

> Statement of Objectives

Upon successful completion of this lesson, you should be able to:

1. Discuss ways in which to take an active role in managing patient depression.
2. Discuss the signs and symptoms of depression; identify these symptoms in patients and intervene.
3. Understand the pharmacological and non-pharmacological treatment of depression.
4. Manage side-effects of pharmacological treatment of depression.
5. Recognize the signs of non-compliance and how to intervene.
6. Discuss ways in which to take a proactive role in reducing non-compliance in a patient with a depressive illness.



HOW PHARMACISTS CAN HAVE AN IMPACT ON THE TREATMENT OF DEPRESSION

A pharmacist-motivated approach

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> Instructions

1. After carefully reading this lesson, study each question and select the one answer you believe to be correct. Circle the appropriate letter on the attached reply card.
2. Complete the card and mail, or fax to (416) 764-3937.
3. Your reply card will be marked and you will be advised of your results in a letter from Rogers Publishing.
4. To pass this lesson, a grade of 70% (14 out of 20) is required. If you pass, your CEU(s) will be recorded with the relevant provincial authority(ies). (Note: some provinces require individual pharmacists to notify them.)

 **1.5 CEUs**

Approved for 1.5 CE units by the Canadian Council on Continuing Education in Pharmacy.

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INTRODUCTION

The facts about depression

Depression affects all ages, ethnic and social groups, and both genders. Depression is a severe mental illness that interferes with all aspects of daily life. Depression is not considered by some to be a real medical condition (such as diabetes or asthma), and available statistics show that it is vastly under-treated. In North America, it is estimated that 18% of the population will have at least one episode of depression in their lifetime. Diabetes, in comparison only affects 5% of the population.¹ Approximately 45% of depressed patients seek treatment, and only 23%, for various reasons, actually get treatment. Of these, only 10% receive adequate treatment.¹ Depression affects all socioeconomic classes equally, however, women are twice as likely to be affected by it.² There is an increased risk of depression with advancing age and indeed, 25% of long-term care residents suffer from bouts of depression.³ Depression is seldom seen in children (less than 2.5%), but when children do suffer from depression, it can lead to impaired development, decreased academic achievement and more severe psychiatric disorders later in life. Suicide is the second leading cause of death in teenagers and depression is thought to be, in many cases, the precipitating factor.^{2,4,5}

Depression also creates a financial burden on society. The total annual cost of depression in Ontario is estimated to be \$500 million.² Depression can lead to increased absenteeism, impaired ability to function at work, disturbed family life, substance abuse and suicide.

As pharmacists, we must examine our role in improving the care of people who suffer from depression. From the statistics shown earlier, it is apparent that many patients seen

in the pharmacy setting have depression and will not receive adequate treatment. In the traditional role, pharmacists have been limited in their response to these patients.

Pharmacists on the "front line" of health care need to be cognizant of the signs and symptoms of depression in order to refer patients to their physicians for diagnosis. Pharmacists should be prepared to follow up and monitor the prescribed treatment to ensure the desired outcome. Follow-up can be as involved as a direct consultation session or as simple as a phone call.

SIGNS AND SYMPTOMS

THERE ARE MANY TYPES OF DEPRESSION, EACH with specific traits. (See Table 1.) The most common form is Unipolar, affecting 90% of patients. Pharmacists must be alert to observe character changes in patients. Character changes include altered moods, irritability, disturbed sleep patterns and physical appearance. Pharmacists need to ask questions to discover how patients are really feeling. If you are suspicious that a patient has depression, examine the patient's profile for drug-related problems (DRP) and/or medical conditions that may be precipitating the depression. (Table 2 lists some of the medications and conditions that trigger depression.)

Bereavement is not mentioned in Table 2. A short bout of depression is normal following the loss of a loved one. If this depression lasts longer than 2 months, or severely disrupts a patient's ability to function, it should be classified as "reactive depression" (see Table 1), and these patients should be referred to their physicians for treatment.² Likewise, if post-partum depression lasts longer than 2 months, it should be considered abnormal

and classed as "reactive depression."²

If a medication is suspected of causing depression, and the timing appears to fit with the onset of depression, pharmacists should suggest an alternative medication to the physician. If a medical illness appears to be the root cause, communicating with the physician to outline your concerns is appropriate. The use of illicit drugs or alcohol should be ruled out as the cause of the symptoms identified. After these considerations, the pharmacist can proceed to verify whether the patient has depression by conducting a simple test. The "Beck Depression Inventory" (see Table 3) is one example of a test for depression which can be used as part of a counselling session. The questions in the inventory are used to select the key symptoms of depression. They measure the degree of a patient's depression and indicate when it is time to refer the patient to a physician.

Because depression is under-treated,⁶ watching for the signs of depression and guiding patients to treatment is the first step pharmacists can take to improve the treatment of depression.

