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**Quirky as this comic is, real depression is nothing to laugh about. Everyone gets down in the “blues” now and then: your boyfriend or girlfriend dumps you; you can’t get a date for the dance; you flunk an important test. Those are some of the normal disappointments of life as a teenager. However, for some people, depression extends beyond life’s normal ups and downs to become a crippling illness. Sometimes, it is due to a traumatic event—say the death of a relative or your parents getting divorced—but sometimes people suffer from depression for no apparent reason.**



# MORE THAN BLUE

*By Doris R. Kimbrough*

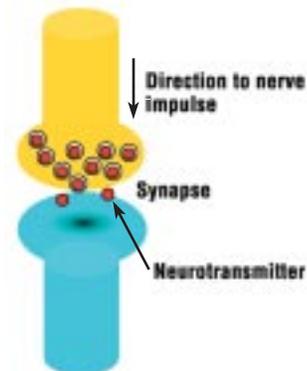


**D**epression becomes a problem when it interferes with your normal day-to-day functioning. Clinical depression is diagnosed when a person either loses or has no interest or pleasure in usual activities. Symptoms can include feeling helpless or worthless, being indecisive, or lacking motivation to complete even simple tasks, such as dressing or eating. People suffering from clinical depression may have trouble sleeping or may sleep constantly. It affects their appetite and productivity and, in extreme cases, the depressed patient may seriously consider suicide. Historically, depression has been much misunderstood, misdiagnosed, and mistreated. In the Middle Ages, depression was thought to be caused by “black bile” or the curse of a witch. More recently, people suffering from depression were often told to “count their blessings” or “just get over it”. It was thought to result from childhood traumas or mistreatments, and doctors were often unable and/or unwilling to treat it successfully. Many of the world’s famous artists and authors suffered from depression (e.g., Ernest Hemingway and Vincent Van Gogh). People suffering from depression or its close relative, bipolar disorder, will sometimes resort to abusing alcohol or drugs in an attempt to ease their symptoms.

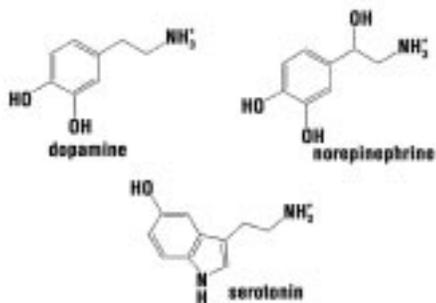
More careful research has revealed that, like most interesting and important things in the world, depression involves some pretty interesting chemistry in the brain. Scientists now realize that chemical imbalances in the brain can be involved in depression, and using other chemicals to rebalance that brain chemistry can bring relief for millions of people suffering from the disease.

There are numerous chemicals in the brain that act as neurotransmitters. That is, they are the chemical connections that enable brain cells to communicate with one another. In general, they function in similar ways. Each neurotransmitter binds to a particular receptor site on the outside of the cell and triggers a particular response inside the cell. In the case of your mood, the neurotransmitters involved are a class of compounds called **monoamines**.

A monoamine involved in depression is serotonin. Typically, people suffering from depression



#### Monoamines





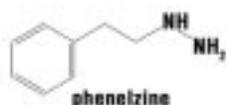
DIGITAL STOCK

have much lower levels of serotonin than nondepressed people. No one really knows why the serotonin levels are lower. Maybe their brain cells don't make enough, or maybe they use it up too fast, but either way, the goal for scientists trying to treat depression is to figure out a way to boost the amount of serotonin in the brain.

Why can't people suffering from depression just take serotonin directly, say in a pill or capsule? The problem with this approach is that serotonin taken this way does not make its way to the brain. It gets converted to an amino acid in the intestine. Doctors might be successful by injecting serotonin directly into brain cells, but they would probably find it difficult to convince their patients to allow brain injections! And it turns out that there is an easier way. Let's look at what happens to the serotonin in the brain.

Serotonin is produced in the brain from the amino acid tryptophan, which comes from the food you eat. It is released by one nerve cell and triggers a response in another. Once it has done its job, two things happen. First, it is reabsorbed by the cell, either in the brain or through the bloodstream into the liver. Then, it is metabolized by an enzyme called monoamine oxidase, or MAO. If either of these two steps

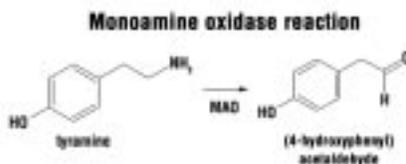
A MAO inhibitor



can be successfully blocked, then you have a way of getting higher levels of serotonin in the brain. Voila! Problem solved. Thus, scientists have discovered two types of drugs that interfere with this process: the selective serotonin reuptake inhibitors (SSRIs) and MAO inhibitors. Let's look at the MAO inhibitors first.

