

Depression Subtyping: Treatment Implications

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The complexity of subtyping depression and the implications that such subtyping has on treatment choices are discussed in this article. The most recent edition of the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition* (DSM-IV) directs clinicians to classify the mood disorders in depressed patients as unipolar, bipolar, due to a general medical condition, or due to substance abuse. The focus of this article is unipolar (major depression and dysthymia) and bipolar I and II disorders with and without feature specifiers for atypical depression, seasonal affective disorder, psychotic depression, and postpartum depression. Anxious depression, which is not a DSM-IV classification, is also reviewed.

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The importance of subtyping clinical depression in patients diagnosed with mood disorders has been recognized for almost a century since Emil Kraepelin¹ first separated manic depressive illness from schizophrenia. Many approaches have been used to create meaningful diagnostic categories that could potentially assist the clinician in determining the type of treatment that may be successful. A well-known example of such a classification is bipolar versus unipolar affective disorders.²⁻⁴ The different subtypes of depression proposed throughout the years, including those delineated in the most recent edition of the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition* (DSM-IV),⁵ may or may not represent discrete disease entities. Indeed, there is often overlap of symptoms between depressive subtypes described in DSM-IV. However, subtyping the clinical depression presented by the patient provides direction in the choice of treatment.

DSM-IV directs that depressed patients presenting with a disturbance in mood as the predominant feature should first be classified into 1 of the mood disorder categories. These categories include depressive disorders (unipolar), bipolar I and bipolar II disorders, mood disorder due to a general medical condition, and substance-induced mood disorder. The depressive disorders, including major depressive disorder, dysthymic disorder, and depressive disorder not otherwise specified, are all unipolar; that is,

there is no history of the patient ever having manic, mixed, or hypomanic episodes. Bipolar I disorder is characterized by a clinical course with 1 or more manic or mixed episodes in patients who have also had 1 or more major depressive episodes; bipolar II disorder is used as the diagnosis when a patient has 1 or more major depressive episodes accompanied by at least 1 hypomanic episode. Patients can be further classified, according to DSM-IV, with specifiers that describe the current or most recent mood episode (e.g., psychotic, with atypical features, and with postpartum onset) or the course of recurrent mood episodes (e.g., with a seasonal pattern). All of these subtypes are characterized by single or recurrent major depressive episode(s), and all but double depression can be present in patients with either unipolar or bipolar depression (Table 1). Thus, the initial diagnostic step a clinician should take in the determination of the subtype of a depressive episode is to ascertain if the patient is within the bipolar spectrum.

The criteria and treatment implications for the DSM-IV classifications of dysthymic disorder and major depressive disorder (double depression), atypical depression, seasonal affective disorder, psychotic depression, and postpartum depression, in addition to anxious depression,⁶ are defined and reviewed, and appropriate treatments are described in this article.

UNIPOLAR DEPRESSIVE DISORDERS

Major Depressive Disorder

Major depressive disorder and dysthymic disorder are 2 of the most prevalent disorders classified in DSM-IV (see Table 2).^{7,8} Major depressive disorder is characterized by 1 or more major depressive episodes without manic, mixed, or hypomanic episodes. Major depressive episodes last at least 2 weeks and are characterized by at least 5 of 9 criteria, including at least 1 of the 2 primary criteria of de-

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Table 1. Mood Disorder Subtypes*

| Subtype | Major Depression, | | |
|-------------------------------|---------------------|----------------------|-----------------------|
| | Single or Recurrent | Bipolar I Depression | Bipolar II Depression |
| Double depression (dysthymia) | + | - | - |
| Anxious depression | + | + | + |
| Atypical depression | + | + | + |
| Seasonal affective disorder | + | + | + |
| Psychotic depression | + | + | + |
| Postpartum depression | + | + | + |

*Symbols: + = a positive subtype of the axis I category, - = cannot be part of the axis I category.

