

Understanding and Managing Major Depressive Disorder

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Purpose

The purpose of this course on major depressive disorder (MDD) is to educate healthcare professionals on the symptoms, treatment, and management of MDD. The course contains useful information on vulnerable population groups and treatment options for application to individual nursing care plans.

Learning Objectives

After successful completion of this course, you will be able to:

1. Name two symptoms of MDD that are not typical reactions to stress.
2. List at least three risk factors for developing MDD.
3. Explain the consequences of untreated MDD.
4. Identify at least two medications used to treat depression.
5. Discuss the effectiveness of therapies for MDD.

Introduction

Major depressive disorder (MDD) is the most serious form of depression.

Depression can range from the “blues” to a major psychiatric diagnosis. It is only in the last 10 years or so that MDD has lost some of its stigma. We realize now that MDD is often caused by a neuro-endocrine problem, and is not a “weakness” of an individual’s personality.

Clarification of Terms

According to the American Psychological Association (APA, 2013), Mood Disorders are divided into the Depressive Disorders (“unipolar depression”), the Bipolar Disorders, and two disorders based on etiology:

1. Mood Disorder Due to a General Medical Condition
2. Substance-Induced Mood Disorder

The Depressive Disorders include Major Depressive Disorder, Dysthymic Disorder, and Depressive Disorder Not Otherwise Specified, which are differentiated from the Bipolar Disorders by the patient not having a history of a Manic, Mixed, or Hypomanic Episode.

Depression: A state of sadness.

Depressive disorders: Mood disorders characterized by prolonged or recurring symptoms of psychological depression without manic episodes.

Types:

Dysthymia: A chronic mild depression.

Major Depressive Disorder: Depression of sufficient severity to require treatment.

Other names include:

- Major Depression
- Clinical Depression

Bipolar disorder: A mood disorder characterized by alternating episodes of depression with mania or mild non-psychotic excitement.

Other names include:

Manic-Depression

Bipolar Affective Disorder

(APA, 2013)

Statistics

The most likely mental health problem you will encounter in primary healthcare patients is a major depressive disorder (MDD), previously known as a unipolar depression.

Major depressive disorder is the leading cause of disability in the United States for people ages 15 to 44. Projections are that by 2020, depression will be second only to heart disease in its contribution to the global burden of disease (Centers for Disease Control and Prevention [CDC], 2010).

MDD affects about 9% of the U.S. population ages 18 and older (approximately 17.1 million) in a given year (CDC, 2010). In 2012, approximately 16 million adults aged 18 or older in the U.S. had at least one major depressive episode in the past year, representing 6.9% of all U.S. adults (National Institute of Mental Health [NIMH], n.d. b).

Hardest hit are women, non-Hispanic whites, with the average age of onset at 32 years (NIMH, n.d. a).

Women are affected more often than men. Recent statistics estimate that women are 70% more likely to experience MDD at least once in their lives compared to men. (NIMH, n.d. a).

Childhood and Adolescence Statistics

Major depressive disorder occurs in every age group but case numbers peak during adolescence.

Major depressive disorder affects approximately 8.5% of youth, with an incidence in children estimated at 2.8% and increasing up to 5.7% in adolescents. Major depressive disorder is related to significant morbidity and mortality. This may be associated with impairment in school performance, poor interpersonal relationships, early pregnancy in teenage girls, increases the incidence of physical illness, substance abuse, and the risk of suicide. Accurate screening is therefore essential when the child or adolescent patient with suspected depression presents (Cincinnati Children's Hospital Medical Center, 2010).

In addition, research indicates that depression onset is occurring earlier in life today than in past decades. A recently published longitudinal prospective study found that early-onset depression often persists, recurs, and continues into adulthood, and indicates that depression in youth may also predict more severe illness in adult life. Depression in young people often co-occurs with other mental disorders, most commonly anxiety, disruptive behavior, or substance abuse disorders and with physical illnesses, such as diabetes (Giardino & Benton, 2014).

Etiology of MDD

According to the National Institute of Mental Health (NIMH), depression is caused by a combination of biological, genetic, psychological, and environmental factors.

Depressive illnesses are disorders of the brain. There are longstanding theories about depression; which suggest important neurotransmitters are out of balance in depression. These theories have not yet been proven. (NIMH, n.d. a).

Technological brain-imaging, such as magnetic resonance imaging (MRI), have revealed that the brains of individuals with depression look different than those of people without depression. The portions of the brain involved in mood, sleep, appetite, thinking, and behavior appear different. But these images do not indicate the cause of depression, and cannot be used in diagnosis.

Some types of depression are familial, although this is not exclusive. Potential genetic links are currently being researched, and indicate a risk for depression with several genes acting along with environmental or other factors. In addition, trauma, loss of a loved one, a difficult relationship, or any stressful situation may trigger a depressive episode. Depression may occur with or without a known trigger (NIMH, n.d. a).

Test Yourself

True or false: Causes of depression have been well-proven through research.

Answer: False. Although there have been long-standing theories of causes, it has been difficult to prove (NIMH, n.d. a).

