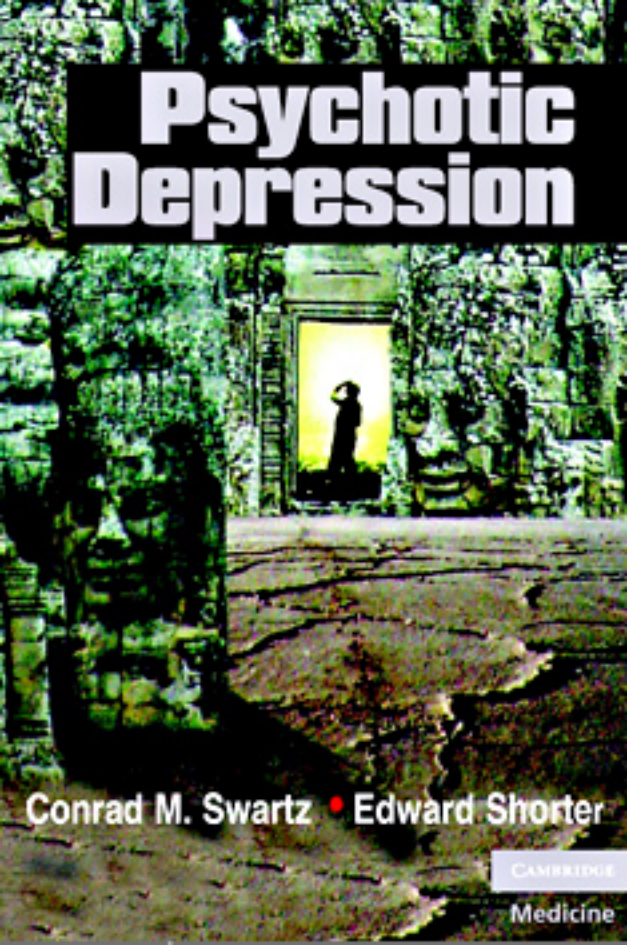
Psychotic Depression



Conrad M. Swartz • Edward Shorter

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PSYCHOTIC DEPRESSION

Psychotic depression is a distinct and acute clinical condition along the spectrum of depressive disorders. It can manifest itself in many ways and be mistaken for schizophrenia. It often induces physical deterioration, mortally dangerous acts toward self or others, or completed suicide. This book aims to help clinical practitioners and trainees describe their observations of psychotic depression, formulate treatment, and express expectations of recovery from illness. It focuses on all facets of the disorder, from clinical history to coverage of the current state-of-the-art diagnostic and treatment protocols. Medical readers of this book will come away able to diagnose and readily treat psychotic depression and thus will be able to serve their patients better. Non-physician readers will come away with the message that this is a terrible illness, but there is hope. This book fills an important gap in the realm of psychiatric literature.

Dr. Conrad M. Swartz is a board-certified psychiatry professor who has written and lectured extensively on depression, anxiety, and the use of electroconvulsive therapy for severe depression.

Edward Shorter is a historian of psychiatry who has written three books on the history of psychiatry and psychosomatic illness.

Also by Edward Shorter

A History of Psychiatry (1997)

Historical Dictionary of Psychiatry (2005)

Psychotic Depression

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To Cynthia and Anne Marie

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Preface

Psychotic depression is an alloy of psychosis and depression that is not separable into psychosis and depression. Psychosis is a symptom that thought and behavior have become unrelated to reality. It is, in other words, a symptom of madness just as biological as delirium. Psychologists and psychodynamicists often understand illnesses as psychological conditions, caused by psychological conflicts and blamed on unconscious psychological mechanisms. Saying "illness" does not denote "biological" to them. We should like readers to perceive the old-time biological meaning of madness, not through the psychology of the unconscious. Depression is an illness that includes, among other symptoms, the loss of ability to think things through. Patients with psychotic depression have an illness with symptoms of disordered thought, behavior, and mood. They are both delusional and suffer a mood disorder. They are truly physically ill, and their illness represents a terrible suffering for patients and their families, worse so because they cannot describe it. This book aims to help health care professionals find

the words to describe their observations of psychotic depression, to work together with their patients to formulate treatment, and to express expectations of recovery from illness. The following pages contain the past, the present, and the future of patient-centered concerns about conventional, and some not entirely conventional, ideas concerning its diagnosis and treatment.

We are trying to reach mainly physicians here, because it is upon their shoulders that responsibility for diagnosis and treatment rests. But we have tried not to make the book so forbiddingly "medical" as to be inaccessible to those outside of medicine such as the patients themselves, their friends and families, and all others interested in or curious about psychiatric illness. It's hard to write both for doctors and patients, for obvious reasons. The pharmaceutical armamentarium so familiar to physicians is a jumble of unfamiliar terms to everyone else. Physicians are accustomed to thinking cooly about diagnoses that patients experience as the horrors of hell and to rationally considering treatments that everyone else deeply fears. The whole alphabet soup of instruments and procedures that doctors take in with the mother's milk of medical school is usually entirely unfamiliar to patients, except terms such as "EEG" that they have encountered in their own experience.

