the International Brain Research Organization (IBRO/UNESCO).

The Child as Father to the Man.

Joel's recollections of his early life and the manner in which they may have influenced his future career are derived from three sources: (Ban, 2011a; Elkes, 1997, 2011a) and (Elkes, 1997).

Joel Elkes was born in Königsberg, capital of eastern Prussia, on November 12, 1913. His father became a medical officer in the Russian Army during the First World War and the ensuing Russian Revolution, so Joel's first five years were spent in Russia before they settled in Kovno, capital of the new Lithuanian Republic. His father, Elkhanan, was the leading physician in the region and, while his "waiting room was always full of patient's who could not pay" he also cared for the President, Prime Minister and Diplomatic Corps. Joel describes his father as follows; "I recall his clean features and his smile. His movements were small and graceful. He rarely raised his voice in public, but when he spoke there was warmth and interest and humor in it, which gave anyone in his presence a sense of closeness and courage. Human frailty – including his own – was to him part of the Almighty's prescription for a good and full life. Only in the presence of bigotry, prejudice, and cruelty would his demeanor change. He would then grow silent: a silence often followed by a statement of such devastating directness as to render his hearer dumbfounded and confused. On his desk rested a little tablet carrying an inscription of Emmanuel Kant. "Two things continue to astonish the mind, the more it dwells on them. One is the starry sky above me, and the other is the moral law within me" (Elkes, 1997).

In the same memoir he also paints a picture of his mother. She was, "blessed with warmth, vitality, curiosity and extraordinarily well read, she assimilated the best of German and French culture, while always drawing on the wellsprings of Jewish heritage. Much was self-taught. Her cheerful temperament complemented my father's somber mood. She was his complete confidante and life companion. She was a wonderful mother, a fount of joy, optimism, adventure, sheer lifemanship, and full of sound practical advice. I still treasure some of her letters from my student days, written in impeccable copper-plate."

Joel attended a Jewish high school (Schwabe's Gymnasium) founded by a group of idealists to provide a good education and prepare students for a hoped for future life in Israel (Palestine). Lessons were taught in Hebrew, although German was spoken at home. Joel was an excellent, prize winning student, graduating with honors and described by a teacher as a "mature poet" in Lithuanian. Initially he developed a deep interest in physics, fascinated by structure, particles, force-fields and "how the world is held together. Lacking mathematical skill he switched his main interest to chemistry as a means to enter medical school, inspired by his father as a role model and aspiring to become a "scientist serving medicine." He states: "I went to

medicine because I had a secure example of good physicianship and a good person in my father and because I also hoped that medicine would lead me to a sort of relationship of science to life and nature" (Elkes, 2011a). In a talk to the ACNP Joel also identifies three other "heroes" who inspired him, Einstein in physics, Ehrlich and his work on receptors, and Goethe as an example of "the rare combination of humanism, scientific creativity and spirit … a master of both prose and poetry." He also read Freud and was impressed by "his view that the future would produce physical markers for mental events" (Elkes, 2011a).

After graduating from the Gymnasium Joel studied for a year in Königsberg to matriculate from a German school and quickly caught up with his peers in German literature and the French language, graduating at the top of his class. Following this he spent four months in Lausanne, Switzerland, attending lectures at the University on pre-medical topics as a prelude to medical school in England. His father was physician to the British Ambassador to Lithuania who encouraged Joel to seek training in his country and provided a letter of recommendation.

In 1930 Joel left Kovno for England where he eventually enrolled in medical School at Saint Mary's Hospital in London, taught by a distinguished faculty that included Sir Charles Wilson (later Lord Moran, Churchill's physician), Sir Almroth Wright who developed a typhus vaccine, Alexander Fleming, who discovered penicillin, and Alec Bourne, a distinguished obstetrician who later became his father in law.

Despite this cadre of brilliant clinicians the hospital was devoid of role models in the as yet unborn field of psychopharmacology. So, while still a student, in the mid 1930s, he was invited to join Alastair Frazer, Senior Lecturer in physiology as a Student Demonstrator. Frazer was working on the absorption of fat from the gut and concerned about the structure of chylomicrons entering the circulation from the thoracic duct following a fatty meal. Joel developed a micro-electrophoretic cell to study their mobility in an electric field. This resulted in his first publication in the *Journal of Physiology* while still a student (Elkes, Frazer and Steward 1939), work that was cited by Starling in his classic textbook *Principles of Human Physiology.*

While still in medical school, in 1937, Joel embarked on a Training Analysis at the renowned Tavistock Clinic at the suggestion of John Bowlby, one of his mentors and a friend. This venture was interrupted by the war when his analyst (Bion) was inducted into the Army.

Joel later completed his analysis in 1955 at Washington D.C. under Winifred Whitman, a training requirement the head of NIMH stipulated for his entire faculty. One can only speculate on how this experience stimulated and informed his later integration of social and psychological factors with his primary early interest in biological matters.

At the start of World War II Joel was cut off from support sent by his father and having financial difficulty supporting his sister and only sibling, Sara, who had joined him in 1937. Alastair Frazer found him a job at the Transfusion Service, where he met his future wife, Charmian Bourne, daughter of his obstetrics professor.

Joel graduated in 1941 and fulfilled the obligatory pre-licensing requirement as a rotating intern in orthopedic surgery, ophthalmology and internal medicine. Enjoying clinical work, he contemplated opening an office in London to practice medicine, but fate intervened when Alastair Frazer was appointed Chairman of the Department of Pharmacology in Birmingham UK, and invited Joel to join him as his research assistant.

We shall see how his upbringing, experiences, education and opportunity would shape Joel's future career but, meanwhile as the war raged on, events in Lithuania were unfolding in tragic fashion that he would only learn about after the war's end and would eventually incorporate in a memoir, "Values, Belief and Survival: Dr. Elkhanan Elkes and the Kovno Ghetto" (Elkes, 1997). In the first eighteen months of the war the Nazi regime established the apparatus of the Holocaust in the homeland, but in June 1941 they began to export *The Final Solution* to nearby Lithuania. The Jews in Kovno were herded into a ghetto and instructed to nominate a leader (*Oberjude),* expected to serve as a trusted servant of the community as well as the conduit for Nazi directives, not to be questioned on fear of death. As the most respected member Elkhanan accepted this impossible task under considerable pressure and with great reluctance. For over two years he fulfilled this role with skill, integrity, exceptional dignity and courage while the Nazi juggernaut rolled on. As the balance of war shifted in the Allies direction, the Nazis moved to bring *The Final Solution* to a speedy and complete conclusion. In mid-1944 the ghetto was destroyed and the remnant of the population murdered or transferred to concentration camps.

In frail health, Dr. Elkes pens a last long letter to his children dated October 19th 1943 that is smuggled into England after the war ends, and which Joel does not read until the autumn of 1945. It ends: "I am writing this at an hour when many desperate souls – widows and orphans, threadbare and hungry – are camping on our doorstop, imploring us for help. My strength is ebbing. There is a desert inside me. My soul is scorched. I am naked and empty. There are no words in my mouth. But you, my most dearly beloved, will know what I wanted to say to you at this hour.

And now, for a moment, I close my eyes and see you both standing before me. I embrace and kiss you both; and I say to you again that until my last breath, I remain,

Your loving father."

On July 13th 1944 Dr. Elkes leads a small group of his surviving community to the railway station and, transferred like cattle, they arrive at Landsberg-Dachau around July 15th. He lived barely three months, striving till the end to help and serve others until finally, his brother, a fellow prisoner, in a letter to Joel describes Elhanan's state of mind in his own words, "Such a life is unseemly. I cannot watch this suffering; I must be away". He begins a hunger strike and his brother tells of his final days: "He laid there for 14 days, a few teaspoons of water his only nourishment. He remained conscious until his last breath, and, on the 17th of October, 1944, at 4:15 am was gone."

Joel's mother mercifully survived concentration camp, joined him in London and eventually moved with Sara to Israel where she died twenty years later.

Blessedly unaware of the unfolding events during the remainder of the war, in 1941 Joel was ready to begin his career, turning his experiences, ideals and hopes into reality.

Joel Elkes'Career

From the end of medical school to official retirement Joel's career began in 1942 and ended in 1974. During these 32 years he worked in three settings, Birmingham UK (1942-1957), NIMH at St. Elizabeth's (1957-1963), and Johns Hopkins (1963-1974). During this period his CV records 40 publications but their quality and impact far outweigh their quantity partly

because of his reluctance to add his name to the work of those he mentored – an unheard of and mostly unfollowed precedent.