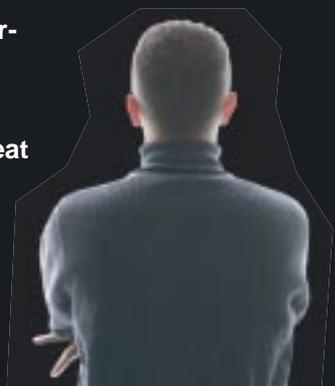
## MAO inhibitors

MAO inhibitors were discovered by accident while treating patients with tuberculosis in the 1950s. Not surprisingly, patients with this life-threatening disease tended to be depressed. One of the antituberculosis drugs doctors tried in those days didn't help the tuberculosis much, but it seemed to improve the mood of these patients. This drug was later found to inhibit the enzyme monoamine oxidase.



**On October 15, 2004, the Food and Drug Administration (FDA) directed the manufacturers of all antidepressant medications to add a “black box” warning that describes the increased risk of suicide in children and adolescents given antidepressant medications and notes what uses the drugs have been approved or not approved for in these patients.**

**Prozac is currently the only medication approved to treat depression in children and adolescents.**



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They react with the enzyme in place of the serotonin and tie up the enzyme, more or less permanently, so that the serotonin levels can gradually increase, decreasing the depression.

One of the problems with this group of drugs is a potentially life-threatening side effect for patients taking MAO inhibitors who eat too much food containing another chemical called tyramine.

Tyramine is found in beer, aged cheese, wine, dried meats and fish, fermented foods (sauerkraut or yogurt), and chocolate. Normally, these foods are not a problem because MAO in your intestines converts the tyramine to harmless molecules. But if you are taking a drug that inhibits MAO, then the tyramine can build up, which causes the body to secrete more noradrenaline, causing an increase in blood pressure. Mild symptoms of tyramine buildup may include headaches; more severe reactions involve liver, kidney, and heart damage; and super high spikes in blood pressure can result in brain hemorrhage and death!

This side effect can be prevented by following a careful diet, but some patients find the diet too restrictive (No chocolate?!) Other side

effects of MAO inhibitors include dizziness and nausea, but these usually go away after awhile. MAO inhibitors also interfere with many other medicines, so doctors monitor these patients very carefully.

More recent research shows that there are actually two kinds of MAO enzymes, cleverly named MAO-A and MAO-B. MAO-B is found in the peripheral nervous system and is involved in tyramine digestion in the intestines. MAO-A is the enzyme in the brain that reacts with serotonin, and early studies indicate that chemicals that inhibit MAO-A but not MAO-B do not produce a “cheese effect” when patients eat the wrong foods, making them safer and more effective.

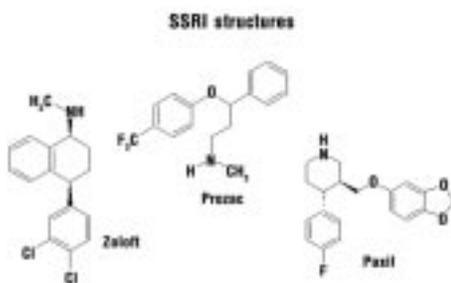
## Serotonin reuptake inhibitors

A newer class of effective antidepressants works by slowing down the reuptake of serotonin into the cell. The first of these was Prozac, and subsequent similar compounds



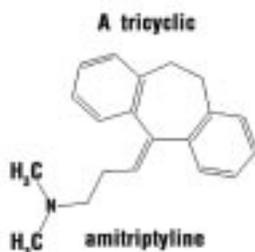
ARTVILLE

include Paxil, Zoloft, and others. This class of chemicals inhibits the “reuptake” of serotonin, meaning that the serotonin does not get reabsorbed as easily by the cell, and thus, levels outside the cell gradually increase.



**Serotonin and the SSRIs are remarkably similar in structure.**

The SSRIs have revolutionized treatment of depression in that they tend to have many fewer side effects than the MAO inhibitors, and often, these side effects go away over time. There is a vast assortment of these medicines, many of which have variations in their specific activity, so that they can be used to



treat a variety of associated disorders, such as obsessive-compulsive disorders, anxiety disorders, seasonal affective disorders, or eating disorders (anorexia, bulimia). In extreme cases, doctors will prescribe combinations of MAO inhibitors and SSRIs.

There is a third class of drugs that have historically been prescribed to treat depression: the “tricyclics”. Tricyclics have three rings (hence, the name), with six-seven-six atoms in each ring and various other atoms hanging off in different directions. They were discovered through a combination of luck and observation. This third class of drugs also blocks reuptake of serotonin, but they are thought to do it in a different way because they also block the reuptake of other neurotransmitters. Tricyclics tend to have more pronounced side effects than the other SSRIs, affecting heart rate and blood pressure and causing weight gain and drowsiness, but are very effective in some groups of patients that don’t respond well to the newer class of SSRIs. Tricyclics can also be used to treat the related conditions mentioned above.

## Teenage depression

Most of you reading this article are teenagers, so we should mention a bit about how difficult it is to treat teenage depression. Because teenagers’ bodies are changing and growing so rapidly, it is especially difficult to treat depression in this age group. Some of the SSRI drugs, for example, have been linked to increased occurrence of suicide or self-destructive behaviors in children and teenage patients. Many doctors try to avoid prescrib-

ing these drugs to teens because their brains continue to grow and develop until the age of at least 20.

