Treating Depression and Anxiety in Primary Care

This ACADEMIC HIGHLIGHTS section of The Primary Care Companion to The Journal of Clinical Psychiatry *presents the highlights of the planning teleconference series "Treating Depression and Anxiety in Primary Care," which was held in November 2007. This report was prepared by the CME Institute of Physicians Postgraduate Press, Inc., and was supported by an educational grant from Forest Pharmaceuticals, Inc.*

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Depression and anxiety are common psychiatric conditions that frequently co-occur and are often underdiagnosed and undertreated. These psychiatric conditions may be accompanied by physical symptoms, and patients often present in primary care offices with physical rather than psychological complaints. In this ACADEMIC HIGHLIGHTS, experts review how to recognize depressive and anxiety symptoms and formulate individualized treatment plans that use the most appropriate therapeutic strategies to address patients' physical and mental health care needs.

Interpreting the Signs of Depression and Anxiety

Anita H. Clayton, M.D., defined 3 subtypes of comorbid depression and anxiety.[1] Patients who meet the criteria for both a depressive episode and an anxiety disorder should be diagnosed with major depressive disorder (MDD) with comorbid anxiety disorder. Patients who meet the criteria for MDD but have subthreshold anxiety symptoms should be diagnosed with anxious depression. Patients with subsyndromal symptoms of both anxiety and depression should be diagnosed with mixed anxiety and depression.

The cardinal symptoms of depression include low, sad, or depressed mood and/or loss of interest or pleasure in activities that were previously enjoyable.[2] In addition, physical symptoms of depression include changes in appetite and weight, sleep disturbances, psychomotor activation or retardation, and fatigue. Patients may also have problems with concentration, memory, or decision-making; have thoughts of death or suicide; and have feelings of worthlessness, hopelessness, helplessness, and inappropriate guilt. As part of the depressive syndrome, functional impairment may present, particularly in occupational or scholastic functioning, relationships with family or friends, or everyday social interactions. Symptoms of anxiety may include excessive worry, avoidance, sympathetic arousal, chest palpitations or pain, shortness of breath, and gastrointestinal distress.

Prevalence and Onset of Depression and Anxiety

Dr. Clayton noted that depression and anxiety are common in the U.S. general population. In the National Comorbidity Survey Replication,[3] which had 9090 respondents, the 12-month prevalence of depression was 6.6%, and the lifetime rate was 16.2%. Among patients with MDD, the rate of comorbid psychiatric disorders was 78.5% in the 12-month prevalence group and 72.1% in the lifetime prevalence group. Of the patients with MDD and comorbid disorders, anxiety disorders were the most prevalent, accounting for comorbidity in 57.5% of the participants with 12-month MDD and 59.2% of the participants with lifetime MDD. In patients with MDD and comorbid anxiety, the onset of the anxiety disorder usually happened first. In patients with anxious depression, the onset of both types of symptoms was typically simultaneous. The order of onset for patients with mixed anxiety and depression was unclear because the subsyndromal symptoms occurred in a low percentage of patients.[3]

Presentation and Course

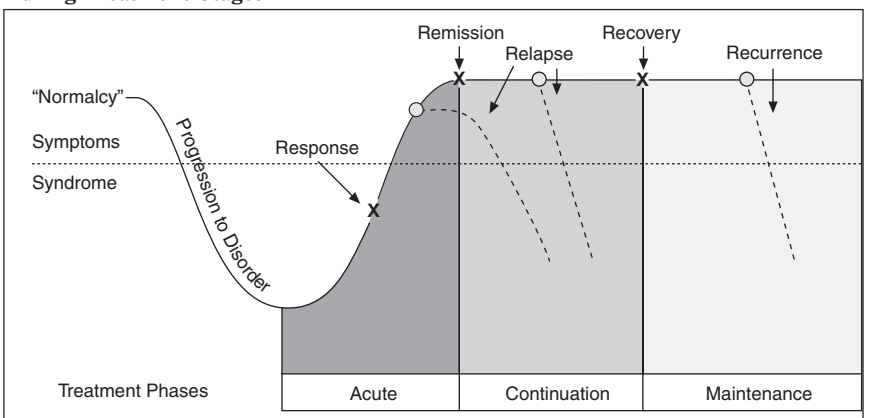
In primary care, more than half of outpatient medical visits are for somatic complaints, which are often associated with depression and anxiety.[4] However, even if patients with depression and anxiety complain of only somatic symptoms, they will answer

questions about the presence of depressive or anxious symptoms if asked.