Thus, patients may not consume avidly every last line of the diagnosis chapter because they are mainly interested in the one illness that they have, not in the entire range of phenomena that they could conceivably have but don't. And physicians may smile indulgently at the chapter on subjective aspects of psychotic depression – psychotic depression as the patients experience it. But they should not. Knowing your patients' experience of illness, and being able to succor and advise them appropriately, is part of the practice of medicine. At some level doctors realize they do not feel what their patients experience until they go through the same condition themselves or with a close relative. Of course, this awareness is easily overlooked in the everyday demands of clinical practice. Doctors, please do not imagine that you know all that your patients go through, because you cannot.

Medical readers of this book will come away able to diagnose and readily treat psychotic depression, and thus be able to serve their patients better. Nonmedical readers will come away with the message that this is indeed a terrible illness, but that there is hope. This can be a precious message.

Conrad Swartz is a practicing psychiatrist and an academic scholar who has published on many subjects, and a specialist in medical treatment, electroconvulsive therapy, and psychopharmacology. Much of his research reflects his engineering PhD along with his MD. Edward Shorter specializes in the history of psychiatry and psychopharmacology, and is a PhD. Shorter comes to the story via the trail of age-old suffering; Swartz has spent a lifetime treating patients. Both perspectives are useful and offer a comprehensive picture of what one is up against in this disease called psychotic depression.

Conrad M. Swartz
Edward Shorter

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Susan bélanger, Heather Dichter, and Ellen Tulchinsky in the History of Medicine Program of the University of Toronto have been of great help in various aspects of the preparation of this book. We should especially like to acknowledge the sage advice and practical experience of Marc Strauss of Cambridge University Press and our copy editor Anula Lydia.

1

Introduction

On June 20, 2001, Andrea Yates of Houston, Texas, drowned her five children one by one in the bathtub in her home. She was clearly seriously ill and had been treated with the drugs sertraline (Zoloft), olanzapine (Zyprexa), haloperidol, and lorazepam among other remedies. Her attending psychiatrist had rejected electroconvulsive therapy (ECT) for her on the grounds that it was "for far more serious disorders" (Denno, 2003). She was said to have committed this terrible act in the grips of major depression. But that cannot be right. "Major depression" is not a specific illness. She had psychotic depression. She was improperly diagnosed, evaluated, and certainly inadequately treated. Her illness gave her an overwhelming compulsion or she would not have pushed the heads of her children underwater in the delusive belief that she was saving them from Hell.

Andrea Yates herself was caught in the jaws of Hell. An editorial in the British medical weekly *Lancet* in 1940 called depression "perhaps the most unpleasant illness that can fall to the lot of man"

(*Lancet*, 1940), and in the midst of a psychotic depression, Yates had opportunity to experience this. Psychiatry could have rescued her, but confusion about her diagnosis and her treatment interfered.

The Andrea Yates story had one more chapter, in which the reality of her illness from psychotic depression was finally understood. An appeals court overturned her original conviction because of inaccurate evidence from Park Dietz, a forensic psychiatrist who had testified for the prosecution. In July 2006, Yates again went before a jury, which found her not guilty. "The jury looked past what happened and looked at why it had happened," said her former husband. "Yes, she was psychotic. That's the whole truth." This time Yates was sentenced to an indefinite term in a maximum security hospital (Associated Press, 2006). Thus the story had an end that lifted slightly the flap of public ignorance about this disorder.

What happened to Andrea Yates between her 2002 and 2006 courtroom trials is also noteworthy. In 2002 she was physically fit. In 2006 she was hardly recognizable, flabby and overweight. In television views of her in prison before the 2006 trial she was unkempt and poorly groomed. Under psychiatric treatment her appearance strikingly deteriorated. What types of psychiatric treatments cause such deterioration, and what do not? People avoid psychiatrists because they are afraid of being stigmatized or controlled by psychiatric treatment. Success in treatment includes avoiding stigmatization and behavioral deterioration from the treatment.

Marc Cherry was the producer and scriptwriter of the TV series *Desperate Housewives*. He said that, like Andrea Yates, his mother was at the cusp of a similar experience. He and his mother had been watching the news coverage of the Yates trial one evening and she grunted, "I was once almost there myself." Cherry was so surprised that he said to himself, "If my own mother was once so desperate, then every woman has probably felt the same thing" (Kreye, 2005).

