MAJOR DEPRESSIVE DISORDER AND GENERALIZED ANXIETY DISORDER

Dana Bartlett, RN, BSN, MSN, MA

Dana Bartlett is a professional nurse and author. His clinical experience includes 16 years of ICU and ER experience and over 20 years of as a poison control center information specialist. Dana has published numerous CE and journal articles, written NCLEX material and textbook chapters, and done editing and reviewing for publishers such as Elsevier, Lippincott, and Thieme. He has written widely on the subject of toxicology and was recently named a contributing editor, toxicology section, for Critical Care Nurse journal. He is currently employed at the Connecticut Poison Control Center and is actively involved in lecturing and mentoring nurses, emergency medical residents and pharmacy students.

ABSTRACT

Major depressive disorder and generalized anxiety disorder are psychiatric conditions with primary symptoms that often overlap. The treatment of each condition is often similar. Medication, psychotherapy and lifestyle changes are typically recommended as part of the patient treatment plan. Although often diagnosed as separate conditions, major depressive disorder and generalized anxiety disorder often co-occur, and thoughtful consideration by psychiatric and primary care providers and nurses of selective treatment strategies to target primary symptoms will support patient compliance, progress and remission.
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Statement of Need:
Nurses need to understand the diagnostic criteria, and treatment for a major depressive disorder and generalized anxiety disorder in order to best support and to educate patients and their families.
**Course Purpose:**
To provide nurses with knowledge of the common psychiatric conditions of major depressive and generalized anxiety disorder.

**Learning Objectives:**
1. Identify risk factors for major depressive disorder and generalized anxiety disorder.
2. Identify environmental stressors that contribute to the etiology of these diseases.
3. Identify screening tests used to detect major depressive disorder or generalized anxiety disorder.
4. Identify signs or symptoms associated with major depressive disorder and generalized anxiety disorder.
5. Identify the first-line medications used to treat these diseases.

**Target Audience:**
Advanced Practice Registered Nurses, Registered Nurses, Licensed Vocational Nurses, and Associates

**Course Author & Director Disclosures:**
Dana Bartlett, RN, BSN, MA, MSN, William S. Cook, PhD, Douglas Lawrence, MS, Susan DePasquale, CGRN, MSN, FPMHNP-BC - all have no disclosures.

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Reviewed by Susan DePasquale, CGRN, MSN, FPMHNP-BC.

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1. **Risk factors for major depressive disorder include:**
   
   a. Chronic disease and substance abuse.
   
   b. Smoking and obesity.
   
   c. Male gender and high socioeconomic status.
   
   d. High level of education and age > 65.

2. **People who have major depressive disorder are:**
   
   a. Depressed only during stressful life events.
   
   b. Depressed once or twice a week.
   
   c. Depressed almost every day.
   
   d. Depressed only during episodes of substance abuse.

3. **Screening for depression should be done:**
   
   a. If the patient has noticeable signs and symptoms.
   
   b. For every patient ≥ age 18 if there is appropriate clinical support.
   
   c. Only during stressful life events.
   
   d. Only for patients who request screening.

4. **First-line medications used to treat major depressive disorder would be:**
   
   a. Diazepam and imipramine.
   
   b. Bupropion and phenelzine.
   
   c. Amoxapine and trazodone.
   
   d. Citalopram and fluoxetine.

5. **True or false: ECT is effective for treating major depressive disorder.**
6. **Risk factors for generalized anxiety disorder include:**
   a. Male gender and age > 16.
   b. Depression and female gender.
   c. Age > 65 and substance abuse.
   d. Stressful life events and smoking.

7. **Generalized anxiety disorder is a disease that:**
   a. Is typically brief in duration and responds easily to treatment.
   b. Is typically chronic in nature but is almost always curable.
   c. Is typically chronic in nature and the severity fluctuates over time.
   d. Is typically responsive only to psychotherapy.

8. **First-line medication to treat generalized anxiety disorder are:**
   a. Benzodiazepines.
   b. Atypical antipsychotics.
   c. MAOIs.
   d. Selective serotonin reuptake inhibitors.

9. **A common treatment for generalized anxiety disorder is:**
   b. Group therapy.
   c. Psychoanalysis.
   d. Behavioral therapy.

10. **Generalized anxiety disorder is typically:**
    a. brief in duration and responds easily to treatment.
b. chronic and often does not respond to treatment.
c. characterized by rapid, progressive worsening.
d. is typically characterized by rapid, progressive improvement.

**Introduction**

Major depressive disorder and generalized anxiety disorder are two of the most common psychiatric disorders. These diseases are not as prevalent as medical illnesses, such as cardiovascular disease and diabetes, but they result in a significant cost to the individual and society. This problem is compounded because major depressive disorder and generalized anxiety disorder are chronic in nature and often resistant to treatment. Psychotherapy and pharmacotherapy can be effective, but availability, cost, patient compliance issues, and a relative lack of clinical evidence supporting who should be treated, how, and for how long have restricted the successful treatment of major depressive disorder and generalized anxiety disorder.