Patients with MDD and comorbid anxiety disorders tend to have more depressive episodes, greater functional impairment, and greater severity of episodes than individuals with MDD alone. Evidence[5,6] suggests that about twice as many depressive episodes occur in patients with anxiety and MDD than occur in patients with only MDD.

Patients with depression and anxiety are also at an increased risk of suicide[7,8] and have severe impairments in daily activities.[5,8] In patients with MDD and generalized anxiety disorder (GAD) or posttraumatic stress disorder (PTSD), health-related quality of life appears to be worse than that in patients with MDD alone.[9] Patients with comorbid anxiety and MDD also have greater symptom severity and persistence,[5] thus increasing health care utilization.[8]

Figure 1. Response, Remission, Recovery, Relapse, and Recurrence of Depression During Treatment Stages[a]



[a]Reprinted with permission from Kupfer.[10]

Take-Home Points

The overlap between depression and anxiety symptoms and the tendency toward somatic presentation make the diagnosis of depressive and anxiety disorders difficult. Because patients with this comorbidity have greater functional impairments, more severe course, and an increased risk for suicide than patients without comorbid anxiety and depression, Dr. Clayton concluded, early recognition of anxiety disorders and components of depression in patients with anxiety disorders is vital for early intervention and perhaps prevention of the onset of depression.

Tailoring Treatment to Optimize Response and Minimize Side Effects

Jeffrey L. Susman, M.D., explained how to tailor treatment plans to individual patients with comorbid depression and anxiety. Clinicians should first rule out other concomitant psychiatric disorders, including substance abuse. Suicidal ideation must be addressed with every patient. After the acute symptoms have responded to treatment, patients should be led to full remission (Figure 1).[10] Once at remission, continuation therapy should last for approximately 9 months. Maintenance therapy should be considered for patients with recurrent or initially severe depression.

Screening Tools

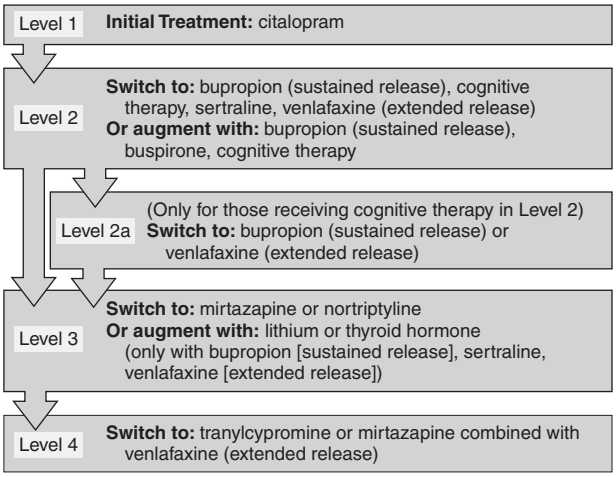
One effective tool for identifying and measuring the severity of depressive symptoms is the 9-item Patient Health Questionnaire (PHQ-9), which is based on 9 *Diagnostic and Statistical Manual of Mental Disorders,* Fourth Edition (DSM-IV) criteria for the diagnosis of MDD.[11] The PHQ-9 is quickly and easily filled out, can be self-administered, and provides a way not only to assess the patient at initial diagnosis of major depression but also during his or her course of therapy.[12] A PHQ-9 score of 19 indicates that robust therapy may be in order, while a patient who scores 9 may only require counseling, relaxation, and exercise. Other instruments, such as the Beck Depression Inventory,[13] Zung Self-Rating Depression Scale,[14] and the 16-item Quick Inventory of Depressive Symptomatology (QIDS),[15] are also useful tools for assessing depressive symptoms, according to Dr. Susman.

