# ELECTROCONVULSIVE THERAPY

Richard Abrams

FOURTH EDITION

# Electroconvulsive Therapy

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## Fourth Edition

Richard Abrams, M.D.

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*For Trudy, again and always*

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# PREFACE

Electroconvulsive therapy (ECT) entered the new millennium as the oldest surviving biological treatment in psychiatry—it is now 54 years old and still going strong. Thirty-four years after the introduction of imipramine, the first antidepressant drug, no medication has been found that equals ECT in antidepressant potency, which is doubtless why more than 100,000 patients will receive ECT this year in the United States alone. Of these, the overwhelming majority will be major depressives, of whom a remarkable 85%–90% will respond with marked improvement or full recovery when the treatment is properly administered.

For the first time since 1988 (the year this book first appeared) I have added an entirely new chapter, on nonconvulsive transcranial magnetic stimulation (TMS), a new technique for electrical stimulation of the brain. Although this treatment method has not yet been approved for use in the United States, it has been the subject of numerous carefully-controlled studies, and when it ultimately receives approval it will be the only other biological treatment in psychiatry besides lithium to have its efficacy demonstrated by double-blind, placebo-controlled studies prior to its introduction for general use.

In preparation for this 4th edition, I reviewed all of the more than 1000 articles on ECT published since the previous edition, as well as almost 500 articles on the psychiatric use of TMS since this method was first introduced. Of these approximately 1500 articles the 200 most important ones have been analyzed in detail in the present volume.

It is far too early to specify the relative indications, advantages, and disadvantages of the two electrical stimulation methods—one convulsive, the other nonconvulsive—as years of general clinical experience with nonconvulsive TMS will be needed before such judgments can reliably be made. Although the history of biological therapies in psychiatry is strewn with the graves of nonconvulsive electrical stimulation methods, my reading of the literature leads me to believe that nonconvulsive TMS will not share this fate.

Like Man, ECT is at the end of an evolutionary line, but, also like Man, rather than facing imminent extinction it is flourishing. I do not see this millennium bringing any exciting new advances in ECT instrumentation or technique—indeed, it is hard to see how the treatment might be further improved at this point other than through refinements in patient selection, prediction of response, and more effective dissemination of knowledge. I view this as a satisfactory state of events for patients everywhere.

*Chicago, Illinois* R.A.

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# Electroconvulsive Therapy

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# 1

# History of Electroconvulsive Therapy

The traditional litany on the history of the medical uses of electricity, beginning with the Roman use of electric fish to treat headaches (Harms, 1956; Sandford, 1966; Brandon, 1981), is simply beside the point; electroconvulsive therapy (ECT) evolved solely as a result of Ladislaus von Meduna's original investigations on the effects of camphor-induced convulsions in schizophrenic patients. It is the chronology of the medical (and specifically, psychiatric) uses of convulsions that provides the appropriate historical perspective to his work.

This chapter draws extensively, and often without specific attribution, from the excellent historical reviews of the subject by Mowbray (1959), Sandford (1966), Fink (1979, 1984), Brandon (1981), Kalinowsky (1982, 1986), Endler (1988), and Endler and Persad (1988); from Cerletti's (1950) personal recollections; from the English translations of the autobiography of Meduna (1985); from Accornero's (1988) eyewitness account of the discovery of ECT; and from my own numerous conversations over 25 years and my published interview with Lothar Kalinowsky (Abrams, 1988a).

According to Mowbray (1959), Paracelsus, the 16th-century Swiss physician and alchemist, ". . . gave camphor by mouth to produce convulsions and to cure lunacy." The first published citation, however, is generally attributed to Leopold von Auenbrugger, the originator of the percussion method of examining the heart and lungs, who, in 1764, treated "mania vivorum" with camphor every 2 hours to the point of convulsions (Mowbray, 1959; Sandford, 1966). The next publication (and the first in English) was by one Dr. Oliver, whose case report in 1785 in the *London Medical Journal* described the successful use of camphor in a patient who had been "seized with mania with few intervals of reason" (Kalinowsky, 1982). Fifteen minutes after a single dose of camphor, the patient had a grand mal seizure and awakened in a rational state. The case was later cited by Burrows in his 1828 textbook, *Commentaries on Insanity*:

> In a case of insanity, where two scruples of camphor were exhibited, it produced a fit and a perfect cure followed. When given to the same gentleman two years afterwards, upon a relapse, i.e., a recurrence, it had the same effect, even to an alarming degree; but the patient did not, as before,

> progressively recover from a single dose, for it was repeated afterwards in smaller doses of ten grains.

Next came Weickhardt, a councilor of the Russian Imperial College, who reported in a Viennese textbook in 1798 that he had obtained cures in 8 out of 10 cases of mania with camphor-induced seizures (Mowbray, 1959; Sandford, 1966; Meduna, 1985). The last citation given, before the method fell into obscurity for almost a century, is from an unpublished 1851 manuscript in Hungarian by a Dr. Szekeres, who described the technique for treating mania recommended by a Dr. Pauliczky, who gave

> . . . camphor, beginning with a dose of 10 grains and increasing the dosage by five grains daily up to 60 grains a day. After this the patient will have dizziness and epileptic attacks. When he awakes from these, his reasoning will return. (Sandford, 1966).

An English translation of Meduna's autobiography (1985) reveals that none of this work was known to Meduna until a year after he had published his first report on induced seizure therapy in schizophrenia, at which time a Hungarian psychiatrist accused him of plagiarizing Weickhardt's 18th-century ideas. Stung by the unfairness of the accusation, which was subsequently published in a Hungarian medical journal, Meduna says

> . . . I began to read old manuscripts and found that the convulsive method had been used 20 years before Weickhardt by Auenbrugger . . . I found other reports: Simmon, whose nationality I could not ascertain, used camphor to produce epileptic attacks to cure insanity; as did Pauliczky, a Polish scientist of the 18th century, and a Dr. Laroze of Paris, probably at the beginning of the 19th century.

Meduna's decision to treat schizophrenic patients by inducing epileptic seizures stemmed directly from the results of neuropathologic studies (Meduna, 1932) in which he observed an "overwhelming and almost crushing growth of the glial cells" in the brains of epileptic patients compared with an equally evident lack of glial-cell growth in the brains of schizophrenic patients. He thought these observations to be evidence of a "biological antagonism" and decided to pursue this line of inquiry further. He was encouraged in this approach by a friend and colleague, Dr. Julius Nyirö, who had observed that epileptic patients had a much better prognosis if they were also diagnosed as having schizophrenia; Dr. Nyirö actually had attempted (unsuccessfully) to treat epileptic patients with injections of blood from schizophrenic patients (Nyirö and Jablonszky, 1929). Not mentioned by Meduna in his autobiography or in Fink's (1984) historical review is Mowbray's (1959) assertion that these earlier authors also had reported using pentylenetetrazol to produce convulsions in their schizophrenic patients.