By the way, both exercise and diet can affect serotonin levels in the brain. Because serotonin is synthesized in the body from the amino acid tryptophan, eating a meal that is high in carbohydrates and protein containing tryptophan (say turkey and mashed potatoes) can result in a feeling of sleepiness and well-being due to increased serotonin. Similarly, vigorous exercise raises brain serotonin levels, although it is not really understood how or why. So the next time you are feeling a little low, consider eating some carbohydrates and protein (say milk and cookies) and head out for a brisk walk. 🏃

**If you feel a little low, try vigorous exercise to raise serotonin levels.**



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**February 2005 Teacher's Guide**

**"More than Blue"**

## Puzzle: Missing Letter

Here are four groups of words used often by chemists . Each group has something in common. Some letters are given for each word; the letters that fill in the remaining blanks are also used in the category name ( perhaps more than once). Your task for each group is twofold: determine each word and determine the theme phrase. You'll be able to go back and forth as you proceed.

For example, suppose the category is \_\_\_\_\_ and three of the clues are  
M \_ \_ C \_ B \_ E , D \_ \_ \_ \_ E, and \_ \_ \_ V E \_ \_ .

A little thought generates the words MISCIBLE, DILUTE, and SOLVENT and the category phrase SOLUTIONS can be made from the underlined letters.

Note that seeing the letter M in clue 1 means that the category type does NOT contain an M in its spelling and that the seven different letters that make up the word **SOLUTIONS** are to be found in the BLANKS of the clues.

### Completing all four makes you a super missing-letter sleuth !

1. Category : \_ . \_ . \_ \_ \_ \_ \_ 2. Category: \_ \_ \_ \_ \_ \_ \_ \_

K E L V \_ \_ \_  
\_ \_ E C O \_ \_ D  
J O \_ \_ L E  
W A \_ \_ \_  
C \_ \_ B \_ \_ C M E \_ \_ E R

B O Y \_ \_ E  
\_ \_ \_ Y - \_ \_ U \_ \_ \_ \_ C  
C H \_ \_ R \_ \_ E \_ \_  
\_ \_ R \_ \_ H \_ \_ M  
\_ \_ V O \_ \_ \_ D R O

3. Category : \_ \_ \_ \_ \_ \_ \_

V \_ \_ L T A G \_ \_  
\_ \_ \_ \_ \_ U C T I \_ \_ N  
\_ \_ \_ I \_ \_ I Z \_ \_  
C \_ \_ L L  
A N \_ \_ \_ \_ \_

4. Category: \_ \_ \_ \_ \_ \_ \_ \_

C \_ \_ V A L E \_ \_ T  
\_ \_ \_ \_ \_ C  
\_ \_ \_ P \_ \_ L E  
\_ \_ R \_ \_ \_ T A L  
S \_ \_ \_ M A

## Puzzle Answers

### 1. S.I. UNITS

Kelvin  
Second  
Joule  
Watt  
Cubic meter

### 2. GAS LAWS

Boyle  
Gay-Lussac  
Charles  
Graham  
Avogadro

### 3. REDOX

Voltage  
Reduction  
Oxidize  
Cell  
Anode

### 4. BONDING

Covalent  
Ionic  
Dipole  
Orbital  
Sigma

# Student Questions

## More Than Blue

1. What are the main features that distinguish clinical depression from the normal “blues” that everyone experiences from time to time?
2. What are neurotransmitters, and how do they function?
3. What neurotransmitter is involved in depression, and how is it affected?
4. How is serotonin produced in the body, and what happens to it?
5. What are the two most common types of drugs used to treat depression, and how do they function, in general?
6. What is one advantage that SSRIs have over MAO inhibitors?
7. What “black box” warning has the FDA recently directed manufacturers of all antidepressant medications to add to their products?

## The Great Hartford Circus Fire

1. Using chemical principles, explain why a mixture of paraffin and gasoline would make an excellent (although flammable) waterproofing material.
2. What is meant by the term “flash point?”
3. Why won't paraffin ignite if touched by a lit cigarette or match, but a mixture of paraffin dissolved in gasoline will?
4. Explain how soap can allow a nonpolar substance like oil to be suspended in a polar substance like water.
5. How do the sizes of the particles in a colloid differ from the particles in a true solution? Can colloidal particles be seen with an optical microscope?

## The Silent Killer

1. What kinds of conditions typically result in the production of carbon monoxide?
2. What are typical levels of carbon monoxide in a home with properly adjusted gas stoves? At what level do most people begin to experience symptoms of carbon monoxide poisoning? What standards have been established for carbon monoxide levels for indoor air and outdoor air?
3. Explain how an electrochemical carbon monoxide detector works.
4. Explain why carbon monoxide is so toxic.

5. Why didn't the mother suffer from carbon monoxide poisoning even though she was breathing the same air as the rest of her family and the baby inside her was suffering from carbon monoxide exposure?
6. What is the standard therapy for carbon monoxide exposure? How rapidly can the levels of carboxyhemoglobin in the affected person's blood be expected to decrease?
7. How does a hyperbaric oxygen chamber work to help victims of carbon monoxide poisoning recover?

