Barry Blackwell: Pioneers and Controversies in Psychopharmacology

Chapter Three: Joel Elkes

Preamble

This Chapter is one of three biographies based on significant personal interaction (See Chapter 15, 1&2). I first met Joel Elkes in 1970 at the Baltimore Conference on *Discoveries in Biological Psychiatry* where, at age 57, he presented his paper, "*Psychopharmacology: On Beginning in a New Science.*" I learned more about him when I collaborated with Tom Ban on *The Oral History of Psychopharmacology* for which he was interviewed at age 82 by Fridolin Sulser in 1995 (Volume 1: Starting Up). When Joel celebrated his 100th birthday in 2013 Tom suggested I write his biography for the INHN website. After some reading and research, I met Joel Elkes and his wife Sally Lucke at their summer home in Chicago and spent several hours interviewing him and socializing with them.

The eponymous title "Father of Modern Neuroscience," implying a successor to Thudichum, was not a title Joel chose for himself, but he suggested the adjective "Integrative" for this biography which reflects the broad scope of his achievements and is reminiscent of Thudichum's nickname among his contemporaries as "The Multiple Man." Both were polymaths.

Justification for Joel's historical role in the modern development of psychopharmacology is briefly related in this chapter and deserves amplification. As a young student, he was fascinated with physics but lacked aptitude in arithmetic so chose chemistry as a focus for earning admission to medical school.

Like Thudichum, he was born in Germany and migrated to Britain at the early age of 17; Einstein and Ehrlich were his role models when he began medical training at St. Mary's Hospital in London. The outbreak of war between Britain and Germany, coupled with his Jewish heritage, created financial problems that prolonged his training and required he seek student employment.

Neither biochemistry nor psychopharmacology were then part of medical education so he obtained work under Alistair Frazer in physiology and, after graduation, followed him to Birmingham in the Department Pharmacology. His work there on the lipoproteins and structure of myelin led to research on the peripheral nervous system of the frog and diffusion of drugs across membranes. During this time (1944-1950) he worked and learned psychiatry at the local mental asylum along with his wife, a family doctor. Together they studied the effects of barbiturates, amphetamines and mephenesin on patients with catatonic schizophrenia. Working with Philip Bradley Joel also developed the EEG to study the effect of drugs on electrical activity of the brain and behavior.

Conceptually Joel Elkes had moved from the composition of the nervous tissues to the relationship between chemical substances, cerebral function and behavior. In doing so he crossed the Rubicon from structure to function, from chemistry to physiology, the barrier which impeded Thudichum who lacked both the knowledge and tools which Joel created, ushering in the new discipline of psychopharmacology.

This accomplishment led to Joel's visit to America on a Fulbright Scholarship after which he returned in 1951 to Britain at age 44 to become Chair and Professor of a new Department of Experimental Psychiatry in Birmingham.

All this was before the discovery of chlorpromazine for psychotic disorders, after which Joel and his wife Charmian published the first double blind study scientifically confirming its efficacy and describing methodology in an asylum setting that served as a model for burgeoning psychopharmacology research at State asylums and the Veterans Administration hospitals throughout the United States.

Joel's time in Birmingham was supported both by the Rockefeller Foundation in America and the Medical Research Council of Britain. He set up a 40-bed experimental facility, the Uffculme Clinic, the first experimental facility worldwide devoted to psychopharmacology. Joel described the work there as resting, "On the assumption that the various manifestations of gross mental disorder and milder dysfunction have their counterpart in disturbed physiology of the brain, and that the study of the chemistry, the cellular constitution and electrical activity of the brain may contribute to an understanding of its function as the highest integrating organ" (Elkes 1955).

Joel's reputation was well established by 1954 when he convened the First International Neurochemical Symposium in Oxford devoted to regional differences in cerebral circulation and neurotransmitters. Three years later in 1957, as Consultant to the World Health Organization (WHO), he planned the First International Symposium on psychotropic drugs, the logical next step from structure and function to treatment.

In that same year, he left Britain to head up the first Neuropharmacology Research Center in America at Saint Elizabeth's Mental Hospital, sponsored by the NIMH. As described in the biography, this was a "Camelot Era" during which Joel recruited, mentored and nurtured promising young scientists in the new discipline and hosted visiting experts from around the globe.

Not surprisingly, in 1961 Joel Elkes became the first President of the American College of Neuropsychopharmacology (ACNP). Earlier, in 1957 the corresponding international organization was created, the Collegium Internationale Neuro-Psychopharmacologicum (CINP). Joel became a Fellow in 1960, presented a paper at the First Congress on the drug induced changes in schizophrenia and was later honored with CINP Pioneer's Award. In the volume "The Rise of Psychopharmacology and the Story of CINP" (Ban, Healey and Shorter 1988), the first chapter is by Joel Elkes, "Towards Footings of a Science: Personal Beginnings in Psychopharmacology in the Forties and Fifties," with the subtitle "A Program on 'Drugs and the Mind' – Experimental Psychiatry in Birmingham, England."

