Barry Blackwell: Pioneers and Controversies in Psychopharmacology

Chapter 15: Career role models; vicissitudes and zeitgeists

Ervin Varga biography

Kanellos Charalampous biography

PREAMBLE

As noted in the Introduction, a significant number of pioneers in American psychopharmacology were immigrants born in the 1920s and 1930s who became victims of ethnic cleansing at the hands of Fascists, Nazis, Communists and often fellow citizens before, during and after the Second World War.

This chapter provides the inspiring biographies of two remarkable individuals, Ervin Varga and Connie Charalampous, both of whom contributed significant autobiographical material describing their early lives in Hungary and Greece.

The main purpose of the chapter is to explore how their family upbringing, culture and early role models shaped not only their capacity to survive but to thrive in their own country, obtain a medical education and begin a career in psychiatry before migrating to America and contributing as pioneers in the evolving psychopharmacology revolution.

ERVIN VARGA: Family, Culture, Persona and Career.

By

Barry Blackwell

As the title implies, Ervin Varga's career path has been determined, perhaps more than most, by complex and unusual circumstances. The accomplishments and challenges of his life's work

are viewed through the prism of his family origins, the culture he grew up in, the way these shaped his adult persona and responses to the challenges he faced.

Ervin Varga's Own Memoir

Ervin is the scion of a large, industrious and successful Hungarian Jewish family for whom ambition and drive had survival value in an anti-Semitic culture until they became "extras in an immense drama ... with a grotesque message; how and why the morally unthinkable became socially acceptable." Ervin comments: "The first half of the twentieth century was, uniquely bloody ... marked by pitiless social and radical ideologies." First Fascism and then the "Final Solution" followed by Communism and its totalitarian ethos.

This story is told in *Living and Dying in Hungary: A Jewish Psychiatrist Looks Back* (Varga 2012). Ervin tells the story in lucid and unsentimental prose of how, "Most of my family members were killed before reaching the age of sixty." The events and facts garnered from books, chapters, articles, archives and survivors of the Holocaust took place almost seventy years before he put pen to paper and what begins as a family history also turns into a memoir, published at the age of 87, recording events with photographic clarity that took place between his birth until, at age 20, "We had returned from hell ... I was impatient to embark on my medical studies, an untenable dream before."

The account of Ervin's career begins where the memoir ends, initiated in part by Tom Ban's awareness of Ervin's interesting but "under the radar" career, due to their common roots growing up in wartime and post-war Hungary, from which Tom also escaped, but earlier, to Canada. As adolescents, but ten years apart they shared a tutor, Michael, who played a significant role in shaping their world views and personas as well as a mentor, Gyula Nyiro, whose teaching shaped their clinical ideology in profound ways described later.

This biography, like those previously documented on the INHN website in *Biographies*, shares a theme common to that literary mode; an awareness that "The child is father to the man"; that a persona shaped in childhood, adolescence and early adult life invariably influences the choice and shape of a career, especially in confronting the ever changing but challenging and unpredictable scientific, personal and social Zeitgeists.

Ervin's detailed memoir and unusual upbringing are particularly informative in this regard. What follows is a synopsis chosen entirely from Ervin's own words, modestly edited and presented without quotation marks for ease of understanding and flow. This is what he has to say.

He traces his Jewish cultural and genetic roots on both maternal and paternal sides. On the maternal side the Richters were upwardly mobile, well to do and endowed with drive, sheer guts and common sense. His grandfather was first in the dynasty to graduate from a gymnasium and, eligible for university, he attended a famous seminary to become a Chief Rabbi and Professor at the local gymnasium, teaching divinity and Judaism. His maternal grandmother Emily's kinfolk were the Reichs; she had incredible resources of moral strength and dignity with an aristocratic gift for gentle comments. Deeply religious, so that Ervin concealed his own lack of faith to avoid offending her.

His mother's eldest brother, Uncle Anslem, lacked the Richter's traits but had a keen curiosity and thrived as an antique dealer. In November 1944, aged 60, he was the first relative to die in the Holocaust. Seized by Hungarian fascists, he was force marched towards Vienna. Unable to keep up, he was pushed to the end of the line, shot in the head and buried in a ditch. His daughter, the same age as Ervin, was taken to Ravensbruck concentration camp a month earlier, survived, was liberated in April 1945 but was shot and killed by a Russian soldier a few days later; possibly resisting rape.

Ervin's second uncle Hugo was the most remarkable member of the clan and an important role model. After graduating from gymnasium, he attended Budapest Medical School and graduated *magna cum laude* in 1910, before working in the laboratory of the renowned neuropathologist, Karoly Shaffer, then spent a year in Berlin at the Kaiser Wilhelm Institute and finally worked with Nobel Laureate Wagner Jauregg in Vienna. Returning to Budapest, he was an unpaid Instructor in neuropathology, living in a one room sublet, tutoring medical students to support his mother and her eight children. After serving as an army doctor in World War I, he returned to the University as an Assistant Professor and made discoveries in neurosyphilis, migraine and Pick's dementia. In 1925, he became Chairman of Neurology and Psychiatry at Budapest Jewish Hospital after declining to accept a full Professorship at the University on condition he converted to Catholicism, an offer Ervin and his brother both declined later in the forced labor camps in order to exchange the yellow star worn by Jews for a white one.

In 1929, Hugo was appointed a "private docent", the highest academic rank and in 1939, a year after Kristallnacht, he declined an offer to work in the United States, reluctant to leave his mother and with the false hope Britain would stop Hitler before Hungary entered the war on Germany's side.

Hugo felt Freud was neither a scientist nor a clinician, a skillful writer who reduced complex issues to a sexuality that remained vaguely defined. These opinions did not deter Ervin, encouraged by his tutor, Michael, from devouring all Freud's books, moving on to analyze his classmates in the gymnasium, interpreting dreams right and left, making a strong impression on girls.

For Erwin, Hugo was the silent witness who shaped his choice of medicine, an early influence that encouraged him at age 7 to introduce himself as "Doctor" to friends and visitors. Later on, his view became more nuanced; comparing himself to his idol he says, "Yet I have never felt fully satisfied with myself because of the relentless challenge to live up to his expectations. I got everything, the ambition, the goal, the style but apparently not made of the same fabric." This insight and conviction would later color career decisions he made.

Two of Hugo's female cousins, one Chair of the English Department and the other Professor of Philology at the University of Vienna, were killed by the Nazis as Jews in 1938, although both were lifelong Catholics. Hugo met a more fortunate fate. In 1944, he was placed in a forced labor camp to dig ditches but reprieved, due to political patronage and his reputation, he returned to his post at the Jewish Hospital, now part of the Ghetto. In 1945, after the liberation, he was hit by a Russian truck and died from his injuries shortly after Ervin was able to visit him and bid farewell.

The story of the remaining Richter aunts, uncles and cousins was both colorful and tragic; first under the "White Terror" after World War I when both Jews and Communists were purged in primitive pogroms and then under the burgeoning Nazi regime. The sole survivor, Uncle Mauricio migrated to Mexico and thrived, dying at the age of 90, socially and financially successful but plagued by feelings of inferiority.

Ervin's paternal ancestors were the Weiszes. His grandparents lived in semi-feudal rural surroundings, dwelling in a relatively decent cottage but without sanitation. His grandfather managed a distillery on the estate of the local Count, while his grandmother tended a family menagerie of fowl, cows, horses and water buffalo. Both were murdered at Auschwitz in 1944.

Ervin's father served in the Austro-Hungarian army in World War I, was captured by the Russians, escaped and travelled home on foot through the war-torn countryside without knowing the language or having a penny in his pocket. He was a soft, sensitive and loving man, a travelling salesman, married to a strong wife, who edited, corrected and proofread him like a never ending story.

From these grandparents and parents Ervin learned the lessons of life. He was expected to "behave like a man"; it was fine to seek advice or help but totally unacceptable to solicit sympathy, dramatize accomplishments or feel sorry for yourself. With hindsight and psychiatric training, Ervin realized how systematically he was encouraged to develop inhibitions, repress basic urges and feelings, to pretend strength and suppress anxieties. He rationalizes these as self- regulatory techniques essential to civilized, disciplined behavior.

One other Weisz, Uncle Andor, became a physician. He graduated from Budapest, married, set up a rural medical practice and converted to Catholicism. Despite this, he was taken with his wife and daughter to the ghetto and then to the gas chambers at Auschwitz, among the first Hungarians to die there. Before they were murdered, they were forced to send a handwritten postcard home, "We are all well and in a nice resort."

Ervin Weisz was born February 20th 1925 on Jozsef Boulevard in Budapest, four years after his older brother Feri. It was a comfortable home, presided over by his grandmother and mother while his father was often on trips as a salesman to bring home the family bread. The family kept Kosher and observed traditional Jewish rituals. Included was the annual Yom Kippur sacrifice of live chickens, first held over the adults' heads as they danced around the room, while Ervin and Feri hid beneath the table, from where they viewed the chickens, beheaded by a ritual butcher, running around headless and gushing geysers of blood. Ervin developed a lifelong aversion to eating the flesh of fowls and at age 9, suffered his first real panic attack.

Ervin traces his educational and emotional evolution through childhood and the teen years, during which the family was upwardly mobile. He moved from a parochial elementary school to a private Jewish institution with a strict impartial teacher, who demanded discipline and gave praise only when deserved. Pupils learned not only how to read and write but how to behave. They sat with hands clasped behind straight backs, developed the smallest genteel manners, including to eat slowly in small bites, to end meals while still hungry and wait till it went away.

At age nine, Ervin began Cub Scouts, where they were taught larger morals, collective responsibility, sharing and more discipline; it was praiseworthy to be strong, tough and do good to others. During this pre-adolescent phase, Ervin was sensitive and naïve, exposed to sexual innuendo and bullying by older boys and girls, which leads him to reflect on how, over a lifetime, he has been controlled by people, institutions, principle and duty.

At age ten, Ervin entered the rigorous eight year-long academic environment of the gymnasium, where they learned Latin daily. It was also rife with anti-Semitism and patriotic heroism, expressed by teachers eager for national revenge over the two thirds of territory lost from Hungary due to the Trianon Peace Treaty after World War I. At age 12, Ervin and his brother enrolled in the Jewish Gymnasium, a simple move that created a new look on life. It was among the best schools in Hungary, a spectacular modern building letting in light everywhere, a metaphor for an enlightened curriculum in science and arts, staffed by above average teachers, including some brilliant former university professors. Exposed to a socio-political climate of anti-Semitic hatred, the pupils felt propelled to academic excellence. His mother hired Michael as a tutor to reinforce the academic and moral climate. Under his guidance, Ervin read Hebrew, the verse of the English Poets, devoured Freud and the German philosophers. He kept a literary diary and was viewed by the family as modestly superior - knowledgeable but not a show off. After work was over, Ervin attended Boy Scouts, played tennis, ice skated and swam – sports he enjoyed but never excelled at.

On the eve of his Bar Mitzvah, on March 12, 1938 at age 13, Ervin learned that Hitler had annexed Austria and German troops had occupied Vienna. People knew the fascists were coming and felt the winds of hatred but ignored the coming storm. In the summer of 1939, Ervin hiked with a friend in the Carpathian Mountains —a gift to Hungary from Hitler for implementing a restrictive "Jewish Law", which included the *numerus clausus* rule, limiting university admission for Jews. Among the victims, Ervin's brother Feri was forced to become a skilled laborer and then drafted to a notorious labor camp.

At age 16, in the bloom of adolescence, Ervin joined a Zionist group preparing its members to live on a Kibbutz in Israel, a phase that only lasted until his provocative dissensions led to his departure, taking with him a lovable girl Anna. Together they eagerly turned adolescent romance into adult love, living in fragile denial that passive compliance with fascism might divert

persecution. But, in 1941, one of the brightest and bravest students at school was arrested by the Hungarian Political Police, taken away and disappeared; soon after an anti-Semitic crowd broke the schools widows with rocks.

Ervin and Anna continued in a Romeo and Juliet state of bliss that sustained the element of denial until he graduated from gymnasium in spring of 1943. Now all Jews were banned from university and Ervin and his friends were anticipating the forced labor camps. His application to medical school was denied unless he converted to Christianity, even though Uncle Hugo (who had rejected the same offer) knew the President and advocated on his behalf.

