Barry Blackwell: Pioneers and Controversies in Psychopharmacology

Chapter 14: A pioneer psychopharmacologist

Karl Rickel's biography

Preamble

Karl Rickels' memoir is a unique and inspiring account of how a German prisoner of war in America came to love the country and returned after the war ended to become one of our 20th century's leading psychopharmacologists, (Blackwell 2014).

Karl's moderate voice in the preceding Chapter 13 provided a balanced viewpoint in the contentious debate concerning the meaning of anxiety in both depression and medical disorders as well as promoting a conservative role for the use of minor tranquilizers.

Karl was also known throughout his career for identifying non-specific factors that influenced outcome in drug therapy, particularly the placebo response. He also explored the role that anxiety played in depression and its response to different drug categories.

A SERENDIPITOUS LIFE: FROM GERMAN POW TO AMERICAN PSYCHIATRIST

By

Karl Rickels, M.D.

Noting Hill Press, Evergreen, CO, 2011

Reviewed by Barry Blackwell

Karl Rickel's memoir, *A Serendipitous Life,* is a rich tapestry which weaves together personal and professional life, yielding a satisfying and revealing portrait of both man and scientist.

This slender volume compresses the author's 87 years and a distinguished academic career into 201 pages plus photographs and appendices. Karl dedicates his work to his grandchildren

because, “there is much to be learned by looking back,” a purpose that applies equally to those neophyte neuroscientists wise and fortunate enough to read it.

The contents are almost equally divided between personal and family affairs (Chapters 1-4, Chapter10 and three appendices) followed by accounts mainly of work as a clinician and scientist (Chapters 5-9). But this dichotomy is illusory and arbitrary. The seeds of Karl’s success, embedded in nature and nurture, blossom into a purpose driven and integrated life, both professional and personal.

For example, Chapter 5, *“The Era of Psychopharmacology,”* is interrupted by two domestic interludes: the adoption of a son in Germany that ends his wife’s infertility producing a second son within a year, *“Adding to Our Family”,* and introspection about why he has spent his whole life at Penn eschewing lucrative offers of department chairs in America and Germany, *“Homebody.”* These twin tales bookend an intervening piece on *“Research and Discovery.”* Throughout the book the warp and weft of family and work mingle vacations on the Jersey shore and international travel with academic tasks and scientific commentary. Chapter 5 ends with the following passage (Author’s italics): *“Serendipity may have provided me with lots of opportunities in life, but it was still up to me to decide which paths to take. I took the ones that were more about people, family and patients, not money.”*

Karl Rickels was born in 1924 in Wilhelmshaven, a large North Sea naval port, two years before his parents moved to Berlin where he spent his entire youth. His character and talents owe much to an ancient and distinguished heritage *(Appendix 1: “Family Matters).* On his father’s maternal side, he is descended from a priest born in 1487 who became a professor of physics at Wittenberg University where he defended his theological thesis before Martin Luther. On the paternal side, the Rickels name is traced back to the same medieval era when they were farmers in Holstein, near Denmark.

According to family folk lore, young Karl’s earliest trait was curiosity and his favorite words were: “What is this?” By age 10 he was academically accomplished enough to be enrolled in the Gymnasium where doctoral level teachers prepared students for university in a multi-ethnic environment. So, he learned French in fifth grade, Latin in seventh and English in ninth. Karl was academically precocious enough to skip the eighth grade. By grade 10 Karl knew he wanted to be

a physician and he selected a natural science track; asked to write about what he intended to become he wrote surgeon in German, but was mortified when the teacher admonished him for misspelling the word. Karl was active in long distance running, gymnastics, handball and rowing – the archetypal team sport. He was also an avid reader.