PHARMACOLOGICAL THERAPY

THE GOALS OF THERAPY, LISTED IN ORDER OF importance are:⁷

1. prevent suicide
2. relieve symptoms
3. restore function
4. prevent recurrence

Suicide is the first priority of therapy due to its prevalence in individuals with depression. The rate of suicide in patients with depression is 15%, compared to 1% in the general population.² Suicide is the single most important reason why pharmacists need to be alert to the signs and symptoms of depression and refer those patients who warrant it.^{2,5,8} The symptoms of suicide should be taken seriously and dealt with quickly and efficiently.² Therapy may consist of medications, psychotherapy or both, depending on the physician and the severity of the case.^{1,2,9,10}

Restoring normal function in depressed patients takes time. It should be emphasized that treatment for the depressive episode will take a minimum of 6 months. A recurrent case of depression can take years.^{1,2} Preventing recurrences is also a key issue. Continuing therapy for an adequate period of time has been shown to prevent recurrences.^{1,2,11,12} It has been shown that up to 40% of depressed patients will experience a recurrence over time.⁸

The cause of depression is not completely

TABLE 1 Types of Depression¹⁵

Type of depression	Prevalence	Characteristics
Unipolar	Most common	Depressed mood Anhedonia* Low self-esteem Thoughts of death Fatigue Decreased sleep Weight loss Lasts 6-12 months
Bipolar	10%	Mania to depressed swings Increased weight – overeating Increased sleep – oversleeping Seldom goes into remission
Psychotic	10%	Unreal thoughts Disorganized thinking Delusions – mood congruent** Low self-esteem
Anxious	Common	Anxiety, phobia Persistent fear or panic Increased time to wellness, recurrences
Melancholic	Often seen in the elderly	Very severe Significant weight loss Night and early-morning wakefulness Complete loss of interest Agitation Guilt – unreasonable
Double	Uncommon	Unipolar and dysthymia at same time Recovery slow, dysthymia stays Relapses common
Atypical	Uncommon	Part of SAD or bipolar sometimes Mood reactivity Overeating and oversleeping Sensitive to rejection Extreme fatigue
Dysthymia	Less common	Chronic – low-grade depression Less severe – lasts longer
Reactive	Common	Episode triggered by life event Also called situational All regular symptoms
Seasonal	14%	SAD – seasonal affective disorder Recurrent disorder, usually connected to time of year (light) All regular symptoms

*Anhedonia – loss of interest in things that give pleasure

**Mood congruent – changes with the mood

Each type of depression has most of the basic symptoms of unipolar depression.

understood. Research shows that depression may have a hereditary link, often triggered by trauma. Researchers have also suggested that a chemical imbalance involving neurotransmitters may occur in the brain.¹ More research is required to further investigate this theory and

search out other causes. Medications presently used to impact these neurotransmitters do not seem to solve the whole problem. The neurotransmitters that have been implicated so far are norepinephrine, serotonin and dopamine. Most of the medications used to treat depres-

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ABOUT THE AUTHOR

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REVIEWERS

All lessons are reviewed by pharmacists for accuracy, currency and relevance to current pharmacy practice.

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TABLE 2 Medications and Conditions Causing Depression^{1,2}

Drugs that may cause depression	Medical conditions that may cause depression
Anabolic steroids	Thyroid disease
Interferon	Heart disease
Systemic corticosteroids (long-term use)	Arthritis
Alcohol	Cancer
Benzodiazepines	Cerebral vascular accidents
Narcotics	Cushing's disease
Hallucinogens	Fibromyalgia
Barbiturates	Multiple sclerosis
Hormones - contraceptives, HRT	B12 deficiency
	Parkinson's disease
	Alzheimer's disease
	Other dementias

TABLE 3 The Beck Depression Inventory

Have you experienced any of the following symptoms for at least a two-week period? Have these symptoms lasted almost all day long?

Symptoms	Yes	No
Feeling down, low or blue almost every day		
Lost interest in things that you used to enjoy		
Lost energy, feeling physically tired or fatigued		
Had trouble concentrating or making decisions		
Feeling agitated, restless, very sluggish or slowed down		
Thinking about death or wanting to die; feeling life isn't worth living		
Worried or feeling guilty about things you have no control over or didn't do		
Trouble sleeping or oversleeping		
Lost appetite or weight loss; overeating or weight gain.		

SCORING AND EVALUATION
Add up all of the YES responses and evaluate the score as follows.
Total 2 or less: Major depression is unlikely, but patient may have other health problems.
Total 3: Major depression is unlikely, but patient may still benefit from assessment by a physician.
Total 4: Depression is likely. Patient should see doctor.
Total 5: Depression is highly likely. Patient should be advised to see a doctor immediately.

sion cause an increase in one or more of these neurotransmitters. Older antidepressants, such as tricyclics (TCAs), are non-selective and affect a wide variety of neurotransmitters, possibly causing added side-effects. Newer agents, such as Selective Serotonin Reuptake Inhibitors (SSRIs), have fewer side-effects because they are more selective for the targeted neurotransmitters than TCAs. Table 4 is a summary of the different categories of antidepressants, including their starting and target doses and primary mode of action.

Creating an atmosphere that promotes patient compliance for those patients with depression is important. Research has shown that treatment failure is most often caused by the improper use of, or failure to take the prescribed medication properly, or even at all.^{1,2,6,13,14,15}

It has been found that between 28 and 44% of all patients fail to take the medications they have been prescribed.² Working to improve compliance is the second step the

pharmacist can take to have a positive impact on the treatment of depression.

