In the prior PL issue, a discussion of the diagnostic interview, was presented, with a plan for two parts. However, the material in the July 2016 PL issue already covers that topic more fully, so this month PL will proceed to new but related material.

The importance of diagnostic interviewing has to do with the perspective that clinicians should treat diagnoses or diseases, not symptoms. The Special Article this month is about Hippocratic psychopharmacology, or the notion of treating diseases not symptoms.

The Article of the Month and the Case of the Month both relate to first-episode or treatment-naive depression. The Drug of the Month is fluoxetine, Prozac, the classic modern antidepressant. A new Concepts and History of Psychiatry column provides ideas from the famed British psychiatrist Aubrey Lewis on the nature of knowledge in psychiatry. Curbside consult questions are provided.

We invite readers to attend either of the two summer CME courses described in the side bar, one in Eastham, Cape Cod, and the other in Martha’s Vineyard, or the fall CME seminar in Santa Fe New Mexico. The last page provides details.

Nassir Ghaemi MD, Editor

New truths begin as heresies and end as superstitions - T. H. Huxley
As discussed in the last issue of PL, making a correct diagnosis is central to psychopharmacology. This approach is not followed in practice, where most clinicians simply treat symptoms. In this issue, PL analyzes this symptom-oriented psychopharmacology, with a critique derived from the Hippocratic tradition in medicine.

**Principles of psychopharmacology: Implications of a Hippocratic approach**

The father of modern medicine William Osler advised his students: “Read the journals and the old books.” The journals keep us up-to-date on recent research; the old books give us perspective and provide universal principles. Among the old books, none are more central than the Hippocratic writings.

The principles of psychopharmacology follow from the principles of medicine, among which the Hippocratic approach is oft-misquoted and misunderstood. Hippocrates’ view of medicine, in contrast to other schools, was that disease comes from nature: it is not unnatural. It’s not something to fight against, but rather a natural process which nature itself can heal. The job of the physician is to help guide nature towards health, using measures such as diet and exercise, rather than to engage in combat with nature through medicines and toxins. The key Hippocratic idea is that nature heals, and doctor is only to handmaiden into nature. Nature cures, the doctor assists.

Many, if not most, illnesses improve naturally, and our role is to not get in the way of nature, but to help nature along. Hence, the Hippocratics divided diseases into the self-limited, the treatable, and the incurable. In the first and third cases, treatments in general are unnecessary and often harmful; in the second case, they are needed. The art of medicine is to distinguish between these three cases.

It’s important to realize that Hippocrates never said “First do no harm.” This is a false statement, made up by a 19th century British physician and attributed to Hippocrates. In fact, Hippocrates is quoted as saying: “Practice two things with disease: Either help or do not harm the patient.” (Epidemics, Book I, Chapter 11) This correct quotation makes the point that there was no “First” to not harming. The first job of the physician was to help diseases, to treat diseases, not to take a generic conservative attitude of not harming. The idea of not harming grows out of treating those diseases we can treat, and not treating those diseases we cannot treat, as well as not treating those symptoms which don’t reflect diseases.

Many clinicians practice non-Hippocratically. They think they should treat everyone who enters their offices. There is precedent for this view in the founder of American psychiatry, Benjamin Rush, who directly attacked the Hippocratic philosophy of treatment and who was a strong advocate of active intervention to treat all kinds of illnesses, including mental illness, through
bleeding. The Hippocratic approach was long forgotten in the Middle Ages and into the modern era. In the US, the Hippocratic philosophy was resurrected in the late 19th century by Oliver Wendell Holmes and William Osler.

Based on their writings, two rules can help clinicians engage in Hippocratic psychopharmacology.

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<th>Osler’s Rule</th>
<th>Holme’s Rule</th>
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<td>Treat diseases, not symptoms.</td>
<td>All drugs are guilty until proven innocent.</td>
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**Osler’s Rule**

The first rule is derived from the father of modern medicine, William Osler, who urged in 1895: “A man cannot become a competent surgeon without a full knowledge of human anatomy and physiology, and the physician without physiology and chemistry flounders along in an aimless fashion, never able to gain any accurate conception of disease, practising a sort of popgun pharmacy, hitting now the malady and again the patient, he himself not knowing which.”