After unsatisfactory animal trials of strychnine, thebaine, nikethamide, caffeine, brucine, and absinthe (!), Meduna learned from the International League Against Epilepsy that one of its officers had written a monograph

about producing artificial convulsions with camphor monobromide. Choosing the less toxic simple camphor, Meduna successfully produced experimental epilepsy in guinea pigs (Meduna, 1934). Two months later, on January 23, 1934, Meduna injected camphor in oil into a schizophrenic patient who had been in a catatonic stupor for 4 years, never moving, never eating, being incontinent, and requiring tube feeding.

> After 45 minutes of anxious and fearful waiting the patient suddenly had a classical epileptic attack that lasted 60 seconds. During the period of observation I was able to maintain my composure and to make the necessary examinations with apparent calm and detached manner. I examined his reflexes, the pupils of his eyes, and was able to dictate my observations to the doctors and nurses around me; but when the attack was over and the patient recovered his consciousness, my legs suddenly gave out. My body began to tremble, a profuse sweat drenched me, and, as I later heard, my face was ashen gray.

Thus, convulsive therapy was born. The patient went on to full recovery after a short series of seizures, as did the next 5 patients treated; by the end of a year, Meduna had collected results, which he then published, from a sample of 26 schizophrenic patients: 10 who recovered, 3 who enjoyed good results, and 13 who did not change (Fink, 1984). Meduna soon replaced camphor with the chemically related pentylenetetrazol (Cardiazol, Metrazol), which he preferred because of its solubility and rapid onset of action.

Pentylenetetrazol convulsive therapy spread rapidly throughout Europe; however, the extremely unpleasant sensations induced in conscious patients during the preictal (or myoclonic) phase of the treatment soon led investigators in Rome to seek alternative methods of induction (Cerletti, 1956). Von Fritsch and Hitzig had already demonstrated that epileptic seizures could be produced in dogs by electrical stimulation of the exposed brain, and von Schilf had suggested the feasibility of producing convulsions in humans with extracerebral electrodes (Mowbray, 1959; Sandford, 1966).

In 1934, Chiauzzi, working in Cerletti's laboratory, produced seizures in animals by passing a 50-Hz, 220-V stimulus for 0.25 seconds across electrodes placed in the mouth and rectum; in May of 1937, Bini, another of Cerletti's assistants (and himself a fine clinician who later wrote a leading Italian textbook on psychiatry), reported similar animal studies at an international meeting in Munsingen, Switzerland, on new therapies for schizophrenia. About 50 of the dogs thus stimulated died, and, according to Kalinowsky (1986), it was Bini who first realized the danger of passing current through the heart with oral-rectal electrodes and who demonstrated the safety of applying both electrodes to the temples of the dogs he was studying. Bini confirmed this during a visit with another of Cerletti's assistants, Fernando Accornero, to the Rome slaughterhouse where, they had been told, pigs were killed by electricity. In actuality, the pigs were first convulsed by an electrical stimulus to the head and then dispatched while they were comatose. The fact that such transcerebral electrical stimulation did not actually kill the

pigs provided encouragement for continued attempts by Cerletti and Bini to define the electrical stimulus parameters that might be safe and effective for application to humans (Cerletti, 1950; Accornero, 1988).

This goal was soon accomplished, and the first patient to receive electroconvulsive therapy was a 39-year-old unidentified man found wandering about the train station without a ticket. He was delusional, hallucinating, and gesticulating, and alternated between periods of mutism and incomprehensible, neologistic speech (Cerletti, 1940, 1956).

After he was observed for several weeks, he was diagnosed as having schizophrenia; he received his first treatment on 11 April 1938. Present were Cerletti, Bini, and only one or two others. An initial stimulus of 80 V for 0.25 seconds was subconvulsive. Two subsequent stimuli of the same voltage, but with durations of 0.5 and 0.75 seconds each, were administered several minutes apart (Bini, 1938), despite the statement of the patient that he did not want a third stimulus. No effect was observed on the patient, and no further attempts to induce a seizure were made that day.

A few days later, a second attempt was made, this time with the entire research team in attendance. Again the initial stimulus was unintentionally subconvulsive (80 V for 0.2 seconds): The patient exhibited a brief myoclonic reaction without loss of consciousness and began to sing loudly. He lapsed into silence while those in attendance discussed what to do next, and then solemnly intoned clearly and without jargon, "Not again, it's murderous!" Despite this ominous warning, which understandably caused some apprehension among those present, the patient was restimulated at 110 V for 0.2 seconds and a grand mal seizure ensued. After awakening,

> The patient sat up of his own accord, looked about him calmly with a vague smile, as though asking what was expected of him. I asked him: "What has been happening to you?" He answered, with no more gibberish: "I don't know; perhaps I have been asleep."

The patient's eventual full recovery with a course of 11 ECTs was dramatic, but not the important contribution made by the Italian investigators —the striking effectiveness of induced convulsions had already been shown many times since 1934—rather, it was the demonstration that such convulsions could be induced safely, reliably, and inexpensively by electrical means, that constituted the technical advance for which Cerletti and Bini justly achieved fame, and that stimulated the rapid spread of this uniquely effective therapeutic modality.

Cerletti and Bini (1938) published their results a few months later in an Italian journal, but Bini (1938) enjoyed the first English-language publication on the topic when his paper on "Experimental Researches on Epileptic Seizures Induced by the Electric Current" was published in a supplement to the *American Journal of Psychiatry*. (The topic was his research in dogs, but he alluded to the first use of ECT in man in the cryptic sentence: "These experiments have so far been conducted almost exclusively in animals.")

## Electroconvulsive Therapy in the United States

Present during the second ECT administered several days after the first was Lothar B. Kalinowsky, a young German psychiatrist who had left Berlin for Rome in 1933 when Hitler came to power. Along with Bini, Accornero, and several other associates, Kalinowsky was a member of a research team that investigated the multiform effects of ECT on the organism and eventually published its results in a special issue of an Italian journal of experimental psychiatry (Cerletti, 1940). Kalinowsky left Rome with his wife in 1939—one jump ahead of the Nazis (his mother was Jewish)—and traveled extensively in Switzerland, France, Holland, and England before emigrating to the United States in 1940, where he received an appointment at the New York State Psychiatric Institute. While in England, he and Dr. J. Sanderson McGregor treated some patients at the Netherne Hospital at Coulsdon with a device constructed according to plans Kalinowsky brought with him from Rome; the results of this work provided the basis for the first English-language publications on the clinical use of ECT (Kalinowsky, 1939; Shepley and McGregor, 1939).

Kalinowsky was not the first to give ECT in the United States as all of the possessions that he had shipped, including his ECT device, were delayed for 10 years by the war. That honor belongs to Drs. Renato Almansi and David Impastato, who administered the first treatment at Columbus Hospital in New York City in early 1940, with a device Almansi had obtained in Rome (Almansi and Impastato, 1940). A few months later, Dr. Douglas Goldman—who subsequently invented nondominant unilateral ECT—demonstrated ECT at the annual meeting of the American Psychiatric Association (Fink, 1987). Later that same year, Kalinowsky—who by then had had another device built—started giving ECT at the Psychiatric Institute, which, because of its academic reputation as a research center, soon became a focal point for the spread of the new treatment method in this country.

