

# CLINICAL COURIER®

Vol. 21 No. 32 September 2003 ISSN 0264-6684

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*Physician Assistants* – The program has been reviewed and is approved for a maximum of 2.0 hours of clinical Category 1 (Preapproved) CME credit by the American Academy of Physician Assistants (AAPA). Physician assistants should claim only those hours actually spent participating in the CME activity.

Program Release Date: September 2003

Program Expiration Date: September 30, 2004

## ACHIEVING REMISSION IN DEPRESSION: Managing Women and Men in the Primary Care Setting

PRESENTED BY:



The Office on Women's Health  
of the  
US Department of Health and Human Services



IN COOPERATION WITH:



American Psychiatric Association

American College of Physicians



American Academy of Physician Assistants

National Association of Managed Care Physicians



SOCIETY FOR  
WOMEN'S HEALTH RESEARCH

Society for Women's Health Research

This program is supported through an unrestricted educational grant provided by Wyeth.

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September 2003

Dear Colleague,

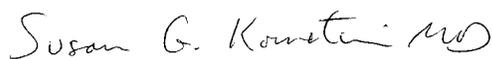
We are pleased to provide you with this continuing medical education newsletter *Achieving Remission in Depression: Managing Men and Women in the Primary Care Setting* developed from the proceedings of a roundtable meeting presented by the Office on Women's Health of the Department of Health and Human Services.

Depression is a greatly underdiagnosed and undertreated disorder that has significant economic and personal costs for patients and for our society at large. Unrecognized depression can result in morbidity and mortality; however, appropriate early diagnosis and treatment can significantly reduce these risks. Primary care providers are often the first medical contact that patients suffering from depression encounter. Therefore, it is vital that healthcare providers are able to identify and treat the disease effectively. Achieving and maintaining remission in depression is the ultimate goal for healthcare providers and their patients and is specifically addressed in this educational program.

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We thank you in advance for your participation and believe you will find this newsletter to be an invaluable resource in the management of depression to achieve and maintain remission.

Best regards,



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## ACHIEVING REMISSION IN DEPRESSION: Managing Women and Men in the Primary Care Setting

Presented by The Office on Women's Health of the US Department of Health and Human Services

Depression is an important public health problem with an estimated annual cost of \$44 billion.<sup>1</sup> It is currently ranked by the World Health Organization as the fourth most disabling illness and is projected to be the second by the year 2010.<sup>2</sup> Depression is both underdiagnosed and undertreated and may be lifelong for many patients.<sup>3-5</sup> The personal price of depression includes not only mental anguish but also impaired family and social functioning, impaired work performance, increased morbidity from comorbid medical conditions, suicide (10% to 15% in patients with major depressive disorder), and other mortality risks.<sup>3,4,6</sup> With appropriate treatment, however, 80% to 90% of patients can be treated successfully.<sup>3,4,6</sup>

Primary care providers play a key role in the provision of mental health services—both in terms of identifying patients in need of mental health services and in managing these patients and their needs. Many primary care physicians (PCPs) have given increased responsibility to their nurse practitioners (NPs) and physician assistants (PAs) in diagnosis, treatment, and, more importantly, patient education to ensure compliance with therapy. Even further, NPs in most states currently have prescribing privileges. According to the 2002 American Academy of Nurse Practitioners Survey, NPs have the authority to prescribe FDA-approved drugs in all 50 states and the authority to prescribe these drugs under their own signature

### EDUCATIONAL OBJECTIVES

Upon completion of this program, participants should be able to:

- Identify differences in the evaluation and treatment of depression by gender and across the female reproductive cycle.
- Differentiate remission and response as goals of the treatment of depression.
- Discuss strategies to achieve and maintain remission long term in patients with depression.
- Discuss the role of patient education as a treatment strategy.
- Identify patient groups with specialized education needs.

### TARGET AUDIENCE

Healthcare professionals who care for patients with depression.

**Table 1**  
**Treatment Outcomes in Depression<sup>4,10</sup>**

|              |  |
|--------------|--|
| • Response   | Clinically significant reduction in baseline symptom severity  |
| • Remission  | Absence of symptoms; return of premorbid psychosocial functioning; no longer meets criteria for major depression |
| • Relapse    | Return of depressive symptoms within 6 months following remission  |
| • Recovery   | Sustained period of remission of at least 6 months following an episode of major depression                      |
| • Recurrence | New episode of depression following recovery from previous episode   |

in 49 states and the District of Columbia.<sup>7</sup> This multidisciplinary team, made up of the PCP, the NP, and the PA, is the backbone of America's mental health system, and these are the only professionals with mental health training in many communities.<sup>8</sup> They provide a larger proportion of mental health services than do specialists in mental and addictive disorders.<sup>8</sup> Approximately 20% to 30% of patients in a primary care practice present with symptoms of depression.<sup>3,9</sup> Many patients, therefore, rely on their provider of primary care services for the diagnosis and treatment of their symptoms of depression. An estimated 50% of antidepressant prescriptions are written in primary care office settings, an indication that providers of primary care services are responding to the challenge.

**"Depression should be seen as another chronic medical illness with all of the nuances of treating a chronic medical illness."**

**M.H. Trivedi, MD**

Treatment outcomes in depression are defined in Table 1.<sup>4,10</sup> It is only in the last 5 to 10 years that the psychiatric community has

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moved the treatment paradigm for depression from symptom relief or response to one of treating to remission. Increasing evidence indicates that depression is a chronic and recurrent illness and not an episodic one. These shifts in concepts about depression necessitate a change in approach to its treatment and evaluation: providers of primary care services need to approach the treatment of depression as they do other chronic medical illnesses. A recent meta-analysis of 31 randomized trials demonstrated a 70% reduction in the odds of relapse of depression with continued treatment versus treatment discontinuation,<sup>11</sup> which underscores the feasibility of both achieving and maintaining remission with treatment.

