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Melancholia: a conceptual history

*Depression, most people know, used to be termed “melancholia”. . . Melancholia would still appear to be a far more apt and evocative word for the blacker forms of the disorder, but it was usurped by a noun with a bland tonality and lacking any magisterial presence, used indifferently to describe an economic decline or a rut in the ground, a true wimp of a word for such a major illness . . .*

*The Swiss-born psychiatrist Adolf Meyer had a tin ear for the finer rhythms of English and therefore was unaware of the semantic damage he had inflicted by offering “depression” as a descriptive noun for such a dreadful and raging disease. Nonetheless, for over seventy-five years the word has slithered innocuously through the language like a slug, leaving little trace of its intrinsic malevolence and preventing, by its very insipidity, a general awareness of the horrible intensity of the disease when out of control.*<sup>1</sup>

A scientific classification of behavior disorders is still an unreachable goal. The efforts in the past two centuries are reminiscent of the many attempts to bring order into the universe of plants and animals before the singular rules of Linnaeus and Mendel allowed meaningful classifications to emerge. The maladaptive variations in human mood, thought, and motor behavior observed over the millennia offer a myriad of images that have captured the attention of one observer or another who attempted to formulate these observations into an understandable framework. More organized systems emerged at the end of the Eighteenth Century with the attentions of German and French physicians.<sup>2</sup> The classifications often lacked a central thesis and, for the most part, clinicians have been attracted by one aspect of behavior or another, allowing the behaviors to be classified by the dominant symptom or presumed etiology. Patients have been lumped or split into classes or described as categories or continua according to idiosyncratic opinions.<sup>3</sup>

Neurosyphilis is an interesting neuropsychiatric disorder that offered a potpourri of images and therapies. So varied were its presentations that clinicians dubbed it the “great imitator.”<sup>4</sup> Descriptions filled volumes, but once the common cause was identified and a laboratory test developed, the variations assumed less significance. An effective treatment gave descriptive syphilology the *coup de grâce*.

The classification of mood disorders presents the same dilemma. Which disorders of mood are expressions of a common pathology and which are not? How many pathopathologies are represented in the mood disorders? How many disorders are

derived from one cause? Acknowledging our limited understanding of human neurobiology, is it prudent to support the many disorders of mood characterized in the *Diagnostic and Statistical Manual* (DSM) classification or is it better to seek a simpler basis?

For a medical classification to be useful it should be precise in its criteria of differentiation, predict the probable course of an illness, and guide the selection of the most optimal intervention. It should also offer the scientist a lodestone for the selection of homogeneous populations for research study.<sup>5</sup>

The psychiatric classifications embodied in DSM-IV and the 10th *International Classification of Diseases* (ICD-10) are not precise, and do not predict the course of illness nor effectively guide intervention. A simplified classification of depressive mood disorders under the rubric of “melancholia” achieves these aims better. “Melancholia” is recognized as a syndrome of gloom, apprehension, inhibited motor activity, slowed thoughts, homeostatic distress, and psychosis. Clinical criteria of the disorder are definable, laboratory tests offer support, and course of illness is predictable with the available therapeutic options. The burden of this report is to establish melancholia as a definable syndrome in psychiatric classification.<sup>6</sup>

Origins of the concept

Melancholia is a concept of depressive illness with an extensive literature and a detailed history. Its recognition as a form of “madness” with “bodily causes” has been consistent for 3000 years. Except for two periods in western history – the Middle Ages, when church teachings dominated western thought, and again in the twentieth century, particularly in the USA, when psychoanalytic notions dominated psychiatric thinking – melancholia was identified as a disorder in brain function. Modern writers who offer detailed histories of the syndrome are Hopewell-Ash (1934), Lewis (1934a), Schmidt-Degenhard (1983), Jackson (1986), Goodwin and Jamison (1990), and Parker and Hadzi-Pavlovic (1996). Discussions of melancholia are to be found in Hunter and Macalpine’s *Three Hundred Years of Psychiatry* (1982), Berrios and Porter’s *A History of Clinical Psychiatry* (1995), Shorter’s *A History of Psychiatry* (1997), and Porter’s *Madness* (2002). Literary writings are presented by Hefferman (1995) and Radden (2000). A review of the role of psychotherapies in the history of depression is offered in a special number of *Psychiatric Annals*.<sup>7</sup>