Among the postwar generation of physicians who became interested in studying the ECT process from a scientific point of view, none was more influential than Dr. Max Fink, a neurologist by training, whose rapidly-developing interest in brain-behavior relationships subsequently led him to obtain residency training in psychiatry and certification in psychoanalysis.

During his medical student and internship days, Dr. Fink actively participated in two research trials of note. In the first, as a medical student at Bellevue Hospital, he administered intravenous infusions of the dye trypan red to Huddie (Leadbelly) Ledbetter in an unsuccesful experimental attempt to treat the amytrophic lateral sclerosis (ALS)[1] that eventually killed the noted folksinger (who, ironically, had already survived two death sentences for murder, pardoned in each instance after singing for the prison warden). In the second trial, as an intern at Morrissania Hospital, Dr. Fink participated in one of the earliest comparisons of sulfadiazine with the new antibiotic, penicillin, for the treatment of empyema secondary to pneumonia. It soon

became apparent that penicillin was indeed a miracle drug, and when a severely ill young mother of two chanced to be assigned to receive sulfadiazine, Dr. Fink gave her penicillin instead, resulting in a rapid cure. When Dr. Eli Rubin,[2] the chest surgeon conducting the study, detected the switch, he threw Dr. Fink off his service.

After medical school and internship, Dr. Fink was called to active duty in the Army, where, after 4 months' training at the School of Military Neuro-Psychiatry, he spent the remainder of his military career as Chief of Psychiatry at a military hospital.

By the time he had completed his residency in Neurology at Bellevue in 1951, Dr. Fink had performed the first carotid angiogram ever done at that institution, confirming a diagnosis of subdural hematoma (Fink and Green, 1950), submitted an article on the results of 102 consecutive carotid angiograms (Fink and Stein, 1952), and published, with his teacher, Dr. Morris Bender, a seminal article on the face-hand test (Fink, Bender, and Green 1951), a neurological "soft sign" assessment that was to become a standard part of every neurological examination for decades.

He then took a residency in Psychiatry at Hillside Hospital from 1951 to 1952, and the following year did a fellowship with Dr. Bender, obtained certification in psychoanalysis at the William Allanson White Institute (which he had attended since 1948), published his first psychoanalytic paper —one of the earliest applications of statistical methods to psychoanalytic hypotheses—(Tarachow and Fink, 1953), and opened an office in Great Neck, New York, for the practice of neurology. His career in private practice (which included occasionally administering ECT, unassisted, to patients in their homes) lasted only a few years, however, as he was appointed Chief of the ECT Service at Hillside Hospital in 1954, and Director of the Department of Experimental Psychiatry there in 1958, a research division created expressly for him. At this point he entered academic medicine full-time to more effectively pursue his several ongoing research grants.

His first papers in electroencephalography (EEG) appeared in 1957, describing the EEG effects of the CNS stimulant megimide (Green and Fink, 1957), and the relation of ECT-induced EEG delta activity to treatment response in ECT (Fink and Kahn, 1957), the latter a classic in the field, its results abundantly confirmed 40 years later (Sackeim et al., 1996). Among the first to recognize the importance of EEG as a research tool for the burgeoning fields of both psychopharmacology and ECT, Dr. Fink also pioneered the application of computer-analytic quantitative EEG methods in his studies of ECT and psychopharmacology.

Because a simple listing of his research accomplishments would occupy the rest of this chapter, and would, in any event, be incapable of conveying the essence of Max Fink's importance to the field of ECT, I am reproducing here an editorial I wrote a number of years ago for a special Festschrift issue of *Convulsive Therapy* honoring him as founding editor of the journal (Abrams, 1994b):

This, the first Festschrift issue of *Convulsive Therapy*, honors Max Fink, founder and Chief Editor of the journal from its inception in 1985 through his retirement as editor in 1993.

Max Fink's first—and, for me, foremost—contribution to the field was his introduction of the scientific method into ECT research in the US in the late 1950's, during his tenure at Hillside Hospital. At a time when many of the leading ECT practitioners in this country were purveying their anecdotal and often self-serving claims for one or another particular treatment method, Max was conducting and publishing carefully-controlled studies on virtually every aspect of ECT: Clinical, electrophysiological, pharmacological, neuropsychological, biochemical, psychosocial, and, of course, theoretical. For example, the 1956 paper of Korin, Fink and Kwalwasser on the relation of changes in memory and learning to the clinical efficacy of ECT was arguably the first neuropsychological study of ECT to be conducted with modern methodology, and remains a classic in the field.

When ECT fell into desuetude following the introduction of psychopharmacological agents, Max indefatigably stalked the corridors of power in the American Psychiatric Association, National Institutes of Mental Health, and Congress Internationale Neuropsycho-Pharmacologium, collaring the movers and shakers of psychiatry, shaming them into including a section on ECT in their programs. When the parvenu geniuses of psychopharmacology tolled the death-knell of ECT, who but Max (himself a leading psychopharmacologist) was there to remind them that their report of its demise was premature? When the first American Psychiatric Association Task Force on ECT was convened in 1978, who but Max was capable of initiating its Chairman into the scientific basis of this apparently arcane therapy?

Probably the determining event for the eventual healthy survival of ECT was not so much the publication of the 1978 American Psychiatric Association Task Force Report as the appearance a year later of Max' magnum opus: *Convulsive Therapy: Theory and Practice*, the first U.S. textbook devoted entirely to ECT. Until that time, the several editions of Lothar Kalinowsky's textbook on somatic treatments had been the standard in the field, but that text's inclusion of considerable material on psychosurgery, insulin coma, and miscellaneous other somatic treatments (many of them already long-defunct)—as well as a long and distractingly Europeanized section on psychopharmacology—had diluted the impact of the chapters on ECT, which, were in any case largely anecdotal and tended to cite uncritically the conclusions of most of the papers published on the subject.

In contrast, Max' volume (which essentially constituted the basis for his later receipt of the *Anna Monika* award) was mainstream and data-oriented, presenting in full scientific detail his more than 20 years of studies on the nature of the ECT process, as well as extensive critical evaluations of the works of others. The book remained in print for over a decade, during which time it became the undisputed bible of ECT, influencing practice in virtually every corner of the globe.

Now that the number of papers published on ECT once again swells annually—due in no small measure to Max' stewardship of *Convulsive Therapy*—and the media has perceptibly toned down its strident attacks on any physician callous enough to subject his patients to the barbaric torture of ECT, it is easy to forget the time, not so long ago, when Max virtually single-handedly nursed ECT back to life while the rest of the psychiatric community looked the other way.