While study data convincingly demonstrate the benefits of treating depression to remission, the challenges to providers of primary care in clinical practice settings, such as NPs and PAs, are to get patients to initiate prescribed treatment and to adhere to the regimen long term—challenges that are common in the treatment of all

chronic medical illnesses. An important component of depression treatment is patient guidance and education regarding the goals of therapy and the need to continue treatment long term for optimum outcomes. Knowledge about differences in clinical presentation and response to treatment between men and women and for women in different stages of the reproductive life cycle as well as common comorbidities shape management and education strategies for patients with depression. As NPs and PAs spend the most time in the patient/healthcare provider interaction, they have an intensified role in this patient education.

## GENDER DIFFERENCES IN DEPRESSION

**“A patient’s gender and for women, their menopausal status, should be considered in both the evaluation and treatment of depression.”**

**S.G. Kornstein, MD**

### Method of Participation

The program consists of a 12-page *Clinical Courier*® with a CME Post-test.

This *Clinical Courier* should take approximately 2 hours to complete. The participant should, in order, review the educational objectives, read the newsletter, and return the completed Post-test and Evaluation Form to the address indicated to receive credit. The Evaluation Form provides each participant with the opportunity to comment on the extent to which educational objectives were met, the quality of the instructional process, the perception of enhanced professional effectiveness, the perception of commercial bias, and participant views on future educational needs. This credit is valid through September 30, 2004. No credit will be given after this date.

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*Achieving Remission in Depression: Managing Women and Men in the Primary Care Setting*, as published in this issue of the *Clinical Courier*, reports highlights from a meeting of experts in treating depression held in Washington, DC, on March 17, 2003. This publication is intended for healthcare professionals who care for patients with depression. This newsletter was developed and produced by SynerMed Communications under an unrestricted educational grant from Wyeth.

The views presented herein are those of selected faculty and not necessarily those of the publisher, grantor, or the University of Minnesota Office of Continuing Medical Education, The Office on Women’s Health of the US Department of Health and Human Services, or the following cooperating organizations: American Psychiatric Association, American College of Physicians, American Academy of Physician Assistants, National Association of Managed Care Physicians, and Society for Women’s Health Research. This material is prepared based upon a review of multiple sources of information, but it is not exhaustive of the subject matter. Therefore, healthcare professionals and other individuals should review and consider other publications and materials about the subject matter before relying solely upon the information contained within this *Clinical Courier*.

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Recognition of gender differences in the prevalence, presentation, and treatment of psychiatric illnesses, including depression, is an outgrowth of the women’s health movement. Epidemiologic data indicate that the prevalence of major depression in women is about 2 times higher than in men—a difference that begins in early adolescence and persists through the mid-50s, corresponding roughly to the reproductive years in women.<sup>12</sup> Biologic and psychosocial factors may contribute to the difference in prevalence. Gender differences in the clinical features of depression include more atypical symptoms, anxiety, and eating disorders in women, whereas men have an increased risk of completed suicide and are more likely to have comorbid alcohol and substance abuse (Table 2).<sup>13,14</sup>

Gender differences also have been shown in response to treatment of depression (Table 3, page 4).<sup>15-18</sup> Women may respond better to selective serotonin reuptake inhibitors (SSRIs) and monoamine oxidase inhibitors (MAOIs) than to tricyclic antidepressants (TCAs). Both women and men can be successfully treated to remission with appropriate therapy, with higher remission rates reported in both women and men treated with a serotonin–norepinephrine reuptake

**Table 2**  
**Gender Differences in Clinical Features and Response to Treatment of Depression<sup>13,14</sup>**

|                                  |  |
|----------------------------------|--|
| • Symptoms                       | Atypical symptoms more common in women<br>Completed suicide risk increased in men        |
| • Course                         | Episodes may be longer in women<br>Depression may be more chronic and recurrent in women |
| • Comorbidity                    | Anxiety and eating disorders in women<br>Alcohol and substance abuse in men              |
| • Precipitating factors in women | Stressful life events<br>Seasonal changes<br>Reproductive events                         |

inhibitor (SNRI) like venlafaxine compared with an SSRI.<sup>18,19</sup> Gender differences in response to psychotherapy are less apparent, although some differences by gender and age in response to psychotherapy with/without pharmacotherapy have been shown.<sup>15,16</sup> For example, response to combined treatment with psychotherapy plus TCAs was greater than the response to psychotherapy alone in men and older women, but not in younger women.<sup>16</sup> The data regarding gender differences are preliminary in that they are based primarily on post hoc analyses of studies underpowered to demonstrate gender differences. Nonetheless, healthcare professionals need to consider gender in their evaluation and treatment of patients with depression.

## DEPRESSION ACROSS THE FEMALE LIFE CYCLE

Within the female life cycle, there are periods that require special consideration with regard to recognition and treatment of depression, as well as education and counseling about treatment options. Several factors, including physiologic and psychosocial factors and psychiatric history, contribute to the increased risk of depression and relapse as well as to the likelihood of achieving remission in women.