**Epidemiology Of Major Depressive Disorder**

Major depressive disorder has been identified by the World Health Organization (WHO) as the leading cause of disability worldwide.\(^1\) Approximately 20% of all adults will have an episode of major depression at some point\(^2\) and the lifetime prevalence of major depression has been estimated to be 7%-12% in men and 20%-25% in women.\(^3\) These statistics vary depending on the clinical setting, and there is strong and consistent evidence that major depression is often undetected or underdiagnosed.

Major depressive disorder is more common in women, it is substantially more common in people who have co-existing medical
problems such as coronary atherosclerosis, diabetes, Parkinson’s disease, stroke, or traumatic brain injury,\(^3\) and the rate of major depressive disorder increases with the seriousness of medical morbidity.\(^4\) Major depressive disorder is associated with a very high risk for suicide\(^5\) and many people who suffer from major depressive disorder never receive treatment.\(^6\)

The pathogenesis of major depressive disorder is unknown, but it is probably a complex interaction between genetic, biological, social or environmental, and psychological factors.\(^2,7,8\) Risk factors for major depressive disorder are listed in Table 1.

**Table 1: Risk Factors for Major Depressive Disorder**

<table>
<thead>
<tr>
<th>Risk Factor</th>
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<tbody>
<tr>
<td>Age (18-29)</td>
</tr>
<tr>
<td>Childhood adversity and/or trauma</td>
</tr>
<tr>
<td>Chronic diseases</td>
</tr>
<tr>
<td>Cognitive impairment, i.e., dementia</td>
</tr>
<tr>
<td>Gender (Female)</td>
</tr>
<tr>
<td>Low socioeconomic status</td>
</tr>
<tr>
<td>Poor social support</td>
</tr>
<tr>
<td>Race (White)</td>
</tr>
<tr>
<td>Serious medical illness</td>
</tr>
<tr>
<td>Stressful life events</td>
</tr>
<tr>
<td>Substance abuse</td>
</tr>
<tr>
<td>Unemployed</td>
</tr>
</tbody>
</table>
• Genetics:

Depression is to some degree an inherited disease.\(^8\) People who have major depressive disorder are three times more likely to have a first-degree relative (parent or sibling) who has or had depression than people who do not,\(^9\) and twin studies have estimated that the risk of developing depression is approximately 30%-50% associated with genetic variations.\(^{10-12}\) However, despite a consistent body of evidence that indicates people inherit a susceptibility to depression, genome-wide association studies and gene-environment interaction studies have not yet clearly defined the role and contribution of genetics in the development of depression.\(^8\)

• Biological:

Biological causes of major depressive disorder include abnormal changes in brain structures, impaired and/or abnormal neurotransmitter function, and immune system dysfunction that can cause inflammation and oxidative stress.\(^{2,13-22}\) Whether these changes in structure and function are cause or effect has been difficult to determine, given the heterogeneity of major depressive disorder and the treatments for the disease.

• Environmental:

Major life stressors are considered to be a strong predictor for the development of major depressive disorder.\(^2,6,23-27\) Chronic diseases such as cancer, chronic obstructive pulmonary disease, diabetes, heart disease also increase the risk for developing depression, as do acute illnesses such as stroke.
Diagnostic Criteria For Major Depressive Disorder

The American Psychiatric Association’s diagnostic criteria for major depressive disorder, located in the Diagnostic and Statistical Manual of Mental Disorders, are listed in Table 1.28

Table 2: Diagnostic Criteria for Major Depressive Disorder

<table>
<thead>
<tr>
<th>1. Five or more of the following symptoms have been present during a two week period; they are a significant change from the patient’s previous mood and functioning; at least least one of the symptoms is depressed mood or loss of pleasure or interest, and; the symptoms are not caused by a medical condition.</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Depressed mood most of the day, nearly every day. The depressed mood can be subjective (i.e., the patient reports feeling sad, hopeless) or can be observed by others. In children or adolescents irritation is often present.</td>
</tr>
<tr>
<td>• Markedly diminished interest or pleasure in daily activities. This happens nearly every day and is reported by the patient or by others.</td>
</tr>
<tr>
<td>• Significant weight loss (&gt; 5% of body weight) when not dieting or a decrease or increase in appetite nearly every day. (Note: In children, consider failure to make expected weight gain).</td>
</tr>
<tr>
<td>• Insomnia or hypersomnia nearly every day.</td>
</tr>
<tr>
<td>• Psychomotor agitation or retardation nearly every day: this should be observable by others and not just the patient’s feelings of restlessness or feeling lethargic.</td>
</tr>
<tr>
<td>• Fatigue or loss of energy nearly every day.</td>
</tr>
<tr>
<td>• Feelings of worthlessness or excessive or inappropriate guilt nearly every day.</td>
</tr>
<tr>
<td>• Diminished ability to think or concentrate, or indecisiveness, nearly every day, reported by the patient or observed by others.</td>
</tr>
<tr>
<td>• Recurrent thoughts of death; recurrent suicidal ideation without a specific plan; a suicide attempt or a specific plan for committing suicide.</td>
</tr>
</tbody>
</table>
2. The symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.

3. The episode is not attributable to a substance or another medical condition.

4. The occurrence of the major depressive episode is not better explained by schizoaffective disorder, schizophrenia, schizophreniform disorder, delusional disorder, or other specified and unspecified schizophrenia spectrum and other psychotic disorders.