Improving compliance begins by providing patients with an appropriate explanation of what the medication(s) will do, how long before an effect will be noticed, how long to take the medication(s) and what side-effects to expect. The issue of alleged addiction potential should also be addressed. To provide this information, pharmacists must have a good working knowledge of antidepressant medications. Research shows that this initial counselling session is essential in achieving complete remission of symptoms.^{1,2,13} Ongoing counselling is also important because depressed patients are often resistant to treatment and are afraid of feeling self-conscious or foolish for being depressed. They require reassurance that depression is a very real medical condition that requires treatment that is best achieved through ongoing counselling.

These counselling sessions should be con-

ducted in a quiet, peaceful setting, free from distractions. Answering patient questions and addressing these very real concerns increases the pharmacist's rapport with patients and ultimately aids in compliance. It should be noted that simply distributing educational material about the medications, without counselling, has actually been found to negatively impact compliance. Perhaps this is due to the fear caused by reading the lists of warnings and side-effects that this type of literature usually contains. When the literature is given out in conjunction with counselling, the information can be explained and the issue of side-effects can be discussed in a proactive manner.¹⁶

The fear of addiction is prominent and most adults resist taking medications that cloud their normal thinking ability or cause them to be dependent. It must be emphasized that antidepressant medication is not addictive. If SSRIs are to be discontinued, the dose should be tapered down over a long enough period of time to allow the brain sufficient time to adapt to the change in neurotransmitter levels, in order to prevent rebound effects. Rebound effects include excessive sweating, palpitations and nausea. The dose should be tapered to a point below the initial starting dose before discontinuation. If discontinuation of the SSRI becomes too traumatic for the patient, the original therapy may be reinstated or a single dose of fluoxetine may be tried. Fluoxetine leaves the body more slowly due to its long half-life and does not cause the rebound effect.²¹ Patients beginning therapy should be cautioned about rebound, in case they decide to quit taking the medication on their own. Patients should be encouraged to call their pharmacist before discontinuing any medication to prevent rebound effects. This action provides the pharmacist with another opportunity to encourage ongoing therapy and the need for it. If the patient is determined to discontinue a medication, the pharmacist should attempt to discover the reason.

Side-effects caused by this class of medication is one of the primary reasons for discontinuation of therapy.^{1,2,7} In this instance, a good rapport with the patient and knowledge of the medications will aid in continuing treatment. There are many ways to deal with side-effects, and there are many alternative medications that can be tried. The goal is to encourage the patient to continue therapy for at least 6 months. Pharmacists can show care and interest by listening carefully to the patient's concerns, finding ways to deal with side-effects that impede therapy and discussing suggestions with the patient. If the patient is willing, set up a care plan and schedule a follow-up consultation by phone or in person. If a solution cannot be found, the pharmacist should be prepared to act as an advocate for the patient by offering to phone the physician to discuss the situation. If a SSRI has caused the problem, suggest another class of antidepressant such as a SNRI, as it may be better tolerated.

Before suggesting an alternative medi-

cation, take the time to examine the dosage of the current antidepressant with respect to the patient's age, weight and ethnic suitability. Interestingly, it has been found that there are genetic variations that affect the hepatic enzymes. Because the most commonly used antidepressants, namely SSRIs and SNRIs, are metabolized by the P-450 (CYP) isoenzymes (in particular CYP3A4, CYP2D6 and CYP2C9)³ this will affect the dosage within certain ethnic groups. Thirty-three percent of African-Americans and Asians have gene alterations which decrease the metabolic rate of the CYP2D6 and CYP2C9 isoenzymes. This generally necessitates reducing dosage to one-half the normal dose.^{2,7} The goal of therapy is to achieve a complete absence of symptoms to prevent relapse and recurrence. Once remission has been achieved, therapy should continue for at least 6 months. If a patient has had several previous bouts of depression, the therapy may have to be of a long-term nature. Research has demonstrated that the length of remission becomes shorter with each new episode of depression.² Older patients (>50 years) have been found to be prone to relapses with more intense episodes. It has been suggested that long-term therapy be considered for these patients. Table 5 lists the different classes of antidepressants and their side-effects.

SIDE-EFFECT MANAGEMENT

SOME SIDE-EFFECTS ARE MORE DIFFICULT TO MANAGE than others. Most antidepressants are capable of producing each of the side-effects listed in Table 5, but to different degrees because they all impact the neurotransmitters. The first step in managing side-effects is to check the dose of the medication. It is generally felt that starting at a low dose and titrating up slowly is an effective way of minimizing side-effects. If a side-effect becomes intolerable, then titrate down to the most tolerated dose and observe how this affects therapy. If the side-effect persists, move the dosage regimen within the day to observe if this improves the side-effect. For example, if the medication causes sedation, move it to the evening. Many antidepressants may be given once a day¹⁷ with equal efficacy to split dosing, with fewer side-effects and better compliance. Fluoxetine has actually been researched as a once-weekly dose and been found to be equally effective and well-tolerated.¹⁸ Determine which schedule best suits the patient and talk to the physician about shifting the medication to the most workable time frame.