Osler emphasized that we need to learn first about diseases before we can do much about treatment. Osler’s Rule is that we should treat syndromes (based on underlying diseases), not symptoms. Symptoms are not what need to be treated; they are signs which point to the disease (or diagnosis), which is what needs to be identified and treated. If clinicians followed this rule, they would avoid using drugs for multiple symptoms, which leads to a haphazard polypharmacy. In treating bipolar illness, for example, patients often receive antidepressants for depressive symptoms, antipsychotics for manic symptoms, anxiolytics for anxiety symptoms, sedatives for insomnia, and mood stabilizers for mood swings. This symptom-oriented approach to treatment is prescientific rather than scientific, 19th century-based rather than up to date, and anti-Hippocratic. The Oslerian approach would be to focus on the diagnosis (not the symptoms), namely bipolar illness, and emphasize mood stabilizers, as much as possible by themselves, as the only class of treatment that treats the whole illness (acute depression, acute mania, and prophylaxis of mood episodes). In cases where the disease is not well-identified, or where perhaps no disease exists, treatment is symptomatic, of a band-aid nature, and the risk-benefit ratio for medication treatment would become more unfavorable to extensive prescription of such treatments. Such is not the case with bipolar illness, however, a diagnosis that has been well described since the Roman physician Arataeus of Cappadocia (2nd century AD) and whose biological basis is well-established.

This need not mean that we should never use medications merely to relieve symptoms. It does mean that this approach goes against the Hippocratic view of medicine, and we should take it only in the short-term, reluctantly, and for immediate relief of symptoms. In psychiatric populations where diseases are either poorly understood (as in children and the elderly), there is rampant symptomatic polypharmacy. And many psychiatrists consider this state of affairs to be acceptable. Osler’s Rule would give us pause.

**Holmes’ Rule**
The second rule is derived from the physician and writer Oliver Wendell Holmes Sr, who said in 1861: “Presumptions are of vast importance in medicine, as in law. A man is presumed innocent until he is proved guilty. A medicine...should always be presumed to be hurtful. It always is directly hurtful; it may sometimes be indirectly beneficial. If this presumption were established...we should not so frequently hear...that, on the whole, more harm than good is done with medication. Throw out opium, which the Creator himself seems to prescribe, for we often see the scarlet poppy growing in the cornfields, as if it were foreseen that wherever there is hunger to be fed there must also be pain to be soothed; throw out a few specifics which our art did not discover, and is hardly needed to apply; throw out wine, which is a food, and the vapors which produce the miracle of anesthesia, and I firmly believe that if the whole materia medica, as now used, could be sunk to the bottom of the sea, it would be all the better for mankind, – and all the worse for the fishes.”

Thus, Holmes’ Rule is that there must be empirical proof that a treatment is effective so as to outweigh the presumption against the use of a medication. If clinicians followed this rule, they would avoid treatment with medications whose efficacy has not been proven. As Osler put it, all medications are toxic; it is only the indication and the dosing that makes them therapeutic. Before using any medication, one must presume harm; the burden of proof is on the medication to be shown effective, not on anyone to show that the medication isn't harmful. Risk-benefit calculations should begin, not on the risk side, but on the benefit side. Otherwise we end up with a kind of “gabapentin syndrome”—giving people safe, though ineffective, drugs (or alternatively, widely using drugs effective only for a few conditions).

For example, in the case of antidepressants for bipolar illness clinicians have been breaking Holmes’ rule egregiously. They have engaged in the extensive long-term use of antidepressants despite two decades of randomized maintenance data demonstrating that they are ineffective, at best, and harmful, at worst, in bipolar illness.

Often clinicians say they want more evidence to stop using antidepressants. If they were practicing Hippocratic medicine, and following Holmes’ rule, they would want evidence to start using medications, not to stop them. The burden of proof isn't that medications should be used unless proven ineffective and unsafe, but that they shouldn’t be used unless proven effective and safe. With antidepressants, and with amphetamines as well in ADD, many clinicians have gotten it backwards.

