

## **An Update on Treatments and Medications for Manic Depression and Major Depression**

*Summarized by Thomas T. Thomas*

Major depression seems to be more widespread than previously thought. A recent study in *The Menninger Letter* (October 1994) found that, in a nationwide sample of 8,000 people, 5 percent had experienced depression within the last 30 days, and 17 percent had experienced an episode of major depression at some time in their life. Depression can have effects that are worse than some chronic medical conditions.

The speaker at our January 24 meeting, **Thomas Morrissey, MD**, Medical Director of the Garfield Mental Health Center, explained the new treatments and medications now being used to combat this crippling emotional state.

Dr. Morrissey made a distinction between two mood disorders: manic depression (now often called bipolar disorder) and major depression. The former is characterized by an onset in the late teens or early twenties, with a high risk of occurrence up until the mid-thirties. Major depression, even a first occurrence, can strike at any time in a person's life.

In manic depression, the period between episodes usually gets shorter: starting about three years apart, then two, then one. Approximately 45 percent of sufferers eventually enter what is called "rapid cycling," experiencing four or more episodes a year. This occurs mostly in women and may be related to alcohol use. With manic depression, recurrence is the rule not the exception, and a person remains at risk for episodes up until the eighties.

The treatment for acute episodes of mania—the elevated portion of the disorder, which may be marked by rage and violence as well as by euphoria— involves getting the sufferer into a quiet environment with reduced stimulation. The first line of medication is antipsychotics such as Haldol or Thorazine instead of lithium, which only takes effect over a period up to ten days. Other useful medications for acute episodes are sedatives or tranquilizers.

The mainstay treatment for long-term maintenance of bipolar disorder is lithium, which is used following an acute episode and is more effective against mania than depression. Lithium is hard to take, because it causes side effects in 30 to 35 percent of users, who experience nervous tremors, trouble in thinking and concentrating, memory loss, or weight gain. Some people take years to accept the drug and stay on its regimen, even though it does curb their illness.

Strategies for reducing lithium's side effects include taking smaller doses several times a day, which lowers the peak in blood level, or taking it with food. Some experiments have tried lowering the overall blood level from the ideal range of 1.0 to 0.75 down to 0.5. This can work, but the risk of relapse is high.

A popular alternative medication, for use alone or in combination with lithium, is carbamazepine (trade name Tegretol). This was originally an anticonvulsant for use in epilepsy. It has side effects such as nausea, rash (in 10

percent of cases), drowsiness, dizziness, and a mild decrease in white blood cells. In rare cases, Tegretol can cause hepatitis, so users must have regular tests of their liver function.

Another anti-mania medication is valproic acid (Depakote or Depakene), which is an anticonvulsant with side effects similar to Tegretol, including the potential for liver damage. Studies have shown this drug to be about twice as effective as the placebo (that is, no drug at all), and there is no evidence that either of these newer drugs have any long-term benefit, while lithium has years of proven effectiveness.

Other medications used to treat mania include:

- Propranolol—a hypertension medication, used with lithium to treat tremors.
- Lecithin—a type of fat found in the brain and used as a food supplement.
- Verapamil—another blood pressure medication.
- Clonazepam—a tranquilizer and anticonvulsant used to treat acute episodes.

Most of these newer drugs have been used in a last-ditch effort to treat patients who cannot tolerate lithium or the other medications.

Treatment for major depression falls into three main categories: electroconvulsant therapy (ECT, sometimes called “shock treatment”), psychotherapy, and medication.

ECT is still the gold standard, having proven to be the most effective way to treat severe incapacitating depression. It is safer than many of the antidepressant drugs, especially for pregnant women. However, it is not commonly used because of the controversy and stigma surrounding it, although nowadays patients receive a muscle blocker so that their bodies remain calm and nonconvulsed while the electric current works on their brains.

Psychotherapy is an important part of any treatment for depression. There are two basic types:

- **Cognitive therapy** works with thoughts and feelings which may be caused by negative views. The therapist challenges these ideas and tries to recast them in a positive light.
- **Interpersonal therapy** focuses on the here and now, working on the patient’s relationships in marriage, family, and work. The therapist helps the patient to strategize responses that will lead to a more positive outcome.