When Karl was eight the Nazis came to power and by the time he was in the ninth grade when World War 2 erupted bringing lost class time and frequent nights in air raid shelters. Throughout childhood Karl thrived in a warm and supportive family environment. Both parents encouraged his educational efforts and accomplishments; his father, Vati, was enamored with books about popular medicine and browbeat the family in correct ways to walk, eat and breathe. In the winter family members had to sit awhile in front of an ultraviolet lamp to absorb vitamin D. Vati was also an accomplished artist and unpublished author of poetry and plays. He was an eternal optimist, always positive.

In 1941 Karl was 17 and the Russians had switched sides, declaring war on Germany. Vati, convinced Germany would lose, sat Karl down to discuss by whom he would rather be captured, the Russians or the British? The Russian reputation for brutality made the answer obvious. To escape the Russian front and find the British in North Africa he would have to avoid the draft and volunteer so as to select the type of service and where that would be. In addition, he qualified for officer training.

This type of forward (anticipatory) thinking would pass from father to son so, after graduating from gymnasium in 1942, Karl joined the Signal Corps. At boot camp the recruits were arbitrarily divided into two groups: wireless or telephone; Karl was assigned to the first but preferred the latter. Breaking rank for a spurious visit to the bathroom, he marched into the colonel's office, requested and was assigned his choice. More forward thinking! After six months of officer training Karl was required to complete three months of front line experience as a private first class before being commissioned. In June 1943, aged 18, he joined the Africa Corps serving under Field Marshal Rommel. Both father and son's expectations were prescient; by the time Karl reached the front lines with telephone wires Montgomery had defeated Rommel at El Alamein and the tide of war turned in Britain's favor. In May 1943 the Africa Corps surrendered to the British who turned their prisoners over to the newly arrived American army. This was providential. Karl writes: "We received ice-cold potato salad, the best hot dogs I have ever eaten, and vanilla ice

cream… I certainly knew then that the Americans would win the war!" Using an English dictionary his father insisted he take with him Karl spent his free time improving his language skills. In June 1943 he boarded ship for America at the height of the U- Boat war in a convoy attacked by German submarines. "For the first time I prayed for the Americans, not the Germans."

At Camp Swift in Texas Karl's facility with English earned him a job as the hospital interpreter while he "worked hard to replace my book-learned English with American idioms and words." Three months later his belongings, confiscated in Africa, were returned: "…I was once again convinced that America would win the war. Surely this was the most efficient country in the world. This was probably the first time I thought about returning to America after the war."

Karl was not idle. Transferred to another camp he became chief of the ration detail, perfected his English and, with a colleague, became "the ping pong champions of our camp." Later, he also won a chess tournament. Meanwhile he matriculated by mail as a medical student at Berlin University in Germany whilst a POW in America. The camp environment was congenial and relaxed with fraternization between guards and prisoners: "We were all soldiers, not politicians. None of us soldiers started the war. Camaraderie just developed. We all wanted the war to end so we could go home and get on with our lives."

When the war did end in mid-1945 rumors circulated that German prisoners might be shipped as slave labor to France or England. By now Karl had become the interpreter and friend of the officer in charge of selecting prisoners for democratization an "Anti-Nazi" training program: "I helped him and put my name at the top of the list." Graduates from this program received a certificate stating that they were "Good Germans ready to help the occupying authorities in the rebuilding of Germany." Aboard ship to Europe Karl was leader of 1,500 fellow prisoners, now registered as a German medical student, identified as "the young doctor" and comfortably ensconced in the ship's infirmary. Allowed to choose which occupied zone (American, British or French) he wished to be discharged to he chose British where his mother's relatives lived. Unfortunately, the British authorities, unfamiliar with the American democratization process, were set on sending all healthy prisoners to England to work as farm laborers. Examined by a German doctor for fitness Karl fabricated a history of headaches and dizziness following a motorcycle accident, revealed he was a medical student and was sympathetically declared "unfit for work."

As Karl anticipated medical school at age 22 he reflected on his three years as a POW in America: *"The experience allowed me to grow and mature, to become self-reliant, to learn to fight for things I wanted and not worry about things I could nor change"* (Author's italics). True, but the seeds were planted early in genetic heritage, family upbringing and sage paternal mentoring.