## Water of Life

1. Explain why the fact that ice is less dense than water may be a critical property for living things.
2. How does the boiling point of  $\text{H}_2\text{O}$  compare to that of similar compounds  $\text{H}_2\text{S}$  and  $\text{H}_2\text{Se}$ ? What accounts for this unusual property?
3. How does water affect the folding patterns of proteins?
4. Explain how the properties of water are critical to the construction of cell membranes.
5. What are some arguments that ammonia,  $\text{NH}_3$ , might possibly be able to function as the basis for a life system in a manner similar to the way that  $\text{H}_2\text{O}$  functions as the basis for ours?
6. What are some arguments that  $\text{NH}_3$  probably would not be able to function as the basis for a life system?
7. Why might alien beings find it inconceivable that a life form could exist in an atmosphere that contained significant concentrations of oxygen?

## Question from the Classroom

1. Where does most of the heat and light given off by a burning candle come from?
2. What is candle wax actually made of?
3. Describe the process that occurs when a candle is burning.

Describe four different purposes achieved by the flame.

What is meant by the “flash point” of a substance?

Explain why a lit match that is brought close to a container of liquid pentane will immediately ignite the pentane, but the same thing will not happen if it is brought close to a container of candle wax.

How could you ignite candle wax without using a wick?

# Student Question Answers

## More Than Blue

1. What are the main features that distinguish clinical depression from the normal “blues” that everyone experiences from time to time?

Clinical depression is diagnosed when a person either loses or has no interest in usual activities and takes no pleasure in them. It is characterized by feeling worthless or helpless, being indecisive, or lacking motivation to complete even simple tasks, such as dressing or eating. People suffering from depression may have difficulty sleeping or may sleep constantly, and their appetite may be affected. Depressed individuals can contemplate suicide.

2. What are neurotransmitters, and how do they function?

Neurotransmitters are chemicals that allow brain cells to communicate with each other. Each neurotransmitter binds to a particular receptor site on the outside of the cell and triggers a particular response inside the cell.

3. What neurotransmitter is involved in depression, and how is it affected?

The neurotransmitter serotonin is involved in depression. People suffering from depression have much lower levels of serotonin than nondepressed people.

4. How is serotonin produced in the body, and what happens to it?

Serotonin is produced in the brain from the amino acid tryptophan, which comes from the food you eat. It is released by one nerve cell and triggers a response in another nerve cell. Once this is done, two things occur. First, it is reabsorbed by the cell, either in the brain or through the bloodstream into the liver. Then it is metabolized by an enzyme called monoamine oxidase, or MAO.

5. What are the two most common types of drugs used to treat depression, and how do they function, in general?

The two most common types of drugs are selective serotonin reuptake inhibitors (SSRIs) and MAO inhibitors. The MAO inhibitors work by inhibiting the enzyme monoamine oxidase. They react with the enzyme in place of the serotonin. Since the serotonin is not being destroyed, it can build up in the brain.

The SSRIs work by slowing down the reuptake of serotonin into the cell. Since the serotonin isn't reabsorbed by the cell, levels outside the cell can gradually increase.

6. What is one advantage that SSRIs have over MAO inhibitors?

They have fewer side effects and do not require that the patient follow a special diet that avoids certain foods.

7. What “black box” warning has the FDA recently directed manufacturers of all antidepressant medications to add to their products?

The warning describes the increased risk of suicide in children and adolescents who take antidepressant medications and notes what uses the drugs have been approved or not approved for in these patients.

## Content Reading Guide

<b>National Science Education Content Standard Addressed</b> As a result of activities in grades 9-12, all students should develop understanding	<b>More Than Blue</b>	<b>The Silent Killer</b>	<b>The Great Hartford Circus Fire</b>	<b>Water of Life</b>	<b>Question from the Classroom: Candles</b>
<b>Science as Inquiry Standard A:</b> about scientific inquiry.	✓	✓	✓	✓	✓
<b>Physical Science Standard B:</b> of the structure and properties of matter.	✓	✓	✓	✓	✓
<b>Physical Science Standard B:</b> of chemical reactions.	✓	✓	✓	✓	✓
<b>Physical Science Standard B:</b> of conservation of energy and increase in disorder			✓		✓
<b>Physical Science Standard B:</b> of the interaction of energy and matter.		✓	✓		✓
<b>Life Science Standard C:</b> of the cell.	✓	✓		✓	
<b>Life Science Standard C:</b> of the behavior of organisms.	✓				
<b>Life Science Standard C:</b> of matter, energy, and organization in living systems.		✓		✓	
<b>Science and Technology Standard E:</b> about science and technology.	✓	✓	✓	✓	✓
<b>Science in Personal and Social Perspectives Standard F:</b> of personal and community health.	✓	✓	✓	✓	
<b>Science in Personal and Social Perspectives Standard F:</b> of natural and human-induced hazards.		✓	✓		
<b>Science in Personal and Social Perspectives Standard F:</b> of science and technology in local, national, and global challenges.	✓	✓	✓		
<b>History and Nature of Science Standard G:</b> of science as a human endeavor.	✓	✓	✓		
<b>History and Nature of Science Standard G:</b> of the nature of scientific knowledge.	✓	✓		✓	✓
<b>History and Nature of Science Standard G:</b> of historical perspectives.	✓		✓		

## Anticipation Guides

Anticipation guides help engage students by activating prior knowledge and stimulating student interest before reading. If class time permits, discuss their responses to each statement before reading each article. As they read, students should look for evidence supporting or refuting their initial responses.