Neurotransmitters

Many of the theories surrounding MDD include an imbalance of neurotransmitters in the brain. Neurons in the brain require communication between each other, which occurs by signals that activate chemical messengers, or neurotransmitters. The release of a neurotransmitter from one neuron can activate or inhibit a second neuron. If the signal is excitatory, the message continues to pass farther along. If it is inhibitory, the signal will be suppressed.

The neurotransmitter also affects the neuron that released it. Once the first neuron has released a certain amount of the chemical, a feedback mechanism instructs the neuron to stop pumping out the neurotransmitter and start bringing it back into the cell (Scanlon, 2011).

For more information about the anatomy and physiology of the brain, check out *RN.com's Assessment Series: Neurological Anatomy and Physiology*

Neurotransmitters and MDD

With MDD receptors may not be able to sense a specific neurotransmitter appropriately; which can cause an excessive or inadequate response. Reuptake may also be imbalanced, usually causing an inappropriate increase in reuptake of the neurotransmitter before they bind to the receptors on other neurons. Any of these system faults could significantly affect mood (Tesar, 2015).

Some of the main neurotransmitters which may be affected with MDD include:

- Acetylcholine: affects memory, learning, and recall
- Serotonin: influences sleep, appetite, mood and pain
- Norepinephrine: affects blood vessel constriction, and may affect anxiety, motivation and reward
- Dopamine: has an effect on movement, motivation, and perception of reality

Medical Illness and MDD

Medical disease or illness can present with depressive symptoms, or be linked with actual MDD. Biological conditions associated with MDD include:

- Neurological: Cerebral vascular accident, impaired cerebral blood flow

- Cardiac: Myocardial infarction, congestive heart failure
- Endocrine: Cushing's disease, Addison's disease, hypothyroidism, diabetes
- Hematologic: anemia, lymphoma, leukemia
- Infection: Human immunodeficiency virus, mononucleosis
- Cancer: Particularly with malignancy
- Pregnancy

(Mental Health in Multicultural Australia [MHIMA], 2011)

Medications and MDD

Of the many medications that predispose to depression, some that you may encounter more commonly are beta blockers, Reserpine, methyldopa, antihistamines, digoxin, levodopa, NSAIDs, oral contraceptives, corticosteroids, anabolic steroids, chemotherapy medications, anticonvulsants, alcohol, benzodiazepines, barbiturates, narcotics, opiates, marijuana, and amphetamine and/or cocaine withdrawal (MHIMA, 2011).

Signs and Symptoms of MDD

Although depression is usually associated with sleep disturbances, changes in appetite and weight, difficulty concentrating, fatigue, irritability, agitation or involuntary movements, sad thoughts and feelings, these symptoms are also typical during stress or bereavement.

What sets MDD apart is the additional experience of anhedonia (inability to experience pleasure), hopelessness, suicidal thinking, feelings of worthlessness, and inappropriate guilt.

Unfortunately, depressed people do not usually complain of despair. External cues such as unexplained somatic complaints, behavior problems and functional incapacity may speak for your patient instead. Sometimes an accurate diagnosis can only be made with the help of multiple informants.

A composite picture of a child's behavioral symptoms might come from parents, teachers, and coaches. Similarly, an evaluation of depression in an elderly patient cannot be made without input from people knowledgeable about the patient's lifetime personality (APA, 2013; NIMH, n.d. a)

Comparison of Common Symptoms of MDD

Children/Adolescents	Elderly
Excessive sleeping	Insomnia, early a.m. rising
Change in friends, social isolation, irritability	Noticeable unhappiness, noticeable discomfort
Behavior + temper problems	Disagreeable mood
Prominent anxiety	Foggy thinking
Physical complaints	Physical complaints
Boredom	Apathy
Alcohol + substance abuse	Involuntary movements
Greater likelihood of auditory hallucinations, if psychotic features occur	Greater likelihood of delusions, if psychotic features occur

American Psychiatric Association [APA], 2013; NIMH, 2012

Interactive Activity

Match the symptoms of depression with the correct age group:

- | | |
|----------------------|-----------------------|
| Elderly | A. Excessive sleeping |
| Elderly | B. Insomnia |
| Children/Adolescents | C. Substance abuse |
| Children/Adolescents | D. Apathy |

Answers: *Elderly= B, D; Children/Adolescents= A, C*

Risk Factors: Familial and Traumatic

A family history of depression is linked to MDD. People with this risk factor have a greater likelihood of MDD onset occurring in childhood rather than in adolescence. The risk for developing MDD when there is a family history is two to four times that of those without a family history (NIMH, n.d. a).

Childhood trauma is also a risk factor for MDD. Your patients are apt to have a history of maltreatment, neglect, or deprivation. These circumstances predispose people to a life pattern of having increased reaction to stressors.

Risk Factors: Gender

As noted earlier, females are highly represented in MDD statistics. Some reasons for this are biological. Females may experience emotional stressors more intensely than males, due to differences in the endocrine system. Postpartum depression affects 5% to 20% of women within six months of giving birth. Although there is an increased risk of depression during menopausal changes, there is a decreased incidence in post-menopausal women (NIMH, n.d. a).