But no! Andrea Yates killed her children in the grips of a delusional depression. However stressed, every woman does not have a psychotic

depression, any more that every woman has a pancreatic tumor or a spinal infection. Psychotic depression is as much a medical illness as tuberculosis. It is not a blip on the stress continuum. Mrs Cherry, at one point, as her son said, set to throw her children out the car window, may or may not have had a psychotic depression. But it is a disease, not a normal response.

What is psychotic depression?

There is a classical psychiatric tradition of dividing depression into two types.[1] As Michael Shepherd, the dean of British psychopharmacology, pointed out in 1959, there were hospital depressions and then there were "large groups of loosely termed 'neurotic,' 'reactive,' or 'exogenous' depression often admixed with the clinical manifestations of anxiety. Many of them run a chronic, fluctuating course." They were certainly not suitable for admission to hospital. Most of these patients "do not come to medical attention at all but rely rather on the advice of the chemist [pharmacist] or on self-medication" (Shepherd, 1959).

In one type of depression – Shepherd's hospital depression – brain biology takes over. The depression happens out of the blue. The patients

1 Aaron T. Beck seems to prefer, among possible polar depression types, the "distinction between endogenous and reactive depressions." A. T. Beck. 1967. *Depression: Clinical, experimental, and theoretical aspects*. New York: Hoeber/Harper & Row, p. 66. For his discussion of the difference between "neurotic" and "psychotic" depressions, see pp. 75–86. See also David Goldberg and Peter Huxley. 1980. *Mental illness in the community: The pathway to psychiatric care*. London: Tavistock. The authors argue that there may be a continuum in depressive illness. Yet "... [s]omewhere on this continuum the line must be drawn between those whose mood disorder is impairing their social and psychological functioning, and those in whom normal homeostatic mechanisms may be expected to operate." (p. 15) See, e.g., P[er] Bech. 1988. A review of the antidepressant properties of serotonin reuptake inhibitors. *Adv Biol Psychiatry* 17: 58–69; "We will analyze the depressive inpatients and the depressive outpatients as two different diagnostic entities" (p. 60).

are very sick and may have delusions and hallucinations or sink into stupor. In 1920 German psychiatrist Kurt Schneider, then in Cologne, proposed a term for this kind of depression in which the patients were terribly slowed. He called it endogenous depression,[2] borrowing from the great German nosologist Emil Kraepelin the term "endogenous," by which Kraepelin meant biological, indwelling in the brain, and dominating the body. Schneider contrasted endogenous depression with a second type, which he called "reactive" depression, usually seen outside of hospital settings. Reactive depression has almost nothing in common with psychotic depression except maybe sadness. Yet reactive depression can also be quite serious, the patients hovering on the brink of suicide. But reactive patients are not psychotic nor do they experience the same kind of "psychomotor retardation," to use the technical term for thought and action being slowed. There are two different illnesses here, one involving a terrible, pathological slowing among other symptoms and the other dependent on external events.

Whether there are two depressions or one – and, if two, whether they may be divided into endogenous and reactive – has long been controversial.[3] We step into a snake pit here. But the massive evidence of the history of psychiatric illness does indeed suggest that there are two. For the sake of convenience we call them here endogenous and reactive-neurotic, fully aware that future generations may find these

2 K. Schneider. 1920. Die schichtung des emotionalen lebens und der aufbau der depressionszustaende. *Zeitschrift fur die gesamte Neurol Psychiatr* 59: 281–6. "Bei der betrachtung der depressionszustaende gehen wir von den beiden, in ihren extremen auspraegungen wohl characterisierten typen aus, der reinen motivlosen 'endogen' und der rein reaktiven depression" (In considering the types of depression, we use as a basis the two forms that have been best characterized in their extreme forms, the purely motiveless "endogenous" and the purely reactive depression; p. 283.)

3 Joe Mendels and Carl Cochrane (1968) began the revival of the endogenous-reactive split: The nosology of depression: The endogenous-reactive concept. *Am J Psychiatry* 124 (Suppl): 1–11. Another important early contribution was I. Pilowsky et al. 1969. The classification of depression by numerical taxonomy. *Br J Psychiatry* 115: 937–45. See also the work of Michael Feinberg and Bernard J. Carroll. 1983. Separation of subtypes of depression using discriminant analysis. *J Affect Disord* 5: 129–39.

terms inadequate. Yet the present state of science does not permit us to go beyond them, and whatever one chooses to call them the fundamental reality is that two classes of depressive illness exist, as unalike as chalk and cheese. Most practitioners will probably agree with this, even though they are forced into the procrustean one-depression bed by the official diagnostic schema – the *Diagnostic and Statistical Manual (DSM)* of the American Psychiatric Association – that is now current.