**The PL Bottom Line**

- The Hippocratic approach is not about general conservatism of treatment.
- Hippocrates never said: “First do no harm.”
- The Hippocratic approach is about avoiding treating symptoms without disease, but also about identify and treating diseases.
- Treat diseases not symptoms.
- All drugs are guilty until proven innocent.
Current Study of the Month: Treatment response in first-episode depression

Effects of patient preferences on outcomes in the predictors of remission in depression to individual and combined treatments (PReDICT) study. BW Dunlop et al, American Journal of Psychiatry. 2017; 174:546-556

All treatments are similar

The holy grail has long been sought: Prove that one treatment for depression is better than another. The STAR*D trial was funded by NIMH in large multi-center style to prove that one drug is better than another, or that combination of antidepressants might be more effective than a single agent. STAR*D found they were similar.

This trial reluctantly reaches the same conclusion.

In this NIMH-sponsored study, the special feature was supposed to be that all patients would be treatment-native, having never been treated for depression before, and most would be in their first depressive episode. In practice, it’s quite difficult to identify and treat the actual first depressive episode of many patients, since most people don’t seek treatment immediately. Rather, such “first episode” studies really reflect “first treated episode.” In this study of the first treated episode, in fact about one-half of patients were in their first depressive episode. The other half had one or more prior depressive episodes.

This study is unique in that there are few if any prior first episode depression studies (in contrast to numerous first episode mania studies in bipolar illness and first episode psychosis studies in schizophrenia). To find first episode subjects, the researchers, centered in Atlanta at Emory University, had to resort to advertising for subjects. They also recruited from a large inner-city public institution, Grady Hospital, at a Spanish-speaking clinic where subjects were identified who hadn’t been previously engaged by the healthcare system.

A reasonably large sample of 344 patients was obtained, blindly randomized for 12 weeks of acute depression outcome to one of three arms: a pure SRI (escitalopram), a SNRI (duloxetine), and cognitive behavioral therapy (CBT). There was no placebo control, which is an unfortunate weakness. (One should prove, not assume, that these treatment-naive patients wouldn’t have improved by natural history or based on nonspecific psychological factors).

The main outcome was the Hamilton Depression Rating Scale (HDRS) score, which reduced similarly in all groups (10.2 improvement with CBT, 11.1 escitalopram, 11.2 duloxetine). The one point difference between CBT and medications was clinically small and not statistically significant. However, at each week by week visit, CBT was slightly less effective than the medication options. Despite the vaunted marketing of “dual-action” on norepinephrine reuptake as well as serotonin, duloxetine was exactly the same in efficacy as escitalopram. This result contradicts the neuromythology that affecting two neurotransmitters systems produces more efficacy than affecting one.

The researchers had wanted to find means to support “personalized medicine,” a popular phrase these days. But they found nothing, or very little. In effect, it didn't matter if patients received a...
pure SRI, a SNRI, or CBT: the result was more or less the same. Differences were minor.

In an accompanying paper, the same researchers report neuroimaging results that differentiate the antidepressant medication response groups from the CBT response groups. These distinctions involve the subcallosal cingulate cortex (SCC) connectivity to other areas of the brain. These findings may be important, but they were not the primary hypotheses of the study, and could reflect post-hoc false positive statistical findings. Nonetheless, they are interesting, suggesting that different regions of the brain may predict CBT response to medication response. However, again, no distinctions were found in comparing one kind of antidepressant medication to another.

Another aspect to understanding this study is the overall response rates, defined as 50% or more improvement in depression symptoms. Those response rates were 42% for CBT, 47% for escitalopram, and 55% for duloxetine. These response rates do tend to support somewhat increasing efficacy in moving from psychotherapy to single neurotransmitter effects to multi-neurotransmitter effects. But again, the effect sizes are relatively small, and not statistically significant.

Lastly, overall, as with STAR*D, only about one-third of patients had remission, meaning resolution of almost all depression symptoms. This is the same result as STAR*D, where most patients had recurrent episodes and prior treatment. Here in the PReDICT study, we have half the sample in its first episode, and none ever treated previously. And still the results of this treatment-naïve sample are the same as in STAR*D. In other words, the poor results in STAR*D didn't reflect a treatment-refractory sample.