Hypothyroidism, a medically correctable cause of depression, is more prevalent in females also (NIMH, n.d. a).

Test Yourself

True or false: The risk for depression increases following menopause.

Answer: False. Although there is an increased risk of depression during menopausal changes, there is a decreased incidence in post-menopausal women (NIMH, n.d. a).

Risk Factors: Stress

Another reason females experience MDD more often than males has to do with psychosocial factors. Females tend to have a different coping mechanism than males, and respond to events in a manner that may predispose them to depression. Traumatic or stressful events, additional personal and professional responsibilities, and other situations that cause stress produce very different reactions in women. Research has demonstrated that women can react in a manner that actually prolongs feelings of stress, which can increase the risk of depression (NIMH, n.d. a).

Risk Factors: Relationship Stress

Circumstances come into play to increase the risk of MDD at any time across the life span. Relationship stress is a major contributor to depression. It can be experienced in the form of ambivalence, abuse, rejection, or dependence within a family or work environment. The death of a loved one is naturally followed by grief, but a quarter of the time the survivor's symptoms are extreme enough to meet the diagnostic criteria for MDD, even several months after the death (NIMH, n.d. a).

Risk Factors: The Elderly

The elderly are at greater risk of developing MDD for several reasons:

- Physical illness and inadequate social support are powerful predictors of MDD in this vulnerable group. Social isolation increases because of inevitable losses of significant others and functional declines associated with aging (Skoog, 2011).
- Cardiovascular disease, stroke, cancer, chronic lung disease, arthritis, Alzheimer's disease, persistent insomnia, and Parkinson's disease are common conditions in the elderly (Skoog, 2011). Degenerative changes in the brain associated with aging make less norepinephrine and dopamine available too, providing an organic basis for depressive symptoms (Skoog, 2011).

Risk Factors: Substance Abuse and Personality

Substance abuse is frequently cited as a risk factor for MDD. In studies of adolescents with coexisting mental illness and substance abuse the mental disorder is present prior to the substance abuse disorder in a high number of cases. This does not mean that substance abuse does not cause depression. Using alcohol and drugs can cause brain damage that meets the criteria for depression (NIMH, n.d. a).

Certain personality traits that disable people from coping well with stress are also considered a risk factor for MDD. Some people have a distorted interpretation of stress that signals threat or entrapment instead of loss or adversity. They develop a learned helplessness and/or provoke further adversity by their reaction. A personality disorder may form that constitutes an ineffective attempt to defuse the stressful situation (NIMH, n.d. a).

Differential Diagnosis

Research suggests that depression frequently goes unrecognized. You may encounter patients who put up their own barriers to addressing depression as they believe they can treat the depression themselves, or they deny the need for intervention.

Time restrictions may not allow you the routine screening of every patient. However, clues to depression may come from persons who accompany the patient and volunteer information. You can test your suspicions with a screening instrument as a first step. A simple two-question tool, the Patient Health Questionnaire (PHQ-2) includes asking the patient if over the past two weeks he or she has:

- *"Felt down, depressed, or hopeless?"*
- *"Felt little interest or pleasure in doing things?"*

(Institute for Clinical Systems Improvement, 2013, p. 3)

If the answer is yes to either question, follow-up is necessary, including administering a more detailed depression instrument.

Diagnostic Criteria for MDD

Diagnostic criteria from the American Psychological Association (APA) Diagnostic and Statistical Manual of Mental Disorders (DSM-V) include:

- Symptoms that are new, a change from past functioning.
- Symptoms that cause clinically significant distress and impairment in the person's life.
- Symptoms not explained by a general medical condition, a psychosis, substance use, side effects of medications, or recent bereavement following the loss of a loved one.
- Symptoms that do not meet the criteria for a mixed episode (bipolar disorder).
- The presence of five of the following nine symptoms almost every day for at least two weeks. One of the symptoms must be loss of interest or depressed mood:
 - Depressed mood
 - Significantly diminished pleasure and interest in most activities
 - Weight loss or gain (over 5%), or increased or decreased appetite
 - Insomnia or hypersomnia
 - Psychomotor agitation or retardation
 - Fatigue or loss of energy
 - Feelings of worthlessness or inappropriate guilt
 - Difficulty thinking or concentrating, or indecisiveness
 - Recurrent thoughts of death or suicide

(APA, 2013)

Test Yourself

Which of the following is a quick tool to assess for potential depressive symptoms.

- A. PHQ-2
- B. DSM-V
- C. MMPI

Differential Diagnosis in Children and Adolescents

The diagnostic criteria of major depressive disorder in children and adolescents are the same as they are for adults. However, recognition of the disorder is more difficult in youth as symptoms vary according to the developmental stage of the youngster.

In addition, children and youths may have difficulty in properly identifying and describing their internal emotional or mood states.

Signs that may be associated with depression in children and adolescents:

- Frequent vague, non-specific physical complaints such as headaches, muscle aches, stomachaches or tiredness.
- Frequent absences from school, poor performance in school, and talk of or efforts to run away from home.
- Outbursts of shouting, complaining, unexplained irritability, or crying or increased irritability, anger or hostility, and reckless behavior in older adolescents.
- Lack of interest in playing with friends, leading to social isolation and poor communication.
- Alcohol or substance abuse.
- Extreme sensitivity to rejection or failure and fear of death.