In 1942 he joined his friend and mentor, Alistair Frazer, as the Sir Halley Stewart Research Fellow in Pharmacology. Among the first papers published was a continuation of his research as a medical student. Three of the authors were Sir Halley Stewart Research Fellows (his mentor Frazer and Stewart, his colleague at St Mary's, as well as Schulman from the Colloid Research Center at Cambridge University). The paper was presented in 1944 at the Royal Society in London (Elkes, Frazer, Schulman and Stewart, 1944). In 1945 he was promoted to Lecturer and in 1948, only six years after joining the Pharmacology Department, he became Senior Lecturer and Acting Director of the Department.

His research accomplishments during this time were significant, producing 16 publications. He began work on the physical chemistry, constitution and structure of biochemical membranes, the lipoproteins. "Suddenly I realized the nervous system was full of lipoproteins. It was myelin, a beautiful para-crystalline structure ubiquitously distributed in the nervous system." Aided by his first Ph.D. student, Bryan Finean, a crystallographer, they developed a technique for the X-ray diffraction of the living frog's sciatic nerve in response to temperature changes and chemicals, including ether. "I suppose it was in the vain hope of seeing the penetration of molecules of an anesthetic into the molecular structure of myelin ...suddenly I was in the nervous system" (Elkes & Finean,1949). "At that time there was no real neurochemistry and very few people I could talk to." Between 1949 and 1953 they produced five publications. At this time Joel also began to study the anticholinesterases and the role of acetylcholine, "the main molecule in the central nervous system" in the firm belief that pharmacology was the path to understanding physiology.

A few years after moving to Birmingham UK Joel and his wife Charmian (a family physician) began clinical training and part time clinical work at the City Mental Hospital working with both inpatients and outpatients. During this time (1944-1950) they began to study the effects of amobarbital, amphetamine and mephenesin on patients with catatonic schizophrenic stupor. This work yielded paradoxical results. Amobarbital caused awakening from catatonic stupor; amphetamine deepened the stupor and mephenesin led to muscular relaxation without affecting states of consciousness. This suggested specificity of the action of

drugs and possible regional chemical differences in distribution of controlling cells within the brain. This experiment also established the Elkes' place in the mental health culture in England.

Difficulty translating his pharmacology from lab animals to humans convinced Joel "we needed another intermediate point." The missing piece fell into place when his second Ph.D. student, Philip Bradley, developed techniques for recording electrical activity in conscious and unrestrained cats. Now they could study the effects of anticholinesterase, acetylcholine blockers and amphetamine on electrical activity of the brain and behavior.

The development of this methodology continued while Joel was awarded a Fulbright Traveling Fellowship in America (1950) where he worked as a resident at the New England Hospital in Boston (under John Nemiah, later Editor of the American Journal of Psychiatry) and at Norwich State Mental Hospital (under Dr. Kettle).

Upon his return from America in 1951 he was appointed Chair and Professor of a new department he named "The Department of Experimental Psychiatry" at the University of Birmingham, UK.

Joel's ground breaking work with Philip Bradley now began to bear fruit in these techniques and results (Bradley and Elkes, 1953; Elkes and Bradley, 1957; Elkes, Elkes and Bradley, 1954). It was into this environment that the serendipitous discovery of chlorpromazine in France intruded leading to the first controlled trial of its efficacy in schizophrenia described earlier and published in the *British Medical Journal* (Elkes and Elkes, 1954). Joel's work in Birmingham laid the foundation for developing a concept of regional neurochemistry leading to the first International Conference focusing on this topic in 1954, mentioned earlier. Joel describes this evolution thus, "We began to talk about regional neurochemistry. Seymour Kety thought about regional differences in cerebral circulation and I thought about regional differences of neurotransmitters and families of naturally occurring compounds that had arisen in evolution to modulate and guide the interaction of neurons, and regulate excitation an inhibition in the nervous system. I thought of regional field effects in the nervous system" (Elkes, 2011a).

Joel's visit to America must have made him aware of the burgeoning interest in neuroscience coupled with vast resources available to support research in the Eisenhower years when America was indeed "the land of opportunity." By the mid-1950s Joel's research was

increasingly bearing fruit and he had established an international reputation in the emerging field of psychopharmacology for leadership and innovation. The coupling of talent and resources made it inevitable that he eventually move to greener pastures. And so, when he was invited to develop the first Clinical Neuropharmacology Research Center in America, he decided the time was ripe to make the move from Birmingham to Washington D.C.

Joel's work during the six years he was at Saint Elizabeth's yielded nine publications of his own and many more by young scientists he mentored. His own publications included eight ground breaking book chapters in five years on diverse topics including, *Psychopharmacology: the Need for Some Points of Reference* (1959), *Psychotropic Drugs* (1961a), *Drugs Influencing Affect and Behavior* (1961b), *Schizophrenia in Relation to Levels of Neural Organization* (1961), *Regional Neurochemistry* (Kety and Elkes, 1961d), *Amines in Relation to Behavior* (1962a), *Behavioral Pharmacology in Relation to Psychiatry* (1962b) a large review paper comprising over 500 references and *Biological Bases of Psychiatry* (1963).

Among the distinguished alumni Joel recruited was Mayer-Gross the German psychiatrist who persuaded him to write an article for the prestigious handbook he edited, *Psychiatrie der Gegenwart*, This paper, "Behavioral Pharmacology in Relation to Psychiatry" was *a tour de force* worthy of a book in its own right. Its publication was delayed and it did not appear until 1967 and was not published in English until his *Selected Writings* in 2001.

But the value and influence of what Joel Elkes created at Saint Elizabeth's was reflected not only in the literature published but in the atmosphere he initiated and the work of the scientists he recruited and mentored. Joel regarded the Institute as a "greenhouse" in which he toiled as "a good gardener." He describes the culture as follows, (Elkes, 2011a). "It was a wonderful, heady, exciting time in the middle of a very chronic mental hospital. There were people coming virtually from all over the world and there were talks and discussions and excitement. At the same time, there was always and always, which is what we had hoped, the presence of the patient. For example, you go to the canteen for lunch and there's a patient with schizophrenia hallucinating under a tree. You're never very far away from the problem that brought you here. And, gradually there developed a sense of place, of belonging. Gradually, I realized that, my God, together we created something pretty wonderful."

Joel relates his capacity to nurture others to his upbringing (Elkes, 2011a): “That brings me back to my parents. They were extraordinary, nurturing people. They made me feel wanted and secure, and at the same time, there was always, always the questioning spirit, the wish to understand.”

In 1963 Elkes left the research center he created to become Chairman of Psychiatry at Johns Hopkins. Satisfied as he was with the accomplishments at St. Elizabeth’s Joel may have wished for a broader palette, one where he could exert an influence on the place of psychiatry in medicine and the training of future practitioners in both disciplines. He joined an already talented faculty whose interests ranged from biology and sexuality to psychoanalysis. The breadth of his own aspirations is reflected in renaming his new domain, *“The Department of Psychiatry and Behavioral Sciences”,* possibly the first academic program to employ “behavioral” as a semantic link between psychiatry and the rest of medicine. To demonstrate and cement this relationship he invited the Chairs of all the other departments in the School of Medicine to give lectures in the students’ introductory course. Joel’s first two papers in this period reflect these widening interests; “On Meeting Psychiatry: a Note on the Student’s First Year” (Elkes, 1965a) and “Psychoanalysis and the Community” (Elkes, 1965b).

Joel’s educational innovations included all levels of care and disciplines. Not surprisingly his Department’s reputation attracted stellar psychiatric residents, among them Sol Snyder, Joe Coyle, Ross Baldessarini and Joe Brady. In addition Joel founded and was first chair of the Hopkins M.D.-Ph.D. Program in Medicine and the Behavioral Sciences. He was also Founder and First Chairman of the Board of Fellowship House a residential, intermediate care facility for people with mental illness. Sol Snyder’s meteoric rise led to the development of a separate Department of Neurosciences. Finally, Joel and Charmian founded a Master’s program for Mental Health Counselors.