Melancholia was identified by Hippocrates in the fifth century BCE as a persistent sadness and morbid thoughts that had their source in a disorder of the brain. In ‘*The Sacred Disease*,’ he wrote:

And men ought to know that from nothing else but thence [from the brain] come joys, delights, laughter and sports, and sorrows, griefs, despondency, and lamentations. And by this, in an especial manner, we acquire wisdom and knowledge, and see and hear, and know what are foul and what are fair, what are bad and what are good, what are sweet and what are unsavory . . . And by the same organ we become mad and delirious, and fears and terrors assail us, some by night, and some by day, and dreams and untimely wanderings, and cares that are not suitable, and ignorance of present circumstances . . . All these things we endure from the

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brain when it is not healthy, but is more hot, more cold, more moist, or more dry than natural . . . And we become mad from humidity [of the brain].<sup>8</sup>

Hippocrates described a specific syndrome, not a vague dysphoria or dourness of character. Although rooted in beliefs in the essential balance of four body humors for health, other early images of melancholia define the same syndrome. Galen and Arateus, both writing in the first century CE, considered melancholia as an affliction of the brain. Arateus described:

And yet in certain of these cases there is mere anger and grief and sad dejection of mind . . . they are suspicious of poisoning or flee to the desert from misanthropy or turn suspicious or contract a hatred of life. Or if at any time a relaxation takes place, in most cases hilarity supervenes. The patients are dull or stern, dejected or unreasonably torpid . . . they also become peevish, dispirited and start up from a disturbed sleep.<sup>9</sup>

Plutarch noted that when a man is melancholic:

Every little evil is magnified by the scaring spectres of his anxiety. He looks on himself as a man whom the gods hate and pursue with their anger . . . Awake, he makes no use of his reason; and asleep, he enjoys no respite from his alarms. His reason always slumbers; his fears are always awake. Nowhere can he find escape from his imaginary terrors.<sup>10</sup>

In western Europe from the tenth to the eighteenth centuries, mental disorders were often ascribed to demons and witchcraft.<sup>11</sup> Relief was theorized to come with exorcism. The medical teachings that psychiatric disorders resulted from aberrations in the brain were officially denied. Many physicians, however, continued to recognize melancholia as disease. Bright (1586) described a “natural” form of mental disorder that resulted from “the mind’s apprehension” and an “unnatural” illness of the humors of the body. The “natural” is recognized today as “reactive depression”, the “unnatural” as “major depression.”<sup>12</sup> A similar division is presented by Robert Burton in *The Anatomy of Melancholy* (1621), the most detailed and poetic description of melancholia in the literature.<sup>13</sup> Another description is that of Richard Baxter (1716) (Hunter and Macalpine, 1982, p. 241):

Melancholy Persons are commonly exceedingly fearful . . . Their Fantasie most erreth in aggravating their Sin, or Dangers or Unhappiness . . . They are still addicted to Excess of Sadness, some weeping they know not why, and some thinking it ought to be so . . . They are continual Self-Accusers . . . They [apprehend] themselves forsaken of God . . . They are utterly unable to rejoice in anything.

A great part of their Cure lieth in pleasing them, and avoiding all displeasing Things, as far as lawfully can be done . . . As much as you can, divert them from the Thoughts which are their Trouble.