These results aren't terrible. Half the patients improved short-term. But they aren't overwhelming either. Further, for those who interpret the limited benefits of antidepressant medications as implying a need to use more psychotherapy, the CBT results in this study indicate that psychotherapy isn't any better.

Perhaps because the treatment efficacy results weren't very exciting, this primary paper for this study emphasizes in its title the question of whether patient preferences for randomization influenced outcome. Before randomization patients were asked whether they preferred one of the three options; they were randomized irrespective of their preferences. The Hispanic subgroup had a preference against medication, while the African-American subgroup had a preference for CBT, and the white subgroup had no overall preference. These stated preferences didn't predict any differences in treatment outcomes, though. Instead, a mismatch of preference to randomized treatment (i.e., getting medication if you preferred CBT) predicted less treatment adherence, as expected.

The PL Bottom Line

• Antidepressant response in a treatment-naïve, partly first-episode depression population was not better than in the treatment-refractory STAR*D study.
• Duloxetine was only slightly more effective than escitalopram, if at all.
• Except for neuroimaging possibly, predictors of treatment response couldn't be identified
Drug of the Month: Fluoxetine (Prozac)
Once weekly dosing, ideal for cross-taper off other SRIs

Biological mechanism
Fluoxetine is the classic serotonin reuptake inhibitor (SRI), the first marketed in the US in the late 1980s. It is not a “selective” SRI, contrary to popular marketing, but instead has notable norepinephrine reuptake inhibition, similar in potency to medium-dose venlafaxine.

Clinical efficacy
Fluoxetine is FDA indicated for acute and maintenance treatment of major depressive disorder, bulimia nervosa, obsessive-compulsive disorder, and panic disorder. Combined with olanzapine it is FDA indicated for acute depressive episodes in bipolar illness, and for treatment-resistant depression.

Besides these mood effects, fluoxetine and all SRIs have direct and immediate anxiolytic effects, especially at low doses. Patients with anxiety symptoms feel “better” but this effect can be misinterpreted as depression benefit. It may underlie the “better than well” phenomenon.

Dosing
The standard dose is 20-40 mg/d, with a maximum of 80 mg/d. The half-life is very long, being 4-6 days for fluoxetine, and 16 days for its active metabolite norfluoxetine. Given this very long half-life, it only needs to be dosed once weekly, and a trade Prozac Weekly formulation is proven effective in MDD at 90 mg/weekly.

Side effects
Nuisance side effects are nausea, diarrhea, apathy syndrome, and sexual dysfunction. Medically risky side effects include akathisia, which can lead to suicidality, which has been shown repeatedly to occur with fluoxetine, especially in children and young adults. As with all antidepressants, mania occurs with fluoxetine, though less given with dopamine blockers.

Serotonin withdrawal syndrome occurs after stopping this agent after long-term use, but it is less severe than with other SRIs. In fact, fluoxetine is useful as a cross tapering agent to allow for taper off other SRIs with less serotonin withdrawal syndrome.

Fast Facts: Fluoxetine
- **Typical dose:** 20-40 mg/d
- **Biological mechanism:** Serotonin and norepinephrine reuptake inhibition
- **Typical side effects:** sexual dysfunction, akathisia
- **Medically important side effects:** suicidality
- **Clinically proven efficacy:** FDA indication for major depressive disorder, OCD, panic, bulimia

The PL Bottom Line
- Fluoxetine is not a pure SRI but has noradrenergic effects.
- It is a powerful immediate anxiolytic, more so than an antidepressant.
- The half-life for its active metabolite is 2 weeks. It need only be dosed once weekly.
- It causes akathisia and suicidality in young adults and children.
- It is useful as a cross-tapering agent with other SRIs for serotonin withdrawal syndrome.
Concepts and History of Psychiatry

Aubrey Lewis: Between guesswork and certainty in psychiatry - 1958

[In this issue of PL we are beginning a Concepts and History of Psychiatry section in the newsletter, seeking to provide readers with primary source material access to thinkers in psychiatry, along with commentary and context from PL.