pressed mood and loss of interest or pleasure in nearly all activities. The other 7 criteria are significant weight loss or gain, insomnia or hypersomnia nearly every day, psychomotor agitation or retardation nearly every day, fatigue or loss of energy nearly every day, feelings of worthlessness or guilt nearly every day, diminished ability to think or concentrate or indecisiveness nearly every day, and recurrent thoughts of death, wishes to be dead, suicide ideation, or a suicide attempt or plan. Major depressive disorder can consist of a single depressive episode or recurrent episodes (approximately 50% to 60% of patients who have had a single major depressive episode will have a second one, 70% of those who have 2 episodes have a third, and 90% of those who have 3 episodes have a fourth; see DSM-IV⁵) and can be further specified to describe the current or most recent major depressive episode or pattern of such episodes. Major depressive disorder is associated with a high mortality (15% die by suicide), may be preceded by dysthymic disorder (10% to 25% of the population), frequently occurs with other disorders (e.g., anorexia nervosa, obsessive-compulsive disorder), is associated with sleep electroencephalogram (EEG) and neurotransmitter abnormalities, is twice as common in women as in men, and may begin at any age but has its highest rates in individuals 25 to 44 years of age (see DSM-IV⁵).

Dysthymic Disorder

Dysthymic disorder is a highly prevalent disorder as indicated by the data from the National Institute of Mental Health (NIMH) Epidemiologic Catchment Area study (lifetime prevalence rate for dysthymia = 3.1% and for major depression = 4.4%).⁹ This disorder is characterized by a chronically depressed mood that occurs most of the day, for more days than not, for at least 2 years. During this chronic depression, the patient experiences at least 2 of the following characteristics: poor appetite or overeating, insomnia or hypersomnia, low energy or fatigue, low self-esteem, poor concentration or inability to make decisions, and feelings of hopelessness (DSM-IV⁵). Other criteria include persistence of the aforementioned characteristics during the 2-year period (not free of symptoms for

Table 2. Depressive Disorders (DSM-IV) Trials (Total N = 524 Patients)*

| Disorder | Point Prevalence, % ^a |
|---------------------------------|----------------------------------|
| Major depressive disorder | 44 |
| Double depression | 22 |
| Dysthymia | 14 |
| Recurrent brief depression | 1 |
| Minor depression | 4 |
| Depressive personality disorder | 41 |

*Data from references 7 and 8.

^aNot mutually exclusive.

more than 2 months at a time); no major depressive episode; no manic, mixed, or hypomanic episode; symptoms do not occur during course of a chronic psychotic disorder; symptoms are not due to effects of a substance or existing medical condition; and the symptoms cause clinically significant impairment of functioning. The duration of dysthymic disorder is 3, 5, or 10 years or more in 96%, 73%, and 42% of patients, respectively.¹⁰

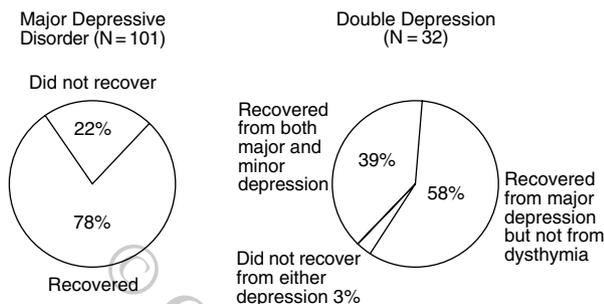
Major Depressive Disorder Versus Dysthymia

The differences between dysthymic disorder and major depressive disorder are in onset, duration, persistence, and severity of symptoms. However, dysthymic disorder is associated with many of the same features as major depressive disorder, especially feelings of inadequacy, generalized loss of interest or pleasure, social withdrawal, feelings of guilt or brooding about the past, irritability and excessive anger, and decreased effectiveness, activity, and productivity. Indeed, several epidemiological and family studies conducted to evaluate the subtyping of major depressive disorder and dysthymic disorder have not provided sufficient evidence to indicate that these 2 disorders are distinct entities. In the longitudinal, prospective epidemiologic community study of 292 males and 299 females from Zurich, Angst¹¹ concluded that there were no significant differences in symptoms or family history between major depressive disorder and dysthymia. Also, the diagnosis of dysthymia was very unstable; that is, only 4 of 19 patients initially diagnosed with dysthymia still met the criteria for diagnosis 2 years later. Results of the DSM-IV mood disorders field trial⁸ are in agreement that many of the symptoms of major depressive disorder and dysthymic disorder overlap, but they are not concurrent. Patients with major depressive disorder had significantly higher rates of 7 of 12 somatic/vegetative symptoms but only 4 of 19 cognitive/affective symptoms.