Side-effects are generally split into two groups: less severe and severe. Less severe side-effects include visual sensitivity to light, dry lips and skin, stomach upset, constipation, lethargy, mild restlessness and weight gain. Visual sensitivity to light may be alleviated with the use of sunglasses and broad-brimmed hats. Sucking on hard, sugarless candies or ice chips may help with dry lips/mouth. Stomach and bowel issues are often solved by taking the medications with food or by altering the diet to include less gas-producing vegetables, and more fibre. To treat

TABLE 4 Types of Antidepressants

Type	Generic Name	Trade Name	Starting Dose	Target Dose
NDM Norepinephrine-Dopamine Modulator	Bupropion	Wellbutrin	100 mg	150-300 mg
TCA (Tricyclics) and Non-Selective Cyclics	Amitriptyline Nortriptyline Protriptyline Clomipramine Desipramine Doxepin Imipramine Maprotiline Trimipramine	Elavil Aventyl Triptil Anafranil Norpramin Sinequan Tofranil Ludomil Surmontil	50-75 mg 25-50 mg 10-20 mg 50-75 mg 50-75 mg 50-75 mg 50-75 mg 50-75 mg 50-75 mg	100-250 mg 75-150 mg 30-60 mg 100-250 mg 100-250 mg 100-250 mg 100-250 mg 100-250 mg 100-250 mg
RIMA Reversible Inhibitor of Mono- amine Oxidase	Moclobemide	Manerix	150-200 mg	450-600 mg
MAOI Irreversible Inhibitor of Mono- amine Oxidase	Phenelzine Tranylcypromine	Nardil Parnate	15-30 mg 10-20 mg	30-75 mg 20-60 mg
SSRI Selective Serotonin reup- take Inhibitors	Fluoxetine Fluvoxamine Paroxetine Sertraline Citalopram	Prozac Luvox Paxil Zoloft Celexa	10-20 mg 50-100 mg 10-20 mg 25-50 mg 10-20 mg	20-40 mg 100-200 mg 20-40 mg 50-150 mg 20-40 mg
SARI Serotonin, Antagonist Receptor inhibitors	Nefazodone* Trazodone	Serzone Desyrel	50-100 mg 50-100 mg	200-400 mg 200-400 mg
SNRI Selective Serotonin Norepinephrine Reuptake Inhibitors	Venlafaxine	Effexor	37.5-75 mg	75-225 mg

Adapted from ref.^{2,7}

* Nefazodone has been withdrawn from the European market due to rare, but life-threatening liver damage that can occur with the use of this drug. It is still available in Canada.²³

lethargy and dizziness, the medication can be taken at bedtime. Mild muscle stiffness can be improved with a regular exercise program. If the effect worsens, then the patient should be referred to the physician. Weight gain, frequently seen with antidepressants, can be controlled with diet and exercise.

Side-effects considered severe include blurred vision, swallowing difficulties, body tremors, diarrhea, major rigidity, rashes and skin discoloration, sexual difficulty, excessive sleepiness and urination problems. Most of these side-effects require the assistance of the physician and the patient suffering from these side-effects should be referred. Pharmacists should recommend alternatives to physicians when these effects do occur. For example, sexual dysfunction is a side-effect which often leads to non-compliance and patients often have difficulty discussing this issue. Pharmacists need to be sensitive to the signals a patient may display regarding this problem. For example, a patient may simply say that he doesn't like the medication or that it doesn't suit him. During the initial counselling ses-

sion, it may be helpful to use an information sheet that lists the side-effects and indicate to the patient that sexual dysfunction is a possibility. This may make it easier for patients to discuss this side-effect later on. If a patient does complain of sexual dysfunction, then a switch to bupropion can be suggested to the physician to eliminate this side-effect, while still providing sufficient therapy.

The pharmacist can improve compliance by addressing the patient's concerns about the medication. Listen carefully to what the patient has to say and discuss possible solutions. The patient should be referred to his or her physician if an appropriate solution cannot be found. The pharmacist should be prepared to work with the physician to find a solution to the patient's concerns. This cooperation will build trust and improve the patient-pharmacist-physician relationship to aid in future compliance.

ALTERNATIVE TREATMENTS

ALTERNATIVE TREATMENTS ARE THOSE THERAPIES which do not involve medications. Alternative

TABLE 5 Antidepressants: Side-effects and Comments^{2,17,20}

Antidepressant	AC	AH	AA	SE	AD	Other	Comments
Norepinephrine-Dopamine Modulators	0	0	0	0	2	No sexual dysfunction	High seizure potential
Tricyclics	4*	4*	3*	2*	3*	Each drug differs slightly *average finding	Nortriptyline least AC, Amitriptyline most AC
MAOI	3	3	3	3	3	Priapism, insomnia	Hypertensive crisis, needs special diet, watch interactions
RIMA	2	1	3	2	2	Insomnia	No diet restrictions, watch interactions
SSRI	0	0	0	4	3	Citalopram least AD	Watch withdrawal syndrome with abrupt stops. All but fluoxetine
SARI	0	0	2	1	3	Trazodone more AA, no sexual dysfunction	Nefazodone, visual disturbances
SNRI	0	0	0	4	2		High doses – watch blood pressure

Anticholinergic (AC): Dry mouth, blurred vision, constipation, urinary retention, sweating, tachycardia, confusion

Antihistaminergic (AH): Drowsiness, weight gain

Anti-alpha Adrenergic (AA): Orthostatic hypotension, dizziness, reflex tachycardia, sedation.

