Melancholia

This book provides a comprehensive review of melancholia as a severe disorder of mood, associated with suicide, psychosis, and catatonia. The syndrome is defined with a clear diagnosis, prognosis, and range of management strategies, differentiated from other similar psychiatric, neurological, and general medical conditions. It challenges accepted doctrines in the classification and biology of the mood disorders and defines melancholia as a treatable mental illness. Described for millennia in medical texts and used as a term in literature and poetry, melancholia was included within early versions of the major diagnostic classification systems, but lost favor in later editions. This book updates the arguments for the diagnosis, describes its characteristics in detail, and promotes treatment and prevention. The book offers great hope to those with a disorder too often misdiagnosed and often fatal. It should be read by all those responsible for the management of patients with mood disorders.

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Melancholia

The diagnosis, pathophysiology, and treatment of depressive illness

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Preface

O Lord, all my desire is before you;
From you my groaning is not hid.
My heart throbs; my strength forsakes me;
The very light of my eyes has failed me.
My friends and neighbors stand back
Because of my affliction;
My neighbors stand afar off. *Psalm 38*

At any point in time on this planet, almost two and a half times as many persons are depressed as are demented. Counting all variations on the theme, about 10% of men and 20% of women are at lifetime risk for experiencing a depressive illness. Based on numbers of persons affected, the World Health Organization estimates that depressive illnesses are the fourth highest cause of medical disability and premature death worldwide in years of illness, treatments required, lost productivity during episodes, and death rates.[1]

Ten to 15% of depressed persons die by suicide. This rate translates into about one million persons annually, worldwide, and 30000–90000 persons annually in the USA. The first figure is the accepted count and the latter figure is estimated from analyses that acknowledge underreporting. In the USA, suicide is the 11th leading cause of death. Most persons over age 50 have known at least one individual who has committed suicide. Among depressed persons, sufferers of melancholia have the highest suicide rates.

Depressive illness is increasing in frequency among persons born closer to the present (a period effect), and first episodes are occurring at younger ages (a cohort effect). These trends result in more ill persons with more years of illness.

Of the persons who kill themselves annually in the USA, nearly 50% (15000–45000 individuals) seek help from a physician within the 3 weeks before they commit suicide – a sad sign of a public health failure because suicide is preventable. In treating depressed patients, psychiatrists meet *minimal* standards of care about 80% of the time, whereas generalist physicians, who see most sufferers of depression, meet the standards of care only 20% of the time. Although the mood is often recognized, a depressive illness is frequently interpreted as disappointment, bereavement, or

demoralization, and is ignored as the brain disease that it is. Although misfortune can precipitate a depressive episode, once the sequence of pathophysiologic events that become a depressive illness unfolds, the changes in brain functioning sustain the expression of the illness. Depressive illness is highly responsive to proper treatment, but more often than not, depressed persons are inadequately treated.

Many forms of depressive illness are recognized. The most prominent are identified as the mood disorders of major depression, dysthymia, bipolar depressive disorder, and depressive illnesses associated with a general medical condition. To this list are added specifiers of frequency (single or recurrent), severity, psychosis, catatonia, and pattern (typical or atypical). Other syndromes of depressive mood are found throughout the *Diagnostic and Statistical Manual* (DSM) classification system. This varied taxonomy lacks supporting psychopathological or pathophysiological evidence and, as a consequence, the taxonomy lacks validity. Reliable diagnosis, prognosis, selection of treatment, and outcomes for sufferers of depressive illness are often poor.[2] Decades of research, however, identify a central pathophysiology in the neuroendocrine system. This theme is *melancholia*, and identifying this syndrome clarifies diagnosis, prognosis, and treatment for more successful outcomes.

Melancholia is a severe disorder of mood, often fatal, that has been described for millennia in medical texts and by poets, novelists, and playwrights. Melancholia is definable by measurable signs and symptoms, characteristic neuroendocrine and neurophysiologic profiles, and its treatment-responsiveness to electroconvulsive therapy (ECT) and to pharmacodynamically broad-spectrum antidepressant drugs. Melancholia is often associated with stupor, catatonia, psychosis, suicide, and manic-depressive illness.[3] Melancholia is a lifelong process with a genetic risk.