Double Depression

The concept of double depression, introduced in the NIMH Collaborative Program on the Psychobiology of Depression (CDS) that was begun in the early 1970s, is a combination of major depressive disorder superimposed on preexisting dysthymia.^{8,10} The prevalence of double depression is intermediate between that of major depressive

Figure 1. Rates of Recovery for Patients With Major Depressive Disorder or Double Depression*



*Data from reference 10.

disorder and dysthymia (Table 2). Although it is difficult to clearly delineate the disorders of major depressive disorder, dysthymia, and double depression, the rates of recovery from these disorders do vary. Of the 133 subjects who were followed up for 2 years in the CDS study (Figure 1), 31 (97%) of 32 patients with double depression recovered only from the major depression compared with 80 (79%) of 101 patients with major depressive disorder alone. Thirteen (41%) of the 32 patients with double depression recovered from both disorders.

Treatment of Unipolar Depression

Reports in the literature indicate that patients with various subtypes of unipolar depression (i.e., dysthymic disorder, major depressive disorder and double depression) are undertreated,^{5,12-17} yet treatment of these patients with antidepressants has been effective.¹⁸⁻²² For example, in a recent study by Shelton et al.²³ of patients with dysthymia for an average of 30 years, only 41.3% were treated with antidepressants and only 56.1% were treated with psychotherapy. Patients with previous episodes of major depression (double depression) were slightly more likely to have received treatment (45.7% received antidepressants and 59.4% received psychotherapy). Comparison of the outcome of treatments in the latter group indicated much improvement in 37.9%, minimal improvement in 24.2%, and no change in 37.9% of the 95 patients who received antidepressants. Fewer patients who received psychotherapy (129 total) reported much improvement (26.4%) and more reported minimal improvement (54.3%). The 3 patients who received electroconvulsive therapy (ECT) were much improved.

Results of studies of pharmacotherapy for the treatment of patients with double depression or dysthymia alone indicate variable efficacy of different types of antidepressants (Table 3). Duarte et al.²⁴ compared the selective reversible monoamine oxidase A (MAO-A) inhibitor moclobemide (300 mg/day) with the selective serotonin reuptake inhibitor (SSRI) fluoxetine (20 mg/day) for the treatment of patients with double depression and found these agents to be of equal efficacy as assessed by the Hamilton Rating Scale

Table 3. Treatment of Double Depression*

| Drug Type | Examples |
|--------------------------------|---|
| Tricyclic antidepressant | Clomipramine Imipramine |
| Secondary amine antidepressant | Desipramine Nortriptyline |
| MAOI | Moclobemide Phenelzine Tranylcypromine |
| SSRI | Fluoxetine Paroxetine Sertraline |
| Atypical antidepressant | Bupropion Mirtazapine Nefazodone Venlafaxine |

*Abbreviations: MAOI = monoamine oxidase inhibitor, SSRI = selective serotonin reuptake inhibitor.

for Depression (HAM-D). Another treatment approach, the use of ECT, has been shown to be as effective in 25 patients with double depression as in 75 patients with major depression only.²⁵