Joel’s bridge-building, integrative cognitive and administrative style, carried with it drawbacks as well as benefits. In his time at Hopkins Joel was at the cusp of a changing Zeitgeist; between the hegemony of psychoanalysis and the burgeoning field of neuroscience he pioneered. Joel’s efforts to integrate these two poles, to bring psychodynamics, biological psychiatry and medicine closer together were, perhaps inevitably, disparaged by those whose

polarizing viewpoints were devoted to the integrity and dominance of their own domains. This discomfort would contribute to his decision to move on.

Upon leaving Hopkins Joel accepted a named professorship at McMaster University in Canada where he stayed six years (1974-1980) “seized by interest in the laboratory of everyday life” (personal communication). His adolescent attraction to Freud’s prediction that physical markers underlie thoughts and feeling was fulfilled with his pioneer work in neuropsychopharmacology; what lingered on from his experience in analysis was the need to complete “the inner examination of the self” an idea expressed in his essay “On Awareness and the Good Day” (Elkes, 1981). As usual with Joel, this personal insight soon translated to the broader context of holistic and behavioral medicine, integrating social and psychological dimensions with the biological foundations he had already created.

The ideas incubated at McMaster blossomed in full after he became Emeritus Professor of Psychiatry at Louisville University when public and professional concerns were increasingly expressed about the dominance of technical over humanistic skills in medical education and practice (Blackwell, 1977). Here Joel collaborated with like-minded faculty and therapists in efforts to ‘humanize medical education’. At first, this involved a four day voluntary Health Care Awareness Workshop for incoming medical students. (Dickstein and Elkes, 1985). The curriculum included mode of life as a factor in illness and disability; stress and the stress response; the physiology of nutrition, exercise and relaxation; the psychology of time management and study skills; dyadic listening; the place of beliefs in healing and the ethics of medical practice.

This pioneer work became the platform for a more ambitious program, “Arts in Medicine,” for which he obtained funding, and designed to integrate twin cultures,; “soft” Arts and ”hard” Sciences in a well-established School of Medicine (Ban, 2001). The program’s objectives were to demonstrate the value of this unity in therapeutics, biomedical research, self-awareness among health professionals as well as personal well-being and creativity.

Asked in 1995, at age 82, to put modesty aside and name his greatest contributions at the three major institutions he headed Joel names four (Elkes, 2011a). First, “the role of regional neurochemistry in understanding the mode of action of psychoactive drugs.” Second,

"pharmacology as the gateway to physiology, to understanding how the brain works naturally without the chemical prostheses of drugs; as a way of exploring the phenomena, the layering, the organization of mental life, and giving us an insight into schizophrenia as a disorder of information processing in the brain." Thirdly, "the importance of understanding the environment, the social setting, the action and even the dose of a drug on these variables." Lastly, "providing a setting where intelligent conversation between, neurochemistry, electrophysiology, behavior and subjective experience could take place, and where experiment interacts with clinical experience."

Family Matters

Like other pioneers in our field Joel Elkes' professional and family life have been intertwined in collaborative and creative ways, with rare tragic moments. Joel's first marriage incubated in medical school when he met Charmian Bourne, daughter of a leading obstetrician at St. Mary's Hospital. It was a relationship built on the future hopes of a young couple facing the vicissitudes and uncertainty following World War II, later cemented by joint work in psychiatry and their seminal early research on chlorpromazine (Elkes and Elkes, 1954), collaboration that became part of their dream. The marriage bore fruit with a daughter Anna and, in turn, a grandchild Laura, both deeply involved in Mindfulness and Spirituality, twin fields akin to Joel's lifelong interests. This marriage sadly ended in divorce. Charmian died in 1996.

Joel's second marriage was to Josephine Rhodes afflicted with severe, painful and crippling rheumatoid arthritis who Joel hoped vainly to comfort and help, consistent with his nurturing nature. It was a relationship that ended unfortunately in a mix of fond memories and deep disappointment.

Joel's present marriage is to Sally Lucke, an innovator and educator in Sarasota; Sally founded a major Art Museum and a Holocaust Library in the Liberal Arts College she had envisioned. She lectured at Harvard on Art Therapy, taught at the Museum of Modern Art and was a scholar at the National Gallery. Sally also created a Public School for the Gifted and another for the Visual and Performing Arts. Their shared interest in healing through the Arts, Mindfulness and Meditation, brought Sally and Joel together at the beginning of their relationship and they continue to develop this knowledge and create organizations reflective of their shared commitment.

Sally also shares Joel's nurturing instincts and talent; while still his fiancé she took into her care and shelter a homeless minority high school student in the seventh grade, tutoring him till Larry became a National Honor Scholar, then graduate of a renowned law school, now a practicing attorney and much beloved member of their family.

Life as a Whole

It is likely that "retirement" was a notion or a word unlikely to appear in Joel Elkes' mind or lexicon. He left Johns Hopkins in 1974, age 61, with a 32-year career behind him, and has added 41 productive years to that – and still counting! As events would unfold he had much left to explore and contribute, some of it described above. Why he made such a change at a relatively early age is speculative but may be enlightened by reciting Joel's own description of his father's determination to conserve energy for what he did best and "to keep away from committees and councils." (Elkes, 1997) Perhaps Joel's fertile integrative mind was seeking fresh fields to plow, free of administrative burdens and constraints?

Elkhanan Elkes' reluctance to seek or accept organizational responsibility was tragically prescient, ending in heartbreak and disaster during the Holocaust despite heroic efforts to serve his community. Joel's administrative skills were considerable when deployed in a fruitful era and environment. But never the less, perhaps they sapped energy needed to pursue broader horizons?

His CV, between 1974 and when it was last updated (1987), lists an additional 10 book chapters on educational, public health, behavioral medicine, community affairs, psychotherapy, self-regulation and self-awareness.

Throughout his lifetime Joel has been dedicated to supporting the affairs of his Jewish faith, a member of the Board of Trustees of Hebrew University in Jerusalem and Chair of the Israeli Center for Psychobiology. When his sister Sarah Elkes established a lecture series in honor of their parents, Joel gave the inaugural address in 1991 at the Stanley Burton Centre for Holocaust studies in Leicester, England, and six years later published the material as a memoir (Elkes, 1997).

Over the span of his life Joel has been a member of several international organizations dealing with his major areas of interest in brain research, psychopharmacology and psychotropic drugs. He has served on the Editorial Boards of six journals, been an invited participant in more than 35 international symposia and given many invited or named addresses to professional organizations, institutes and universities at home and abroad.

Joel is a Distinguished Professor Emeritus of Psychiatry at the Universities of Johns Hopkins and Louisville. He is also a Charter Fellow of the Royal College of Psychiatrists of Great Britain, a Fellow of the Royal College of Physicians of Canada, Life Fellow of the American Psychiatric Association, Life Fellow of the ACNP and a Life Fellow of the American College of Psychiatrists.

Over the span of his life Joel has been a member or fellow of almost 50 societies or professional organizations, testimony to the breadth of his interests, gregarious temperament and abundant energy.

Among the prestigious awards he has received are the Salmon Medal (1964), Taylor Manor Award (1969), Governor's Citation for Distinguished Service, State of Maryland (1969), Benjamin Franklin Fellow, Royal Society of Arts and Sciences (1974), and the Pioneer Award, CINP (1998).

To celebrate Joel's one hundredth birthday the CINP published a selection of his writings (Ban, 2011). Titled "*Selected Writings of Joel Elkes,"* the book is organized thematically in a manner that reflects Joel's breadth of interests and span of influence. The 12 topics are, Overviews; Early Papers; Electrophysiological Studies in Birmingham & an Early Clinical Trial; Reviews; Schizophrenic Disorder, a disorder of information processing in the Brain; Humanizing the Education of Physicians and Behavioral Science in the Service of Medicine; Five Named Lectures; The Community as an Agent of Proactive Health Care & Health Enhancement; Holocaust & Israel; Two Friends (Jonas Salk & Norman Cousins), and On Art & Healing. This alone is testimony to a multi-tiered life but it also speaks to abundant and prevailing energy. There are publications from every decade of Joel's career from the 40's (1), 50's (4), 60's (10), 70's (4), 80's (3) and 90's (6). This surely gives the lie to William Osler's opinion about, "The =comparative uselessness of men above forty years of age" (Osler, 1932).