5. There has never been a manic episode or a hypomanic episode.

Screening For Depression

Screening for depression is recommended by the U.S. Preventive Service Task Force (The Guide to Clinical Preventive Services) in non-pregnant adults 18 years and older when staff-assisted depression care supports are in place to provide accurate diagnosis, effective treatment, and follow-up. Screening for depression should also be considered in certain high-risk populations, i.e., people who have cancer or cardiovascular disease, people who have recently had a stroke or a myocardial infarction, or people who have chronic pain.

There are a variety of screening tools available and comparative studies indicate that they are reasonably equal in effectiveness and ease of use. The Patient Health Questionnaire - 9 (PHQ-9) is a screening test that is often used, it is available without charge, and it has been shown to be accurate, specific, and sensitive.
Table 3: The Patient Health Questionnaire-9

<table>
<thead>
<tr>
<th>Over the Last 2 weeks, How Often Have You Been Bothered by Any of the Following Problems?</th>
<th>Not At all</th>
<th>Several Days</th>
<th>More Than Half the Days</th>
<th>Nearly Every Day</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Little interest or pleasure in doing things</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>2. Feeling down, depressed, or hopeless</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>3. Trouble falling or staying asleep, or sleeping too much</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>4. Feeling tired or having little energy</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>5. Poor appetite or overeating</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>6. Feeling bad about yourself — or that you are a failure or have let yourself or your family down</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>7. Trouble concentrating on things, such as reading the newspaper or watching television</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>8. Moving or speaking so slowly that other people could have noticed? Or the opposite — being so fidgety or restless that you have been moving around a lot more than usual</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>9. Thoughts that you would be better off dead or of hurting yourself in some way</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
</tbody>
</table>

\[0 + \quad \quad + \quad + \quad = \text{Total Score: } \]

If you checked off any problems, how difficult have these problems made it for you to do your work, take care of things at home, or get along with other people?

Not difficult at all   Somewhat difficult   Very difficult   Extremely difficult

A score of 10 or higher indicates the possibility of a depressive disorder, and scores of 5, 10, 15, and 20 indicate the presence of mild,
moderate, moderately severe and severe depression, respectively.\textsuperscript{37} The diagnosis of depression requires that there is a score of 2 or higher on one of the first two questions.\textsuperscript{37} A shortened version, the PHQ-2, uses the first two questions of the PHQ-9 and it appears to offer good sensitivity and specificity as well.\textsuperscript{37}

The SIGECAPS mnemonic is another useful screening tool for detection of major depressive disorder.\textsuperscript{38}

\textbf{Table 4: SIGECAPS Mnemonic}

<table>
<thead>
<tr>
<th>S</th>
<th>Sleep disturbance – either insomnia or hypersomnia.</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Loss of interest in everyday activities – anhedonia.</td>
</tr>
<tr>
<td>G</td>
<td>Guilt – helplessness, hopelessness, worthlessness</td>
</tr>
<tr>
<td>E</td>
<td>Lack of energy</td>
</tr>
<tr>
<td>C</td>
<td>Difficulty concentrating</td>
</tr>
<tr>
<td>A</td>
<td>Appetite disturbance – either increased or decreased</td>
</tr>
<tr>
<td>P</td>
<td>Psychomotor blunting or agitation</td>
</tr>
<tr>
<td>S</td>
<td>Suicidal thoughts, thoughts of death</td>
</tr>
</tbody>
</table>

Also ask the patient if they feel depressed.

Patients who have a major depressive disorder often complain of lack of energy, decreased appetite, dizziness, inability to concentrate or think, fatigue, insomnia, pain, restlessness, and they frequently have many non-specific somatic complaints.\textsuperscript{3,28,39,40} These complaints should be evaluated, but it should be remembered that many patients
who are depressed may have somatic complaints but will not admit to or cannot express feelings of depression.\(^3,39-41\) These somatic complaints and patients not reporting feelings of depression may contribute to a missed diagnosis,\(^42\) and Deneke et al., (2014) noted that there is evidence that many cases of depression are not detected by primary health care providers or in a medical setting.\(^3,43\)

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**Learning Break:**

Is screening for depression effective? Williams et al., (2014) states that depression is frequently undetected if targeted screening is not done and that screening is not harmful.\(^39\) There is also evidence that for screening to be helpful beyond increasing detection and diagnosis rates it must be used in conjunction with appropriate follow-up and effective care; i.e., screening alone is not enough.\(^39,43\)

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**Clinical Course Of Major Depressive Disorder And Consequences Of The Disease**

The clinical course of major depressive disorder is quite variable.\(^3\) The disease typically has its onset when the patient is in his or her mid-20s or 30s\(^28,43\) but a later onset is not uncommon.\(^44\) Most patients who have major depressive disorder will eventually remit, but some patients will never have a remission (two months or more with no symptoms, or one or two symptoms to a mild degree) and others may have many years in which they have no signs and symptoms of depression.\(^28\) Early recognition and treatment and a short duration of depressive symptoms are associated with spontaneous recovery, a better response to treatment, and a higher chance of remission.\(^28,45,46\)
Patients who have had severe depression or who have had an onset at a relatively young age are more likely to have recurrent depression, and depression accompanied with anxiety, personality disorders, or psychotic features has a poor prognosis for remission. Gender and age do not seem to affect the progression of major depressive disorder.