### *The Anti-Electroconvulsive Therapy Lobby: Scientology*

Absent Scientology there would hardly be an organized anti-ECT movement in the United States or anywhere else. According to Burton (1991), Scientology's vitriolic attacks on psychiatry, psychopharmacology, and ECT are financially motivated:

> Scientologists' central belief is that human beings have a soul-like entity called a "thetan" that is perfect and travels from galaxy to galaxy. Their goal is to help their thetans get rid of something called engrams—essentially bad memories. To this end, Scientology developed a lie-detector-like device called an E-meter, which is used to treat mental problems often at hundreds of dollars per session. Psychiatrists consider these "treatments" quackery.

Founded in the late 1940s by science-fiction writer L. Ron Hubbard (who reportedly died in hiding in 1986 after 5 years of successfully evading an Internal Revenue Service indictment for tax fraud), Scientology portrayed itself as a religion despite an Internal Revenue Service ruling that stripped the mother "church" of its tax-exempt status[3] by arguing that it was more a business than a church (Behar, 1991; Burton, 1991). A *Time* magazine cover story describing the self-styled church as "a hugely profitable global racket that survives by intimidating members and critics in a Mafia-like manner," further noted that "in the early 1980's, eleven top Scientologists, including Hubbard's wife, were sent to prison for infiltrating, burglarizing, and wiretapping more than 100 private and government agencies in attempts to block their investigations" (Behar, 1991).

### *The California Legislative Experience*

The disproportionate effectiveness of the anti-ECT lobby is amply demonstrated by the history of the introduction and passage of the highly restrictive Assembly Bill 4481 for legislating ECT use in California (Moore, 1977), as well as the saga described below of the US Food and Drug Administration's unsuccessful effort to reclassify ECT devices (Isaac, 1990; Abrams, 1991b).

California Assembly Bill 4481 was written by a member of the Network Against Psychiatric Assault and presented by California Assemblyman Vasconcellos. It passed with only one dissenting vote and was signed into law by then Governor Ronald Reagan.[4] A successful challenge of AB 4481 was mounted by the International Psychiatric Association for the Advancement of Electrotherapy (now the Association for Convulsive Therapy), leading to replacement of AB 4481 by the somewhat less restrictive AB 1032, which continues in force at this time.[5]

In 1991, the San Francisco Board of Supervisors passed a resolution against the use or financing of ECT (Peterson, 1991). Although the resolution had little practical effect, it provided impetus for the anti-ECT forces to sponsor California Assembly Bill 1817 that, in addition to broadening pa-

tients' rights advocacy, permitted local restrictions on the use of ECT and a ban on its use for patients under 16 years of age. The California Alliance for the Mentally Ill opposed the bill, citing FDA and Alcohol, Drug Abuse, and Mental Health Administration support for the safety and efficacy of ECT. After a public hearing of the Committee in which patients, their families, and the California Psychiatric Association, testified enthusiastically for ECT, the bill was withdrawn for reconsideration the following year, and subsequently died in committee.

Interestingly, although the availability of ECT steadily declined during the 7 years after the enactment of AB 1032, there was little year-to-year variation in its use in California: Approximately 1.1 persons per 10,000 population per year received ECT during 1977–1983 (Kramer, 1985), a figure that is just below the range of the national average of 1.3 to 4.6 per 10,000 when sampled in 1978 (Fink, 1979), but less than the reported 2.42 patients per 10,000 population who received ECT in Massachusetts from 1977 to 1980 (Kramer, 1985).

A subsequent review of the use of ECT in California (Kramer, 1999) covering the decade from 1984 to 1994 found the average annual rate of administration of ECT to be 0.9 per 10,000 population, only marginally below the average for the years 1977–1983. However, the rate recorded for 1994, the last year of the decade studied, was only 0.8 per 10,000 population, suggesting a significant decline since the earlier study. There was no change from the previous period in the number of counties where ECT was available, and a slight increase in the number of facilities offering ECT.

## *Regulation of Electroconvulsive Therapy Devices in the United States*

When the Medical Device Amendment to the Food, Drug, and Cosmetic Act[6] gave the Food and Drug Administration (FDA) regulatory responsibility for medical devices in 1976, FDA placed ECT devices in Class III, which requires manufacturers to provide data demonstrating safety and efficacy of new devices they intend to market. However, because existing ECT devices, as well as those subsequently introduced as "substantially equivalent" to pre-1976 devices were exempted from such premarket approval procedures under a grandfather clause, there was no practical significance to the FDA's action.

In 1978 the FDA recommended reclassifying ECT devices into Class II, which assumes ECT to be both safe and efficacious and requires only that devices meet a performance standard for safety of construction and instructions for use. Under fire from Scientologists and other antipsychiatry activists, the FDA quickly reversed its opinion, placing ECT devices back into Class III in 1979, while simultaneously inviting the American Psychiatric Association (APA) to submit a petition requesting that ECT devices be reclassified to Class II.

The APA procrastinated 3 years before finally filing the petition[7] in 1982, following which the FDA again recommended that ECT devices be reclassified into Class II, but this time contingent on the development of a performance standard.[8] A year later, the FDA published notice of its intent to reclassify ECT devices into Class II, and there the matter stood for the next 7 years while the FDA waffled to the tune of the Scientologists and other anti-ECT activists, despite the fact that various national and international performance standards (e.g., IEC 601) had already achieved worldwide acceptance.

Finally, in 1990, the FDA proposed a definitive rule[9] to place ECT devices in Class II (still, however, contingent on the development of a performance standard) but this time only for devices labeled as intended solely for use in patients with "severe depression," which the FDA defined as DSM-III major depressive disorder with melancholia. (ECT devices intended for use in other conditions, including mania, catatonia, and schizophrenia, were to remain in Class III, requiring manufacturers to undertake enormously expensive controlled trials of safety and efficacy and to seek FDA approval separately for each condition.)

Although the FDA claimed that its decision to severely limit the clinical indication for ECT was "based on its review of new, publicly available, valid scientific evidence," the task force conducting the review included one identified physician, three individuals with non-medical doctorates, and one person without a stated degree, none of whom were psychiatrists or had published on ECT. The 200 articles referenced in their report omitted numerous controlled studies of the use of ECT in nonmelancholic depression, mania, catatonia, and schizophrenia that had appeared in major world journals during the years reviewed. Most egregiously, the FDA report relied mostly on long-outdated studies in support of its decision to exlude nonmelancholic major depression from the approved incidations for ECT (4 of the 5 studies cited were from 1953–1965), while ignoring every single random-assignment, double-blind, sham ECT-controlled study of the modern era that had demonstrated the efficacy of ECT in such patients. Equally flawed was the FDA's justification for excluding from approval for ECT other diagnoses, including especially mania and catatonia.

About this time, in 1990, the House of Representatives, apparently fed up with the FDA's dawdling incompetence, introduced a proposed new section of the Safe Medical Devices Act[10] calling for judicial review of any of the promulgated regulations that were contested—effectively taking the final decision out of the FDA's hands. The Senate followed with its own committee report[11] stating that it was not its intention to require that a performance standard must exist before such Class III devices could be placed in Class II.