One distinguished believer in the two-depression concept is Joe Schildkraut at Harvard. In 1965 Schildkraut devised one of the most influential ever biological theories in psychiatry. He said that affective disorders (depression and mania) result from disturbances in the metabolism of the neurotransmitter norepinephrine. Chemically, norepinephrine belongs to the "catecholamine" class of neurotransmitters, and Schildkraut's ideas became famous as the "catecholamine hypothesis of affective disorders."[4] Schildkraut, as other observers, saw that there were two kinds of depression. Later, he characterized the endogenous disorders as "running out of gas depressions" and the reactive as "chronic characterological depressions." (He actually did not use the term reactive but rather "depressions with much more in the way of . . . self-pity and histrionics." Yet it means the same thing: a chronic character meets a distressing environmental event.) Schildkraut called the endogenous concept "more a European notion, a notion that might be called by some vital depressions, because you didn't have to have a depressed mood. It was based on having a loss of vitality, anergia, anhedonia and psychic retardation." He said that such depressions, unlike the reactive, "did not readily change with ongoing interpersonal interactions or environmental events. It was a kind of fixed-stuck disorder."[5]

4 Joseph J. Schildkraut, interview. 2000. The catecholamine hypothesis. In David Healy (ed.) *The Psychopharmacologists*, vol. 3. London: Arnold, pp. 111–34, at p. 131.

5 See note 4.

A tradition exists of calling endogenous depression melancholia. Psychiatrists once resisted the term melancholia because it harked back to the days when deep depression was associated with humoral theories of "black bile" and the melancholy constitution. Yet the term melancholia has such historical heft that many prefer it to the rather jargonish-sounding "endogenous." Bernard Carroll affirmed emphatically in 1982, after discovering that a biological test (the dexamethasone suppression test) was relatively specific for melancholia, "Our results give unequivocal support to the view that melancholia is a categorically distinct entity from non-endogenous depression" (Carroll, 1982). In 2006 Michael Alan Taylor and Max Fink re-endorsed in a comprehensive overview the existence of melancholia as a separate diagnosis (Taylor and Fink, 2006). In our view, melancholia is one type of endogenous depression, but when speaking generalistically the two terms are interchangeable.

There are various types of endogenous depression. In catatonic depression, the extreme form of which is stupor, movement and speech are slowed. In melancholic depression, the patient has a sickly persona, and movement and speech may also be "retarded." In this book, we are interested in the type of endogenous depression called "psychotic," characterized by delusions and hallucinations. As Chapter 3 explains, there are various forms of psychotic depression that are really more or less independent illness entities in their own right. Psychotic depression is not actually a disease of its own but a collective term for a number of illnesses having the common properties of depression and psychosis. Of hospitalized patients with endogenous depression, about half are psychotic.[6]

Psychotic depression is highly dangerous. The patients' thinking becomes so delusive that, having lost contact with reality, they

6 Of 225 patients with primary unipolar affective disorders admitted to the Iowa University Psychiatric Hospital between 1935 and 1940 (part of the "Iowa 500 Study"), 52% revealed delusions. See William Coryell and Ming T. Tsuang. 1982. Primary unipolar depression and the prognostic importance of delusions. *Arch Gen Psychiatry* 39: 1181–4.

contemplate suicidal behavior, taking poison perhaps to kill off the hallucinated bug infestation (although it kills them). As London psychiatrist Thomas A. Munro, a psychiatrist at Guy's Hospital in London, pointed out in 1949, "The treatment of depression is always a great responsibility. The patient's life is at stake" (Munro, 1949).

Psychotic depressions can also be risky for others. As with Andrea Yates, periodically there are terrible stories of psychotically depressed parents who murder their children to save them from the fires of Hell or the doom the parents know lies ahead. Thus, the English *Drug and Therapeutics Bulletin* advised in May 1965 as follows: "Another reason for admitting severely depressed patients to hospital is that on occasion they murder relatives or friends in an attempt to spare them imagined pain."[7]

In psychotic depressive illness we are therefore discussing a variety of endogenous depression, depressions that may end up in hospital. Reactive depressions, on the other hand, come on slowly, under stress, and are filled with anxiety, anger, or dissatisfaction. The symptoms of reactive depressions tend to be vague, formless, and primarily subjective. In today's psychiatry, reactive distress tends to be called by a range of terms that are really all over the map, from adjustment reaction, major depression, depression "not otherwise specified," or dysthymia, to the whole anxiety spectrum, such as generalized anxiety disorder or some other anxiety diagnosis, to personality disorders such as borderline personality, or even dissociative disorder. The term neurosis formerly applied in many cases. The psychoanalysts once considered these patients, perhaps not incorrectly, as having a character disorder. A number of additional conditions doubtless huddle under the shelter of reactive distress, including chronic fatigue syndrome (formerly neurasthenia), weltschmerz, and the emotional consequences of poverty, pain, and threatening medical illness.

