A 55-year-old woman comes to a psychiatrist complaining of experiencing a depressed mood over the past 3 months. She notes that her mood has been consistently low (3 on a scale of 1 to 10, with 10 being the best she has ever felt), and she describes her condition as “just not me.” She has also noticed a decrease in energy and a weight gain of 6 to 7 lb occurring over the same period of time, although her appetite has not increased. She has never visited a psychiatrist before and does not remember ever feeling this depressed for this long before. She states that she has no medical problems that she is aware of and that she takes no medication. Her family history is positive for a history of schizophrenia in one maternal aunt.

On a mental status examination the patient appears depressed and tired, although she has a normal range of affect. Her thought processes are linear and logical. She is not suicidal or homicidal and does not report hallucinations or delusions. Her physical examination reveals a blood pressure of 110/70 mm Hg and a temperature of 98°F. Her thyroid gland is diffusely enlarged but not painful. Her heart has a regular rate and rhythm. She has coarse, brittle hair but no rashes.

◆ What is the most likely diagnosis?

◆ What is the next diagnostic step?
ANSWERS TO CASE 4: Hypothyroidism With Depression

Summary: A 55-year-old woman presents to a psychiatrist with a depressed mood, decreased energy, and a weight gain. She has never had these symptoms before. The results of the rest of her mental status examination are normal. Her physical examination is notable for a diffusely enlarged thyroid gland.

◆ Most likely diagnosis: Mood disorder secondary to a general medical condition.

◆ Next diagnostic step: Obtain thyroid studies for this patient, including determinations of thyrotropin (TSH), triiodothyronine, and thyroxine levels.

Analysis

Objectives
1. To recognize mood disorder occurring secondary to a general medical condition.
2. To be able to use the most likely diagnosis for this patient to guide the laboratory examination required for a patient with suspected hypothyroidism.

Considerations
Although this patient’s history is consistent with that of major depression, two elements are atypical, and one very much so. A weight gain is observed in patients with atypical major depression, but this condition is usually accompanied by an increase in appetite. A weight gain in the absence of an increase in appetite is a clue to the metabolic changes caused by this patient’s hypothyroidism. At times the clinical features of hypothyroidism are evident (Figure 4-1). An enlarged thyroid is not seen in patients with major depression but is a clue that guides the specific laboratory examinations chosen in this case.

APPROACH TO MOOD DISORDER DUE TO A GENERAL MEDICAL CONDITION

Clinical Approach
Diagnosis of this disorder requires a disturbance in mood that causes significant distress or an impairment in functioning. It can resemble either an episode of depression (depressed mood or decreased pleasure) or an episode of mania (elevated or irritable mood). The history, the physical examination, or the laboratory findings must demonstrate a causal physiologic relationship between the medical illness and the change in mood. In other words, the depression or
mania cannot result only from the stress of having a medical condition. The mood episode also should not occur only during a delirium.

**Differential Diagnosis**
The differential diagnosis for mood disorder due to a general medical condition is large given the numerous medical and neurologic conditions that can cause depression or another mood state. Table 4-1 lists many of them. Also important in this differential diagnosis are substance-induced mood disorders caused not only by alcohol and illicit drugs (in intoxication and in withdrawal) but also by a vast number of medications. See Table 4-2 for a partial list of medications that can cause depressive symptoms. Making a distinction between primary (psychiatric) and secondary (induced) mood disorder can sometimes be difficult, especially because stressors such as medical illnesses themselves can trigger episodes of both major depression and mania.

**Treatment**
The treatment of mood disorder due to a general medical condition entails addressing the underlying medical condition first, if possible, and obtaining improvement in the symptoms. For example, in the above case, if the woman is found to have hypothyroidism and subsequently treated with thyroid supplementation, she will likely experience an improvement in mood. Mood symptoms caused by medical or neurologic conditions that are recurrent, chronic, or otherwise untreatable (eg, dementias, strokes, malignancies) often respond to typical psychopharmacologic treatments such as selective serotonin reuptake inhibitors, tricyclic antidepressants, mood stabilizers, and electroconvulsive therapy.
<table>
<thead>
<tr>
<th>MEDICAL CONDITION</th>
<th>MOOD DISORDER</th>
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<tbody>
<tr>
<td>Parkinson disease</td>
<td>Depression</td>
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<tr>
<td>Huntington disease</td>
<td>Depression or mania</td>
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<tr>
<td>Wilson disease</td>
<td>Mania</td>
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<tr>
<td>Cerebrovascular accident</td>
<td>Depression or mania</td>
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<tr>
<td>Cerebral neoplasm</td>
<td>Depression or mania</td>
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<tr>
<td>Cerebral trauma</td>
<td>Depression or mania</td>
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<tr>
<td>Encephalitis</td>
<td>Depression or mania</td>
</tr>
<tr>
<td>Multiple sclerosis</td>
<td>Depression or mania</td>
</tr>
<tr>
<td>Temporal lobe epilepsy</td>
<td>Mania</td>
</tr>
<tr>
<td>Hyperthyroidism</td>
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<td>Depression</td>
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<td>Depression</td>
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<tr>
<td>Uremia</td>
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<tr>
<td>Cushing syndrome</td>
<td>Depression</td>
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<tr>
<td>Addison disease</td>
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<td>Systemic lupus erythematosus</td>
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<tr>
<td>Rheumatoid arthritis</td>
<td>Depression</td>
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<tr>
<td>Folate deficiency</td>
<td>Depression</td>
</tr>
<tr>
<td>Vitamin B₁₂ deficiency</td>
<td>Depression or mania</td>
</tr>
<tr>
<td>Human immunodeficiency virus disease</td>
<td>Depression</td>
</tr>
</tbody>
</table>

