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A Tribute to Eli & Lee Robins— Citation Superstars. A Citationist Perspective on Biological Psychiatry

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One of the most influential researchers in the field of biological psychiatry, Eli Robins, is highlighted in this essay. His most-cited works and contributions to the field of psychiatry are examined. Among the publications described are three *Citation Classics*®: on the histochemical study of the central nervous system, on research diagnostic criteria, and on suicide. Research-front analysis indicates his continuing influence. The work of spouse Lee N. Robins in psychiatric epidemiology is also reviewed.

For the sake of historical accuracy, this essay began in response to a single information request. The response grew, like Topsy, to its present proportions. This past summer I was contacted by Winston W. Shen, School of Medicine, St. Louis University, Missouri, for information on fellow Missouri Psychiatry Society member Eli Robins. Shen knew that Robins was a highly cited researcher and wanted current citation data for a news story he was preparing for the newsletter he edits—*Missouri Psychiatry*.¹

I hadn't realized that Robins was a close colleague of Oliver H. Lowry, Washington University School of Medicine, St. Louis, internationally recognized not only as the author of the most-cited paper ever published,^{2,3} but also for his other major contributions to biochemistry. Robins himself has produced over 175 publications that have been cited in over 10,000 papers. This essay is, in part, a tribute to Robins—not only to his being a citation superstar, but also to his determination. Most of his cited works were written after he was diagnosed during the early 1960s with multiple sclerosis. Despite his condition Robins remains a prodigious researcher and author. In addition, I am pleased to acknowledge the work of his wife, Lee N. Robins.

Biographical Data

Eli Robins was born in Houston, Texas, on February 22, 1921. He received his BA degree from Rice University, Houston, in 1940, and his MD degree from Harvard University Medical School, Boston, Massachusetts, in December 1943.

From January 1944 through June 1949, Robins interned at Mt. Sinai Hospital, New York, and served residencies in psychiatry at Massachusetts General Hospital, Boston, and McLean Hospital, Waverly, Massachusetts, and a residency in neurology at Pratt Diagnostic Hospital, Boston.

From 1951 through the present, Robins has been affiliated with Barnes and Allied Hospitals, St. Louis, as a psychiatrist. From 1963 through 1975, he was psychiatrist-in-chief and head of the Department of Psychiatry, Washington University School of Medicine.

Awards/Memberships

Robins has been honored by various groups and associations, including the Gold Medal Award of the Society of Biological Psychiatry, 1974; the Paul H. Hock Award of the American Psychopathological Association, 1977; the Distinguished Service Award, National Alliance for the Mentally

Ill, 1983; and the AACP Achievement Award, American Academy of Clinical Psychiatrists, 1986. He was awarded an honorary Doctor of Science degree from Washington University in 1984 and is the only Washington University faculty member ever to receive this honor. He is also a member of Sigma Xi, the Honorary Research Society.

Robins is also one of the two honorary chairmen of the Scientific Council of the National Alliance for Research on Schizophrenia and Depression of Chicago, a newly established nongovernmental organization that funds research in biological psychiatry. The other honorary chairman is Nobel laureate Julius Axelrod (1970, physiology or medicine), discoverer of neurotransmissions of the brain.

Robins has membership in many august societies, including the American Academy of Neurology, the American College of Neuropsychopharmacology, the American Federation for Clinical Research, the American Psychiatric Association (life fellow), the American Psychopathological Association, the Association for Research in Nervous and Mental Disease (vice-president, 1960), the Histochemical Society, and the Society of Biological Psychiatry.