### Premenstrual Phase

In the premenstrual phase of the menstrual cycle, there is increased vulnerability for the onset of an episode of depression or worsening of an ongoing depression, and psychiatric hospital admissions and suicide attempts are increased.<sup>20</sup> Approximately 40% to 60% of women with a chief complaint of premenstrual syndrome (PMS) have an underlying mood or anxiety disorder.<sup>20,21</sup> Women who suffer from moderate to severe symptoms of premenstrual depressed mood, anxiety, irritability, and mood swings as part of premenstrual dysphoric disorder (PMDD) experience relatively high levels of impairment that are nearly comparable to levels observed in major depression.<sup>22</sup>

Although a number of treatments have been studied for PMS and PMDD, antidepressants, specifically SSRIs and the SNRI venlafaxine, show consistent improvement in both mood and physical symptoms beginning in the first cycle.<sup>22,23</sup> Several studies indicate that intermittent treatment (day 14 or 15 through the first day of menses) with an antidepressant is effective therapy for PMDD.<sup>23-26</sup>

### Pregnancy and Postpartum Periods

**“Treatment decisions in women who are pregnant or breast-feeding are based on risk/benefit assessments of the impact of prenatal or neonatal exposure to psychiatric medications and the impact of untreated psychiatric disorders on the fetus or newborn.”**

***L.S. Cohen, MD***

There is a growing consensus that pregnancy does not protect against mood and anxiety disorders or other types of psychiatric illness.<sup>27,28</sup> It is necessary, therefore, to have strategies for treating women who become pregnant and have been on maintenance therapy for mood disorders or who develop symptoms during pregnancy. Depression prior to or during pregnancy is the strongest

**Table 3**

### Gender Differences in Response to Treatment of Depression<sup>15-18</sup>

- Women may respond better to SSRIs and MAOIs than TCAs
- Menopausal status may affect response to treatment
- Augmentation strategies may differ (eg, thyroid hormone, estrogen)
- Response to cognitive behavioral and interpersonal therapies is similar in women and men
- Combined psychotherapy and pharmacotherapy with TCAs is better than psychotherapy alone in men of all age groups and in women  $\geq 50$  years

MAOIs = monoamine oxidase inhibitors; SSRIs = selective serotonin reuptake inhibitors; TCAs = tricyclic antidepressants.

predictor of postpartum depression (PPD), with another strong risk factor being a history of a psychiatric disorder.<sup>29</sup> The prevalence of PPD is 5% to 10%, which is equivalent to the prevalence of depression in nonpuerperal, age-matched women.<sup>27</sup> Although all antidepressants are found in breast milk in varying concentrations, the milk:plasma ratio is a poor indicator of fetal exposure.<sup>30</sup> No antidepressant is contraindicated or safer than another during the postpartum period.<sup>30,31</sup> There is a general recommendation to avoid prenatal exposure to psychiatric medications when possible. A growing body of evidence indicates that SSRIs and SNRIs do not adversely affect pregnancy outcome or the risk of teratogenesis.<sup>32-35</sup> Women with depression who are pregnant or postpartum, therefore, need education and counseling regarding the risks/benefits to both mother and fetus or newborn of medications and the impact of untreated psychiatric illness on fetal outcome or the newborn. Since no decision is risk-free, it is important that women understand the risks/benefits associated with both untreated and treated illness. A useful resource for assistance in risk/benefit decisions during pregnancy and postpartum is the website of the Massachusetts General Hospital's Center for Women's Mental Health: <http://www.womensmentalhealth.org>.

### Peri- and Postmenopausal Periods

Women transitioning into menopause, especially those with a previous history of depression, are at increased risk of developing depressive symptoms,<sup>13</sup> and are another group who may require education and counseling by the multidisciplinary team regarding the risks/benefits of treatment. Some studies indicate that estrogen improves both depressive and physical symptoms in peri-/postmenopausal women.<sup>36</sup> Preliminary evidence suggests that estrogen therapy improves both response and remission rates for SSRIs but not for SNRI therapy.<sup>37,38</sup> However, estrogen as an adjunctive treatment for depression requires further study in peri-/postmenopausal women. Other preliminary evidence suggests that the SNRI venlafaxine may be more effective for achieving remission in postmenopausal women than SSRIs, which

is similar to findings in younger women.<sup>38</sup> Although younger women appear to respond better to SSRIs than to TCAs, response rates to these antidepressant classes are similar in postmenopausal women.<sup>17,18</sup> However, many women have abruptly discontinued hormone therapy because the Women's Health Initiative (WHI) showed a greater overall risk than benefit from this therapy.<sup>39</sup> Providers of primary care may see an increase in the number of peri-/postmenopausal women with symptoms of mild depression now that hormone therapy is prescribed less often. Education about the risks/benefits of this and other treatments will be necessary for women with depression for whom hormone therapy may be a treatment option.

## DIAGNOSIS OF DEPRESSION AND COMORBIDITY

**“A yes to either or both of the following questions is a good positive screen for depression:**

- **In the last month, have you lost pleasure in the activities you normally enjoy?**
- **In the last month, have you felt sad, down, depressed, or hopeless?”**

*J.A. Lieberman III, MD, MPH*

Providers of primary care are expected to recognize in a limited amount of time both general medical and mental health problems in their patients. There are easy and quick techniques to facilitate recognition of mental health problems that can be used during the screening process at each visit to assess whether patients have symptoms of depression. When NPs and PAs are examining patients for depression, a positive screen is a yes to either or both of the following questions: In the last month, have you lost pleasure in the activities you normally enjoy? In the last month, have you felt sad, down, depressed, or hopeless? Another screen for mental health problems is the BATHE interviewing paradigm, which utilizes the problem-oriented medical record format (Table 4).<sup>40</sup>