Major depressive disorder is associated with a high mortality risk and most of this risk is from suicide. Major depressive disorder is considered to be a significant risk factor for suicidal behavior, and suicide attempts or threats of suicide are considered to be consistent risk factors for suicide in patients who have major depressive disorder.

Major depressive disorder is a risk factor for the development of chronic diseases (and it negatively influences the progression of these diseases) such as cardiovascular diseases, diabetes, and neurological disorders. People who have major depressive disorder are more likely to smoke, abuse alcohol and drugs, they report a lower quality of life, and this disorder has a profound effect on the patient’s family life, personal relationships, and professional and social life.

**Treatment For Major Depressive Disorder**

Antidepressant medication and psychotherapy are the two primary treatments for major depressive disorder. They will be discussed separately, but they can be and often are used together.
Antidepressant Medication

The antidepressant medication used to treat major depressive disorder are often classified as first-generation or second-generation. First generation refers to the monoamine oxidase inhibitors (MAOIs) such as phenelzine and selegiline and the tricyclic anti-depressants (TCAs) such as amitriptyline and nortriptyline; second-generation refers to all other drugs used to treat major depressive disorder. These terms are still commonly used, but the antidepressants cannot be easily or usefully divided into these two categories. These medications work by affecting the activity or level of neurotransmitters, but the mechanism of action is specific to each drug.

Learning Break:
The MAOIs and the TCAs are called first-generation simply because these drugs were developed and used many years before the advent of the so-called second-generation antidepressants.

The generic name is provided first and the trade name is in parentheses. Some of the older medications are rarely if ever prescribed with trade names.

Table 5: Currently Available Antidepressants/Atypical Anti-Depressants

<table>
<thead>
<tr>
<th>Monoamine Oxidase Inhibitors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Isocarboxazid</td>
</tr>
<tr>
<td>Phenelzine</td>
</tr>
<tr>
<td>Selegiline, transdermal</td>
</tr>
<tr>
<td>Tranylcypromine</td>
</tr>
</tbody>
</table>
Selective Serotonin Re-Uptake Inhibitors/Receptor Partial Agonists

- Citalopram (Celexa)
- Escitalopram (Lexapro)
- Fluoxetine (Prozac)
- Fluvoxamine (Luvox)
- Paroxetine (Paxil)
- Sertraline (Zoloft)
- Vilazodone (Viibryd)

Serotonin-Norepinephrine Re-Uptake Inhibitors

- Desvenlafaxine (Pristiq)
- Duloxetine (Cymbalta)
- Milnacipran (Ixel)
- Venlafaxine (Effexor)

Tricyclic and Tetracyclic Anti-Depressants

- Amitriptyline
- Amoxapine
- Clomipramine
- Desipramine
- Doxepin
- Imipramine
- Maprotiline
- Nortriptyline
- Protriptyline
- Trimipramine

Atypical Antidepressants (unrelated to serotonin, tricyclic, tetracyclic, and MAO inhibitors)

- Bupropion (Wellbutrin)
- Mirtazapine (Remeron)
- Nefazadone (Serzone)
- Trazodone (Desyrel)
- Vilazodone (Viibryd)
A drug that is representative of each of these categories is briefly discussed below. However, it is important to remember that the mechanism of action described (and thus the category each medication is placed in) is the primary way the drug works; and, to lesser or greater degree, all of the antidepressants can affect other neurotransmitters and bind to other receptor sites. For example, the antidepressant effect of the TCAs is mediated through re-uptake of norepinephrine and serotonin but the TCAs also bind to peripheral α-adrenergic receptors and histamine receptors, and postural hypotension and anticholinergic effects such as dry mouth and dizziness are common side effects of the TCAs.

- Bupropion:
  The mechanism(s) of action of bupropion is not completely understood, but it most likely affects adrenergic and dopaminergic activity.

- Phenelzine:
  Phenelzine inhibits the activity of monoamine oxidase, an enzyme that is responsible for the breakdown of endogenous dopamine, norepinephrine, and serotonin.

- Fluoxetine:
  Fluoxetine inhibits the re-uptake of serotonin, thus increasing central nervous system (CNS) concentrations of serotonin.
• **Venlafaxine:**

Venlafaxine inhibits the re-uptake of norepinephrine and serotonin, thus increasing the CNS concentration of these neurotransmitters.

• **Nortriptyline:**

Nortriptyline and the other TCAs are believed to have antidepressant effects by inhibiting the re-uptake of norepinephrine and serotonin. However, these drugs also down-regulate beta and serotonin receptors and as previously mentioned they have other important pharmacologic effects, *i.e.*, binding to peripheral alpha receptors and histamine receptors.

**Choosing an Antidepressant**

Effectiveness, safety and tolerability are the primary factors to consider when choosing an antidepressant; the patient’s co-morbidities, other prescription medications that she or he takes, and patient preference, must also be considered. The effectiveness of the antidepressants is considered to be essentially comparable, but at this time the selective-serotonin re-uptake inhibitors are usually the first choice. These medications, along with serotonin-norepinephrine re-uptake inhibitors, are the most commonly prescribed antidepressants, primarily because when compared to the MAOIs and the TCAs they have more tolerable side effects and are far less dangerous when taken in overdose.
Common adverse effects or side effects of the antidepressants are listed in Table 6. The incidence of, and risk for these, varies for each drug.