Screening for bipolar disorder is also an important part of patient assessment because these patients are much more likely to seek treatment when they are depressed than when they are manic. The Mood Disorder Questionnaire[16] is a useful tool in this regard. A family history of bipolar disorder and an early and exaggerated response to antidepressant monotherapy—particularly mixed depression or a switch to mania—are also signs to look for when screening for bipolar disorder, noted Dr. Susman. Hirschfeld et al.[17] found that, in a primary care clinic, 21% of patients taking an antidepressant for depression screened positive for bipolar disorder. If a patient has bipolar disorder and not depression, the treatment plan, including pharmacotherapy, will be quite different.

Suicide Risk

Dr. Susman stated that clinicians should always be mindful of the risk of suicide associated with MDD and anxiety.[7,8] Asking a patient to talk about suicidal ideation should be a routine part of any mental status examination. A suicide assessment gives the clinician an idea of the level of risk facing the patient, and patients may feel relieved after discussing their suicidal thoughts. The clinician should query the patient as to the availability of the

Figure 2. Sequenced Treatment Alternatives to Relieve Depression (STAR*D) Algorithm[a]



[a]Reprinted with permission from Rush et al.[18]

means to commit suicide, the lethality of those means, and the patient's seriousness of intent. The clinician must also try to learn if the patient is apt to be impulsive, is using or abusing substances, and has social and family supports. In patients with major affective disorders, the following characteristics were associated with suicide: panic attacks, severe psychic anxiety, diminished concentration, global insomnia, moderate alcohol abuse, anhedonia, hopelessness, suicidal ideation, and a history of previous suicide attempts.[7]

Stepwise Therapy for Depression

Dr. Susman stated that the first step in treating a patient who has severe MDD is to start effective medication.[18] For patients with mild or subthreshold depression, treatment may entail support, exercise, informal counseling, or formal psychosocial interventions such as cognitive-behavioral therapy, interpersonal therapy, or problem-solving therapy. These strategies may also be needed in patients taking medication. The acute phase of treatment typically lasts 6 to 10 weeks, but response can be assessed after 4 to 6 weeks. Clinicians should be alert for medication nonadherence throughout treatment because, even after remission, most patients need to continue medication for 6 to 9 months. Some patients (e.g., those who had psychotic depression or a depressive episode lasting more than 6 months) warrant longer continuation pharmacotherapy. Maintenance pharmacotherapy should be considered for patients with recurrent depression, initially severe depression, or those in whom remission was difficult to achieve.

Specific classes of antidepressants work with various levels of success in specific patients. Dr. Susman suggested that the clinician consider other factors, such as the patient's comfort in using a particular medication, the patient's comorbidities, the patient's insurance coverage, drug-drug interactions, and side effects when deciding what medication to prescribe. The Sequenced Treatment Alternatives to Relieve Depression (STAR*D; Figure 2) study[19] examined the treatment of 3671 individuals with nonpsychotic MDD. At baseline, 44.6% of patients had anxious features of depression, and the rates of concurrent agoraphobia, GAD, obsessive-compulsive disorder, panic disorder, PTSD, and social phobia ranged from 10.5% to 29.1%. Over a third of the patients were treated in primary care settings. About 17% of subjects had attempted suicide.

The STAR*D study[19] used a methodical, stepwise design to treat MDD. Because patients were given the option of switching or augmenting therapies at different steps, the STAR*D study design is separated from that of typical randomized controlled trials. Each acute treatment step lasted 12 to 14 weeks.

The STAR*D study illustrated that several augmentation and switch strategies may be needed to bring patients with depression to remission (see Figure 1). Almost two thirds of patients failed to achieve remission with the first step of treatment, citalopram.[19] In step 2, patients chose between switching to bupropion SR, cognitive therapy, sertraline, or venlafaxine XR or augmenting the original citalopram dosage with bupropion SR, buspirone, or cognitive therapy. In this step, 30.6% of patients achieved remission. Treatment-resistant patients continued to step 3, in which they were switched to mirtazapine or nortriptyline or received augmentation with lithium or triiodothyronine. The rate of patients who achieved remission after this step was 13.7%. Step 4 offered a switch to tranylcypromine or augmentation of venlafaxine XR with mirtazapine, which led 13.0% of patients to remission.