(Cincinnati Children's Hospital Medical Center, 2010)

Differential Diagnosis in the Elderly

When MDD is diagnosed for the first time in an elderly person, the likelihood of coexisting illness is high. Depression amplifies pre-existing physical symptoms, so a diagnosis of depression is often secondary to a diagnosis of a somatic disorder. When the degree of disability does not match the expectation for a medical illness, comorbid depression can be a factor.

It may not be easy to distinguish between normal aging, dementia and depression, especially if a patient is known for a long period of time. Many individuals over age 85 have some form of dementia; Alzheimer's disease being the most common form seen. Major depressive disorder alone causes cognitive impairment that can mimic dementia, confusing the picture further (Skoog, 2011).

Diagnosis in the Elderly: Sorting Out Three Different Conditions

Normal Aging	MDD	Dementia
Forgets names of acquaintances	Slower thinking	Forgets names of family
Forgets where things were put	Reports difficulty in thinking, but still able to think well	Forgets where they live

Slow recall of new information		Denies problems with thinking
Problems with nonverbal memory, perception of spatial relationships, abstract reasoning		Unlikely to express depression
		Agitation, tearfulness

Depressive symptoms that do not meet the diagnostic criteria for MDD can be present in the elderly. This “minor depression” is not yet recognized as a standardized disorder but is just as disabling as MDD. Symptoms of this milder depression deprive the elderly of an enjoyable quality of life and lead them to frequent healthcare utilization (Skoog, 2011).

Psychiatric Disorders and MDD

Psychiatric disorders other than MDD may complicate your patient’s situation. Many patients that have MDD beginning before adulthood have an additional mental disorder. Bipolar disorder frequently begins with a depressive episode but time reveals a set of symptoms that do not match the criteria for MDD. Differentiating between unipolar (MDD) and bipolar disorder is crucial because antidepressants given to a bipolar patient may trigger a manic phase associated with an increased risk of suicide. Mood swings in reaction to stressful events that last no longer than two weeks do not meet the criteria for MDD (APA, 2013).

Common Psychiatric Co-Morbidities

Common psychiatric comorbidities with MDD are dysthymia (chronically mild depressive state), anxiety, antisocial behavior, and substance abuse and/or addiction. Anxiety usually coexists with MDD and has similar physiological consequences associated with a long-term stress response. Dysthymia is a chronic depression with its own DSM-V diagnostic criteria. It lasts longer than a year in children and at least two years in adults, with an average duration period of four years. A high percentage of children diagnosed with dysthymia experience their first episode of MDD within five years (Giardino & Benton, 2014). This is called “double depression.”

Differential Diagnosis of Major Depression

Type	Specific Cause
Drugs	Corticosteroids, contraceptives, reserpine, alphas-methyl-dopa, anticholinesterases, insecticides, cimetidine, ranitidine, indomethacin, phenothiazine, thallium, mercury, cyclosporine, vincristine, vinblastine, disulfiram, metoclopramide, interferon, H ₂ Blockers (cimetidine, famotidine, ranitidine)
Drug withdrawal	Amphetamine, cocaine
Infection	Tertiary syphilis, influenza, AIDS, viral pneumonia, viral hepatitis, infectious mononucleosis, TB
Endocrine	Hypothyroidism, apathetic hyperthyroidism, diabetes, hyperparathyroidism, late luteal phase dysphoria, Cushing's disease and syndrome, adrenal insufficiency
Collagen	SLE, rheumatoid arthritis, fibromyalgia, polymyalgia rheumatica
Neurologic	MS, Parkinson's disease, head trauma (post concussive syndrome), complex partial seizures, CNS tumors, stroke, early dementia, sleep apnea, frontal lobe syndrome, Huntington's disease
Nutritional	Vitamin deficiencies (B ¹² , C, folate, niacin, thiamine)
Neoplastic	Pancreatic cancer, disseminated carcinomatosis
Psychiatric	Bereavement, adjustment disorder with depressed mood, bipolar disorder, generalized anxiety disorder, somatization disorder, post-traumatic stress disorder
Organic mental disorders	Delirium (acute confusional state), subcortical dementias, neuroleptic-induced Parkinsonism

(Tesar, 2015)

Interactive Activity: Assessing for MDD

The following brief video is a vignette showing how to assess a patient for depression. It can be viewed at <https://www.youtube.com/watch?v=Gm3FLGxb2ZU>

Treatment Options

The goal of treatment for MDD is a remission of the current episode that lasts for at least four to six months (Tesar, 2015). It is estimated that one out of three patients achieve this goal (Gaynes, Lux, & Gartlehner, 2012). However, clinicians generally look for a 50% response to treatment, rather than a total remission of symptoms. Residual symptoms linger in 30% to 45% of patients even after there is improvement in reducing the number, frequency, and intensity of symptoms. These residual symptoms increase the risk of relapse. An estimated 75% will have another episode within ten months (Gaynes, Lux, & Gartlehner, 2012).