The Robins/Lowry Connection

Robins has been affiliated with the Washington University School of Medicine since 1949. Lowry was appointed head of the Department of Pharmacology at the university in 1947. In his connection with Lowry, Robins recalls:

My association with Oliver Lowry goes back a long way. In 1949, I became what I believe must have been the first pharmacology Fellow funded by the National Institute for Mental Health. This distinction came about because I had that year accepted an appointment in the Department of Psychiatry at Washington University Medical School in St. Louis, the same medical school that had recently...[hired] Oliver Lowry as head of the Department of Pharmacology. I wanted to learn something about biochemistry and pharmacol-

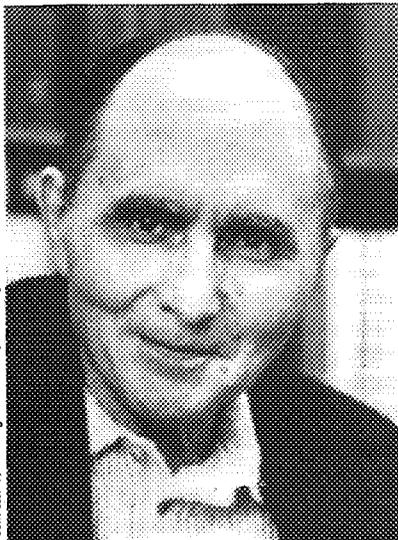
ogy and [Lowry] agreed to be my teacher. He gave me space in his lab. I, in turn, shared my consulting office with the rats we used in our experiments; my patients never commented.... These were extremely pleasant years because of Ollie's influence on the pace and ambiance of the lab and its undertakings. There was never a feeling of pressure, but always a sense of steady forward progress. Of great benefit to his students, postdocs, and colleagues was the time he made available for at least two luncheon seminars each week.⁴

From this fruitful collaboration, Robins and Lowry coauthored three methods papers through 1956.⁵⁻⁷ (Indeed, his first published paper in 1951 was with Lowry,⁵ the same year Lowry published his paper on the Folin phenol reagent.²) From there, Robins went on to appointments in the School of Medicine as a psychiatrist—first as an instructor in neuropsychiatry and eventually as head of the Department of Psychiatry at Washington University from 1963 to 1975, when his multiple sclerosis started to prohibit the execution of his demanding administrative duties. Currently, Robins is Wallace Renard Professor of Psychiatry.

In a recent conversation, Robins described himself as a biological psychiatrist.⁸ For *Current Contents*® (CC®) readers who are not familiar with the term, I have decided to provide some background on what biological psychiatry is, and whence it came. The information presented here definitely indicates that psychiatry is not a static discipline, but one in the throes of rapid evolution.

Biological Psychiatry: A Background

In facing the puzzle of mental illness in the early twentieth century, some psychiatrists hoped that Freudian theory alone would provide the answers. According to Joseph Wortis, Department of Psychiatry and Behavioral Science, School of Medicine, State University of New York, Stony Brook (who introduced insulin shock treatment to the US for the treatment of schizophrenia and who also worked with Freud), the heyday of psychoanalysis was in the decades of



Eli Robins

the 1940s through the 1960s.⁹ However, in the second half of the century, scientific research has uncovered evidence that biological malfunctions are central to mental illness and that much of the accepted psychological emphasis can be misleading if seen in isolation from other factors.¹⁰ There is ample evidence of the complex interrelationship between psychological and biological variables, and, at least in some cases, the disease state arises as a result of an interaction between genetic endowment, biological functioning, and personal and psychological experiences and responses. There are well-established interrelationships between psyche (the mind) and soma (the body).¹¹

Biological psychiatry has made fundamental contributions to the field of psychiatry as a whole. These are primarily in terms of treatment and in providing the original discipline with a third cornerstone, neurobiology, to join psychology and medical sociology.¹² Biological psychiatry deals with the biological nature of behavior and its disorders. Because of its broad scope, biological psychiatry includes aspects of electrophysiology, neurology, nutrition, pharmacology, biochemistry, genetics, psychology, human behavior studies, and molecular biology. Traditionally, medicine has recog-

nized the importance of psychology, social setting, and emotions in the care of patients. In this sense biological psychiatry uses the traditional medical model.

According to H.M. van Praag, Department of Psychiatry, Albert Einstein College of Medicine, Montefiore Medical Center, New York, biological psychiatry was the saving element in keeping the field of psychiatry connected with the rest of the medical sciences.