**Directions for all Anticipation Guides:** In the first column, write "A" or "D" indicating your agreement or disagreement with each statement. As you read, compare your opinions with information from the article and complete the second column. In the space under each statement, cite information from the article that supports or refutes your original ideas.

### More Than Blue

Me	Text	Statement
		1. Chemical imbalances in the brain are sometimes involved in depression.
		2. Neurotransmitters help brain cells communicate with each other.
		3. Serotonin, a chemical often lacking in brain cells of depressed people, can be taken in pill or capsule form.
		4. Drugs that inhibit the enzyme monoamine oxidase can decrease serotonin levels.
		5. Serotonin levels can be increased by allowing cells to reabsorb serotonin.
		6. Some drugs used to treat depression may increase self-destructive behaviors in teens.
		7. Vigorous exercise and eating carbohydrates and proteins increase brain serotonin levels.

## Reading Strategies

These content frames and organizers are provided to help students locate and analyze information from the articles. Student understanding will be enhanced when they explore and evaluate the information themselves, with input from the teacher if students are struggling. If you use these reading strategies to evaluate student performance, you may want to develop a grading rubric such as the one below.

Score	Description	Evidence
4	Excellent	Complete; details provided; demonstrates deep understanding.
3	Good	Complete; few details provided; demonstrates some understanding.
2	Fair	Incomplete; few details provided; some misconceptions evident.
1	Poor	Very incomplete; no details provided; many misconceptions evident.
0	Not acceptable	So incomplete that no judgment can be made about student understanding

## More Than Blue

Complete the chart below comparing monoamine oxidase (MAO) inhibitors, serotonin reuptake inhibitors (SSRIs), and tricyclics.

	MAO Inhibitors	SSRIs	Tricyclics
How they work			
Side effects			
Structure			

# More Than Blue

## Background Information

### Definition of Clinical Depression

As might be suspected, diagnosing a condition like clinical depression is not as clear cut as diagnosing something like a broken bone, acne, blocked arteries or a specific type of cancer. As the article points out, everyone is depressed at many points in their lives, often for understandable reasons. There is no sharp dividing line between “normal” bouts of temporary depression (the “blues”) and clinical depression. The article doesn’t present a specific definition of clinical depression, but rather states that depression “becomes a problem” when “it interferes with your normal day-to-day activities.” But “becoming a problem” really isn’t an adequate criteria to label something as clinical depression. The loss of a loved one, for example, can often result in a temporary period of grief and depression that would certainly be expected to interfere with normal day-to-day activities but wouldn’t be classified as clinical depression because of its obvious and understandable cause and the reduction in severity with time. People can and do “get over” normal bouts of depression. Most of us probably do it several times over the course of our life.

One accepted definition of clinical depression is: *a state of depression and anhedonia (loss of interest in life) so severe as to require clinical intervention.*

Understandably, the phrase “so severe as to require clinical intervention” will be interpreted differently by different individuals. Nevertheless, it is clear that many people suffer extended bouts of depression whose symptoms are so severe that they become debilitating to the point where clinical intervention is necessary if they are going to have a good chance to recover in a reasonable period of time.

Sometimes clinical depression is defined as depression whose severity reaches levels that meet criteria that are generally accepted by clinicians. Once again, this is somewhat ambiguous, but this may involve a state of depression that lasts more than two weeks and is so severe that it interferes with daily living.

In an effort to shed more light on exactly how clinical depression is diagnosed, I contacted a former student who is now a practicing psychiatrist. The following question was posed:

“Internet sources indicate that clinical depression is defined as ‘a state of depression and anhedonia so severe as to require clinical intervention. But how does one determine when it has reached that state?’”

His response was:

*The formal diagnosis of depression for a psychiatrist has to fulfill criteria laid out in the DSM-IV-TR (Diagnostic and Statistical Manual, Fourth Edition). There are nine potential criteria and a diagnosis of major depression requires five of them present for at least two weeks. One criterion that must be present is either depressed mood or anhedonia. The others are things like appetite changes, changes in sleep, energy, concentration, or suicidal thoughts.*

*Most depression is diagnosed by non-psychiatrists, for example primary care doctors. There it’s more art than science, but does generally rely on the same criteria. A few key factors that usually catch the attention of any doctor are depressed mood, crying, suicidal thoughts, and impairment of function at work or at home.*

*As you may know, a number of more “objective” instruments have been developed to diagnose and monitor the progress of treatment. One commonly used is the Beck Depression Inventory (BDI). The patient answers about 20 questions indicating symptom severity on a 0-3 scale, and the scores are summed. Another common tool is the Hamilton Rating Scale for Depression (HAM-D).*

Approximately 5% of the population of the United States will experience a depressive episode that will require psychopharmacological treatment. A number of studies put the average age of onset in the late 20s. Women are about twice as likely as men to undergo treatment, although this discrepancy is shrinking and is no longer present after menopause. The greatest danger comes from suicide. Some estimates put the suicide rate for patients whose symptoms are severe enough to require hospitalization at about 15%.

