DEPRESSION & MANIC-DEPRESSION

SOURCE: WHEN TREATMENT FAILS

Medical advances over the last three decades have made it possible to help most people suffering from depression and manic depression (unipolar and bipolar disorders). However, no single treatment can be expected to help everyone. Different individuals may require different medications or combinations of therapies to achieve relief. As many as 20 percent of those with mood disorders do not respond to the first treatment tried.

That is why managing depression or manic-depression is a life-long process -- one in which you, as the patient, must actively participate. The more you know about your illness and participate in the treatment, the more successful your results may be.

This information discusses the various treatments available for depression and manic depression and helps explain treatment resistance. It also points out the value of carefully tracking your medications and your response to each.

What is Treatment Resistance?

Treatment resistance is a lack of satisfactory response to treatment over a period, often after several approaches have been tried. The potential reasons a medication may fail or appear to fail are quite varied, and can include any of the following:

- **Side effects** - Most medications used for treating mood disorders have side effects. Sometimes these reach intolerable levels and the drug regimen must be altered. In many cases, however, another drug can be used to block the unwanted effect, or a small dosage adjustment will reduce the side effect to a tolerable level. These decisions must be made jointly by you and your physician. You should not discontinue your medication without consulting your physician first.

- **Inadequate time** - Often a treatment may appear to have failed when, in reality, it hasn't had time to take effect. Most treatments for mood disorders require at least two to four weeks before noticeable results appear. Therefore, when beginning a new medication, you should be patient and give the medication time to do its job.

- **Insufficient dose** - For most medications used to treat mood disorders, the actual amount reaching the brain following a given dose will vary widely from one individual to another. Since a medication must reach the brain to be effective, doses that produce inadequate levels may falsely suggest that the medication has failed.

- **Non-compliance** - A medication may fail because it is not taken regularly. This lack of compliance may be a consequence of the disease. For example, mania's characteristic confusion and distractibility may cause scheduled doses to be forgotten. Conversely, a depressed patient may think, "What's the use?" and discontinue medication.

- **Other medical conditions** - Sometimes a medication may truly fail but for reasons unrelated to your fundamental illness. Medical conditions as varied as hypothyroidism, chronic fatigue syndrome, and brain injury can lead to depression or mania and limit the effectiveness of medications used to treat mood disorders.

- **Adverse drug interactions** - Medications used to treat other illnesses may interfere with treatment of your depression or manic-depression. For example, some medications may decrease the amounts of mood-stabilizing drugs in the blood stream, possibly preventing them from reaching effective levels. Others, ranging from beta-blockers to arthritis drugs, may directly render antidepressant or antimanic drugs less effective in treating your symptoms.

- **Substance abuse** - Drug or alcohol abuse is another factor that may cause medical treatment of depression or manic-depression to be ineffective. For example, alcohol reduces the effectiveness of certain antidepressants.

- **Non-response** - Response to any medication, and especially those for treating depressive and manic-depressive illnesses, is highly individual. In any instance, a certain proportion of treated patients will fail to respond. If you are one of these patients, however, do not give up hope as there are multiple alternative treatment strategies. Even if several have already failed, one of those remaining is likely to prove successful.

Treatments for Unipolar Mood Illness (Depression)

- **Tricyclic Antidepressants.** Most patients with unipolar disorder are initially treated with tricyclic and related antidepressants. These are sold under various brand names such as Tofranil (imipramine), Elavil (amitriptyline), Trazadone (Desyrel), and Pamelor (nortriptyline).

- **Selective Serotonin Reuptake Inhibitors (SSR/s).** A newer group of medications, often used similarly to the tricylics, includes Prozac (fluoxetine) and Wellbutrin (bupropion). Patients often find these have a more favorable side effect profile.

- **Monoamine Oxidase Inhibitors (MAOIs).** Most physicians will try two or three of the tricyclic-related antidepressants before switching to another class of drugs. This may be a different type of antidepressant known as monoamine oxidase inhibitors, or MAOis. MAOis are likely to prove helpful as the more usual antidepressants. However, patients on these medications must avoid certain foods that, in combination with the MAOI, can produce very high blood pressure levels.

- **Potentiators.** An alternative strategy is combination therapy involving a 'potentiator' -- a compound that, while rarely useful by itself, often seems to render other medications more effective. Potentiators may be used with either tricyclic-related antidepressants or MAOis; the most common examples are lithium and thyroid hormone. Your physician can

explain how these might fit into the treatment of your disease.

Treatments For Bipolar (Manic-Depressive) Disorder

In thinking about manic-depressive disorder, it is important to understand that mania and depression are not two different diseases that can be addressed in isolation. Rather, they are two different aspects of the same illness. Thus, any truly effective treatment for the disease must address both aspects simultaneously.

Lithium. At the time of diagnosis, a manic-depressive patient is typically in either a manic or a depressive phase. The traditional treatment -- lithium -- will gradually bring most manic patients down to a normal mood level and may help lift the mood of those initially depressed. If you are initially depressed, you may need short-term treatment with an antidepressant. In bipolar patients, however, all these medications have been known to include manic episodes. There is also evidence that antidepressants can increase the frequency of mood swings and thus render lithium treatment more likely to fail.