In 1958, psychiatry was detached from the rest of medicine. The concepts of psychosomatic medicine were restricted and the psychoanalytic language was too arcane to be taken seriously by mainstream medicine. In the 1960s, Western Europe... attempt[ed] to sever all ties between psychiatry and the medical disciplines and to promote the social sciences as psychiatry's home port. Biological psychiatry played an important role in preventing this.... Biological psychiatry has provided psychiatry not only with a new basic science and new treatment modalities, but also with the tools, the methodology, and the mentality to operate within the confines of an empirical science, the only framework in which a medical discipline can survive. Psychiatry is on its way to becoming a scientific discipline, and in no small measure biological psychiatry has facilitated that process.¹²

Two Biological Psychiatric Treatment Successes: General Paresis and Pellagra

While the term "biological psychiatry" has been current for half a century, the methods used in this approach had their beginnings long before. Two psychiatric illnesses, general paresis and pellagra, were among those to be comprehended and approached by physiological methods that characterize biological psychiatry. It should be said here, however, that the realized solutions took decades for both diseases.

General paresis was described hundreds of years ago as a progressive dementia and paralysis frequently associated with behavior change and psychotic symptoms. This malady accounted for one-tenth of the admissions to state institutions as late as 1930. The relationship of this disease to syphilis was

confirmed in 1913, but the successful treatment of general paresis was not achieved until the 1940s with the introduction of penicillin. According to published data by Robins and Vincent E. Ziegler, a psychiatrist in private practice, less than a decade after the introduction of penicillin, the admission rate to New York State institutions of patients with general paresis declined 66 percent.¹³

While general paresis begins with infection by bacteria, the origin of pellagra is nutritional deficiency. Pellagra has been recognized for two centuries, along with its tendency to occur in poor rural communities existing on cereal diets. The symptoms of this disease were depression, psychosis, and dementia. The disease was first suspected of being nutritional in origin back in 1914; however, it was not until 1938 that the basis of successful treatment was found with the isolation of nicotinic acid as the specific missing nutritional factor responsible for the manifestations of the disease. Nicotinic acid is now one of many vitamins and minerals known to be essential to normal central nervous system function.¹³

Psychopharmacology

Perhaps one of the greatest contributions of biological psychiatry to its mother discipline was the discovery of psychotropic drugs in the treatment of mental illness. The first such drug, chlorpromazine (Thorazine), was synthesized in 1950. First used in anesthesia and later in psychiatry, this drug marked the beginning of the modern era of pharmacotherapeutics in psychiatry. According to Robins,

With the introduction of this drug, the negative effects of sedation were separated from the therapeutic effects, later, best described by the terms "tranquilization" and "antipsychotic." Within a few years the similar effects of reserpine, the antidepressant effect of Niazid and later imipramine, and the anti-anxiety effects of meprobamate and the benzodiazepines were discovered and introduced into clinical practice. The development of these compounds...is

given partial credit by most and total credit by some, for revolutionizing the practice of psychiatry.¹³

My own connection with Thorazine development will be mentioned later.

Eli Robins: His Publications and Most-Cited Works

Looking over Robins's 175 published papers and books, the works can be categorized under four general topics: neurochemistry, suicidology, homosexuality, and psychiatric illnesses. All four subject areas are represented in the list of his most-cited works in Table 1.

Robins's works have remained very influential. For example, from 1987 through mid-1989, over 110 papers cited publications written by Robins. The topic breakdown is also worth noting—51 of the citing papers were on suicide; 35 on depression; 17 on schizophrenia; 6 on biochemical studies of the brain; and 5 on alcoholism. Of Robins's 175 published works through 1989, roughly 35 percent of them concern brain neurochemistry and histology. This is no accident, for during his early years in research, Robins worked a great deal in the field.

Early Histochemical Studies

Much of Robins's published output in the 1950s concerned histochemical and biochemical examinations of brain functions. Indeed, a 1958 paper on "The fluorometric measurement of dexoyribonucleic acid in animal tissues with special reference to the central nervous system"¹⁴ was discussed in a 1986 *Citation Classic*[®] commentary by coauthor John M. Kissane, Department of Pathology, Washington University School of Medicine.¹⁵ The work described in the paper has links to quantitative histochemical methods formulated by Lowry.¹⁶ Although over 30 years have passed since publication, over 1,400 other research articles have referenced this paper (in 1988 alone it was cited 68 times)—indicating its continued use and relevancy in central nervous system studies.

