Psychiatry Primer DVR, 2010

Practicing psychiatry is making decisions. These decisions are most effective when they are informed by sound principles applied to accurate diagnoses. Accurate diagnoses require an accurate catalog of lifetime symptoms organized into sound diagnostic categories.

These diagnoses in turn must then be related to each other according to the treatment hierarchy of diagnoses. Once these diagnoses have been established and prioritized, there are decision-making principles that can be applied to make rapid and effective treatment decisions. The objective of all this is to recover our patients as rapidly as possible.

I. Establishing accurate diagnoses:

The lifetime catalog of symptoms.

Diagnoses are assigned by comparing the catalog of lifetime symptoms against the established criteria of DSM-IV tr. This catalog of symptoms should include the symptoms of these diagnostic categories only. Use of an instrument structured to collect these data is invaluable. At Scott P. Hoopes, M.D., we use our customized version of the MINI International Neuropsychiatric Interview. This instrument allows the skilled interviewer to complete the critical lifetime catalog of psychiatric symptoms in 30 minutes or less.
The MINI includes modules for each of the major psychiatric illnesses organized around required symptoms that serve as screening questions for each module. If the patient does not endorse the screening questions the interviewer moves to the next module and so on through the entire interview. When the patient endorses the screening questions the interviewer works through the entire module to create the catalog of symptoms.
Within the depression module there is a question probing for feelings of worthlessness or guilt. When these feelings are present, it is important to establish whether or not these feelings reach the point of a conviction. Ask the patient whether they are able to accept reassurance that they are not worthless or to consider the possibility that they are not responsible for terrible things happening to themselves or others. If they cannot accept reassurance or consider that they are not responsible for misfortune to themselves or others, they may be suffering from delusional worthlessness or guilt, which should be indicated within the MINI by checking the box by the Y.

The mood disorder module is designed to facilitate the identification of mania and mixed states. The euthymia module precedes the mania modules because the euthymia module allows the interviewer to establish euthymia as the point of comparison for the description of mania. Use the question about sleep in the depression module to start to distinguish Major Depression Disorder (MDD) from Bipolar Disorder (BD) by probing for and describing depressions featuring hypersomnia first. If the patient endorses another type of depression during which they do not sleep well (hyposomnia), defer the description of this mood to the mixed state module.
When the patient endorses the symptoms of any module, it is essential to establish the age of onset of the symptoms, their duration, and the frequency of their occurrence.

The power of normal.
The euthymia module is one of the most important modules of the interview. It allows the interviewer to orient the patient to their own euthymic moods. If necessary, as it sometimes is, it creates an opportunity to describe a "normal" mood to people who have been ill so long they have forgotten what a normal mood feels like (neutral, able to experience happiness, joy and pleasure, negative emotions occur in negative contexts, and overall emotions are proportional to circumstances). This provides the point of comparison for the patient's past to identify times of hypomania and mixed states.

The euthymia module also allows the interviewer to distinguish primary from secondary states. The catalog of symptoms that the MINI creates does not of itself distinguish independent conditions from those conditions that occur only in the context of other conditions. For example, 60 % of depressed patients will experience significant anxiety, but they only experience this anxiety when they are depressed. The depression, therefore, is the primary condition and the anxiety is secondary to the depression. This is established by determining whether or not the anxiety occurs when the depression is not present. If the anxiety is present when the depression is not present, then the anxiety is independent of the depression and therefore another primary condition. The euthymia module, therefore, allows the interviewer to ask the patient whether each identified symptom cluster is present when their mood is not disordered. Those conditions that are only present when the mood is disordered are secondary to the mood disorder. Those conditions that are still present when the mood is not disordered represent independent or primary conditions that will need to be addressed separately in the treatment plan. The secondary conditions are expected to resolve as the mood is established to euthymia and therefore are not addressed separately in the treatment plan.

The Treatment Hierarchy of Diagnoses
Once a list of primary diagnoses has been created, it is necessary to determine the order in which to treat these diagnoses. This order is created by adhering to a hierarchy of diagnoses created by three considerations. First, conditions attributable to medical conditions should be treated first (for example, delirium must be addressed before depression). Second, those conditions should be treated earlier that carry the greatest risk to the patient (for example, psychotic disorders carry more risk than ADHD). Third, those conditions should be treated later whose treatments can worsen other conditions (for example, anxiety disorders are often treated with SSRIs that can worsen Bipolar Disorder). Applying these principles to the major psychiatric diagnoses yields a listing in the following order for treatment: medical illnesses, psychotic disorders, bipolar disorder, major depression, anxiety disorders, eating disorders, impulse control disorders, ADHD, and personality disorders. The primary diagnoses placed in this order become the basis of the treatment plan.

