Q and A about Dysthymic Disorder (Chronic Depression)

"Over the past few decades, there has been a revolution in the treatment of chronic depression. We really can treat this illness effectively in many people. This couldn't be said twenty or twenty-five years ago…"

—David Hellerstein, MD

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1) What is dysthymic disorder and how is it diagnosed? And how has the new DSM-5 changed the categorization of chronic depression?

Dysthymic disorder (abbreviated as DD) is *chronic low-grade depression*. It is one subtype of what the DSM-5 now calls "Persistent Depressive Disorder," or PDD. [See this document for a summary of DSM-5 changes: Changes from DSM-IV-TR to DSM-5.]

The new category of PDD includes several forms of chronic depression, of which dysthymic disorder (DD) is at the milder end and chronic major depressive disorder (chronic MDD) is at the more severe end. To qualify for the diagnosis of Persistent Depressive Disorder, a person must have been feeling depressed for at least two years. In practice, people often after have suffered from depressive symptoms for twenty or thirty years or more before seeking treatment!

It is not difficult for people to realize that chronic major depression (chronic MDD) is a severe disorder, since on a day-to-day basis a person is likely to have significant and obvious symptoms. In contrast, dysthymic disorder is more subtle, and is easily overlooked. Yet the authors of the DSM-5 included dysthymia as a subtype of PDD because it is similar to chronic MDD and other forms of chronic depression in clinical course, in genetic risk, in family history, in neurobiological profile, and in its impact on people's lives.

Indeed, even after decades of research, dysthymic disorder is still under-recognized and under-treated. Thus, now as in previous decades, dysthymia can be thought of as a paradoxical disorder. Though its symptoms are fairly mild on a day-to-day basis (especially in comparison to chronic MDD), over a lifetime DD is actually a *severe* disorder—leading to high rates of suicide, work impairment, and social isolation. In fact, the risk of suicide is higher with dysthymia than in acute major depression! Another aspect of the paradox is that because people think of dysthymia as mild they often do not seek treatment. Or if they do seek treatment, it is with types of medicine or therapy that are unlikely to help them feel better.

2) What are the main symptoms of dysthymic disorder?

The main symptoms of DD include: depressed mood (lasting 2 or more years); feelings of hopelessness; poor concentration or difficulty making decisions; low self-esteem; low energy or fatigue; poor sleep; and poor appetite or overeating.

Our research studies have shown that there are more subtle symptoms of DD as well, which may be even more common. People with DD are also often socially withdrawn, and perform below their abilities at work and school. They often find it difficult to take normal day-to-day risks such as asking someone out on a date, or calling to apply for a job. They are often easily discouraged, and often have difficulty completing tasks. They are often overly pessimistic.

Indeed, the impairment in life functioning that is often associated with dysthymic disorder probably results from at least 3 sources: 1) core depressive symptoms; 2) social avoidance and decreased willingness to take normal day-to-day social risks; and 3) often-subtle cognitive impairment.

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3) How is dysthymic disorder different from other types of depression?

Most of the time when people talk of “depression,” they have meant what the DSM-5 would call “acute major depressive disorder.” Major depressive episodes are generally severe, and may be fairly brief in duration—lasting perhaps weeks or months. In major depression, mood drops markedly, and is usually accompanied by poor sleep, loss of appetite, weight loss, hopelessness, and often with suicidal ideas. In contrast, DD is not as severe on a day-to-day basis, and (by definition) it lasts for years (even decades) rather than weeks or months.

Many times, people who present for treatment of depression actually have “double depression.” That is, they have a longstanding problem of chronic low-grade depression, but now they are also in a state of major depression. (This is another subtype of the DSM-5 category of Persistent Depressive Disorder, in which a person would be considered to have PDD with 'intermittent major depressive episodes, with current episode' of MDD.)

It is important to try to tell if a person has double depression—since if they are treated and merely return to their usual chronically depressed state, they have not really gotten well! That is, if the major depression has gotten better but the person now has merely returned to their usual dysthymic state, then it is a mistake to say that the treatment is a success!