We begin with Sir Aubrey Lewis (1900-1975), who was the most prominent figure in British psychiatry through most of the 20th century. He was the leader of the Institute of Psychiatry at the Maudsley Hospital for much of the middle of the 20th century. That institution in London was the most influential educational center for psychiatry in the nation. Through his leadership there, Lewis was extremely influential. His articles and essays are masterpieces of psychiatric thinking in English prose. Their style and clarity are impressive, even where the reader might not agree fully with the content. PL hopes to present other articles and essays by Lewis in future issues too.

In this 1958 essay, Lewis addresses the general question of the extent to which psychiatrists know anything. This article, published in the Lancet (Volume 1, pages 171-5 and 227-30, 1958), was directed toward a medical audience that was skeptical about the professional credibility of psychiatry. The original text follows.]

It is the common state of reflective and inquiring minds to be somewhere between untrammeled guesswork and certainty....We [psychiatrists] are, however, sometimes suspected of luxuriant speculation and of invincible faith in our tenets: and I propose to soldier how this reputation has arisen.

More than most branches of medicine, psychiatry can be regarded as an art. One of its distinctive procedures - psychotherapy - manifestly depends on subtle relationships and incommunicable qualities of personality...Psychiatry in this is like the rest of medicine, combining moral and personal principles of action with those arrived at by the methods of science, and depending on the last for any increase in its power to prevent and control disease....'

It would be easy to pile up instances showing that psychiatry is not the only branch of medicine - or of knowledge - to be pilloried for lax thinking and complacent dogmatism. It has, however, troubles which seem peculiar to itself, and some ministrants who seem peculiarly indifferent to the scientific method as understood by the rest of the world....

The aims of medical treatment are ordinarily to remove or lessen disabilities and pain, to put an end to morbid changes in the patient's body of which he may not be aware but which must sooner or later cause disability, and thirdly, to enable him to lives satisfying a life as possible, in spite of persistent disability and morbid process. Applied to mental illness, all this becomes equivocal. The patient will often be unaware of disturbances very plain to others; he may not complain of his symptoms; he may even cherish them. He may lead a less satisfying life when his symptoms have been got rid of than when he had them. The morbid process often has no physical substrate that we know of: and the psychopathology may be obscure and inaccessible. The criteria of recovery are therefore hard to specify, and like the criteria of improvement, depend on an assessment of the patient's happiness, competence, and well-being which involves moral and social values as well as plainly medical ones....

A rather silly but often repeated truism says that the aim of psychiatric treatment is to promote mental health. It is hard to tell what the latter phrase means. Mental health is an invincibly obscure concept.... [It] is an abstraction which is very loosely interpreted....
Lewis goes on to criticize our ability to know if our treatments work, whether they be physical, like insulin coma or drugs, or psychotherapeutic.

...the medley of ‘tranquilizing’ drugs may pass... into the like chiaroscuro of approval and rejection. But the doubts which attend physical methods of treatment are dwarfish alongside the giant misgivings and disputes which envelop psychotherapy in dust and fog. The trouble is of long standing, and has divided psychiatrists bitterly...Psychotherapists are seldom skeptical or, as one might say, ambivalent about the treatment they give, and ‘philosophic doubt’ is not in keeping with their metier....Here then is a great domain of psychiatric practice in which there has been an excessive proportion of guesswork and rather a lot of subjective certainty....

There are some awful warnings of what a craving for certainty can lead to. You may remember the philosopher Cratylus who, as Aristotle tells us, decided never to say anything but what was certainly true, and so he ceased to talk at all and confined himself to wagging his finger. Psychiatry suffers much from hopeful illusions and cliches used as incantations, just as a few decades ago it suffered, even more, from pessimistic and resigned inertia....It is easy to lay failings like those at the door of psychiatrists, blaming their lack of scientific training, their loose habits of thought, their incuriosity, their passion for psychoanalysis or for physical methods of treatment, their preoccupation with the fascinating art of understanding other people. To think this seems to me facile and unjust. More important than the deficiencies of doctors are the inherent complexity of the problems.....