In 2011 the ACNP celebrated its 50th anniversary, a few weeks past Joel's 98th birthday, when he presented a History Lecture, supported by over a hundred references and a pamphlet (Elkes, 2011) reprinting three seminal papers included in his *"Selected Writings"* (Ban, 2001). Together these cover a span of 43 years (1952-1995) and, perhaps, represent his most treasured contributions, his "*Alpha & Omega."* They are: "Prospects in Psychiatric Research" (Elkes 1952), "The ACNP: A Note on its History, and Hopes for the Future" (Elkes, 1962) and "Psychopharmacology: Finding One's Way" (Elkes, 1995). The latter of which includes photographs of key places and events.

Joel is also an artist from his childhood days, whose talented paintings are on exhibit in a number of institutions of art. They constitute the final theme in the CINP tribute as a collection of 15 paintings from 1988 to 1992. Joel's artistic oeuvre at that time was dominated by somber tones and broad brush strokes, all black and white, painted in the three years before and a year after the memorial lecture to his much beloved father. A subsequent collection painted at and published by the Fetzer Institute, where he is Founding Fellow and Senior Scholar in Residence begins to explore the brighter colors of the spectrum (Elkes, 2003).

An art critic comments as follows, "In a threatened society Joel Elkes creates beautiful images to lighten the soul. Using a new process, his prints reflect, with magical skill, his original paintings. They are alive with a light that carries us from the beginning of time to a life that will not be destroyed" (Kasle, 2003). As in all other areas of his prodigiously productive and long life this multi-tiered scientist, humanist and scientist continues to evolve, moving beyond the Holocaust to happier times.

Envoi

It remains to better define the nature and origins of Joel Elkes' unique contributions to neuroscience and medicine.

Joel was genetically well endowed by parents who raised him in an environment imbued with intellectual, artistic and moral precepts. His father was a noted physician role model and his mother a nurturing overseer of his growing years. Inherent insight, empathy and sensitivity were enhanced by a personal analysis begun early and completed later. Scientific principles were

implanted by medical and physiology training in both humans and animals. These seedlings bore fruit in mature integrative thinking and behavior.

Joel's intellectual approach possesses all three of the characteristics identified in creative scientists (Blackwell, 1971). These are an ability to see analogies, the tendency to seek original solutions and a type of Gestalt thinking that views parts in relation to the whole. These talents are reflected in his prescient grasp of the need to integrate neurochemical and physiological methods of study, the specificity of drugs on different cell populations and the need for a translational approach from animals to humans.

In the clinical arena Joel pioneered the empirical use of double blind controlled study to confirm or refute clinical observations. He stressed this in the early testing of the first psychotropic drugs used in State Mental Hospitals and the V.A. Joel influenced the design and scope of these studies at both the national and international level through his work with the NIMH at St. Elizabeth's Hospital in Washington, D.C., and in convening the first international study group on psychopharmacologic agents by the World Health Organization.

After psychiatry in America divorced itself from patient centered sites to academic medical centers Joel developed innovative methods to connect psychiatry with medicine including combining M.D. with Ph.D. training programs, humanizing medical student education and advocating for an integrative biopsychosocial approach to diagnosis and treatment.

The tension Joel Elkes' experienced in mid-life occurred in the context of a changing Zeitgeist and is not uncommon in the career patterns of pioneers in our field as illustrated in the INHN series of biographies. (See Jean Delay, Jose Delgado, John Smythies and Frank Berger.) Like Joel each of these eminent scientist-clinicians found late life solace in other talents: literature, art and philosophy.

Joel Elkes' incomparable lifetime accomplishments serve as a beacon to encourage and sustain present and future neuroscientists and psychopharmacologists at a bleak moment in our history, when progress seems sparse and the future uncertain.

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August 20, 2015

IN MEMORIAM: LEST WE FORGET

Joel Elkes - November 12, 2013 – October 30, 2015

A Personal Recollection by Barry Blackwell

As a young resident in 1962, at the Maudsley Hospital in London, I knew of Joel Elkes by name and reputation only, but in 1970 we met in person when he gave the opening talk at the first Taylor Manor Awards Conference in Baltimore, organized by Frank Ayd and me. His topic, "Psychopharmacology: On Beginning a New Science" (Elkes, 1971), was a *tour de force* of personal recollections on his role in launching the discipline of psychopharmacology from his first meeting with Alistair Frazer as a medical student in 1934, over tea and anchovy toast, until he became the First President of the new American College of Neuropsychopharmacology (ACNP) in 1960.

The peroration to this spellbinding talk was a reflection on the role of psychopharmacology as a science. He begins …

“I know of no other branch of science which, like a good plough on a spring day, has tilled as many areas in Neurobiology.” Joel then itemizes them:

“...synaptic transmission in the central nervous system … regionalization of chemical process in the brain…the interaction of hormones and chemical process in the brain … tools for the study of the chemical basis of learning… dependence of pharmacologic response on situational and social setting… a hard look at the semantics of psychiatric diagnosis … to have resuscitated the oldest of remedies, the placebo response for careful scrutiny … to have encouraged the Biochemist, the Physiologist, Clinician, the Mathematician and Communication Engineer to join forces at the bench level is no mean achievement for a young science.”

Elkes ends with a paragraph that emphasizes how psychopharmacology is “compelling the physical and chemical sciences to look behavior in the face.” The sentiments he next expresses epitomize Joel’s unique capacity to integrate disparate themes.

“There is no conflict between understanding the way things are and the way people are, between the pursuit of science and the giving of service. Where does one find a field as rich and powerful as ours?”

Joel spoke these words when he was midway through his tenure as Chair at Johns Hopkins.

I did not fully understand the meaning behind these words until I met Joel again almost half a century later. In 2015 Tom Ban suggested I write a biography of Joel Elkes, a process that involved reading much of his writing, talking to him by phone and eventually meeting face to face when, with his wife Sally, he moved to their summer residence north of Chicago, only an hour’s drive from my home in Milwaukee.

When Joel spoke in 1970 his focus was shifting from the science of psychopharmacology to its broader behavioral implications in medical education, medical practice, and an inner understanding of the self. Behind him were the early years of neuroscience and mostly bench research in Birmingham UK, when he picked up where Thudichum left off; moving from the anatomical structure and basic chemical composition of the brain to an understanding of its physical function and neurochemistry. This was followed by Joel’s Camelot years as Chief of the

NIMH research program at Saint Elizabeth's Hospital in Washington DC where his talents as a nurturing overseer of both basic and clinical research were highly productive.

His next move to a pre-eminent medical school with prestigious faculty in all the clinical disciplines broadened Joel's palate bringing novel opportunities and challenges. The shift in Joel's interests that underlay this move may well have been completion of the psychoanalysis begun as a medical student, disrupted by the Second World War and not accomplished until a quarter century later in Washington DC. Once again he was highly successful in building a program he named the Department of Psychiatry and Behavioral Sciences, a prescient appellation that was quickly copied across the nation. It was replete with one of the first MD-PhD programs, attracting stellar residents, as well as other innovative programs described in the biography. But the time and environment presented problems. This was on the cusp between psychoanalytic hegemony over academic psychiatry and the burgeoning dominance of neuroscience pioneers. Joel's efforts to integrate these poles were vigorous but perhaps under appreciated by leadership devoted to preserving the integrity and dominance of their own domains. Certainly the environment was less compatible and more challenging to someone who, like his physician father, was not adept at administering a complex and hostile environment.

Having accomplished what he could Joel moved on to the final phase of his academic career, a six year respite for reflection and incubating fresh ideas, filling a named Chair at McMaster University in Canada. Although these years were fallow in terms of research and publications he emerged with renewed vigor as Emeritus Professor of Psychiatry at Louisville University where he undertook to "humanize medical education," developing innovative programs that integrated the twin cultures of Art and Medicine with success.

When the time came to retire from teaching Joel settled into a contented life in Sarasota living with his talented wife Sally, an idyllic relationship bonded by shared interest and enthusiasms in art, education, mindfulness and social justice.

As one surveys the panorama of Joel's life and accomplishments one perceives core characteristics identified by sociologist Robert Merton and others in creative scientists. These are an ability to see analogies, to view parts in relation to the whole and pursue original, integrative

solutions. In Joel's case this yielded a lifetime of successful and evolving innovation against a changing Zeitgeist. One wonders if it has received the merit deserved. As the field of neuroscience has become more complex and unyielding there may be a tendency to regard the original discoveries as simplistic. Joel's constantly evolving and innovative accomplishments may attract less approval than those of scientists who persist in a single area of endeavor. History will be the judge. Thudichum, also a man of multiple talents, underwent a long period of competitive disparagement before his contributions were eventually accorded the universal praise they deserved.