### Different subgroups of clinical depression

Clinical depression has been subdivided into a number of subgroups. Included among them are:

*affective disorder, emotional disorder, emotional disturbance, major affective disorder*—these refer to any mental disorder that does not appear to be caused by some detectable organic abnormality of the brain but still involves a major disturbance of emotions.

*agitated depression*—a state of clinical depression marked by significant irritability and restlessness.

*anaclitic depression*—a severe and progressive depression in infants who have lost their mother and for whom no suitable substitute was obtained.

*dysthymia, dysthymic depression*—this refers to mild but chronic depression—a person who seems to always be in a “bad mood” and has been that way for years.

*melancholic depression, endogenous depression*—a state of depression that does not appear to be related to any obvious cause.

*exogenous depression, reactive depression*—a state of depression that has an obvious cause, but the depth and duration of which is more severe than might be considered a normal reaction to the event(s).

*major depressive episode*—a state of depression that has all the classic symptoms, such as anhedonia, lethargy, sleep disturbance, despondency, morbid thoughts, feelings of worthlessness and perhaps even attempted suicide, but for which there is no known organic dysfunction.

*neurotic depression*—a term used for any state of depression that is not psychotic.

*psychotic depression*—a state of depression so severe that the person loses contact with reality and is severely functionally impaired.

*retarded depression*—a state of depression marked by extreme lethargy.

### **What causes depression?**

No specific cause has yet been identified, but a number of different factors appear to play a part. Included among these are:

*Heredity*—there is some evidence that there may be a genetic link to the tendency to suffer from depression.

*Physiology*—Changes or imbalances in chemicals which transmit information in the brain—the neurotransmitters, as discussed in the article.

*Psychological factors*—This includes things such as low self-esteem and/or self-defeating or distorted thinking. There is a cause vs. effect question here, i.e., which came first, the distorted thinking or the depression? But it has been established that sufferers who can correct their thinking patterns can show significant improvement in both their mood and their self-esteem.

*Early experiences*—If one suffers trauma early in life, one is much more likely to suffer from severe depression later in life. Trauma can include things such as the loss of a parent, abandonment or rejection, neglect, chronic illness and severe physical, psychological or sexual abuse.

*Life experiences*—Loss of a spouse or family member, financial difficulties, including the loss of a job, divorce, long term stress, etc.

*Medical conditions*—some medical conditions can contribute to depression. Included are hepatitis and mononucleosis. Some medications such as birth control pills and steroids can also precipitate bouts of depression.

*Alcohol and other drugs*—including tranquilizers, sleeping medications and narcotics.

*Post-partum depression*—About 10% of new mothers experience some form of depression after childbirth. The most common time of onset is about three months after delivery. About 0.2% of new mothers have symptoms so severe that they include hallucinations or delusions.

*Living with a depressed person*—A person living with a depressed person is more likely to become depressed themselves.

### **Treatment of clinical depression**

As the article points out, there is no one way to treat clinical depression. Individuals differ, and their reaction to and the success of any particular treatment scheme will vary. There are two main modes of treatment, medication and psychotherapy, often employed together. Although not mentioned in the article, another treatment alternative involves the use of electroconvulsive therapy.

### **Approaches using medications**

The article does a very good job of presenting the three major kinds of medications used to treat clinical depression, namely the Serotonin Reuptake Inhibitors (SSRIs), MAO inhibitors and the tricyclics.

The use of Selective Serotonin Reuptake Inhibitors (SSRIs), such as fluoxetine (Prozac), paroxetine (Paxil), sertraline (Zoloft) and nefazodone (Serzone) currently constitutes the most commonly used treatment involving medication. As the name suggests, these pharmaceuticals operate by reducing the reuptake of serotonin by nerve cells. This leaves higher serotonin levels in the brain. Since lower levels of serotonin have been connected to depression, raising these levels often leads to a lessening of the condition. One advantage attached to the use of SSRIs in place of other medications is that they typically have fewer side effects than the tricyclics or the MAO inhibitors, although side effects can include drowsiness, dry mouth and decreased sexual performance.

The Monoamine Oxidase Inhibitors (MAOIs) are often prescribed if the use of SSRIs proves to be ineffective. As the article points out, there can be serious side effects if the patient consumes too much food containing tyramine. These potentially serious and possibly fatal side effects have resulted in SSRIs largely replacing the use of MAOIs in the treatment of depression. A new MAOI has recently become available. Moclobemide (Manerix) is classified as a reversible inhibitor of monoamine oxidase A (RIMA). Its use does not demand that the patient follow a special diet.

As pointed out in the article, the oldest group of chemicals used to treat depression are tricyclics such as amitriptyline and desipramine, but their use has decreased because of the more serious side effects attached to their use and the availability of better alternatives. These side effects can include increased heart rate, drowsiness and memory impairment.