I have not enlarged on the attainments of psychiatry, its solid groundwork of detailed, minute, and orderly observations, its empirical successes, its accretions thorough application so the basic medical sciences to clinical problems....

Clearly we are a long way from certainty, and when we meet anyone who is sure that he knows how to tackle the problems of mental disorder and to remedy the failings of psychiatrists and psychologists, we may recall Lord Landsdowne’s remark: ‘I wish I could be as sure of anything as Tom Macaulay is of everything.’ Guessing, too, has its perils and is arduous: it takes unkindly to the discipline which is good for it. Yet between those who are nearly certain and those who guess much there is the bond which Isaac Newton spoke of: ‘I doubt not we have one common design: a sincere endeavor after knowledge, without valuing uncertain speculations for their subtleties, or despising certainties for their plainness.’

**PL Comment:**

In his analysis, Lewis places the limitations of psychiatry in context. Our knowledge in psychiatry, Lewis asserts, lies somewhere between guesswork and certainty. It is not pure guessing, nor is it certain knowledge; yet much of medicine and science is the same. Lewis emphasizes the extent to which psychiatrists can feel overly certain about their theories, and how much they can be deeply unscientific, failing to test those theories. Lewis concludes that the largest part of the problem is the complexity of the nature of psychiatric problems. We know so little, and our most basic concepts, like mental health, are inscrutable.

PL appreciates Lewis’ frankness, but he veers too far at times toward his own version of excessive skepticism. Yet there is much to learn from his clear thinking, which future issues will explore.
Case of the Month

A first depressive episode at age 18

An 18-year-old male has a first depressive episode. For the last two months, he reports decreased interest, energy, concentration, and appetite. Two weeks ago, his parents took him to his primary care doctor, who diagnosed depression, and began treatment with fluoxetine. The patient had no prior psychological problems or treatment, and has done quite well in school. A few days after starting fluoxetine, the patient reported some suicidal ideation, but denied any intent or plan. He also admitted to drinking some alcohol with friends. He has no other medical problems, no allergies, and is taking no other medications. There is no history of trauma, and he was raised in an intact and supportive family. He has multiple family members with depression, and one aunt diagnosed and treated for bipolar illness.

PL consultation was obtained. The observation was made that the course of illness and genetics of this case are more consistent with bipolar illness than major depressive disorder (MDD). The occurrence of suicidal ideation after treatment with fluoxetine was noted and a causal relationship implied. It was observed that the whole concept of MDD was associated with a lack of bipolar genetics and an age of onset around 30, as opposed to bipolar illness which began around age 19 and had bipolar genetics. The concern was raised that this depression may be the first episode of bipolar illness (with future mania), or at least cannot be the first depressive episode of MDD, given bipolar genetics and course of illness. The PL recommendation was to discontinue fluoxetine and begin lithium.

The patient saw a psychiatric nurse practitioner who concurred with the diagnostic and historical assessment, but concluded that lithium was a "third line" treatment for more severe illness than this patient possesses. In contrast, fluoxetine was a less intensive and more conservative treatment. Fluoxetine treatment was continued, with a plan to consider lithium later.

The PL perspective is that fluoxetine is not a more conservative treatment than lithium in this case. Fluoxetine increases suicidal ideation and suicide attempts by about 70%, whereas lithium reduces completed suicides by about 90%, as discussed in a prior PL issue. Thus lithium is a more conservative treatment than fluoxetine from the perspective of suicide risk. Since this patient has suicidality, this issue is important. Further, the increased risk of suicidality with fluoxetine specifically occurs in patients in this young adult age group. Finally, the bipolar genetics of this patient raises the possibility that the patient may have bipolar illness, or at least does not have straightforward “MDD.” Lithium is proven effective for both unipolar depression and bipolar illness, and is the only drug proven to reduce suicide risk. The psychiatric nurse practitioner’s concern may have had to do with the perception that there are many more side effects with lithium than with fluoxetine, especially medical risks like kidney impairment. But, as discussed previously, lithium’s kidney risk occurs in a 20-year time frame, and is irrelevant to treatment for an acute depressive episode. Also, even though lithium has a long list of side effects, most patients don’t experience any of them, and they are dose related. Fluoxetine has its own list of concerning side effects as well, besides suicidality (which is bad enough), including severe sexual dysfunction and serious long-term serotonin withdrawal syndrome risk.
Curbside Consults