News that the German Army had stalled and was facing defeat in Russia bred a brief false optimism but also fueled Hitler's determination to complete the Final Solution. In March 1944, Germany invaded and occupied Hungary, its erstwhile ally, after the interim government attempted to broker an armistice with Britain and Russia. Two weeks later, the Americans started to bomb Budapest. A new pro-fascist government took over and the civilian population felt empowered to escalate its latent anti-Semitic ethos in support of the Nazis. All Jews were required to wear a yellow star over their heart. Anna's father was taken away and the Gestapo sealed their house but not before Anna escaped to take refuge in a tenement where Ervin was able to visit her. In less than a month, all Jews were herded into internment camps, a gateway to concentration camps and the gas chamber. On June 5 1944, Ervin was commanded to report to the forced labor camp at Felsohangony. What started as a six month period in military style housing with enforced hygiene and adequate food, soon deteriorated into an increasingly rabid anti-Semitic environment administered by guards delivering senseless cruelty, blind hatred and officially sanctioned sadism. Treated as objects of intense abhorrence, the prisoners struggled to survive as decent human beings, an irrational hope.

In mid-July, Ervin's unit was taken to a camp in the Carpathian Mountains to build an airfield, where they worked for three months like slaves, 6 days a week for 12 hours daily. In October, at two hours' notice, they began a month long forced march to the town of Kassa, where they were loaded and locked into boxcars, 80 or more at a time. They travelled this way for uncounted days, stopping intermittently to be given soup with a small piece of bread and to carry the dead into the surrounding fields.

On New Year's Eve 1945, they arrived at Hidegseg (Hungarian for coldness) and crowded 50 or more into sheds with frozen mud floors covered with a few reeds. A voice from outside the shed demanded silence: "This is a death camp. If you speak loudly you will be shot. If you are sick you will be killed. If you don't obey fast enough you will be beaten to death." This was delivered without anger or empathy in a voice ice-cold, clear and factual.

Over the next three months, ending on March 29, 1945, this proved an accurate description of unimaginable cruelty and barbarity which Ervin witnessed and endured. Instructed to dig trenches to obstruct Russian tanks, equipped with shovels and axes they could hardly lift, they struck at frozen earth. In the evening, they were fed soup made of potato and carrot peelings boiled in unsalted water, with a slice of bread every three days. People died of starvation, exhaustion, beating, shootings and freezing. Typhoid, dysentery and lice were endemic. The living undressed the dead and distributed the clothes to those unable to move. Those who survived buried the dead.

In February, on Ervin's birthday, the survivors were ordered to stand in a large circle. The guards dragged a small emaciated young man into the center, barefoot, half frozen in rags, hands tied behind his back. Sentenced to death for attempting to escape, he was shot in the back of the head and went down like a marionette when the string is let go.

Following the execution, Ervin became ill. Terribly thirsty, he faded in and out of delirium. He could not stand, his toes were frost bitten and he developed bed sores. During roll call his companions held him up, then smuggled him back to the shed and covered his body in rags. The only person Ervin could think of was his mother, only she meant redemption.

By mid-March, Ervin began to recover and learned to stand by climbing up his own legs, like a child with muscular dystrophy. Starving and craving food, the prisoners minds were filled with thoughts of it, a craving that brought them to the edge of decency and dignity. They counted their dead comrades and ruminated on why they remained alive. It was a question with no logic or principle to explain the luck of survival; existence was a statistical aberration.

The guards no longer let them out to work but continued to rampage. They shot a man in Ervin's hut for no reason and when a heroic rabbi attempted to fulfill his obligation to bury the dead they shot him too. The bodies lay alongside, unburied.

By the time of their delivery, the prisoners had buried 800 (about half) of their fellows and in Ervin's shed only eight were still living. As the Russians came close, the guards prepared to flee as darkness fell; they stopped outside the shed and demanded to know how many were alive. Hearing the answer "eight" they opened fire, repeating the question till the answer was "four". Satisfied, believing no witness would survive, they disappeared.

In the morning three men were wounded and one dead. Sitting quietly, the survivors tended the wounded. Suddenly the locked door was broken open by a young Russian soldier, soon followed outside by a tank with an officer on top. He spoke in broken German: "You are free, the camp is yours; your guards have run away. Go and eat from the storeroom, there is plenty of food. Take off your yellow ribbons."

Ervin was happy not to feel hungry or cold and relieved from constant fear of being brutalized, but overall being free was characterized by numbness, a lack of feeling. Ervin could not walk more than 100 yards but made up his mind to head for home as best he could. In three weeks, he travelled 200 miles by foot, truck and train, stopping briefly in a local hospital and an unexpected guest in the homes of two peasants, finally crossing the Danube on the only remaining bridge to reach Budapest, one of the first to return from a death camp.

Ervin went first to the Jewish Hospital and sat by the bedside of Uncle Hugo the day before he died from his injuries. Also giving comfort were his mother and grandmother. Added to the joy of re-union was the news that his brother had somehow escaped from his labor camp and was also safely home.

On liberation, their mother had left the ghetto and single-handed evicted the fascists who had occupied the family home, which remained in surprisingly good condition. Their father also survived two concentration camps; now fifty years old, he had returned reasonably healthy. Of all those closest to Ervin, only his sweetheart Anna failed to return. Three months later, her name was listed on those who died in Bergen-Belsen concentration camp.

Ervin had regained most of his weight and health by the summer but developed tuberculosis and spent time in a sanitarium; absent the availability of drugs to treat the condition, he stayed only until he enrolled in medical school among the 1000 applicants, many of them Jewish men and women previously denied acceptance.

By this time, Ervin and his brother had decided to shed their Jewish name Weisz, which attracted anti-Semite attention and was of little historical significance to them. Paging through the Budapest Telephone Directory, they picked an ecumenical run of the mill name with the longest list. Ervin Weisz became Ervin Varga, now embarked on what he hoped would become a discrimination free life as a future physician in Hungary.

Hungary Post World War II

Ervin's Memoir ends at age 20, when the social and political climate in Hungary left much to be desired. Russia pursued its aggressive role of Communist hegemony and neo-colonialism, invading the countries adjacent to its borders and establishing totalitarian regimes where the defeat of Nazi Germany had created a political vacuum embracing Greece, Hungary, Czechoslovakia, Latvia, Bulgaria and Poland, ultimately bringing down the Iron Curtain. For centuries anti-Semitism had been endemic in the Hungarian population, covert or overt, depending on the political climate. A majority of the population had actively or passively endorsed the Nazi goal of eliminating Judaism and after the Nazis left, it did not disappear overnight. The strategy of seeking secular anonymity with a name change would serve as only a slender shield for someone with Ervin's experiences and innate sensitivity.

Now medical school was a much awaited, long delayed reality but not an easy one, particularly the first year with 1000 students jostling for space and attention. But their numbers dwindled rapidly, more than two thirds dropped out and only 300 graduated, Ervin among them, as well as a future wife, found once the pain and loss of Anna had slowly melted away. In a population culled of young men by the Nazis, women outnumbered the male survivors.

To best understand the roots of Ervin Varga's medical and psychiatric education and its branches requires some background. Semmelweis University in Budapest was founded in 1789 and became independent of Budapest University after World War II, at the time Ervin began his studies. It enrolls around 10,000 students annually from 60 nations, offering undergraduate and graduate level courses in medicine, pharmacy, dentistry, health sciences and administration taught in English, Hungarian and German. It is home to the biggest medical library in the country and produces the greatest number of scientific publications (Wikepedia Encyclopedia, 2015).

The University of Pecs is the oldest University in Hungary with its own Medical School. As a medical student, Ervin attended both Universities, beginning at Semmelweis and transferring to

Pecs after five semesters, as his interests evolved and then returning to Semmelweis for psychiatric residency.

A crucial influence on psychiatric education during that period was the Semmelweis Professor of Psychiatry, Gyula Nyiro. In 1933, he had worked with Von Meduna to introduce what became known as "shock therapy" for psychotic patients, induced first with chemical convulsants and later by electricity. Nyiro, a brilliant clinician, diagnostician and teacher, published little but exerted a profound influence on a trio of students all of whom went on to make significant contributions in psychopharmacology. The first two were Ervin Varga and his contemporary in gymnasium and medical school, Joseph Knoll. The third was Tom Ban, younger by ten years when he enrolled at Semmelweis. For a fuller understanding of Nyiro's contributions, see Tom Ban's e-book on INHN (INHN in e-books; 10/10/2013). Tom believes that Nyiro provided the link between Wernicke's nosology and Pavlovian reflexology, bridging psychopathology with pathophysiology. When Tom escaped from Hungary in the mid 1950's, leaving most of his possessions behind, he tucked Nyiro's lecture notes into his briefcase.

Nyiro's influence on Ervin's career was direct and profound. As a medical student, his teaching reinforced Ervin's determination to follow in Uncle Hugo's footsteps as both a neurologist and psychiatrist. This motivated him to move to Pec's University to work under Professor Lissak, where he learned about high quality neurophysiology research. Here he also met his future wife Vera, a *magna cum laude* medical student. Ervin finished medical school at Pecs, completed a rotating internship there and obtained his MD Diploma in June 1951 from that University.

From 1951 to 1959, he returned to Semmelweis for residency training in both neurology and psychiatry in Nyiro's sphere of influence. He obtained boards in psychiatry in 1955 and neurology in 1962. During this time, his still untreated tuberculoma (due to the absence of drugs) was surgically removed along with an entire lobe of one lung, taking half a year to fully recover. While in residency, he embarked on a thesis supervised by Nyiro that led to a Ph.D. equivalent in 1962 as a Candidate in the Academy of Sciences. The core of his dissertation was the observation that normal speech made no sense until it was vocalized, after the brain had completed the words and sentence. Ervin hypothesized that patients with schizophrenia lacked this ability; their utterances were immediate and often nonsensical. Over four years, Ervin developed neurophysiological

methods to measure this phenomenon which Nyiro had named "delayed inhibition." Ervin published nine papers in both English and German, culminating with his Thesis, *Schizophrenic Perception*. *An Experimental Investigation* (Varga 1961).

During this time period, chlorpromazine became widely used to treat schizophrenia but Ervin did not study its effects on delayed inhibition, a missed opportunity he feels would be worth revisiting today.

In the brief interval between finishing residency and starting his academic career, Ervin decided to attempt to implement an intrepid urge to visit the Maudsley Hospital in London, recognized as one of the leading centers in European excellence under Aubrey Lewis. This was a challenging task; under Communist rule, he needed a connection to the Hungarian authorities, a minimum fund for support and a letter of invitation to give a lecture. He obtained the economic support from his brother in California and the invitation from a former schoolmate working as biochemist at the Hammersmith Hospital in London. He rented a small apartment for a month's stay and his host arranged for him to meet Michael Shepherd, the number two academic at the Maudsley.

Shepherd was by no means the most popular person at the Maudsley but he and Ervin hit it off. "We immediately liked each other, I enjoyed his slightly manneristic, sarcastic style and he was glad to speak real psychiatry. He took me everywhere, tested my diagnostic skills, took me to his home, and gave me books to read." Michael also introduced him to senior colleagues well known for their research. Altogether, "My visit to the Maudsley changed my life ...I liked everything." It also cemented a relationship that would have later consequences for Ervin's career and which energized him to engage in almost a decade of intense academic achievement.

Ervin returned to take up his post as Assistant Professor of Psychiatry and Neurology at Semmelweis and three years later was promoted to Associate Professor and Director of Psychopharmacology. While completing his thesis, Ervin had also worked as Chief of the Depression Unit, where he was disappointed with the effects of ECT and began developing an interest in the new drug treatments. His classmate, friend and now colleague, Joseph Knoll had decided to pursue bench research rather than clinical work and had joined the Department of Pharmacology, where he remained for the rest of his life. He became a Full Professor in 1963 and Head of the Department from 1962 until his academic retirement thirty years later in 1992,

although still doing active research at the age of 91. His early research was with the MAO inhibitors and he had already supplied Ervin with Niamid for use in humans (Varga 1964). Aware of the "cheese effect" in humans treated with MAOI (Blackwell, 1963), Knoll was intrigued to find that the MAO inhibitor he was now working on, Deprenyl (E-250), also inhibited the noradrenaline releasing effect of tyramine in rodents.

Ervin Varga's early role as the clinical component of this translational research is told in an interview of Knoll by Tom Ban at Budapest in 2002 for the *Oral History of Neuropsychopharmacology* (OHP) (Vol. 3; Series Ed. Ban TA; Vol. Ed. Sulzer F). This 32 page interview is probably the most lengthy of those in all ten volumes of OHP and is an enthralling micro biography of Joseph Knoll, as well as a powerful and enlightening testimony to the virtue of translational collaboration between bench and clinic.