Table 6: Adverse Effects and Side Effects of Antidepressants

<table>
<thead>
<tr>
<th>Adverse Effects and Side Effects of Antidepressants</th>
</tr>
</thead>
<tbody>
<tr>
<td>Agitation</td>
</tr>
<tr>
<td>Anticholinergic signs/symptoms, i.e., dizziness, dry mouth</td>
</tr>
<tr>
<td>Constipation</td>
</tr>
<tr>
<td>Drowsiness</td>
</tr>
<tr>
<td>Gastrointestinal effects</td>
</tr>
<tr>
<td>Insomnia</td>
</tr>
<tr>
<td>Orthostatic hypotension</td>
</tr>
<tr>
<td>Palpitations</td>
</tr>
<tr>
<td>Restlessness</td>
</tr>
<tr>
<td>Serotonin syndrome</td>
</tr>
<tr>
<td>Sexual dysfunction</td>
</tr>
<tr>
<td>QTc prolongation</td>
</tr>
<tr>
<td>Weight gain</td>
</tr>
</tbody>
</table>

Learning Break:
The selective serotonin re-uptake inhibitors are required to include a boxed warning (typically called a “black box” warning) in the prescribing information that states that the use of these drugs has been associated with an increased risk for suicidal thinking and behavior in children, adolescents, and young adults. These medications can be prescribed for these patient populations but only with close monitoring for emergence and/or worsening of suicidal behavior or thoughts.
A response to an antidepressant is usually considered to be a > 50% reduction in symptoms as measured by an assessment tool such as the PHQ-9. Responses are usually seen in one to two weeks but longer response times are possible. If the patient does not respond the clinician can decide to: 1) increase the dose; 2) wait several more weeks to see if a response occurs; 3) prescribe a different drug; or, 4) add another antidepressant or an adjunctive treatment to the regimen.

The addition of psychotherapy is an adjunction treatment option, which will be discussed in a later section. These approaches have their own risks and benefits and there is no universal consensus as to which one is best. Clinicians should also be aware that non-adherence to antidepressant therapy is relatively common and if the patient is not responding he or she should be questioned about the level of compliance. The goal of treatment is full remission of symptoms. If an antidepressant or antidepressants are an effective regimen, then treatment is usually continued for at least six months to a year. Most patients should be started on a single antidepressant. There is no conclusive evidence that dual therapy for initial treatment provides an advantage, and it increases the risk for side effects.

**Discontinuing and Switching Antidepressants**

The topic of discontinuing and switching antidepressants will not be discussed in depth. A discontinuation syndrome with withdrawal signs and symptoms can occur when antidepressants are stopped. Tapering the dose over a period of two to four weeks rather than abruptly stopping treatment is recommended, but there is some doubt as to whether this strategy is truly effective for preventing
discontinuation syndrome.\textsuperscript{66} Regardless, patients should be instructed not to abruptly discontinue their antidepressant medications \textit{or} to decrease the dose. The approach to switching from one antidepressant to another is specific to the drug being stopped and the one being started.

**Other Treatments/Therapies for Major Depressive Disorder**

There are many treatments aside from antidepressants that have been used to treat major depressive disorder, however, a complete review of these would be too extensive for this study. Deep brain stimulation, transcranial magnetic stimulation, and vagus nerve stimulation are used much less often than the therapies discussed in the module and they will not be described. Other medications that have been and can be used to treat major depressive disorder is listed in Table 7.\textsuperscript{68,69} Clinical experience with these drugs is limited and they are considered adjunctive therapy.

**Table 7: Other Medications for Treatment of Major Depressive Disorder**

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Amphetamine</td>
<td></td>
</tr>
<tr>
<td>Aripiprazole (Abilify)</td>
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</tr>
<tr>
<td>Buspirone (Buspar)</td>
<td></td>
</tr>
<tr>
<td>Carbamazepine (Tegretol)</td>
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<tr>
<td>Ketamine</td>
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<tr>
<td>Lithium</td>
<td></td>
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<tr>
<td>Methylphenidate, long-acting</td>
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<tr>
<td>Olanzapine (Zyprexa)</td>
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<tr>
<td>Pindolol</td>
<td></td>
</tr>
<tr>
<td>Quetiapine (Seroquel)</td>
<td></td>
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<tr>
<td>Thyroid hormone</td>
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</tbody>
</table>

(including other Atypical Antipsychotics and Psychostimulant drugs)
Lifestyle interventions, *i.e.*, abstinence from alcohol, drug, and tobacco use, changes in diet, exercise patterns, and sleep patterns have been investigated for a beneficial effect on depression.\(^\text{58}\) A sensible, moderate diet, regular exercise, smoking cessation, moderate alcohol use, and abstaining from drug use all have undeniable health benefits, but there is no substantial evidence that these interventions or other lifestyle changes have a strong effect on alleviating depression.\(^\text{70,71}\)

Animal-assisted therapy, music therapy, meditation, and various types of relaxation therapy have shown some benefit for treating major depressive disorder, but a recent review noted that more clinical experience and controlled trials are needed before they can be judged to be effective.\(^\text{58}\)

Electroconvulsive therapy (ECT) is considered to be an effective therapy for treatment-resistant depression, *i.e.*, patients who have not responded to two drugs from a different class used for a sufficient length of time or patients who have not responded to four or more different therapeutic regimens.\(^\text{72,73}\) It can also be used for geriatric patients, patients who have depression and Parkinson’s disease, patients who have severe major depression,\(^\text{58}\) those whose depression is accompanied by catatonia or psychotic features, or patients who have been, or may be non-compliant with medication regimens.