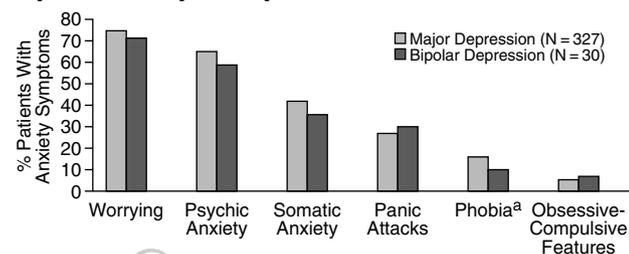
In studies of patients with dysthymia, sertraline (an SSRI) and imipramine (a tricyclic antidepressant) were significantly better than placebo at improving psychosocial outcomes and increasing full remission rates.^{23,26} In addition to imipramine, mianserin and dothiepin have been shown to be effective in reducing the symptoms of dysthymia, whereas other tricyclic antidepressants (e.g., doxepin, amitriptyline, desipramine) have been shown to be ineffective (no difference compared with placebo). Similarly, the monoamine oxidase inhibitors (MAOIs) have been shown to be effective in some cases (phenelzine) but not in others (isocarboxazid).³

The variability of the results of antidepressant efficacy studies may be due to small sample sizes and/or overlap of disease entities. More studies are needed to clearly define the efficacy of antidepressant therapy for patients with dysthymia or double depression. However, existing data suggest that patients with dysthymia respond to antidepressant therapy in a manner similar to that of patients with major depressive disorder,⁷ so prompt and aggressive treatment of these patients may prevent development of a more severe disorder and the associated prevalence of drug and alcohol abuse.²³

ANXIOUS DEPRESSION

Anxious depression is not a DSM-IV classification but is worthy of note because of the overlap of depressive symptoms and anxiety noted by many clinicians and investigators.⁶ This concept goes back to the origins of diagnosing depression when Sir Aubrey Lewis described anxiety as a qualifying term for the agitated depression associated with melancholia.²⁷ Anxious depression is different from DSM-IV atypical depression and can be part

Figure 2. Anxiety Symptoms in Patients With Major Depression or Bipolar Depression*



*Data from reference 6 and P.J.C., unpublished data, 1992.

^aOnly phobia occurred more frequently in women.

of major depression or bipolar I or bipolar II depression (see Table 1). Literature findings indicate that many depressed patients can be described as having anxious depression: 15% to 33% of depressed patients have frequent panic attacks, and an even larger proportion of depressed patients exhibit anxiety symptoms along with agitation, obsessive-compulsive symptoms, anorexia/weight loss, gastrointestinal symptoms, hypochondriasis, depersonalization, and diurnal variations.²⁸⁻³⁶ In this clinical entity, patients must fulfill the criteria for major depression according to DSM-IV but, in addition, have a number of anxiety symptoms. A different condition, in which patients present with both anxiety and depressive symptoms that do not fulfill criteria for DSM-III-R diagnoses of either depressive or anxiety disorder, has been defined as mixed anxiety and depression by *The Tenth Revision of the International Classification of Diseases, Injuries and Causes of Death (ICD-10)*.³⁷

Anxious depressed patients are more severely ill than nonanxious depressed patients according to HAM-D results.^{9,23} They have poorer responses to treatment in naturalistic studies⁶ and in treatment studies using imipramine, desipramine, and phenelzine.^{38,39} Finally, psychic anxiety and panic attacks in depressed patients are predictive of an outcome of suicide in the first year.^{40,41}

In a study of 327 patients with primary unipolar depressive disorder as indicated by Research Diagnostic Criteria, Clayton and coworkers⁶ demonstrated a high frequency of anxiety symptoms (Figure 2) such as worry, psychic anxiety, somatic anxiety, panic attacks, acute phobias, and compulsions. For instance, between 25% and 30% of patients had panic attacks during an episode of depression. These same diagnoses are also seen in bipolar depressed patients (P.J.C., unpublished data, 1992). The depressed patients with higher ratings for anxiety took longer to recover (26 weeks compared with 13 weeks). There was also a significant relationship between anxiety in depressed probands and the risk for primary unipolar depressive disorder in 832 first-degree relatives. The usefulness of subdividing depressed patients according to anxiety symptoms is supported by the results of this study because these symptoms predict family illness and patient outcome. In