At our meeting a few months ago with Joel and Sally we found Joel engrossed with a painting in progress, the walls of their house hung with his completed art of high caliber. After a delightful lunch and informative conversation Sally invited us to attend a showing of his most recent work in Sarasota timed to celebrate Joel's 102nd birthday on November 12th.

Later, we wrote to accept the invitation but two weeks before the event Sally phoned from a hospital to say that Joel was admitted with a syncopal episode or a small heart attack. She handed the phone to Joel who sounded optimistic so I wished him a speedy recovery and looked forward to seeing him at the art exhibition. On October 30th Sally phoned again, this time with the sad news that Joel's cardiorespiratory function had rapidly failed leading to his death. Conscious till close to the end he was holding her hand. Sally has decided to turn the Art show into a celebration of Joel's life and we shall be there. Before she hung up Sally told me Joel called her "The Oracle of Delphi, well of my being, compass of my life." What a sentient human being; and talented scientist to boot. What a creative pioneer; a role model for aspiring neuroscientists.

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November 12, 2015

Samuel Gershon's comment

This is a marvelous piece on Joel Elkes and Barry is right in stating that he generously contributed his ideas to widely help a new enterprise or offered specific points of view that would benefit the development of an existing enterprise. He was a kind and generous man. Moreover, it should be mentioned that Joel and Seymour Kety were the two most important people in bringing the impact of biological psychiatry to Israel. Psychiatry in Israel was dominated by European analytic psychiatry and these two leaders brought in help, ideas, plans, projects and funds to set up labs. The warriors they brought to this effort were Elliot Gershon, Bernard Lerer and others. So their efforts were unceasing.

January 7, 2015

Paul Grof's comment

Barry Blackwell's writing captured the central points of Joel Elkes' life admirably. I want to add a few words about a part of his life that is less familiar. When Joel retired from the chair at Johns Hopkins, he had several options to consider. However, his former student, Nahum Spinner, convinced him to come to McMaster University in Hamilton, Ontario, Canada. Part of the attraction was the task of radically improving undergraduate medical education. McMaster was the place where such transformation started back in 1968 and the new approach was quickly catching in many medical schools.

There were several characteristic elements of the new educational system. The most important principle was to teach what a physician needs when he enters practice rather than, as in

the past, lecturing on what the faculty wanted to teach. Joel, with his pioneering spirit, made several new contributions. For example, the creation of a large, integrated Brain and Behavior program was a significant achievement that benefited from the combination of his exceptional knowledge of neurosciences and interpersonal skills. Furthermore, his lifelong interest in the functioning of the human consciousness led to including group meditations into tutoring and mentoring students.

The educational principles that he nourished at McMaster, he later transferred to the University of Louisville in Kentucky. It was also during his tenure at McMaster that he became increasingly involved in painting. He bought a cottage on Prince Edward Island, as he felt that the location has unique colors and lighting.

I would be remiss not to mention that Joel had a profound positive influence on our family. He brought my brother from Prague to Johns Hopkins, because of their shared interests, and I had the pleasure of working with him at McMaster, eventually inheriting his position as the Director of research and education. Our lives kept connecting many times, on various occasions.

January 28, 2016

Barry Blackwell's reply to Paul Grof's comment

I thank Paul for casting further light on Joel Elkes' time at McMaster University and subsequently at Louisville. This was a period when Joel was incubating and evolving his innovative ideas about medical education, as well as recharging his batteries. It was not a time he chose to dwell on or speak much about. Although he was proud of his accomplishments at Johns Hopkins (the Department named him Emeritus Professor and has preserved his reputation), Joel's exit was accompanied by bruised feelings. Neither the psychoanalysts nor the biological purists fully understood or appreciated the way his creative mind was moving on from pioneering work in neuroscience to a novel area of integrative thinking; the task of blending the arts and science to train a "complete physician."

There is irony to the fact that the Flexner Revolution in medical education, moving from an apprenticeship to a scientific model, put down its firm roots at Johns Hopkins at a time when Osler's ideas foreshadowed Joel's. The model Osler espoused, involved seeing and talking to patients beyond the lecture hall, and is epitomized by one of his many pithy sayings: *"He who studies medicine without books sails an uncharted seas, but he who studies medicine without patients does not go to sea at all."* Osler's personal philosophy of inner tranquility, espoused in his valedictory address at Philadelphia, *"Aequanimitas,"* is prescient of Elkes' late life adoption of Buddhist principles and practice of Mindfulness Meditation.

Especially interesting is that the shared beliefs of Osler and Elkes provide evidence that from its earliest days, the Flexner tradition has struggled with a dark side as it strives to adapt to an ever expanding encroachment of technical advances. In 1927, Francis Peabody, in an address to medical students at Harvard, complained, *"Young graduates have been taught a great deal about the mechanisms of disease but very little about the practice of medicine."* In 1978, over half a century later, George Engel echoed those words, "*Medical education has grown increasingly proficient in conveying to physicians sophisticated scientific knowledge and technical skills about the body and its aberrations. Yet at the same time it has failed to give corresponding attention to the scientific understanding of human behavior and the social and psychological aspects of illness and patient care."*

From the mid 1960's to the mid 1970's, the Federal Government funded over 30 new community medical schools with a goal of graduating humanistic primary care physicians. This was accompanied by a massive increase in the Behavioral Medicine curriculum, often interdepartmental, embracing Osler's ideals, Engel's biopsychosocial model and Elkes' vision of uniting arts with science (Blackwell and Torem, 1982). In 1974, I became founding Chairman of Psychiatry in one of these schools and some years later, after graduation of the charter class, wrote a paper documenting the failure of the experiment titled *"Medical Education and Modest Expectations"* (Blackwell, 1985).

Well into the 21st century, things continue to deteriorate. Bedside teaching in the Osler tradition has virtually disappeared since the DRGs, with sicker inpatient populations and briefer stays, ushered in salaried Hospitalists, not paid or provided time to teach. Massive educational debt is driving medical students away from primary care and towards the more lucrative

procedure oriented specialties. Independent primary care has given way to salaried employees of so-called, not-for-profit health care corporations, the "productivity" requirements of which value revenue over quality, discouraging doctors from teaching or from treating complex, time consuming patients, especially those on Medicare and Medicaid.

I never discussed these gloomy thoughts with Joel, whose contributions to neuroscience and medical education will always stand as testimony to his unique ability to synthesize and integrate disparate disciplines in prescient ways.

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April 14, 2016

Robert H. Belmaker's comments

I met Joel Elkes on my first day of arrival in Israel on July 1st 1974, together with Charles Smith, a well-known Washington D.C. builder and philanthropist. Joel Elkes was already a legend in psychiatry, but I had not met him before. He had met Charles Smith by chance on an airplane flight and they talked about new understandings of depression as a biochemical illness. Charles Smith was intrigued, and Joel Elkes translated that opportunity into a 40-year relationship with the Smith Family Foundation that created the National Institute for Psychobiology in Israel. I was an early recipient of grant support and a lifelong beneficiary of

Joel Elkes' wisdom, friendship and generosity. A laboratory in Jerusalem of the National Institute for Psychobiology in Israel is dedicated in the name of Charles Smith and Joel Elkes.

Joel Elkes came to Israel frequently, even in his later years. He skillfully and honestly maintained the Smith family as major private supporters of psychiatric research in Israel, due to his openness, optimism and willingness to give freely of his time. He was very proud of the successes of the National Institute for Psychobiology in Israel and he served as the Chairman of the Board of Trustees for 30 years. He went through the list of young investigator grants personally each year with pride. We will sorely miss him

February 4, 2016

Ross J. Baldessarini's comment

Recollections of Joel Elkes from the 1960's

I first met Joel Elkes in 1965, under somewhat unusual circumstances. Following a year of internal medicine at Boston City Hospital, and during a laboratory research fellowship in neuropsychopharmacology at the National Institute of Mental Health (NIMH) in Bethesda, Maryland (1964–1966), I became increasingly interested in training in psychiatry. However, following two nationwide visits to leading US training programs, I came away skeptical and unconvinced that the field was keeping up with progress in general medicine and surgery, and considered pursuing a laboratory career. The NIMH research program director at the time was Seymour Kety (1915–2000), who had recently chaired the Department of Psychiatry at Johns Hopkins in Baltimore (1961–1962), but without training in clinical psychiatry, found it a difficult fit and left in less than a year. He suggested that I contact his good friend and colleague, Joel Elkes (1913–2015), who then led a major and innovative program of neuroscience research with a psychiatric orientation, at the St. Elizabeth's Hospital laboratories in Washington DC, associated with the NIMH, and was about to take the chair at Johns Hopkins.