Another Senate Report issued in late 1994 required the FDA to complete its reclassification of all pre-amendment Class III devices into classes II or I, or retain them in Class III, by December, 1995, while at the same time authorizing anyone who felt adversley affected by the regulation to petition the US Court of Appeals for a judicial review. A month later, the

FDA announced it would issue an immediate call to all manufacturers of ECT devices to submit a summary of and citation to any data known to them respecting safety and efficacy of their products. The FDA would then be required by law to publish a proposed regulation to reclassify ECT devices to Class II or I or retain them in Class III, providing up to 90 days for public comment before taking final effect.

The call was issued and the responses duly submitted, but nothing further was ever heard from the FDA on the subject—the status of ECT devices in the United States at the time of this writing, 8 years after the 1994 Senate report, remains in the same limbo in which it was placed a quarter-century ago.

Fortunately, this has prevented neither US ECT device manufacturers from introducing new models, nor US psychiatrists from administering the latest forms of ECT according to their best clinical judgment, with one important exception: the FDA has steadfastly refused to allow US doctors to administer the higher ECT dosages required to deliver clinically effective treatment—or even to obtain a seizure—in a significant number of patients (Sackeim, 1991b; Lisanby et al., 1996; Abrams, 2000; Krystal, Dean, and Weiner, 2000), dosage levels that have long been available to psychiatrists in many other countries. Indeed, during the late 1980s, the Royal College of Psychiatrists (1989) issued the requirement that all ECT devices offered in the United Kingdom be able to deliver twice the dosage level presently permitted for ECT devices sold in the United States.

## *Electroconvulsive Therapy Use in the United States*

An analysis of the National Institutes of Mental Health national survey data for the years 1975, 1980, and 1986 showed that the declining use of ECT ended in the 1980s (Thompson,Weiner, and Myers, 1994). In 1986, 36,558 patients received ECT, which represented a decrease from the 58,667 who received ECT in 1975, but an increase over 1980, when 31,514 patients were so treated. Strikingly, recipients of ECT were primarily older white patients in private institutions; patients in state hospital facilities rarely received ECT. The figures presented are doubtless underestimates of the true use, primarily because of sampling error such as chance omission from the sample of a few large-volume ECT centers. The authors estimated that the 36,558 patients treated in 1986 received approximately 300,000 ECTs—equivalent to the number of procedures performed for coronary bypass, tonsillectomy, inguinal hernia, or appendectomy—thus making ECT one of the most common procedures carried out in patients given general anesthesia.

Analyzing data from the American Psychiatric Association Professional Activities survey of 1988–1989, Hermann et al. (1995) found that 1102 psychiatrists reported treating 4398 patients during the previous month. Extrapolating from these results, the authors estimated that 4.9 patients per 10,000 population received ECT annually—a modest increase over the 1978 American Psychiatric Association estimate of 4.4 per 10,000 population—

yielding an estimate of 100,000 patients treated in the United States during 1995. Because ECT is given in virtually every other country of the world —and not infrequently at much higher rates of use than in the United States —it is likely that between 1 and 2 million patients per year receive ECT worldwide.

The aging of the US population has resulted in an increasing number of geriatric patients who receive ECT. Rosenbach, Hermann, and Dorwart (1997) studied a 5% sample (representing about 4000 individuals) of all Medicare part B claims for 1987–1992 and found a 30% increase in receipt of ECT during the period (equal to an extrapolated total national increase from 12,000 to 15,500 Medicare patients treated). The rate of use of ECT in this group increased from 4.2 to 5.1 per 10,000 population, which is consistent with the overall use of ECT reported in the previous paragraph. During the study interval, outpatient use of ECT more than doubled: from 7% to 16% of all treatments administered. This study is the first to show a clear increase in ECT use in the United States, after 30 years of generally declining, and, more recently, stable, use.

Olfson et al. (1998) analyzed inpatient ECT data from the 1993 Healthcare Cost and Utilization Project of the Agency for Health Care Policy and Research, which comprises a sample of 6.5 million case records from 913 community hospitals in 17 states (approximately 20% of US community hospitals). Close to 10% of the 22,761 general hospital patients admitted with a principal diagnosis of recurrent major depression received ECT during the survey year. The highest rates of ECT use were found in older, white, privately-insured, more affluent patients, with sharply lower use among black, Hispanic, and low-income patients. After controlling for patient selection bias, prompt administration of ECT was found to be associated with shorter and less costly hospital stays.

It is apparent from the above surveys that ECT is alive and well in the United States. It is also apparent that ECT is markedly underutilized in economically disadvantaged, and state-hospital, populations—presumably for the same economic reasons that these populations receive the lowest-echelon treatments available in every other branch of medicine as well. When health insurance becomes available to members of these populations, as it has in recent decades through Medicare, ECT utilization rates increase sharply; those patients entering state facilities because they could not afford a higher level of care, find themselves candidates for admission or transfer to community hospitals, where, for the first time, they become eligible to receive more effective treatments, including ECT. If and when a national health insurance program is introduced in the United States, there will doubtlessly be a corresponding substantial increase in ECT use.

## The Future of Electroconvulsive Therapy

As Fink (1979) pointed out, convulsive therapy burst on the scene during an era of unprecedented therapeutic optimism in psychiatry, following hard

on the heels of Wagner-Jauregg's malarial fever therapy for general paresis of the insane (1917) and Klaesi's prolonged sleep therapy (1922), and virtually coeval with Sakel's insulin coma therapy (1933) and Moniz' psychosurgery (1935). One by one, the other treatments flourished briefly and then fell into disuse, to be replaced by less complex and more definitive methods. Only ECT flourished and remains widely used to this day, doubtless because of its demonstrable efficacy, safety, and relative ease of administration, all due in large measure, to the advances in technique (e.g., succinylcholine muscle relaxation, barbiturate anesthesia, oxygenation, unilateral and bifrontal electrode application, seizure monitoring, brief- and ultrabrief-pulse stimulation) that have been introduced over the years.

Will ECT ultimately be replaced by a less intrusive, pharmacologic therapy that alters brain function in the desired direction (e.g., via a hypothalamic neuropeptide) but without the auxiliary convulsion and its attendant risks and drama? Perhaps, but not in the foreseeable future. The rate of accumulation of new techniques and discoveries in the application of neurotransmitter pharmacodynamics to the treatment of major depression has been excruciatingly slow. Despite manufacturers' claims, no significant improvement in the therapeutic potency of antidepressant drugs has materialized since the introduction of imipramine and amitriptyline nearly a half-century ago (Barbui and Hotopf, 2001).

Moreover, incremental advances in the technique of ECT have refined the treatment to the point that, with high-dose right unilateral ECT, or moderate-dose bifrontal or bitemporal ECT, administered with brief- or ultrabrief-pulse technique, many patients can now enjoy the full therapeutic benefit of ECT without the prominent cognitive side effects that were so common with sine-wave bitemporal ECT. Most importantly, those patients requiring bitemporal ECT can now receive it in a more physiological form than before, using the shorter pulse-widths and longer stimulus trains that are more consistent with the parameters of neuronal depolarization and recovery (see Chapter 6), and therefore less likely to impair memory and cognition.