Eager to start medical school immediately Karl faced a final hurdle. At Bonn the Dean of Admissions told him he was too late to enroll and would have to join the winter semester. Instead, Karl travelled 100 kilometers to Muenster, a city 80% destroyed by allied bombs and, once again, was rejected as too late for the summer semester, first by the admissions committee and then by the Dean on appeal. Karl turned to the British university officer, producing his POW democratization certificate. Impressed, the official wrote a formal recommendation on official stationary, "*His Majesty's Service,*" stating Karl was one of the first students to have applied (from America). Presented with this documentation the Dean "Almost stood to attention, and I was admitted the same day."

In medical school two preclinical years followed by three clinical years in various hospitals were coupled with a doctoral dissertation involving rat research on the nutritional value of essential amino acids. During the last two years Karl met his future first wife, Crista, a PhD student in German and English literature. Post war conditions were arduous, hot water for bathing once weekly, shortage of food (ration coupons provided only 1,200 calories daily), no toilet paper, no student accommodations, living in four or five different rented apartments and poor quality clothing. But Karl also notes the generous clothing and food supplied by many charitable organizations and above all the Marshall Plan: "One of the greatest acts of modern charity, executed by the occupying forces of a victorious nation." Faced with all this and financial hardships marriage was inevitably postponed for four years, until April 1963.

Following graduation from medical school in July 1951 Karl began a 15-month internship in three different settings, an X-Ray Institute, an Institute of Hygiene and the Medical Department of the City hospital in Dortmund. During this time, he published his first scientific paper on blood typing in paternity suits.

After internship Karl's interests turned toward public health, microbiology and pathology. He learned to do autopsies, did lab research on the interaction of antibiotics with bacteria and

published three scientific papers. His hope was to apply to Harvard for a job in public health: “At this time, psychiatry was the furthest thing from my mind.” Three objectives were foremost: academia, research and America.

In 1954 Karl saw an ad in a German medical journal offering sponsorship to emigrate to the United States subject to spending one year at the Mental Health Institute in Cherokee, Iowa. Crista was now pregnant, but they were both eager to escape the harsh economic conditions in Germany spurred on by Karl’s idyllic memories of America. Their flight from Frankfurt landed on American soil on September 1, 1954, and less than two weeks later Karl, now aged 30, began life as a psychiatrist in rural Iowa. Housed in a comfortable apartment on the hospital grounds with a four-year-old Buick for Karl and a sewing machine for Crista their son Larry was born three months later.

Psychiatry was on the cusp between custodial asylum care and the impending revolution in psychopharmacology (Chapter 12). Karl describes the scene thus: “It was still a time when barbiturates and bromides, the only sedatives available, did not work and straightjackets, cold water baths, electroshock therapy (without anesthesia), insulin coma and trans-orbital lobotomy were treatments to control violent, aggressive but also just unruly patients.” Karl takes pains to point out this was “definitely not a snake pit.” There were ample support and nursing staff, the psychiatrists were almost entirely well-trained immigrants and although treatment was primitive it was humanely administered. Karl had only been in Cherokee a few months when he was witness, in early 1955, to the effects of the first samples of chlorpromazine and reserpine provided by the pharmaceutical manufacturers. “Suddenly, patients who had been violent and aggressive for many years were quiet and comfortable. They could dress themselves, eat on their own and no longer soiled themselves. The stench that had been pervasive on the wards where these violent patients lived disappeared. It was truly a wonder” (Chapter 7).

