

# When the Patient Asks

MARY L. HEWETT, PA-C, MS

## Q: What do I do about my depression?

Depression is a treatable condition. Evidence-based psychotherapies and antidepressant medications are equally effective in the treatment of mild to moderate depression. For patients with severe recurrent depression, combining pharmacotherapy and psychotherapy is recommended.<sup>1</sup>

### ▶ TREATMENT RESISTANCE

Only 40% of patients in primary care respond to the first choice of antidepressant medication. The causes of treatment resistance are multiple. Obviously, patients who do not adhere to their drug regimen often present with what appears to be treatment resistance. Patients who meet the criteria for psychiatric comorbidities are more likely to be resistant to their first antidepressant medication. Those patients with severe depression that has been present for a substantial period of time are also frequently resistant. Chronic social stressors can limit antidepressant response. Finally, one of the more common causes of patients failing to respond to depression therapy is undiagnosed bipolar disorder.<sup>2</sup>

### ▶ THE STAR\*D TRIAL

The STAR\*D trial was designed to compare long-term outcomes of various pharmacologic and nonpharmacologic treatments for depression. This randomized trial also addressed the issue of treatment resistance. Patients who either did not achieve remission or who could not tolerate a 14-week trial of citalopram (selective serotonin reuptake inhibitor [SSRI]-Celexa) were randomly assigned to one of three groups. Group 1 substituted sustained-release bupropion (atypical antidepressant-Wellbutrin SR) for citalopram. Group 2 substituted

sertraline (SSRI-Zoloft), and group 3 substituted venlafaxine (serotonin-norepinephrine reuptake inhibitor-Effexor). After treatment with one of these three medications for up to 14 weeks, remission was achieved in 25% of patients and response was achieved in an additional 25%.<sup>2</sup>

The STAR\*D trial also investigated the response of treatment-resistant patients to augmentation of citalopram therapy with either bupropion or buspirone (serotonin type 1A receptor stimulant-BuSpar). Remission was achieved in approximately 30% of patients in both groups. Multiple randomized trials using aripiprazole (atypical antipsychotic-Abilify) as an adjunct medication have shown this regimen to be effective. The use of lithium for augmentation has also been studied and found to be effective. Lithium is the only medication that has been shown to decrease the rate of suicide in major depression.<sup>3</sup>

The STAR\*D trial went on to study patients who did not remit with the medication switching or augmentation. This group of patients was randomized to either switching to nortriptyline (tricyclic antidepressant-Pamelor) or mirtazapine (tetracyclic antidepressant-Remeron) or to augmentation with lithium, triiodothyronine, sertraline, or venlafaxine. Patients who received either mirtazapine or nortriptyline did not demonstrate lower remission rates. Augmentation with either lithium or triiodothyronine was found to be effective for treatment-resistant patients.<sup>3</sup>

There exists reluctance on the part of both clinicians and patients to push antidepressant treatment to full remission. Additionally, treatment times longer than those used previously are required to achieve remission. A modest improvement at 6 weeks may

require a dose increase or a longer time period (up to 12 weeks) at the same dose for a full response.

### ▶ BOTTOM LINE

Patients who are resistant to monotherapy for depression should be evaluated carefully for medication compliance, substance abuse, bipolar disorder, and social stressors. The combination of antidepressant medication and psychotherapy is more effective than either treatment alone for patients with severe recurrent depression. Patients who fail to remit after the institution of one SSRI may achieve remission when a second SSRI is substituted. Patients who fail to remit after two trials of SSRIs should be switched to a different class of medication, and dual-action medications may be more effective in patients with severe depression. Augmenting SSRI therapy with a second antidepressant or with an atypical antipsychotic medication are also effective strategies. **JAAPA**

Mary Hewett is Assistant Professor, Division of Physician Assistant Studies, Medical University of South Carolina, Charleston, and the department editor for When the Patient Asks. She has indicated no relationships to disclose relating to the content of this article.