"The first clinical trial with racemic Deprenyl in depression was done by my childhood friend, my schoolmate in gymnasium and classmate at the university. The preliminary results were presented at a conference in Budapest in 1965 (Varga 1966 c). The study was extended and was published (Varga and Tringer, 1967). The first clinical trial with the minus isomer, the drug now in use, was published by Tringer, Haits and Varga in 1971 (Knoll, 2002). In spite of their favorable findings, the possibility of introducing Deprenyl as an antidepressant remained unexploited for many years after."

That Ervin Varga was the first to show that Deprenyl did not interact with tyramine and was safe, but that this failed to save the MAOI from oblivion, contributes to my own expressed concern that these "drugs were too useful to be quickly abandoned" (Blackwell, 2014). This occurred despite the fact that we never fully defined the clinical characteristics alleged to benefit or took account of the fact that tranylcypromine (Parnate), probably the most widely used MAOI, also had mild amphetamine like euphoriant effects, a property that proved useful for the treatment of outpatient depression long before imipramine was discovered.

From an historical viewpoint, it is interesting to note that Knoll subsequently discovered that Deprenyl was the first catecholaminergic enhancer and that it prolongs the life span and sexual activity of rodents, an action that is under clinical investigation today in Japan.

The implementation of Ervin's plan to establish solid academic and research credentials, incubated at the Maudsley, ranged far beyond psychopharmacology influenced by his mentor's

interests and teaching. In seven short years, he published 27 scientific contributions in German and English, of which he was first author on 25, covering nosology, natural history and social features of psychoses, neuroses and personality disorders (Varga 1965, 1966 a,b,c; Varga and Haits 1966). This culminated in an authored book, *Changes in the Symptomatology of Psychotic Patients* (Varga, 1966 d). This prescient volume documented the decline of positive symptoms such as hallucinations but not the negative cognitive and behavioral features. This aspect of the response to antipsychotic drugs was a prelude to the ease with which patients could be released from asylums only to founder in the community.

Ervin notes two publications during this creative period he considers his most important contributions. The first, which had international implications, involved his return to the Maudsley for a second visit, sponsored by the World health Organization. Over a period of three months in London during 1966, he worked to support the work of Michael Shepherd and Jules Angst (from the Burgholzli Hospital in Zurich) in carrying out a retrospective evaluation of 910 depressed patients treated at the Maudsley between 1957 and 1963, in an attempt to replicate and validate the findings of the Medical Research Council's study of a similar population, published the previous year in the British Medical Journal (Report of the Clinical Committee, 1965). This creative and unique design resulted in supporting the conclusion that ECT and imipramine were superior to the MAO inhibitor phenelzine, failed to support the earlier finding of a gender difference in favor of females but was unable to clearly identify which clinical, demographic or social criteria characterized a failure to respond to all forms of therapy. Paradoxically, this finding may have made its own contribution to the demise of the MAO inhibitors, although its conclusion was based on the performance of only phenelzine. An earlier operational study of the use of MAOI at the Maudsley established that prior to 1965, tranyleypromine was the MAOI in widest use and suggested that it was more effective than other MAOIs (Blackwell and Taylor, 1967). After the identification of the tyramine interactions in 1963, its use declined rapidly at the Maudsley, replaced by phenelzine.

After the study was complete, Ervin was invited by Jules Angst to visit the Burgholzli on his way home; he was a guest in Jules house, attended the teaching conferences chaired by Bleuler and served as a consultant in helping to diagnose a complex case of a woman who spoke only Hungarian, before returning to Budapest a week later. His interactions with Angst cemented a relationship that stood him in good stead when he later escaped from Hungary.

After returning to Hungary, Ervin undertook a study of a smaller sample of 249 patients with severe depression treated at the Budapest Psychiatric Clinic with ECT, imipramine and phenelzine. The results confirmed the superiority of ECT over drug treatments noted in the London sample (Varga, Angst & Shepherd, 1967).

The second contribution identified by Ervin as important had its greatest impact within Hungary itself. Because of his established position as an expert in schizophrenia, he was asked by the Hungarian Academy of Science to review the history of the life and death of the famous Hungarian poet, Joseph Attila, regarded by many Communist citizens as "the poet of the proletariat." Ervin's findings were controversial (Varga, 1966), provoking debate and angry rebuttals that continue to this day. These focus on an interpretation of the poet's death, regarded by his many admirer's as martyrdom by suicide. The facts suggested otherwise. Attila had approached a stationary train at a crossing, unlatched the gate, crawled under the engine and fallen asleep. When the train started to move, he was crushed and died, an accident Ervin considered the result typical of schizophrenic thought and behavior. It is worth noting that Ervin's mentor Nyiro was admired for his willingness to stand up and maintain his independence under both Fascist and Communist regimes. Perhaps Ervin Varga was a kindred spirit?

Family Matters

The biographies of neuroscientists indicate that marriage does indeed matter, at times in a pre-emptive manner (See those of Jean Delay, Karl Rickels, Heinz Lehmann and John Smythies, in particular, on the INHN website in *Biographies*). There are reasons to suppose this may be even more so in understanding Ervin Varga's career choices and trajectory.

To begin with his marriage lasted almost 67 years and was a highly successful union. It took Ervin four years to resolve the grief and loneliness following news of the loss of his beloved Anna in 1945. But when he met Vera at Pec's University in medical school in 1949, they were married within three months, a union lasting until her death in July 2015. The couple bore two sons, Peter and John, born a year apart and ages 13 and 14 when they escaped from Hungary. Each is now a successful physician in Chicago, where Ervin lives in an apartment overlooking Lake Michigan, comforted by his dog, a Bassenji, and in frequent touch with his sons. Peter is an Associate Professor of Pediatrics at the University of Chicago and an expert in non-invasive cardiac imaging.

John is the John and Nancy Hughes Distinguished Professor of Rheumatology at Northwestern University and a national expert in Scleroderma and its treatment.

So all four members of the Varga family have been talented physicians. The tone and tenor of the parent's marriage is revealed in a eulogy John delivered at his mother's memorial service. As a 12 year old he was so proud of his physician mother that he advertised her services to the neighborhood kids, offering free check-ups and emergency services. "Anyu was an understanding lifelong partner to my Dad. The two of them were inseparable through 67 years of challenges including Communism, revolutions and emigration. *One of her enduring gifts to us, and to our children is her example of this special partnership*" (John's italics).

"Mom was the family bedrock as we rebuilt our lives in the new world. Peter and I never knew how hard she and Dad worked during these years, completing a demanding Residency at 40, while sending my brother and I to elite colleges ... she never complained nor looked back."

John portrays her persona: "Most of all Mom had a big heart...She had a passion for words, literature and books. Mom was the most well-read person I knew, but she wore her erudition lightly. She could read and speak Hungarian, German, French and English but also knew some Russian, Spanish, Italian and even a smattering of Japanese. There will never be another one like her."

In addition to this extraordinary union to a unique partner, one must reflect on the valence and significance of marriage for Ervin. He grew up in a close knit and loving family disrupted by fascist anti-Semitism and in a decade, as a teenager and young adult, lost 40 of his family members to the Holocaust.

Every talented scientist devoted to his or her work must titrate that goal with a competing desire and love for family. For Ervin circumstances would dictate that the balance sometimes tilted more towards family.

Escape from Hungary

Towards the end of 1967, events came to a head in Budapest. Ervin's mentor, senior colleague and friend, Julius Nyiro, Head of the Department of Neurology and Psychiatry, died suddenly. Ervin Varga was expected by many friends and colleagues to be a natural successor, influenced by the solid academic credentials he had accumulated in eight short years as a faculty member. But

Ervin's searing experiences inside Hungary and friendships with Shepherd at the Maudsley and Angst at the Burgholzli had exposed him to the very best in European psychiatry, on the far side of the border. Both Ervin and his wife were eager for a life free of totalitarian constraints with better prospects for their two boys. They had been planning and making preliminary moves for some time but Ervin was concerned that the husband of one of his patients might be a Communist spy. Events finally determined the outcome. A school friend, whose son he had treated, worked for the police and called to warn him it was 'now or never'. The Russians had invaded Czechoslovakia and the borders were about to close.

Leaving everything, except what they could carry, the family took flight for Italy and spent the next five months of 1968 in Rome, where Peter and John attended an international school. Jules Angst cared for their money in Zurich and his brother provided funds from California while Ervin cast about for a job opportunity in Britain or America.

Ervin and his wife were charged and convicted *in absentia* to two and a half years in prison. Years later, when a Democratic Government was elected, the sentence was annulled with apologies. A relative bought back some of their confiscated possessions at exorbitant and inflated prices, including several valuable pieces of art. The pictures were hanging on the walls of the family room when we visited in January 2016 to interview Ervin and meet his sons for lunch at a nearby Asian café.

Through his contacts at the Maudsley, Ervin knew there were no job openings in the U.K. but he was soon contacted by Nathan Kline in New York who, presumably, had heard of Ervin's availability from European contacts. He began an exhaustive and exhausting effort to recruit Ervin, calling from New York weekly and eventually sending an emissary to close the deal with increasing financial incentives that doubled what he might have expected in Britain. Eventually Ervin succumbed and the family moved to New York.

America: Stranger in a Strange Land

Ervin Varga is blunt; moving to America was the worst mistake of his life. By far, he would have preferred Britain whose people, culture and academic climate he preferred. In 1968, American academic psychiatry was dominated by psychoanalytic hegemony. Almost every academic department was chaired by an analyst; most of the residents were in analysis with a faculty member and as the US-UK cross-cultural study would show, nosology and taxonomy were

derelict. Truth to tell, he was somewhat sheltered from this reality. The real work of psychopharmacology first took root in the state asylums, the V.A. and with a few private practitioners, like Frank Ayd (Ayd, 2011). Nathan Kline's research was done at Rockland State Hospital in New York (named after him following his premature death) and supplemented in Nate's fashionable and lucrative New York City private practice.

What was, however, inescapable was the culture at large and the shock it inflicted on Ervin's fragile temperament. From the rigid constraints of a totalitarian system he was in a land where he was unsure of the rules and had too many choices to make, creating feelings of insecurity that aggravated his strong sense of family responsibility. It felt like, "I was driving on the freeway without knowing the rules."

His initial assignment was to work with Nate Kline on a pet project – doing a demographic study of computerized psychiatric nosology in the seven Atlantic States. Computers were not a strong interest and, in addition, Ervin had to accommodate to Kline's controversial style. As editor of the 9th volume of the OHP, I dedicated it to Nathan Kline and described him in the Introduction as follows, "Nate was intensely energetic, creative, curious, challenging, provocative and entrepreneurial ... a researcher, busy practitioner, publicist, politician and world traveler (Blackwell, 2011). Among Nate's comments when he first met Ervin was, "For someone as bright as you are, why aren't you rich?" Nate's dominating, self-aggrandizing approach was the polar opposite of Ervin's innate reserve and modesty concerning any accomplishment of his own. Nonetheless he saw and appreciated the good side of Nate's character and worked with him for two years, during which he published two papers, a follow up to an earlier paper on archaic schizophreniform symptoms in depression (Varga, 1971 a) and a psychopharmacology paper on Loxapine in destructive behavior (Varga, 1971 b).

After two years working with Nate, Ervin made a brief visit to Europe where he visited the Maudsley and renewed his acquaintance with Shepherd. There were clearly still no suitable work opportunities in Britain but he returned to America with written endorsements that might stand him in good stead in America. They provide an interesting view of the impression Ervin's career accomplishments created on two of the most critical thinkers in European psychiatry. Michael Shepherd wrote, "On the basis of my personal contacts and his professional reputation I know Dr. Varga to be a physician of outstanding ability and integrity. He is also a helpful and reliable

colleague. On all these grounds I would strongly support Dr. Varga's petition for medical licensure in the State of New York."

A second letter by Sir Aubrey Lewis, Director of the Maudsley Hospital and Institute of Psychiatry is more broadly intended but equally positive coming from a person respected for his accurate but critical assessments (Goldberg and Blackwell, 2015). "Dr. Varga's medical attainments are those of a mature and well trained psychiatrist. He is engaged in research into problems of schizophrenic speech and thought disorder, psychopharmacology and social psychiatry. His publications include a valuable monograph on the changes that occur in the clinical pattern of mental illness. His numerous other publications show that he is a research worker of proved ability.

In personality, clinical attainments and research record Dr. Varga seems to me to be fully equipped to hold a responsible post in a psychiatric research department or academic centre."

Armed with such an endorsement from a highly respected source, Ervin might well have felt equipped to look elsewhere in the America. That he chose to remain where he was may have been influenced by the dominance of psychoanalytic influence over academic domains and sources of research funding as well as to existing opportunities at Rockland State with its established reputation, research support and large patient population. There were also research workers whose styles and temperaments were more compatible to Ervin.