4) How is dysthymic disorder different from normal sadness or unhappiness?

Any sort of normal life loss, or transition, or stress may be accompanied by a few weeks of low mood. This is what the DSM-5 call an “adjustment disorder with depressed mood,” and puts in the category of 'Trauma- and Stressor-Related Disorders.'

Generally with an adjustment disorder, things improve after a few weeks to months. In contrast, the person with DD remains depressed for years, even decades. This is not “normal sadness or unhappiness”—it is an illness.

It is worth noting, as psychiatrists and neuroscientists are well aware, dysthymic disorder is what we call 'heterogeneous.' That is, there may be different neurobiological circuits involved between different people who present with similar symptoms. This is clearly a limit to our current psychiatric diagnostic system, the same being true of other conditions like schizophrenia or bipolar disorder. On the other hand, this problem is common to all of medicine: what we call hypertension or diabetes may come from many, many different causes!

That said, the symptom profile presented by people with PDD or DD is striking, particularly because it is so long-lasting and persistent within one person's experience, even though specific symptoms may differ from one person to the next. Whereas normal sadness or unhappiness generally improve once one's life circumstances improve, the typical person we see for our dysthymia program describes being 'depressed as long as I can remember' or since primary school, middle school, or 'over the past ten years.'

5) How common is Persistent Depressive Disorder?

PDD is one of the most common mood disorders. It affects as many as 3 to 5% of the general population. It occurs about equally in men as in women, though women are generally more likely to seek treatment. Different studies suggest that the percentage of people with 'pure' dysthymia, or without a history of major depression, is about 1-2 %, and the rest of people with PDD have either intermittent or chronic episodes of major depression. Regardless of subtype, many people with PDD have no idea that they have a mood disorder. They often think that they are “meant” to be depressed, or that negativity, pessimism, sadness, low energy and so on are just part of their “personality.”

6) Is Persistent Depressive Disorder physical or mental, or both?

There has been a lot of debate about this over the years. Until the Diagnostic and Statistical Manual, 3rd edition (the DSM-III) was published in 1980, individuals suffering from longstanding depressive symptoms were thought to have “neurotic depression.” If their depression was a “neurosis,” the logical treatment was psychoanalysis -- which hoped to cure neuroses. [An aside: the original meaning of neurosis was an inflammation of the brain, but in common parlance a la Woody Allen neurosis means psychic experiences related to unconscious mental conflict].

However, the 1980 DSM-III reclassified chronic depression “dysthymia” as a “mood disorder”—in the same category as major depression and other forms of severe depression.

Since then, there have been many studies of DD, which have generally shown that dysthymia (or as the DSMIV put it, dysthymic disorder; and, as the DSM-5 now puts it, Persistent Depressive Disorder) *does* respond to antidepressant medicines.

[See here for a Cochrane review of medication studies of dysthymia, which reviews the 17 double-blind placebo controlled studies that had been done as of 2005. And here for another recent medication review.]

People with dysthymic disorder, the mildest presentation of PDD, show abnormalities in sleep, brain images, hormone levels, and even their immune systems, that are generally similar to those seen in other forms of biological depression.

So PDD is physical, but it is also mental! And it may respond best to treatments that work on both mind and body.

7) What are the causes of PDD?

There are probably a variety of causes of chronic depression among different people. (As noted above, depression is 'heterogeneous'!) Clearly, people who face increased life stresses are at increased risk of developing chronic depression—loss of a parent, chronic stresses of poverty or unemployment, chronic medical illnesses or pain -- these are associated with greater risk of developing persistent depression. [One useful term to describe this risk-increasing situation of chronic stress is allostatic load]

Some people may have genes which predispose them to, or protect them from, chronic depression—an often quoted study reported in *Science* by Caspi and colleagues suggested that polymorphisms (variants) of the serotonin transporter could 'moderate the influence of stressful life events on depression.' Some people may be protected against developing PDD, and others may develop DD no matter how supportive their family environment may have been.