I called Joel to ask for an appointment to discuss psychiatric training and the future of the field in this country. He invited me to visit at his home nearby, in Bethesda. This memorable first encounter included having tea in his very English-style rose garden, where he showed me a collection of his own recent, modern paintings, and laid out a remarkable vision for the future. Quite convincingly, he predicted that psychiatry was about to enter a new era, based on what would soon become known as "neuroscience."

At the time, the only obviously clinically relevant component of such science was the emerging application of effective and tolerably safe medicines to treat psychotic and major mood disorders and some anxiety disorders. Examples of each of these innovative treatments had been discovered (more by serendipity than by rational, scientific prediction) and initially tested by 1960—between 1949 (lithium) and during the 1950's (chlorpromazine, chlordiazepoxide, clozapine, iproniazid, imipramine (Baldessarini, 2013). Indeed, a major contribution to Elkes' reputation was his early trial of chlorpromazine with his first wife Charmian (Bourne) Elkes (1920–1995), at his innovative experimental psychiatry program at the University of Birmingham, England, which opened in 1951(Elkes, 1995; Elkes and Elkes, 1954).

This study (Elkes and Elkes, 1954) is worthy of comment and re-reading, if only to appreciate how far the design, analysis, and reporting of experimental therapeutic trials have come in the past half-century. At its time, the study was as advanced as any in general medicine by including efforts at double-blinding and use of a placebo-control. It is appropriately considered a landmark study in psychopharmacology. By today's standards, however, it seems frankly primitive. It used a within-subject, crossover design and neither specifically contrasted average outcomes with placebo versus chlorpromazine, nor controlled for drug-discontinuation and carryover artifacts. The study was hampered by lack of knowledge of appropriate drug-dosing, or of times in which improvement and worsening might be expected to occur after starting or stopping chlorpromazine. Exposure times were increased from two weeks initially, to six weeks, later during the conduct of the trial, and there were 2–7 changes per person between drug and placebo over approximately 22 weeks. Drug doses were determined empirically during the trial, and are reported as total grams given per patient rather than as daily mean doses (which averaged approximately 150 mg/day). Diagnoses also varied: most of the 27 subjects, 48.2%, had probable manic-depressive disorders (bipolar or melancholic), 40.7% had schizophrenia-like,

chronic psychotic or delusional conditions, and 8.1% were demented, but all were chronically ill, currently agitated and difficult to manage clinically. "Definitely beneficial" responses with chlorpromazine (sometimes followed by worsening with placebo) were found in only 7/27 cases (25.9%), with a nonsignificantly higher response rate among mood-disorder subjects (4/11 [36.4%]) than in psychotic (3/13 [23.1%]) or demented (0/3 [0.0%]) patients (chi ^{2} = 1.54; *p*=0.22). Data for responses during drug-versus-placebo phases are not provided, and assessments were impressionistic, severely limiting interpretation of the findings. Notably, although this trial is widely considered a first controlled test of the phenothiazine for schizophrenia, the majority of subjects and most responders were manic-depressive.

At our initial meeting, Joel reviewed this and other developments in which he had been involved in England and the US, including early studies of the structure of myelin, the differential pharmacology of catatonia (worsened with amphetamine and improved with amobarbital), on the neurophysiological and behavioral effects of anticholinesterases and muscarinic antagonists, and promotion of the concept of regional, cerebral neurochemistry. His work in neurochemistry followed the tradition of Johann Ludwig Thudichum (1829–1901), another British immigrant from Germany (Elkes was born in the former Königsberg in eastern Germany in 1913 and raised in Lithuania before moving to England at age 17) (Elkes, 1995; Blackwell, 2015). He considered this work as only the beginning of a new, more biomedical era in psychiatric therapeutics. He also expressed great optimism for the pursuit of biological contributions to the causes and pathophysiology of major mental disorders, in part based on the questionable, highly *pharmacocentric* idea (Baldessarini, 2013) that knowledge of the actions of new drugs might lead to testable hypotheses about a biology of the illnesses for which they provided symptomatic benefits. Finally, he outlined his hopes for the Department of Psychiatry and Behavioral Sciences at the Henry Phipps Psychiatric Clinic at Johns Hopkins, which he was about to chair, and encouraged me to apply there for residency training.

Suffice it to say that Elkes' views, enthusiasm and achievements were highly persuasive, and led me to apply to return to Hopkins. I had finished medical school there in 1963, having been taught in freshman year by John Whitehorn (1894–1974), successor to Adolf Meyer (1866–1950) as the second director of the department of psychiatry. Almost from the beginning, and consistently throughout my years at the Phipps Clinic (1966–1969), I was forced to conclude that

Joel's biological vision was, at best, premature, with limited direct clinical relevance. Nevertheless, in the years since then, a more biomedical and descriptive approach to clinical psychiatry, with a very heavy reliance on psychopharmacology, has come to dominate the field (Baldessarini, 2013, 2014).

In the US, the biomedical approach forced a previously dominant psychodynamic perspective aside, at least from leadership positions in academic, publishing, governmental, administrative and other organized aspects of the field. It has also had a profound impact on clinical practice, particularly in shifting toward the application of psychotropic drug treatments rather than psychotherapy (Baldessarini, 2013, 2914). This impact on clinical practice has often been dramatically effective, and has profoundly changed the nature of psychiatric training and practice, and altered the organization of psychiatric facilities and services. Nevertheless, it can risk loss of other progress, particularly clinical progress, made over the past century (Baldessarini, 2014). Moreover, the hope that a neurobiological approach would succeed at the level of explaining the causes of major mental illnesses, or support a more rational, experimental, psychiatric therapeutics continues largely to be elusive (Baldessarini, 2013, 2014). However, the scientific contributions of biological psychiatry and of neuropsychopharmacology, in particular, have been stunning. They include spectacular technical advances in brain imaging, cerebral metabolism and genetics that are being applied usefully to clinical problems as well as advancing molecular understanding of the actions of known (but not necessarily of innovative) psychotropic drugs (Baldessarini, 2013). Nevertheless, the promise of a clinical psychiatry, based on methods arising in Europe and North America from the late 19th century and refined by clinical experts (including psychoanalysts) throughout the 20th century, has remained elusive.

I received intensive and appropriate clinical training and experience at the Phipps Clinic (1966–1969), where I also met my wife, then a psychiatric nursing supervisor. In addition, I owe a specific debt of gratitude to the late Charmian Elkes, who was a favorite clinical supervisor and first introduced me to the then rather un-American concept that there was a lot more to psychotic illness than schizophrenia. The insight first arose in reviewing with her the case of a seemingly psychotic and very hypersexual adolescent female patient. Charmian encouraged me to read deeply into the European literature on manic-depressive illness, which gradually became a sustained and sustaining interest. My earliest interests in bipolar disorder in Baltimore included

an ill-advised, but successful effort as a resident to obtain permission (Investigational New Drug [IND] authorization) from the US Food and Drug Administration to supervise use of lithium carbonate for the entire Johns Hopkins medical center. This manifestation of my extraordinarily poor judgment and risk-taking led to interesting comments by senior colleagues in internal medicine, who predicted disaster by encouraging mere psychiatrists to use such a toxic agent clinically.

His years at Hopkins (1965–1973) appeared to be frustrating to Joel Elkes. Barry Blackwell, in his recent biographical notes on Elkes (Blackwell, 2015), suggests that an essential problem at the Phipps Clinic in the 1960's was a clash between highly entrenched and influential psychoanalysts versus anyone who would pursue a biomedical orientation. However, combining work in basic neuroscientific research with strong clinical interests had been a tradition initiated by neuropathologist Adolf Meyer (chairman, 1909–1941) and continued by his successor, John Whitehorn (chairman, 1945–1960), who had been a chemist at Harvard, working with Otto Folin (1866–1934) at McLean Hospital, as well as by Elkes' immediate predecessor, Seymour Kety (chairman, 1961–1962). I suspect that Elkes' greater challenge was to command sufficient resources with which to establish major new laboratory and clinical research programs, as he had known in Birmingham and at St. Elizabeth's, and to exercise the administrative skills required to bring his hopes to fruition. However, I agree with Blackwell that Joel Elkes' career was an "integrative life."