So began a four year period (1972-1976) as an Attending Psychiatrist at Rockland Psychiatric Center when he collaborated with other like-minded scientists and clinicians in producing 14 publications on a wide variety of topics. Most prominent among his fellow workers were George Simpson and Tom Cooper, both migrants from the British Isles.

Ervin liked and admired both these men. Simpson's origins, temperament and career accomplishments as both a clinician and psychopharmacologist are related in Volume 4 of the OHP (Ed. Levine J, 2011) as a brief biography (Blackwell in *Dramatis Personae* lxxxvi-lxxxviii) and interview with Leo Hollister (Simpson, 2011 pp 373-384). Ervin's collaboration with George involved 6 publications. A report on the use of psychotropic drugs in a State Hospital (Laska, Varga & Simpson, 1973), a study of dosing schedules in schizophrenia (Lee, Branchey, Haher, Varga & Simpson, 1974), the equivalency of 3 brands of Thorazine (Simpson, Varga et al., 1974), prognosis and diagnosis of tardive dyskinesia (Simpson & Varga, 1974 a), a new antipsychotic

clozapine (Simpson Varga, 1974 b) and psychotic exacerbation produced by neuroleptics (Simpson & Varga, 1976).

Tom Cooper's background, career and expertise in biochemical pharmacology and the metabolism of drugs are related in Volume 7 of the OHP (Ed. Blackwell B, 2011) as a brief biography (Blackwell in *Dramatis Personae*, liii-liv) and interview with Tom Ban (Cooper 2011, pp 125-137). Ervin's collaboration with Tom involved 4 publications, 3 on lithium in the prevention of alcoholism (Kline, Wren, Cooper, Varga & Canal, 1973), (Kline, Wren, Cooper, Varga & Canal, 1974 a), and (Kline, Wren, Cooper, Varga & Canal, 1974 b). The other was on bioequivalency of 3 brands of Thorazine (Simpson & Varga et al, 1974). The 4 papers with Ervin as first author in collaboration with others were on depression, osteoporosis and osteoarthritis (Varga & Kline, 1973), neuroleptic-induced Kluver-Bucy syndrome (Varga et al, 1975), a 2 year trial of Loxapine in chronic schizophrenia (Varga et al, 1976) and schizophrenia 50 years after the death of Kraepelin (Varga & Kroll, 1977).

First among Ervin's cultural concerns at this time were the economic issues of survival in an aggressively capitalist country. Accustomed to the socialist ideal of state funded education for all those able to benefit, he was confronted with the dilemma of finding and paying for College once his son's reached the appropriate age. As fate would have it, they applied for and were accepted to the two most expensive private institutions in New York, Peter at NYU and John at Columbia. Their parents had no knowledge concerning scholarships or tuition breaks and, only one year apart in age, they were heavily burdened with escalating debt.

This played a role in Ervin's decision to move from Rockland, when he was recruited by Arthur Sugerman, who had joined the Carrier Clinic in 1972 as Research Director. Arthur had worked collaboratively with Nate Kline and George Simpson on ECDEU projects from 1961 to 1972, so knew of and admired Ervin's work on the Kluver-Bucy syndrome at Rockland.

Arthur Sugerman's background, training and career are related in Volume 2 of the OHP (Ed. Fink. M), first in a brief biography (*Dramatis Personae*, xli) and then, in an interview with Tom Ban (Sugerman 2011).

Arthur began his education at the Jewish International School and then University in Ireland (Dublin) and medical school in England (London). Ervin and Arthur worked together for 9 years

at the Carrier Clinic in what was a wonderful, friendly relationship. Ervin later joined him on the faculty of the Robert Wood Johnson Medical School as a Clinical Professor (1982-1992).

In his time at the Carrier Clinic, Ervin published 10 articles, 4 of them with Arthur, all on different topics; the prevention of ECT amnesia (Menken, Sugerman & Varga, 1979), the safety of hemoperfusion in schizophrenia (Kinney, Varga & Sugerman, 1979), codeine in involutional and senile depression (Varga & Sugerman, 1982 a) and the prevalence of spontaneous oral dyskinesia in the elderly (Varga & Sugerman, 1982 b).

Private Practice

By 1985 Arthur Sugerman stepped down as Medical Director at Carrier and was replaced by an administrator. This change triggered Ervin's decision to enter private practice, initially with a recent graduate from the Harvard residency program whose knowledge helped Ervin adapt to a new way of life. After a few months, he decided to become a completely independent solo practitioner working in two separate settings; an office in Princeton, where many of his patients were faculty members and another in Somerville, a nearby industrial area. Much to his own surprise, Ervin took to private practice like a duck to water. He liked working on his own and thoroughly enjoyed clinical work where his skills in diagnosis, psychopharmacology and psychodynamics ensured good results and personal satisfaction. He is proud of the fact he never had a patient commit suicide.

After 8 years, in 1993, he decided to cut back and switched to doing locum tenens work for a couple of months each year, much of it in New York and Manhattan but occasionally, as far afield as San Francisco. Apart from the fact that he could stay in the best hotels and dine in fashionable restaurants, he could synchronize his trips with visits to family and friends. This continued until 2015, when he finally retired (so he says) to live at leisure.

Synthesis

In relating Ervin Varga's family, culture and persona to his career challenges and accomplishments one must apply caution. The biographical details in his excellent, well documented memoir, "Living and Dying in Hungary: Jewish Psychiatrist Looks Back" (XLibris, 2012) are viewed with hindsight, recorded seven decades after he reached early adult life and

perhaps colored by his career as a psychiatrist. But it remains a highly credible story, told with photographic precision in lucid prose.

The account suggests a genetic endowment from both paternal and maternal sides of a strong, upwardly mobile work ethic, coupled with an ethos of modest claims for personal accomplishments. The metaphor of "bread" is invoked on both sides; what work provides and what one does with it are vitally important. Ervin's father works diligently lifelong to "bring home the bread" while his maternal grandfather admonishes "who does not slice bread properly does not deserve to eat it." Advice to which Ervin responds, "I still to this day slice bread properly"; a modest claim to which his abilities and how he uses them attest.

In addition to these dual generational role models, one takes note of others; a strong nurturing and protective mother, the only image Ervin can conjure as his life hangs in the balance towards the end of the *Holocaust*. His mother survives and it was she who earlier arranged for a tutor, Michael, to assist with Ervin's gymnasium studies and who became a powerful influence on his intellectual, literary and moral development.

More directly influencing his choice of medicine as a career was his Uncle Hugo Richter, a distinguished academic psychiatrist and neurologist, an early role model that led 7 year old Ervin to introduce himself to others as "Doctor". Ervin's admiration came with a caveat as, in late adolescence, he compares his own talents with Hugo's. "I got everything; the ambition, the goal, the style, but was apparently not made of the same fabric." The attribute Ervin believes he lacks is the confidence to face "the relentless challenge to live up to his expectations."

Finally, important to note, was the role of Gyula Nyiro, a distinguished mentor and role model whose guidance was a crucial element in shaping Ervin's early academic career and whose untimely death triggered his life changing decision to leave Hungary for America.

To these personal influences, one must wonder about the extent to which they are modulated by Ervin's experience in growing up in an increasingly hostile, dangerous and brutal anti-Semitic environment culminating in a *Holocaust* that caused the deaths of 40 of Ervin's relatives across both blood lines and several generations. Ervin declares that 'What decisively defined me was that I belonged to a persecuted minority." At the end of the war, Ervin and his older brother decided to erase their patronymic identity of Weisz in favor of the most common "run of the mill" surname they could find in the Hungarian telephone directory, emerging as Varga. Although the Nazis were

gone, the family still sought secular anonymity among native Hungarian citizens, who had often supported the invader's barbaric ideals, and many of whom were now Communists.

Ervin's families of origin and the value placed on them formed the template for his own idyllic and successful marriage with a nurturing spouse and two successful sons, all four of them physicians in different fields of endeavor. He never failed to place family interests and values at the forefront, preserving a balance between work and home.

Ervin's innate sensitivity to stress and control issues are suggested by the onset of panic attacks in childhood and a lifelong phobia, avoiding the flesh of fowls. To what extent might this vulnerability have been influenced by exposure to brutal and life threatening events in captivity during the final months of Nazi occupation?

The term "Post Traumatic Stress Disorder (PTSD)" entered the psychiatric lexicon of the Diagnostic and Statistical Manual (DSM) during the Vietnam War, but not with any clear or useful meaning. The existence of a catalogue of symptoms creates a stereotype that diminishes the nuances and individuality of human responses to extreme harm and threat. An important book, *Shook Over Hell* (Dean, 1997), brings an historical perspective to bear by comparing a sample of Civil War Veterans with other wars, including Vietnam and both World Wars. Among the author's conclusions is the following, "*The very real problems of Veterans, which are difficult to quantify, understand and discuss in the first place, are frequently, if not routinely, manipulated and exaggerated for a variety of purposes.*" (page 215). The data challenges the veracity that all veterans can be viewed as victims and advances the novel idea, citing examples, that some may achieve heightened coping responses. Ervin vehemently rejects the idea that such savage brutality can engender benefit of any kind although, after his own trial by fire, he sheds the victimization invited by his Jewish name and embarks on an arduous career path with a commitment to excel in his chosen profession. He is protected, however, to some degree, by the family ethos, avoiding immodest claims to success, shunning the limelight and minimizing exposure to undue stress.

The burdens and stress of a totalitarian regime, shared by his wife, certainly influenced Ervin's decision to escape into what he hoped might be a more enlightened environment of the kind he briefly experienced in Britain (the Maudsley) and Switzerland (the Burgholzli). Denied those possibilities, he opted for America, a choice that exposed him to culture shock – the stark difference between a totalitarian regime and an aggressive capitalist one. In his initial exposure to

Nathan Kline he met a prototype of American exceptionalism; enormous talent and charm wed to brazen confidence and self-aggrandizement – the mirror image of his own family ethos of modest claims and muted accomplishments.

The absence of stress due to external control was replaced by the internal stress of adapting to a culture whose rules and mores were foreign to him. Initially, this tested his tender temperament but, as always, his adaptation was eventually exemplary, sufficient to meet his own expectations as a family breadwinner and talented collaborative scientist. The facts of his resume speak for themselves. For over two decades, living in an alien culture, Ervin worked on the frontiers of psychopharmacology alongside some of its leading figures with results that touched many of the growing points in our field.

In his dealing with colleagues, nurturance of family and care of patients, Ervin Varga did indeed "Slice bread properly."

Author's Note: Ervin's second visit to the Maudsley in 1966 and his friendship with Michael Shepherd overlapped with my time as a registrar and work as a Research Fellow with Shepherd. We were never introduced although my own doctoral research on MAOI and tyramine was relevant to Ervin's experience with Knoll and to my comment on the findings of the MRC replication study concerning phenelzine. It was truly a delight to meet and get to know the person whose path I had unwittingly crossed and of whose work I had been ignorant.

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KANELLOS CHARALAMPOUS: CONFRONTING THE ZEITGEIST

By

Barry Blackwell and Kanellos Charalampous

"Zeitgeist"

OED: "The defining spirit or mood in an historical period"

For more than two years it has been my privilege and pleasure to pen brief biographies for INHN of pre-eminent pioneers in neuropsychopharmacology. But an historical website also has an obligation to portray the endeavors, accomplishments and struggles of the journeymen in our field, like myself, whose more mundane lives may realistically mirror and shape the expectations of future aspiring neuroscientists. This is especially true at a time when the entire field of psychiatry is under duress, filled with questions and concerns about the future and viability of our profession.

We have documented how even the careers of distinguished neuroscientists such as Jean Delay (Blackwell 2014) and Jose Delgado (Blackwell 2013) have been shaped or disrupted when a changing Zeitgeist presents unanticipated social, political, scientific or economic barriers to their plans or progress. This essay will draw attention to how three characteristics of an individual's persona can help navigate the minefield of professional life; these are **prescience**, the ability to anticipate future trends, **fortitude**, courage in the face of adversity and **flexibility**, an ability to mobilize multiple talents in novel and creative ways.