Also, there are certain habits which can increase the chance of a person staying depressed—for instance, having a negative style of thinking, a tendency toward pessimism, a feeling that nothing can help, and reluctance to do anything to change unpleasant realities in one's life. All these things may make chronic depression a self-fulfilling prophecy.

8) What is going on in the brain of someone who has Persistent Depressive Disorder?

Depression has been shown to be a "brain-mind-body problem." People with chronic depression are likely to have greater abnormalities in their brain than people with only one or two brief episodes of depression. Chronic depression is a state of chronic 'stress activation': the body's stress-response systems are revving nonstop. Hormones (like cortisol) stream through the body, preparing you for dangers which may never materialize. The effects of this long-term "activation of the stress response systems"

are devastating for the brain and the body. The body responds by increasing adrenaline, by elevations in blood pressure, by increased blood levels of sugars and fats.

The brain responds by having its alarm systems in an "always-on" state. The amygdala, the brain's panic system, actually grows in size! The hippocampus, the brain's center of working memory, and the prefrontal cortex, the area of planning and reflection, actually wither and shrink! Chronic depression is toxic for your brain!

DD is also toxic for your body. Because of stress activation, people who are chronically depressed are at greater risk of heart disease, diabetes, osteoporosis, and many other medical problems, not just the psychiatric symptoms of depression. Not to mention that they are likely to eat worse diets, to smoke more, to drink more alcohol, and to use more recreational drugs—all of which can make you feel better in the short run, but are obviously bad for health in the long run.

9) You mentioned above that people with dysthymia are more likely to be suicidal than people with major depression—is that really true?

Surprisingly, yes. Daniel Klein, a researcher at SUNY Stonybrook, did a study following people with dysthymia over a 5 year period. He found that over time they are at higher risk of suicidal behavior than people with acute depression! When you think about it, though, this is not as surprising as it may seem. People with dysthymia are almost certain to eventually develop major depression (and go into a state of "double depression"). They often have health problems, and poor work histories, not to mention problems with their intimate relationships.

Compounding this is the fact that people with DD can't look forward to feeling good once their more severe depression goes away—they may just return to their baseline "funk."

10) Does dysthymia run in families, and if so, why do some people in a family get it and others not? What should you for the kids of someone with dysthymia?

A person with dysthymia is likely to have other relatives with various types of depression. With early-onset dysthymia, the rate of depression in family members may be >50%. Other family members may have DD, or major depression, or bipolar disorder. Also there is an increased likelihood of other problems such as alcoholism. Patients in our practices and research projects often realize that "it runs in my family"—and will then begin to refer their relatives for treatment. Of note, the DSM-5 category of Persistent Depressive Disorder brings together different forms of chronic depression because of an 'inability to find scientifically meaningful differences between these two conditions led to their combination with specifiers included to identify different pathways to the diagnosis.' This includes similar risk of mood disorders in family members among people who have chronic major depression and those who have 'pure' dysthymia.

As far as kids go, research on children suggests that depression (or persistent anxiety) starting early in life may lead to all kinds of problems in development, school performance, relationships with peers, and so on. If a kid appears to show signs of depression, or ongoing behavioral problems, an evaluation is usually indicated.

11) If you have chronic depression, what should you do to get evaluated?

You should definitely see your primary care doctor, and have a physical exam and laboratory tests. A variety of medical conditions may cause, or worsen, chronic depression—everything from diabetes to thyroid disease to various types of infection.

If there's "nothing wrong" medically, then you should consider getting a psychiatric evaluation, which should include evaluations of not only whether you have a "disorder" but also the life issues that may be contributing to your depression. It makes sense to do a "self-evaluation" as well, to consider what aspects of your current life may contribute to depression. Too much alcohol, marijuana, caffeine, and other drugs, or a lack of physical activity, can contribute to depression.