The theoretical cumulative remission rate of the study[19] was 67%, meaning one third of the STAR*D participants were left to cope with ongoing depression. Patients who improved but had not reached remission were more likely to relapse than those who had reached remission. These STAR*D results confirmed the importance of not settling for response alone, but rather pushing to remission.[20]

Maintenance Therapy and Recurrence

According to Dr. Susman, remission of symptoms should be followed by continuation therapy for approximately 9 months. Maintenance therapy to avoid recurrence is then an option (see Figure 1). Data[21] have shown that 85% of

patients had a recurrence of depression within 15 years after recovery, including 58% of those who had remained well for at least 5 years after recovery. In light of these data, Dr. Susman suggested that a patient with depression complicated by anxiety may be a candidate for ongoing maintenance therapy. He stated that virtually all professional guidelines recommend long-term maintenance therapy for patients with 2 or more prior episodes, as well as for selected individuals following the second episode.

Take-Home Points

Lastly, Dr. Susman listed 4 steps for treating depression and anxiety: (1) use a formal instrument to diagnose depression and anxiety; (2) screen patients who present with depressive symptoms for anxiety, bipolar disorder, substance abuse, and suicidal ideation; (3) treat to remission by using continuation therapy; and (4) follow-up with maintenance therapy after remission has been achieved.

Depression as a Significant Comorbidity

Larry Culpepper, M.D., M.P.H., addressed the associations between MDD and chronic medical conditions such as arthritis, diabetes, stroke, and heart disease. These associations affect the management of both the depressive disorder and the comorbid medical illness.

In primary care settings, physical complaints have been shown to increase the likelihood that the patient has a mood or anxiety disorder.[22] Researchers have found that depression and anxiety not only increased the likelihood of chronic disease but also markedly worsened the course and long-term outcome of illnesses such as arthritis,[23,24] diabetes,[25–27] stroke,[28,29] and cardiovascular disease.[30,31]

Mechanisms of Risk

The average age at onset for MDD is the mid-20s, and for many anxiety disorders, it is childhood to mid-20s.[2] Depression and anxiety convey an increased stress response, that is, a chronic alteration in hypothalamic-pituitary axis function and sympathetic nervous system function.[32] This increased stress response over the years may explain the onset of diabetes, stroke, and heart disease in middle age.

Possible mechanisms of cardiovascular risk associated with depression include increased platelet activation/aggregation,[33] reduced heart rate variability, and alterations in cardiac autonomic tone.[30] Patients with MDD may also be less likely to comply with medical regimens and recommended lifestyle changes.[34,35]

Depression and Arthritis

Arthritis is a chronic condition, the outcome of which is worsened by comorbid depression. Mortality over 4 years for patients with rheumatoid arthritis and depression was increased by a hazard ratio of 2.2 (95% CI = 1.2 to 3.9, p = .01) compared with arthritis patients without comorbid depression.[23] Among patients with rheumatoid arthritis, 65% reported depression (with 37.5% having moderate or severe depression) and 44% had anxiety.[24] Depression and anxiety were both correlated with arthritis-related pain and functional impairment.

According to Dr. Culpepper, because arthritis outcomes are affected by psychiatric comorbidity, psychiatric treatment can help patients with arthritis. Lin et al.[36] found that collaborative care of depression and arthritis resulted in the reduction of depressive symptoms, a significant reduction in pain intensity (p = .009), and a significant reduction of interference in daily activities due to pain (p = .002). Overall health and quality of life were also improved relative to control patients after 12 months of depression treatment.[36]

Depression and Diabetes

Diabetes is a serious disease that carries the risk of many health-related complications, and MDD appears to be a risk factor for the onset of diabetes. The Epidemiologic Catchment Area Program[25] demonstrated, over a 13-year follow-up period, a relative risk of 2.23 (95% CI = 0.90 to 5.55) for the onset of type 2 diabetes in patients with MDD compared with those without MDD. Depression not only increases the risk for diabetes but, if untreated, also worsens the course of diabetes. A 5-year follow-up study[26] found that patients with MDD had significantly worse glycemic control than patients without depression (p = .03). Conversely, better glycemic control in patients with type 2 diabetes led to improved mood and well-being and fewer physical symptoms associated with the disease.[27] Successfully treating depression in patients with diabetes should, therefore, improve the course and outcome of both illnesses.