If other means will not do, neglect not Physick; and tho’ they will be averse to it . . . yet they must be perswaded or forced to it . . . I have known a Lady deep in Melancholy, who a long time would not speak, nor take Physick; nor endure her Husband to go out of the Room; and with the Restraint and Grief he Died, and she was Cured by Physick put down her Throat, with a Pipe by Force.<sup>14</sup>

In the nineteenth century melancholia was recognized as a core illness among many forms of insanity. One writer defined six classes of insanity: melancholia, mania,

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fatuitas, stupiditas, amentia, and oblivio”.<sup>15</sup> Another offered five “species” of insanity: melancholia, mania with and without delirium, dementia, and idiocy.<sup>16</sup> Yet another author divided insanity into three orders, with mania and melancholia combined as one.<sup>17</sup> Mania was considered a higher form of melancholia or as the same illness in a different form. A specific view is expressed by the apothecary of London’s Bethlem Hospital, John Haslam, in 1809 (Hunter and Macalpine, 1982, p. 580):

As the terms Mania and Melancholia are in general use, and serve to distinguish the forms under which insanity is exhibited, there can be no objection to retain them; but I would strongly oppose their being considered as opposite diseases. In both there is an equal derangement.<sup>18</sup>

Other observers emphasized the connection between the mood disorders of depression and mania. Descriptions of a circular insanity were detailed by Falret (1854) and Baillarger (1854).<sup>19</sup> Falret described melancholia:

At the commencement of this phase . . . the patients begin to withdraw and now speak only rarely. Sometimes they express remorse over their previous condition . . . the patients withdraw, remaining all alone and motionless . . . they are now meek, and their humility may go so far as for them to refuse treatment in the belief that they do not deserve it. This despondency becomes more pronounced daily . . . [and] the patient is transformed into a statue . . . were he not coaxed to eat, the patient would not bother to seek food . . .

The thought processes are very slow; rarely this may result in complete cessation of all intellectual activity . . . his movements are sluggish or absent. The face is pale; the features sag, suggesting dejection rather than anxiety . . . Appetite is decreased, and the patient eats little; digestion is equally slow and defecation is laborious.

Nevertheless, there are a certain number of patients who present with specific preoccupations, among which we have noticed ideas of humility, of ruin, of being poisoned, or of guilt.<sup>20</sup>

The lack of a coherent formulation of psychiatric disorders encouraged two camps to develop, one dividing the behaviors into many conditions and the other offering a single disorder of the brain as the basis for many forms of psychiatric illness.<sup>21</sup> The single cause for psychiatric disorders was formulated when anatomic studies showed diverse forms of mental illness to be associated with thickening of the brain’s meninges, later seen as secondary to cerebral syphilis.<sup>22</sup> The brain diseases took various forms, one dissolving into another, and arguments ensued as to the relevance of a single brain disorder (*Einheitspsychose*) or multiple disorders.<sup>23</sup>

Of many attempts to develop a coherent nomenclature, Emil Kraepelin’s formulation of melancholia as an abnormal mood state was widely accepted.<sup>24</sup> An active and agitated form of the illness was grouped with manias, and the periodicity of recurrences was highlighted. He recognized two forms of the psychoses – a progressive deteriorating illness of dementia praecox (*Verblödungsprocesse*) and a non-deteriorating form of periodic illnesses (*das periodische Irresein*). The latter term was replaced in his next edition by *das manisch-depressive Irresein* which established a condition of manic-depressive illness. Melancholia was retained as a separate depressive syndrome that occurred in a perceived “involuntional period.” In writings in the first half of the Twentieth Century it became the syndrome of *involuntional melancholia*.

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For mania, Kraepelin described a progression in severity from hypomania to mania to delirious mania. For melancholia, he described a parallel progression of simple retardation, retardation with delusions and hallucinations, and stuporous conditions.<sup>25</sup>

Various attempts to distinguish depressive mood disorders were made. One attempt divided depressed patients with anxiety as “reactive” to stress (psychoneurotic), and an autonomous form that had a systemic or biologic basis.<sup>26</sup> The arguments were of popular interest at the beginning of the twentieth century, with prominent British authors arguing for a unitary model.<sup>27</sup>

Melancholia was described as a specific disorder by Aubrey Lewis (1934b) in his detailed study of 61 melancholic patients:

*Melancholia* is one of the great words in psychiatry. Suffering many mutations, at one time the tenacious guardian of outworn schemes or errant theories; presently misused, cavilled at, dispossessed, it has endured into our own times, a part of medical terminology no less than of common speech. It would seem profitable to consider the history of this word, and of the states of fear and distress with which it has from the beginning been associated.<sup>28</sup>

The concept of melancholia was brought to life in the description by Hopewell-Ash (1934).<sup>29</sup>

MELANCHOLIA is a depressed state [meaning subdued, not a diagnostic category] of the entire personality reaction. Depression of spirits, psychomotor retardation and general torpidity of mind and body are its essential features. Invariably associated with these are insomnia, indigestion and constipation. It is true that morbid, restless anxiety often colours the depression, but in typical cases it is the general slowing up of the rhythm that characterizes the clinical picture. Mental depression may be due to many causes, both physical and mental; toxemia reflex irritation and physical fatigue on the one hand and psychological stress on the other are responsible for many instances. But in the melancholic state – using that term to indicate a particular clinical condition – there is a sluggishness of mind manifested by difficulty in thinking, poverty of ideas and loss of attentive control that is not found in any kind of simple nervous depression. In well-developed cases the “slow-motion” life of melancholia is extraordinarily characteristic; slow movements, retarded reaction and difficulty of ready response combine to present us with appearances that are familiar to all who have much to do with cases of mental disease. It is a clinical picture accentuated by the foetid breath, furred tongue and story of digestive troubles which express the inhibited gastro-intestinal functions. The lacklustre expression, lifeless hair and greasy complexion, which are equally common, complete a characteristic facies. In more severe degrees of melancholia one finds, as will be noted later, such symptoms as the above combined with hallucinations and delusions. The latter are usually concerned with ideas of wrong-doing, evil, disaster and death. The man who believes that he has committed the “unpardonable” sin and will not admit any doubt about it is always suffering from melancholia. No anxiety state representing a psychoneurosis ever produces a reaction of this kind.

A contemporary, Denis Hill (1968), found no merit in the subdivisions of the mood disorders, concluding that the treatments defined the condition:

It is a striking fact that the antidepressant drugs and ECT have their profoundest therapeutic effect when the primary functional changes of depression are most in evidence and that, given

these, the secondary symptoms disappear as the primary functional changes are alleviated. To put the matter at its greatest simplicity there is little to contradict in the statement that biological therapeutic agents operate only on biological functional systems.<sup>30</sup>

**The psychodynamic interruption**

Kraepelin’s formulation of melancholia as a core mental disorder had many critics. The strongest attacks came from Freud and his followers, who offered a “mental” or “psychological” basis for melancholia.<sup>31</sup> Their theory pictured active exchanges of energies within a tripartite mental apparatus defined as the *superego*, *ego*, and *id*. Mourning for the loss of a love object deranged the energetics so that melancholia emerged. The physical attributes of the illness resulted from a displacement of energies from the *ego* – the emotional part that related to the outside world – to the *id* – the hidden source of drives and emotions. When a loss could be associated with a specific subject or event in the subject’s history, “reactive depression” ensued. When a loss was not identifiable and the condition seemed unrelated to history, a “psychotic depression” ensued.<sup>32</sup> As psychodynamic theory came to dominate American psychiatry, interest in the biological aspects of melancholia diminished.

Adolf Meyer, a leading professor of psychiatry in the USA, is described as:

desirous of eliminating the term melancholia, which implied a knowledge of something that we did not possess, and which had been employed in different specific ways by different writers. If, instead of melancholia, we applied the term depression to the whole class, it would designate in an unassuming way exactly what was meant by the common use of the term melancholia; and nobody would doubt that for medical purposes the term would have to be amplified so as to denote the kind of depression . . . We might distinguish the pronounced types from the simple insufficiently differentiated depressions. Besides the manic-depressive depressions, the anxiety psychoses, the depressive deliria and depressive hallucinations, the depressive episodes of dementia praecox, the symptomatic depressions, non-differentiated depressions will occur.<sup>33</sup>