Table 4. Treatment of Anxious Depression*

| Drug Type | Examples |
|--------------------------|-----------------|
| Tricyclic antidepressant | Clomipramine |
| MAOI | Phenelzine |
| | Tranlycypromine |
| SSRI | Fluoxetine |
| | Paroxetine |
| | Sertraline |
| Atypical antidepressant | Mirtazapine |
| | Nefazodone |
| | Venlafaxine |

*Add benzodiazepines; augment with lithium. ECT or bupropion probably should not be used in treating anxious depression.

addition, the choice of drug therapy may depend on the presence of anxiety symptoms; for example, Joffe et al.³⁹ reported that patients with anxious depression are slightly less likely than nonanxious depressed patients to respond to tricyclic antidepressants. Other treatments include the SSRIs and MAOIs⁴² (Table 4). With mirtazapine, the addition of a benzodiazepine may not be necessary because mirtazapine has anxiolytic properties that have been shown to be efficacious in this group.⁴³

ATYPICAL DEPRESSION

According to DSM-IV, atypical depression is a specifier that can be used to further describe a current or most recent major depressive episode in patients diagnosed with major depressive disorder, dysthymic disorder, bipolar I disorder, or bipolar II disorder. The essential criteria are mood reactivity and at least 2 of the following features: increased appetite, weight gain, hypersomnia, leaden paralysis, and chronic pattern of extreme sensitivity to perceived interpersonal rejection.

The prevalence of atypical depression was studied by Robertson et al.⁴⁴ in 79 unipolar and 30 bipolar patients who were diagnosed according to DSM-IV criteria. The patients were assessed with the Atypical Depression Diagnostic Scale, and no differences were found between the 2 populations in atypical symptom profile or prevalence of a diagnosis of atypical depression (28% of unipolar and 30% of bipolar patients). Asnis et al.⁴⁵ reported a similar prevalence (29%) of atypical depression in their population of 114 depressed outpatients. Atypical depression is more common in women (29 of 33 women in the study by Asnis et al. had atypical depression)⁴⁵ and is usually chronic (> 2 years).⁴⁶

The symptoms of atypical depression are similar to those of melancholic depression, but patients with atypical depression have a significantly younger age at onset (16.8 versus 32.2 years) and more chronic course of illness (227 versus 46 months).⁴⁶ In addition, mood response to intravenous amphetamine differentiates these 2 groups. In a test of mood response to dextroamphetamine, a dysphoric mood was observed in significantly more patients with

Table 5. Treatment of Atypical Depression*

| Drug Type | Examples |
|-----------|--|
| MAOI | Moclobemide Phenelzine Selegiline Tranylcypromine |
| SSRI | Fluoxetine Paroxetine Sertraline |

*Electroconvulsive therapy should not be used in treating atypical depression.

atypical depression (15/24, 63%) than in patients with melancholy (2/19, 11%).⁴⁶ Familial history of patients with atypical depression compared with that of melancholic patients also indicates that the 2 disorders are distinct. In a study of 330 patients with unipolar depression, those with atypical depression had significantly more family members with dysthymia (87/173) and atypical depression (25/173) than did those with melancholic depression (10 of 53 relatives had dysthymia, and 3 of 53 relatives had atypical depression).

Treatment outcome also distinguishes atypical depression from melancholia. Patients with atypical depression preferentially respond to MAOIs compared with tricyclic antidepressants,^{46,47} whereas patients with melancholic depression are equally likely to respond to MAOIs and tricyclic antidepressants.⁴⁶ Indeed, it was this preferential response that prompted West and Dally⁴⁸ to coin the term atypical depression for patients who were responsive to iproniazid but did not have the typical endogenous characteristics of depression. Another type of antidepressant, the SSRIs, has also been shown to be effective in the treatment of atypical depression (for example, fluoxetine⁴⁹). Moclobemide, a reversible inhibitor of MAO-A, was superior to fluoxetine as determined by some scales (the Montgomery-Asberg Depression Rating Scale [MADRS] and the Clinical Global Impressions [CGI] scale), but not others (HAM-D).⁵⁰ The results of these studies indicate that any of the therapeutics shown in Table 5 would be possible successful treatments for patients with atypical depression. The difference between patients with atypical and melancholic depression is also evident in their responses to electroconvulsive therapy; that is, patients with melancholia improve, but patients with atypical depression actually worsen.⁴⁶

