

Other advantages in grouping mental disorders into these clusters include (1) because psychiatrists already use these modes of explanation, rendering them more explicit dispels mystery from this field; (2) each cluster encourages research directed at uncovering the hypothesized causal elements in the examples (for diseases: pathogenesis; for dimensions: psychometric validation; for behaviors: mechanisms provoking and shaping habit; for encounters: life histories and their contexts); and (3) distinctions identified by these simple clusters render psychiatric practice more intelligible to all observers but particularly to medical colleagues. This strengthened explanatory structure indicates why recognizing symptoms, such as depression or anxiety, despite their reliable definitions or even symptomatic remedies, is insufficient for full understanding of a patient.⁸ One must strive to find the generative sources of the symptoms. Given that alleviating diseases, interrupting disordered behaviors, guiding patients with dispositional vulnerabilities, and rescripting the meaning-filled assumptions of those patients troubled by life-encounters are distinct therapeutic exercises, these clusters affirm and identify the skills used by psychiatric specialists.

Leahy⁹ quotes a Chinese adage, "The beginning of wisdom is calling things by their right name," an adage identifying the historic value of the *DSM-III*. To be coherent, psy-

chiatrists must explain to their patients, themselves, and their medical associates what they have named. Psychiatrists could advance toward this goal if, as the fifth edition of *DSM* is planned, they consider organizing the disorders already reliably described into etiopathic clusters, such as those suggested here.

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The Increasing Medical Burden in Bipolar Disorder

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BIPOLAR DISORDER IS ONE OF THE WORLD'S 10 MOST disabling conditions, taking away years of healthy functioning from individuals who have the illness.¹ With no predilection for nation, race, or socioeconomic status, classic manic-depressive illness has a prevalence of approximately 1% across all populations.² However, the personal and societal costs of bipolar disorders are not limited to the more traditional bipolar I subtype, which includes episodes of full-blown mania and major depression.³ Bipolar II disorder, involving episodes of less severe hypomania and major depression, and bipolar spectrum subtypes, which probably bring the prevalence of all bipolar disorders to more than 3% of US individuals, can also be devastating conditions. All bipolar disorders are chronically recurring illnesses associated with substantial morbidity and mortality.^{1,6}

The morbidity, mortality, and personal suffering associated with bipolar disorder are not simply a result of psy-

chiatric symptoms and the attendant dysfunction. A wide range of medical problems have been cited in the few studies focused on medical illness in this population; the most common being cardiovascular disease, diabetes mellitus, obesity, and thyroid disease.⁷ The accumulation of key medical risk factors related to excessive nicotine use, use of alcohol and other drugs, and co-occurring anxiety disorders and eating disorders may lead to the early onset of medical diseases with poor long-term outcomes.⁸ Furthermore, because patients with bipolar disorder spend most of their time in the depressive phase of the illness, there is often a loss of the discipline and motivation required to reduce such medical risk factors. Katon⁹ has established a relationship between depression and a host of negative health behaviors, including smoking, poor diet, overeating, and a sedentary lifestyle. Furthermore, he has shown that depression has

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direct adverse physiological effects, including decreased heart rate variability and increased adhesiveness of platelets, and negative effects on adherence to medical regimens.⁹

Bipolar disorder is almost always treated in mental health settings, with patients viewing their psychiatric care as their most important form of medical care. This notion has led to a relative underrecognition of and inattention to the many physical diseases these patients experience. Furthermore, it would appear that bipolar disorder itself is generally underrecognized in primary care settings.¹⁰ Only recently has a greater awareness of medical burden and medical risk factors, stimulated by the introduction of atypical antipsychotic medication for bipolar disorder with its attendant medical problems, led clinicians and investigators to focus on these issues. However, there is still little recognition that advances in the treatment of bipolar disorder must go together with increased medical risk factor assessment, ongoing laboratory surveillance, and treatment that integrates medical and psychiatric care. Cardiovascular disease and obesity provide 2 examples of the medical needs of this patient population.

The high prevalence of cardiovascular disease among those individuals with bipolar disorder may be related to an increased prevalence of traditional cardiovascular risk factors, such as smoking, obesity, and diabetes mellitus. Alternatively, it may be related to unrecognized increased prevalences of emerging risk factors, such as inflammation, high-risk lipoprotein particle subfractions, abnormal metabolism (insulin resistance, the metabolic syndrome), and mild renal insufficiency.¹¹ For example, insulin resistance coupled with visceral adiposity and associated hypercortisolemia can act synergistically with a diathesis for bipolar disorder to worsen cardiovascular outcome and augment risk for development of type 2 diabetes mellitus and the severity of hyperglycemia.¹² In addition to differences in cardiovascular disease risk factor profiles, the pathophysiology and presentation of atherosclerosis associated with bipolar disorders may differ from that in the general population through a common mechanism that may play a role in both disease states. Until more is known about the source of the increased risk of cardiovascular disease in patients who have bipolar disorder, it is incumbent upon physicians to provide careful surveillance for both traditional and nontraditional risk factors for cardiovascular disease in this population. It is also important to try to reduce these modifiable risk factors.