By the age of 50 in 1963 Joel Elkes had accumulated an impressive and unique record of "first place" accomplishments in the new and rapidly evolving field of neuropsychopharmacology. A more complacent and less talented human being might have rested on these laurels and coasted to a comfortable retirement but his creative and fertile mind dictated the next step. In that year Joel took the Chair of Psychiatry at Johns Hopkins University, the premier medical school in the United States. This is where William Osler served as Dean and established a curriculum that became a model for the Flexner Revolution, transforming the profession from an apprenticeship into a scientific discipline (Blackwell 2016).

Joel's mission was to secure the place of psychiatry as an integral part of that discipline, an intention heralded by choosing to rename his domain "The Department of Psychiatry and Behavioral Medicine," a prescient choice that would make the two disciplines synonyms in a

nationwide attempt to rid psychiatry of stigma. This intent was reinforced by initiating a joint M.D.- Ph.D. program in medicine and neuroscience.

But Osler's genius, turning medicine into a scientific enterprise, had a down side; beginning in the 1930s and continuing into the 1950s distinguished educators and internists, first Peabody and then Engel, raised valid concerns about an over emphasis on the biomedical aspects of treatment to the detriment of humanistic and psychosocial input (Blackwell 1985).

Overall, this novel aspect to Joel's task was one for which his integrative persona was well equipped. He had begun an analysis as a medical student, interrupted by the onset of World War II when his analyst was inducted into the Army. Joel completed the analysis while in Washington so had the credentials and training to introduce psychosocial issues into the curriculum.

But the 1960s were a difficult time to implement such a transition. The hegemony of psychoanalysis over academic psychiatry was crumbling and the relevance of biological psychiatry was growing rapidly. Neither side in the struggle for dominance was eager to yield curriculum time. Meanwhile, frustrated by the lack of primary care physicians the Federal Government initiated programs in the 1960s and 1970s to fund over thirty new medical schools in community settings, away from academic ivory towers and equipped to graduate humanistic doctors, able to meet a public's perceived expectations for a new brand of family physician (Blackwell 1985).

There is no doubt that Joel faced covert opposition to implementing the kind of curriculum that would address this need. He was aware of these undercurrents, transformed into criticism of his administrative skill, but was reluctant to discuss them other than acknowledge they played a part in his decision to leave Hopkins after almost ten years of qualified success.

Joel sought refuge in a named professorship at McMaster University in Canada, a seedbed of novel ideas for medical education and practice where he spent six years incubating his own ideas for curriculum change. He emerged to enter the final epoch of his professional life as Emeritus Professor of Psychiatry at Louisville University where he developed programs and obtained funding to support humanizing and broadening the curriculum, including integrating the Arts with medicine.

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Joel finally quit formal academia in 1988, at the age of 75, and spent the last quarter of the

20th century engaged in scientific, family and artistic endeavors described in the last three segments

of the biography: Family Matters, Life as a Whole and the Envoi which places his lifetime

accomplishments in perspective.

After the biography was completed and presented to Joel and Sally they invited us to attend a

public showing of Joel's much-admired art, combined with a celebration of his 102nd birthday. A

few weeks before Sally called from a hospital where Joel had been admitted and was recovering

from a mild heart attack. I was able to speak to Joel and found him to be in his usual optimistic

frame of mind and looking forward to seeing us at his birthday. It was not to be; a few days later

Sally called again to say Joel had succumbed to a fatal heart attack so the art showing would now

be coupled with a memorial service. I joined several colleagues in brief eulogies and we returned

home with one of Joel's much-admired paintings. It serves as a daily reminder of a true pioneer

whose accomplishments are inadequately appreciated or acknowledged today.

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JOEL ELKES: AN INTEGRATIVE LIFE

By

Barry Blackwell

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

At this writing, Joel Elkes is now in his 102^{nd} year of a distinguished life and is the oldest living pioneer in our field, recognized as the "father of modern neuropsychopharmacology" (See 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, 12 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 (Ban 2001). 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 patient's 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 Collegium Internationale Neuro-Psychopharmacologicum (CINP) or American College of Neuropsychopharmacology (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 in1954 (Elkes 2011a). It was attended by Seymour Kety, Heinrich Waelsh, Louis Flexer and Jordi Folch-Pi from the USA, with Geoffrey Harris, Derek Richter and himself 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 ACNP in 1962 and when the history of the 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, (Elkes 2011a; Ban 2001; Elkes 1997).

Joel Elkes was born in Koenigsberg, capital of eastern Prussia, on November 12, 1913. His father, Elkhanan, 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 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 Koenigsberg 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 microelectrophoretic 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 in 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 18 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 more than 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. Elkhanan 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 20 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 in 1942 to official retirement in 1974, Joel's career began and ended. 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 and 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 Fullbright Travelling 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, Elkes and Bradley 1954; Elkes and Bradley 1957). 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 (1961c); 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 Counsellors.

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 the 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." Third, "the importance of understanding the environment, the social setting, the action and even the dose of a drug on these variables." And last, "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 a graduate of a renowned law school and 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 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 nevertheless, 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 & Sciences (1974); and the Pioneer Award, CINP (1998).

To celebrate Joel's 100th 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 40s (1), 50s (4), 60s (10), 70s (4), 80s (3) and 90s (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 more than 100 references and a pamphlet (Elkes 2011) reprint of 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 VA. 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 PhD. 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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