Treatment programs usually consist of three stages to more effectively manage the residual symptoms of MDD and ensure long-term management of MDD (Tesar, 2015).

Interactive Activity: Screening Tools

A treatment response is measured by a self-reporting screening tool that takes the patient about two to five minutes to complete. Some of the more commonly used tools are:

- The Beck Depression Inventory (an example can be found at http://nyulangone.org/files/BDIForm_for_New_Patients.pdf)
- The Zung Self-Rating Depression Scale (an example can be found at <http://healthnet.umassmed.edu/mhealth/ZungSelfRatedDepressionScale.pdf>)
- The Center for Epidemiological Studies Depression Scale (an example can be found at http://www.valueoptions.com/providers/Education_Center/Provider_Tools/Depression_Screening.pdf)
- The Children’s Depression Inventory (for ages 7-17) (an example can be found at <http://www.psych.uic.edu/csp/images/stories/physicians/rating%20scales/CES-DC.pdf>)
- Patient Health Questionnaire-9 (an example can be found at <http://www.integration.samhsa.gov/images/res/PHQ%20-%20Questions.pdf>)

Treatment Stages

	Acute Stage	Continuation	Maintenance
Length	4-8 weeks	6+ months	Years
Program	<ul style="list-style-type: none"> • Weekly or biweekly monitoring for pharmacotherapy. • 6-20 weeks of pharmacotherapy. 	Monthly or bimonthly monitoring.	<ul style="list-style-type: none"> • Monthly or quarterly monitoring. • Pharmacotherapy required for history of three or more episodes.
Response	<ul style="list-style-type: none"> • Hospitalization required in 5-10%. • Outpatient response 50-80%. • Combination of psychotherapy and medications is not more effective than one treatment alone, except for severe or recurrent MDD. 	Cuts relapse almost by half	

(Tesar, 2015)

Patients Who Require Special Consideration

There are groups of patients who require special consideration:

- Older adults take longer to show a treatment response and are usually taking many different prescription medicines concurrently. Thus, physicians are often reluctant to add another medication that may increase the risk of drug-drug interactions.
- People with personality disorders are prone to MDD but do not respond to antidepressant medication as well as other patients. They have more residual symptoms that foster social impairment.
- Patients with substance abuse disorders have poorer prognoses than others with MDD and are more likely to require hospitalization. Detoxification is usually complete prior to starting an antidepressant medication because of the danger of substance-drug interactions. The diagnostic procedure for patients with a co-existing mental disorder and a substance abuse disorder (called a dual diagnosis) is complex and time-consuming. You will need to refer these patients to a mental health or substance abuse specialist.
- Women of childbearing age who have MDD need to weigh the risks of becoming pregnant while taking medication. Birth defects are the major concern associated with medication, although miscarriage and developmental problems are also risks.
- Children and adolescents require special consideration for treatment options.

(Cincinnati Children's Hospital Medical Center, 2010; Skoog, 2011; NIMH, n.d. a).

Test Yourself

Which group of patients are more likely to require hospitalization?

- A. Older adults
- B. Patients with personality disorders
- C. Patients with substance abuse disorders**

Medication and MDD

The use of antidepressants offers hope for those with MDD. The abnormal brain chemistry noted in MDD may be reversed by antidepressants (Tesar, 2015).

Studies show that patients who remain on antidepressant medication for the number of months recommended by their physicians (usually at least six months up to a year) increase the levels of specific proteins needed for nerve cell regeneration.

Medication Classes and MDD

Existing antidepressants are known to influence the functioning of certain neurotransmitters in the brain. The newer medications, chiefly the selective serotonin reuptake inhibitors (SSRIs), are generally preferred over the older medications, including tricyclic antidepressants (TCAs) and monoamine oxidase inhibitors (MAOIs), because they have fewer and less severe potential side effects.

Norepinephrine and dopamine reuptake inhibitors (NDRIs), norepinephrine-serotonin reuptake inhibitors (NSRIs), and other newer medications have similar effects as SSRIs, with favorable side effects. All generations of medications are effective in relieving depression, although some people will respond to one type of drug, but not another (Tesar, 2015; McEvoy, 2011).

Mechanism of Action of SSRIs

SSRIs are believed to treat depression by slowing down the reuptake of serotonin by pre-synaptic neurons. Serotonin molecules thus remain in the synapse longer than they normally would, and have more time to activate the post-synaptic neuron. There are several types of serotonin receptors, and some medications work on specific receptors better than others (Tesar, 2015).

Response to Medications

There is no way to predict individual responses to antidepressant medication in general or to any one agent in particular. Experimental trial and error is needed, with a favorable response in roughly 50% and remission in nearly 30% of patients with a single therapeutic medication trial. If the first agent is ineffective, the diagnosis should be reviewed for accuracy and if confirmed, another antidepressant should be tried. At least one alternative medication within the same class should be tried before switching to an agent from a different class (Tesar, 2015).