Electroconvulsive therapy has been shown to achieve a substantial remission rate,\(^\text{74}\) and a review of randomized controlled trials indicates that ECT combined with medications is superior to the use of medications alone for preventing relapse.\(^\text{75}\) Anterograde and retrograde memory deficits and other cognitive deficits are relatively
common after ECT,\textsuperscript{76,77} but fortunately these are in most patients of short duration.\textsuperscript{77} Electroconvulsive therapy is comparatively time consuming and logistically complicated.

St. John’s wort is a flowering plant and extracts from the plant are widely used to treat depression. St. John’s wort preparations are available over-the-counter but the evidence for its effectiveness is mixed,\textsuperscript{78,79} and it is not currently recommended as a treatment for major depressive disorder.\textsuperscript{80} It should be used with caution as it can interact with, and reduce the effectiveness of, many commonly used medications such as antidepressants, digoxin, oral contraceptives, and warfarin.\textsuperscript{80}

S-adenosyl methionine (SAMe) is an endogenous substrate that is involved in metabolic processes. Synthesized SAMe preparations have been used to treat depression and SAMe is available over-the-counter. As with St. John’s wort, the evidence for the effectiveness of SAMe for treating major depressive disorder is at best mixed and it is not currently recommended as a therapy for this disease.\textsuperscript{81-83}

**Success Rate of Antidepressants**

Aside from psychotherapy (which will be discussed in the next section) antidepressants are the most commonly used therapy for major depressive disorder. They are widely prescribed and the second-generation antidepressants, particularly the SSRIs, are safe and generally well tolerated and pharmacotherapy is less expensive and more convenient than psychotherapy. However, many patients do not respond to antidepressants; non-compliance with antidepressant therapy is common, and relapses during remission and before recovery
are common features of antidepressant therapy. Continuing antidepressant therapy for a period of time after remission has proven to be successful in preventing relapses. However, poor patient compliance and living for one to two years with antidepressant side effects are significant limitations to this approach.

**Psychotherapy for Major Depressive Disorder**

There are many types of psychotherapy that are available for the treatment of major depressive disorder. Several reviews indicate that no type of psychotherapy is superior in effectiveness. Psychotherapy alone can be an effective treatment, but there is considerable evidence that psychotherapy combined with an antidepressant is superior to either psychotherapy alone or antidepressants alone for treating major depressive disorder. The effectiveness of psychotherapy appears to be associated with the number of sessions per week; more sessions being more effective.

**Generalized Anxiety Disorder**

Generalized anxiety disorder is a common psychiatric condition. Population studies have found a lifetime prevalence of generalized anxiety disorder of 5.0%-5.7%. Generalized anxiety disorder is more common in women and it is a common psychiatric disorder in the elderly.

**Etiology Of Generalized Anxiety Disorder**

The pathogenesis of generalized anxiety disorder is complex and incompletely understood. Risk factors for generalized anxiety disorder are listed in Table 8.
Table 8: Risk Factors for Generalized Anxiety Disorder

<table>
<thead>
<tr>
<th>Depression</th>
</tr>
</thead>
<tbody>
<tr>
<td>Family history of psychiatric disorders</td>
</tr>
<tr>
<td>Financial strain</td>
</tr>
<tr>
<td>Female gender</td>
</tr>
<tr>
<td>Poor parenting</td>
</tr>
<tr>
<td>Negative life events</td>
</tr>
<tr>
<td>Physical ailments/disabilities</td>
</tr>
</tbody>
</table>

- Genetics:
  Twin studies and other genetic research indicate that generalized anxiety disorder is moderately heritable, but the genetic influences have not been clearly identified.\(^{103-106}\)

- Biological:
  There is data and research that suggest that brain function and brain metabolism are significantly different in patients who have generalized anxiety disorder.\(^{107-109}\)

- Environmental:
  Environmental influences are clearly associated with the development of generalized anxiety disorder, \textit{i.e.}, stressful life events, poor parenting, and physical ailments and disabilities.
Learning Break:
People who have generalized anxiety disorder often have personality traits of chronic worry, difficulty recovering from emotional distress, emotional hyperactivity and intensity, hypersensitivity, and hypervigilance.98

The American Psychiatric Association’s diagnostic criteria for generalized anxiety disorder, located in the Diagnostic and Statistical Manual of Mental Disorders, are listed in Table 9.28