Table 1: E. Robins's most-cited works. Data are from the *SCI®/SSCI®*, 1945-1988. A=number of citations. B=bibliographic data. Asterisks (*) indicate works that are *Citation Classics®*.

A	B
*3,733	Feighner J P, Robins E, Guze S B, Woodruff R A, Winokur G & Munoz R. Diagnostic criteria for use in psychiatric research. <i>Arch. Gen. Psychiat.</i> 26:57-63, 1972.
*1,667	Spitzer R L, Endicott J & Robins E. <i>Research diagnostic criteria (RDC)</i> . New York: Biometrics Research, New York State Psychiatric Institute, 1975. 34 p.
*1,414	Kissane J M & Robins E. The fluorometric measurement of deoxyribonucleic acid in animal tissues with special reference to the central nervous system. <i>J. Biol. Chem.</i> 233:184-8, 1958.
1,405	Spitzer R L, Endicott J & Robins E. Research diagnostic criteria: rationale and reliability. <i>Arch. Gen. Psychiat.</i> 35:773-82, 1978.
*267	Robins E, Murphy G E, Wilkinson R H, Gassner S & Kayes J. Some clinical considerations in the prevention of suicide based on a study of 134 successful suicides. <i>Amer. J. Public Health</i> 49:888-99, 1959.
211	McCaman M W & Robins E. A fluorimetric method for the determination of phenylalanine in serum. <i>J. Lab. Clin. Med.</i> 59:885-90, 1962.
160	Robins E & Guze S B. Classification of affective disorders: the primary-secondary, the endogenous-reactive, and the neurotic-psychotic concepts. (Williams T A, Katz M M & Shield J A, eds.) <i>Recent advances in the psychobiology of the depressive illnesses</i> . Washington, DC: US Government Printing Office, 1972. p. 283-93.
154	Saghir M T & Robins E. <i>Male and female homosexuality; a comprehensive investigation</i> . Baltimore, MD: Williams & Wilkins, 1973. 341 p.
150	Spitzer R L, Endicott J & Robins E. Clinical criteria for psychiatric diagnoses and <i>DSM-III</i> . <i>Amer. J. Psychiat.</i> 132:1187-92, 1975.
147	Robins E & Guze S B. Establishment of diagnostic validity in psychiatric illness: its application to schizophrenia. <i>Amer. J. Psychiat.</i> 126:983-8, 1970.
123	Purtell J J, Robins E & Cohen M E. Observations on clinical aspects of hysteria. A quantitative study of 50 hysteria patients and 156 control subjects. <i>J. Amer. Med. Assn.</i> 146:902-9, 1951.
114	Stokes P, Stoll P M, Koslow S H, Maas J W, Davis J M, Swann A C & Robins E. Pretreatment DST and hypothalamic-pituitary-adrenocortical function in depressed patients and comparison groups: a multi-center study. <i>Arch. Gen. Psychiat.</i> 41:257-67, 1984.
101	Hirsch H E & Robins E. Distribution of gamma-aminobutyric acid in the layers of the cerebral and cerebellar cortices: implications for its physiological role. <i>J. Neurochem.</i> 9:63-70, 1962.

During the 1960s, while Robins was still active in studies of the brain and central nervous system, a new issue in psychiatry attracted his attention—the problem of vague descriptions of psychiatric disorders.