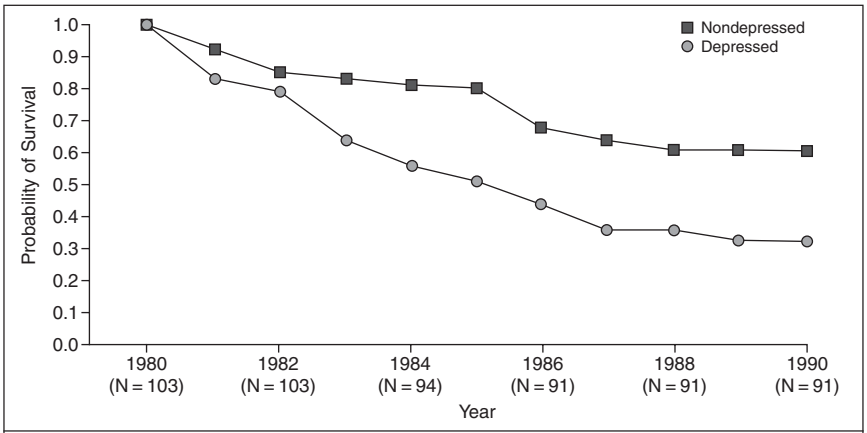
Depression and Stroke

Patients with a history of MDD were found to be 2.6 times more likely to experience a stroke than individuals without depressive illness.[28] Patients with depression were also more likely to suffer a fatal stroke.[29] Individuals with depression who experienced a stroke were 3.4 times more likely to die in the next 10 years than those who were not depressed (Figure 3).[29] Functional recovery after a stroke may be accelerated by improvement in depressive symptoms, although cognitive and neurologic factors influence the level of improvement.[37]

Depression and Heart Disease

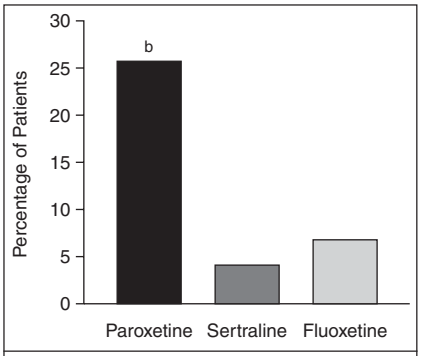
Among patients with acute coronary syndromes, 15% to 23% have MDD, which is an independent risk factor for morbidity and mortality associated with heart disease.[38] Dr. Culpepper noted that the literature on cardiovascular disease is impressive in its depth and consistency about the worsening of cardiac outcome in patients with depression.[30,31] Cardiologists often look for presentations of depression in their patients because of the wealth of

Figure 3. Probability of Survival Following Stroke for Depressed and Nondepressed Patients[a]



[a]Reprinted with permission from Morris et al.[29]

Figure 4. Percentage of Patients With ≥7% Weight Gain at Endpoint After 26 to 32 Weeks of Therapy[a]



[a]Reprinted with permission from Fava et al.[44]
[b]Significant difference for paroxetine vs. sertraline ($\chi^2 = 5.78$, df = 1, p = .016) ($\chi^2 = 8.63$, df = 1, p = .003) and paroxetine vs. fluoxetine at endpoint.

compelling evidence concerning the exacerbation of heart disease by depression. One study[39] showed that the occurrence of myocardial infarction (MI), angioplasty, coronary bypass surgery, and death over a 12-month period was predicted by the presence of MDD before cardiac catheterization. Other studies found that depression was associated with cardiac mortality after MI[40,41] and in patients with coronary artery disease.[42]

Dr. Culpepper then explained that comorbid depression alters treatment selection. Cardiac medications and antidepressant medications should be selected to minimize not only drug-drug interactions but also adverse effects such as MI. Cohen and colleagues[43] found that tricyclic antidepressants, which have significant norepinephrine effects, increased sympathetic nervous system tone and may adversely affect cardiac rhythm and cardiac output.

