

# Robert Hedaya, MD: Depression and the Practice of Whole Psychiatry

Interview by Craig Gustafson

**Robert J. Hedaya, MD, ABPN, DFAPA**, is the founder of the National Center for Whole Psychiatry in Chevy Chase, Maryland. He is board certified by the American Board of Psychiatry and Neurology and is a Distinguished Fellow of the American Psychiatric Association. He is a clinical professor of psychiatry at Georgetown University Medical Center, an active member of The Endocrine Society, certified as proficient in psychopharmacology by The American Society of Clinical Psychopharmacology, and has been recognized as a master clinician in functional medicine by the Institute for Functional Medicine. Dr Hedaya is a recipient of the Physician's Recognition Award from the American Medical Association and has been voted Outstanding Teacher of the Year multiple times by the Georgetown University Medical Center's Department of Psychiatry. He has authored books for both practitioners and consumers, has been featured as an expert consultant numerous times in the media, and writes a blog for Psychology Today.

Dr Hedaya is the developer of the Whole Psychiatry methodology, which offers a comprehensive physiological and psychosocial-spiritual approach to mental health and chronic physical illness. His method evaluates and treats mind and body dysfunction by focusing on the detailed evaluation and bidirectional interactions between and among a person's hormonal system, immune system, gastrointestinal system, nutrition, environment, socio-spiritual status, genetics, detoxification, cell signaling, life circumstance, age, and gender.

**Integrative Medicine: A Clinician's Journal (IMCJ):** At what point in your life did you realize you had a passion for medicine and psychiatry?

**Dr Hedaya:** For medicine, it was in college, while my passion for psychiatry developed in my last year of medical school. I was matched to be a surgeon and decided to take an elective in child psychiatry, since I had a child and thought it might make me into a better father. I fell in love with psychiatry.

**IMCJ:** Please describe your educational path and how that influenced your development as a practitioner.

**Dr Hedaya:** I applied to medical school and actually did not get in, and I was waitlisted at Georgetown. I decided to go to Mexico for medical school. That was very difficult for a lot of reasons. Being an American in Mexico is very challenging. After 2 years, I decided to take 6 months off, study for my boards, and transfer back to the States. That was a wonderful opportunity because it allowed me to actually integrate the basic sciences. I spent 6 months studying 10 hours a day. I could go from—if I was studying say lung cancer—the pathology to the anatomy to the histology to the biochemistry. I was really able to integrate the whole body of basic science. That was wonderful.

In psychiatry, reductionist thinking was predominant. There were many schools of thought about the root causes of mental illness. Each was really its own religion, whether it was behaviorism, family systems, neurobiology, or psychodynamics. At the time, it was estimated that there were over 600 types of psychotherapy. It was jarring and confusing. As a way of coping with the anxiety of not knowing, we were encouraged to choose just one theoretical approach and learn it well. I consciously decided to maintain an open mind for 4 years—to tolerate the anxiety of not knowing. By the end of my 4 years, I had become able to integrate the major theories of mental illness into a whole perspective, without leaving any one of them out, and consequently I had more tools with which to help people.

Most people have what I call *premature closure*. They close their thinking down and have too much anxiety to allow for the introduction of paradigm-breaking ideas. I think it is important for clinicians to keep their minds open to new paradigms and to always work toward integrative thinking.

In 1995, I wrote my first book, where I started to integrate medicine and psychiatry. Following that, I developed a mild case of chronic fatigue syndrome. I did a workup on myself and was horrified to see that my natural killer cells were suppressed. That spurred me to do research. One thing led to another, and that is when I realized that the head was connected to the body by the neck. I successfully treated myself using functional medicine principles.

Because it made sense and had cured me, I pursued training in functional medicine and learned about all the

systems that are involved in physiology, including the physiology of the brain, and began to integrate that into my practice. That has been developing steadily since then.

**IMCJ:** You evolved from a traditional psychiatric practice with a more open-minded approach to incorporating physiology and functional aspects of the body and their impact on the brain. When did the formal idea of *whole psychiatry* first come together for you?

**Dr Hedaya:** I first started to think about whole psychiatry as a concept formally in the late 1990s—I would say 1998 or 1999. My general idea is that one's understanding of mental health, and even physical health, depends on the lens one uses. If you use a very high-powered lens, you see atoms and molecules. As we lower the power of the lens, we might see metabolic pathways. Then if we lower the power of the lens some more, we see organ systems, and then the whole body. If we lower the power of the lens further, we see relationships. If we lower it further, we see family systems, and then community, culture, political systems, economic systems, environmental factors, and at the lowest power the whole earth, and even the sun and moon. That might seem far-fetched, but it is well known that there are more emergency room visits around the full moon.

The power of the lens and the nature of the lens that you use determine what you see. It is very important to have the flexibility to use lenses that vary. This led me to the concept of whole psychiatry. It is not just about functional medicine and traditional psychiatry. It is about always trying to see the whole picture and also leaving space for what we do not know. There will always be things we do not know. One very important idea to add to the mix is the spiritual dimension of things. It cannot be ignored and is, I would say, the most powerful type of psychosocial therapy.

**IMCJ:** Could you describe a couple of examples of how the spirituality aspect impacts physiology?

**Dr Hedaya:** I saw a patient last week who originally came to me about 2 years ago with a very severe depression. She was very upset about being irritable with her children. We worked on her physiology and I also repeatedly suggested cognitive behavioral therapy. In the course of discussion, I

told her that I was hoping cognitive behavioral therapy would give her more resilience, a way of thinking about things in a more realistic way. She was resistant.