While lithium is usually effective in relieving acute manic episodes, it does so relatively slowly. When severe symptoms require rapid relief, neuroleptics have traditionally been used and more recently, benzodiazepines have also proven helpful. Use of either is typically discontinued after the patient is stabilized.

Once a normal mood has been achieved, lithium will often prevent the recurrence of depressive as well as manic phases of the illness. Nevertheless, anywhere from 20 to 40 percent of patients treated with lithium will either not be able to tolerate its side effects or will not show satisfactory improvement. In many cases, this inadequate improvement will reflect repeated breakthrough depressive or manic episodes.

As with antidepressants for unipolar disorder, there is no effective way to predict which bipolar patient will fail to benefit from lithium. Certain characteristics do suggest patients who are less likely than others to benefit from the drug. Even among these patients, however, the number who will benefit is great enough to make lithium the typical choice for a first therapeutic trial. As well, anticonvulsants are increasingly being used in these instances.

Other Mood Stabilizers. When lithium fails, the major alternatives are Depakote (valproate) and Tegretol (carbamazepine). Both these drugs are marketed primarily as anticonvulsants for the treatment of seizure disorders (i.e., epilepsy), but recent research suggests they help certain manic-depressive patients as well. This usefulness in manic depressive disorder, however, appears to be unconnected to their common identity as anticonvulsants. Not only do the manic-depressive patients benefit, they typically show no sign of any convulsive disorder, but some other drugs effective as anticonvulsants provide no help at all in bipolar illness. What's more, response to one anticonvulsant is not predictive of response to another.

Recent research suggests the anticonvulsants may bring acute manic episodes under control more rapidly than lithium. The benefit is usually noticeable

within one or two weeks, in comparison to the two to four weeks typical of lithium. The most apparent drawback to these medications is that they may provide greater benefit in acute mania than in depression.

The rapid relief provided by anticonvulsants may reduce or eliminate the need for neuroleptics as supplemental short-term therapy. Since anticonvulsants, unlike neuroleptics, are suitable for long-term maintenance treatment, a patient's acute response provides information about appropriate maintenance therapy, which is lost when neuroleptics are employed instead. Even if you are not helped by lithium or by anticonvulsants alone, you may benefit when the two drug types are used together. In some cases, your physician may simply add one of the anticonvulsants to your on-going lithium therapy, without first trying it as a single-drug treatment.

Electro Convulsive Therapy

Although medications represent the foundation for today's approach to therapy of mood illnesses, electroconvulsive therapy (ECT) may play a significant role in treatment of some cases. ECT involves inducing a controlled seizure while a patient is under anesthesia.

Although this may sound frightening, the positive effects are well demonstrated and the side effects quite mild. More significantly, the effectiveness of ECT in extreme cases of both depression and mania makes it the best choice for many such individuals.

Psychotherapy

Evidence has shown that short-term psychotherapy, when used alone or in combination with pharmacological treatment, is an effective treatment for depression, especially in less severe cases. Some therapists utilize cognitive therapy, which seeks to normalize the patient's overly negative view of the world. Other therapists utilize interpersonal therapy to assist you in improving personal relationships. Once the acute episode is over, long term psychotherapy can help maintain stability and prevent further episodes.

Maintaining Stability

Both unipolar and bipolar mood disorders are recurrent diseases. If one episode occurs, it will probably be followed by others. Your course of treatment will depend on your personal circumstances. More and more physicians, however, are coming to believe that mood disorders should be managed with continuous medication -- if not after the first episode, then certainly after the second or third.

Typically, the medication that relieved your acute episode will be used for maintenance therapy. Many physicians prescribe a lower dose for maintenance therapy, while others favor continuing the dose already proven effective if it is tolerated.

Even when medication is used continuously, an occasional episode may break through this protective shield. While distressing, this does not mean maintenance therapy will fail to help in the future. If episodes become frequent or severe, however, then an alternative therapy should be sought.

What can you do?

As the patient, you can often help in this endeavor. No one knows better than you the symptoms and the side effects that you are experiencing. If you record these effects daily, along with the medication being taken, your diary can provide extremely valuable guidance in further medication choices. With this detailed record of responses to medications, your physician can avoid repeated trials of medications, which have already proven ineffective or impossible to tolerate.

What's more, you and your family need not feel you must deal with your illness alone. Patients and family members have come together to form groups for education, advocacy, and mutual aid. Many of these groups are usually associated with a local mood disorders association. Through contact with support groups, you and members of your family can gain information about your illness and support from those who understand what these diseases mean to everyday life.

No one can discount the difficulties that accompany depressive and manic-depressive illness. Today there are multiple and sophisticated treatments available. If one approach is not successful, others should be sought. With continued research, new medicines and approaches will be developed -- approaches that should enhance both acute and long-term treatment for these illnesses.

"Treat it - Defeat it."