In the previous edition, I described the possibility that ECT might someday be replaced by magnetic convulsive therapy. My view now is that the economic realities detailed in Chapter 13 make this unlikely to occur for many years, if ever. Improvements in instrumentation and stimulation parameters for administering nonconvulsive repetitive transcranial magnetic stimulation ($_r$TMS) might elevate its efficacy in major depression to the level of ECT, although it would be hard to improve significantly on the 87%–95% remission rate recently achieved in a 4-hospital collaborative study of brief pulse bitemporal ECT (Petrides et al., 2001). Certainly, it would be an important advantage if nonconvulsive $_r$TMS were at the same time to have fewer side-effects than ECT on memory and cognition, and definitive information on these points should be available within a few years.

Most likely brief pulse ECT will continue to benefit from further fine-tuning of its stimulus parameters—the reintroduction of the ultrabrief stim-

ulus providing a typical example—and advances in techniques for ensuring the maximum possible benefit from each treatment session. Given the facts that recent research has clearly demonstrated how to administer ECT with a degree of efficacy that equals or surpasses any other treatment in medicine, yet with a morbid and mortal risk below that of many drugs, and virtually all other procedures carried out under general anesthesia, the long-term survival of ECT seems assured.

## NOTES

[1]An autotoxic theory of ALS was then in vogue, which the trypan red was intended to combat by preventing transfer of autotoxins across the blood-brain barrier.

[2]Dr. Rubin subsequently published the extremely favorable study results in his 1947 volume, *Diseases of the Chest.*

[3]The tax-exempt status of the Church of Scientology was subsequently meekly restored by the IRS after the Church threatened to bring IRS operations to a halt through lawsuits and various other actions.

[4]When later criticized for this action, Reagan typically disclaimed responsibility, stating that he "had no respect for the type of people who had supported the Vasconcellos law" and had signed the bill at the end of the legislative session when he had had more than 1000 legislative actions to consider (Bennett, 1983).

[5]A few years later, in November 1982, the citizens of Berkeley, California, approved by referendum a Board of Supervisors ordinance that made administering ECT in city hospitals a crime punishable by a fine of $500 or 6 months in prison, or both (Bennett, 1983). This ordinance was subsequently reversed by the Alameda County Superior Court on a technical point of law.

[6]May 28, 1976: Congress enacts Medical Device Amendment to Federal Food, Drug & Cosmetics Act (FFDCA).

[7]August 13, 1982: APA submits petition 82P-0316/F820007 to FDA under section 513(e) of FFDCA (21 USC 360c(e)) to reclassify the ECT device to Class II.

[8]November 4, 1982: FDA Advisory Panel agrees to APA's request, contingent on development of mandatory Safety & Performance standard under section 514 of the FFDCA (21 USC 360d).

[9]September 5, 1990: FDA proposes rule (55 FR 56378-90).

[10]October 5, 1990: House Report #94-583, p. 53.

[11]October 9, 1990: Senate Report #101-513, p. 17.

# 2

# EFFICACY OF ELECTROCONVULSIVE THERAPY

## Experimental Data

It is axiomatic that rigorous experimental methods are required to demonstrate the efficacy of a medical treatment. Whether the comparison is with placebo (sham treatment) or with an alternative active therapy, a prospective design with random assignment of consecutive patients to treatment groups and blind assessment of outcome using objective measures are absolute requirements. Both the diagnostic criteria and the precise treatment parameters must be specified, and appropriate statistical analyses must be employed (or the data presented in sufficient detail for readers to perform their own calculations). Scrupulous adherence to these rules is especially crucial when studying an emotionally charged and physiologically active treatment such as ECT, for it is often used for illnesses (depression, mania) with a high spontaneous remission rate.

The first part of this chapter assesses the efficacy of ECT by reviewing the evidence from controlled trials in the three disorders for which such data are available: depression, schizophrenia, and mania. The results of uncontrolled or otherwise methodologically weak studies, anecdotal reports, and case history studies are referred to in the second part.

## *Depressive Illness*

### Sham Electroconvulsive Therapy Studies

The studies of genuine versus sham ECT published through 1966 and reviewed by Barton (1977), Fink (1979), and Taylor (1982) generally support the efficacy of ECT in treating severe depression, although each suffers from inadequate methods of varying degree (Crow and Johnstone, 1986). The following review concentrates on the random assignment studies published since then, each of which satisfies the methodological requirements outlined earlier.

Freeman, Basson, and Crighton (1978) treated 40 primary depressives with either 2 genuine (bilateral, partial sine-wave) or 2 simulated ECTs during their first week of treatment, after which, for ethical reasons, all patients

received genuine bitemporal ECT for the remainder of the course. Anesthesia was identical for both groups and included atropine, barbiturate, and muscle relaxant. Mean scores on the Hamilton, the Wakefield, and the Visual Analogue depression scales after the first 2 treatments were significantly lower after genuine than after simulated ECT, and patients in the simulated ECT group ultimately received significantly more treatments prescribed by clinicians who were blind to group assignment. (The Beck self-rating depression scale did not reveal any significant between-group differences, perhaps because depressed patients, particularly those with retardation, have difficulty completing it.)

Lambourn and Gill (1978) assigned 32 patients with psychotic depression to receive either 6 brief-pulse, low-dose (10 joules [J]), unilateral ECTs, or an equal number of identical anesthesia inductions without the passage of electricity. Mean Hamilton rating-scale scores obtained 24 hours after the sixth treatment did not differ significantly for the 2 groups.

In the Northwick Park ECT trial, Johnstone et al. (1985) gave 70 endogenous depressives a 4-week course of 8 partial sine-wave bitemporal ECTs or 8 anesthesia inductions without electrical stimulation. Mean Hamilton depression scale scores after 4 weeks were significantly lower in the genuine ECT group by about 26, a difference that was no longer present at 1- and 6-month follow-up intervals, during which additional treatment (including ECT) had been given ad libitum. The advantage of genuine over sham ECT in this study was most marked in the subgroup of delusional depressives (Clinical Research Centre, 1984).

West (1981) treated 22 primary depressives with courses of 6 genuine or sham ECTs. The patients then completed the Beck self-rating scale for depression, were blindly rated on both doctors' and nurses' rating scales, and were then switched to the alternate treatment if indicated. There was a highly statistically significant and clinically important improvement in the genuine compared with the sham ECT group, and 10 out of 11 sham ECT patients (but no genuine ECT patients) were switched to the alternate method, from which they derived the expected degree of improvement.