7 See May 28, 1965, Antidepressant therapy, *Drug and Therapeutics Bulletin* 3(11): pp. 41–3, at p. 42.

In the vast mass of "depression" diagnoses that are handed out today, many patients will have such a reactive depression: the depression comes on in response to bad news rather than out of the blue. The patients' thought and movement are not abnormally slowed as in endogenous depression. Unlike psychotic depression, which answers readily to ECT, reactive depressions do not respond so well to ECT. The phrase "reactive depression," by the way, was abolished in 1980 in American psychiatry with the advent of a new recipe-based classification manual called *DSM*-III. Yet, the term reactive depression delineates a basin of distressed patients with a mixture of sadness, weariness, and anxiety that is difficult to circumscribe well, and there is no reason why it should not soldier on.[8]

Endogenous depression is an entirely different beast. The patients are not necessarily sad but slowed in thought and deed, sometimes to the point of stupor. The patients complain that their minds move slowly and their movements are laborious and painful. In the psychotic variety of endogenous depression the patients are not always slowed, and may have a hint of mania, exhibiting such features of agitation as pacing and repeating "It's my fault, it's my fault." Yet the main point is that the patients are tormented by delusions of various kinds; in an earlier era their delusive thoughts often involved their irremediable sinfulness; today, hypochondriac delusions about one's organs turning to concrete and the like come to the fore. Endogenous illness does not have the same favorable promise of remission that is lent to reactive depression, although after about 8 months most untreated endogenous patients get over it (for the time being). Patients with endogenous depression are often inclined to seek oblivion, so that suicide is always to be feared, as

8 It is true that reactive depression has not been without its critics. As Swiss psychiatrist H. J. Bein put it, "It must, of course, be borne in mind that . . . in all the so-called reactive depressions, the qualifier 'reactive' is only a reflection of the investigator's empathy for a given situation." H. J. Bein. 1978. Prejudices in pharmacology and pharmacotherapy: Reserpine as a model for experimental research in depression. *Pharmakopsychiatrie Neuropsychopharmakologie* 11: 289–93, at p. 291.

actually happens in perhaps one in seven of the untreated cases. (But in nonendogenous depression too the patients may attempt suicide, and the psych emergency wards are very familiar with them.)

"Endogenous depression should be looked upon as an acute disease, like appendicitis; it cannot wait," one Swedish psychiatrist told a Scandinavian symposium from the floor in 1960. He remembered a patient from his practice in Linköping, referred with the following information, "The patient is recommended for examination at a psychiatric clinic." There was nothing more. "We phoned the doctor but he was not in, and then we wrote – as we usually do – requesting details of the case. Three days passed before we got any news and the same day the patient committed suicide, taking with him a daughter of five years."[9]

Finally, endogenous depression is "autonomous"; it does not get better with good news.[10] Your lover has just moved back in? Guess what, your psychotic depression has not improved. As psychopharmacologist Donald Klein once told Robert Spitzer, the mastermind of *DSM*-III, in a moment of irritation, "I think that the distinction between the relatively autonomous depression and the relatively reactive depression is a strikingly important one that should be present in this edition [the forthcoming *DSM*-III-R in 1987]. That also speaks for the utility of a mood-reactive depressive disorder."[11]

DSM-IV in 1994, no longer under Spitzer's control, did incorporate the notion of mood reactivity, but made it a characteristic of major depression with "atypical features," meaning what is often called "atypical depression." Yet the disease designers included alongside "mood reactivity," "interpersonal rejection sensitivity," which means basically

9 Gerdt Wretmark, in discussion. In Erik S. Kristiansen (ed.) 1961. *Depression: Proceedings of the Scandinavian Symposium on Depression, 26–28 October 1960*. Copenhagen: Munksgaard, pp. 138–9.

10 Pioneering the distinction between "autonomous" and "reactive" depressions was English psychiatrist R[obert] D[ick] Gillespie. 1929. The clinical differentiation of types of depression. *Guy's Hospital Reports* 79: 306–44.

11 Klein to Spitzer, March 19, 1986; American Psychiatric Association, Williams Papers, *DSM-III-R*, box 2.

thin skin (American Psychiatric Association, 1994). The disease designers had in effect asserted that thin skin is the autonomous dimension of major depression.

The basic problem with *DSM*, though, is that it fails to recognize endogenous depression. The manual styled itself as "atheoretical," meaning making no assumptions about causation. But by dismissing causality, *DSM* is more agnostic than diagnostic. In all other fields of medicine, causality is crucial in diagnosis and intimately tied to evidence and scientific observation. Psychiatrists must not be so totally agnostic (if they want to be effective or to practice on the basis of modern science).