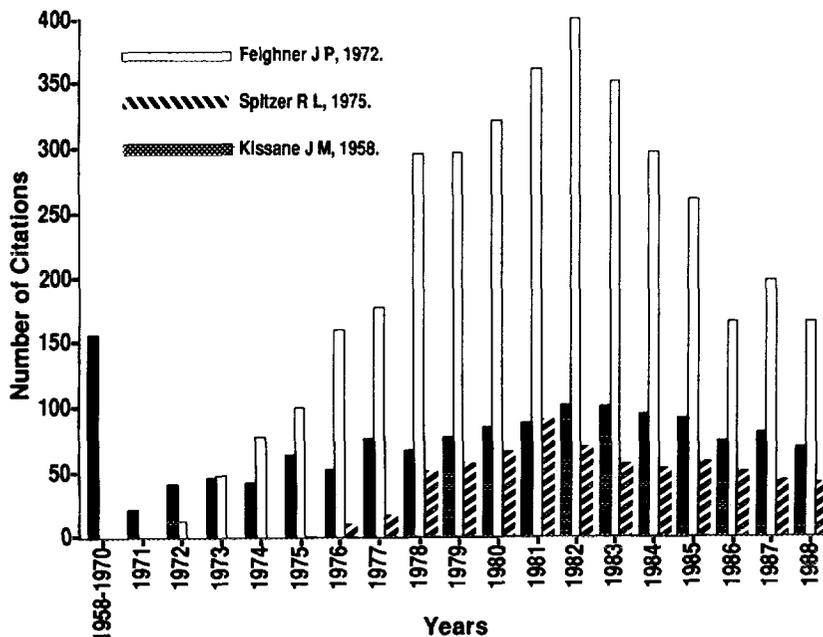
The Search for Sound Diagnostic Criteria

One of the main problems of psychiatry has been how to assess the validity of psychiatric diagnosis. In the 1960s psychiatric diagnosis was believed by many to be so unreliable as to be factually unsound (due to less-than-reasonable reliability). But some psychiatric researchers believed that diagnostic reliability was achievable—if the criteria were clearly specified and the validity of the diagnostic categories could be assessed. In 1970 Robins and Samuel B. Guze, professor of psychiatry, Washington University School of Medicine (who is also co-editor of the journal *Psychiatric Develop-*

ments), published a paper that proposed five indirect indicators for assessing the validity of psychiatric diagnosis.¹⁷ Their paper envisioned that assessing validity was achievable because clearly defined diagnostic criteria referred to in the paper could be applied reliably. Specific criteria appeared two years later in a paper entitled “Diagnostic criteria for use in psychiatric research,” commonly known as the “Feighner criteria” (so named after the first author on the paper).¹⁸ Robins considers this paper one of his two most important publications.⁸ Figure 1 is a graph of Robins’s most important (as well as most-cited) work, his 1958 histochemical classic, and a third *Citation Classic* work that will be discussed in the next section.

The “Feighner criteria” specified the symptoms that characterized a disorder, as well as the number of symptoms that had to be present and by what age and with what

Figure 1: Year-by-year distribution of citations received by three of E. Robins's most-cited works.



severity and frequency. With over 3,700 explicit citations, this paper is not only the most-cited work from the *Archives of General Psychiatry*, but is also the most-cited paper published in the field of psychiatry. Indeed, recently in *CC*, a *Citation Classic* commentary by John P. Feighner, Department of Psychiatry, University of California, San Diego, has addressed these issues.¹⁹ Not surprisingly, the second most-cited paper for this journal is Robins's 1978 paper on research diagnostic criteria.²⁰

Improving the "Feighner Criteria"

The "Feighner criteria" were widely adopted by clinical researchers, but some of the psychiatric disorders needed further changes to their identifying criteria, as well as the addition of categories not included in the original Feighner paper. This need resulted in the publication in 1975 of the booklet *Research Diagnostic Criteria (RDC)*. In a *Citation Classic* commentary on this work, coauthor Robert L. Spitzer, Biometrics Research, New York State Psychiatric Insti-

tute, New York, talks about the worldwide effect of this publication.