Either course of therapy is better than the placebo, and the approaches may work better together than either does alone.

Of the many types of medications to treat depression, all seem to be about equally effective. In fact, depression is such a loosely defined syndrome, Dr. Morrissey said, that it is hard to prove that the antidepressants work at all. In choosing one drug over another, patients should consider ones they have taken before and found effective, or whether someone in the family has taken the drug successfully (because there may be a genetic component to the disorder).

For any of these drugs to work, the patient needs to take an adequate dose and stay on it long enough, usually six weeks, to show its effectiveness. Most drugs fail because patients take too little or quit too soon because of side effects. Other reasons for ineffectiveness include alcohol and drug abuse or a concurrent medical illness. The point is to get up to the recommended dose of an antidepressant as

quickly as possible. If the patient shows no effect after six weeks, then increase the dose.

Dr. Morrissey cited some myths about antidepressants. One is that, once the depression is treated, the patient only needs to keep up the dose for six months. This is too short a time. To prevent a relapse, one needs to keep using the drug for at least a year. If depressive episodes came less than two years apart, the recommended maintenance period is five years. Another myth is that once the treatment works, the prescribing physician should cut the dose in half. No, Dr. Morrissey said, the dose should stay at full strength.

If the medication helps only a little bit, then the doctor can try several strategies, such as adding lithium (even in cases without mania); adding thyroid hormone, which has a big effect on mood; or adding Tegretol or valproic acid.

Antidepressants come in several broad classes, upon which Dr. Morrissey commented briefly, noting their side effects. One strategy that does *not* seem to be effective, he said, is switching between drugs within the same class, because they all work in more or less the same way.

The first class comprises the tertiary amine and secondary amine *tricyclics*. The tertiaries are older, including amitriptyline (Elavil), imipramine (Tofranil), and doxepin (Sinequan). The secondaries are newer, including nortriptyline (Pamelor, Aventyl), desipramine (Norpramin), and protriptyline (Vivactil). The secondaries are better tolerated, with fewer side effects such as drowsiness, dry mouth, and constipation.

Next is the class of *heterocyclics*, such as amoxapine (Ascendin) and maprotiline (Ludiomil). These are used to treat delusions and hallucinations.

The third class is the *monoamine oxidase inhibitors*, including isocarboxazid (Marplan), phenylzine (Nardil), tranylcypromine (Parnate), and Deprenyl. These are used against atypical depressions, characterized by sleeping too much instead of insomnia, eating too much instead of appetite loss, or hypersensitivity in relationships instead of apathy. Common side effects are weight gain and postural hypertension, which means loss of blood pressure—to the point of passing out—when the patient stands up.

The last class of antidepressants is the *serotonergics*, including trazodone (Desyrel), fluoxetine (Prozac), bupropion (Wellbutrin), sertraline (Zoloft), paroxetine (Paxil), fluvoxamine (Luvox), nefazodone (Serzone), and venlafaxine (Effexor). These drugs are so new that there are no studies to compare one against the other, although all seem to be better than the placebo. The choice among them is mainly in their side effects:

- Luvox and Paxil can cause drowsiness.
- Prozac and Zoloft can cause insomnia.
- Zoloft, Paxil, and Luvox seem to cause less appetite and anxiety disorders than Prozac, but they can cause more dry mouth and constipation.
- Serzone can cause headaches, dizziness, nausea, and drowsiness.
- Trazodone can cause a painful erection in men, called priapism.
- Wellbutrin can cause a sustained elevation in the diastolic (lower number) blood pressure.

The good news is that, of up to ten listed side effects for each drug, the average person experiences only one or two.

The major difference among these newer class of antidepressants is that, while most are flushed from the body four or five days after the patient stops taking them, Prozac usually lingers for weeks. Their cost is comparable; that is, the average dose will cost \$55 to \$65 per month on a wholesale basis. In his conclusion, Dr. Morrissey suggested that someone suffering a severe depression should usually try the more established drugs, if tolerated, and wait for the newer medications to prove themselves.