Meyer stated that depressive mood disorders were individualized “reactions”:

The conditions which we meet in psychopathology are more or less abnormal reaction types, which we want to learn to distinguish from one another, trace to the situation or condition under which they arise, and study for their modifiability.<sup>34</sup>

Meyer’s formulations were adopted in the concept of “reactions” that became the basis for the American Psychiatric Association classification of psychiatric disorders (Table 1.1) in DSM-I (1952) and the revision of DSM-II (1968).<sup>35</sup>

The concepts of Freud or Meyer, or those of the adherents to their philosophies, would not have been so widely accepted had there been a competing biological model of psychiatric illness or effective treatments for psychiatric disorders. Neuroscience technologies and laboratory procedures were primitive and no somatic treatment was established. The introduction of malarial fevers (1917), insulin coma (1933), convulsive therapy (1934), and leucotomy (1935) challenged the psychodynamic model. The success of these treatments in quickly relieving the most severe psychiatric

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**Table 1.1.** Diagnostic and statistical manual, 2nd edition (DSM-II) “depression” formulations

DISORDERS OF PSYCHOGENIC ORIGIN OR WITHOUT CLEARLY DEFINED PHYSICAL CAUSE OR STRUCTURAL CHANGE IN THE BRAIN
Psychotic disorders
<b>Disorder due to disturbance of metabolism, growth, nutrition, or endocrine function</b>
Involutional psychotic reaction
<b>Disorders of psychogenic origin or without clearly defined tangible cause or structural change</b>
Affective reactions
Manic-depressive reaction, manic type
Manic-depressive reaction, depressive type
Manic-depressive reaction, other
Psychotic depressive reaction
Schizophrenic reactions
Schizophrenic reaction, schizoaffective type
Psychoneurotic disorders
<b>Disorders of psychogenic origin or without clearly defined tangible cause or structural change</b>
Psychoneurotic reactions
Anxiety reaction
Depressive reaction

illnesses changed clinical psychiatric practice and once again directed attention to the brain as central to psychiatric disorders.<sup>36</sup> A new therapeutic optimism improved the tenor of psychiatric institutions.<sup>37</sup>

The recognition of melancholia in psychiatric classification

New typologies were envisioned as the basis for more effective prescription of the available treatments. Altered mood states were now labeled as *vital* or *personal*, *primary* or *secondary*, *atypical*, *vegetative*, *endogenomorphic depressions* and *anxious thymopathy*.<sup>38</sup>

In an unusual study, Klein and Fink (1962a, 1962b) randomly assigned patients of varying diagnoses (depression, mania, psychosis) referred for medication treatments in an inpatient hospital setting to one of three treatments – imipramine, chlorpromazine (combined with the antiparkinson agent, procyclidine), or placebo.<sup>39</sup> Imipramine relieved depressed mood in both the retarded and agitated forms. Chlorpromazine relieved psychosis but also relieved depressed mood. The labeling



of the new psychoactive substances as either “antidepressant” or “antipsychotic” was challenged.

The diagnostic criteria of DSM-II served as poor guides in the prescription of the compounds.<sup>40</sup> Many psychopharmacologists described their frustration with DSM-II criteria for the selection of treatments.<sup>41</sup> They struggled with a confusion generated by the varying proposed causes of depression: being rooted in life events (*reactive depression*) or in body physiology (*endogenous, vital depression*), or dominated by neurotic symptoms (*neurotic depression, dysthymia*), psychosis (*psychotic depression*), or character pathology.