Early *International Classification of Diseases* (ICD) editions and DSM-I and DSM-II classifications identified melancholia, but these classification systems were not helpful in prescribing newly introduced treatments (e.g., insulin coma, psychosurgery, convulsive therapy) that were found to be effective in schizophrenia and then in manic-depressive illness. The efficacy of psychotropic drugs was also weakly correlated with heterogeneous DSM categories, discouraging the search for treatment response as a feature of classification. The DSM-III and subsequent classifications, introduced as operationally defined and more "scientific," produced no better results. To achieve the approval of the largest segments of the diverse memberships of professional organizations, the DSM definition of mood disorder became overly broad and criteria for the diagnosis of major depression overly liberal. The "worried well" with characterological depressive moods were conflated with melancholia into the category of "major depression." The neuroendocrine, neurophysiologic, and psychopathologic delineators of melancholia were confounded, and discarded as diagnostic and prognostic clinical laboratory aids. Under the DSM-III system, the dexamethasone suppression test (DST) identified melancholia in 50% or more of depressed patients, but rather than concluding that the other 50% represented different forms of distress, the DST was discarded as a measure of melancholia.[4]

In the decades after the introduction of DSM-III, intrusive actions of the pharmaceutical industry encouraged a weakening of criteria to justify the use of antidepressant

drugs in the largest number of persons. The safety and efficacy of the older, no longer patentable agents (tricyclic antidepressants, monoamine oxidase inhibitors, and lithium) were maligned through aggressive marketing that relied on unsound industry-sponsored comparison studies. Academic psychiatry went to the highest bidder.[5]

In response to weakened criteria and confusing classification, we reintroduce melancholia as the classic depressive illness with definable diagnostic criteria and effective treatment algorithms. We write this book for physicians and other health care professionals who treat severely ill depressed patients. It is intended to spur better modeling of disorders in psychiatric classification schemes.[6] Our approach is that of the clinician-scientist, not the bench researcher, although we detail the biology of depressive illness and the evidence that it is a brain disease.

We set the historical stage and describe the remarkably consistent conceptual image of melancholia over millennia. We describe the disorder and review studies that systematically delineate melancholia, mirroring the historical record, and validating melancholia as a definable syndrome. Laboratory findings that support the melancholia syndrome and its variations (e.g., psychotic depression) are presented. We offer a systematic examination for the classic psychopathology of melancholia.

A variety of labels have splintered the melancholia concept. We show these to be variations of melancholia. We offer criteria on how to separate melancholia from depressive-like syndromes that have been inappropriately attached to it, and from other conditions in which apathy and psychomotor slowing are features. Suicide is a principal risk in melancholia, and we discuss the recognition of suicide and suicide prevention. Convulsive therapy is the syndrome's most effective treatment and we discuss how to maximize its effect. We detail medication management of patients suffering from melancholia. Newly proposed treatments are critiqued. We review the evidence that depressive illness is a lifelong process, discuss its pathophysiology, and offer the evidence that melancholia is an expression of brain dysfunction. Finally, we offer our conclusions that melancholia is a syndrome that warrants separate classification in the mood disorders category. We present prevention strategies, and how research needs to be refocused to provide a better understanding of melancholia.

We come to this book after decades of treating depressed patients, often those so severely ill that their deaths seemed imminent. One of us, (MAT) has been a career-long student of descriptive psychopathology in the nineteenth-century tradition, detailing the characteristics of patients with mania, depression, psychosis, and catatonia. He has been a teacher of neuropsychiatry for medical students, psychiatric residents, neurologists, and psychologists. He prescribes and administers ECT. The other (MF) has encouraged the development and administration of modern ECT, which is recognized as the most powerful antidepressant treatment. He has an extensive experience in clinical and experimental psychopharmacology, in the electrophysiology of psychoactive drugs, and in psychopathology.

Together, we have witnessed the birth and infancy of the psychopharmacology era and experienced its promises to treat patients with mood disorders better. We are

concerned about the effects on psychiatric practice, education, and research, as well as on popular culture that we see in the unhealthy relationships between academia and the pharmaceutical industry. Despite the escalation of new agents, remission rates are lower than ever and "treatment resistance" is said to be common.[7]

We write this book, however, with optimism because we know that when physicians "get it right" – the diagnosis and treatment – depressed patients have a good response and many achieve remission of their symptoms and return to productive lives. There is nothing more elating in clinical psychiatry than to see an animated and cheerful person who only a few short weeks before was immobilized with indecision and overwhelmed by apprehension, gloom, and thoughts of death.

To understand melancholia is to understand depressive illness and the care of patients with mood disorder. If we improve this understanding, we will have achieved our goal.

NOTES

1 Murray and Lopez (1996); Uston *et al.* (2004).
2 At a 2003 presentation of brain metabolic abnormalities in depressive illness to a large group of depression researchers, the chairperson opened the session by stating that the present DSM depression taxonomy was inconsistent with clinical evidence and unhelpful in research and clinical practice. The audience agreed. (University of Michigan Depression Center symposium series: M.A. Taylor, personal observation.)
3 We prefer the classic term "manic-depressive illness" to that of "bipolar disorder." It offers historical continuity and captures the essence of the disease better. Chapters 2 and 5 discuss manic-depressive disorder and its relationship to melancholia.
4 Chapter 4 provides a discussion of laboratory tests for melancholia.
5 Chapter 10 discusses industry influence on antidepressant treatment trials.
6 We have taken a similar approach in presenting the evidence for catatonia as a distinct syndrome (Fink and Taylor, 2003; Taylor and Fink, 2003).
7 Montes *et al.* (2004).

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