Conversely, selective serotonin reuptake inhibitors (SSRIs) inhibit serotonin-mediated platelet activation. Glassman and colleagues[38] found that after hospitalization for MI or unstable angina, 14.5% of patients with MDD who took an SSRI for 24 weeks experienced severe cardiovascular events compared with 22.4% of those who took placebo. Recurrent MIs decreased by about 30% and total mortality decreased by 61% with SSRI treatment. The study was not designed to assess mortality and thus did not enroll a large enough population for statistical significance on that outcome (p = .07). However, Dr. Culpepper stated that the data[41] suggest a potent effect of SSRIs on improving cardiac outcome.

Weight gain is a side effect of SSRIs that must be considered. Fava and colleagues[44] compared weight gain during long-term treatment with the SSRIs fluoxetine, paroxetine, and sertraline. Patients with MDD (N = 284) were randomly assigned to treatment with 1 of the 3 SSRIs for 26 to 32 weeks. Patients given paroxetine gained more weight than those given fluoxetine or sertraline (Figure 4). Finally, Dr. Culpepper suggested using an antidepressant with an intermediate or long half-life so that, if the patient misses a dose, he or she does not mistake withdrawal symptoms for cardiac symptoms.

Conclusion

Dr. Culpepper concluded that MDD and anxiety are chronic disorders that tend to be episodic in ways similar to arthritis, diabetes, stroke, and heart disease. Patients may be stable for a while but then have a period of worsening and require medication adjustment or other treatment. Physicians must treat psychiatric disorders and chronic medical illness together because each influences the other. Effective treatment of comorbid psychiatric disorders and chronic medical conditions requires an integrated treatment strategy to ensure the best possible patient outcomes.

Treating Severe Depression: A Case Model

Joseph A. Lieberman III, M.D., M.P.H., presented the following case model as an illustration of treating depression in primary care.

Case report. Mr. A, a 38-year-old certified public accountant (CPA), came to the primary care office with a chief complaint of "There must be something medically wrong with me." The primary care clinician had cared for Mr. A's family for the past 5 years, but Mr. A's cardiologist had been the primary source of care for Mr. A himself because of high cholesterol. However, Mr. A believes that his current problem is not within his cardiologist's area of expertise.

Mr. A related that over the past few weeks he has become increasingly moody, withdrawn, and irritable. He reported not eating or sleeping regularly, that he no longer enjoys playing with his children, and that he has begun to miss work.

Table 1. BATHE Technique Sample Questions[a]

Mnemonic	Sample Questions	Clinical Significance
Background	"What is going on in your life?"	Defines the patient's unique situation
Affect	"How do you feel about that?"	Ascertains the patient's feelings about the situation
Trouble	"What troubles you the most about this?"	Ascertains what about the situation troubles the patient most
Handling	"How are you handling that?"	Gives a sense of the patient's problem-solving skills and coping mechanisms
Empathy	"This must be very difficult for you."	Empowers and supports the patient

[a]Based on Stuart and Lieberman.[45]

Table 2. SIG E CAPS: Sample Case Evaluation of Minor Symptoms of Depression[a]

Mnemonic	Mr. A's Responses
Sex/sleep	He says he does not enjoy sex anymore, has trouble falling asleep, sleeps fitfully, and then awakens early in the morning and cannot get back to sleep. As a result, he is "tired all the time."
Interest	He has lost interest in activities he used to enjoy.
Guilt	He acknowledges that "he is the problem," not his wife and children. He feels guilty about that.
Energy	He acknowledges that his energy level is falling.
Concentration	He has difficulty concentrating, particularly at work, and even more after an unusually poor night's sleep. Now he takes the day off after an especially bad night.
Appetite	He says food does not appeal to him and his appetite is "way off."
Psychomotor agitation or retardation	He denies agitation but admits to sluggishness and hesitancy in speech.
Suicide	He admits that to him "life is pointless," and thoughts of death are commonplace lately. However, he denies having a suicide plan or having access to lethal means.

