

What happens if a person presents with both anxiety and depression? Or, as it often happens as the depression is treated, which was the primary presenting problem masking the anxiety, the anxiety is revealed? What do you do then? Attached is a nice, somewhat clinical, but good explanation of treatment options from a medical perspective. Added to a therapeutic approach this approach may have some interesting outcomes.

### ***Helping Hearts Heal***

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#### Expert Column in Depression

Anxiety Symptoms and Treating Depression

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## **Introduction and Clinical Tools**

### **Introduction**

Over the past 10-15 years, the pharmacologic treatment of depression has been greatly advanced, with the introduction of many new medications that have achieved much wider use. However, a variety of problems continue to exist. Many patients do not respond to first-choice treatments, which are usually selective serotonin reuptake inhibitors (SSRIs), and there are no clear guidelines as to what to do next for such patients. Further, substantial portions of the patients who do benefit from the SSRIs do not achieve full remission, and here also guidelines are lacking as to what to do next. Finally, many depressed patients manifest substantial anxiety symptoms as well; here again, guidelines are lacking as to how these anxiety features should influence treatment selection.

### **Clinical Tools**

Unfortunately, at present, psychiatry lacks many of the diagnostic techniques that have advanced the precision of treatment selection in other fields of medicine, such as blood tests, x-rays and other imaging techniques, biopsies, and cultures. Instead, we must rely on clinical presentation and histories of the patient's illness, their prior treatment response, and family illness and treatment response to guide medication selection. While this approach is far from perfect even in the most expert of hands, there are a number of clinical markers that can enhance treatment selection that are not yet widely employed.

## Diagnostic Clarity

Most clinicians are aware of the need to distinguish between bipolar and unipolar disorders when evaluating a depressed patient. However, the evaluation of bipolarity is usually confined to trying to detect a history of bipolar 1 (full mania alternating with depression) or bipolar 2 (hypomania alternating with depression) disorders. Less often is the full bipolar spectrum explored, including extended prior periods of productive high energy that may signal vulnerability to antidepressant-induced mood cycling. This manifests itself clinically as responses to antidepressants that are not sustained, as patients cycle from well to depressed, and back to well again, on a given antidepressant.<sup>[1]</sup> It must be distinguished from antidepressant "poop out," where the positive effects of a drug are lost and not regained. Many clinicians confuse the two and mistakenly treat antidepressant-induced cycling with additional antidepressants or switches to other drugs with similar mechanisms, which does not rectify the situation. The optimal response in such situations is to see if the patient can be treated without antidepressants; if not, then efforts must be made to use mood-enhancing agents that do not induce cycling, such as lithium or lamotrigine.

Turning to the unipolar depression spectrum, there are a number of useful distinctions that can be made that will enhance a clinician's ability to get good effects with the first antidepressant chosen.

## Distinguishing Subtype

The first distinction I try to make once I am sure that we are in the unipolar spectrum is whether the patient is suffering from the melancholic subtype of depression. If the patient has appetite loss, middle or terminal insomnia, diurnal variation (worse in the AM), and complete or near complete anhedonia (loss of capacity for joy or pleasure), then he/she meets criteria for melancholia.<sup>[2]</sup> Such patients do better, I believe, with dual serotonergic-noradrenergic reuptake inhibitors (SNRIs) than they do with SSRIs. Examples of SNRIs are the older tricyclic antidepressants, extended-release venlafaxine, and the still investigational drug duloxetine. I have seen many melancholically depressed patients who showed poor responses to an SSRI do very well when changed to extended-release venlafaxine or augmented with a tricyclic antidepressant. Unfortunately, before coming to me, some of these patients had already been switched from one SSRI to another by other clinicians, greatly delaying the onset of symptom relief. For the unipolar patients with nonmelancholic symptoms, I have not seen strong evidence of a differential response to SSRIs vs SNRIs.