II The Treatment Plan

The initial treatment plan is formed to address the diagnoses established as described above in the order of The Treatment Hierarchy of Diagnoses. The following principles are valuable in forming the initial treatment plan.

Treat the Primary Diagnoses in the order of The Treatment Hierarchy of Diagnoses.

Addressing the diagnoses from the first to last diagnosis in the hierarchy will result in the utilization of fewer medications because secondary conditions will resolve as primary conditions improve and one will not be in the position of aggravating conditions higher in the hierarchy by treatments of conditions lower in the hierarchy. In addition, one will less often be in the position of treating side effects of medications with other medications.

Stabilize first and then treat depression.
Bipolar Disorder consists of two components: the fluctuation between the four possible mood states of Bipolar Disorder (euthymia, depression, mania and mixed mania); and the mood itself. That is to say, one cannot really discuss a person's mood state when their mood changes from day to day or week to week. Antidepressants can aggravate mood lability. Mood stabilizers, therefore, should be prescribed before antidepressants.
The mood can be stabilized in depression or euthymia (mania is unstable by definition). It is important to help the patient understand that in stabilizing their mood they may end up feeling more consistently depressed than they did when they presented for treatment. This is progress. Once the mood is stabilized, then one can beneficially address the mood by addinga medication to the mood stabilizer to nudge the depression into euthymia while maintaining the stability of the mood.

III Applying the treatment plan.

As one works to apply the treatment plan, one will necessarily use the developing experience of the patient to modify the treatment plan. These modifications occur in "medication management" appointments after the application of the initial steps of the treatment plan. The following principles can be valuable in this regard:

Change one variable at a time.
There is often a temptation to change more than one aspect of the treatment plan at once. When one does this, all possibility of learning from adverse or favorable events is abdicated. It is far wiser, and much more scientific, to change only one variable of treatment at a time so that one can learn more about the biology of the individual being treated that in tum will allow the next treatment decision to be more individualized. This principle is reasonably disregarded when trying to recover a patient rapidly to avoid hospitalization.

Treat diagnoses, not symptoms.
Symptoms, as noted above, can be present in more than one diagnosis. When the diagnosis is treated, the symptoms of the diagnosis will improve. For example, many patients complain bitterly of the anxiety of mixed mania. This anxiety, if treated as a symptom with SSRIs, without regard to diagnosis, may be worsened by the treatment, because SSRIs typically aggravate mixed states. If the anxiety is treated as a symptom of mixed mania with a mood stabilizer, say with Depakote, the anxiety will improve as the mixed state improves.

Never chase symptoms.
Always reduce or eliminate a medication first.
After one has identified the diagnosis that contains the symptom(s) of the chief complaint, one mentally prepares a list of possible interventions. For many reasons

prescribers think first of adding or increasing medications. This leads to unnecessary polypharmacy at best and at worst to treating inadvertently side effects of one medication with another medication. This approach often leads to excessively sedated patients who are partially functional at best, increasing the cost of pharmacological treatment, and often increasing the burden of consequent adverse events.
Better to discipline oneself to consider the psychopharmacotoxicology of the medications we prescribe, i.e. consider that the symptoms the patient endorses are a result of one of the medication they are already taking. Then, from the list of possible interventions, always choose first to reduce or eliminate medications. This creates a bias against the medications and helps ensure that we are treating our patients with the smallest number of medications possible. This principle requires a working knowledge of psychopharmacotoxicology.

Anxiety in bipolar disorder is mixed mania until proven otherwise.
Our bipolar patients often present for treatment of anxiety. Population surveys suggest that anxiety disorders are often comorbid with Bipolar Disorder. Our experience, by contrast,finds that symptoms of anxiety in Bipolar Disorder nearly always indicate mixed mania. Resist the temptation to treat this anxiety during follow-up as an independent anxiety disorder, and address the anxiety as part of an active mixed mania. Instead of adding SSRIs, one will usually instead reduce antidepressants first (see above under "Always Reduce or Eliminate Medications First") and then if necessary increase the dose of an already established mood stabilizer to optimal levels (often guided by serum levels of the medication). The anxiety disorders are proven to be primary or secondary by the principles reviewed above under "The Power of Normal".