SEASONAL AFFECTIVE DISORDER

The essential feature of seasonal affective disorder (SAD) is the onset and remission of major depressive episodes at recurrent and distinct, regular times of the year. According to DSM-IV,⁵ SAD is a specifier that can be applied to patients with major depressive disorder, bipolar I disorder, or bipolar II disorder. The other criteria for this specifier are full remissions (or change to mania or hypo-

mania) at a characteristic time of the year, 2 seasonal and no nonseasonal major depressive episodes in the last 2 years, and seasonal episodes that substantially outnumber nonseasonal episodes over a lifetime. Most patients with SAD (65% to 85%) have increased appetite, carbohydrate craving, weight gain, and hypersomnia (these symptoms are sometimes called reverse vegetative symptoms).⁵¹

According to DSM-IV,⁵ the prevalence of SAD is greater at higher latitudes, in younger people, and in women (60% to 90% of SAD patients are women). In an epidemiologic study, Dam et al.⁵² report that 12% of an unselected cohort of 3556 people in Denmark have SAD as measured by high Global Seasonality Scores (GSS) assessed by the Seasonal Pattern Assessment Questionnaire (SPAQ). There also appears to be a relationship between SAD and polarity of depression. The results of several studies (for review see Goodwin and Jamison⁵³) indicate that 8% to 100% of patients with SAD also have bipolar I or II disorder. The symptoms associated with SAD also overlap with those of atypical depression. However, only 26% of 53 patients with SAD met the DSM-IV criteria for atypical depression in the study by Tam et al.⁵⁴ The reverse vegetative symptoms overlapped in these patients, but not the classic atypical depression symptoms of mood reactivity, rejection sensitivity, or leaden paralysis, and SAD is an episodic disorder compared with the chronic course of atypical depression.

Schwartz et al.⁵⁵ studied the long-term course of 59 patients with SAD for 8.8 years. The depressive disorders in 42% of this population remained purely seasonal, whereas nonseasonal depression appeared in 44% over the time period studied. Total remission of SAD was noted in 14% of the patients.

Possible treatment of patients with SAD include light therapy, sleep deprivation, and antidepressants. Patients with SAD are effectively treated with light therapy.^{56,57} Schwartz et al.⁵⁵ reported that the use and efficacy of light treatment remained stable over time and many patients are often successfully treated with light therapy alone. However, 63% of these patients required supplemental antidepressant medication at some time. There are only a few studies in the literature comparing the efficacy of different antidepressants. Both moclobemide, a reversible MAO-A inhibitor, and fluoxetine were shown to be efficacious in patients with SAD.^{58,59} In addition, sleep deprivation under stringently controlled conditions has been shown to improve patients with SAD.⁶⁰ The response rate was similar to that seen with antidepressants in SAD patients, equal to the response of non-SAD patients, and better than that seen in controls.

PSYCHOTIC DEPRESSION

Another DSM-IV specifier that can be assigned to major depressive disorder, bipolar I disorder, and bipolar II disorder is psychotic depression, which indicates the pres-

ence of delusions or hallucinations. These delusions/hallucinations can be mood-congruent and consistent with depressive themes (e.g., delusions of guilt or deserved punishment, and nihilistic or somatic delusion), or the delusions can be mood-incongruent and unrelated to depressive themes (e.g., persecutory delusions and delusions of thought insertion, thought broadcasting, and control).