One treatment-relevant subtype of nonmelancholic depression is atypical depression, characterized in DSM-IV by mood reactivity (retention of the ability to be temporarily cheered by pleasant events) and 2 or more of the features of overeating, oversleeping, feelings of leaden fatigue, and extreme sensitivity to rejection or criticism.<sup>[2]</sup> Such patients were found to respond better to monoamine oxidase inhibitors (MAOIs) than to tricyclic antidepressants,<sup>[3]</sup> but have not been well studied with regard to their responses to SSRIs or SNRIs. Drugs that enhance dopaminergic activity seem especially useful in

this population, either as monotherapy (eg, MAOIs) or more commonly in conjunction with SSRIs or SNRIs (eg, bupropion, amphetamines, or other dopaminergic agonists).

## **Depression Plus Anxiety**

Many unipolar depressed patients present with considerable anxiety symptomatology, and data exist to suggest that these patients are harder to treat successfully and have higher suicide rates than depressed patients who are not highly anxious as well.<sup>[4]</sup> In terms of evaluating the anxiety symptoms, it is useful to distinguish between an earlier-onset anxiety condition such as panic, posttraumatic stress, social anxiety, generalized anxiety, or obsessive compulsive disorder and anxiety symptoms stemming directly from the depression. In either case, selection of an antidepressant with proven antianxiety efficacy is sensible. The proven efficacy of SNRIs like venlafaxine and several of the SSRIs for one or more anxiety disorders adds, I believe, to their usefulness in unipolar depression with prominent anxiety symptomatology. For depressed patients who are highly anxious, it is useful to add a benzodiazepine as initial adjunctive therapy to provide symptom relief for the first several weeks until the antidepressant begins to have significant effects.

The time course of response of the various symptom constellations in patients with depression and a comorbid anxiety disorder is interesting to consider, and has not, in my estimation, been studied sufficiently. My colleagues and I conducted one open trial of patients with social anxiety disorder with comorbid major depression using an SSRI.<sup>[5]</sup> We considered the major depressions to be secondary to the more longstanding social phobias in these patients. Therefore, we expected that the social anxiety disorder would improve first, followed by the depressive symptoms. However, contrary to our expectations, the patient group showed a very significant drop in depression ratings over the first 4 weeks, while a meaningful drop in social anxiety symptoms took about 8 weeks to emerge. Thus, in these comorbid states, each condition responded in a manner similar to what is seen when it occurs alone. The clinical lessons we learned were twofold: first, depression comorbid with even a chronic anxiety disorder can respond even before the anxiety disorder is significantly improved. Second: longer medication treatment is required for amelioration of some of the anxiety disorders that are frequently comorbid with major depression. While our study illustrated this for social anxiety disorder, it is probably true for obsessive-compulsive disorder and posttraumatic stress disorder as well, since these conditions have also been shown to typically require longer treatment periods than major depression before showing significant improvement.

Some unipolar depressed patients present with agitated depression, a very serious and fairly common clinical picture colloquially known as a "nervous breakdown." These patients are almost always melancholic. In addition to their anhedonia, insomnia, and loss of appetite, they show psychomotor activation in the form of pacing, rubbing their hands together, and/or a feeling that they are "jumping out of their skin." SNRIs are the treatment of choice for such patients, augmented initially with antianxiety drugs like a benzodiazepine, or even more usefully, low doses of atypical neuroleptics. The augmenting agents help bring about quick relief of the extreme agitation, and can usually

be tapered after several weeks when the antidepressant begins to have significant effects. It is very important to recognize and effectively treat agitated depressions because of the extreme distress and incapacitation they engender.

## Conclusion

Unfortunately, many of the issues tackled above, while of great import to clinicians and patients, have not received systematic research attention. There are multiple reasons for this. Some of them are hard to study, and some of them have not been of interest to federal or pharmaceutical industry funding sources. The data to support the positions taken, therefore, come as much from clinical experience as from systematic research studies. Nevertheless, given the scientific limitations of our field at present, I believe the guidelines suggested above will be helpful to both patients and practitioners.

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