Karl had only been at Cherokee six months when he decided psychiatry was his calling: “I wanted to be involved in this revolutionary development from its beginning and hoped to become an important player in the new field.” Knowing he needed further expert training he applied to Harvard, Johns Hopkins and the University of Pennsylvania (Penn). Penn offered an opening subject to an interview that Karl couldn’t afford to attend. They agreed to a phone interview perhaps impressed with his three publications. Seeking collateral information, the interviewer

called the hospital Superintendent who issued a lukewarm endorsement intended to retain someone he couldn't afford to lose. Asked if they were going to let Karl go and hearing an emphatic denial the astute interviewer saw through the deception and promptly offered Karl a position.

Karl arrived at Penn in late summer 1955 and remains there today, 59 years later. He joined a residency program that was "small and elite" with a salary of $2,800 that matched the first of those adjectives – but it was supplemented by the Chair, Dr. Appel, with additional funds to attend the newly appearing conferences on biological psychiatry that kept them both up to date. At Penn, like almost every academic department in America, psychoanalysis was king. The department headquarters was located at the University hospital but the hub and heart of the program was at the Institute, a large private practice located on "large grounds in a palatial setting" where patients from the "most famous and rich families" were treated by "all the leading psychiatrists and analysts in the city." Patients lingered for months, some "for their whole lives."

In this environment Karl was given time for basic research, mentored by the professor of pharmacology under whose direction he did primate work on the effects of anticonvulsants and human studies on the cold pressor test in anxious and non-anxious patients. Results from both were published and the latter would portend a lifetime interest in the anxiety disorders. Karl was also mentored by Dr. Appel after he had seen his last psychotherapy patient at the Institute, often around midnight. He describes two lessons learned in supervision. First, his psychotherapy patient, who was benefiting less and less from a barbiturate, regained the effects after a pink capsule was replaced by a green one containing the identical dose of sedative – a placebo response, one of the nonspecific factors in therapy Karl would later become renowned for studying. The second lesson had generic implications. After Karl failed to connect with a female patient during a 50-minute therapy session Dr. Appel intervened. In a brief 15-minute chat he elicited the missing information while holding constant eye contact, expressing caring and warmth. This "amazed me and served as one of the most important examples of how I wanted to act and treat my patients." On the hospital consultation service seeing medical patients Karl quickly learned the value of practical, often biological, advice that the surgeons and internists found more helpful than psychoanalytic interpretations.

In 1956, the year after Karl began residency as a second-year fellow, the National Institute of Mental Health (NIMH) established the Psychopharmacology Service Center under the direction

of Jonathan Cole with several million dollars of funding from Congress. The following year, after completing residency, Karl submitted a grant proposal to NIMH to study drug treatment in neurotic outpatients. It was funded on the first attempt. This began a unique half century of continuous NIMH funding lasting from 1959 to 2009 when Karl was 85. His final application required several submissions but Karl persisted as a mentoring example to junior faculty on how to seek and obtain NIMH funding. In 1956, while still a resident, Karl planned and carried out one of the earliest, perhaps the first, double blind placebo controlled study in anxious medical outpatients, collaborating with internists, not psychiatrists. This innovative strategy and population reflected the fact that anxiety is a common symptom in medical conditions for which treatment often reduces medical morbidity. The results were published in the Journal of the American Medical Association (JAMA) and this strategy was adopted three years later in Britain by David Wheatley co-operating with a large group of family practitioners (also funded by NIMH). Karl's study was prescient of the now well-established fact that primary care physicians prescribe the majority of drugs to treat anxiety and depression. Noteworthy is the fact that Karl's choice of population was also dictated by the reluctance of psychoanalysts in 1956 to prescribe medication for anxiety on the mistaken belief it might reduce motivation for psychotherapy. Despite this fact it was Karl's mentor, Dr. Appel, who encouraged him to go ahead. From this Karl derived the principle of always going to the person in charge for approval because "He or she has more wisdom than the people reporting to them."