Serotonergic (SE): GI distress, headache, nervousness, akathisia, EPS, sweating, sexual dysfunction, anorexia

Adrenergic (AD): Tremors, tachycardia, sweating, insomnia, sexual dysfunction.

Ratings: 0=none 1=least 5=most

treatments can be used alone or in combination with pharmacological therapy. These therapies include psychotherapy, electro-convulsive therapy, light therapy and lifestyle issues.

Psychotherapy involves establishing a relationship between a therapist and a patient so that the illness can be discussed. While effective in many cases, it usually takes longer to achieve remission. There are fewer side-effects than with pharmacological therapy and the results have been found to last beyond pharmacological therapy.

Severe depression may not be treatable with psychotherapy alone. There are two types of psychotherapy that have proven effective: cognitive behavioural therapy (CBT) and interpersonal psychotherapy (IPT). CBT is based on the theory that people who are depressed think in a dysfunctional manner, which may predispose them to depression. The therapy involves correcting the distorted attitudes and teaching the patient to think differently. CBT has been shown to be effective in 60% of mild-to-moderate depression cases. It takes 3-5 months to reach the full effect.¹

IPT is based on the theory that depression comes from dysfunctional relationships. The therapy essentially consists of improving these relationships. Long-term remissions (>3 years) have been seen with IPT, but the therapy is still fairly new, so the full effects are not yet known.¹

Electro-convulsive therapy (ECT), also

known as shock treatment, is an electrical impulse delivered to the brain that produces a seizure. Therapy involves 6 to 12 treatments over 4 to 5 weeks. It is very effective for all types of depression, especially psychotic, and it is relatively quick-acting. Some memory loss is usually experienced with ECT, but this improves after 6 months. The downside of ECT is that the beneficial effects do not last longer than a few months. ECT usually has to be followed by pharmacological treatment.¹

Light therapy is usually reserved for people with seasonal affective disorder (SAD). Light is delivered to the eyes for 30 to 60 minutes per day for up to 2 weeks to evaluate effectiveness.^{1,22} The lamp used for light therapy blocks the UV light (unlike tanning lamps).¹ Broad spectrum wavelengths of light are preferred as they mimic natural light.²² It is the intensity of the light that appears to be the important factor. The recommended intensity of light is 10,000 lux.^{1,22} If there is no improvement in mood after 2 weeks, light therapy is deemed ineffective and should be discontinued.¹

Lifestyle issues should be evaluated in depressed patients. These include exercise, activities and diet. It has been found that managing lifestyle issues contributes to the successful management of depression. Statistics show that 30% of depressed people gain weight during the course of their illness.^{1,2,19} This contributes to low self-esteem, which worsens the

condition. Many antidepressants aggravate this situation by causing weight gain, especially older antidepressants such as MAOIs and tricyclics.

Exercise has been shown to improve self-esteem and contribute to weight loss. A March 2002 study¹⁷ found that aerobic exercise was the most effective form of exercise in reducing depressive symptoms. Aerobic exercise includes walking, biking, running and swimming. Exercise also helps depressed patients focus their energies on an activity. Often, a depressed person will not leave the house or associate with other people. This provides excessive time for dwelling on problems. Exercise is a motivator offering them achievable goals. Aerobic exercise can begin at home with video exercise programs, a treadmill, stationary bike or even a skipping rope. Encourage patients, as therapy progresses, to join an exercise group. Aerobic classes are available for all fitness stages and ages. It can be fun and uplifting. If these classes are of no interest to a patient, suggest walking with a friend, at least 3 times per week to start. For seniors, walking clubs provide an opportunity to gather several times a week to walk around the local mall. These clubs offer exercise and decrease loneliness (a contributing factor in depression in the elderly). Most community centres also offer aqua-exercise classes. This form of low-impact aerobic exercise, called aquatics, is suitable for physically-impaired individuals. Aquatics provides an opportunity for people to meet and establish relationships. Improving the heart and lungs promotes better circulation and more oxygen to the brain, promoting feelings of well-being.

Another component of lifestyle is diet. When depression strikes, patients often lose interest in eating. Scientific evidence has shown that many vitamins and minerals contribute to the regulation of mood. B complex, folic acid, calcium, magnesium and l-tryptophan have been found to affect mood regulation. L-tryptophan, an amino acid, is a building block for neurotransmitters and has a direct link to depression. There is some evidence to support its use to augment regular antidepressant therapy. Some medications can cause food cravings and a dry mouth which may lead to an increased intake of soda pop and other foods. Being aware of these problems and promoting sugarless products to quench these cravings will help the depressed patient.¹ A proper diet that includes dairy products, meat, fish and grains will yield most of the vitamins and minerals necessary to regulate mood.¹ Controlling the diet and participating in activities that include aerobic exercise will help the depressed patient to achieve a positive treatment outcome. Pharmacists should be prepared with handouts on the role of diet and exercise. Keep a current list of activities in your area to distribute to patients and encourage them to participate.

