



Jonathan O. Cole, MD (1925–2009): Innovator in Clinical Psychopharmacology and of the ECDEU/NCDEU Tradition

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To honor the 50th anniversary of the ECDEU/NCDEU meetings, *The Journal of Clinical Psychiatry* is publishing a series of articles reviewing the past and anticipating the future in clinical psychopharmacology. This note is designed to provide a brief account of Jonathan Cole's key role in initiating the meeting that has become the New Clinical Drug Evaluation Unit (NCDEU).

Jonathan O. Cole, MD, was a unique leader in the creation of the field of clinical psychopharmacology. Obituaries from the American College of Neuropsychopharmacology¹ and the Collegium Internationale Neuro-Psychopharmacologicum,² the leading organizations in the field, and a memorial celebration of his life in September 2009 paid tribute to his seminal contributions. He was a distinguished administrator—Chief of the Psychopharmacology Service Center (PSC) at the National Institute of Mental Health (NIMH) and Superintendent of the Boston State Hospital. He was a much revered teacher of generations of residents at the McLean Hospital in Boston, Massachusetts. His textbooks, written in collaboration with Alan F. Schatzberg, MD, communicated these teachings to countless individuals who never had the opportunity to

learn directly from his prodigious knowledge of the field.³ He was an imaginative and rigorous researcher. One of his early publications on treatment of schizophrenia (1964) was formally authored by the National Institute of Mental Health Psychopharmacology Service Center Collaborative Study Group and is indexed under "Anonymous" by the National Library of Medicine.⁴ This was the first in a series of seminal multicenter collaborative studies he initiated at the PSC.^{5,6} His later contributions to the treatment of depression with medications remain as valid and insightful today as when they were published.⁷

In 1960, as Chief of the PSC, Jon Cole was using a variety of means to "jump start" the then nascent field of clinical psychopharmacology. As he recounted the story later, one strategy was to claim research already being supported by NIMH as clinical psychopharmacology.⁸ A lasting contribution was to establish the Early Clinical Drug Evaluation Unit (ECDEU) program at universities and clinical centers around the country. Started with 15 grantees in 1950, the program was designed to provide open-ended support that would allow investigators to design and conduct research to examine the new medications quickly as they became available. Given that the discovery of chlorpromazine as a medication to treat psychosis had been serendipitous, the idea was that researchers poised to translate new discoveries into treatment through observation and rapid initiation of experiments would speed discovery into practice. The

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studies conducted by the ECDEU investigators were often small; sometimes they were placebo controlled and sometimes open. They relied heavily on the clinical acumen and impressions of the investigators to document both the efficacy and the safety of the drugs being studied. The leaders of these units came together once or twice a year for closed meetings to share their findings (and problems) in conducting research in this new area. From its inception, the ECDEU program was international; Pierre Deniker, MD, of France, one of the discoverers of the potential of chlorpromazine as a psychiatric treatment, was one of the original ECDEU investigators. These small, closed meetings were the beginning of the ECDEU/NCDEU tradition. As recounted by Cole at the 25th anniversary of the NCDEU meeting,⁸ the meeting gradually expanded. Pharmaceutical company representatives were invited to attend sessions at which their drugs were being discussed, investigators who no longer had support continued to attend, the US Food and Drug Administration sent representatives, and international investigators joined the meeting.

In 1976, the meeting was renamed the NCDEU (New Clinical Drug Evaluation Unit) Meeting. Many of the important characteristics embedded in the evolving program designed by Jonathan Cole continue in the renamed meeting. These include the early recognition of the value of multicenter studies⁴⁻⁶; the NCDEU meeting as a venue that supports partnership and collaboration among academia, government, and industry; and the recognition of the NCDEU meeting as the setting to report and discuss methodological advances.

At the 25th anniversary of ECDEU/NCDEU, Jon Cole⁸ said, "If I am partially responsible for the development of the unique and excellent program, I am glad." That statement reflects his characteristic modesty about his accomplishments. To the contrary, the ECDEU program was his unique vision to establish a community of investigators dedicated to development of a new field. The ECDEU/NCDEU meeting represents a continuing demonstration of his accomplishment in providing a focused and open forum. The expanding community of academic researchers, pharmaceutical industry

scientists and drug developers, United States and international regulatory authorities, and others involved in medication development in psychiatry continues to meet to report on findings, discuss methodological advances, and interact informally. The meeting now includes a special program dedicated to support and development of new investigators in the field. His spirit of modesty, honest, and unpretentious communication and the single agenda of the pursuit of new knowledge established a tone for the meeting that remains the NCDEU goal going forward, despite the more complex array of problems and constituents. NCDEU at 50 represents a fitting legacy to Jonathan Cole's early vision.

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