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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-I" 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.