It is important to know that it could take as many as six to eight weeks for the full therapeutic effect to occur. All patients being treated with antidepressants should be monitored appropriately and observed closely for worsening depression symptoms, suicidal thoughts or behavior, and unusual changes in behavior, especially during the first few months of treatment, or when the dose is increased or decreased.

Medications and MDD

Antidepressant drugs increased the risk of suicidal thinking and behavior in studies of children, adolescents, and young adults (ages 18-24) with major depressive disorder (MDD) and other psychiatric disorders. No increased risk has been shown for adults over age 24, and the risk decreased for those aged 65 and older (Tesar, 2015).

Common medications for MDD are Prozac® (fluoxetine), Zoloft® (sertraline), Celexa® (citalopram), Paxil® (paroxetine), Effexor® (venlafaxine), Wellbutrin® (bupropion), and Luvox® (fluvoxamine). There is no single best medication, and selection should be based on the patient's treatment history, potential drug interactions, and preferred side-effect profile (Tesar, 2015). See antidepressant side effects described later.

Other medications, such as the atypical antipsychotic drugs aripiprazole (Abilify®) and quetiapine fumarate (Seroquel®) are now used as add-on treatments for major depression. These adjunctive treatments can increase effectiveness of MDD medications (Tesar, 2015).

Prozac®

Fluoxetine (Prozac®) is used for the treatment of major depressive disorder, and should not be used in combination with monoamine oxidase inhibitors (MAOIs) or thioridazine (used to treat psychotic disorders, severe depression or anxiety or severe behavior problems in children). In addition, care should be exercised when Prozac® is used in combination with NSAIDs as this increases the risk of bleeding. Side effects of Prozac® include chest pain, chills, hemorrhage, hypertension, increased appetite, nausea and vomiting. There is also a risk of developing Serotonin Syndrome (McEvoy, 2011).

Zoloft®

As with Prozac®, sertraline (Zoloft®) should not be used with MAOIs or thioridazine. In addition, people taking Zoloft® should not take pimozide (Orap), a medication used for the treatment of Tourette's disorder. Zoloft® may also affect a person's lithium levels (used for the treatment of bipolar disorder), so close monitoring may be necessary. Side effects of Zoloft® may include impotence, heart palpitations, chest pain, hypertonia (increased muscle tightness), increased appetite, back pain, myalgia (muscle pain), yawning, male and female sexual dysfunction, rhinitis, and tinnitus. As with Prozac®, there is also a risk of Serotonin Syndrome when taking Zoloft® (McEvoy, 2011).

Celexa®

Celexa® (citalopram) should not be used with MAOIs or pimozide (Orap). Celexa should not be used with patients who have a prolonged QT complex, as it can cause lethal arrhythmias, including ventricular tachycardia. Celexa® should be used with caution with warfarin or NSAIDs, as there is an increased risk of bleeding. Side effects of Celexa® may include increased suicidal thoughts, ECG changes, impotence, nausea and vomiting, diarrhea, dry mouth, male and female sexual dysfunction, yawning, and respiratory infection. There is also a risk of Serotonin Syndrome when taking Celexa® (McEvoy, 2011).

Paxil®

Paxil® (paroxetine) should not be used with MAOIs, pimozide, or thioridazine. Side effects of Paxil® may include increased suicidal thoughts, anxiety, anorexia, nausea and vomiting, constipation, shaking, dry mouth, male and female sexual dysfunction, yawning, and infection. There is also a risk of Serotonin Syndrome when taking Paxil® (McEvoy, 2011).

Effexor®

Effexor® (venlafaxine) should not be used with MAOIs. It should be used with caution with warfarin or NSAIDs, as there is an increased risk of bleeding. Side effects of Effexor® (may include sleepiness or insomnia, constipation, nausea and vomiting, dry mouth, male and female sexual dysfunction, anorexia, and weakness (McEvoy, 2011).

Wellbutrin®

Wellbutrin® (bupropion) should not be used with MAOIs. It should not be used with patients who have a seizure disorder, as it may increase the risk of seizures. Wellbutrin® should be used with caution with dopaminergic agent (such as levodopa), as it can increase the risk of CNS toxicity. Side effects of Wellbutrin® may include hypertension, suicidal thoughts, tachycardia, agitation, myalgia, constipation, nausea and vomiting, dry mouth, male and female sexual dysfunction, and anorexia (McEvoy, 2011).

Luvox®

Luvox® (fluvoxamine) should not be used with MAOIs, pimozide, or thioridazine. It should be used with caution with warfarin or NSAIDs, as there is an increased risk of bleeding. Side effects of Luvox® may include increased suicidal thoughts, sleepiness, weakness, anorexia, nausea and vomiting, shaking, dry mouth, male and female sexual dysfunction, and increased urination. There is also a risk of Serotonin Syndrome when taking Luvox® (McEvoy, 2011).

Test Yourself

It can take _____ weeks for full therapeutic effects of medications for treatment of MDD.