After Kraepelin lumped mania and depression together in 1899 as a single illness,[12] "manic-depressive psychosis," for about the next half century endogenous depression often was referred to as manic-depressive illness. Yet the majority of patients had no evidence of mania, and many patients with mania had no history of depression. Today, authors distinguish between genuine manic-depressive illness, also called "bipolar-1" disorder, and unipolar disorder (depression without mania). This book is mainly about unipolar disorder and about psychosis in the depressive phase of bipolar illness. But, to be frank, some clinicians think that sooner or later many of the depressed hospitalized patients will develop an episode of mania, and that on a lifetime basis the distinction between unipolar endogenous depression and bipolar disorder is meaningless.[13]

To recap, this basic distinction between endogenous and reactive depression has today almost been lost sight of. Since Kurt Schneider, the classification of depression has become rather a parlor game for insiders, with countless varieties being proposed. In particular, the all-encompassing amorphous label of major depression and a pseudospecific

12 Emil Kraepelin. 1899. *Psychiatrie: Ein Lehrbuch für Studirende und Aerzte*, vol. 2, 6th edn. Leipzig: Barth, pp. 359–425.

13 See, e.g., Heinz E. Lehmann. 1971. Epidemiology of depressive disorders. In Ronald R. Fieve (ed.) *Depression in the 1970's*. Amsterdam: Excerpta Medica, pp. 21–30; proceedings of a conference held in 1970.

subtype called atypical depression enjoy popularity at the moment. Yet there are not countless varieties. There are really only two master illness entities here. Schneider's distinction between endogenous and reactive has a solidity that has withstood the test of time. This book is about psychotic depression in its varieties because it is threatening, yet repairable.

There are commonalities between the two depressions. They may have sadness in common or a diminished sense of self-worth and overarching distress. Both may be triggered by stress, but endogenous depression must also have a biological trigger, not just a psychological one. Jet lag, high cortisol, insomnia, starvation, and stimulant drug abuse may all serve as behavioral disturbances that provoke the physical brain changes of endogenous depression. As L. G. Kiloh and R. F. Garside at the University of Durham observed in 1963 in a classic article, "It is often correctly pointed out that many attacks of endogenous depression are precipitated by adverse circumstances and are therefore in this sense reactive, but this does not necessarily indicate that the precipitants play an important causal role" (Kiloh and Garside, 1963).

And sin! While psychotically depressed patients are covered in it, patients with community depression feel they deserve to be treated better. They do not dread punishment for having sinned unforgivably in the eyes of God, or fear that they are dead.

Thus, two diseases. It is just as tuberculosis and pneumonia are two different diseases, although they may have fever and coughing up phlegm in common. Lumping the diseases of endogenous and reactive depression together as "depression" makes about as much sense as lumping tuberculosis and pneumonia together: They have different prognoses, entirely different responses to treatment, and presumably different biochemistry and genetics. That means we are talking about utterly different diseases, not variations on a theme.

In this book we look at the whole question of the diagnosis and treatment of psychotic depression afresh, without the preconceptions of industry-marketed psychopharmacology and *DSM*-nonspecific nosology

that have made psychiatry today a field that needs upstanding principles instead of accommodating every viewpoint. It is not as though we had a huge conventional wisdom about psychotic depression to overturn, because in the past 30 years psychiatry has not paid much attention to the condition (nor has psychiatry bothered much about the other kinds of endogenous depressions either). But psychiatry has paid inordinate attention to the public marketing of what is officially called "major depression," which is a mixture of melancholia and dissatisfaction, or of psychotic depression and reactive depression if one will. A single class of drugs – the selective serotonin reuptake inhibitors (SSRIs) – has been offered by industry as the treatment of choice of major depression, although the drugs are not effective for serious depressions.[14]

So there is a conventional wisdom out there: the SSRIs as the ideal treatment for major depression. And the conventional wisdom is wrong. There is no specific thing as major depression, and the SSRIs are poor antidepressants, although they have efficacy in treating other types of mood changes, such as worry. The enormous success of the SSRIs as the treatment of choice for major depression – a nontreatment for a non-illness – has left many clinicians frustrated as their patients fail to recover until their illnesses have run their natural cycle. It has also left the patients chasing futilely one ineffective treatment after another rather than receiving accurate diagnoses and therapies that might make them genuinely better.

