

## ... CASE 1

A 42-year-old man comes to his outpatient psychiatrist with complaints of a depressed mood, which he states is identical to depressions he has experienced previously. He was diagnosed with major depression for the first time 20 years ago. At that time, he was treated with imipramine, up to 150 mg/day, with good results. During a second episode, which occurred 15 years ago, he was treated with imipramine, and once again his symptoms remitted after 4 to 6 weeks. He denies illicit drug use or any recent traumatic events. The man states that although he is sure he is experiencing another major depression, he would like to avoid imipramine this time because it produced unacceptable side effects such as dry mouth, dry eyes, and constipation.

+ **What is the best therapy?**

• **What are the side effects of the proposed therapy?**

## ANSWERS TO CASE 1: Major Depression, Recurrent

*Summary:* A 42-year-old man complains of symptoms of major depression identical to two prior episodes he experienced in the past. Previously, he was successfully treated with a tricyclic antidepressant (TCA), although this class of medication often produces anticholinergic side effects such as dry mouth, dry eyes, and constipation, which this patient complains about. The question becomes what medication should be used to treat recurrent major depression when tricyclics are not an option.

- + **Best therapy:** A selective serotonin reuptake inhibitor (SSRI) such as sertraline, paroxetine, citalopram, or fluoxetine is one of the first-line choices of medication for this patient.
- **Common side effects: Gastrointestinal symptoms**—stomach pain, nausea, and diarrhea—occur in early stages of the treatment. Minor sleep disturbances—either sedation or insomnia—can occur. Other common side effects include tremor, dizziness, increased perspiration, and **male and female sexual dysfunction** (most commonly delayed ejaculation in men and decreased libido in women).

### Analysis

#### Objectives

1. Understand the treatment of uncomplicated major depression without psychotic features.
2. Be able to counsel a patient in regard to the common side effects of **SSRIs**.

#### Considerations

Although the patient has been successfully treated with a **TCA** (imipramine) two times in the past, these medications are no longer considered first-line treatments because of their **common side effects and their potential lethality in overdose** (cardiac arrhythmias). For a patient such as this one, one might consider using imipramine again. However, the patient specifically requests another type of medication because of his previous discomfort with the side effects. One of the current first-line treatments for patients with major depression. SSRIs are thus the logical choice; they have fewer side effects and are safer.

Table 1-1 lists the criteria for major depression, recurrent.

**Table 1-1**  
**DIAGNOSTIC CRITERIA FOR MAJOR DEPRESSIVE**  
**DISORDER, RECURRENT**

- Two or more episodes of major depression diagnosed by the following:  
Five or more of the following symptoms have been present most of the time for at least 2 weeks:
  1. Depressed mood
  2. Anhedonia
  3. Significant weight change or change in appetite
  4. Insomnia or hypersomnia
  5. Psychomotor agitation or retardation
  6. Fatigue or loss of energy
  7. Feelings of worthlessness or excessive guilt
  8. Decreased ability to concentrate or indecisiveness
  9. Thoughts of death or suicidal ideation
- There has never been a manic, hypomanic, or mixed episode.
- Symptoms cause significant distress or impairment in functioning.
- Symptoms are not caused by a substance of abuse, medication, or a medical condition.
- Symptoms are not better accounted for by schizophrenia, schizoaffective disorder, delusional disorder, or a psychotic disorder not otherwise specified.
- Symptoms are not better accounted for by bereavement (i.e., symptoms last longer than 2 months: marked functional impairment, suicidal ideation, and/or psychotic symptoms are noted)

## APPROACH TO MAJOR DEPRESSIVE DISORDER, RECURRENT

### Definitions

**Anhedonia:** Loss of interest or pleasure in activities that were previously pleasurable.

**Selective serotonin reuptake inhibitor:** An agent that blocks the reuptake of serotonin from presynaptic neurons without affecting norepinephrine or dopamine reuptake. These agents are used as antidepressants and in treating eating disorders, panic, obsessive-compulsive disorder, and borderline personality disorder.

### Clinical Approach

Major depression is a common problem. In the United States, approximately one in seven individuals will suffer from this disorder at some time in their lives. Women are affected twice as often as men, with a mean age of occurrence at 40 years. A common hypothesis concerning the etiology of

major depressive disorder involves the alteration of biogenic amines, particularly norepinephrine and serotonin. Genetics plays a role, as evidenced by family studies.