In addition to chance and serendipity, synchronicity also played an important role in Karl's career development. He was in the right place at the right time. As other clinicians around the world experienced the same epiphany evoked by witnessing the remarkable reduction in psychotic symptoms due to the first drugs, an impetus to convene and share information evolved. Karl became a prominent participant in three key organizations founded to achieve this end (Chapter 6). The earliest was the *Collegium Internationale Neuro-Psychopharmacologicum* (CINP) in Europe. It was informally convened in Zurich during the Second World Congress on Psychiatry in 1957. Invited members from 13 nations included six basic scientists and 27 clinicians of whom four were from America: three clinicians, (Brill, Denber and Kline) and one basic scientist (Brodie). The CINP held its first Congress in Rome in 1958, addressed by Pope Pius XII, membership was opened and Karl was one of 13 new members from the United States. He presented a paper on the *Methodology of Drug Evaluation in Neurotic Outpatients.* Subsequently

Karl published several papers at the Second Congress (Basel 1960) and the Third Congress (Munich 1962) dealing with placebo controlled drug studies and the role of non-specific factors in treatment outcome. In *"The Story of the CINP*" (Eds Ban, Healey & Shorter, CINP, 1988) Karl's early contributions to the field are cited by several distinguished colleagues.

Perhaps due to the hegemony of psychoanalysis America lagged behind Europe and it was not until 1961 that the *American College of Neuropsychopharmacology* (ACNP) was created and Karl was a member of the charter class of 90 individuals; fewer than 20 still survive among which he must be one of the few still active in the field. He became a Life Fellow in 2002 at which time he received "Special commendation for excellent, outstanding service to the field."

The third organization of which Karl became a founding member was the Early Clinical Drug Evaluation Unit (ECDEU) established and funded by NIMH in 1960 to develop methodology to evaluate the safety and efficacy of new drugs to treat mental illness. A dozen research centers were spread among State hospitals, the Veteran's Administration and a few Academic Medical Centers like Penn where Karl's unit was initially the only one studying outpatients. In the early 1980s industry became more involved in drug trials, several NIMH funded centers closed and the program changed its name to the New Clinical Drug Evaluation Unit (NCDEU).

Karl was still active in all three organizations when they celebrated their 50th anniversaries; at the NCDEU in 2010 he gave an invited lecture on *"Trial Methodology over Five Decades."*

Five years after completing residency Karl was well established at Penn in a successful career; now a member of the three most prestigious organizations in the heyday of new psychotropic drug development, already an accomplished investigator and confident grant writer. He was domestically settled in a beautiful home, Crista had resumed her graduate studies and their son Larry was a happy seven-year-old doing well in the local elementary school. All of this was when misfortune struck, the antonym of serendipity. Crista developed ovarian cancer in early summer 1962 and died only nine months later. Karl was devastated: "I was a workaholic then (and since), working late hours and even in the evening when I got home. When we were finally settled, and Crista could enjoy a good life, suddenly it was over."

Now a single parent of a young son, deeply engaged and a hard-working scientist, Karl went to Europe for eight weeks as a respite, spent much of the time with Larry and on their return

flight discovered how serendipity can accommodate life-changing social encounters as well as profound scientific contributions. During the flight to Philadelphia Karl became engaged with a family returning home to New Jersey after a European vacation. Included was Linda, a student majoring in sociology and elementary education at Salem College. “We talked about my work and I gave Linda my business card asking her to give me a call. Linda must have wondered if I thought she needed to see a psychiatrist.” Socially she did! Just over a year later, in June 1964, they were married, a union that produced two sons, lasted 44 years and established another spousal alliance that successfully merged domestic with professional life.