Becoming Acquainted

Kanellos Charalampous, known to colleagues and friends as "Connie", is a Member-Emeritus of ACNP since 1965: he was interviewed by Tom Ban for the *Oral History of Neuropsychopharmacology* in 1999 (Charalampous, 1999). Recently, Connie became acquainted with the INHN website and our postings. Curious to learn more and perhaps contribute, Connie contacted me and I invited him to visit. Facing the vicissitudes of air travel at age 84, he flew from his home in Houston to Milwaukee. We may have met briefly in the past, perhaps many years ago, when we were both involved in drug testing on prison volunteers (Blackwell 1971) but we did not know each other well enough to be sure we would recognize one another. So I greeted him at Mitchell Field Airport wearing a pink cap and red shirt to facilitate recognition. In return, he had sent me a flattering photo attached to his C.V., which didn't alert me to his diminutive size (5 foot 3 inches at a stretch), a pronounced Greek accent, immaculate attire and dexterous handling of two suitcases, the larger of which I later learned contained the C-PAP machine that minimizes the late life sleep apnea that has hardly slowed him down.

We spent three days together indulging Connie's lifelong interest in art by visiting the Calatrava, Grohmann and Harley Davidson Museums, in between times, dissecting his interesting life and career experiences, which mirrored my own.

After he returned home Connie sent me over twenty essays he had written during his life and career. They display descriptive talent, humor and gentle satire, adding insight and anecdotal color to the material we had already shared. The outcome is an unusual hybrid document in which Connie's verbatim comments are inserted in italics to the larger text, resulting in an account partly autobiographical (KC) and partly conventional biography (BB).

What we discussed or viewed, what we have shared and concluded is what follows, embedded in the matrix of Connie's life.

Growing up in Greece

Kanellos D. Charalampous was born in Aigion, a city 80 miles west of Athens, in Greece in 1931 and he was 8 years old at the outbreak of the Second World War, when the Nazis occupied his homeland. This was followed, in 1944, by a Communist insurrection. His father, a family physician, served briefly in the Greek army fighting both these foes and having settled down in guerilla held territory, he was viewed with suspicion due to his right wing and religious convictions. He was an excellent role model for Connie, whom he occasionally took with him on patient rounds; his mother was an attractive, flirtatious coquette, determined and controlling but seldom nurturing. Connie was the eldest of four children for all of whom she chose predestined careers. Connie was to be a doctor, his younger sister a dentist and the two youngest boys an engineer and a lawyer. Only the putative dentist rebelled, while all three boys achieved their allotted careers.

The stark background to this benign family portrait is revealed in Connie's essay, "Diogenes".

On October 28, 1940, Benito Mussolini's Italian army attempted to occupy Greece. The Greeks mounted a strong resistance, and the Italian armies were repulsed into Albania. This was the only victory of the Allies over the Axis in 1940-41. Nevertheless, Greece fell to the onslaught of the German Armies in April 1941. Two months later, in the summer of 1941, my family moved to a mountain village, Ampelokepoi, in northern Peloponnese. We left the city we had lived in since 1936.

The main reason for the move was my father's anxiety and other symptoms of stress. After his capture by German paratroopers at the Isthmus of Corinth, following the collapse of the front, my father was detained with a fellow soldier, both in uniform. Repeated attacks by the Stukas of the Luftwaffe roused sirens, the terror of which, coupled with many explosions of ships in the harbor, led to panic attacks. His blond friend became white-haired overnight. Following his release and return home, every time my father met German soldiers in the street, his symptoms worsened.

Another reason for the move was the need to raise some food. People in the cities were starving and over 300,000 died, in part because the Allies refused to allow the Red Cross to deliver provisions for fear the Germans would commandeer them. In the winters of 1941 and 1942, a cousin, a high school junior and her classmates, for weeks, would enter the homes of those who died of starvation to retrieve the bodies.

So, in the village, we planted wheat in the few fields that belonged to our family, and in a few more no one claimed. In the summer of 1943, our wheat was already harvested and we had time to secure an open space for threshing. The previous year, not having found an open space, we were obliged to thresh and store our wheat at the entrance to the village cemetery, where I had to sleep to guard the crop. Sleeping in a cemetery was not a pleasant experience for a lad of eleven.

Also malaria was endemic in Greece in the 1940's. Every summer, my mother with the four children would take shelter in the mountain village, above the mosquito line and stagnant waters of the littoral, taking our pink quinine tablets.

Village life had its own routine. After lunch people usually went home for a siesta; summers in Greece are hot. I would spend the noon hours in the village square; on one side was the church, on the other a coffee shop, the communal fountain on the third and a ravine on the fourth. A plain tree, genus Platanus, in the center of the square, provided ample shade with a little breeze and the cacophony of cicadas. The tree must have been there for centuries; two men with outstretched arms could barely encircle the trunk.

During the noon hour, the square was empty except for me but around 2:30 an average size man with receding blond hair joined me. He would sit across the table and read the daily papers, one at a time and then place them in a basket that contained about a dozen papers from Athens. Each was only four to six pages long, since newsprint was scarce and the news meager. The

farmers showed up at the end of their workday to drink coffee, socialize, retrieve and read their newspapers before returning home for an early supper.

Every noon, before the farmers arrived, this man and I would read every newspaper in the basket. I learned he was a lawyer, a university graduate and an "intellectual". Disinclined to work and not expected to do so, he was supported by his family, while an attractive sister in-law fixed his meals and did his laundry. He was a serious man who rarely smiled and did not express much humor. But he had the illustrious name of Diogenes and was secretary of the Communist party in our area. Guerillas with fictitious names, supported by the Communist party, would come and go.

Diogenes and I did not talk politics. After reading the papers, when the heat subsided, I would go home, snack and then take my donkey to graze in the fields outside the village.

By that summer, I had completed the first two years of gymnasium and in the fall was due to attend classes in the city where we used to reside, living alone in our large empty house where an elderly aunt, almost blind, came in twice a week and cooked for me. On a cold winter morning, it took me twenty minutes to walk to school through the center of town, past the city square and on to the gymnasium a mile away. The all-male student body convened for a brief outdoor prayer, the announcements of the principal and inspection of the length of one's hair.

One morning, as I approached the square, from the corner of my eye I caught sight of a helmeted German soldier standing behind a machine gun on the balcony of the hotel facing the square. It was surrounded by acacia trees that shed their leaves in winter. Looking around I caught another sight. Five men were hanging, each from an acacia tree. I approached. The sight was ghastly. Two of the men were tall and almost touched the ground, with their heads in grotesque positions. Another had fallen in an awkward way; his eyes were open and his bluish tongue protruded.

The man in the middle, wearing a long khaki army coat, was hanging with his head facing forward and his eyes closed. He had not resisted the execution and I recognized him. It was Diogenes, my reading companion from the previous summer.

The Germans, during a sweep through the countryside, had picked him up. Apparently, they knew of his political affiliation. Although he had a rope attached to the sill of his second floor bedroom window in order to escape, he did not make the effort. When the Germans knocked at his

door he opened it. He was brought to town and, the following morning, he and four others were hanged as a reprisal for the assassination of a German officer by the guerillas.

I watched the hanging men for a minute or two and continued my walk to school. My concentration in class was poor; that night and the following nights, my sleep was interrupted by nightmares.

In later essays (*The Pre-Med Experience and A Tumultuous Adolescence*) Connie tells of his late adolescent years and transition from Greece to America.

The gymnasium required a lot of study and was difficult. From 400 students that entered only 79 of us graduated. Ancient Greek and Byzantine history were my great pleasures. Every week we had to write a composition; I memorized whole paragraphs from different books and would insert them in the text. This made the results spectacular and often the professor would ask me to read my composition to the class. However, he never failed to complain about my terrible handwriting and the hard work I was putting him through to read and make corrections. Homework was always demanding and often I would get up at 4:30 am to study.

The teachers in the gymnasium, although Greek, taught in the French and German manner; didactic, remote, indifferent and punitive, contributing to an altogether toxic environment that incubated an unspoken determination to escape my native country for America at the earliest opportunity.

In the summer of 1943, as the Nazis were withdrawing, many people who had not joined the Communist Party were arrested. This included women and their children. They would be taken further up the mountain to be tortured and slaughtered. One summer evening after I had left Aigion to join the family, all the dogs in the village started barking. Alarmed, my mother went to find Triandaphyllos, a family friend, and asked him to find seven mules. During the night, we packed and at 8 o'clock mother went to the village square. The commandant of the guerillas was having his morning coffee. Calmly, she explained that usually in the late summer, we departed from the village and returned to Aigion for the kids to attend school. The commandant graciously gave a written note to my mother, who returned to the house, gathered us up, and we left. Forty minutes after our departure, the provincial leader of the Communist Party appeared in the village square and informed the commandant that the Charalampous family was on the list of reactionaries,

suspected anticommunists, who would later be arrested and executed. A squad of guerillas was dispatched to bring us back. Fortunately, we had reached German occupied territory. We barely escaped.

After the departure of the Nazi forces, the Civil War continued. It came close to putting Greece behind the Iron Curtain. From 1947 to 1949, Aigion was attacked regularly by bands of communist guerillas every third night. Imagine the effects, not only from fear but lack of sleep. It was a period when every good friend I had perished. Also, the house I was born in and loved for its size and elegance was burnt to the ground. Another conflict related to the knowledge that my future depended on higher education, and the realization that my family lacked the resources to support me. The probability of following in my father's footsteps was always there but I had doubts about my ability to get into medical school and having the money.

I finished gymnasium with good grades and in the summer of 1949 I left for Athens to take entrance exams to the University. Walking down a corridor, I headed for the room where the candidates for law school were taking their exam but instead entered the room where the candidates for theology were. I passed that exam easily. When I announced to my parents I would be attending theology school my father was pleased. But my mother asked, "What for?" Well, I said flippantly, "I'll become a bishop." In the Greek Orthodox Church priests can marry but bishops are celibate. Mother asked, "What do you propose to do for sex?" I had no answer.

In another essay (*Triantaphyllos*; *The Last Time I Saw Rebecca*) Connie tells the story of a family friend who helped out with family chores and assisted their escape from the Communists but whose ambition was also to become a priest.

Triantaphyllos was a tall man, with wavy brown hair, a charming smile and a pleasant voice. He was a carpenter. Often I saw him on the roof of the new church under construction. Triantaphyllos had only a grammar school education but he read a lot, particularly ecclesiastical books. He wanted to become the priest of our village. Despite the support of my parents and other families, he was not selected but he did not give up. When a position opened in a nearby village he applied. The local people had their own candidate and the bishop, although sympathetic was reluctant to make an early decision.

More than a year later, one cool night after finishing my homework, I went to bed around 9pm and fell fast asleep only to be awakened a few minutes later by Triantaphyllos, who said, "Connie, get up. We will go to my last movie show. The bishop just told me he is going to ordain me." Priests did not go to the movies in those days. We headed for the movie theater four blocks away and on the screen there were Lawrence Olivier and Joan Fontaine in Du Maurier's drama, Rebecca.

When I got up the next morning to go to school, Triantaphyllos was already gone. I never saw him again. A German soldier had been killed by the guerillas and true to their edict they had swept the countryside to arrest 30 civilians including Triantaphyllos. Those opposed to his selection as village priest had falsely betrayed him to the Germans as a communist.

The execution platoon of helmeted troops appeared early next morning with a heavy machine gun on the back of an army truck, and stopped outside a small warehouse. The prisoners were kept there and knew the moment had come. Triantaphyllos moved forward, faced the officer in charge and begged for a few minutes to prepare communion for himself and others who wished to partake. The request was granted. A little time later, the prisoners were taken outside, placed in a row against the wall and machine-gunned. The German officer was reported to have said, "Well that fellow surely was not a communist."

Connie continues his story (Pre-Med Experiences). Because the theology courses at the University of Athens were inadequate, I started attending the Panteion University of Political Sciences as well. In Greece, it was not customary for a student to work while going to school but I thought to try. The National Bank of Greece offered exams so I applied. I made 100 on the test but the Director of Personnel told me I could not get a job because of my poor handwriting. I understood clearly that in Greece you could not get a job without connections.

At this time, my Uncle Haralabos was visiting Athens on one of his regular business trips. He was a prominent businessman with important connections. On his visits to Athens, Uncle Haralabos would invite me out to lunch on a street where the restaurants specialized in succulent, charcoal-roasted lambs. During one such visit, he noticed that I looked unhappy. I related my experience at the bank and he said he knew the President of the Bank of Commerce and would recommend me for a job. They sent me for a pre-employment physical examination conducted by Professor Patronicolas, a tuberculosis specialist and brother in law of Aristotle Onassis. He took a chest x-ray and there was a Ghon tubercule, early pulmonary tuberculosis. At the time, I was

practically starving, eating only watermelons and honey, a stupid and insufficient diet. The Professor told me he could let me work at the bank but in his best judgment he recommended a course of two medications, streptomycin and PAS with bed-rest for a few months. I followed his recommendation and was one of the first recipients of streptomycin in Greece. I continued attending classes at the two universities but never took the job at the bank.