COMPLIANCE

STUDIES HAVE DEMONSTRATED THAT THE FOLLOWING factors contribute to poor compliance:^{1,2}

1. Diseases requiring longer therapy.
2. Diseases where the outcomes are difficult to measure.
3. Diseases that are undervalued by society (i.e. depressed people often feel that they don't deserve treatment).
4. Diseases that affect the brain – increasing forgetfulness, or causing poor motivation.
5. Polypharmacy.
6. Gender differences – women are least compliant (perhaps due to side-effects).
7. Substance abuse.
8. Age – younger patients and elderly are least compliant.
9. Low economic status – perhaps driven by an inability to pay for drugs.
10. Drugs that take a long time to become effective.
11. Drugs that produce a number of side-effects.

Many of the factors that produce non-compliance are applicable to the treatment of depression. This answers the question of why compliance is such an issue with this condition.

It has become increasingly apparent that treatment of depression must be continued for a minimum of 6 months; for patients with recurrent episodes, treatment may last a lifetime. Unipolar depression is now considered a chronic, disabling condition, requiring long-term treatment with acute doses of antidepressants. The need for long-term therapy stems from the observation that the severity and frequency of episodes increases as the number of past episodes increases.¹³ The risk of recurrence is 50% after 1 episode, 70% after 2 episodes and 90% after 3 episodes.² Therefore, preventing the recurrence of depression is key to a positive treatment outcome. Studies have shown that 28% of patients discontinue their medication(s) in the first month and 44% stop within 3 months.²

Pharmacists are in a good position to notice signs of non-compliance. The signs are: late refills, not returning for refills, no obvious improvement in character/mood after a month, constant complaints about side-effects and comments such as, "I feel much better now, the problem is solved." indicating a belief that treatment is no longer required. Once these signs are detected, what can be done to prevent non-compliance?

THE PHARMACIST'S ROLE IN COMPLIANCE

MUCH OF THE GROUNDWORK FOR COMPLIANCE CAN BE done when the prescription is dispensed. Begin by establishing a good relationship with the patient. As discussed previously, pharmacists need to be attentive, empathetic listeners. A good initial counselling session with the patient, where the disease and the treatment are discussed in full, lays the foundation for compliance. Pharmacists should emphasize the following:

1. Depression is a legitimate illness that is quite common.
2. Depression needs to be treated. Treatment can be successful, but success is dependent on compliance.

FIGURE 1 Manual Call-back System Bulletin Board

Today	Next week	Next month

CALL-BACK FORM	
Call-back date	Instructions 1) Fill in the call-back form 2) Place on bulletin board under the correct time-frame 3) Check the bulletin board daily 4) Make appropriate calls
Name	
Telephone	
Rx# and filling date	
Reason for calling	
Outcome	

3. Treatment will take a minimum of 6 months.
4. Antidepressants are non-addicting.
5. Most antidepressants need to be discontinued slowly. Ask the pharmacist for help.
6. Antidepressants have side-effects. However, most side-effects can be managed. Review the major side-effects and how they can be managed. Do not hand out an information sheet on antidepressants without discussing the side-effects in detail. The side-effects most likely to be experienced should be emphasized so the patient isn't surprised by them. Ways in which the patient can cope with these side-effects should be discussed. Assuring the patient that most side-effects will not occur will help ease fear of therapy and encourage the patient to give therapy a fair trial.
7. Encourage the patient to call or see you if side-effects bother them, so that you can help.
8. A response to the medication(s) may take 2 to 4 weeks.^{1,2,7,12} The dose may have to be adjusted before treatment is successful.
9. Encourage patients to keep a record/diary of how they are feeling: patients should rate mood, irritability, appetite and fatigue so that they will be able to tell when they are feeling better.
10. Obtain the patient's permission for follow-up consultations during the initial consultation, and arrange these follow-up consultations by phone, or in person, at the following intervals.

1) After 1 week to ask about side-effects and tolerance.

2) At 2 to 3 weeks to ask about effect.

3) At 6 weeks to check on outcome and to suggest referral if the outcome is not satisfactory. Consultations will improve compliance and show that you care about your patient's welfare. In the follow-up consultation, focus on the specific aim of the call, but also ask about the

record/diary that the patient has been keeping, how the patient is tolerating the medication, suggesting ways to manage side-effects if present. Encourage the continuation of therapy, pointing out that treatment, until there is complete remission (no symptoms), is the goal and the best way to prevent future episodes. Monitor refills and phone the patient as a reminder. Be an advocate for the patient.

AIDS TO COMPLIANCE

SOMETIMES COMPLIANCE REQUIRES THE HELP OF AIDS to promote memory. Such aids include blister pill packs, dosettes, pillboxes with timers and special calendars. Be inventive in thinking of ways to help patients remember to take their medications. Programs that prepare medications in pill packs and monitor their use are particularly helpful to patients who are severely cognitively impaired. Be alert to recognize these patients and be prepared to offer assistance.