**Comprehension Questions**

For the following clinical vignettes (questions [4.1] through [4.4]), choose the one most likely diagnosis (A through E):

A. Bipolar disorder, manic  
B. Episode of major depression  
C. Mood disorder due to a general medical condition  
D. Substance-induced mood disorder  
E. Bipolar disorder, mixed state

[4.1] An 18-year-old man presents with 3 days of an irritable mood, decreased sleeping, talkativeness, increased energy, and distractibility. He has no personal or family psychiatric history and no current
medical problems. His mental status examination is remarkable for psychomotor agitation and an irritable affect. He is paranoid but denies delusions or hallucinations. His physical examination is notable for a slightly elevated pulse rate and blood pressure as well as markedly dilated pupils bilaterally. The results of his urine toxicology screening are positive for cocaine.

[4.2] A 39-year-old woman presents with 1 month of a gradually worsening depressed mood, with increased sleeping, low energy, and difficulty concentrating but no appetite or weight changes. Her medical history is significant for multiple sclerosis, but she is currently not taking any medication. Her mental status examination is notable for psychomotor slowing and depressed facies. Her physical examination demonstrates several different sensory and motor deficits.

[4.3] A 52-year-old male executive presents with an onset of depression, early-morning awakening, decreased energy, distractibility, anhedonia, poor appetite, and weight loss for the past 3 months. His symptoms began shortly after he suffered a myocardial infarction. Although he did not experience significant sequelae, he has felt less motivated and fulfilled in his life and work, believing that he is now “vulnerable.” As a result, he does not push himself as he used to, and his output is beginning to decline.

[4.4] An 80-year-old woman without a psychiatric history is examined after a left-sided cerebral vascular accident has left her paralyzed on her right side. Since her stroke, she complains of an absence of pleasure in anything that she formerly enjoyed. She describes frequent crying spells, increased sleeping, a decreased appetite with weight loss, and feelings of hopelessness and helplessness.

[4.5] A 33-year-old woman complains of epigastric discomfort radiating to her back and of feeling “blue” for the past 2 months. She has lost 10 lb over the past 4 weeks without trying. Which of the following is the most likely diagnosis?
A. Peptic ulcer disease
B. Diabetes mellitus
C. Esophageal spasm
D. Pancreatic carcinoma

Answers

[4.1] D. The most likely diagnosis for this man is substance (cocaine)-induced mood disorder. Although he presents with classic manic symptoms (irritable mood, decreased sleep, etc), he has no psychiatric or family history of mood disorder. His physical examination reveals several findings not necessarily consistent with mania, namely, elevated vital signs (pulse rate and blood pressure) and dilated pupils. The
important factor in this case is his obvious cocaine use, which can produce symptoms mimicking those of acute mania.

[4.2] C. The most likely diagnosis in this case is mood disorder due to a general medical condition, namely, multiple sclerosis. Although this woman displays the characteristic symptoms of an episode of major depression (depressed mood, increased sleeping, low energy), she does not exhibit the appetite or weight changes commonly seen in this illness. Steroids often cause mood symptoms such as depression or mania, but she is currently not taking any medication. The results of her physical examination are also consistent with a flare-up of her multiple sclerosis and demonstrate a temporal relationship to her depression. The central nervous system white matter lesions seen on imaging are known to cause a depressive state.

[4.3] B. The most likely diagnosis for this man is major depression. He has symptoms typical of the disorder, both depressed mood and neurovegetative symptoms lasting for more than 2 weeks. Although his condition was preceded by a heart attack, it was not a physiologic cause of his depression. Rather, his medical illness (and subsequent feeling of vulnerability) was the stressor that brought on his episode of depression.

[4.4] C. The most likely diagnosis in this case is mood disorder due to a general medical condition, namely, a cerebral vascular accident. The patient has obvious symptoms of a depressive illness, including anhedonia. These symptoms also have a clear temporal relationship to her stroke, which has left her with significant motor deficits. Cerebral vascular events, especially those affecting the left frontal region (where the stroke occurred), are well known to result in depression.

[4.5] D. Pancreatic carcinoma is commonly associated with depression. Discomfort radiating to the back and painless jaundice are typical symptoms.

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**CLINICAL PEARLS**

❖ A complete medical history, a physical examination, and routine laboratory tests, including thyroid studies, are essential in the workup for an individual presenting with a first episode of mood disorder.

❖ Atypical symptoms, such as weight gain without an increase in appetite, suggest mood disorder due to a general medical condition.

❖ The medical condition is required to have a causal physiologic relationship to the mood episode for mood disorder secondary to a medical condition to be diagnosed.

❖ Strokes, especially left frontal strokes, commonly cause subsequent episodes of depression.
REFERENCES