There also is a newer group of pharmaceuticals called Selective Norepinephrine Reuptake Inhibitors (SNRIs) such as venlafaxine (Effexor) and reboxetine (Edronax). These work by maintaining a constant level of noradrenaline in the brain while also acting upon serotonin. Fewer side effects have been connected to their use and they appear to have a positive affect on both concentration and motivation. One negative is that discontinuation of the drug appears to be associated with withdrawal symptoms.

Occasionally other types of medications may be used for particular patients. These may include tranquilizers and sedatives, antipsychotics and lithium, but the potential addiction issues as well as several serious possible side effects generally limits their use to treat depression.

### **Psychotherapy**

Psychotherapy is often used in conjunction with medical approaches. The goal is to help the patient both understand the problems that are contributing to his/her condition and then take steps to resolve these problems. Psychotherapy can be done in either a group or individual setting. While only a licensed psychiatrist can prescribe medication, psychotherapy (or counseling) can be administered by a number of different health care professionals such as psychiatrists, psychologists, social workers or psychiatric nurses.

Some of the goals of psychotherapy are to help the patient make changes in his/her thinking patterns, to deal with relationship issues and to gain insight into the factors that are contributing to the depression and learn ways to deal with them. They also help the patient deal with relapses.

Different approaches can be used. *Cognitive therapy* focuses its efforts on how patients think about themselves and their relationships to the rest of the world. It tries to get them to correct negative thought patterns, improve

their self-image, develop better interpersonal skills and reduce stress. *Behavioral therapy* is based on the idea that behaviors are learned. It tries to replace ineffective and destructive behaviors with better and more effective alternatives. *Supportive therapy* focuses on getting people to discuss their problems, and then share information, ideas and strategies for coping while providing emotional support.

### **Electroconvulsive therapy**

As the name suggests, this type of therapy involves subjecting the patient to convulsive electrical shocks. It employs short bursts of carefully controlled electrical current. These bursts induce an artificial epileptic seizure.

Unfortunately, this type of therapy conjures up a very repulsive and negative image in the minds of most people, which may be largely due to the way the therapy was performed and misused in the past as well as its portrayal in movies such as "One Flew over the Cuckoo's Nest."

ECT was first used in the 1930s. During the 1940s and 1950s, ECT was used to treat severe mental illness. It was often administered to severely disturbed patients residing in large mental institutions. And it was often misused. It was administered for a wide variety of illnesses, many of which did not respond to this type of treatment. It was given in large doses and for extended periods of time. In some cases it harmed rather than helped the patient. It was sometimes used to manage and control unruly patients rather than as a form of therapy designed to help them.

The development of effective psychopharmacological medications and the imposition of judicial and regulatory restrictions designed to prevent abuses greatly diminished the use of ECT. Today it is mainly used in psychiatric hospitals or the psychiatric units of general hospitals. Although there is an ongoing debate as to what type of psychiatric disorders it should be used for, there is a growing concern that the curtailment of this type of therapy may be depriving many patients of what might be an effective treatment method.

First, ECT is no longer administered the way it has been portrayed in the movies. The patient is given a general anesthetic and is asleep during the procedure. Then the drug succinylcholine is administered. This drug temporarily paralyzes the muscles, which is a positive thing, since this means that they will not contract during the treatment. In the traditional treatment two electrodes are placed on the patient, one above the temple of the nondominant side of the brain and a second in the middle of the forehead. A current is applied for about one second. The patient's seizure activity is monitored with an electroencephalogram (EEG) while his/her heart rhythm is monitored with an electrocardiogram (EKG). During the procedure the patient is ventilated with pure oxygen. The induced seizure typically lasts about 30 seconds to perhaps slightly over a minute. The patient generally awakens from the anesthesia about 10-15 minutes later. Common side effects upon awakening may include some confusion, headache or muscle stiffness. These generally diminish significantly in about an hour. Because the procedure can sometimes produce an increase in blood pressure and/or temporary heart arrhythmia, patients who suffer from hypertension or cardiovascular problems need to be carefully evaluated before undergoing the procedure.

After initial improvement it is common for patients to relapse, so ECT is often readministered at intervals of perhaps six weeks.

The one major problem associated with this treatment is the potential for persistent memory loss. Although most patients return to normal, a small percentage appear to suffer severe loss.

How distressing is it to the patient? One study interviewed seventy-two patients that had undergone the procedure. While some did find the procedure terrifying and/or shameful and others reported persistent memory loss, the majority spoke positively of the benefits. Among the patients who were interviewed, 54% said that a visit to the dentist was more stressful and 81% stated that they would agree to have the procedure performed again.

Is ECT effective, and if so, for what specific conditions? A report on ECT prepared by the National Institutes of Health (NIH) states that studies that have used various controls for comparison, including "sham" ECT (e.g., all of the elements of the ECT procedure except the electric stimulus), the use of MAOIs, tricyclics and other combinations of antidepressants and placebos have demonstrated the efficacy of ECT in the treatment of delusional and severe endogenous depressions. It does not appear to be effective for patients with milder depressions such as dysthymic disorder.