[a]Based on Lieberman.[47]

When asked, "How has your health been in general?" Mr. A responded that he has always been reasonably healthy. He was hospitalized on 1 occasion as a teenager for observation following an automobile accident. He had a tonsillectomy as an outpatient when he was 6 years old. He had been taking a statin drug for moderately elevated cholesterol and an occasional aspirin for headache. The only symptoms he reported were that he is "out of sorts" and "can no longer see the point of most things." Mr. A denied grandiosity or episodes of euphoria and other markers of bipolar disease.

Primary Assessment: BATHE

To elucidate Mr. A's symptoms, Dr. Lieberman suggested using the BATHE technique (Background Affect Trouble Handling Empathy)[45] to perform a focused psychosocial interview (Table 1). The BATHE technique is designed to illuminate issues of a sensitive and psychosocial nature in a timely and efficient manner.

Mr. A was asked, "What is going on in your life?" (**B**ackground) and he responded, "Not much. I get up, go to work, come home, eat dinner, watch TV, and go to bed. I used to play with the kids and go to their games, but I don't do that much anymore. Everything just seems so pointless." When asked, "How do you feel about that?" (**A**ffect) he said, "I don't know. I just don't enjoy things the way I used to." When asked about the most troubling aspect of his situation (**T**rouble), Mr. A replied, "Well, is this all there is? I mean, it's really depressing." When asked how he was handling the current situation (**H**andling), Mr. A replied, "Well, I guess not very well. My wife complains about my mood, but she and the kids aren't the problem. I am, but I don't know what to do about it." In line with an empathetic response, the clinician supported him with an encouraging statement concerning his decision to seek treatment (**E**mpathy).

Then, the clinician stated that he felt that Mr. A could be helped, but first the clinician needed to elicit some additional information. Depressed mood or anhedonia are the primary symptoms of MDD, but secondary criteria must be confirmed for a diagnosis of MDD.[2]

Secondary Assessment: SIG E CAPS

Dr. Lieberman recommended employing the SIG E CAPS[46] mnemonic device to either confirm or rule out a diagnosis of MDD. This mnemonic aids clinicians in remembering secondary symptoms of MDD (Table 2).[47] If a patient has at least 1 major symptom (e.g., depressed mood or anhedonia) and 4 minor symptoms or 2 major symptoms and 3 minor symptoms in the same 2-week period, and these symptoms represent a change from previous functioning, then the patient meets the DSM-IV criteria for MDD.[2]

In this case, Mr. A met the criteria for a diagnosis of MDD. The absence of other psychiatric symptoms, such as excessive worry or mania, ruled out other psychiatric diagnoses. Dr. Lieberman emphasized that being compassionate, caring, and kind is important when inquiring about suicidal thoughts and plans.

Medical, Family, and Social History

The next step in treating Mr. A, according to Dr. Lieberman, was gleaning additional medical history, medications, history of alcohol and/or substance abuse, family history, and social history. Mr. A's medical history was as stated, with the addition of the usual childhood illnesses. He had no known food or drug allergies and was seen regularly by his cardiologist for hypercholesterolemia.

In addition to the statin drug, Mr. A took 1000 mg of vitamin C and 81 mg of aspirin daily, plus an occasional full-strength dose of aspirin for a headache or general aches and pains. Mr. A stated that he used to "enjoy a cold beer" after strenuous exercise, but he was not "doing much of that," and the beer "had no appeal" for him.

Mr. A reported that his mother was 60 years old. She had an episode of postpartum depression after the birth of his youngest brother, but she was now healthy. His father was 62 years old, took a multivitamin and medication for high blood pressure, and did not plan to retire for at least 5 more years. His brothers, ages 35 and 28 years, were doing well.

According to his social history, Mr. A was a CPA for a large firm in his hometown. He said he was happily married, but because his home life was affected by his current mood, he sought treatment.