The SIG E CAPS system (Figure 1), which includes the symptom criteria for depression, is useful for identifying which symptoms the patient is experiencing.<sup>41</sup> A positive response to 5 of the 8 symptoms including depressed mood or anhedonia correlates with a diagnosis of depression.

|                         |                                   |
|-------------------------|-----------------------------------|
| • <b>Background</b>     | “What is going on in your life?”  |
| • <b>Affect/feeling</b> | “How are you feeling about that?” |
| • <b>Trouble</b>        | “What troubles you most?”         |
| • <b>Handling</b>       | “How are you handling that?”      |
| • <b>Empathy</b>        | “That must be very difficult.”    |

## Comorbidity

**“Depression is frequently comorbid with many common medical conditions; accurate diagnosis and treatment of depression in these patients may have a significant beneficial effect on the course of the primary medical condition.”**

*S.P. Roose, MD*

As a common comorbidity with medical conditions such as cardiovascular disease (CVD) and chronic pain, depression can have a deleterious impact on prognosis. A common misconception is that CVD is a leading cause of death in men only. In fact, more women than men die of CVD annually (505,661 vs 440,175), and women's death rate from CVD is more than 10 times that from breast cancer.<sup>42</sup> The estimated prevalence of significant depressive symptoms post myocardial infarction (MI) is 45%, while major depression occurs in approximately 15% to 22%. Depression is an important independent risk factor for the occurrence of major cardiac events, and it is an independent risk factor for death following MI. This is supported by a prospective study that examined the impact of depression on 6-month survival. The results showed that depression was a significant predictor of mortality.<sup>43</sup>

A large study found that the prevalence of chronic painful conditions increased dramatically with age and was higher across all age groups in women than in men.<sup>44</sup> A correlation also has been shown between the number of depressive symptoms and the rate of chronic pain conditions: two depressive symptoms were associated with a 29% rate of pain conditions, compared with a rate of 62% for eight symptoms.

In addition to recognition and treatment, education regarding the probable need for adherence to treatment regimens long term for both the medical illness and depression is important for improving prognosis.

**Figure 1**  
**SIG E CAPS System<sup>41</sup>**

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- S** Increased or decreased **sleep** and **sexual** desire
- I** Decreased **interest** or pleasure in almost all activities
- G** Inappropriate **guilt** or feelings of worthlessness/hopelessness
- E** Decreased **energy** or fatigue
- C** Decreased **concentration**
- A** Increased or decreased **appetite** with weight gain or loss
- P** **Psychomotor** agitation or retardation
- S** **Suicidal** ideation, plan, or attempt

Adapted with permission from Lieberman JA III. Depression: a common illness uncommonly diagnosed. *Psychiatric Ann.* 2002;32:522-526.

## ACHIEVING REMISSION—A MODEL OF EFFICACY

**“Treating to remission, ie, achieving a virtually asymptomatic state, rather than response is the ultimate goal of antidepressant therapy.”**

*M.H. Trivedi, MD*

Treating to remission, ie, achieving a virtually asymptomatic state, rather than response is now the accepted goal of antidepressant therapy. However, remission as a goal of treatment has not been evaluated in most randomized clinical treatment trials conducted to date. The shift in the treatment paradigm for depression to one of sustained remission requires a redefinition of long-term treatment goals, a reassessment of how to evaluate ongoing treatment for symptom relief after the usual 8- to 12-week treatment period of clinical trials, and patient education to promote adherence to long-term treatment regimens. Not treating to remission increases the economic burden of depression due to a higher risk of relapse,<sup>11,45-48</sup> more rapid relapse, increased rate of recurrence, and increased risk of suicide,<sup>45</sup> as well as shorter well intervals and fewer symptom-free weeks.<sup>46</sup>

Strategies to achieve remission are summarized in Table 5.<sup>49</sup> Three factors that commonly contribute to poor treatment outcomes in depression are an inadequate treatment trial with a particular agent, use of a suboptimal dose, and lack of monitoring for symptomatic and functional improvement. Recent studies question the common perception of the necessity for changing treatment if significant improvement is not achieved in 4 to 6 weeks.<sup>50,51</sup> Treating for 12 or more weeks resulted in an additional 30% to 40% of patients achieving remission who were not in remission after the initial 6 to 12 weeks of treatment. Treating with the maximum tolerated dose, not the minimum dose to relieve symptoms, is another key strategy to optimize treatment outcomes.

The addition of depression-targeted psychotherapies may be necessary in some patients. Psychotherapy interventions such as

| Treatment Phase | Goal   |
|-----------------|--|
| • Acute         | Symptomatic remission<br>Resolve tactical issues<br>(eg, dosing, compliance)   |
| • Continuation  | Recovery from episode<br>Restore psychosocial functioning (follows symptomatic remission by 1 to 3 months)<br>Reduce likelihood of relapse |
| • Maintenance   | Required for most patients<br>Prevent recurrence   |

cognitive behavioral therapy may be successful in some patients who have failed antidepressant treatment trials, and, when added to successful antidepressant treatment, they can sustain remission and prevent relapse.<sup>52,53</sup> Cognitive behavioral therapy also prolongs the time to relapse in successfully treated patients with residual symptoms, which are more common in severely ill patients and are a strong predictor of early relapse.<sup>46,52,53</sup>