Table 9: Diagnostic Criteria for Generalized Anxiety Disorder

1. Excessive anxiety and worry, happening more days than not for at least six months, about activities or events.
2. The individual finds it difficult to control the worry.
3. Anxiety and worry are associated with three (or more) of the following six symptoms and some of the symptoms have been present more days than not for the prior six months. Only one of these is required to be present in children.
   a. Restlessness, feeling keyed up or on edge.
   b. Easily fatigued.
   c. Difficulty concentrating, mind goes blank.
   d. Irritability.
   e. Muscle tension.
   f. Difficulty falling asleep or staying asleep, restless or unsatisfying sleep.
4. The anxiety, worry, or physical symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.
5. The disturbance is not attributable to the physiological effects of a substance (i.e., a drug of abuse, a medication) or another medical condition (i.e., hyperthyroidism).
6. The disturbance is not better explained by another mental disorder (i.e., anxiety or worry about having panic attacks in panic disorder, negative evaluation in social anxiety disorder [social phobia], contamination or other obsessions in obsessive-compulsive disorder, separation from attachment figures in separation anxiety disorder, reminders of traumatic events in posttraumatic stress disorder, gaining weight in anorexia nervosa, physical complaints in somatic symptom disorder, perceived appearance flaws in body dysmorphic disorder, having a serious illness in illness anxiety disorder, or the content of delusional beliefs in schizophrenia or delusional disorder).

**Screening For Generalized Anxiety Disorder**

Patients who have generalized anxiety disorder typically have a wide range of physical and psychiatric complaints. The primary symptoms include anxiety, difficulty concentrating, fatigue, headache, insomnia, and pain. If no medical explanation for the patient’s complaints can be found a screening test for anxiety should be applied.

Screening tools for detecting generalized anxiety disorder include the Beck anxiety inventory, the generalized anxiety disorder-7 or 2 (GAD-7, GAD-2), the hospital anxiety and depression scale (HADS), the Symptoms Driven Diagnostic System-Primary Care (SDDS-PC), and the Prime MD tool. The GAD-7 is free, and it has good sensitivity and specificity, and it can also help identify patients who suffer a disability from the disorder. The specificity and sensitivity of the GAD-7 may be population-specific.
## Table 10: The GAD-7

Over the last 2 weeks, how often have you been bothered by the following problems.

Not at all  Several days  More than half the days  Nearly every day

1. Feeling nervous, anxious or on edge.
2. Not being able to stop or control worrying.
3. Worrying too much about different things.
4. Trouble relaxing.
5. Being so restless that it is hard to sit still.
6. Becoming easily annoyed or irritable.
7. Feeling afraid as if something awful might happen

Scores for the answers are 0, 1, 2, or 3, respectively. If the score is $\geq 8$ then a provisional diagnosis of generalized anxiety disorder can be made.

If you checked off any problems, how difficult have these problems made it for you to do your work, take care of things at home, or get along with other people?

Not difficult at all  Somewhat difficult  Very difficult  Extremely difficult

---

### Clinical Course And Consequences Of Generalized Anxiety Disorder

Generalized anxiety disorder is typically a chronic disease and most patients experience fluctuations in the severity of symptoms.\(^{96,99}\) Complete and lasting remission can occur but the incidence of lasting remission is not high and for many patients who do have remission, some levels of anxiety remain.\(^{99}\) Unfortunately, many patients who have generalized anxiety disorder do not respond to therapy.\(^{99}\) The
consequences of generalized anxiety disorder can be serious. It is associated with significant functional impairment;\textsuperscript{96,112} and, is associated with an increased risk for depression\textsuperscript{96} and cardiovascular disease. It also has been associated with an increased incidence of suicidal ideation and suicide attempts,\textsuperscript{99,113} and has a significant negative effect on a person’s quality of life.

**Treatment For Generalized Anxiety Disorder**

**Pharmacotherapy**

The selective serotonin re-uptake inhibitors (SSRIs) and the serotonin-norepinephrine re-uptake inhibitors (SNRIs) are considered the first-line drugs for the treatment of generalized anxiety disorder.\textsuperscript{114,115} These medications have been shown to be effective and, although there is little evidence, available data suggests that all of the selective serotonin re-uptake inhibitors are comparable in effectiveness for this purpose.\textsuperscript{114} A response is usually seen within four weeks of initiation of therapy. If there has been no response in six to eight weeks then the original medication should be tapered and a new one started.\textsuperscript{114}

Second-line drugs for treating generalized anxiety disorder are the benzodiazepines (*i.e.*, alprazolam, diazepam) and the tricyclic antidepressants (TCAs).\textsuperscript{114} The TCAs and the benzodiazepines have been shown in some reports to be equally effective for treating generalized anxiety disorder.\textsuperscript{116} Concerns for the TCAs were discussed in the section on major depressive disorder, and the benzodiazepines are not without risk, *i.e.*, dependency, overdose, and significant side effects such as drowsiness, tolerance, and withdrawal. However a 2014 study noted that long-term use of benzodiazepines may be safer
than was previously thought, and that using them in combination with an antidepressant and psychotherapy can be very effective.117

**Learning Break:**

Benzodiazepines bind to a specific receptor that is associated with gamma-aminobutyric acid (GABA) receptors. Gamma aminobutyric acid is one of the major inhibitory neurotransmitters and when benzodiazepines bind to benzodiazepine receptors this action increases the activity and duration of GABA, thus causing sedation and anxiolysis.