12) What are the best treatments? And what are the worst treatments?

The best treatments are those which help reasonably quickly. Generally, antidepressant medicine should relieve symptoms of DD within 1 or 2 months after it is started. Most classes of antidepressants have been shown to work in DD. Psychotherapy should also have some effect on the symptoms of chronic depression within a number of months (not years!!). If the treatment isn't working, you should discuss this with your doctor or therapist, and you might consider getting a consultation, or changing treatment approaches.

The worst treatments are those which are pursued for a long time even if they aren't helping. People with chronic depression may enter therapy (or take medications) and keep going for a very long time without asking themselves, "Is it working?" Note: there are a number of useful self-rating scales for one's level of depression, including the Quick Inventory of Depressive Symptoms.

Oftentimes, people with DD and other forms of chronic depression are given the wrong type of medicine. For instance, their anxiety may be treated with Valium-like drugs, or benzodiazepines. Or their cognitive symptoms may be treated with stimulants such as Adderall or Ritalin. These medicines have their benefits, but don't particularly help chronic depression, and may become addictive.

The very worst treatments are "self-medication," in which people use alcohol, cocaine, or other substances, to try to make themselves feel better. Obviously, these solutions may create problems of their own.

13) When should you get psychotherapy? When should you get medication? And when you need both treatments?

We don't know for sure who will respond best to medication and who will get better from therapy. It often makes sense to try one type of treatment first—go into therapy for several months, or try medication. If you don't improve after a number of months, then you could either switch treatments or add the other type of treatment. People with more severe depression often need both therapy and medication—for instance if you have "double depression," both DD and major depression at the same time. A person who is suicidal or unable to function or is facing severe life stresses generally needs both medication and therapy.

Sometimes combined treatment can be very helpful. In one of our studies, people with DD were first put on medication. After they had responded to antidepressant medicine, we then put them into group therapy—to help them to address the many psychological consequences of having had been depressed for so many years. While continuing medicine, they worked on improving social relationships, changing their negative thought patterns, and taking more chances in life. The results of that study suggested that they did better overall—in more areas of life, symptoms, psychological functioning and social functioning—than people who just stayed on medicine. In another study, we added Behavioral Activation Therapy, a specific form of behavioral therapy that focuses on increasing time spent doing rewarding activities.

The bottom line is that when people with chronic depression receive effective treatment, whether medication or therapy or both, the large majority of people can have a good outcome. As dysthymia experts Haykal and Akiskal put it, "With sustained pharmacotherapy and specialized clinical care, 3 of 4 patients immersed in gloom for much of their lives achieved for the first time good to superior levels of functioning that were maintained for an average of 5 years."

14) What are the best things a person can do to help him or herself recover from chronic depression?

Take an active approach. Review your life situation, your health habits, even your psychological approach to life. What are the main stresses that you face? Can you make life changes that will make you happier? Think about your relationships and your connection to your community, and how they might be improved. It is important to find meaningful social connections in order to recover from depression, especially from chronic depression.

15) Does exercise help? Diet? Changing your sleep habits?

Some fascinating recent studies suggest that exercise can have a significant effect on depression. In animals, it has been shown that the brain shrinkage caused by depression can be reversed by antidepressant medicine, and it can also be reversed by exercise. Amazingly, the combination of exercise and antidepressants leads to an additive effect! We don't know for sure if this is the case in humans, but it is possible. There are many studies showing that exercise does help depression in humans, so it often makes sense to add it to a treatment plan. (Some studies also suggest that

learning makes your brain grow—so maybe we should encourage people with DD to study something new as well!) As far as sleep goes, chronic sleep deprivation has been shown to worsen depression, so normalizing sleep is likely to be helpful.

All that said, people with DD often have done all the lifestyle changes possible and still find that they suffer from depressive symptoms, and that consequently psychiatric treatments are still helpful.

16) Does St John's Wort work for dysthymia? What about Sam-E? Omega fatty acids?