My Uncle George also visited Greece from his home in Detroit for the first time since leaving at age 16. He was one of seven siblings and his father sent him to America with instructions to get an education, find work and, when successful, send money back to Greece. On Ellis Island, George changed his name to Harris and then worked for several years with Irish immigrants laying down railroad tracks, before going into the restaurant business in Detroit, close to the Ford Company executive offices, where many of the executives dined.

During George's visit, Uncle Haralabos spoke to him as businessman to businessman suggesting he help me find a university to enroll at in America.

A few weeks later, a letter came from Uncle George. On his way by train to retire in Arizona, at his physician's advice, he stopped in Fort Worth and remembered what he had been asked to do. A lawyer he consulted told him that Texas Christian University, a fine school, was situated there and he registered me as a student. I obtained a visa after many months of delay, on Christmas 1950, packed my bags, bid farewell to my family and set out for America.

On the Cusp

I extracted the first paragraph of Connie's account of his *Pre-Medical Experience* and placed it here, as he is about to embark for America to fulfill his hopes and expectations. Understandably he is filled with anxiety from the past, projected onto his future, unaware of the assets his experience has accumulated. It reads as follows:

It is often said that many people would dearly love to regain some of their younger years, together with acquired maturity. I believe that very few would like such a time to include years from adolescence. My personal experience supports this notion. Not only adolescent turmoil, but the experience of the Communist Civil War that extended four more years beyond 1945 had created for me an unhappy and stressful period.

When one views the panorama of Connie's life after birth in Greece, one understands the desire to repress what he experienced in adolescence; the turmoil and torment of a nation torn by Axis and Communist barbarity; near starvation, dodging malaria and tuberculosis and negotiating the obstacles to obtain a university education.

But that hardscrabble crucible shaped a persona that created the traits, which would ensure success in his adopted country and chosen profession. This was, and always will be, the core of the immigrant experience, the sustaining lifeblood of a nation built by people who escape poverty and persecution for safe harbor.

Early Life in America

Connie already had ideas of medical school but with the mistaken expectation he could enter direct from high school. Fortunately, he was already enrolled in Texas Christian University (TCU) with a double major in Biology and Chemistry. Within a year, he determined medicine was his best choice and severed obligations to his uncle, became independent, but financially vulnerable. So he worked as a janitor to earn his tuition and then became a laboratory assistant and Instructor in marine biology at TCU. While doing so he obtained a fellowship to the Virginia Marine Institute, where he studied oyster mortality supported by, and in defense of, the oil company accused of drilling that was alleged to destroy the crustaceans' habitat. A taste for his research subjects developed and we watched him consume Oysters Rockefeller with gusto at the Wisconsin Club.

In his junior year at TCU, Connie decided on medical school but when he graduated, in 1954 without citizenship, he was unable to enroll in a State Medical School. Although lacking funds from Greece, he was accepted by Baylor College of Medicine and, once again, needed work to support tuition. He did this exhibiting a vigorous work ethic as told in *In Pursuit of an Academic Career*.

Besides my work at the VA, I had another job at Hermann Hospital Xeroxing old hospital records. Also, I worked off and on in the Jones Medical Library classifying old books. At other times, I assisted the nursing staff at the Methodist Hospital making beds and other menial jobs. At Jefferson Davis Hospital, I prepped several hundred prospective mothers before delivery. While a junior at the medical school, during lunch at the VA, I was asked by a group of senior medical students to join them and do physical examinations on new admissions to the psychiatric wards.

When I told them I didn't have enough experience, they assured me they intended to teach me. Thus I was doing physicals at the VA for room and board until graduation from medical school.

When I did physical exams on the psychiatric ward, I had to go through many locked doors. In addition, two black attendants walked in front and two behind; it looked like a small safari! A few years later, I was interviewing a patient on the same ward. Guided by some delusion or hallucination, he stood up, grabbed his chair and broke it into pieces, striking my desk. A nurse heard the commotion, locked me in the office with the patient and went for help. Minutes later, after she had collected six staff people, they unlocked the office door. By that time, the patient and I were standing there like nothing had happened. Obviously the arrival of psychotropic drugs made it routine for a doctor and patient to be left alone as with any other patient.

Connie does not bother to mention his capacity to remain calm in the face of danger, a trait acquired long before, with an obvious tranquilizing effect on an agitated patient.

Connie also obtained a number of paid stipends from the medical school, including assisting in a study of oxygen metabolism in polio patients on respirators. At the VA, he worked as a Lab Tech and phlebotomist before moving on to do statistical analysis for two psychiatrists on an early study of chlorpromazine in patients with mental illness. He notes, that was probably the only study worldwide that found chlorpromazine to be ineffective in schizophrenia. Another lesson; if you don't believe something you may affect the outcome of a study. In another study during his junior and senior year, he assisted the chairman of anesthesiology in studies on the control of postoperative surgical pain. These research projects may have influenced his choice of specialty but Connie's main preoccupation was to mirror the faculty role models who inspired him with the idea that a complete physician should be a clinician, teacher and researcher. Among them were cardiac surgeon Michael DeBakey, for whom he scrubbed and Hebel Hoff, Professor of Physiology, who invented the physiograph to replace smoked drums – something we still used and I frequently smudged doing research in rats on tyramine and MAOI at the Maudsley Hospital in 1963. Also an influence was pioneer psychiatrist John Kinross-Wright, who was Director of one of the first six ECDEU Units funded by NIMH for psychopharmacology research.

By the time Connie began his rotating internship at Houston City Hospital, he fit in easily with his fellow interns outstripping them with skills he acquired as a lab tech and phlebotomist, inserting catheters with ease in the emergency room. For a short while, he contemplated surgery or internal

medicine but was deterred by lifestyles he deemed too frantic. Considering psychiatry, he compared Europe with America and decided the latter was the new frontier in brain science. Despite fulfilling his mother's expectation, he had become a physician but she disapproved of his choice of both specialty and country. It did not deter him.

Clearly viewed as a top candidate, Connie began residency (1959-1962) at Baylor, then affiliated with the Texas Psychiatric Institute (for research and training) the VA and Jewish Institute (for clinical and research experience) and the Jefferson Davis Hospital.

My class had six residents and my first rotation was the VA Hospital. Two were women, two were doctors who had been in medical practice and were invited to come to psychiatry with stipends from NIMH three times the amount the rest of us received, and a foreign colleague from Bulgaria who was assigned to the Jefferson Davis Hospital, where he received free room and board while I had to pay for mine at the VA. I visited the vice-chairman of the department, described this disparity and the following week I was transferred to the Jefferson Davis Hospital, where I began work as a resident, also with free room and board.

At that hospital, I had rotations on the inpatient service, outpatient clinic, emergency room and consultation-liaison service. Starting at the inpatient service, I walked into the treatment room, where the chief resident was rendering trans-orbital lobotomies with what appeared to be an ice pick. I walked out and never saw the procedure performed again. On the inpatient service of 40 beds as many as 20 patients were receiving electroshock every morning.

The faculty director of the outpatient clinic left his position shortly after I arrived. Later I learned he could not accept research activities for patients with mental illness. His humanitarian concerns had to be respected but if there was a branch of medicine that needed research it was psychiatry. What stands out in my memory from the first year of residency is how little the faculty had to teach and how wise was the saying "the best teacher is the patient."

Unlike his contemporaries who concentrated their efforts on psychoanalysis, Connie chose to do a research elective under John Kinross-Wright who, while supportive, was aloof. Clearly, Connie had a mind of his own and was assertive in meeting his needs – an attitude that reminds one of those early immigrants whose flag and motto was "don't tread on me"; an effective ideology for a fellow immigrant of short stature with a pronounced accent.

Fluphenazine Enanthate

By his third year of residency, Connie had established a reputation for hard work and accomplishment; he received the unusual compliment of being appointed Faculty Instructor, devoted to full time research. So, in 1961, he began pioneer work on fluphenazine (Prolixin) enanthate, first working in dogs and monkeys and then progressing to Phase 1 and early Phase II studies in prisoner volunteers at the Baylor facilities (Kinross-Wright & Charalampous, 1965). The manufacturer, Squibb, was tepid about the potential for this first long acting antipsychotic given by injection every two weeks. Deinstitutionalization had not begun in earnest and compliance did not emerge as a named problem until the mid-1970's (Blackwell 1997). But Connie knew enough of the benefits from oral medication to foresee a need for a maintenance drug in patients discharged from closely supervised inpatient care to a community setting, a lengthy distance away with questionable continuity of care and the risk of non-compliance.

Connie began his postgraduate career in 1963 as an Assistant Professor at Baylor. His tasks were threefold. First, he became the Assistant Chief of Psychopharmacology under Kinross-Wright and during the next three years, until 1966, they worked on over 100 experimental compounds in early Phase II studies. This was facilitated by his directing efforts to create a 380 bed psychiatric facility at the Wynne Unit of the Texas Department of Corrections. The body of drug research during this time produced 19 publications, on 15 of which he was first author.

Much of the drug research Connie accomplished was in prison volunteers in a correctional setting. He relates a colorful account of this in *My Life in Prison*.

In the 1950's, the Texas Department of Corrections (TDC) was a national disgrace. The barbarity of poorly paid guards was reflected in the brutal incarceration of 11,500 inmates. In the daytime they did agricultural work of a primitive kind, including picking cotton for hours under the hot Texas sun, sometimes lacerating their Achilles tendon to avoid working in the fields.

TDC acquired a new director, the remarkable pioneer O.B. Ellis, who transformed work to indoor acquisition of future work and educational skills. With a significant number of inmates with mental illness he contracted with Baylor Department of Psychiatry to develop a special program to meet their needs. As a second year resident, I was to spend one day a week developing the psychiatric unit, where we also hoped to begin drug research. Inside the prison for the first time,

I felt self-conscious but the Superintendent and major in charge of security greeted me warmly, almost with a sense of relief.

The Wynne unit contained 400 individual cells on three floors guarded by uniformed officers and mental health trustees – prisoners who wore white uniforms, different from the striped ones of other inmates. Prison lore had it that unlike the general population many were sociopaths and the best were those who had committed murder. Polite and cordial, they introduced themselves and showed me the examination room, EEG and EKG labs then another room with locked cabinets for the pharmacy drugs. Preoccupied and under stress, absorbing all the security and other protocols, I drifted backwards towards the iron bars of the cells, when several of the trustees screamed at me to move away. I was standing in front of a cell containing "the beast", a large inmate, incarcerated for life and probably demented who, two weeks before, had killed two fellow inmates standing in front of his cell when he passed his huge arms through the bars, grabbed each inmate by the neck and crushed their skulls, killing both.

In a house nearby the closed unit, I met the full time psychiatrist in residence, an ex-general practitioner, who received a large NIMH stipend to obtain residency training in psychiatry. We had a pleasant visit, enjoying a beer until, at midnight, he explained he did rounds on the inmates at 2 am; during the day the temperature rose making the place unbearable. Obviously, I did not accompany him and going to the prison only once a week I did not meet him again until the trustees told me a few weeks later that he had stopped making rounds. I learned this talented man, also a great musician and vocalist, was a manic-depressive who injected himself with large doses of thorazine to achieve a euthymic state in the days before lithium. A year later, this unfortunate colleague committed suicide.

One afternoon, as I was about to leave the Wynne Unit, the trustees ran to the freezers, got out 18 gallons of frozen urine, part of a research project, and loaded them into the trunk of my car. Driving back to Baylor it began to rain. I was thinking how beautiful it might be to sit on the porch of a farm house, looking across the meadow at the tall pine trees of the Sam Houston National Forrest, when suddenly the car drifted across a new concrete surface onto an asphalt pavement and lost traction; it slammed into a wood post on the highway divider, the trunk burst open and the jugs of urine spilled onto the highway. I opened my umbrella, walked up and down

to collect them, fearful of an oncoming car. Fortunately none came, the car was drivable and I returned safely to Houston.

As my prison experience was coming to an end, the trustees asked me to facilitate the release of one of them, our EEG technician. I had a good impression of him, so I arranged with a rancher friend to employ him. A parole office visited me to approve. He was polite and deferential but his half Cherokee eyes looked at me with irony. The trustee got early release, left for Oklahoma, moved into his new apartment and went to work, but for one day only. He pled illness and left. Two weeks later the rest of the story appeared in the Daily Oklahoman. Our rehabilitated trustee, carrying a pistol without a trigger robbed seven Safeway stores before being arrested. The parole officer paid me a second visit, looking at me with unmistakable sympathy. I asked him how he had known. Cryptically he told me that anyone who left the red soil of eastern Oklahoma and saw the city lights was not about to return to a ranch. So much for this psychiatrist and his ability to predict future outcome.