A physical examination revealed a well-nourished, 38-year-old man in no acute distress but somewhat apathetic on questioning. His vital signs were as follows: height, 59 in; weight, 145 lb; blood pressure, 130/78 mm Hg; pulse rate, 78 bpm; respiratory rate, 20 breaths per minute. Head, eyes, ears, nose, throat, chest, abdomen, genitalia, rectum, extremities, and neurologic findings were all normal.

Patient-Administered Screening Tests

Dr. Lieberman said that primary care clinicians may find patient-administered screening tests helpful. Repeating these tests during the course of treatment adjustment and monitoring will give the clinician a sense of how the patient has responded to therapy.

Mr. A scored a 20 on the PHQ-9,[12] indicating severe depressive symptoms. On the Fatigue Severity Scale (FSS),[48] Mr. A scored a 6, indicating severe fatigue. Mr. A scored a 10 on the Epworth Sleepiness Scale (ESS),[49] which indicated excessive sleepiness or a sleep disorder. The primary care clinician concluded from these tests that Mr. A had MDD with severe fatigue.

Treatment

With the diagnosis of MDD with severe fatigue established, the clinician met with Mr. A and, at his request, his wife. The clinician informed the couple that Mr. A's problem originated from an imbalance of brain chemicals that regulate mood. The clinician reassured them that although the medical community does not know everything about this disorder, medications and therapies have proven to be effective in comparable cases. The clinician suggested seeing Mr. A on a regular basis and that Mr. A keep a sleep diary. Lastly, the clinician prescribed an antidepressant medication.

One week after the initial encounter, Mrs. A called the clinician to report that Mr. A's appetite was improved, but his sleep was worse. Mr. A then added that he felt a bit better overall. He exercised as directed and adhered to principles of good sleep hygiene, but these strategies had not helped as much as he had hoped. He also took 3 mg of melatonin for a few nights, but he did not notice any change in his insomnia. Because his sleep had not improved, a hypnotic medication was added to his regimen.

The clinician saw Mr. and Mrs. A 2 weeks after the first encounter. Mr. A appeared a bit brighter but said he was still depressed and suffering from anhedonia, although not to the same degree as 2 weeks earlier. Since he began taking the hypnotic medication, his sleep improved dramatically, particularly his ability to fall asleep, and a review of his sleep diary confirmed his claim. The findings of a new physical examination were essentially unchanged, but he had gained 1 lb. He denied any suicidal ideation. The PHQ-9, FSS, and ESS all showed improvement.

Three weeks after Mr. A's first visit, Mr. A called to report that he was further improved but still not symptom-free. Mr. and Mrs. A were not completely satisfied with the pace of his treatment, but they both conceded that they were told therapy would take time and that he was making progress.

One week later, Mr. A came in for another office visit. His PHQ-9 score was now 10, his FSS score was 4, and his ESS score was 8. He said his biggest improvement was in the area of sleep, but he still took the hypnotic nightly and diligently practiced sleep hygiene. His weight was stable, and he reported that his appetite was better. The findings on the physical examination again remained unchanged.

Six weeks after the clinician first saw Mr. A, both Mr. and Mrs. A were pleased with his progress. She said, "I've got my husband back." His PHQ-9, FSS, and ESS scores were normal. He reported sleeping well with the same dosage of hypnotic medication, which his sleep diary verified. Findings on his physical examination were unchanged, except that he gained 2 lb, which was most likely a result of the return of his normal appetite.

The clinician congratulated Mr. and Mrs. A and commended them for adhering to the program. The clinician also cautioned that pharmacotherapy may have to continue for a full year, with the exception of the hypnotic agent.

Drug names: bupropion (Wellbutrin and others), buspirone (BuSpar and others), citalopram (Celexa and others), fluoxetine (Prozac and others), lamotrigine (Lamictal and others), lithium (Eskalith, Lithobid, and others), mirtazapine (Remeron and others), nortriptyline (Pamelor, Aventyl, and others), paroxetine (Paxil, Pexeva, and others), sertraline (Zoloft and others), venlafaxine (Effexor and others).

Disclosure of off-label usage: The chair has determined that, to the best of his knowledge, lamotrigine, lithium, tranylcypromine, and triiodothyronine are not approved by the U.S. Food and Drug Administration as adjuvant treatment of major depression.

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