Psychotic depression is evident in 14% to 17% of patients with major depressive disorder and is more frequent in females.⁶¹⁻⁶⁴ In a study of 253 patients with affective disorders, this feature has been shown to be more frequent in bipolar than unipolar patients.⁶²

Psychotic depression is associated with nonsuppression of cortisol on the dexamethasone suppression test. The nonsuppression rate in patients with psychotic depression was 64% compared with 41% in nonpsychotic depressed patients.⁶⁵ Patients with psychotic depression also have significantly more episodes of major depression than nonpsychotic patients. Sixty-nine percent of 140 nonpsychotic patients experienced only 1 major depression episode compared with 12% of 25 psychotic patients.⁶⁴

ECT and the combination of antipsychotic and tricyclic antidepressant agents are the treatments of choice for patients with psychotic depression.^{66,67} ECT was clearly shown to improve symptoms in psychotic depression patients in sham-control trials.⁶⁷ Treatment of these patients with a combination of a tricyclic antidepressant and an antipsychotic is significantly more successful than tricyclics alone (76% versus 43%, respectively; see Coryell⁶⁷). The combination therapy must be monitored carefully, however, because the antipsychotics may interfere with the metabolism of the tricyclic antidepressants. Inconsistent results from studies comparing the efficacy of ECT and combination drug therapy indicate the need for careful diagnosis of psychotic depressed patients. Other treatment regimens for patients with psychotic depression include amoxapine monotherapy, SSRIs, atypical antipsychotics (e.g., risperidone), and lithium enhancement.⁶⁷

POSTPARTUM DEPRESSION

Postpartum depression is a DSM-IV specifier that is used to classify a current or most recent major depressive, manic, or mixed episode that begins within 4 weeks postpartum in patients with major depressive disorder, bipolar I disorder, bipolar II disorder, or brief psychotic disorder. Postpartum illness can be characterized as depression or psychosis. Mood lability is common in postpartum episodes, and delusions often concern the newborn infant.

The symptoms of depression were noted at 6 weeks postpartum in 10% of 20 normal pregnant women as determined by 3 different questionnaires (Postpartum Emotional Disorders Questionnaire, the Beck Depression Inventory, and the Differential Emotions Scale/Adjective Checklist⁶⁸). The patient population was small, so conclu-

Table 6. Treatment of Postpartum Depression*

| Type of Depression | Treatment |
|--------------------|------------------------------------|
| Depressive | Lights (if fall/winter) |
| | Psychotherapy |
| | Medication |
| | Antidepressant |
| Psychotic | Not benzodiazepine alone |
| | SSRIs are safe |
| | Mood stabilizers |
| | Antipsychotics and antidepressants |
| | (appropriate to predominant mood) |
| | Electroconvulsive therapy |

*Adapted from reference 76. If first episode, taper treatments at 6 months or at summer (for light therapy); if recurrent, give maintenance medications. Any antidepressant is acceptable except doxepin (see Table 7). Benzodiazepines should not be used alone in treating postpartum depression.

sions about relationships between postpartum depression and other factors (e.g., race, age, marital status) could not be made. More recent studies have shown a similar prevalence using a short postnatal depression questionnaire (Edinburgh Postnatal Depression Scale) developed by Cox et al.⁶⁹ The point prevalence of depression was 12.5% at 8 weeks and 8.3% at 12 weeks postpartum in 1584 Swedish women,⁷⁰ and 11.4% at 3 days and 11% at 6 weeks postpartum in a population of 370 mothers in Dublin.⁷¹ In a study of mood changes after childbirth, Kendell et al.⁷² report that ratings of depression, tears, and lability, but not anxiety or irritability, rose to a sharp peak 5 days postpartum and then declined. The mother's parity or the method of feeding the newborn did not affect this peak. Twenty-seven percent of the 81 women studied had depressive symptoms that lasted about 4 weeks. The peak in depressive symptoms noted at 5 days postpartum was much more prominent for the 22 women with postpartum depression than for the other women.