Questions and cases from you

Question: A 34-year-old woman with severe bipolar illness is prescribed lithium 900 mg/d, aripiprazole 20 mg/d, and hydroxyzine 50 mg BID for anxiety. She stopped taking aripiprazole for a month or so and then reported increasing anxiety. Her sleep is good when her family (child age 3 and husband) are away, but impaired when they are home. How should her anxiety be managed?

PL: Aripiprazole is a complicated medication. It is more effective for depressive symptoms at lower doses (<10 mg/d) and for manic symptoms at higher doses (>15 mg/d). In this case, it isn't clear what her current or recent mood symptoms have been. If she has been mostly depressed recently, then it would be reasonable to reduce aripiprazole to 5-10 mg/d to see if she is willing to take it, assuming she doesn't have akathisia or some other important reason why she can't take it. If she has had akathisia, or was recently or currently manic, then it likely makes sense to replace aripiprazole with a different dopamine blocker, like asenapine or risperidone. Despite her current anxiety, quetiapine would have the disadvantage of weight gain and metabolic syndrome, unlike asenapine. Another option could be to add divalproex to lithium, since divalproex has direct anxiolytic effects. It can cause weight gain, but it doesn't cause metabolic syndrome.

Question: To follow up on a prior PL curbside consult, I am sure I'm not alone in wanting PL's opinion about when/how to treat the painful symptoms of grief with medication when there is no prior history of depressive episode.

PL: The general recommendation made by PL was to differentiate grief from depressive illness by the course of illness. If there are past depressive episodes, then this recurrent condition would be seen as an illness. The setting of grief could be seen then as a trigger, not a cause, of the current depressive episode.

The question seems to be whether and how and when one might consider medication treatment when grief is diagnosed, not recurrent depressive illness. In other words, the patient never had a prior depressive episode, but is currently experiencing severe grief.

Should such patients receive medications, like SRIIs? The PL view is that in such settings the use of medication would be symptom-based, not disease-based. Symptom-based treatment is discouraged by PL, but this is a matter of emphasis not prohibition. One should prescribe medications less frequently, at lower doses, and for shorter durations, when such treatment is purely symptomatic.

So in this case of pure grief that is severe, a clinician might decide that some medication could be given if the patient refuses psychotherapy, or if the latter is not available, or if psychotherapy is not helpful enough. Any SRI could be used, such as citalopram or fluoxetine or sertraline, but PL would recommend as low a dose as possible, for as short a time as feasible. Thus, one might give sertraline 25 mg/d and if the patient remained symptomatic, increase to 50 mg/d. If there was sufficient benefit, it might be continued for 3-6 months, and then stopped.

Cultural considerations are relevant. A colleague in Egypt asked about treating grief there. In Muslim countries, grief is valued, even when severe. However, the clinician should keep an eye on patients so that suffering doesn't become extreme. Suicidality, if present, could be treated with low dose lithium 150-300 mg/d.
Upcoming Courses/Seminars
by PL Editor Nassir Ghaemi MD

July 2017 - Cape Cod, MA
Becoming a Master Clinician: Diagnosis, Drugs and Existential Psychotherapy,
New England Educational Institute,
July 24 - 28, 2017, Cape Cod, MA.
www.neei.org

August 2017 - Martha’s Vineyard, MD
Clinical Psychopharmacology: Principles and Practice,
Harvard Medical School CME series
August 21-25, 2017, Martha’s Vineyard, MA
www.capecodsummerseminars.com

October 2017 - Santa Fe, New Mexico
Becoming a Master Clinician: Diagnosis, Drugs and Existential Psychotherapy,
New England Educational Institute,
October 25 - 28, 2017, Santa Fe, NM.
www.neei.org