The need for call-backs cannot be over-emphasized. A callback system will aid you in helping your patient. Calling the patient to check on therapy and remind them to come in for therapy is an easy and effective way to aid compliance. There are many ways to conduct a callback program. For example, computer systems, presently available in most pharmacies, can flag prescriptions that require call-backs. Daily call-back lists can be downloaded each morning as a reminder. A simple bulletin board will do. A sample set-up is outlined in Figure 1. The method used is not as important as the action taken. Make time for this important function in your daily routine, but be sure to check if your co-worker has already dealt with the situation before calling. Always check the profile before making any calls to acquaint yourself with any recent documented changes.

Many pharmacists are under time constraints that make consultation by phone or in person seem impossible. It may be necessary to think creatively about ways to achieve this aspect of your professional role. One method may be to arrange these callbacks or consultations before beginning your workday or at the end of the day. If you are in a position to do so, arrange some "overlap" time with a co-worker to enable you to do this important job. Consultations are as important as dispensing the prescription.

THE TEAM APPROACH

AS MEMBERS OF THE HEALTHCARE TEAM, PHARMACISTS should look for ways to partner with other health professionals in order to assist patients. Nurses, physiotherapists, dietitians, social workers, psychiatrists and physicians all have a role to play in the management of depression. Good communication with each of these professionals will help patients achieve successful treatment outcomes. In particular, try to partner with the mental health unit in your area to develop communication programs. For example, the Medication Awareness Program (M.A.P., developed in Elliot Lake, Ont., and recently introduced in Sudbury, Ont.) is essentially a pill pack program with a communication component. It is a simple but effective method of partnering with other health workers to monitor the overall treatment of psychiatric and depressed patients. It begins by contacting the local mental health unit and discussing a partnership. The mental health unit refers patients to the program. The pharmacist enrolls patients and sets up pill packs to explain each medication and expected effects. Patients come into the pharmacy each week to pick up the medication and the pharmacist observes compliance and discusses issues with these patients. If a patient does not come in or is not taking their medication, the pharmacist telephones the patient's mental health worker. The mental health worker then locates the patient and tries to encourage them to take their medications. At the end of each month a short report is sent to the mental health unit,

outlining compliance and reviewing present medications. This informs the mental health worker and the psychiatrist of any changes in therapy, as some changes may occur between visits to the psychiatrist.

Pharmacists should not hesitate to call other health professionals to arrange appointments or seek advice that may aid a patient (with the patient's permission).

For instance, dietitians are a good resource for dietary concerns. Make an effort to discover "help groups" (such as AA, community mental health groups, activity groups, exercise classes) available in your area. Provide the patient with a list of these groups, meeting times and places and encourage them to go. Encouraging patients to participate outside of the home aids in achieving a positive treatment outcome.

In conclusion, pharmacists have a tremendous opportunity to improve compliance. And total compliance is the ideal way to achieve the successful treatment of depression.

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QUESTIONS

CASE STUDY #1

Jane is a 15-year-old girl who graduated from public school with a 70% average. She loves to play baseball and to "hang out" with her friends. Over the past year, however, her parents have noticed that she is spending more time in her room and has become quite resistant to answering questions about school and friends.

1. Which of the following symptoms indicate that Jane is suffering from depression?

- a) an increased thirst
- b) sleeping all the time, no energy

- c) constant headaches and achy joints
- d) alopecia

2. What possible outcome(s) should Jane's parents be most concerned about if she does have depression?

- a) A decrease in her social activities and loss of friends.
- b) An inability to graduate from high school, due to lower grades.
- c) An increased risk of suicide.
- d) All of the above.

3. What percentage of the population suffers from depression?

- a) 20%
- b) 40%
- c) 18%
- d) 5%

4. Which of the following is a possible cause of depression?

- a) anabolic steroids
- b) non-steroidal anti-inflammatories
- c) hypertension
- d) cholinesterase inhibitors

5. Unipolar depression is the most common type of depression. What characteristics are most prevalent with this condition?

- a) overeating
- b) anhedonia
- c) oversleeping
- d) severe mood swings

6. The Beck Depression Inventory is a series of symptoms that can be used to diagnose depression. How many positive responses to these symptoms are adequate grounds to suspect depression and refer a patient to a physician?

- a) 2 c) 5
b) 7 d) Must have all symptoms.

7. Research has found that the levels of the various neurotransmitters play a role in the development of depression. All of the following antidepressants affect serotonin levels EXCEPT:

- a) paroxetine c) venlafaxine
b) bupropion d) fluoxetine

8. Which statement is TRUE with regard to discontinuing SSRIs?

- a) Fluoxetine is the only SSRI that requires tapering the dose before stopping.
b) Simply stop taking the drug because it does not cause rebound reactions.
c) The dose must be tapered to below the initial starting dose before stopping.
d) With the exception of fluoxetine, all SSRIs should be discontinued gradually.

9. The side-effects of antidepressants are a major cause for non-compliance with medication therapy. What side-effect(s) can be safely handled by the pharmacist?

- a) sexual dysfunction c) blurred vision
b) dry lips d) major rigidity

CASE STUDY #2

Mrs. R. presents with a prescription for temazepam 15 mg, take 1 capsule hs. Mrs. R. is a regular customer and from your previous discussions, you are aware that her husband has terminal cancer and she is the sole caregiver. She seems very "down" lately and has lost weight. From her profile, you note that she is presently taking Premarin 0.625 mg 1 tab daily, Lorazepam 1 mg prn for anxiety and Adalat XL 30 1 tab daily.