For instance, obesity is both a medical disease and a risk factor for cardiovascular disease and other diseases, including diabetes mellitus.¹³⁻¹⁵ Obesity and being overweight are highly prevalent in patients with bipolar disorder and related to both adverse psychiatric and adverse medical outcomes.^{16,17} A recent review¹⁸ concluded that patients with bipolar disorder may have increased rates of abdominal obesity. It is not yet clear whether obesity is a feature of bipolar disorder itself or of the treatments used to manage it. Nor is it clear whether obesity represents a modifiable risk fac-

tor for poor psychiatric outcomes. What is clear is that many of the treatments used for bipolar disorder substantially increase the risk of overweight and obesity. The physician treating bipolar disorder is called upon to make a complex risk-benefit assessment when selecting a treatment for these patients and then monitoring their change in weight carefully, reassessing the risk-benefit ratio when substantial weight gain occurs.

Despite the increasing realization that the interplay among physiological processes responsible for medical diseases and recurrent psychiatric disease may be similar and interactive, medical care systems continue to operate across a chasm with little direct interaction among specialists. From a public health perspective, the cost of bipolar disorder involves not only health costs for the psychiatric condition but enormous medical care costs.¹⁹ In a sample of health maintenance organization enrollees, Simon and Unutzer²⁰ found that patients with bipolar disorder had total health services costs approximately 2½ times higher than costs for age- and sex-matched general medical outpatients. General medical costs of patients with bipolar disease were approximately 40% higher, with specialty mental health care costs accounting for the remaining percentage. What is not known is whether these costs could be decreased through a more integrated approach for the care of individuals with bipolar disorders.

The discovery of the interaction between mood disorders and medical disease is making it clear that mania and, in particular, depression must be adequately treated to reduce the risks of other adverse medical outcomes. In a similar fashion, the medical burden associated with bipolar disorder needs to be treated more aggressively by psychiatrists working with other clinicians in the long-term treatment of this illness. Both the medical morbidity and health economic data support a fundamental reexamination of how to treat bipolar disorder over the long term. The presence of serious medical conditions and accumulation of medical risk factors, leading to increased adverse psychiatric and medical outcomes, calls for an integrated care model. Such a model should provide patients with both psychiatric and medical care without competing goals and with clear recognition of the extent to which a mood disorder may complicate the treatment of medical disease and risk factors or vice versa.

Customized treatment must be implemented for patients with bipolar disorder in which bipolar disorder and medical risk factor assessment and patient outcomes are considered. Treatment factors such as toxicity from medications (eg, the impact of medications on body mass index and diabetes mellitus), as well as health care factors (eg, access, lack of clinician training, and lack of follow-up with respect to medical conditions), that currently lead to poor outcomes in these patients must be acknowledged. Primary prevention (eg, psychoeducation, increased physical activity, improvements in diet) should be aimed at reducing medical risk factors. An integrated treatment interven-

tion should address such issues at the point of secondary intervention by educating clinicians and providing chronic disease management.

Finally, there is a clear role for basic research in this area. Mood disorders are increasingly recognized as multisystem disorders that affect immunologic, endocrine, vascular, and neural functions.²¹ Elucidating the links between specific medical illnesses and bipolar disorder may clarify the pathophysiology of bipolar disorder and suggest new approaches for secondary prevention and long-term treatments. Although recognition of the convergence of medical and psychiatric needs can lead to a series of integrated interventions that will need to be tested for their efficacy and effectiveness, a second equally important challenge is how best to conduct translational research on bipolar disorder that could lead to a better understanding of the pathophysiology of the disorder and possibly to the development of more specific-targeted interventions, with reduced propensity to increase medical risks. Such a venture will require the application of clinical neuroscience biomarkers to identify appropriate subtypes of bipolar disorder. For example, given current clinical and basic data on circadian and social rhythm disruption in bipolar disorder,²²⁻²³ it may be reasonable to identify a subgroup that has circadian fragility or vulnerability. Such subgroups could be specifically treated with targeted interventions to increase regularity of social and circadian rhythms. In a similar way, it may be possible to identify a subgroup of patients with bipolar disorder who are most prone to develop a high level of medical risk factors for the metabolic syndrome or for specific chronic medical diseases. The availability of markers of prognosis and treatment outcome would tremendously enhance the capability to conduct highly targeted clinical trials aimed at improving long-term outcomes in terms of both psychiatric and medical comorbidity. The opportunities to use the new basic science tools developed for serious medical disease can find an important place in current efforts to understand the increasing medical burden of bipolar disorders.

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