14 In an unguarded moment, Robert Temple, head of the Office of Drug Evaluation I of the Food and Drug Administration (FDA), admitted in front of a microphone at a meeting of an advisory committee, "[We need] to find out whether the [SSRI-style] drugs actually provide some benefit, even in people who seem to be doing well on them . . . I mean, as Tom [Laughren] has pointed out repeatedly, the failure of most of the drugs to show effectiveness doesn't mean they don't work. On the other hand, we don't have evidence that they do work, and that is not irrelevant either." FDA Archives, Joint Meeting of the CDER Psychopharmacologic Drugs Advisory Committee and the FDA Pediatric Advisory Committee, September 14, 2004, transcript p. 55. Although the meeting was given over to pediatric suicide with antidepressants, Temple made this comment in the context of the treatment of adults. Laughren was head of the psychopharmacology evaluation unit of the FDA.

As we said above, the ideal treatment for psychotic depression is ECT. Yet the view has squirmed into today's psychiatry that the way to go is a combination of antipsychotics and antidepressants.

As one warning flag among many: At the University of Iowa, Paul Penningroth collected a series of four patients with psychosis and depression treated with antipsychotics who suicided (at ages 21, 23, 24, and 38), despite seeming to have responded.[15] Antipsychotics do not remove all the thought disorder, and that is the problem. Moreover, they cause substantial impairment. So the combo of antipsychotics and antidepressants is clearly not the first choice. The first choice is ECT. The second choice is a tricyclic antidepressant (TCA) or a drug Glaxo SmithKline markets called generically bupropion (Wellbutrin), to which about a third of psychotic depressives respond. Then comes a miscellany, for example, drugs that inhibit the enzyme monoamine oxidase, called MAOIs, such as phenelzine (Parke-Davis's Nardil); in the miscellany is lithium plus TCAs. In the last place, and not win, place, or show in the horse race, is the combo of TCAs plus antipsychotics.

Patients

The year is 1889. We are in the closed wing of the Holloway Sanatorium for the Insane, in Virginia Water outside of London, a private nervous clinic for the middle classes. Constance, D., 35, is brought in for "acute melancholia." She had given birth about 2 months ago, and 3 weeks after the delivery, as one of the medical certificates stated, she had taken on "a terrified expression, [is] nervous and wrings her hands, is afraid she is going to be boiled alive, and asks for a knife with which to end her life." Before the onset of the present

15 R. Paul Penningroth, "Schizophrenia, depression, and suicide." Psychiatry Grand Rounds, University of Iowa Hospitals and Clinics, November 16, 1976.

illness she was said to have been "strong, active, healthy and temperate, very fond of music." Then after the baby's arrival she started to lose her appetite and was sleepless (a nanny apparently looked after the child). She began to dread impoverishment although there was no objective reason for doing so. As noted in her chart, "She said she was miserable enough for suicide but lacked the necessary courage. She appeared to take no interest in her child." She came into the care of Dr George Savage, a prominent London psychiatrist who also once had Virginia Woolf as a patient, and Savage arranged for her committal to "Holloway House," as it was called.

At Holloway House, the clinicians noted that she had a scar on her left hand, where she had attempted to open a vein. Mentally she is suffering from "melancholia agitata," with delusions that she is about to undergo some horrible torture. She clutches her hair, wrings her hands, looking the very picture of abject misery, begging that she shall be removed to some dark room and just locked up where no nurse can reach her, as they are on the point of taking her into the bath and boiling her alive." Every time the doctor visited her she would say, "This is the last time, all is pretence and sham, that they are now preparing the boiling pitch for her."

That was in March. By May she was well enough to play tennis on the clinic's "airing court," yet filched a nurse's keys and plunged down the embankment in order to launch herself into the Thames. She continued to pick her face into open wounds, "continues the nervous habit of blowing on her hands whilst talking, and adheres to the same absurd statement that this is her last day as she is about to be put into the 'boiling bath.' "

In August, Savage had her discharged to her home in the hope that familiar surroundings might make a difference. (Apparently there were servants enough to keep an eye on her.) By October Savage informed the clinic doctors that Constance D. was indeed much improved, washing and dressing the baby and being mistress of the house at the head of the table. "The only suspicious feature respecting her cure being that she still

says, 'she ought never to have been sent away from home,' and 'that her husband is a fool.' "[16]

This was a psychotic depression, brought on by the birth of a child. Constance D. had been ill for about 10 months, which was fairly standard. In 1889 they had no specific treatment for depression, only weak sedatives such as the foul-smelling paraldehyde for patients who were highly agitated, and her doctors and family just waited the illness out.