Postpartum psychosis is characterized by congruent and incongruent mood features, confusion, disorganization, and homicidal ideation.^{73,74} The onset of this disorder was within the first 2 and 4 weeks postpartum in 38% and 80%, respectively, of the very large cohort provided by the Edinburgh Psychiatric Case Register for the study by Kendell et al.⁷⁵ The symptoms were severe enough in 0.2% of the cases that psychiatric hospitalization was necessary. Several factors were associated with an increased relative risk of admission for postpartum psychosis, such as being unmarried, having a first baby, cesarean section, and perinatal death. Also, women with a history of manic depressive illness had a higher risk of puerperal psychosis than those with a history of schizophrenia or depressive neuroses.

Treatment of patients with postpartum depression is multifaceted (Table 6) and complicated by the risks of fetal side effects with prophylactic therapy and side effects in breastfed newborns with postpartum therapy (Table 7). Postpartum depression with depressive symptoms can be

Table 7. Antidepressants and Breastfeeding*

| Drug | Results |
|---------------|--|
| Amitriptyline | Not found in infant plasma |
| Nortriptyline | Not found in infant plasma |
| Desipramine | Not found in infant plasma |
| Clomipramine | Not found in infant plasma |
| Dothiepin | Not found in infant plasma |
| Sertraline | Not found in infant plasma |
| Fluoxetine | Controversial; some reports of undetectable amounts in infant plasma |
| Paroxetine | Controversial; some reports of undetectable amounts in infant plasma |
| Doxepin | Adverse effects; no problems after 10 wk |

*From references 77 and 78.

treated with light (if seasonally related), psychotherapy, or antidepressants. These treatments can be tapered off at 6 months (or in the summer) in cases of a first episode of postpartum depression. For patients with psychosis associated with their postpartum depression, mood stabilizers, antipsychotics and antidepressants in combination, and ECT are possible treatments. Maintenance medication/therapy may be considered in patients with recurrent episodes of depression. A recent study by Kulin et al.⁷⁶ indicates that new SSRIs (fluvoxamine, paroxetine, and sertraline) are not associated with an increased risk for fetal malformations or higher rates of miscarriages. The prophylactic use of antimanic agents in women with bipolar depression significantly improved the well-being of the patients for 3 months postpartum.⁷⁴ These studies indicate that early identification and treatment of women at high risk for postpartum psychosis is beneficial and safe for the mother. Several drugs used for the treatment of postpartum depression are also safe for the newborn being breastfed as indicated by their absence in infant plasma (see Table 7 and review by Wisner et al.⁷⁷). Possible effects have been reported in some infants breastfed by mothers being treated with fluoxetine, paroxetine, and doxepin, and low levels of these agents and/or their metabolites have been detected in breast milk.^{77,78} However, because the studies conducted to date contain too many confounds, the correlation between antidepressant treatment and adverse effect is unclear. Treatment regimens are difficult to establish.⁷⁹ As suggested by the Committee on Drugs of the American Academy of Pediatrics and discussed recently by Cohen and coworkers,⁸⁰⁻⁸² the decision to administer antidepressants to mothers who are breastfeeding their infants must be made on a case-by-case basis. Alternatives to drug therapy, such as ECT or psychotherapy, or bottle feeding the newborn are options for patients who need treatment for postpartum illnesses.

CONCLUSIONS

In summary, the subtyping of depression has become much more detailed in recent years and is well docu-

mented in DSM-IV.⁵ Knowledge of these subtypes and the symptoms associated with them is crucial for the accurate diagnosis of a patient's illness. Furthermore, as evidenced by the many studies reviewed in this article, proper diagnosis is important for the decision of type(s) of treatment. The guidelines for diagnosis and choice of treatment of each subtype of depression that can be gleaned from the literature are useful tools for the clinician. However, the complexity of depressive disorders dictates that the clinician should consider treatment on a case-by-case basis.

Drug names: amitriptyline (Elavil and others), amoxapine (Asendin), desipramine (Norpramin and others), dextroamphetamine (Dexedrine), doxepin (Sinequan and others), fluoxetine (Prozac), fluvoxamine (Luvox), imipramine (Tofranil and others), isocarboxazid (Marplan), mirtazapine (Remeron), paroxetine (Paxil), phenelzine (Nardil), risperidone (Risperdal), sertraline (Zoloft).

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