The true historical significance of our article was that it heralded the way for the inclusion of specified diagnostic criteria for virtually all of the over 200 specific mental disorders included in the third revision of the *Diagnostic and Statistical Manual of Mental Disorders (DSM-III)*, published in 1980.... *DSM-III* not only changed American psychiatry, but with the inclusion of diagnostic criteria in the mental disorders chapter of the... World Health Organization's [WHO] International Classification of Diseases, psychiatry throughout the world has been changed.²¹

According to Shen, citations to the Feighner criteria paper and *RDC* booklet have been superseded by the *DSM-III* manual (and its 1986 revision, *DSM-III R*) in all its forms. These are now the premier reference works on the subject.¹

Suicide and Depression

Robins has long been interested in depression and suicide. His earliest paper on sui-

cide appeared in 1954,²² while his most recent work was published just three years ago.²³ Suicide may be an uncomfortable subject, but I think that the study of the phenomenon is of fundamental importance. Since 1987 over 500 papers on suicide have been published. In an earlier essay, the topic of suicide in children was discussed.²⁴

Suicide Studies

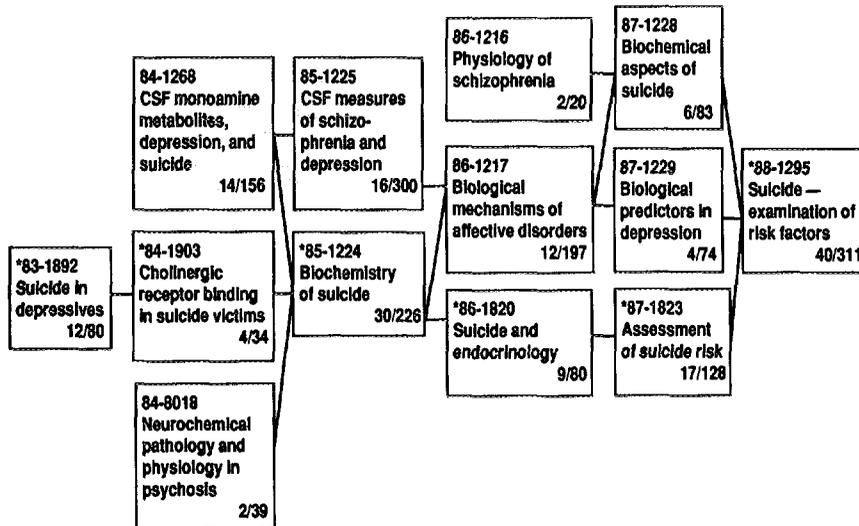
Robins considers that the second of his two most important publications⁸ is the book entitled *The Final Months: A Study of the Lives of 134 Persons Who Committed Suicide*.²⁵ This work is core to two of the research fronts shown in Figure 2. This book was derived from his *Citation Classic* article on this same group of suicides.²⁶ This paper has been core to this field for many years. In a *Citation Classic* commentary, Robins himself writes about the vagaries of trying to conduct a meticulous study on this emotional subject.

On the very first interview...we spoke with the husband of the suicide subject and, although he invited us inside his living room, he remained standing and never offered us chairs. So all of us remained

standing throughout the interview, which lasted three hours.... On another occasion, when [one of Robins's colleagues] arrived, by appointment, to a survivor's home, he was grabbed by two policemen who leapt out of a closet to arrest him just as he began his questioning. Fortunately, he was able to convince them of his legitimate purpose and thus avoid jail.... I think I can see why [the paper] has become so often cited—because of the non-selection of suicide subjects, because of the emphasis on prevention, and because we presented a good many new statistics as to age, sex, length of illness, hospitalization, communication of intent, and diagnosis.²⁷

Whether it has been neurochemistry studies, diagnostic criteria, or suicide, citations to Robins's published research indicate that his contributions were vital, even ground-breaking, for each of these subspecialties. But what of the impact of his work on the field of psychiatry as a whole? Many psychiatrists and researchers consider that influence to have been central. In the opinion of long-time colleague Guze (who has just stepped down from administrative duties as head of the Department of Psychiatry [1975-1989] and vice-chancellor of Washington University Medical Center): "I think

Figure 2: Historiograph tracing research in biological psychiatry of suicide. Numbers of core/citing papers are indicated at the bottom of each box. Asterisks (*) indicate research fronts to which E. Robins is a core author.



he had a profound effect on the field because early on in the United States, he was one of the few psychiatrists who argued about the central importance of improving our diagnostic system. From my perspective, this is a basic step in the advancement of any branch of medicine, and certainly in psychiatry."²⁸

Lee N. Robins: Eli's Well-Cited Spouse

It is not often that a spouse of a citation laureate is also well cited. Lee N. Robins, a psychiatric epidemiologist with a PhD in sociology, is also a professor of psychiatry at Washington University School of Medicine. She has been a consultant in psychiatric epidemiology for many foreign countries, including Taiwan, the Republic of South Korea, and New Zealand. She is well traveled—for instance, she participated in the field trials of WHO's Composite International Diagnostic Interview in 1987.