If the gift of prescience, acquired in his unpredictable youth, had deserted Connie, he must have been comforted by knowing that his psychiatric brethren agreed they were unable to predict suicide or violence with any validity.

Secondly, Connie advocated successfully for the development of a psychopharmacology outpatient clinic in Houston, of which he became Director, linking Houston with the State Hospital in Austin, 164 miles away. He saw the benefit of the Kennedy sponsored Mental Health Act that funded Community Mental Health Clinics. Unlike many others who turned them into psychosocial agencies for the worried well, staffed by social workers, Connie cared for the de-institutionalized patients with serious mental illness, focusing on continuity of care, leaving their current medications intact and avoiding polypharmacy, while using fluphenazine enanthate as a tool when necessary.

Also aware of the needs of a neurotic population, he set up a second clinic to deal with anxious and depressed patients, staffed not by social workers but by nurses.

This creative and innovative planning was modeled on programs in the U.K. Connie had heard about for the rehabilitation of military personnel discharged with post-traumatic and other psychiatric disorders at the end of World War II.

The "Pink Spot"

Thirdly, Connie completed nuclear medicine training in the Endocrine Department and was among the first to undertake isotope studies on the metabolism of the parent compounds and metabolites of anti-psychotic and anti-depressant drugs. But, most importantly, Connie also became involved in studying the metabolism of mescaline, a compound with hallucinogenic effects. This would center on the presence, potential activity and alleged significance of the metabolite DMPEA, the so-called "pink spot" in the urine of some schizophrenic patients but not in normal subjects. This involved Connie in one of the major early controversies in psychopharmacology during the 1950's and 1960's.

The saga of the "pink spot" began in 1952 at the threshold of psychopharmacology with the discovery of chlorpromazine, when two British residents (registrars) speculated that a metabolite of mescaline might play a role in the etiology of schizophrenia (Osmond & Smythies, 1952). This part of the story is told through the eyes of John Smythies on the INHN website (Blackwell 2015, a). Humphrey Osmond would play the major role going forward, when lack of support in England led him to join Abraham Hoffer in Canada (Hoffer, 1998) for ongoing studies of what they termed the "adrenochrome hypothesis of schizophrenia", which also morphed into controversy over "megavitamin" therapy that involved Nobel Laureate Linus Pauling and "psychedelic therapy" advocated by Osmond. From 1954 to 1960, Hoffer and Osmond received a substantial six year grant from the Rockefeller Foundation to pursue these lines of research, which ended abruptly in 1960, when increasing street use of hallucinogenic drugs cast a shadow over psychedelic and megavitamin therapy. Nevertheless, research on the etiologic theory of schizophrenia continued, fueled by an article in *Nature* identifying DMPEA in the urine of schizophrenics (Friedhoff & Van Winkle, 1962). This is the point at which Connie became involved in several years of research funded by the US Public Health Service, studying C14-labeled DMPEA in prison volunteers (Charalampous, 1966). The results showed oral doses of DMPEA, twice those of mescaline that produced hallucinations, were completely inert even when the subjects were pre-treated with the MAOI pargyline in an attempt to enhance activity. These results were presented at the Fourth World Congress of Psychiatry at Madrid, in May1966, published in the Proceedings (Charalampous, 1966) and further elaborated on later (Charalampous, Walker, Kinross-Wright, 1966; Charalampous, Tansey, 1967; Charalampous, 1971).

It is incontrovertible that by the end of 1966 Connie's research clearly established that DMPEA was an inert, non-toxic substance with no conceivable etiologic role in schizophrenia. The research had been published in a leading scientific journal, presented at a World Congress and published in the Proceedings.

Three events would occur in the following year, 1967, which might seem to reflect world scientific opinion but which made no mention of Connie's research findings. The first key event was a symposium hosted by the Department of Psychological Medicine and its Chair, John Smythies, in Edinburgh, Scotland. The symposium was chaired by Seymour Kety and the proceedings were published later that year as a book, *Amines and Schizophrenia*, 1967, co-edited by Harold Himwich, Seymour Kety and John Smythies.

Secondly, a key paper presented at the symposium from the Nuffield Unit of Genetics at the University of Liverpool provided new evidence seemingly supporting the "pink spot" (Bourdillon & Ridges, 1967). It included a study in 296 subjects where the investigators were blind to diagnosis and drug therapy. In 238 subjects assessment was possible; 20 out of 30 non-paranoid schizophrenic patients had the "pink spot" compared to only 7 out of 102 with paranoid schizophrenia and only 1 out of 68 non-schizophrenic patients. The authors concluded the "pink spot" was "a product of a metabolic abnormality connected with the disease process", not due to dietary causes or the duration of hospitalization.

The third occurrence was an anonymous editorial in the British Medical Journal (*Lessons of the Pink Spot*), published in February 1967 (Anonymous, 1967). In withering prose, it exposed the multiple clinical and biochemical flaws in contemporary data on the topic, discredited the results and concluded, "Perhaps it is time to stop investigating schizophrenics *en masse*" and concentrate on individual patients.

It remains to be said that neither the leading scientists who convened the Symposium, those who presented data at it or the author of the editorial cited mentioned Charalamapous' elegant and irrefutable demonstration that DMPEA was an inert substance and its presence in urine of schizophrenics, even if true, was meaningless. One may then ask how this could be possible. Did the protagonists fail to read the literature or attend the World Conference in the months preceding the Symposium? Was it too late to cancel the Symposium and save face? Or was it simpler to look the other way, dismiss the work of a relatively unknown junior scientist and, by doing so, preserve

their reputations and research funding? We may never know but such behavior by senior scientists is not unknown (See Blackwell, 2014, b).

The "pink spot" saga had a 15-year life span. The Greeks have a word that often attaches itself to the birth of an idea but never to its demise, *Kudos*, (OED, praise or honor). Connie learned this lesson the hard way and perhaps it played a role in shaping his career, when his interests moved from bench research to clinical issues, where he demonstrated the same prescience, fortitude and flexibility in facing whatever the Zeitgeist had to offer.

As if professional life was not enough, Connie, with considerable prescience, set up the Dexion Foundation, a private means of sequestering funds for educational, cultural and philanthropic purposes. In addition, in 1965, he obtained a pilot's license, symptomatic of his intrepid temperament. The idea incubated and was implemented much earlier in 1959, at age 28, the year he began residency, stimulated by an article in *Newsweek* about the Greek oligarchs (Onassis, Niarchos and Livanos). Niarchos had taken up flying and the story told of his emergency landing in the East River.

I was invited to my first lesson in September 1959, soloed after 18 hours and when I landed, the instructor was holding a bouquet of wild flowers collected from around the field, adding if I had not come down safely, he would have sent them to the funeral home. In July 1964, I had my first cross country trip, to Alice in Jim Wells County, Texas. A few miles out, I called the tower and was given instructions to land, but where? On Orange Grove Naval Air Landing Field, while Navy jets were flying in and out. A Navy pickup appeared with a large sign on the back FOLLOW ME. A junior officer smiled and said I was not the only one. After I signed close to 28 forms, the control tower told me to take off; a few minutes later I faced the real Alice airport and landed.

Over 40 years, Connie flew trips for business, pleasure and family affairs, twice with near fatal consequences. Once when he ran into a rainstorm and was forced to land on a farm road, where a low hanging cable smashed into the windshield and on another occasion when his pilot's seat pulled back suddenly and he could not reach the pedals for rudder control. Using the ailerons and horizontal control, he managed to land safely, left of the runway in tall wet grass from which a tractor pulled him out. In 1999, at age 68, he took his last flight.

I realized my knees could not support my legs for a jump in an emergency. Flying an airplane is not like riding a bicycle. On three different occasions, I lost my skill and had to learn flying 'de novo'. To maintain one's skills, a pilot should fly for a minimum of 12 hours a month, a large time commitment. A person should still be young or have retired at a young age. This was possible in Greece but we know what that has led to. Productivity and the pursuit of pleasure do not seem readily available to an American physician.

Confronting the Zeitgeist

In 1965, change occurred at Baylor. Shervert Frazer became Chair of the Department and Mental Health Commissioner of the State with a mission to make it a center of psychoanalytic excellence. Connie saw the writing on the wall for psychopharmacology and decided to accept the position of Associate Professor and member of the Clinical Pharmacology Division in the Department of Medicine at the University of Oklahoma as well as Consultant in pharmacology to the V.A. Hospital. Connie was particularly attracted to the chance to work with Jolyon West, a creative, charismatic and flamboyant role model. However, Joly was an "editorial", not a handson researcher, who made a name for himself by killing an elephant in the Zoo with an overdose of LSD, while trying to induce a toxic psychosis. Soon after Connie arrived, Joly left for UCLA where he had friends among the Hollywood stars.

Located in a Department of Medicine with little commitment to psychopharmacology, Connie quickly realized he had made an "out of the frying pan into the fire" move. Looking for a new direction in research, he decided to pursue a timely interest in the use of hashish and marijuana.

Studies in Marijuana

Taking a self-imposed sabbatical, Connie travelled to London where, at the Library of the British Museum, he studied the six-volume report of the Royal Indian Hemp Commission, before flying to Geneva to consult with Dr. Norman Cameron, Director of the Drug abuse section of the World Health Organization. Following his direction, Connie travelled home to Greece to review Dr. M.G. Sringaris' treatise on hashish before discussing the author's findings and extensive experience. Next, he visited a psychiatric hospital in Istanbul, Turkey, where Turan Itil served as a translator, while he interviewed 13 chronic users of hashish. Finally, he travelled to Morocco to consult with other colleagues about their experience with users in that country.

On returning to the United States and after continuing to review all the available literature on the topic, he put the large body of information he had gathered to use in a series of lectures to the students and faculty at several universities, culminating in an invitation to develop a symposium on the topic to the annual meeting of the American Psychiatric Association in Boston, in the summer of 1968. Once again, he had run head on into the Zeitgeist, just at a time when THC had become viewed as the "gateway to heroin' and research on potentially addictive or hallucinogenic drugs was no longer funded or approved of. The symposium was disrupted by student activists from Boston and Harvard so had to be abandoned. Similar midlife turmoil affected the careers of Jean Delay and Heinz Lehmann, as reported in INHN biographies (Blackwell on Delay, 2014, a; Blackwell on Lehmann, 2015). His experiences of the drug culture during this rapidly changing era are described in a paper in the American Journal of Public Health (Charalampous, 1971, a).

Evolving Interests in Dallas

Looking for a calmer and more conducive environment, Connie joined the faculty at Southwestern Texas Medical School in Dallas, in 1968, as an Associate Professor, where he developed three areas of research and clinical interest, two of which were adaptations to a changing environment. His primary purpose was to help set up a Psychiatric Research Institute and he became the Chief of a Psychopharmacology laboratory as well as setting up an outpatient clinic for the treatment of anxiety and depressive disorders. This produced several papers on chlordiazepoxide (Charalampous, 1972 a), Amoxapine (Charalampous, 1972 b) and chlorazepate (Charalampous, Tooley, Yates, 1973). During this period, he was also Clinical Director of an innovative 70 bed adolescent unit at Woodlawn Hospital, an affiliate of Parkland Hospital, which included a club for the patients in the basement. This may also have triggered an evolving interest in alcohol treatment that would later expand (Dun, Smith, Lemere & Charalampous, 1971). Finally, he consulted to the Maximum Security Unit for the criminally insane at Rusk State Hospital in East Texas, introducing upgraded medical care and rehabilitation treatments (Clark, Huber & Charalampous, 1971).

Social and Community Psychiatry

Probably the most prescient of Connie's evolving interests in Dallas was in the rapidly developing field of community psychiatry, fed by the impact of de-institutionalization and the Kennedy administration's initiative providing funding for community mental health centers.

(House Bill 88-164). Between 1968 and 1971, Connie attended three two-week seminars twice yearly taught by Gerald Caplan of Harvard Medical School and completed a fellowship in Community Psychiatry. This laid the groundwork for a life-long commitment to continuous, coordinated and collaborative outpatient care, including family involvement. The principals taught by Caplan built on seminars Connie had attended years earlier in Athens at the Institute of Ekestics, where the City architect and planner, Constantine Doxiades, taught a systems approach and sensitized him to social issues, an input that would broaden his skills in psychopharmacology. He was also influenced by the models of care, developed in 1944 by Querido in Amsterdam and later by Sidney Merlis in America.

