

**Barry Blackwell and Kanellos Charalampous:  
Kanellos Charalampous Confronting the Zeitgeist**

Collated by Olaf Fjetland

This collated document includes the Kanelloos Charalampous biography written by Barry Blackwell and Kanellos Chralampous, and two comments, one each by Thomas A. Ban and John Smythies.

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*“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 Patronicolos, 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 May 1966, 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 hands-on 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 Ekeistics, 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, 1977, c; Charalampous & Skinner, 1977; 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 21<sup>st</sup> 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, anti-manic 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 19<sup>th</sup> 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 16<sup>th</sup> 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 19<sup>th</sup> 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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December 24, 2015

### **Thomas A. Ban's comment**

I read with interest your biography and noted your research related to the "pink spot". It brought back memories from the 1960s, about a time when I was coordinating the Canadian Mental Health Association (CMHA) Collaborative Studies on Nicotinic Acid in the Treatment of

Schizophrenias (Ban 1971 a, b; Ban and Lehmann 1970). At the time the CMHA Collaborative Studies were designed, in the early 1960s, psychotoxic metabolites of catecholamines and indoleamines were implicated as the culprit for schizophrenia and our intention was to test the hypothesis that the presence of one of these metabolites, 3,4-dimethoxyphenylethylamine (DMPEA), in the urine of schizophrenic patients was a predictor of favorable outcome to treatment. The idea was that administration of nicotinic acid that converts into nicotinamide, a methyl acceptor, will prevent the formation DMPEA, a dimethylated dopamine. Yet, by the time we were ready to test this hypothesis, in the late 1960s, we decided not to proceed, in light of findings like yours, which conclusively demonstrated that DMPEA has no psychotoxic effects (Charalampous 1966; Friedhoff and Hollister 1966; Hollister and Friedhoff 1966). The story of DMPEA began, in 1934, with Noteboom's discovery that DMPEA produced experimental catatonia in rats. It continued, in 1952, with Harley-Mason's implication that DMPEA, formed in the body, is the culprit of schizophrenia (Osmond and Smythies 1952) and culminated, in 1962, with Friedhoff and Van Winkle's detection of a "pink spot" with paper chromatography in schizophrenic urine and determination of the chemical responsible for the "pink spot" as DMPEA.

In spite of the demonstration in the mid-1960s that DMPEA has no psychotoxic effects, the controversy about the "pink spot" continued well into the early 1970s (Ban 1973).

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### **John Smythies' comment**

I was never directly involved in work on the "pink spot" nor is there any evidence that mescaline-like metabolites occur in the human body whether in health or disease. However, there is good evidence that the psychotomimetic agent adrenochrome occurs in the brain in normal subjects. The adrenergic neurons of the C1 group in the medulla contain neuromelanin and adrenochrome is a mandatory ingredient in the biosynthesis of neuromelanin. So, it is remarkable that no one has followed up this clue by examining whether the brains from schizophrenic patients contain any abnormalities in the neuromelanin content of the C1 neurons in the medulla.

On another tack, the transmethylation hypothesis has recently taken new life by the observation that brains in MDD and in schizophrenia show abnormalities in DNA methylation, which is a key mechanism modulating the synthesis of brain proteins. This may be the long-missing explanation for the old observation by Seymour Kety that the methyl donor l-methionine exacerbates the symptoms of chronic schizophrenics

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