## TREATMENT STRATEGIES

Treatment of depression in controlled clinical trials is relatively successful. Up to 60% of patients respond to medication, psychotherapy, or a combination of the two treatments. However, 29% to 46% of patients fail to respond fully to adequate antidepressant therapy.<sup>53</sup> Of note is that patients in controlled clinical trials generally are not reflective of those typically treated at primary care practice sites; that is, they typically do not have comorbid conditions, such as anxiety disorders and substance abuse, or concomitant general medical conditions. Successful treatment of depression, like other medical illnesses, requires a systematic approach in which patients are assessed frequently for response to the prescribed treatment and adjustments in therapy are made based on the assessments.<sup>4</sup> It is important for healthcare providers to use a multidisciplinary approach to the treatment of depression. The purpose of this approach is to have the patient achieve remission, particularly early remission, which predicts better outcomes and long-term success.<sup>45,54,55</sup>

**“Focus on improvement in the patient’s target symptoms to guide treatment.”**

*R.R. Krishnan, MD*

What treatment strategies can be used to successfully treat patients with depression to remission? First, it is important for the healthcare provider and patient to establish a partnership by setting the goals of treatment together and for the healthcare provider to ensure that the patient understands that remission of depression is an achievable goal. Second, it is important to recognize the three phases of treatment and the goals and expectations of each phase (Table 6).

**Table 5**

### **Strategies to Achieve Remission<sup>49</sup>**

- Selection of antidepressant (maximize benefits using agents with multiple neurotransmitter effects; prior history of response)
- Maximize antidepressant dose and duration of treatment (higher dose, longer trial)
- Monitor outcomes frequently to optimize treatment
- Augmentation strategies (use of another pharmacologic agent to enhance antidepressant effect)
- Switch to another antidepressant
- Combination antidepressants (concomitant use of  $\geq 2$  antidepressants to achieve effect)
- Antidepressants + psychotherapy

Remission of symptoms and a good prognosis long term are the ultimate goals of all phases of treatment. Maintenance treatment, which is analogous to long-term therapy for cholesterol lowering or control of blood pressure, is necessary for most patients and generally requires patient education to ensure that they remain on therapy. Third, the general principles of treatment summarized in Table 7 provide a helpful framework for initiating and continuing or switching treatments. Focusing on target symptoms for a particular patient is the best way to guide treatment in clinical practice settings. Psychotherapy and newer options (eg, electroconvulsive therapy, transcranial magnetic stimulation, and vagal nerve stimulation) are performed outside the primary care setting and necessitate a multidisciplinary approach.

The many available antidepressant agents belong to one of six major classes. They inhibit serotonin, norepinephrine, and/or dopamine; some are mixed action drugs, and some are MAOIs. No one drug fits most patients even half of the time. Consideration of several factors when selecting the initial antidepressant treatment may improve the generally accepted 50% to 60% response rate (Table 8).<sup>57</sup> In addition, understanding the characteristics of the various antidepressant classes, which are summarized in Table 9 (page 8) and Figure 2, aids in therapy selection.<sup>58-68</sup> Many patients still may require changes in or additions to the medication selected.

Selecting an antidepressant with a low incidence of long-term side effects enhances adherence to treatment, especially long term (Figure 2).<sup>60</sup> Once remission is achieved, the antidepressant should be continued at the same dosage for the continuation and maintenance phases of treatment to prevent relapse and/or recurrence. Sometimes, it may be necessary to adjust the dose to

| <b>Table 7</b>  |  |
|---|--|
| <b>General Principles of Treatment</b>                              |  |
| • Form partnership with patient                                     | <ul style="list-style-type: none"> <li>– Set goals of treatment</li> <li>– Educate patients regarding need for long-term treatment</li> </ul>  |
| • Select medication and dosage                                      | <ul style="list-style-type: none"> <li>– High long-term tolerability</li> <li>– High safety in overdose</li> </ul>   |
| • Medication fails to achieve remission or side effects intolerable | <ul style="list-style-type: none"> <li>– Consider switch within or to another class or augmentation strategies</li> <li>– Consider switch to newer options</li> </ul>  |
| • Provide psychotherapy   | <ul style="list-style-type: none"> <li>– Medication adherence</li> <li>– Early detection of recurrence, residual symptoms</li> <li>– Identification of axis II disorders</li> <li>– Psychosocial issues</li> </ul> |
| • Measure symptomatic and functional outcomes                       |  |
| • Educate patients regarding long-term management                   |  |

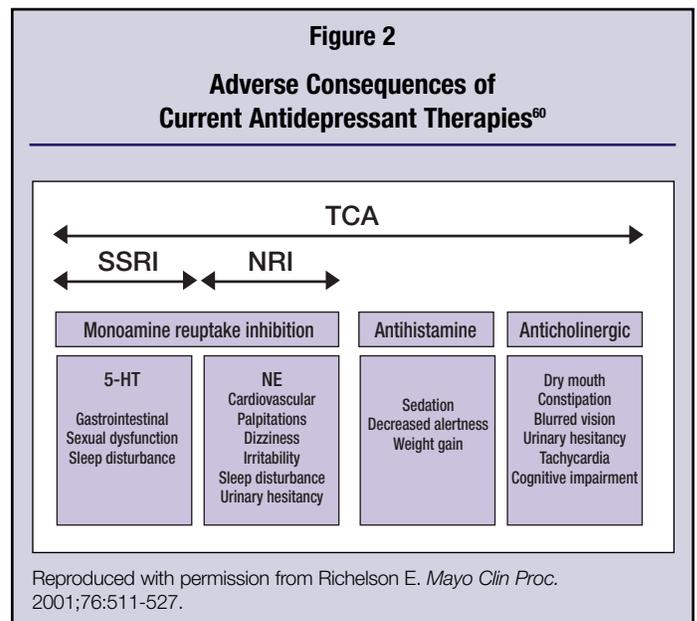
| <b>Table 8</b>                                |  |
|---|--|
| <b>Factors Affecting Medication Selection</b> |  |
| •   | Prior positive response to an agent  |
| •   | History of nonresponse to a specific agent   |
| •   | History of intolerance to a specific agent   |
| •   | Pretreatment symptom features (eg, atypical or psychotic)                                  |
| •   | Response to an agent in first-degree relative(s)   |
| •   | Severity of associated symptoms (eg, anxiety, insomnia) not predictive of response         |
| •   | Side effects beneficial in short term are possible liabilities in long term (eg, sedation) |