Given the frequency with which depression is a presenting complaint in the primary care setting, a mnemonic is helpful in remembering the criteria for an episode of major depression. As lack of energy is common to most of these episodes, the mnemonic relates to "treating" this symptom by "prescribing energy capsules" and is written on a prescription as **SIG: E(nergy) CAPS**. Each letter stands for a criteria (except for depressed mood) used in diagnosing an episode of major depression:

S—sleep changes

I—{decreased} interest

G—(excessive) guilt

E—(decreased) energy

C—(decreased) concentration

A—appetite changes

P—psychomotor agitation or retardation

S—suicidal ideation

## Differential Diagnosis

It is important to rule out other disorders that could be causing a depressed state, including medical diseases (e.g., hypothyroidism or multiple sclerosis), medications (e.g., antihypertensives), or substances (e.g., alcohol use or cocaine withdrawal). Obtaining a thorough history, performing a physical examination, and ordering appropriate laboratory studies are crucial in the assessment of any new onset of depression.

Many psychiatric illnesses are characterized by depressive symptoms, including psychotic disorders, anxiety disorders, and personality disorders. A critical distinction to make, especially in recurrent episodes of depression, is between major depressive disorder, recurrent, and bipolar disorder, depressed. This distinction is essential not only for making the correct diagnosis but also for proper treatment. **Standard therapies for major depression can be less effective and actually worsen bipolar illnesses.** It is necessary to obtain any current or past history of episodes of mania, as well as any family history of bipolar disorder.

## Assessment of Suicide Risk

One of the most important determinations a clinician must make in the case of a depressed individual is the risk of suicide. The best approach is to ask the patient directly using questions such as, "Are you or have you ever been suicidal? Do you want to die?" A patient with a specific suicide plan is of special concern. Also, the psychiatrist should be alert to warning signs such as an individual becoming uncustomarily quiet and less agitated after a previous expression of suicidal intent or making a will and giving away personal property. Risk factors for suicide include older age, alcohol or drug dependence, prior suicide attempts, male gender, and a family history of suicide.

The results of a careful mental status examination, risk factors, prior suicidal attempts, and suicidal thoughts and intent must be all considered.

## Postpartum Depression

As many as 20% to 40% of U.S. women report some emotional disturbance or problem with cognitive functioning during the postpartum period. Many experience what is known as **postpartum blues**, in which there is **sadness, strong feelings of dependency, frequent crying spells, and dysphoria**. These feelings, which do not constitute major depression and therefore should not be treated as such, seem to be attributable to a combination of the rapid hormonal shifts occurring during the postpartum period, the stress of childbearing, and the sudden responsibility of caring for another human being. **Postpartum blues usually lasts for only several days to a week.** In rare cases, postpartum **depression** exceeds in both severity and length that observed in postpartum blues and is **characterized by suicidality and severely depressed feelings**. Women with postpartum depression need to be treated as one would treat a patient with major depression, taking care to educate them as to the risks of breast-feeding an infant when the antidepressant appears in the milk. Left untreated, postpartum depression can worsen to a point where the patient becomes **psychotic**, in which case antipsychotic medication and hospitalization can be necessary as well.

## Treatment

In individuals who suffer from one episode of major depression, there is a **50% to 85% chance of having another episode**. The risk of recurrence increases not only with each subsequent episode but also with the occurrence of residual symptoms of depression between episodes, comorbid psychiatric disorders, and chronic medical conditions. Therefore, adequate treatment resulting in full remission is the goal. The treatment options for recurrent episodes of major depression are not significantly different from those for a first episode: pharmacotherapy, psychotherapy (for mild or moderate symptomatology), a

combination of the two, or **electroconvulsive therapy (ECT)** in **major depression with psychotic features or where a rapid response is required**.

Common first-line pharmacotherapy for episodes of major depression includes SSRIs (such as fluoxetine, sertraline, paroxetine, and citalopram), veniafaxine, bupropion, mirtazapine, and duloxetine. Side effects vary among the specific medications and include sedation or activation, weight gain, headache, gastrointestinal symptoms, tremor, elevated blood pressure (for veniafaxine at higher doses), and **sexual dysfunction**, particularly with **SSRIs and veniafaxine**. Although efficacy is essentially equivalent among all classes of antidepressants, TCAs such as desipramine and nortriptyline are usually **not considered first-line agents** because their **side effects are less well tolerated**, including **anticholinergic effects, orthostasis, and cardiac effects** leading to lethality in overdose. **Monoamine oxidase inhibitors (MAOIs)** are used less frequently because of their significant **drug-drug interactions** and because **dietary restrictions** are necessary.