Mania trumps depression.
In treating our bipolar patients we must often consider how best to treat mixed states. Recall that mixed states are conceived of as the mixture of depression and mania. In addressing mixed mania, therefore, we should "stabilize first and then treat depression". Techniques to treat mania include reducing or eliminating antidepressants (see above under "Always Reduce or Eliminate Medications First") and increasing or adding mood stabilizers. Only when the manic portion of mixed mania has been addressed is it reasonable to address the depression that may remain (and it often does not remain; we find that the high energy of mania often "drives" the dysphoria of mixed mania).

Sunlight is an antidepressant.
Good data supports the use of light (10,000 lux white light; 5,000 lux blue light) in the treatment of seasonal depression. The notion that light is an antidepressant has significant implications in the treatment of all mood disorders, but particularly bipolar disorders. In northern latitudes there is more light in the summer than the winter. One would expect, therefore, depressions to be more common in the winter than the summer, which is true. By the same token mixed states and manias for most patients are more common in the spring and summer. Consider the following equation: antidepressant medication + sunlight = total antidepressant. Hypothesize that the total antidepressant needs to be constant for the mood to be consistently euthymic. That leads to the conclusion that the antidepressant medication will need to be adjusted up in the falVwinter and down in the spring/summer to maintain a constant "total antidepressant" and thus a stable mood. Note that in the fall/winter the emergence of depression will cue the increase in antidepressant medication and that the

emergence of mania or a mixed state will cue the necessity to reduce antidepressant medication. (This last point is very powerful. The "treatment as usual" method is to add a medication for emergent symptoms fall and spring, leading to more and more medication year by year.) For most patients one will be able to identify a seasonal pattern that can be anticipated so that medication changes can be made before moods start moving, thus leading to an even more stable mood. If one thinks enough of a treatment to use it, use it thoroughly.

Often medications are prescribed but abandoned at the first sign of adverse events or of failure immediately to improve the current state of the patient. There are three questions to answer in using any medication: are there adverse effects that will not allow its use (e.g. serious rashes, marked agitation, etc); does the medication seem to do anything of benefit; what is the optimal dose for the most benefit and the fewest and least disruptive adverse events. This last point may require the prescriber to reduce doses as well as to increase doses. Only when limiting adverse events have been experienced or when the medication fails to improve the diagnoses at minimal or maximal doses should it be abandoned. This avoids building up a list of medications that were prescribed but never optimized in a never ending merry-go-round of medications.

Treat the patient, not the package insert.
There are recommended dose ranges of all medications listed in the FDA approved Package Insert. Remember that the dose-response curves they contain" represent a scatter of data derived in study subjects in flexible dose studies. There are people in the studies who did well on doses above and below that dose response curve. For a number of reasons, many psychopharmacologists are more than willing to push medications to doses that exceed recommendations (we seldom find this necessary or advisable), but disregard the possibility that "less is more". It is wise to start medications at low doses and to advance the doses cautiously and systematically. Often patients respond to doses lower than expected. When assaying doses higher than recommended, it is wise to be guided by serum levels of the medication and to monitor key medical parameters, e.g. E.K.G.s for Geodon.

IV General Pharmacotoxicology

An accessible published study to illustrate basic principles of psychopharmacotoxicology is the Beasley analysis of fixed dose studies of fluoxetine (Psychopharmacol Bull, 1990 (26)1; 18-24). This analysis of pooled data from 2 fixed dose studies showed, in general, an inverted-U dose-response curve. That is to say, as the dose increased people generally did well emotionally, but at a certain dose (f1uoxetine 60 mg/d) people felt less well associated with emergence of adverse events. The inverted-U doseresponse curve applies generally to psychotropic medications and should be kept firmly in mind when considering treatment options.