In Europe, St. John's Wort is commonly used for mild depression. Studies in the U.S. on St. John's Wort in the treatment of severe depression haven't shown very positive results. There hasn't been much good research on its use in DD. The same goes for Sam-E or Omega-3 fatty acids. Our overall recommendation is that as with any other treatment you should consult your physician before starting such a treatment. In general, when doctors do a "medication trial" with any drug, we require that the patient take "enough medicine for enough time," and we closely monitor the symptoms that we are trying to treat. Our sense is that these "natural" compounds should be considered like drugs and require similar close monitoring.

17) How does medication work to treat dysthymia? Is it true that antidepressants cause parts of the brain to regrow or changes the activity of brain circuits?

This is a complicated question. The simple answer is that we don't entirely know how the antidepressant medicines work. They do have effects on brain transmitter systems, especially on serotonin and norepinephrine. They appear to interrupt the abnormal cycles of brain activation, and to normalize many things in the brain—they normalize the levels of hormone production, they improve sleep, and so on. People who have responded to antidepressant medicines show changes in their brain functions, which become more normal. Interestingly, new research in the past few years suggests that the parts of the brain which have been shrunken and withered as a result of stress hormones actually do begin to recover after successful treatment. The hippocampus, the brain's center for working memory, actually can grow back! Other areas of the brain begin to reconnect again. This is true for depression in general, not just for dysthymia. It would be particularly encouraging if we can find this to occur in dysthymia, since this is such a chronic disorder: does the brain actually begin to regrow after many years of depression-induced shrinkage? Our research group is beginning a study to look at this issue—using MRI scans before and after antidepressant treatment in chronically depressed people.

One of our recent papers showed that something called the 'default mode network' (DMN), a series of brain circuits that are active during self-focused thought, is more active in people with dysthymia, compared to people without a mood disorder. We measured the activity of this part of the brain by using resting state MRI brain imaging. When a person is told to close their eyes and let their mind wander, the default network

circuits light up, suggesting that this brain network is more active when the mind is wandering. And in dysthymia, like other forms of depression, our study showed the DMN is hyperactive [see our 2013 paper in JAMA Psychiatry]--some people have even hypothesized that depression is a disorder of abnormal mind wandering, in which people are unable to turn off this tendency of their brain even when they need to focus on a task at hand. Interestingly, in this study we found that antidepressant treatment led to normalization of the DMN activity whereas there was no change with placebo treatment. We are now doing another study to try to replicate these findings.

18) What types of psychotherapy are helpful for dysthymia? What types aren't helpful?

Surprisingly there are not many studies of psychotherapy in DD--especially because for so many decades DD was thought to be a "neurotic" condition. We do not know whether psychoanalysis helps DD—even 100 years after Freud. It may, or may not. Most therapy studies of DD have used cognitive or behavioral therapy (CBT) or interpersonal therapy (IPT) approaches. In these studies, such approaches have been promising. There have been a few studies combining therapy and medication—the most famous being the CBASP study, which compared the addition of a type of cognitive-behavioral therapy to antidepressant medicine for fairly severe chronic depression, and found that combined treatment was much more effective than medicine alone.

Types of therapy which are not helpful are those which are pursued fruitlessly for years. If the symptoms of chronic depression aren't better after several months, it is time to ask why.

19) What are the main goals in the treatment of dysthymic disorder?

We think that DD treatment should have phases. Because symptoms have lasted for many years, it may take a while to dislodge the effects of chronic depression from your life! The first goal is elimination of as many of the symptoms of DD as possible—the depressed mood, the hopelessness, the poor sleep, the tearfulness, and so on. This is often accomplished in a few months or less. Then a person enters what has been called a "post-dysthymic" state—they are not depressed, maybe for the first time in their adult life!