### REFERENCES

1. Lyness J, Schwenk T, Solomon D. Depression: clinical manifestations and diagnosis. *UpToDate* Web site. [http://www.utdol.com/online/content/topic.do?topicKey=psychiat/6524&selectedTitle=2%7E150&source=search\\_result](http://www.utdol.com/online/content/topic.do?topicKey=psychiat/6524&selectedTitle=2%7E150&source=search_result). September 8, 2009. Accessed February 1, 2010.
2. Ciechanowski P, Katon W, Schwenk T, Solomon D. Treatment of resistant depression in adults. *UpToDate* Web site. [http://www.utdol.com/online/content/topic.do?topicKey=psychiat/12876&selectedTitle=5%7E150&source=search\\_result](http://www.utdol.com/online/content/topic.do?topicKey=psychiat/12876&selectedTitle=5%7E150&source=search_result). September 10, 2009. Accessed February 1, 2010.
3. Fava M, Trivedi M, Wisniewski S, et al. Medication augmentation after the failure of SSRIs for depression. *N Engl J Med*. 2006;354(12):1243-1252.

For patient information on this topic, please turn the page.

# Patient Information

## Q: What do I do about my depression?

### ›WHAT IS DEPRESSION?

Depression is more than just sadness. It takes over your life, and it makes it hard to work, study, eat, sleep, and have fun. It can make you feel lifeless, empty, helpless, hopeless, and/or worthless. If you have clinical depression, you may have some of these signs and symptoms:

- You can't sleep or sleep too much.
- You can't concentrate or find that you have trouble with easy tasks.
- You feel hopeless and/or helpless.
- You have negative thoughts and can't stop thinking them.
- You don't feel like eating, or you eat all the time.
- You feel short-tempered and irritable.
- You have thoughts that life may not be worth living.

Depression comes in many shapes and forms. Different types of depression have unique symptoms, causes, and effects. Knowing what type of depression you have helps you get better treatment.

### ›WHAT CAUSES DEPRESSION?

Depression is complex. It is caused by a chemical imbalance in the brain and by biological, psychological, and social factors. Your lifestyle choices, relationships, and coping skills also play a role. The causes and risk factors can include loneliness, lack of social support, recent stressful experiences, relationship problems, and financial strain. Other risk factors are childhood trauma or abuse, alcohol or drug abuse, unemployment, health problems, or chronic pain.

### ›HOW IS DEPRESSION TREATED?

The treatment for your depression must be tailored to you. Treatment may include counseling, medicine, or both. If your depression is severe, you may have to take one or more medicines. You may need counseling

at the same time. If you have been depressed before, you may need both counseling and medications. If your depression is mild to moderate, you can probably be treated with either counseling or drugs. You and your health care provider will decide together whether to use medicine or counseling. When you receive the best treatment for your depression, you can expect it to last for a shorter time. You will be less likely to have ongoing symptoms or have a relapse.

### ›HOW DOES TREATMENT WORK?

There are different types of counseling. All involve you and a licensed health care professional talking together about your feelings, relationships, and worries. During therapy, you and the therapist can discuss different ways of thinking or feeling about a situation. This often helps you to cope with your symptoms, improve your social skills, and become more self-confident.

Drugs help to restore the normal balance of chemicals in the brain. Different types of drugs—called *antidepressants*—can relieve symptoms. It is important to allow enough time for a drug to work. New research indicates that it may take up to 14 weeks to learn whether a medicine is working for you. You should take the medicine for at least 6 to 9 months to prevent symptoms from returning.

### ›WHICH ANTIDEPRESSANT SHOULD I TAKE?

Many types of drugs can treat depression. The choice of which to use depends on many things, which you and your health care provider can discuss.

- One type of antidepressant increases levels of a brain chemical

called *serotonin*. Low levels of this substance may be one cause of depression. This class of drugs includes fluoxetine (Prozac), sertraline (Zoloft), paroxetine (Paxil), citalopram (Celexa), fluvoxamine (Luvox), and escitalopram (Lexapro). These drugs have relatively few side effects.

- Another class of drugs includes venlafaxine (Effexor) and duloxetine (Cymbalta). They may work well in persons with depression and physical pain.
- Mirtazapine (Remeron) is a newer antidepressant that increases the activity of two chemicals in the brain.
- Bupropion (Wellbutrin) may work in people who are tired or cannot concentrate.

### ›WHAT IF THE DRUG DOES NOT WORK?

Many studies have been done to find out why a drug might not work and what can be done. You may need both a medication and counseling. Or you may need to address some lifestyle issues. It is also important to make sure the correct diagnosis has been made for you.

If the problem is that you are just not responding to your antidepressant, many things can be done. The dosage of the medicine may need to be increased. A drug from a different class altogether may need to be started. Or a second drug from the same class or from a different class may need to be added.

### ›BOTTOM LINE

Depression can be treated. Together, you and your health care provider can find a way to ease your symptoms and help you return to a rich and productive life. There is help for you. **JAAPA**