Back to Baylor

Connie's accomplishments in Dallas led to an invitation to return, in 1972, to Baylor in Houston, where his heart still was, and two years later, he was promoted to Full Professor in the Department of Psychiatry. Once again, he occupied several roles including initiating studies on cyclic nucleotides supported by NIMH. Also important was administering a large grant from the U.S. Department of Transportation to study vehicular deaths and ways to separate driving from drinking. This involved running an inpatient program for alcohol rehabilitation at Methodist Hospital, including multimodal and multidisciplinary treatments involving Alcoholics Anonymous and Family Education. These activities produced a significant body of research on addictions and their treatment both at the basic science and clinical level (Charalampous & Askew, 1974; Zung & Charalampous, 1975; Charalampous, 1977; Charalampous, 1976; Charalampous, 1997; Askew & Charalampous, 1977, a; Askew & Charalampous, 1977, b; Askew & Charalampous & Askew, 1977, a; Charalampous & Askew, 1977, a; Charalampous & Askew, 1977, b; Skinner& Charalampous, 1978). Connie also produced 7 book chapters on aspects of alcohol treatment between 1976 and 1979 (Publications on record at INHN.org).

As was his custom, Connie ran an anxiety and depression outpatient clinic and was also Chief of Psychopharmacology Research at the V.A., clinical tasks that produced several publications on the treatment of anxiety, psychoses and dementia (Charalampous, Freemesser & Smalling, 1974; Charalampous, Sermas, Newsom & Keepers, 1977; Charalampous, Thornby, Ford, & Freemesser, 1977; Charalampous & Keepers 1978 a; Charalampous & Keepers, 1978 b). He also contributed

a book chapter on the pharmacotherapy of schizophrenia (Charalampous, 1978) and several educational cassettes and motion pictures on psychopharmacology topics funded by Sandoz Pharmaceutical Company.

Based on his now extensive knowledge of the field, Connie developed a curriculum for the training and certification of chemical dependency counselors that was adopted widely throughout the United States.

An Academic Exodus

In 1978, Connie made the final move of his fulltime academic career. He accepted the position as Chairman of Psychiatry at Texas Tech University School of Medicine in Lubbock. He describes this two-year experience as a "watershed moment", a period in which he was overwhelmed with administrative, clinical and teaching responsibilities with no time or money for research in programs distributed over five locations. Amarillo (child psychiatry), Des Plains (a mental health center), Big Springs (a VA and State hospital), El Paso (a County Hospital inpatient program) and Odessa (a Family Practice outpatient program).

During this period, Connie was also active on the Statutory Medical Advisory Committee, appointed by the Texas Mental Health and Retardation Commissioner, he served for 8 years (1974-1982) and was elected Chair by his fellow members. He was also asked to recruit a panel of nationally recognized experts to evaluate and report on the future of the Texas Research Institute of Mental Science (TRIMS). Included in the panel members were authorities like Don Klein and Robert Rose.

This experience must have alerted him to a developing climate that, beginning in the early 1980's, marked the threshold of a long winter of discontent for psychiatry, in general, and psychopharmacology, in particular. This inclement Zeitgeist included many co-occurring ingredients. Among them the parsimony of newly arrived managed care, the cupidity of insurance companies in authorizing that care and the barriers to access care both contributed to. Support for research dwindled as the NIMH closed the federally funded NCEDU programs, switching research priorities from psychopharmacology to neuroscience. Meanwhile, the pharmaceutical industry took control and corrupted the testing of new compounds, initiating three decades of sterile innovation, while the number of low income generating generic drugs increased. The largesse that

created academic conflicts of interest and propped up professional organizations dwindled. Lack of insurance parity between mental and medical illnesses would persist into the 21st century, accentuated by the inadequacy of Medicaid and Medicare's health care and disability benefits and the reluctance of psychiatrists to treat such patients. This contributed to the degradation of County funded outpatient mental health systems of care while the proven model of multidisciplinary Assertive Community Care was diluted to less expensive and fragmented forms of case management. Private sector psychiatric care began to coalesce into large health care corporations, allegedly "not-for-profit" but driven by a bottom line ideology that adopted the catch phrase, "No margin, no mission" (Blackwell, 1994). These regional monopolies began to dictate the patterns of medical care and residency training by turning private independent practitioners into salaried staff and introducing productivity requirements that focused on quantity of care at the expense of quality.

But perhaps the most personal concern Connie felt, at age 49, was time pressing with no adequate program for faculty retirement, including his. After two years, he made a decision to quit academia and enter full time private practice in 1980.

A Model of Private Practice in the Community

Needless to say, Connie approached this aspect of his career with careful planning and considerable energy, developing a model of care in the community surrounding Houston based on principles he had already assimilated. It was designed to meet the radical changes he foresaw occurring in health care in the United States, offering cost-effective multimodal and multidisciplinary programs and services.

He opened five offices in Harris County, partly funded from the Dexion Program of Care – an extension of the family Foundation he incorporated as a 501 © 3 in 1963. These offices were staffed by social work counselors he trained and supervised in the principles of continuity and collaborative care. He obtained staff affiliations with 23 hospitals and inpatient programs and at one time or another, served as Director of inpatient programs at three of them.

Connie also obtained a faculty appointment as Adjunct Professor at the School of Public Health at the University of Texas Health Center in Houston (1980-1984) and later (1988 on), was appointed Clinical Professor of Psychiatry and Behavioral Sciences at the University of Texas

Medical School in Houston. Working with the Texas Psychiatric Society, his Foundation donated funds to support the training of psychiatrists as administrators for this kind of program but these were subverted and the plan never came to fruition as lay administrators with business backgrounds focused on bottom lines took control.

All this helped secure Connie's future as an independent practitioner in a field of rapidly shifting sands, including managed health care, profit-driven health care corporations and deteriorating publically funded community mental health systems. It also attracted public approval. In 1984, he was selected to participate in *Leadership Houston*, a yearlong study of community organizations under the auspices of the Chamber of Commerce, to prepare citizens to serve on boards and executive committees of organizations that promoted quality of life. In 1996, Connie received the *Psychiatric Excellence Award* from the Texas Society of Psychiatric Physicians. Throughout this later time in his career, Connie continued to teach psychiatric and family medicine residents, substance abuse counselors and public health students. He also organized community wide scientific symposia on geropsychiatry and psychopharmacology.

During his long career, Connie was active in 35 professional Associations and Societies becoming a Fellow in the American Psychiatric Association (1961), the Academy of Psychosomatic Medicine (1966), the World Association for Social Psychiatry (1970), the American Association for Social Psychiatry (1983) and a Founding member of the Royal College of Psychiatrists (1965). He belongs to both the American (1983) and Texas (1986) Associations of Psychiatric Administrators. He has been a member of the ACNP since 1965 with Emeritus status.

Connie finally took down his shingle from full time practice in 1995 and for a four year period continued to do locums in South Texas until he grew disappointed with the authoritarian methods and lack of family involvement practiced by the physicians he was covering for.

Asked to look back over his life, he feels proudest of the way in which he could "see the way psychiatry was going", that he contributed "research that was credible" and always "protected his patients." The core of his contributions has been in psychopharmacology integrated with psychotherapy and sociotherapy. An essay on *Basic Research and Clinical Studies in Psychopharmacology* summarizes his thoughts as follows:

Recently with the supervision of psychiatry residents and locum tenens practice in both outpatient and inpatient settings, I came to appreciate the current treatment of psychopharmacology as well as psychotherapy and sociotherapy.

The use of psychotropics is chaotic. With the persistent input of pharmaceutical companies, treatment does not address diagnostic entities but clinical symptoms. As a result, an individual patient may receive four to six psychotropics, including atypical antipsychotics, anxiolytics, antimanic and antidepressant medications. This may be in addition to medications prescribed for hypertension, type II diabetes and other co-morbid conditions.

I have observed the changes in patient care from locked wards to the emptying of the mental hospitals. This has all happened without the parallel activation of adequate mental health community programs envisaged during the Kennedy administration

In the age of managed care with continuously diminished resources, the ageing of the population and the ubiquitous use of drugs of dependence, one questions if the discovery of more and more psychotropic compounds may require greater discrimination in the application of clinical psychopharmacology. However, for me, psychopharmacology remains the most exciting part of my career.

Connie's biggest disappointment was a lack of strong mentoring in his early years and that he left Baylor prematurely, discouraged by a Chairman who was dismissive and discriminatory. His marriage following residency ended in divorce after 13 years to a wife who was not sympathetic or helpful to his career. Altogether, this is the portrait of a humble man of energy and diverse interests with a prescient capacity to anticipate and confront whatever the Zeitgeist offered with fortitude and flexibility.

Perhaps the core of Connie's interests lies in an essay written in 2012, *Psychological Peregrinations*. In it he traces the historical and philosophical origins of his ideal based on the life and teachings of Socrates taught in the *phrondisteron*, the 'thinkery'.

Socrate, (470-399 B.C.) was a son of a sculptor and midwife. He was a philosopher who taught for free, did not develop a system, and wrote nothing. He had studied the natural philosophers but abandoned them for their lack of interest in human conduct. He studied the sophists but attacked them for their indifference to virtue. He believed that virtue comes from understanding, and that

no man knowingly does wrong. Socrates, a patriot, fought and was wounded in battle. He believed that a citizen bound by conscience must obey the laws of the state. The Delphic oracle named him the wisest man of his time, and all his life he pursued the dictum, "know thyself". Socrates was reported to have said, "The unexamined life is not worth living."

Connie uses the Socratic template to compare it with the various forms and ingredients of psychotherapy and its place in the Hippocratic ideal for physicians, contrasting it with the shortcomings of contemporary psychiatric practice and managed care. He concludes:

Hopefully, with the study of both the ancients and contemporaries, we may acquire wisdom conducive to mental health, defined as creativity, productivity and the capacity for pleasure.

This is remarkably similar to the conclusion reached by Frank Berger, discoverer of the first minor tranquilizer in his postmortem book, "A Man of Understanding", on the relative roles of drugs and philosophy in mental health (Blackwell, 2014).

Pastimes and Pleasures

Connie's two greatest pastimes and pleasures have origins in his Greek heritage, books and art. He was a "history buff" in high school and gave lectures to his classmates on such topics. Today, he likes to browse used bookstores seeking ancient tomes about Greek plays, philosophy and historical figures. But his major avocation is collecting art, which he began in the early 1960's, inspired by his sister Doula's interest in the Byzantine era and the manner in which an innate sense of beauty in art made its contribution to the quality of life. His personal collection of over 700 artworks is garnered from world travels in such places as Haiti, Cuba, Vietnam, Mexico, Greece and China. Connie is currently seeking a congenial and caring environment to which he can donate and display a collection worth in excess of a million dollars.

Our time together in Milwaukee was divided between dissecting Connie's career and catering to his artistic interests by visiting three outstanding and unique museums. First and foremost was the internationally renowned Calatrava Museum, its cantilevered wings open towards Lake Michigan. On display this month was a travelling exhibit "From Van Gogh to Pollock" that traced the evolution of schools of art from the late 19th century to the present. Billed as "acts of creative rebellion" this might also be seen as the retrospective of an evolving artistic Zeitgeist.

Next was the Grohmann Museum at the Milwaukee School of Engineering (MSOE). Like Connie's, this is one man's collection of art dedicated to the "evolution of work in all its various forms", including trades, occupations and professions. Dr. Eckhart Grohmann is an engineer and successful entrepreneur; his collection of over 1000 pieces of art and sculpture dates from 1580 to the present, priceless and unique worldwide. Included is a section that portrays the beginnings of medicine at work as apothecaries, alchemists and barber-surgeons. A 16th century masterpiece in oils shows a surgeon operating on himself, a knife in one hand, a coil of intestine in the other, beneath a face distorted in agony. An additional recent display is of twenty 19th century paintings by a Milwaukee German artist, Carl Spitzweg. His most famous painting, "The Bookworm", is hung in proximity to a modern portrait by Norman Rockwell with the same title.

Our final visit was to the Harley-Davidson Museum, which houses motorcycles from the inception of the company in 1903, displaying all the various designs through both World Wars to the present. A new adjacent display is devoted to the talents of Willie Davidson whose grandfather was one of the founders. Willie served as Chief Styling Officer and Head of Brand Development until his retirement in 2012 and is widely regarded as a popular "Brand Ambassador". As a young man, Willie attended art school and is a very talented watercolor painter; several of his works were on display, but not for sale. The synchrony between his vocation and avocation makes him comment, "I never worked a day in my life."

When our three days of talk and viewing were over, we drove Connie to Mitchell Field Airport, telling him on the way that it has the unusual attribute of housing a used bookstore, *Renaissance*, on the departure level, somewhere for a bookworm to browse while waiting for his flight home.

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