In the Leicestershire trial, Brandon et al. (1984) studied 95 major depressives who were allocated to up to 8 genuine (bitemporal, partial sine-wave) or sham ECT, administered twice weekly. A significantly greater improvement in Hamilton depression scale scores was seen in the genuine (compared with the sham) ECT group at 2 and 4 weeks, but not at 12 and 28 weeks. As in the Northwick Park trial, the largest between-group differences occurred in the subgroup of delusional depressives.

In the Nottingham ECT study, Gregory, Shawcross, and Gill (1985) randomly assigned 60 depressives to partial sine-wave ECT with bitemporal or unilateral placment, or to sham ECT. Both genuine methods were superior to sham ECT after 2, 4, and 6 treatments, as measured by the Hamilton and the Montgomery and Asberg depression scales, which were administered blindly.

Thus, 5 out of 6 methodologically impeccable studies of simulated compared with real ECT in the treatment of depressive illness show both a statistically significant and clinically substantial advantage for the genuine article in reducing depression scale scores during and immediately following the treatment course. It is not surprising that evaluations done later in the maintenance phase of the treatment course or at follow-up generally fail to show such an advantage; during the intervening weeks patients typically received a variety of "doctor's choice" treatments, including both ECT and drugs, administered unsystematically.

The single study (Lambourn and Gill, 1978) that failed to show an advantage for real compared with sham ECT also differs from all the others in having used brief-pulse, low-dose (10 J) unilateral ECT as the active treatment. A similar low-dose technique using an even higher stimulus energy (mean = 18 J) was shown by Sackeim et al. (1987a) to be clinically ineffective for right unilateral ECT. Recent evidence demonstrates that this method must be administered with high stimulus dosing to maximize efficacy (Abrams, Swartz, and Vedak, 1991).

## Electroconvulsive Therapy Compared with Antidepressant Drugs

The case for a therapeutic advantage of ECT over antidepressant drugs rests primarily on three studies: Greenblatt, Grosser, and Wechsler (1964), the Medical Research Council trial (MRC, 1965), and Gangadhar, Kapur, and Kalyanasundaram (1982). Although many studies have provided interesting and useful insights into special aspects of the relative efficacy of the 2 treatment methods, none has the scientific rigor necessary for an unequivocal demonstration of the superiority of ECT. Abrams (1982b) and Rifkin (1988) have detailed the methodological flaws of the published comparisons of ECT and antidepressant drugs in the treatment of depressive illness. Half of the studies have to be excluded from consideration because of retrospective design; nonblind evaluation and faulty data analyses account for most of the remainder. These are by no means trivial points. In a retrospective study, for example (they are all chart-reviews), patients have not been assigned randomly to treatments; there is no sure way to equate the groups for psychopathology or illness severity; the reasons why physicians or patients chose one or the other treatment constitute a major source of bias; there is no control over drug dosage or numbers of ECTs administered; and outcome assessment (even if done by "blinded" reviewers) is necessarily based on the nonsystematic observations recorded at the time by nonblind clinicians with unknown biases.

Even studies that apparently follow a rigorous method may fade into insubstantiality on closer scrutiny. A case in point is the previously mentioned study by Greenblatt, Grosser, and Wechsler (1964) that is widely cited as a demonstration of the therapeutic superiority of ECT over imipramine in the treatment of depressive illness. In this trial, 281 patients were ran-

domly assigned to receive either ECT, a maximum obligatory dose of 200 mg/day of imipramine, phenelzine, isocarboxazid, or placebo and evaluated blindly. The authors indeed found ECT to be superior to imipramine across the total sample studied, but diagnoses were heterogeneous and included psychoneurotic depression, schizophrenia, and a large number categorized only as "other," in addition to the diagnostically relevant categories of manic-depressive, depressed, and involutional psychotic reaction. A combined analysis is clearly noninformative with such diagnostic heterogeneity. Although a table provides separate percentages for each diagnostic subgroup of patients who were markedly improved with each treatment, the actual numbers of patients receiving each method are not given, nor are chi-square values or significance levels provided. The authors nevertheless affirm that their analyses show ECT to be significantly more effective than imipramine for the treatment of involutional psychotic reaction (85 versus 42 markedly improved) but not for the depressed phase of manic-depressive illness (78 versus 59 markedly improved); these groups were not combined for analysis.

In the multihospital Medical Research Council trial (MRC, 1965), 269 patients with endogenous depression were randomly assigned to 4 different treatment groups, 2 of which comprised 4 to 8 ECTs (65 patients) and imipramine, 100 to 200 mg/day (mean = 193 mg/day; 63 patients). Fifty-eight patients in each group completed the first 4 weeks of treatment, at which time physicians' blind global assessments showed 71 of the ECT group to have no or slight symptoms, compared with 52 of the imipramine group ($\chi^2 = 8.75$; $p = 0.0005$).

Gangadhar, Kapur, and Kalyanasundaram (1982) studied 24 primary endogenous depressives who were randomly assigned to receive a course of genuine bilateral or sham ECT given over a 12-week trial in conjunction with either placebo capsules or imipramine, 150 mg/day. The first 6 treatments were given over 2 weeks, followed by 1 treatment per week for 2 additional weeks and then 1 "maintenance" treatment at the 6th, 8th, and 12th weeks of the trial (total, 11 treatments). Genuine ECT plus placebo capsules was significantly superior to sham ECT plus imipramine in lowering Hamilton depression scale scores after 6 treatments; no significant between-group differences on this scale were observed at subsequent assessment intervals. Assuming that imipramine does not antagonize the antidepressant effects of ECT—Price et al. (1978) suggest that this may not be the case—this study also demonstrates the efficacy of genuine versus sham ECT. Although the sample size is small and the dose of imipramine used is low, this is the only study to employ the critical format of genuine ECT plus placebo compared with sham ECT plus active drug in conjunction with all of the other methodologic requirements.

All three studies, however, can be criticized for the low drug dosages employed. Although there is little doubt that imipramine, 100 to 200 mg/day, is an effective treatment for some patients, most psychopharmacologists today would peg the therapeutic range of this antidepressant at 200 to 300 mg/day and would also require plasma-level monitoring. The two-phase

study of Wilson et al. (1963) addresses the question of dosage, albeit in a very small sample. In the initial phase, depressives were randomly assigned to 4 treatment groups, of which 2 (6 patients each) were ECT plus placebo and sham ECT plus imipramine at a dose of 150 to 220 mg/day (mean = 180 mg/day). Assessment on the Hamilton Scale after 5 weeks showed a large and highly significant advantage for ECT. In the second phase of the study, 14 new patients were treated—4 with ECT and 10 with imipramine alone—at a higher dosage: 215 to 270 mg/day. After 5 weeks on this regimen, the high-dose imipramine group showed significantly more improvement than the first- and second-phase ECT groups combined (although the authors erroneously describe the 2 methods as identical). The rating procedure, however, presents an important problem in this study: Different numbers of raters were used at different assessment periods; 1 of the raters was never blind; and 1 was not a psychiatrist. Moreover, the authors do not say which raters participated in the second-phase assessments or how the Hamilton scores were derived when more than 1 rater was used.