Programs aimed at integrating basic neuroscientific research with clinical studies in psychiatry departments were widely known long before Elkes moved to Hopkins, and well before he established such a program at the University of Birmingham. These include McLean Hospital (1888), the New York Psychiatric Institute (1895), the Illinois Psychiatric Institute (1907), the Phipps Clinic itself (1913), the German Institute for Psychiatric Research in Munich (1917) led by Emil Kraepelin (1856–1926), and many other "psychopathic institutes" that developed at university medical centers in the early 20th century. Their impact on training, research, and practice has been and continues to be profound. Nevertheless, there is a risk that their scientific contributions may remain largely parallel developments to progress in the clinical assessment and treatment of the severely mentally ill. The vision espoused by Joel Elkes and his predecessors at the Phipps Clinic, aimed at integrating basic neuroscience with clinical research

and improved clinical care was premature and has been followed by decades of still-unfulfilled expectations. Nevertheless, it sustains many of us working in biological psychiatry and neuropsychopharmacology in retaining optimism about continued contributions of neuroscience to clinical psychiatry and in pursuing efforts to integrate neuroscience into psychiatry, while not ignoring the considerable progress in clinical psychiatry over the past century (Baldessarini, 2013, 2014).

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March 10, 2016

Samuel Gershon's comment on Barry Blackwell's biography and Ross Baldessarini's comments

I read Barry Blackwell's biography of Joel Elkes and Ross Baldessarini's comments and agree with them fully. I also want to stress the points made by both authors that Joel was somewhat frustrated by his experiences in the States. He came bursting with enthusiasm. His position in England permitted him to develop project with greater freedom and intellectual support but without the necessary financial resources.

I met him many times in the States and several times in Israel. He, together with Seymour Kety, exerted the major role of transforming Israeli Psychiatry from the old European and psychoanalytic emphasis. Here in this arena he was welcomed and appreciated. He also raised funds in the U.S. for a Biological Research Foundation in Israel. He also had the advantage of speaking perfect Hebrew. He was an example of someone who really would have had a greater impact in Israel than he could achieve in the States. This is not to diminish his contributions in the States, but he and his influence would have grown and multiplied more fruitfully there.

He was a person of great warmth and generosity and was ready to help individuals and groups in any way he could. In short, he must be considered a great man and great scientist and was eager to give in a climate here that was not ready to receive.

March 17, 2016

Barry Blackwell's reply to Ross Baldessarini's comment

Ross Baldessarini's cogent comments on his personal interactions with Joel Elkes and how these helped shape his career are valuable additions to developing a better understanding of Joel's contribution to the evolving relationship between clinical psychiatry, neuroscience and behavioral medicine.

Building on his undergraduate excellence in organic chemistry, Ross was diligent and determined in plotting his future and the education necessary to secure its foundations. After internship in internal medicine and a bench research fellowship in neuropsychopharmacology at NIMH, he explored a career in psychiatry and was disappointed at the two leading programs he visited in America. So Ross consulted Seymour Kety, the head of his research program. Kety had recently vacated the Chair of Psychiatry at John Hopkins he occupied for less than a year, feeling unprepared for the task without having any formal training in the discipline. Seymour suggested Ross speak to Joel Elkes, head of the NIMH neurosciences research program at St. Elizabeth's. He was about to take the Chair of Psychiatry and its residency training program at Johns Hopkins that Kety had vacated.

Ross describes Joel's tenure at Johns Hopkins (1963-1974) as an interlude after the mostly serendipitous discovery of all the major categories of psychotropic drugs and scientific proof of their efficacy by means of randomized controlled trials (RCT's). When Frank Ayd and I invited all the pioneers who made these discoveries to describe them in their own words in 1970, we made the following editorial comment in the book that followed, *Discoveries in Biological Psychiatry* (Ayd and Blackwell, 1971): "Compared to the fruitful years recorded here, biological psychiatry has fallen on more barren times. It is not unusual for an era of productivity to be followed by the kind of slack interval in which we are currently becalmed." Little did any of us know that the "slack interval" would last more than half a century.

Joel's contribution to the scientific process of ratifying the original discovery was one of three such papers in different countries; Britain (Elkes and Elkes, 1954), France (Delay, Deniker and Harl, 1952), and Canada (Lehmann and Hanrahan, 1954). Ross describes the Elkes' study as "primitive", a word that might apply to all three, although theirs is the only one to include

elements of control. All three were conducted on diagnostically heterogeneous groups of agitated, psychotic asylum patients. The title of Joel's paper was *Effects of chlorpromazine on the behavior of chronically overactive psychotic patients.* He was always adamant that this was not linked to any specific diagnosis. The title of Heinz Lehmann's paper was *A new inhibiting agent for psychomotor agitation and manic states.* It included 72 agitated psychotic patients with 12 different diagnoses. But the results and comments made by Pierre Deniker of his work with Jean Delay (three reports, all in 1952 and in French) are the most prescient and compelling (Deniker, 1970):

"Psychiatric wards 20 years ago still included agitated patients who did not respond to common therapeutic procedures. Logically a new drug was tried in cases resistant to all existing therapies. Manic excitation and, more generally, psychotic agitation, immediately became the indication of choice. We had scarcely treated 10 patients, with all due respect to fervent adherents of statistics, when our conviction proved correct. It was supported by the sudden great interest of the nursing personnel who had always been reserved about innovation."

Deniker and Delay's further detailed observations, were more nuanced but equally valuable. They distinguish between what later became known as the positive and negative symptoms of schizophrenia. "Agitated aggressiveness and delusional conditions of schizophrenia improved. Contact with patients could be re-established but deficiency symptoms did not change markedly." This is what secured the patient's release from asylum care and contributed to their failure to thrive in community.

Finally, speaking for the providers of treatment, Deniker comments, "Paradoxically some assumed a certain opposition between chemotherapy and, on the other hand, socio-therapy and psychotherapy. They actually benefit from one another and are inseparable."

However primitive and unsophisticated the trial methodology may appear to have been, skilled clinicians like Deniker, Lehmann and Elkes were able to harvest essential details to inform sound clinical practice. The shortcomings of RCT's, which we recognized almost a half century ago (Blackwell and Shepherd, 1968), were slow to permeate the field until the value of real life effectiveness studies in addition to artificial efficacy designs was recognized.

At the same conference where Deniker made his remarks in 1970, Joel Elkes gave an opening presentation titled, *Beginning in a new science* (Elkes, 1971). Seven years into his tenure at Hopkins (1963-1974), he confines his comments to his neuroscience accomplishments at Birmingham UK and Washington DC. Beneath this silence lie hints about his thoughts for the future when he concludes his presentation with the following: "Psychopharmacology is, for the first time, compelling the physical and chemical sciences to look behavior in the face, enriching both these sciences and behavior. If there is discomfiture in this encounter it is hardly surprising, for it is in this discomfiture that there may well be the germ of a new science …there is here no conflict between understanding the way things are and the way people are, between the pursuit of science and the giving of service. Where does one find a field as rich and powerful as ours?"

This makes clear why he titled his new department, *Psychiatry and the Behavioral Sciences.* Further evidence of this is contained in the few articles he published during his tenure at Hopkins. There are only three. *On meeting psychiatry; a note on the medical student's first year* (Elkes 1965, a); *Psychoanalysis and the community* (Elkes, 1965b) and *Behavioral pharmacology in relation to psychiatry* (Elkes, 1967).

Joel's remarks at the Baltimore Conference, and his literary oeuvre at Hopkins predict his future interest and contributions in medical education, the humanities and a clinical biopsychosocial perspective. These ideas incubated in mid-life (39-50) at Johns Hopkins, were refined (but still largely silent) at McMaster, coming into full bloom at Louisville until his retirement where he continued to write and paint.

With hindsight it seems clear that by 1970 Joel and Ross, as well as the pioneers at large, already saw the limitations of a clinical "pharmacocentric ideal," but perhaps only Joel clearly distinguished neuroscience and behavioral science. This was an innovative but poorly understood posture that may have irritated both the psychoanalysts and traditional clinical psychiatrists.