maintain response and tolerability in the continuation and maintenance phases. Patient education regarding the long-term course of depression and its treatment is important for promoting adherence to the medication regimen.

### Maintenance Therapy

Maintenance therapy is essential for patients with recurrent episodes of depression. For these patients, depression as an illness is analogous to other chronic medical illnesses (eg, hypertension, diabetes) and may require lifelong therapy with periodic assessments at 3- to 6-month intervals after remission is achieved. The goal is to restore and maintain a normal level of functioning with minimal symptoms long term. Practitioners in primary care settings need to be attuned to any variability in mood and symptomatology after patients have been in remission.

In addition, implementing procedures to provide more frequent follow-up of patients after initiation of antidepressant therapy and to educate them regarding the long-term nature of their illness and its treatment are quality improvement initiatives that can be



accomplished by NPs or PAs in primary care settings. Understanding and application of the concepts of treating depression as a chronic illness and to complete resolution of symptoms in primary care settings fulfill the ultimate goal in providing care—improved treatment outcomes in patients with depression.

### Patient Referral

When should a primary care provider refer a patient to a mental health specialist for treatment? At the time of the initial diagnosis of depression, complicating disorders, such as severe anxiety or substance abuse or a diagnosis of bipolar disorder, would prompt a referral for treatment. The need for addition of psychotherapy may prompt a referral. For other patients, the answer, in part, is the comfort level of the healthcare provider and patient with treatment and its progress. Referral for a second opinion is indicated if a

patient has not achieved remission after two adequate treatment trials in 6 months.

### PATIENT EDUCATION AND MONITORING

Providers of primary care, particularly NPs and PAs, who often have face-to-face, open dialogue with patients, are in a unique position to diagnose illnesses associated with significant morbidity and to initiate therapy. With approximately 50% of antidepressant prescriptions being written by primary care physicians, it is apparent that they are initiating therapy. However, follow-up of the patient generally is not optimum for achieving remission of symptoms in that the average prescription is for a 90-day supply and the next scheduled appointment may be in 6 to 12 months. In that period, one of several things may have occurred: the patient may decide not to have the antidepressant prescription filled initially or to take the

**Table 9**  
**Comparison of Major Antidepressant Classes<sup>4,58-68</sup>**

| Antidepressant Class  | Mechanism of Action  | Response and Remission Rates*                | Other Characteristics   |
|---|--|--|---|
| MAOIs, older (phenelzine, tranylcypromine)  | Irreversible inhibition of MAO-A and MAO-B; enhance NE, 5-HT, DA   | 60%-70%                                      | May be better in atypical depression<br>Require dietary restrictions                    |
| TCAs (amitriptyline, amoxapine, desipramine, doxepin, imipramine, nortriptyline, protriptyline, trimipramine) | Block reuptake of NE, 5-HT   | 43%-70% <sup>†</sup><br>25%-60% <sup>†</sup> | Analgesic, anticholinergic, and antimuscarinic actions<br>High side-effect burden       |
| Tetracyclic (maprotiline)   | Block reuptake of NE   | 53%-63%                                      | Similar to TCAs<br>Risk of seizures at higher doses                                     |
| SSRIs (fluoxetine, sertraline, paroxetine, fluvoxamine, citalopram, escitalopram)                             | Selectively block reuptake of 5-HT   | 60%-70%<br>20%-35%                           | Broad comorbidity coverage<br>Less side-effect burden vs TCAs<br>Safe in overdose       |
| SNRI (venlafaxine)  | Block reuptake of 5-HT and NE  | 65%-76%<br>37%-45%                           | Higher remission rates<br>Less side-effect burden vs TCAs<br>Safe in overdose           |
| NDRI (bupropion)  | Block reuptake of NE and DA (?)  | 52%-70%                                      | Effective for smoking cessation<br>Less sexual dysfunction<br>Safe in overdose          |
| SA (mirtazapine)  | Potent antagonist of 5-HT <sub>2</sub> , 5-HT <sub>3</sub> , and H <sub>1</sub> receptors; moderate α <sub>1</sub> -adrenergic antagonist; moderate antagonist at muscarinic receptors | 70%  | Safe in overdose<br>Common TCA and SSRI side effects minimized<br>Sedation, weight gain |
| SA/SRI (nefazodone)   | Antagonist of 5-HT <sub>2</sub> receptors and blocks reuptake of 5-HT and NE   | 35%-67%<br>35%-52%                           | Modest antidepressant<br>Used mainly for hypnotic and anxiolytic effects                |

\* Commonly accepted definitions: response = ≥50% reduction in the Hamilton Rating Scale for Depression (HAM-D) or Montgomery-Asberg Depression Rating Scale (MADRS) score; remission = absolute score of ≤7 on the HAM-D-17 or absolute score of ≤10 on the HAM-D-21 scales.