In his lengthy and prolific career Karl has published almost 600 reviews, articles and book chapters, as well as editing nine books beginning with the classic “*Non Specific Factors in Drug Therapy”* (Rickels 1968) and ending with “*Good Chemistry*” (2004). Chapter 8 of his memoir, *“My Personal Contributions to the Field*,” provides details of eight areas of enquiry covered by Karl’s literary and research oeuvre. Much of this focused on outpatient treatment of anxiety and, to a lesser extent depression, including pioneer work in family medicine and private psychiatric practice. Karl’s findings helped elucidate a strident multinational controversy on the benefits and risks of benzodiazepine (minor tranquilizer) drugs, of which Valium is the prototype, used to treat anxiety. Introduced in 1963, within seven years it became the “most widely prescribed drug in the world.” The ensuing debate focused on the appropriateness of treatment, its length and the risks of dependency or abuse (Chapter 5, *The Era of Psychopharmacology*). Much of the concern emanated from Britain where one psychiatrist called these drugs “the opium of the masses.”

Karl brought both experience and expertise to a debate characterized as hedonists versus puritans. He participated in the development of the Hopkins Symptom Checklist, a patient rating scale widely used worldwide; compared the efficacy and side effects of antianxiety and antidepressant drugs in anxious outpatients; demonstrated the influence of physician attitudes and patient expectations on treatment outcome; quantified the frequency and severity of dependence relative to duration of treatment; and, above all, stressed the importance of a “multifaceted, holistic approach to the pharmacological treatment of emotional symptoms.” All together Karl believes that antianxiety drugs are appropriately used and that dependence is seldom a severe problem (Rickels 1966). In 2008 he chaired an international symposium at the CINP that reviewed the role

of benzodiazepines in the 21st century which concluded: “Benzodiazepines are probably not over-prescribed but under-prescribed.”

Karl’s academic career as Professor of Psychiatry (1969) and Pharmacology (1976) took a midlife turn when he also became the Stuart and Emily BH Mudd Professor of Human Behavior and Reproduction. The duality of the title reflects his pervasive interests and stems from work with non-psychiatric patients in primary care that led to research on infertility and prevention of adolescent pregnancy. In 1993 he co-authored (with Ellen Freeman) “*Early Childbearing: Perspectives of Black* A*dolescents on Pregnancy, Abortion and Contraception.”* Karl also collaborated with his co-author on the treatment of premenstrual symptoms (PMS) in research continuously supported by NIH for 25 years.

Karl has also spent his abundant energies in many additional directions not mentioned in his memoir (Blackwell 2011a). He is Editor of *Pharmacopsychiatry* (1973-) and serves on the editorial boards of eight other leading journals in research, stress, primary care, and neuropsychopharmacology. He serves on numerous University and Hospital Committees and has been a consultant, committee or task force member to pharmaceutical companies, AMA, NIMH, FDA, NIH, APA and the Academy of Sciences.

The memoir’s penultimate chapter (Chapter 9, *Reflections on Psychopharmacology Today*) is a synthesis of the current state of the vineyard in which Karl has toiled for more than half a century. It provides a cautionary tale of troubled times echoing and elaborating on concerns of many of his contemporaries (Blackwell 2011b). Karl’s conclusions are followed by reasons and recommendations for remediation: “New drug development … has stalled. Most new drugs are basically ‘me too” drugs. Though they typically have a different side effect profile there is still little or no improved efficacy… Our tremendous scientific laboratory advances, such as those made in the fields of molecular science and nanotechnology have, regretfully, at least in psychiatry, not yet lead to treatments via completely new mechanisms… Only side effect profiles and excessive marketing, not efficacy, differentiate the newer from the older compounds.” Karl also points out discoveries in the first two decades “were made with much smaller financial investment and fewer researchers than today.”

In search of reasons for this impasse Karl includes being "enthralled with the concept of co-morbidity and diagnostic purity" and he indicts consumer marketing and its support by "medical leaders, academics and non-academics alike" who collude in the creation of diagnostic entities to match a drug profile – such as panic disorder and Xanax. He notes that academia is highly represented on lucrative industry speakers' bureaus or advisers to marketing departments. In an earlier chapter Karl reminds us that he consulted only to research and never to marketing and even there he only dealt with the CEO or the Vice president for Research. As a result: "I was able to shoot down many ineffective compounds early in development, saving hundreds of millions of dollars." He is proud of the fact that his appointment to an FDA review committee was approved after he listed all his industry consulting appointments and, in response to cross questioning, pointed out that all but one of his recommendations was negative. There remains a simplistic assumption today that reciting a list of "conflicts of interest" absolves a researcher form revealing the price paid for his advice and its outcome.