Ross attributes Joel's discomfiture at Hopkins to an inability to garner "significant resources" to pursue a more biological approach. A more sustainable hypothesis is that his behavioral aspirations were triggered by concluding his psychoanalysis in mid-life and a deeply felt need to find better ways to improve medical education and clinical practice. Like Kety, he had no formal training in psychiatry but was self-taught by clinical exposure to patients both he and his wife saw in a Birmingham asylum. He was not about to repeat Kety's failure due to a singular reliance

on neuroscience; as the Chair of Psychiatry in a premier medical school, he saw the need for a broader vision. A common feature in the biographies of pioneers in psychopharmacology, including both Joel and Ross, is a shared belief that drugs alone are never enough.

The final question, perhaps the most important, is whether Ross Baldessarini's residency experience, under Joe Elkes' tutelage, impaired his career. The answer is unequivocally revealed in a 22 page interview between Ross and David Healy in 1998, for the *Oral History of Neuropsychopharmacology* (Baldessarini, 1998).

This archive documents many contributions and accomplishments including a benevolent postscript to the story of Ross's frustrated attempt to study lithium in bipolar disorder during his residency, which I hope will become an important addition to the half century history of this unique substance compiled by members of the INHN network (Blackwell et al., 2013).

By the time Ross began his residency in 1963, lithium was in widespread use worldwide for the treatment of acute mania, except in America where the FDA banned its use due to its toxic and occasionally fatal effects when used as an adjunct to treat hypertension. This ban was not lifted until the mid-1970's, but, in the early 1960's, Scandinavian psychiatrists had begun its use to prevent future episodes of recurrent bipolar disorder, an indication with broad implications. As a junior resident, Ross took the intrepid step of applying for an Investigational IND to study lithium which the FDA granted.

Ross does not reveal his hypothesis or trial design, which was never accomplished, apparently because senior colleagues in medicine objected to a "mere psychiatrist using such a toxic agent clinically." Why Ross and his Chairman Joel Elkes chose not to proceed seems surprising since it was 15 years since lithium's safety had been established by an Australian study in 100 patients monitored by routine plasma levels (Noak and Trautner, 1951). Six years later the Trautner team (Sam Gershon was now a member) fully defined the excretion and retention levels of lithium and its effect on ionic balance in humans (Trautner, Morris, Noak, and Gershon, 1955). Such interference by members of one department in the affairs of another would be highly unusual but Ross took it to heart and continues to berate himself for "extraordinary poor judgment and risk taking."

A quarter of a century after Ross completed his residency, in the early 1990's, he became reacquainted with lithium in a series of studies showing that in patients taking psychotropic drugs for prolonged periods, often for 'prophylaxis', abrupt or rapid discontinuation was much more dangerous than gradual tapering off medication. This was first demonstrated with lithium, then with neuroleptics in schizophrenia and antidepressants, where there was an increased risk of suicide.

During the time I was writing Joel Elkes' biography we had several conversations by phone and in person. While it became clear his time at Johns Hopkins and departure were difficult and troubled, he was scrupulous in avoiding discussion of details and individuals. What was also clear is that with the passage of time, his role and contributions became increasingly acknowledged and appreciated. He was proud to be a Distinguished Lifetime Professor and contributed several of his wonderful paintings to hang on the walls of his former Department.

One of the rewards of history is to share the bard's insight that sometimes, "All's Well That Ends Well" (Shakespeare, circa 1607).

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May 26, 2016

Ross Baldessarini's response to Barry Blackwell's reply

Barry Blackwell's comments on my recollections of early times with Joel Elkes are much-appreciated. However, my experience with lithium during residency needs to be clarified. I have characterized my willingness to take responsibility for clinical use of lithium carbonate under an IND from FDA in the mid-1960s for the entire Johns Hopkins Medical Center as a risky endeavor, and one that I would not undertake now. This was not because other clinical departments interfered with our efforts, but because the risks were substantial and difficult to

manage effectively. Comments about risks of lithium treatment from Baltimore colleagues in internal medicine were offered and received in the spirit of collegial concern. Most of these observations were from older physicians who were present when a series of case reports in 1949–1950 highlighted sometimes severe adverse medical outcomes when lithium was used as an uncontrolled salt-substitute for sodium chloride, often for medically ill patients who least needed exposure to such a potentially toxic material in unmonitored quantities (Corcoran and Taylor. 1949; Greenfield and Zuger, 1950; Talbot, 1950; Waldron, 1949).

In addition, the experience with lithium at Johns Hopkins was not a failed experimental trial, as Barry suggests. The aim was to enable clinical experience with a promising treatment that was accepted internationally but disfavored in the US until the early 1970s, largely owing to concern about the toxic potential of lithium and its status as an un-patentable mineral with limited commercial value or industrial support. Joel Elkes was not involved in our work with lithium. Findings from this work, pertaining to dosing, dose-serum concentration relationships, and adverse effects of lithium, were reported in collaboration with a senior faculty member of the Elkes department, Joseph H. Stephens, MD (Baldessarini and Stephens, 1970). Contrary to Barry's suggestion that this experience "impaired my career" based on criticisms from medical colleagues or by a "frustrated attempt to study lithium," it stimulated an interest that has grown over the years and encouraged a number of laboratory and clinical studies, that included developing evidence of an anti-suicidal effect of lithium (Tondo and Baldessarini, 2015).

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August 11. 2016

Barry Blackwell’s response to Ross Baldessarini's response

I am grateful to Ross for clarifying the fact he did indeed complete work on the basic pharmacology of lithium in collaboration with Joseph Stephens towards the end of his residency, that his Chairman, Joel Elkes, was not involved and that this was the stimulus to a career long interest and research contributions on lithium, including a potential anti-suicide effect. It remains puzzling that the climate in America, in general, and Hopkins and the FDA, in particular, should be so averse to further clinical work long after the safety of lithium was demonstrated in Australia and its benefits in prophylaxis were becoming recognized worldwide (perhaps skeptically in Britain). Also, that senior medical colleagues viewed his enterprise as “extremely poor judgment and risk taking,” a sentiment that did not deter him.

August 18, 2016

Reid Finlayson’s comment

Dr. Joel Elkes was visiting emeritus professor of psychiatry in residence at McMaster University during the 1970's when I was a trainee and junior faculty member under the chairmanship of Dr. Nathan B. Epstein and the late Dr. John 'Jock' Cleghorn. It was a vibrant time, during which he created widely acclaimed approaches to patient care. These programs were designed to apply "Brain and Behavior" to community-oriented, people-centered, interdisciplinary and problem-based approaches to education and clinical care.

I recall Dr. Elkes' personal warmth, humility and enthusiasm. He was an engaging teacher who was always interested and supportive. He was a man of many talents, who excelled in many fields. In addition to recognition as a scientist, expert clinician and wonderful teacher, Dr. Elkes became an accomplished artist in his later years.

March 31, 2016

William E. Bunney's comment

I have read Dr. Blackwell's biography of Joel Elkes. It is truly comprehensive and excellent, and I have little to add. I had limited contact with Dr. Elkes when he was at St. Elizabeth's Hospital in Washington D.C. I also saw him at the annual meetings of the American College of Neuropsychopharmacology. My impression is that he was a broad visionary and, at times, somewhat controversial in his inclusiveness. In my view, he showed great leadership and was one of the most brilliant minds of the century.

April 21, 2016

James Harris' comment

Joel Elkes at Johns Hopkins

Stanislav Grof (1931 -), Paul Grof's brother was brought by Joel to Johns Hopkins as Fellow of the Foundations Fund for Research in Psychiatry in New Haven, CT, originally to start a new research project of psychedelic therapy. Because of the hysteria created by Maimon Cohen's paper of the effect of LSD on chromosomes, Joel decided not to start this project. Grof then joined the existing psychedelic research program at Spring Grove State Hospital, which was later moved to the newly built Maryland Psychiatric Research Center. He also taught psychotherapy as Assistant Professor of Psychiatry at Johns Hopkins and, after the death of Walter Pahnke, he became Chief of Psychiatric Research at the MPRC. He was a co-founder of transpersonal psychology and played an important role in the development of pre- and perinatal psychology.

Another recruit was Roland L. Fischer (1915-1997). He was an experimental psychologist and psychopharmacologist known for his early work on schizophrenia, the perception-hallucination continuum model of altered states of consciousness and for his work on gustation which later contributed to research supporting super tasting.

Fisher had worked with Hoffman in Basel (who had discovered LSD) and was an early proponent of the study of hallucinogens as models of psychosis. His calling card read "cartographer of consciousness and biologist of the fleeting moment."