<sup>†</sup> Variability in response and remission rates due to heterogeneous selectivity on norepinephrine and serotonin within the class; higher rates associated with agents that have an approximately equal effect on both neurotransmitters. DA = dopamine; 5-HT = serotonin; MAOIs = monoamine oxidase inhibitors; NDRI = norepinephrine-dopamine reuptake inhibitor; NE = norepinephrine; SA = serotonin antagonist; SA/SRI = serotonin antagonist/serotonin reuptake inhibitor; SNRI = serotonin-norepinephrine (noradrenergic) reuptake inhibitor; SSRIs = selective serotonin reuptake inhibitors; TCAs = tricyclic antidepressants.

medication for only a few days because of side effects; the patient may respond initially, but then deteriorate; the patient may not respond and discontinue the medication; or the patient may have taken the medication and be doing well at the follow-up visit. Patient education and monitoring are integral to good patient care.

NPs and PAs have established relationships with their patients and know each as a whole person as well as what recommendations or treatments may or may not be complied with. With knowledge about the patient and the paradigm shift in the approach to the management of depression—from one of an episodic illness to a chronic, long-term condition—NPs and PAs in primary care can provide effective patient education using a chronic disease model focus to ensure patient understanding of depression and its treatment. All patient groups (eg, pregnant or peri-/postmenopausal women, patients with comorbid medical conditions, those with residual symptoms, etc) can benefit from patient education efforts.

Some elements of patient education are common to all patient groups, while others are tailored to specific groups. Elements of patient education discussed in this newsletter are summarized in

| <b>Table 10</b>  |  |
|--|--|
| <b>Elements of Patient Education for Depression</b>  |  |
| <b>General</b>   |  |
| • Depression is a chronic disease requiring long-term treatment.                             | – The approach to therapy is similar to that of chronic medical conditions (eg, hypertension, hypercholesterolemia, diabetes). |
|  | – Maintenance therapy is required in most patients.  |
| • The goal of treatment is remission or absence of symptoms and normal level of functioning. | – Adherence to therapy is important for achieving early remission.   |
|  | – Treatment (medical and psychotherapy) is continued after remission is achieved.  |
| • The treatment of depression may be lifelong.   | – Patients may have frequent relapses or recurrences.  |
|  | – Patients may have residual symptoms after achieving remission.   |
| <b>Specialized</b>   |  |
| • Pregnant and postpartum women  | – Risks/benefits of treatment and fetal/neonatal exposure to medications should be assessed.                                   |
|  | – Risks of untreated depression on the fetus or newborn should be considered.  |
| • Perimenopausal and postmenopausal women  | – Risks/benefits of hormone therapy  |
| • Comorbid medical conditions  | – Depression may worsen prognosis.   |
|  | – Adherence to lifestyle changes (exercise, smoking cessation) should be encouraged in heart disease patients.                 |

Table 10. All patients with depression need to understand that depression is a chronic disease, similar to many medical conditions, requiring long-term treatment for patients to be symptom-free and achieve normal functioning. Some patients may have had depression for such a long time that they do not remember what normal functioning is. Maintenance therapy that possibly is lifelong is an important element for patients to understand, particularly those who have had frequent relapses or recurrences or residual symptoms. Specialized or targeted patient education is necessary for those needing to make risk/benefit decisions regarding treatment (eg, pregnant, postpartum, or peri-/postmenopausal women). The goal of all educational efforts is to promote adherence to treatment regimens to achieve sustained remission of depression.

NPs and PAs in primary care practices also are in a position to utilize quick assessment tools to screen patients for symptoms of depression and to implement follow-up procedures for those patients prescribed antidepressant therapy. Although currently there are no good tools for monitoring patients, the consistent use of some tool, such as SIG E CAPS to assess target symptoms or the Patient Health Questionnaire depression module (PHQ-9),<sup>69</sup> is preferable to not using any structured assessment. In the first 24 to 48 hours after the visit at which the diagnosis of depression is made and an antidepressant prescribed, an NP or PA can telephone the patient and ask if he/she had the prescription filled, if the patient is taking the medication, and if he/she has any questions or concerns. The NP or PA can schedule a follow-up visit or telephone call in 3 to 4 weeks to monitor adherence to the medication regimen, any change in symptoms, and any occurrence of side effects. NPs and PAs can ensure that patients are monitored every 3 to 6 months while on antidepressant therapy, including after patients achieve remission and a normal level of functioning.

Another important role for NPs and PAs in primary care settings is to integrate the patient's care, serving as the patient's liaison with the primary care physician and the psychotherapist following referral for additional care. Continued educational efforts may be necessary to ensure that patients adhere to their antidepressant regimen and their psychotherapy. Patients may want to discontinue treatment as soon as they begin to feel better rather than remain on long-term treatment, which is necessary to maintain complete remission of symptoms and return of a normal level of functioning.

## CONCLUSION

Although often considered an episodic illness, depression actually is a chronic debilitating illness that, if left untreated, can significantly increase the risk of suicide.<sup>3</sup> The approach to treatment, therefore, is analogous to the management of other chronic diseases (eg, diabetes, hypertension, hypercholesterolemia) that often present in the primary care setting. The goals of treatment are for patients to have an absence of symptoms and a level of psychosocial functioning similar to that in normal individuals and to prevent relapse or recurrence. Through patient/healthcare provider partnership, distinct treatment goals and expectations, and consistent management, treatment of depression to remission in the primary care setting will result in better prognosis and outcomes.