Another aspect of the imipramine dose-response relation was studied by Glassman et al. (1977), who treated 42 nondelusional psychotic depressives with a fixed milligram per kilogram dose of imipramine and examined the relation of plasma level to clinical outcome. The proportion of imipramine-responders increased directly with plasma levels: 29 for plasma levels of 150 ng/mL, 64 at 150 to 225 ng/mL, and 93 for levels of 225 ng/mL. The study is rendered meaningless, however, by the authors' failure to specify their criteria for defining treatment response.

Thus, although ECT is clearly more effective than moderate doses of imipramine in treating several subtypes of endogenous depression, it is less obvious that this difference would obtain under the optimal conditions of higher drug dosages, perhaps with plasma-level monitoring. To be sure, most practitioners neither administer high-dose antidepressant drugs nor routinely monitor plasma levels; in this sense, ECT can justifiably be considered superior to the mediocre antidepressant therapy that is generally prescribed.

In a different paradigm, Dinan and Barry (1989) randomly assigned 30 severely depressed patients who did not respond to treatment with tricyclics —of whom 23 met criteria for melancholia—to receive either 6 bilateral ECTs or the addition of lithium to the tricyclic. There was no difference between groups in blindly obtained, depression-scale score reductions at the end of 3 weeks, although patients receiving the lithium-tricyclic combination improved faster. This is the most favorable outcome obtained to date for drug therapy of depression when compared with ECT and supports the rapid antidepressant efficacy previously reported for the lithium-tricyclic combination (De Montigny et al., 1983; Heninger, Charney, and Sternberg, 1983).

## Electroconvulsive Therapy versus Drugs in Depressive Illness: Other Studies of Interest

The 1964 study of DeCarolis et al., as reviewed by Avery and Lubrano (1979), provides unique information on an important clinical question: What

is the response to ECT in depressives who have failed high-dose antidepressant drug therapy? These authors intially treated a diagnostically heterogeneous sample of 437 depressives with imipramine, 200 to 350 mg/day. All patients who failed to improve after 30 days on this regimen were then given a course of 8 to 10 ECTs. Endogenous depressives constituted the largest diagnostic subgroup ($n$ = 282), of which 172 (61) responded to imipramine. Of the remaining 109 patients (1 patient dropped out), 93 (85) then responded to a course of ECT. In the subgroup of 181 delusional depressives, only 72 (40) responded to imipramine, compared with 91 (83) of the 109 imipramine nonresponders who went on to receive ECT. Although assessment of outcome was not blind in this study, this seems at least partially counterbalanced by the powerful bias against ECT response introduced by withholding this treatment until patients had first failed high-dose antidepressant drug therapy.

A paper by Coryell (1978) considers a different question: What is the response of patients who had received ECT and antidepressants during different depressive episodes? In this study, hospital charts were reviewed and blindly rated for all patients who received ECT for depression in the pre-antidepressant era (1920–1959) and who later received tricyclic antidepressants from 1961 to 1975 for a different episode. Complete recovery occurred in 94 of the episodes treated with ECT compared with 53 of those treated with antidepressants. Drug dosages were low by present standards, however, and no data are provided on the relative efficacy of the 2 methods within patients (e.g., how often the ECT response was superior to the tricyclic response).

## Electroconvulsive Therapy versus Isoflurane

Because of a superficial analogy between ECT-induced postictal suppression and the total suppression of cerebral activity that can occur with deep isoflurane anesthesia, Langer et al. (1985) conducted an open clinical trial of this procedure in 11 treatment-resistant depressed patients who preferred not to undergo ECT, and claimed thereby to have achieved a very rapid antidepressant effect that was comparable to ECT. Stimulated by that article, Greenberg et al. (1987) conducted an open replication trial in 6 patients with recurrent depressive disorder, 5 of whom had recovered with ECT from prior episodes. No clinical antidepressant activity of deep isoflurane anesthesia was observed during the study, and 5 of the 6 patients went on to recover with ECT.

An open study of isoflurane anesthesia and ECT in depressed patients (Carl et al., 1988) is simply incomprehensible as insufficient methodology is provided to determine what was done to whom, or why, and what the results were. This same group published a subsequent open clinical trial (Engelhardt, Carl, and Hartung, 1993) in which 12 treatment-resistant depressed patients were first given 6 isoflurane inductions, and those who failed to respond—or improved only temporarily—were then given ECT.

In a nonblind assessment, the authors rated 7 of the 12 patients as markedly improved after isoflurane anesthesia, but only 3 of them could be discharged from the hospital. The remaining 9 patients went on to receive ECT, but the authors unaccountably omit mention of whether any of them were subsequently discharged from the hospital. As the authors point out, however, isoflurane anesthesia is contraindicated in patients with coronary or cerebral vascular disease, a fact that would certainly prevent a substantial number of patients who receive ECT from ever becoming candidates for this procedure.

Most recently, Langer et al. (1995) reported an open, nonrandom, clinical comparison of ECT with isoflurane anesthesia in depression, purporting to find isoflurane anesthesia the more effective therapy. Remarkably, all patients continued to receive antidepressant drug therapy throughout the study period.

However, their study is invalidated by inadequate ECT technique. Using a Siemens Konvulsator partial sine-wave device set to the intermittent stimulus mode, with peak current of 500 mA, these authors delivered a stimulus only 2 seconds long. (If they didn't induce a seizure, they immediately restimulated at 600 mA.) Langer et al. (1995) do not provide figures for the mean charge they used, but it is easy to calculate using the correction factor of 0.64 provided by the manufacturer of the Siemens device. Each second of stimulation in the intermittent mode provides 0.125 second (25 pulses per second of 0.005 second each) of current flow, so:

$$500 \text{ mA} \times 0.64 \times 0.125 \text{ sec.} \times 2 \text{ sec.} = 80 \text{ mC}$$

For the 600-mA setting, the dose would have been 96 mC. Such a low dosage range is doubtless responsible for the incredibly poor results these authors obtained with bilateral ECT: just 49% improvement in depression scores after 6 treatments.

In comparison, Lamy, Bergsholm, and d'Elia (1994), who also used an old Siemens Konvulsator, delivered an 800-mA peak current for an average of 6 seconds' stimulation (range 4 to 10 seconds), yielding a mean stimulus charge of 384 mC and achieving recovery in most patients with bilateral ECT. Similarly, Abrams, Swartz, and Vedak (1991) reported 79% improvement with 6 bilateral ECTs, using a mean stimulus charge of 378 mC delivered via a brief-pulse instrument.

## *Efficacy in Mania*

Only one prospective controlled trial of ECT in mania has been published at the time of this writing (Small et al., 1988): A sample of 34 newly admitted manic patients were diagnosed as bipolar I according to the Research Diagnostic Criteria and were randomly assigned to receive a course of brief-pulse ECT ($n = 17$) or lithium therapy ($n = 17$). The mean number of ECTs administered was 9.3, and lithium dosages were adjusted to yield serum