- A. One-Two
- B. Four -Six
- C. Six-Eight**

Side Effects of Medications

Side effects associated with these antidepressants are common, but generally resolved as tolerance develops. The most typical side effects your patients starting on antidepressants will report are:

- Fatigue, weakness
- Nervousness, trembling
- Upset stomach, constipation, or diarrhea
- Appetite and weight changes
- Headache, drowsiness, dizziness
- Dry mouth, sweating, excessive thirst
- Nightmares, insomnia
- Sexual dysfunction
- Increased skin sensitivity to sunlight

(Tesar, 2015; McEvoy, 2011)

More information on antidepressant drug side effects can be found here:

<http://www.clevelandclinicmeded.com/medicalpubs/diseasemanagement/psychiatry-psychology/recognition-treatment-of-depression/table4.htm>

Serotonin Syndrome

Serotonin Syndrome is a potential adverse reaction in depressed patients on MAOI drugs. This is a crisis in which headache, hypertension, and cardiac arrhythmias occur, and may be suddenly brought on by drug-drug or food-drug interactions.

To avoid this syndrome, antidepressants should not be started within 14 days after taking MAOIs, and foods containing high amounts of tyramine are also to be avoided. These include some cheeses, beer, wine, chocolate, and pickled herring (McEvoy, 2011).

Use of Antidepressants in Youth

The use of antidepressants in children and adolescents is under scrutiny by the Food and Drug Administration (FDA). Research on how adults' prescription medications affect youth lags years behind prevalent clinical usage. In January 2008, the FDA began requiring drug companies to monitor suicide warning signs in clinical trials for experimental drugs, since it has been proven that many different drugs can have psychiatric side effects in children and adolescents.

Clinical trials that must add a suicide assessment to their studies include those for drugs combating epilepsy, incontinence, obesity, and smoking, in addition to depression. Most of these drugs were not previously thought to affect the brain (McEvoy, 2011).

Caution in Prescribing

In March 2009, the FDA approval of Lexapro came after new clinical trials, though not all showed success. The FDA reasoned that the drug's effectiveness can be "extrapolated" from adult data.

More caution needs to be exercised in prescribing antidepressants to the general population, and to youths in particular. The National Institute of Mental Health recommends involvement of a mental health specialist in dealing with children and adolescents' depression (Tesar, 2015).

Psychotherapy

Psychotherapy is a proven treatment for MDD whether alone or in combination with medication. If MDD is mild to moderate, psychotherapy is just as effective as antidepressant medication, but when MDD is severe or recurrent, a combination approach is best (ICSI, 2013).

Among the psychotherapies, cognitive behavior therapy (CBT), interpersonal therapy (IPT), short-term psychodynamic psychotherapy (STPP), and problem-solving treatment (PST) are effective for MDD. In mild to moderate depression, psychotherapy can be equally as effective as medication. With severe depression, antidepressants may be necessary. There is documentation to support lower relapse rates and outcomes among patients receiving psychotherapy. A therapy program usually lasts for at least two to three months. Distorted thought patterns that affect your patient's viewpoint on life are addressed in CBT. This approach also encourages new and different behaviors to establish new habits. Social isolation that contributes to depression is addressed in IPT. This approach enhances social skills. With the elderly, guided reflection on life experiences from the past may be used. With children, self-control may be taught. With adolescents and adults, coping skills are emphasized (ICSI, 2013).

Types of Therapy

Cognitive behavior therapy (CBT) is based on a model or theory that it's not actual events that upset us, but the meanings we give them. Cognitive behavioral therapy involves structured sessions, based on goal setting for specific problems. The patient is given "homework" to determine the problems that they want to work on, and are viewed as partners in structuring the therapy. CBT assists in problem solving, developing coping strategies, forming new relationships, and changing beliefs or behaviors (National Alliance on Mental Illness [NAMI], 2012).

Interpersonal therapy (ITP) is a short-term, limited-focus therapy for MDD which addresses interpersonal issues. It has been demonstrated as effective for children, adolescents, and adults. The theory is that MDD affects relationships by occurring within an interpersonal context, by emphasizing how symptoms are associated with an individual's relationships. The therapist focuses on recognizable problems in how an individual interacts with others (or not). By addressing these problems, the patient realizes a benefit in his or her experience of symptoms (ICSI, 2013).

Short-term psychodynamic psychotherapy (STPP) focuses on unconscious processes with behavior, and in gaining insight. There is a goal of understanding past influences on present behavior, and is based on Freudian principles. In its short-term form, the approach assists the patient to examine unresolved conflicts and symptoms that arise from previous dysfunctional relationships (ICSI, 2013).

Problem solving therapy (PST) advanced from delivering psychotherapy by teaching patients psychosocial skills, which involves teaching an individual how to use a step-by-step process to solve life problems. The usual course involves two main points of employing a problem-solving orientation to life and utilizing rational problem-solving skills. Patients are taught to view problems as challenges that can be solved, which requires time and effort (ICSI, 2013).

Alternative Treatment Options

Alternative approaches to managing MDD are plentiful and creative. They include religious, artistic, culturally-based, nutritional and technologically innovative techniques.

Light Therapy

Light therapy for half an hour daily is effectively useful for seasonal affective depression (SAD) that occurs in the darker months of the year (Tesar, 2015). There is also evidence to support the use of bright light therapy for other types of depressive symptoms, and it can be used as an adjunctive treatment, by quickening and enhancing the effects of antidepressant medication (ICSI, 2013).