A thumbnail biographical sketch of Lee: she received her BA in 1942 from Radcliffe College, Cambridge, Massachusetts; received her PhD from Harvard University, Cambridge, and Radcliffe in 1951; and was elected to Sigma Xi. She is a member of many societies and associations including the Institute of Medicine, National Academy of Sciences, 1977 to present; the American Psychopathological Association (president, 1986-1987); and the American College of Neuropsychopharmacology.

Her more than 90 publications listed in ISI[®] databases have been cited in over 2,460

research papers. Her book, *Deviant Children Grown Up: A Sociological and Psychiatric Study of Sociopathic Personality*,²⁹ has been cited about 900 times. Her 1981 paper "National Institute of Mental Health diagnostic interview schedule—its history, characteristics, and validity"³⁰ has received about 560 citations and is already a *Classic*. The topics of Lee Robins's papers are wide-ranging, among them are suicide, substance abuse among adolescents and Vietnam war veterans, alcoholism, and antisocial disorders and behavior in children. Table 2 lists her most-cited works.

Conclusion

With nearly 40 years worth of publications experience behind him, Eli Robins has attained a rare status among researchers. His record demonstrates once again that the major figures central to a scientific field usually publish a prodigious number of high-quality, high-impact papers.

And what of the field of biological psychiatry? Robins thinks that the field at present is still at a nascent stage and that the discovery of specific therapies for any functional psychiatric illness is still a realization for the future.⁸ As it turns out, my connections to the field of biological psychiatry are somewhat tenuous but nevertheless are real. For this reason I have been asked to be a keynote speaker at the May 1990 celebration of the 20th anniversary of the journal *Biological Psychiatry* at the annual meeting of the Society of Biological Psychiatry that will be held in New York. I will help orga-

Table 2: L.N. Robins's five most-cited papers. Data are from the *SCI[®]/SSCI[®]*, 1945-1988. A = number of citations. B = bibliographic data.

A	B
883	Robins L N. <i>Deviant children grown up: a sociological and psychiatric study of sociopathic personality.</i> Huntington, NY: Krieger, 1974. 351 p.
558	Robins L N, Helzer J E, Croughan J & Ratcliff K S. National Institute of Mental Health diagnostic interview schedule—its history, characteristics, and validity. <i>Arch. Gen. Psychiat.</i> 38:381-9, 1981.
348	Robins L N, Helzer J E, Weissman M M, Orvaschel H, Gruenberg E, Burke J D & Regier D A. Lifetime prevalence of specific psychiatric disorders in three sites. <i>Arch. Gen. Psychiat.</i> 41:949-58, 1984.
110	Robins L N & Murphy G E. Drug use in a normal population of young Negro men. <i>Amer. J. Public Health</i> 57:1580, 1967.
106	Robins L N. Sturdy childhood predictors of adult antisocial behavior—replications from longitudinal studies. <i>Psychol. Med.</i> 8:611-22, 1978.

nize a plenary session on scientific communication. Participating in the meeting will be my colleague Williamina Himwich. She was my mentor at the Welch Medical Library Indexing Project,³¹ and through her, I met her husband, Harold (who is certainly one of the fathers of organic psychiatry and was the eighth president of the Society of Biological Psychiatry in 1954).

As a relevant footnote on my connection to biological psychiatry, it was through the Welch Project that I met Theodore Herdegen

of SmithKline & French (SK&F) laboratories. He invited me to Philadelphia to consult for SK&F in 1954 in order to create a machine-based index to the literature of Thorazine.³¹

* * * * *

My thanks to C.J. Fiscus and Peter Pesavento for their help in the preparation of this essay.

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