Antidepressants
People feel depressed and anxious when antidepressant doses are too high. When a patient reports feeling dysphoric, and particularly when they complain of feeling anxious and/or agitated with insomnia, consider reducing antidepressant doses. This is particularly helpful in the Spring and Summer because sunlight is an antidepressant (see above under Sunlight 1S an Antidepressant). Consequently, in the Spring and Summer people taking

antidepressants may become activated, including agitation, anxiety and depression, by the combination of their antidepressant and the increased sunlight (see above under, "Always Reduce or Eliminate an Antidepressant First").
Start at low doses of SSRIs when treating anxiety disorders.
The full dose of an SSRI often initially agitates anxiety disorder patients. It is important, therefore, to start SSRIs at low doses, at least 1/4 usual doses as a rule of thumb, and to titrate minimally in 2 week increments.

The CYP system becomes less efficient with age.
The inefficiency of the CYP system can lead to rising tricyclic antidepressant levels with age even at a fixed dose. It is important to check TCA levels at least yearly in established patients and at intake for new patients (who will continue the TCA). Other antidepressants that are metabolized via CYP systems may require lower doses in people over 55 yo. Note that c10zapine is metabolized via CYP enzymes; consider obtaining levels in patients who develop late and therefore unexpected agranulocytosis.

Atypical Antipsychotics
Atypical anti psychotics can cause depression when the dose is too high. Atypical antipsychotics when used as mood stabilizers have been conceptualized as "stabilizing from above", i.e. pushing manias down into euthymia. This stabilizing from above, however, can sometimes press a patient's mood below euthymia into depression. This type of depression usually includes mild anhedonia, amotivation and psychomotor retardation. This depression can be improved by reducing the dose of the atypical antipsychotic.

Atypical antipsychotics can cause akathisia.
Atypical anti psychotics can cause akathisia which consists of a physical and/or emotional restlessness and agitation that usually is associated with dysphoria that can can be mistaken for mixed mania. The discomfort of akathisia is temporarily relieved physically by movement that often leads the person to appear fidgety and restless. The akathisia is usually dose dependent and improves with reduction in the atypical antipsychotic. If a dose reduction is ineffective and the medication is necessary, the akathisia can be treated with Inderal, amantadine or Cogentin.

Atypical antipsychotics when added to antidepressants can cause agitation.
Atypical anti psychotics increase serotonergic tone via blockade of post synaptic serotonin 2a receptors. Consequently, when agitation emerges when an atypical antipsychotic is added to an antidepressant the agitation can be improved by reducing the antidepressant (this occurs much less often with Zyprexa and Seroquel than Risperdal, Geodon or Ability. Be sure the agitation is not attributable to akathisia, however.).

Benzodiazepines
Patients treated with antidepressants and benzodiazepines who are still very depressed and anxious are usually undiagnosed bipolar disorder. The antidepressants have pushed the patient into a mixed state for which benzodiazepines have then been added. Benzodiazepines are associated with depression, ataxia, and cognitive impairment when used chronically. Sometimes tapering and stopping benzodiazepines is the most effective intervention to relieve depression (see above, "Always Reduce or Eliminate a Medication First").

Antiepileptics used as mood stabilizers.
Lamictal can cause a serious rash known as Stephen Johnson Syndrome (SJS). The risk is directly related to the starting dose and the rate of titration. It is essential to follow the recommended dose titration. Patients should retitrate Lamictal if they miss 2 or more doses.
Depakote interferes with the urea cycle which increases serum ammonia levels. Elevated ammonia levels can cause lethargy, depression, and the confusion of encephalopathy. Always check Depakote and ammonia levels when a patient taking Depakote deteriorates.

Trileptal can cause hyponatremia in up to 15 % of patients. The symptoms of hyponatremia include lethargy, mild anhedonia, parasthesias, and cognitive difficulties. Always check electrolytes when patients taking Trileptal deteriorate. Trileptal can also cause SJS, but the relationship to titration and starting dose is not clear.

Topamax is not a mood stabilizer (failed 7 controlled trials).

Zonegran may be a mood stabilizer, but the studies will likely never be done because it is generic.

Lithium:
Up to 35 % of patients taking lithium chronically will require thyroid supplementation. When a patient taking lithium deteriorates, always check thyroid and lithium levels.
The adverse effects of lithium are directly proportional to dose and include tremors, nausea, diarrhea, cognitive impairment, and others.
Levels of lithium below 0.8 *meQ/L* are helpful for depression, those above 0.8 *meQ/L* are effective for mania.

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