Nutritional Supplements

Improvement in depressive symptoms has been noted with the nutritional supplement S-adenosyl-L-methionine (SAMe). St. John's Wort can be another effective over the counter supplement for treating mild to moderate depression, but not for moderate to severe depression. It is not known how St. John's Wort works but some problems are associated with it. It does interact adversely with MAOIs, HIV medications, anti-rejection drugs or chemotherapy (NIMH, n.d. a).

In addition, increased sensitivity to sunlight is a side effect. Patients should be cautioned against self-treatment of using OTC supplements. Treatment under the supervision of a healthcare professional is required, with FDA approved medications (ICSI, 2013).

Exercise

Exercise is an important recommendation for patients with depression. Many studies show that exercise can produce a positive effect on mood. Additionally, exercise provides a structured activity for patients, and may increase feelings of self-esteem and competence (Tesar, 2015).

ECT

Response and remission rates are higher with Electroconvulsive therapy (ECT) than with any other form of antidepressant treatment with 70%-90% of patients showing improvement. Its use is effective in the acute phase and with MDD maintenance. Considerations for use of ECT in geriatric patients with MDD include:

- An intolerance or medical risk with antidepressants
- Catatonia
- Severe suicide risk
- Predominant melancholic symptoms
- Depression with psychosis
- Depression with medical symptoms
(ICSI, 2013)

Side Effects of ECT

Common side effects associated with ECT include headaches, myalgias, nausea, drowsiness, confusion, and amnesia.

More serious and rare side effects include hypertension, tachycardia, myocardial infarction, cerebrovascular accident, or death (ICSI, 2013).

Recurrence Rates

In adulthood, the number of MDD episodes peaks in the fourth decade and again in the sixth. The disorder features one or more episodes that each last at least two weeks, average from six to nine months if left untreated, and generally remit within two years (Tesar, 2015).

The chance of having only one episode of MDD in a lifetime is slim. Researchers predict a 50-85% recurrence rate, the highest odds based on cases not receiving intervention. The prognosis is less optimistic with more episodes. People with two episodes of MDD have a 70% chance of experiencing a third (Tesar, 2015; ICSI, 2011).

Test Yourself

True or False: The chance of having only one episode of MDD in a lifetime is slim.

Answer: True

Consequences of MDD

Although some MDD episodes remit spontaneously, there are consequences to lack of treatment that diminish the quality of life. Residual symptoms that occur create disability in work and personal life. This affects a huge portion of the population.

Depression is now the leading cause of disability in the USA. Economic losses, missed opportunities, and a dwindling support group of friends increase life stress. Neurological abnormalities in the Central Nervous System (CNS) that correlate to MDD may continue, contributing to a higher risk of recurrent episodes, substance abuse, morbidity, mortality, and frequent utilization of medical services (Tesar, 2015; ICSI, 2013).

Interactive Activity

The following is a short video based on what people with depression want others to know. It can be viewed at <https://www.youtube.com/watch?v=IQR1G1OOEEQ>

The Risk of Suicide

The risk of suicide is a consequence of MDD that can be reduced, but not eliminated entirely, with treatment. This risk is estimated to be 15% for the entire MDD population and the elderly have the highest rate of all age groups, and the highest rate is among those over 85 years old (Tesar, 2015).

Among adolescents with MDD, 7% eventually commit suicide in early adulthood, making suicide the third leading cause of death among 10 to 24 year olds. Some mental disorder is present in 90% of all suicide cases (NIMH, n.d. a).

Suicide Risk

Along with age, there are other factors that place a patient at risk for suicide. These include:

- Gender: females are at higher risk for attempts but males are at higher risk for successfully committing suicide
- Access to lethal means: this may include medications and firearms
- Life events: stressful events such as a death or loss of job
- Previous attempts: previous suicide attempts increase the risk of another attempt
- Other psychiatric disorders: along with depression other psychiatric co-morbidities increase risk
- Substance abuse: inhibitions and impulsiveness can be affected
- Genetics: family history of mental illness or suicide can increase the risk
- Childhood trauma: abuse and neglect can also increase the risk

(Centre for Addiction and Mental Health, 2011)

Approaches with Suicidal Patients

It is important to assess suicide risk by asking the patient directly about suicidal ideation. This should include questions about any plans made, availability of means, and deterrents which

may prevent the patient from acting on suicidal thoughts. Considerations of risk factors are included in the assessment.

It is important to establish a rapport with the patient, and explore their feelings without judgment. Focusing on potential deterrents to suicide, such as religious beliefs or family at home, is essential. A contract with the patient is essential, preferably written, in which the patient agrees not to harm him or herself until treatment can be established.

All suicidal ideation should be taken seriously. Immediate referral for treatment is needed, and documentation should include all details of any conversations with the patient (Centre for Addiction and Mental Health, 2011)

Conclusion

MDD can strike anyone at any time. It is a major mental health problem facing us today.

Treatment is available and is often successful, and can include minimal side effects.

Knowledge about MDD helps you to work successfully with patients who are suffering from this disorder.

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