Often this is the time that psychotherapy really starts to be helpful. Once a person is beginning to feel good, it is often clear how chronic depression has had devastating effects on his or her life. Social withdrawal, undue pessimism, low energy levels, procrastination, chronic irritability, and other symptoms may have laid waste to your life! Beyond this, a person who has experienced a "depressed self" for many decades may feel that to be his or her "true self"—and the beginning of good feelings may be in some ways disorienting or confusing. At this point in treatment, it often becomes important to work on improving your life, your social and intimate relationships, your work life, and so on. It is important to begin to take more risks on a day to day basis, to challenge

yourself with things that may have previously been avoided. So, to make a long story short, medication treatment of DD symptoms may often set the groundwork for successful changes in therapy.

20) How do you know if treatment is working? How long does it take before you should start getting better?

If the main symptoms of DD are beginning to fade away, the treatment is likely to be working. This may begin to occur within the first two to four weeks, and symptoms may continue to improve over eight to twelve weeks or more. The life changes that occur after the DD is under good control may continue to unfold over a year or two years or more.

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21) Are there some people who are less likely to respond to treatment? If so, who? And what kinds of treatment they should get?

People who have several types of problems are less likely to respond than people with only one type of problem—for instance, a person who is using drugs or alcohol and has DD is unlikely to have a good response until they get sober. Also, people who face severe and ongoing life stresses may be less likely to respond. People with very severe chronic depression are less likely to respond to medicine alone—or to therapy alone They need combined treatment, with both medicine and therapy.

One big category of people who are less likely to respond to treatment are those who have been misdiagnosed. If you actually have a medical problem (thyroid disease, cancer, etc.), antidepressant medicine isn't likely to help! On a more subtle level, a person with chronic depression who actually has manic depressive illness (but is misdiagnosed as having DD) may actually get worse rather than better when put on antidepressant medicine!

In brief, anyone who is treated for DD who doesn't get better should get a closer look, perhaps a second opinion!

22) If medication or therapy treatment doesn't work, what to do next?

Consider re-evaluating the problem, as indicated above. If DD really is the diagnosis, and medicine didn't work, then consider switching to therapy, or adding therapy. If therapy was the first option, one might consider adding medicine. If one type of

medicine doesn't work, doctors will often decide between different options: either switching to another class of medicine, or adding a second medicine ("augmenting").

23) What are the main side effects of medicine?

Medicines used for DD are generally the same antidepressant medicines used for major depression. They include the serotonin reuptake inhibitors (SRIs), such as Prozac, Zoloft, and so on; the serotonin-norepinephrine reuptake inhibitors, such as EffexorXR or Cymbalta; and various atypical medicines like Wellbutrin, Remeron, and others. Side effects vary, but the person with DD has special issues to face: since their symptoms are fairly mild on a day-to-day basis, it is important to find medicines which have fairly low side effects and can be tolerated over long term treatment. SRIs can have sexual side effects, for instance, which may be higher for some medicines (Paxil) and lower for others (Celexa, Lexapro). WellbutrinXL is thought to have low sexual side effects. Weight gain also varies, with some medicines associated with more and others with less of this side effect. Our research projects have focused on medicines which seem likely to be low in side effects (such as Lexapro and WellbutrinXL), and this is something we study.

24) Is medicine addictive?

Antidepressant medicines are not addictive. They do need to be taken on a daily basis, and generally need to be discontinued in a gradual fashion rather than abruptly. They do not have the characteristics of addictive medicines like alcohol, heroin, or barbiturates which require greatly increasing doses over time to maintain the same effect.

25) If your depression is better but medicine has ruined your sex life what should you do?

This topic has gotten a lot of attention by psychiatrists, both researchers and clinicians. Sexual side effects of antidepressant medicines are often worst when the medicine is first started, and may improve over time as your body gets used to the medicine. If not, sometimes changing medicine dose may help. Other times, psychiatrists will suggest changes in the type of medicine, or adding a second type of medicine to try to counteract this side effect. There has been some research on Viagra, which seems to help many men. Our research group is planning a study of another medication, which increases brain levels of doptamine. Some antidepressant medicines, such as WellbutrinSR or WellbutrinXL, appear to have fewer sexual side effects.