Fifty years later, psychiatrist Eliot Slater recalled the typical delusional melancholic patient in the early 1930s at the Maudsley Hospital on Denmark Hill in South London: The chronic melancholic "would be a thin, elderly man or woman, inert, with the head lifted up off the pillow. There were some sort of Parkinsonian-like qualities, mask-like face sunk deep in misery, and speaking in a retarded way. If you could get them to say anything, it would be something about how hopeless things were, how they were wicked, doomed to disease, death, and a terrible afterlife, if there was one." Could these patients be helped? "There wasn't anything you could do," said Slater, "except to try to make them sleep, try to get them to take some food, tube-feed them if they were refusing food, which happened frequently." It was when they started to revive from this kind of stupor that suicide was to be feared, said Slater.[17]

At this point psychotic depression, as well as the other endogenous depressions, suddenly became among the most treatable of all psychiatric disorders. In 1935 Budapest psychiatrist Ladislaus von Meduna originated the first of the convulsive therapies, using the convulsive drug pentylenetetrazol, sold in Europe under the trade name Cardiazol, in the United States under Metrazol, to trigger the seizure. Although Meduna intended to treat schizophrenia with Metrazol, it soon became apparent that depression responded even better to the new treatment, including

16 Holloway Sanatorium, patient files, at Wellcome Library for the History of Medicine, London. MS 5157, case no. 404.

17 Eliot Slater. 1993. Interview. In Greg Wilkinson (ed.) *Talking about psychiatry*. London: Gaskell, p. 4.

psychotic depression.[18] Three years later, in 1938, Rome psychiatrist Ugo Cerletti determined an even better way of inducing convulsions, with electricity; ECT was born.[19] ECT was thought to be superior to Metrazol convulsive therapy because it caused the patients less anxiety in the stage of waiting for the fits to begin – with ECT unconsciousness is immediate; also, Metrazol was plagued by the problem of partial seizures. ECT remains today the preferred treatment for psychotic depression.

Questions

These momentous developments left several questions unanswered, and they remain question marks even today.

First, why has the frequency of psychotic depression declined considerably over the years? Today, it is certainly not an uncommon ailment, and 15–30 percent of endogenous depressions are said to have a delusional component. But in mental hospital admissions in the past the figure was much higher. At the Royal Hospital in Edinburgh, a psychiatric hospital, among female patients the number of delusional depressions per 100 depressions admitted dropped from 75 percent in 1892 to 39 percent in 1942–3, to 30 percent in 1981–2. The decrease is statistically significant (the decrease in male patients, though parallel to that of females, is not statistically significant; Eagles, 1983). Of course it is possible that the hospital decided to admit more delusional depressives at one point than another: were the quieter cases kept more at home in the earlier period? Or perhaps later generations of family

18 L. C. Cook and W. Ogden. 1938. Cardiazol convulsion therapy in non-schizophrenic reaction states. *Lancet* 235: 885–7. Four of five patients with "psychotic depression" responded well to Cardiazol.

19 For details on these developments, see Edward Shorter and David Healy. In press. *Shock Therapy: The History of Electroconvulsive Treatment in Mental Illness*, forthcoming from Rutgers University Press, September, 2007.

doctors, intent upon treating their patients' (now treatable) bodily woes, simply missed the delusions in their depressed patients and did not recommend them for admission. It is also possible that "schizophrenia" has increasingly replaced the diagnosis of psychotic depression, given that the presence of psychosis in depression, if chronic, could easily be considered schizophrenia. Thus, in various ways the finding could be an artifact, but it is probably not because several other series confirm it.

In Scotland at the Crichton Royal Hospital (formed out of two nineteenth-century institutions), the percentage of depressed patients with delusions declined in women from 77 percent in 1880–9 to 19 percent in 1970–9; in men from 78 percent to 31 percent. On an epidemiological basis, per 100,000 population at risk, the declines were of a similar magnitude, so it is not just a question of possible changes in the patient mix. Meanwhile in Scotland, the percentage of delusions in patients with schizophrenia was relatively unchanging (and per 100,000 population actually rose).[20]

Finally, in Finland at the Helsinki University Psychiatric Clinic, among patients with severe depression (called "depressive psychosis" but not necessarily delusional), the percentage of patients experiencing "strong manifest guilt," a surrogate for delusions, declined from 30 percent in 1900–9 to 9 percent in 1930–9, to 5 percent in 1960–9. The trend for "religious symptoms in abundance" was similar.[21]

Because the trend in all three of these studies is sharply down, it is unlikely that we are dealing with some kind of artifact of registration; a genuine epidemiological change seems to have occurred, lessening the frequency of psychotic depression. Because big changes over time in

20 A. D. T. Robinson. 1988. A century of delusions in South West Scotland. *Br J Psychiatry* 153: 163–7. For a not entirely convincing critique of this study, see M. J. S. Morton, letter, 1988. *Br J Psychiatry* 153: 710–11.

21 P. Niskanen and K. A. Achté. 1972. Disease pictures of depressive psychoses in the decades 1880–89, 1900–09, 1930–39 and 1960–69. *Psychiatria Fennica* 95–100; delusions increased somewhat between the 1880s and the 1890s.