### **Transcranial magnetic stimulation**

Repetitive transcranial magnetic stimulation (rTMS) is currently being studied as a possible treatment for depression. This technique uses a powerful magnetic field to stimulate the left prefrontal cortex. This area of the brain typically shows abnormal activity in depressed individuals. Preliminary studies appear to indicate that its effectiveness parallels that of ECT, but with fewer side effects.

## Possible Student Misconceptions

There are a great number of misconceptions that students may have about depression and its treatment. The article should dispel many of them. Included may be things such as:

Depression is normal and never requires medical treatment.

Clinical depression is very rare.

Clinical depression is the same thing as “manic-depressive” or bipolar disorder.

Depressed individuals may threaten suicide, but they rarely go through with it.

## Demonstrations and Lessons

1. If your course includes a strong organic component, a careful analysis of the structures and functional groups present in many of the molecules presented in the article could provide either the foundation for a lesson introducing these structural elements and functional groups or an excellent review.
2. There is always an ongoing debate as to whether high creativity is positively connected to mental illness and/or depression. It is easy to have an opinion on the topic and to cite one or two specific examples (Van Gogh always comes to mind), but what is the actual evidence for this view? Many very uncreative individuals suffer from mental illness and/or depression as well. This topic could provide a vehicle for debate designed perhaps not so much to “settle” the question as to analyze the nature of evidence— anecdotal vs. statistical, etc. Such a debate could go far to teach students about the nature and value of different kinds of evidence and argument, especially if students were given an assignment to come prepared for the debate with more than just their opinions.

## Connections to the Chemistry Curriculum

Although this article may not connect as strongly to topics typically included in a high school chemistry course, it does tie in nicely to organic structures and functional groups.

## Suggestions for Student Projects

1. One means of treating depression involves the use of electroconvulsive shocks (see *Background Information*). The way in which this therapy was administered and misused in the past, along with its very negative portrayal in movies such as “One Flew over the Cuckoo’s Nest” has resulted in many people’s rapid and almost reflex rejection of this type of therapy. But the way it is administered today is far different from the way it was administered in the past and the way it has been portrayed in movies. In addition, many studies have shown its effectiveness for some types of depression. Students could prepare and present a report showing how this type of therapy has been portrayed by Hollywood, how it was used and misused in the past, and how the current application differs dramatically, along with a presentation of information relating to some of the studies that support its clinical effectiveness.
2. There has always been an ongoing argument as to whether mental illness and/or depression and creativity are connected. It is certainly true that many creative individuals have suffered from various kinds of mental illness and depression. This issue could be the focus of a couple of different projects. Students could take one specific individual and research both his/her creative achievements and his/her difficulties. Alternately, they could research the arguments and evidence on both sides of the issue.

## Anticipating Student Questions

1. Why don’t people who claim to be suffering from depression just quit feeling sorry for themselves and get on with their lives? I’ve done it, why can’t they?

To quote one Website: (<http://www.free-definition.com/Clinical-depression.html>)

*It is hard for people who have not experienced clinical depression, either personally or by regular exposure to people suffering it, to understand its emotional impact and severity, interpreting it instead as*

*being similar to “having the blues,” or “feeling down.” ..clinical depression is a syndrome of interlocking symptoms which goes far beyond sad or painful feelings. A variety of biological indicators, including measurement of neurotransmitter levels, have shown that there are significant changes in brain chemistry and an overall reduction in brain activity. One consequence of a lack of understanding of its nature is that depressed individuals are often criticized by themselves and others for not making an effort to help themselves. However, the very nature of depression alters the way people think and react to situations to the point where they may become so pessimistic that they can do little or nothing about their condition. Because of this profound and often overwhelmingly negative outlook, it is imperative that the depressed individual seek professional help. Untreated depression is typically characterized by progressively worsening episodes separated by plateaus of temporary stability or remission. If left untreated it will generally resolve within six months to two years although occasionally depression becomes chronic and lasts for many years or indefinitely. Treatment can shorten the period of distress to a matter of weeks. While depressed, the person may damage themselves socially (e.g. the break up of relationships), occupationally (e.g. loss of a job), financially and physically. Treatment of depression can significantly reduce the incidence of this damage, including reducing the risk of suicide which is otherwise a common and tragic outcome. For all of these reasons, treatment of clinical depression is seen by many as very useful and at times life saving.*

2. Is a tendency towards depression inherited?

There does appear to be some individuals whose brain chemistry is predisposed to depression while others appear to be much more resistant, even when they experience the same or similar physical or psychological triggers. Close relatives of people who are bipolar disorder (manic-depressive) are at a higher risk for developing depression than the general population.

3. Are there any other ways to treat depression other than those discussed in the article?

See *Background Information*.

## **Websites for Additional Information and Ideas**

For additional discussion of serotonin:

<http://www.health.uab.edu/show.asp?durki=61541&site=734&return=18687>

For a good general discussion of mood disorders:

<http://www.surgeongeneral.gov/library/mentalhealth/chapter4/sec3.html>