26) What happens if you come off medicine abruptly?

Two things may happen: 1) a person may begin to have "rebound" symptoms, and 2) the depression may come back. Rebound symptoms occur because your brain and body are suddenly deprived of the medicine you have been taking regularly; your brain's receptors are "hungry." Some medicines such as Paxil and Effexor appear to cause

more severe rebound; they should be discontinued particularly slowly. Overall advice: consult with your doctor before coming off medication, to decide when and how to do it best.

27) How long do you need to stay on medication/in therapy for treatment of dysthymia?

There is relatively little research on this topic. About two dozen studies have shown that antidepressants work for short-term treatment of DD. A handful of studies have shown that medicine continues to work for a year or more. But there are very few studies of discontinuing antidepressants. If a person's chronic depression has been "in remission" for a year or more, does it make sense to go off medicine? This is a fairly unknown area. We believe that this area should receive more systematic study.

28) You mention that cognitive symptoms are commonly seen in people with dysthymia and othe forms of PDD. What kinds of problems are there and how can they be approached?

There is relatively little research on this topic. It is clear that depression is often associated with impaired work functioning, and some studies have even shown that among people with *remitted* depression they still have some impairment in their work functioning, and in cognitive functioning. The causes for this are not entirely clear. And the percentage of people who have this problem is not entirely clear either. One way to think about this issue is to ask whether a person may have 2 coexisting conditions, attention deficit disorder (ADD) as well as PDD. Some people clearly do 'meet criteria' for both disorders. And this can be confirmed by neuropsychological testing. Other people may have 'primary' ADD with a 'secondary' depression, in which they have ADD first and later on in life, perhaps as a result of the negative impact of ADD on their life functioning they may develop chronic depression (ADD may be part of their 'allostatic load' referred to above). Other people may have a 'primary' depressive disorder and later in life develop cognitive problems, perhaps because of the negative brain effects of chronic depression.

What to do about this condition? A good evaluation is always indicated, with assessment of both mood and cognitive problems. If mood disorder is thought to be primary, then an active treatment approach for depression (including treatments listed above, considering medication and psychotherapy, as well as exercise, etc. etc.) makes sense, while tracking the cognitive symptoms. Some people such as those with primary ADD may benefit from medication targeted for ADD, which can include stimulants and other classes of medication.

Interestingly, a newly introduced medication, vortioxetine (brand name Brintellix) has been demonstrated to have some beneficial effects on cognitive functioning in people with depression. This hasn't yet specifically been studied in DD or other forms of PDD, and it is still too early to know whether this medicine represents a significant advance or

not. Regardless, it seems likely that future treatments of PDD will take improved cognitive functioning into account as one of the desired outcomes of treatment.

It is also worth noting that there is a new science of 'cognitive remediation' that has the goal of improving memory, attention and problem solving; it has primarily been developed for people with schizophrenia but could be adapted to the needs of people with PDD, and computerized training could possibly be helpful for these difficulties.

29) Any other thoughts?

Just that over the past few decades there has been a revolution in the treatment of dysthymic disorder, and other forms of Persistent Depressive Disorder. We really can treat this illness effectively in many people. This couldn't be said twenty or twenty-five years ago. So, on the whole, we're very optimistic. There's still a lot to learn about this condition—its causes, what's happening in the brain, and in the body (for instance in the immune system). In the brain, we have amazing tools like MRI scanning which can allow us to look not only at the structure of the brain but also at how it works—how activity in different areas of the brain changes when you think about sad or happy things, for instance. And MRI even allows you to measure the amount of transmitters in various parts of the brain, and how they change after medication treatment! On the treatment side, we have many medications that work, and we know how therapy and exercise and other things can help. In a nutshell: chronic depression is treatable. This is a very exciting time to be working in this field.

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