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# ACHIEVING REMISSION IN DEPRESSION: Managing Women and Men in the Primary Care Setting

## Post-test

### Instructions for Continuing Education Credit

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Release Date: September 2003  
Expiration Date: September 30, 2004

1. All of the following statements regarding gender differences are true, except:
  - a. The prevalence of major depression in women is approximately twice that in men.
  - b. Women with depression are more likely to have eating disorders and shorter episodes of depression compared with men with depression.
  - c. Women may respond better to selective serotonin reuptake inhibitors than to tricyclics.
  - d. Gender differences regarding the evaluation and treatment of depression are preliminary and based on post hoc analyses of study data.
2. All of the following statements are true, except:
  - a. The strongest predictor of postpartum depression is depression prior to or during pregnancy.
  - b. Women with moderate to severe symptoms of premenstrual anxiety and irritability have levels of impairment nearly comparable to those observed in major depression.
  - c. The risk of prenatal exposure to antidepressants never outweighs their benefit in women with depression.
  - d. Estrogen therapy may improve response to selective serotonin reuptake inhibitors in postmenopausal women.
3. Which of the following statements is true regarding depression?
  - a. Depression is frequently comorbid with general medical conditions and can adversely affect prognosis.
  - b. Treatment for depression is unsuccessful in 80% or more of patients.
  - c. Depression is an episodic condition that requires only short-term therapy.
  - d. There is no association between depressive symptoms and chronic pain conditions.
4. Which of the following is the goal of the treatment of depression?
  - a. Symptom relief
  - b. Response
  - c. Relapse
  - d. Remission
5. Which of the following statements is true?
  - a. Depression as a diagnosis is almost always missed by primary care physicians.
  - b. The diagnosis of depression requires a lengthy patient assessment using standardized scales.
  - c. The change in target symptoms or the PHQ is useful for monitoring response to therapy.
  - d. Most primary care physicians routinely do frequent monitoring of patients with depression.
6. All of the following are true regarding remission, except:
  - a. Remission is defined as the absence of symptoms.
  - b. Once a patient reaches remission, antidepressant treatment can be stopped.
  - c. Remission is defined as a level of psychosocial functioning similar to that in normal individuals.
  - d. Patients treated to remission are less likely to have a relapse or recurrence of their depression.
7. Which of the following is a principle for treating depression?
  - a. Use of the dose that achieves remission.
  - b. Infrequent monitoring for symptomatic and functional improvement.
  - c. Use of a short-duration treatment trial.
  - d. Use of the minimum dose that relieves symptoms.
8. Which of the following are roles for nurse practitioners and physician assistants in primary care practice sites?
  - a. Patient education.
  - b. Monitoring of therapy.
  - c. Liaison between patient, primary care physician, and psychotherapist.
  - d. All are roles for nurse practitioners and physician assistants.
9. All of the following statements are true regarding patient education for depression, except:
  - a. All patients can benefit from education about depression and its treatment.
  - b. Patient education for depression emphasizes adherence to medication and psychotherapy regimens.
  - c. Patient education is necessary only when the initial prescription for an antidepressant is written.
  - d. A discussion of risk/benefit of treatment is a component of patient education for some patients.
10. Successful monitoring of patients with depression may include all of the following, except:
  - a. Initial telephone call in 24 to 48 hours after initial prescription is written.
  - b. First follow-up contact/visit in 6 months.
  - c. Use of a structured tool to monitor symptoms.
  - d. Integration of patient care when the patient is referred for additional care.

# ACHIEVING REMISSION IN DEPRESSION: Managing Women and Men in the Primary Care Setting

## CME Post-test Answer Key/Evaluation/Registration Form

*Nurse Practitioners:* Approval is being sought by the Continuing Education Approval Program of the National Association of Nurse Practitioners in Women's Health for contact hours and pharmacology hours.

*Physician Assistants:* The program has been reviewed and is approved for a maximum of 2.0 hours of clinical Category 1 (Preapproved) CME credit by the American Academy of Physician Assistants (AAPA). Physician assistants should claim only those hours actually spent participating in the CME activity.

### Post-test Answer Key

- |            |            |            |            |             |
|------------|------------|------------|------------|-------------|
| 1. A B C D | 3. A B C D | 5. A B C D | 7. A B C D | 9. A B C D  |
| 2. A B C D | 4. A B C D | 6. A B C D | 8. A B C D | 10. A B C D |

### Program Evaluation Form

The University of Minnesota would appreciate your comments regarding the quality of the information presented.

- The program objectives were fully met.  
Strongly Agree      Agree      Disagree      Strongly Disagree
- The quality of the educational process (method of presentation and information provided) was satisfactory and appropriate.  
Strongly Agree      Agree      Disagree      Strongly Disagree
- The educational activity has enhanced my professional effectiveness and improved my ability to treat/manage patients.  
Strongly Agree      Agree      Disagree      Strongly Disagree      N/A
- The educational activity has enhanced my professional effectiveness and improved my ability to communicate with patients.  
Strongly Agree      Agree      Disagree      Strongly Disagree      N/A
- The information presented was *without* promotional or commercial bias.  
Agree      Disagree
- What changes will you make in your practice as a result of participating in this program? \_\_\_\_\_  
\_\_\_\_\_
- Comments/suggestions regarding *this* material: \_\_\_\_\_  
\_\_\_\_\_
- Recommendations for *future* presentations: \_\_\_\_\_  
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Expiration date for credit:  
September 30, 2004

Editor: *Clinical Courier*<sup>®</sup>  
SynerMed<sup>®</sup> Communications  
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Vol. 21 No. 32

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Managing Women and Men in the Primary Care Setting**