In Chapter 7, a section on "*Thoughts on Methodology*" elaborates on the drug trial methodologies adopted by industry that contribute to the contemporary sterility of the field. It is influenced more by marketing than research departments and suffers from the following shortcomings: many of the newer compounds are inactive or only mildly so; study subjects are often recruited by advertisement and are not true patients in primary care; combined with the previous problem this leads to increased placebo responses contributed to by spontaneous remission and resulting in low drug-placebo discrimination; all this then results in attempts to increase the sample size and number of study sites often including those from developing countries thus increasing variability and unreliability. An overarching problem is that drug trials have moved from academic and private practice settings to drug company owned or sponsored clinical research organizations (CROs) where the primary motivation has shifted from scientific curiosity and academic advancement to financial gain.

It is difficult not to conclude that in degrading trial methodology the industry has killed the golden goose that lays its eggs. Karl's remedy is to reverse each of the causes he lists.

The final chapter 10, "*Linda,*" is a portrait in praise and gratitude to Karl's second wife who died of brain cancer after a long struggle shortly before Christmas 2008. It is followed by three appendices: the first is a family genealogy; the second is the revealing text of a letter Karl

wrote to his future mother in law conveying his thoughts and feelings towards her daughter including, in a brief postscript, his philosophy of life and marriage; and the third, titled *"Advice of a Husband and Father to his Children and Grandchildren."* It is tool kit of desirable behaviors, values and virtues most of which the reader will recognize from the memoir itself. Included are" "Happy and lasting marriage takes two people …divide roles, and once done respect the other's decision… have a positive outlook… learn from your mistakes… be not afraid to make decisions …a job you like and look forward to is more important than making money… always be polite, politeness opens many doors."

In the same year that Linda died Penn awarded Karl the William Osler Patient Oriented Research Award. With gentle irony it is worth recalling what William Osler said about the role of a physician's wife in the 19th century during an address to medical students entitled, "*The Physician's Life."* He states: "What about the wife and babies if you have them? Leave them! Heavy is your responsibility to yourself to the profession and to the public. Your wife will be glad to bear he share in the sacrifice you make." Two centuries later Karl Rickels modernized this antique ideology in his own career with an enlightened and negotiated integration of personal and professional life. He has expressed his gratitude by endowing two chairs of psychiatry at Penn, one in honor of Vati, his father, and the other in honor of Linda, his wife. They testify to the way in which familial influences shaped and supported a unique career devoted, like Osler's, to caring for others.

Karl chose to title his memoir *"A Serendipitous Life*," which is surely an understatement of the forces governing his career. The word "serendipity" was coined by Horace Walpole in a letter to a friend in 1754 describing a Persian fairy tale, *"The Three Princes of Serendip*" (formerly Ceylon, now Sri Lanka). This tells how one of the princes deduced that a mule, blind in the right eye, had travelled the same path because the grass was only eaten on the left side. The tale does not reveal if the link between the cause (blindness) and the outcome (the shorn grass) was made by someone who knew the mule was impaired in some way beforehand or by an uniformed observer. In the former instance, serendipity might be closer to Pasteur's aphorism that "Chance favors the prepared mind." But by common usage the dictionary definition (OED) of serendipity focuses only on chance: "The occurrence and development of events by chance in a happy and beneficial way." Still, it is this reviewer's opinion that while Karl's contributions may owe

something to benevolent chance, much of his unique bequest to the field of psychopharmacology and the patients who benefited was due to curiosity, forward thinking, persistence, creativity, integrity and loyalty.

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