A rule of thumb in managing recurrent episodes of major depression is that the particular medication that achieved remission in past episodes is likely to achieve remission in subsequent episodes, often at the same dose. Additional factors to consider when choosing a medication are prior side effects, drug-drug interactions, cost, and patient preference.

## Comprehension Questions

- [1.1] A 70-year-old woman presents to her primary care provider complaining of fatigue for the past 7 weeks. She admits to difficulty falling asleep, a poor appetite with a 10-lb weight loss, and thoughts of wanting to die. She admits to having had symptoms similar to these on several occasions in the past, but "never this bad." Her medical problems include asthma and a high cholesterol level. She uses an albuterol inhaler only as needed. Which of the following symptoms is necessary in order to make a diagnosis of major depressive disorder?
- A. Depressed mood
  - B. Decreased appetite
  - C. Fatigue
  - D. Suicidal ideation
  - E. Excessive guilt

- [1.2] A 44-year-old woman comes to your office for a follow-up visit. She recently received a diagnosis of major depressive disorder and began treatment with citalopram (an SSRI) 6 weeks ago. She claims to feel "happy again," without further depression, crying spells, or insomnia. Her appetite has improved, and she has been able to focus at work and enjoy time with her family. Although she experienced occasional headaches and loose stools at the beginning of her treatment, she no longer complains of any side effects. Which of the following is the most appropriate next step in her treatment?
- A. Lower the dose of citalopram
  - B. Maintain the current dose of citalopram
  - C. Increase the dose of citalopram
  - D. Discontinue the citalopram
- [1.3] Which of the following side effects common to SSRIs is the woman in question [1.2] most likely to complain of in the future?
- A. Anorgasmia
  - B. Insomnia
  - C. Nausea
  - D. Tremor
- [1.4] The woman in questions [1.2] and [1.3] is seen one year later for a return visit. She has remained on the citalopram at the same dose, and she is tolerating it well, but she worries about "always having to take medication." What is her risk of recurrence if she is not maintained on antidepressant medication?
- A. 0%-20%
  - B. 20%-50%
  - C. 50%-85%
  - D. 85%-100%

### Answers

- [1.1] A. Although a change in appetite, decreased energy, fatigue, and suicidal ideation are all criteria used in diagnosing major depressive disorder, one of the symptoms must be either a depressed mood or anhedonia.
- [1.2] B. The proper strategy in the management of an episode of major depression that has recently remitted is to continue treatment at the same dose if it can be tolerated. Early discontinuation of medication can lead to an early relapse. A general rule of thumb is. "The dose that got you better will keep you well." A reasonable duration for continuing the medication is 6 to 9 months.

- [1.3] A. Although activation (causing insomnia), gastrointestinal symptoms (including nausea), and tremor are common side effects of SSRIs, only sexual dysfunction generally occurs later in the treatment course (after weeks to months).
- [ 1.4] C. The recommendations for maintenance therapy in major depressive disorder should be made on a case by case basis. However, the illness tends to run a chronic course, especially if treatment is discontinued. Indeed, 50% to 85% of individuals will suffer from at least one further episode, most likely within 2 to 3 years.

## CLINICAL PEARLS

It is important to rule out an underlying substance, medication, or medical condition causing depression, especially if the patient does not have a prior history of depression.

More than 50% of patients who have had one episode of major depression will have recurrent episodes.

The risk of further episodes of major depression increases with the number of prior episodes, the occurrence of residual symptoms of depression between episodes, and any comorbid psychiatric or chronic medical illnesses.

The treatment that was successful for prior episodes of major depression has a higher likelihood of achieving remission in future episodes.

Selective serotonin reuptake inhibitors, as well as bupropion, venlafaxine, mirtazapine, and duloxetine, are all first-line treatment options for major depressive disorder.

## REFERENCES

American Psychiatric Association. Practice guidelines for the treatment of major depressive disorder. Available at: [http://www.psych.org/clin\\_res/depression2e\\_book.cfm](http://www.psych.org/clin_res/depression2e_book.cfm). Accessed July 14, 2005.

Stoudemire A. Clinical psychiatry for medical students, 3rd ed. Philadelphia: Lippincott Williams & Wilkins, 1998:243-245; 257-260.