By the late 1960s it was no longer acceptable to treat all depressed patients as if they were suffering from a single condition because some treatments were effective for some patients and not for others. One group, for example, examined 33 studies that had assessed medication treatments of depression and could not find a diagnostic formulation that had predictive strength.<sup>42</sup> The DSM-II and ICD-8 classifications had poor reliability, best demonstrated in international studies.<sup>43</sup>

An operationally defined diagnostic scheme was offered in the Research Diagnostic Criteria (RDC).<sup>44</sup> Its usefulness encouraged the American Psychiatric Association to update the official classification in DSM-III of 1980.<sup>45</sup> Lacking a defined theory of psychiatric illness, however, the classes represented a consensus among observers who used different texts, idiosyncratic personal clinical experiences, and different psychological and pharmacologic theories as guidelines. For some disorders, a Kraepelinian template can be recognized (e.g., the schizophrenia criteria); for others, a psychological template is apparent (e.g., dissociative disorders). The committees represented diverse constituencies and the final formulations were designed to be accepted by the average psychiatrist who would vote it up or down in an American Psychiatric Association election.<sup>46</sup> Within a few years, dissatisfaction with the classification called for revisions (DSM-III-R in 1987 and in 1994 (DSM-IV)).<sup>47</sup>

Melancholia was ignored as each revision added new categories in response to the needs of different practitioner groups. In the first DSM classification, four different depressive reactions were identified, with four subtypes for “affective reactions.” In the 1968 version, two additional subtypes were added. By 1980, four major mood disorders were identified, with 10 subtypes. For major depression, an additional three subtypes were listed. “Melancholia” could still be specified as either present or absent for major depression but was not recognized as a specific disorder. As the core disorder of mood, the DSM-III commission offered a single concept of “major depression” (with descriptors of single episode or recurrent) and with the variant *bipolar depression* (with mixed, manic, and depressed variants). *Depressive disorder not otherwise specified* and *abnormal bereavement* were two additional entities. *Psychosis* became a specifier of mood disorders. A syndrome of “dysthymia” was revived.<sup>48</sup> The concepts of melancholia, melancholic depression, and involutional depression were discarded.<sup>49</sup>

Bipolar disorder was distinguished as a separate class by the occurrence of excitement, distractibility, agitation, and talkativeness in the patient’s life history. Parallel to



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the subtyping in the DSM category of major depression, the bipolar disorders were divided into *bipolar I* with a *single manic episode* (with more recent episode *mixed* or *depressed* or *unspecified*), *bipolar II* (*with hypomanic but not manic episodes*), and *cyclothymic disorder*.<sup>50</sup> The list of specifiers is similar to those in the major depressive category, with the addition of *rapid cycling*.

The new classification and specific criteria were quickly challenged by clinicians who could not fit their patients within the defined categories. In response, new diagnostic classes were included in the 1987 revision (DSM-III-R) and again in the 1994 iteration (DSM-IV).<sup>51</sup> The number of recognized diagnostic entities dramatically increased. The episodic nature of emotional illnesses was recognized in the definition of *major depressive, manic, mixed, and hypomanic episodes* that were combined into *major depressive disorder* (either *single* or *recurrent*), and further divided by the specifiers of *chronic* and *severity/psychotic/remission* and by the features of *catatonia, melancholia, atypical, or postpartum onset*. To the recurrent disorders, two additional specifiers of *course* and *seasonal pattern* were offered.

This extended list of diagnoses was still considered insufficient. Clinicians labeled variations in the duration of the illness, its seasonal features, differential response to medication, and mixtures of psychopathology as *seasonal affective disorder, atypical depression, double depression, brief recurrent depression, and endogenomorphic depression*.<sup>52</sup> Mood disorders were separated by assumed precipitants and labeled major depression following childbirth (*postpartum depression*), in menopause (*involuntary depression*), with aging (*geriatric depression*), and after the loss of a loved one (*abnormal bereavement*). The labels were offered as if the psychopathology, course, outcome, or treatment of the condition was differentiable from other depressive disorders. In clinical practice, however, these situational precipitants do not define the presentation of the illness, the response to treatments, or the endocrine markers.<sup>53</sup>

The limitations of the present DSM classification are well recognized. The DSM-V iteration planned for the years 2007–2010 seeks a basis in experimental studies of genetic, neuroanatomic, neuroimaging, developmental science, and family criteria.<sup>54</sup> Whether the neurosciences will offer sufficient data to define a more useful classification is unpredictable.