Other medications that are used to treat generalized anxiety disorder include typical and atypical antipsychotics, buspirone (Buspar), hydroxyzine (Vistaril), mirtazapine (Remeron), and pregabalin (Lyrica).114 There is less clinical experience with these for treating generalized anxiety disorder than with the first-line and second-line medications, but if the first-line and second-line drugs are deemed ineffective then these “third-line” medications can be prescribed. Alternative and complementary medicine, herbal medicines, and exercise have been used to treat generalized anxiety disorder and there are some positive reports about these118 but the clinical experience with their use is sparse.114

**Psychotherapy**

Psychotherapy, alone or in combination with drug therapy, can be an effective treatment for generalized anxiety disorder,99,119 and cognitive behavioral therapy is considered to be one of the most effective forms of psychotherapy for this purpose.99,114,120,121 Cognitive behavioral
therapy has been compared to pharmacotherapy and the two have been found to be equal in effectiveness for this patient population, but the data is limited. Combining cognitive behavioral therapy with an antidepressant or a second-line medication may be helpful but more evidence supporting this approach is needed.

**Summary**

Major depressive disorder and generalized anxiety disorder are very common psychiatric disorders. They are associated with significant co-morbidities, and they can have a profound negative effect on personal health, social and professional life. The etiology of these diseases is not completely understood, but they are to some degree inheritable, they are perhaps precipitated by environmental stressors, and abnormal brain function is either a cause or an effect that contributes to their prolongation.

The preferred treatments for major depressive disorder and generalized anxiety disorder are psychotherapy, pharmacotherapy or a combination of both. Cognitive behavioral therapy is the most commonly used psychotherapy for generalized anxiety disorder, and selective serotonin re-uptake inhibitors are the first-line medications for both of these disorders. Major depressive disorder and generalized anxiety disorder are curable, but the rate of complete and lasting remission for both is low.

Please take time to help the NURSECE4LESS.COM course planners evaluate nursing knowledge needs met following completion of this course by completing the self-assessment Knowledge Questions after reading the article. Correct Answers, page 34.
1. **Risk factors for major depressive disorder include:**
   a. Chronic disease and substance abuse.
   b. Smoking and obesity.
   c. Male gender and high socioeconomic status.
   d. High level of education and age > 65.

2. **People who have major depressive disorder are:**
   a. Depressed only during stressful life events.
   b. Depressed once or twice a week.
   c. Depressed almost every day.
   d. Depressed only during episodes of substance abuse.

3. **Screening for depression should be done:**
   a. If the patient has noticeable signs and symptoms.
   b. For every patient ≥ age 18 if there is appropriate clinical support.
   c. Only during stressful life events.
   d. Only for patients who request screening.

4. **First-line medications used to treat major depressive disorder would be:**
   a. Diazepam and imipramine.
   b. Bupropion and phenelzine.
   c. Amoxapine and trazodone.
   d. Citalopram and fluoxetine.

5. **True or false: ECT is effective for treating major depressive disorder.**
   a. True.
   b. False.
6. **Risk factors for generalized anxiety disorder include:**
   a. Male gender and age > 16.
   b. Depression and female gender.
   c. Age > 65 and substance abuse.
   d. Stressful life events and smoking.

7. **Generalized anxiety disorder is a disease that:**
   a. Is typically brief in duration and responds easily to treatment.
   b. Is typically chronic in nature but is almost always curable.
   c. Is typically chronic in nature and the severity fluctuates over time.
   d. Is typically responsive only to psychotherapy.

8. **First-line medication to treat generalized anxiety disorder are:**
   a. Benzodiazepines.
   b. Atypical antipsychotics.
   c. MAOIs.
   d. Selective serotonin reuptake inhibitors.

9. **A common treatment for generalized anxiety disorder is:**
   b. Group therapy.
   c. Psychoanalysis.
   d. Behavioral therapy.

10. **Generalized anxiety disorder is typically:**
    a. brief in duration and responds easily to treatment.
    b. chronic and often does not respond to treatment.
    c. characterized by rapid, progressive worsening.
    d. is typically characterized by rapid, progressive improvement.
Correct Answers:

| 1. a | 2. c | 3. b | 4. d | 5. a |
| 6. b | 7. c | 8. d | 9. a | 10. b |

**REFERENCE SECTION**

The reference section of in-text citations include published works intended as helpful material for further reading. Unpublished works and personal communications are not included in this section, although may appear within the study text.


17. Dunlop BW, Nemeroff CB. The role of dopamine in the pathophysiology of depression. *Arch Gen Psychiatry.* 2007; 64: 327-337


23. Harkness, KL, Tabari N, Monroe, SM, Slavich, GM, Gotlib IH,


36. Gilbody S, Richards D, Brealey S, Hewitt C. Screening for depression in medical settings with the Patient Health...


46. Ghio L, Gotelli S, Marcenaro M, Amore M, Natta W. Duration of untreated illness and outcomes in unipolar depression: a


68. Epstein I, Szpindel I, Katzman MA. Pharmacological approaches to manage persistent symptoms of major depressive disorder:


88. Cuijpers P, Karyotaki E, Weitz E, Andersson G, Hollon SD, van Straten A. The effects of psychotherapies for major depression in


106. Kendler KS, Neale MC, Kessler RC, Heath AC, Eaves LJ. Major depression and generalized anxiety disorder. Same genes,


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