10. You are concerned that Mrs. R might be suffering from depression. Which of the following questions would best give you the extra information necessary to confirm your suspicions?

- a) Has your stomach been bothering you lately?
b) Have you lost weight?
c) Are you still interested in participating in your normal activities?
d) Are you worried about your husband?

11. From your discussions, you conclude that Mrs. R has depression and needs to be referred to her physician. Which of the following points did not contribute to this decision?

- a) Her apparent weight loss.
b) Her excessive worry and anxiety over her husband's condition.
c) Her increased blood pressure.

d) The review of her profile.

12. At your suggestion, Mrs. R. started on venlafaxine SR 75 mg twice daily. Six weeks later, Mrs. R. does not seem to be responding as well as expected. Upon questioning, you find out that she often forgets to take both doses in the day. What would be the most appropriate suggestion?

- a) Switch therapy to amitriptyline and take at bedtime.
b) Switch to fluoxetine once weekly.
c) Modify the dosage schedule and give venlafaxine SR 150 mg once daily.
d) Send the patient back to the physician to solve the problem.

CASE STUDY #3

Mr. J. has been taking sertraline 100 mg every morning for 3 weeks. He wishes to purchase Gravol to treat his persistent nausea which he has experienced for several weeks.

13. What do you do?

- a) Sell him the Gravol and document it in your computer.
b) Ask him when he is taking his sertraline.
c) Check his profile, then sell him Pepcid AC because it suits his condition better and won't make him sleepy.
d) Tell him to discontinue the sertraline.

14. Mr. J. tells you that he is taking his sertraline at 6 a.m. each morning and that he goes back to bed for an hour because he thought he had to wait before taking his other medications. After examining his profile, what would you tell him?

- a) Start taking the sertraline after breakfast. I will call you in 2 days to see if this improves the nausea.
b) Your nausea is caused by lying down immediately after taking the sertraline. Try taking it later in the morning and staying up for at least 30 minutes afterwards.
c) Take it at bedtime instead so the nausea will occur at night while you are sleeping.
d) There is nothing in your profile that will cause nausea. Please see your doctor if this persists.

15. Mr. J. tells you that he has heard really bad things about sertraline. He has decided to discontinue sertraline because he's feeling better.

- a) Tell him that it is a good idea and suggest that he discontinue the medication gradually.
b) Remind him that he needs to follow the physician's orders and remain on the medication until the next visit to the doctor.
c) Listen to his concerns and try to encourage him to remain on his therapy for at least 6 months.
d) Tell him that sertraline is the best choice for treating depression and there are very few side-effects.

16. Despite your encouragement, Mr. J. insists that there are too many side-effects with sertraline and he wants to stop taking it. When asked, he says that nausea, diarrhea and sleepiness bother him the most. He gives you permission to call his doctor and ask for a change in medication. Which of the following will you suggest?

- a) paroxetine
b) bupropion
c) citalopram
d) amitriptyline

CASE STUDY #4

Mrs. P. is a regular customer who has been recently diagnosed with depression. Although she has been provided with a prescription for venlafaxine, she is reluctant to take medications, preferring to find some "natural" way to deal with the condition.

17. What effective alternatives to medications could be suggested?

- a) Go to a chiropractor for a neck adjustment.
b) See a psychiatrist for cognitive behaviour management.
c) Ignore the symptoms, get a bit more rest, go for a walk.
d) Suggest light therapy.

18. Mrs. P. opts for psychotherapy and returns to her physician to be referred to a therapist. Which of the following statements are not true about psychotherapy.

- a) There are 2 types of effective psychotherapy.
b) Interpersonal psychotherapy has been around a long time and has been shown to be 60% effective.
c) Cognitive behavioural therapy deals with dysfunctional thinking.
d) Cognitive behavioural therapy takes about 3 to 5 months to reach full effect.

19. The least effective exercise in reducing depressive symptoms is:

- a) swimming c) walking the dog
b) tai bo d) weight lifting

20. Pharmacists can prevent non-compliance by emphasizing to their patients that:

- a) Depression can be treated successfully if therapy is maintained for a sufficient length of time.
b) Therapy should be maintained for at least 9 months.
c) Antidepressants are addictive, but we can help you deal with that after remission.
d) There are no side-effects that will prevent you from taking your medications.



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HOW PHARMACISTS CAN HAVE AN IMPACT
ON THE TREATMENT OF DEPRESSION
A PHARMACIST-MOTIVATED APPROACH
1.5 CEUs

1.5 CE UNITS IN QUEBEC
CCCEP #934-0203
JUNE 2003

Not valid for CE credits after February 28, 2006

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Feedback on this CE lesson

- Do you now feel better able to provide pharmaceutical care to patients with depression? Yes No
- Was the information in this lesson relevant to your practice? Yes No
- Will you be able to incorporate the information from this lesson into your practice? Yes No
- Was the information in this lesson... Too basic Appropriate Too Difficult
- Do you feel this lesson met its stated learning objectives? Yes No
- What topic would you like to see covered in a future issue? _____

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