Instead of looking to an unsure future classification based on models and studies yet to be reported, there is merit in a simplified classification of the mood disorders based on the classical principles of clinically defined signs and symptoms and course of illness, as offered by nineteenth-century psychopathologists. The psychodynamic and psychopharmacologic interruptions are false trails, misjudgments in the development of a psychiatric science that were attractive for a time. In addition to clinical criteria, biological treatments are remarkably effective and they may be used to define diagnostic criteria. Some laboratory tests hold promise for supplementing treatment response. To redress the present false trail on which psychiatric classification is embarked, a single image of depressive mood disorders is parsimonious. *Melancholia*, recognized as a central theme of depressive illness throughout much of medical history, provides the standard on which to judge mood disorder.

NOTES

1 Styron (1990), pp. 36–7.  
2 Wallace (1994); American Psychiatric Association (1980, 1994).  
3 Parker (2000).  
4 Osler, Wm. Cited among aphorisms. See: <http://www.vh.org/adult/provider/history/osler/5.html>.  
5 Sadler *et al.* (1994).  
6 The evidence for these conclusions is detailed in subsequent chapters.  
7 Beck *et al.* (1977).  
8 Adams (1939), *The Sacred Disease*, p. 344. Hippocrates describes a patient:  
In Thasus, a woman, of a melancholic turn of mind, from some accidental cause of sorrow, while still going about, became affected with loss of sleep, aversion of food and had thirst and nausea . . . On the first, at the commencement of night, frights, much talking, despondency, slight fever; in the morning frequent spasms, and when they ceased, she was incoherent and talked obscurely; pains frequent, great, and continued. On the second, in the same state; had no sleep; fever more acute. On the third, the spasms left her, but coma, and disposition to sleep, and again awaked, started up, and could not contain herself; much incoherence; acute fever; on that night a copious sweat all over; apyrexia, slept, quite collected; had a crisis. About the third day . . . a copious menstruation (*The Epidemics*, p. 346–7.)  
Hippocrates offers treatments such as abstaining from all excesses, a vegetable diet, exercise short of fatigue, sexual abstinence, and bleeding, if necessary.  
9 Mathews M. Theories of depression before the 20th century. <http://www.priory.com/homol/dephist.htm>  
10 Zilboorg (1941).  
11 Middle Eastern physicians such as Avicenna (980–1037 CE) recognized melancholia as a brain disease and not due to the influence of the supernatural (Jackson, 1986, pp. 62–4).  
12 Bright (1586). See Hunter and Macalpine (1982), pp. 36–40.  
13 Burton’s scholarly work is encyclopedic, describing many forms of the illness. It was often reprinted and is now considered a literary classic. Burton was himself a sufferer. For a delightful frontispiece of Burton’s fourth edition, see Hunter and Macalpine (1982), p. 99. A reprint of the three volumes, published in 1932, was recently published by the *New York Review of Books* and also a fully annotated six-volume series by Oxford University Press (Rosen, 2005).  
14 Hunter and Macalpine (1982), pp. 241–3. For a detailed description of psychotherapy recommended for this condition, see Timothy Rogers (1691), *ibid.* pp. 248–51. For a description of the use of opium for melancholia, see George Young (1753), *ibid.* pp. 395–8.  
15 Ascribed to Vogel (1772) by Lewis (1934a).  
16 Pinel (1806).  
17 Melancholia is “a chronic afebrile, brooding delirium fixed on a small number of objects” Boissier de Sauvages, quoted by Lewis, 1934a, p. 6.  
18 From Haslam’s *Observations on Madness and Melancholy*, quoted by Shorter (2005), pp. 36–7.  
19 Portions of Falret’s book are translated by Sedler (1983). Falret’s description of *la folie circulaire* is acknowledged by Kraepelin in his formulation of manic-depressive insanity. A circular insanity was recognized by many authors, including Baillarger (*la folie à double*