Finally, I asked her what her spiritual orientation was. She said she believed in God. I asked her how that was active in her life. She said she prayed. I asked her how she felt when she prayed and what she thought about when she was praying. She said she would experience gratitude and joy when she prayed. I encouraged her to pray more often and more regularly, a suggestion she actually thanked me for, since it gave her permission to take more time with prayer. Now, I was thinking, if she could actually embed that routine behavior and accompanying mind-state into her psyche on a more regular basis, and have consequent neural development along those lines, then she would have more resilience and her stress threshold and response would be markedly improved.

That would have downstream effects on everything from her gut to her hypothalamic-pituitary-adrenal axis, her immune system, her children's development, her social world, et cetera.

Next is a very interesting case because it demonstrates the integrated nature of mental health with the rest of a person's life. I first saw this patient in 1985. He had been hospitalized, had depression, and was suicidal as a result of having panic attacks that were uncontrollable. He was treated in the hospital and was on Nardil, which is phenelzine. That was a monoamine oxidase inhibitor that was used back then. He did well; we did group therapy and individual therapy. After about 5 years,

he was transferred to Prozac. He was stable and I would see him once or twice a year.

After a few years of being stable, he came in and told me he was going to marry a woman who had been abused. I told him there was a high risk that she would develop problems such as chronic fatigue, PTSD, et cetera. He married her and sure enough, after about 5 years she developed chronic fatigue syndrome and fibromyalgia and was unable to work. He had 2 children, which his wife was not able to take care of. At about the same time his father died, leaving a retail store to my patient, who then had to leave his chosen career, take over the store, and also care for his unstable mother.

All of these stresses caused him to feel so anxious that



he would start overeating and he gained about 30 pounds. He went to his internist and said he thought he was having reflux. He was put on Prilosec. After 2 or 3 years on Prilosec he developed panic attacks, again, for the first time in 20 years.

I spent about 6 months trying to convince him to do a workup and finally he consented. We found a number of things, but particularly it revealed that he had a B<sub>12</sub> deficiency. It is known that Prilosec inhibits the absorption of B<sub>12</sub>. When I gave him B<sub>12</sub> injections, his panic attacks went away, his mood improved, and we worked on his diet and learning how to manage stressors.

With this case, you can see the interrelationship of life factors, the domino effect, and how these factors develop into what looks to be a pure psychiatric illness: in this case panic attacks. It was really multifactorial and operated at many different levels. In the past few years, I have been encouraging his spiritual development and he has gradually been able to handle his stresses more and more easily, without resorting to self-defeating behaviors such as overeating.

**IMCJ:** In the latter case, the patient's condition before he came to see you seemed to be exacerbated by the fact that efforts to get it under control were not working. When considering the spiritual aspect of treating depression, what role does hope have in the equation?

**Dr Hedaya:** Hope is critical in all healing—a book written by Jerome Frank, entitled *Persuasion and Healing*, deals with this topic very effectively. Hopelessness is one of the cardinal features of depression, as is helplessness; hope and depression are inversely correlated. Hope assists healing and can, in and of itself, cause healing; but there are many situations, such as the latter case, which cannot be treated exclusively with hope, but also require some detective work and targeted treatments. Hope can keep the patient engaged in the process of healing.

The other issue I want to mention is that of control, helplessness, and spirituality. Depression is thought of as a state of *learned helplessness*, as described by Martin Seligman. Generally speaking, we strive to have control over the experiences that society deems essential to generating self-esteem: love, power, achievement, money, et cetera. When we think that we have lost hope of attaining these things—ie, we are helpless in controlling them—most people slide towards depression.

The issue, which is not often addressed by professionals, is the fact that there is a false, socially embedded assumption here. The hidden assumption is that we can/do/should have control over these things, when in reality these things are, in significant measure, dictated by many circumstances and situations outside of our control. If you just think about it: Did you get to where you are in life without parents, friends, or natural endowment? Is your ability to maintain your function not

contingent on all the people around you functioning in a reasonably consistent and reliable manner? Even the most successful of us can lose our status overnight. The only things under our control, ultimately, are our attitude and the choices we can make. Gratitude—a great attitude—is essential. With that, one can adapt to nearly anything in life. It is even better than a fat bank account. So, whatever it takes to develop skill in maintaining a great attitude, that is what one should engage in, in a deep way. Make the best choices you can, and do not get overly attached to outcome. Along with that, one should associate with people who manifest the characteristics one wishes to develop. The nature of who one is, and one's healing, occurs most easily in community, not in isolation.

**IMCJ:** Last year you responded publicly to a pair of doctors who engaged in a debate over whether antidepressants really work. As part of your response, you had cited societal acceptance of the “one pill for every ill” concept. It accused doctors of basically employing faulty logic in their attempt to treat depression and other chronic illnesses. Would you summarize your response to their opinion that effort should be dedicated to the development of tests to determine who would respond best to which drug therapy?

**Dr Hedaya:** First, I would say they are missing the point. As in the case of the 60-year-old psychotic woman I mentioned, the medications did work when the underlying physiology was corrected. So, it was not an issue of choosing the right antidepressant. In fact, no one antidepressant has ever been shown to be superior or more efficacious. That type of predictive information is not needed. When a patient is not responding to medication, psychopharmacologists embark on a series of medication trials. I know this process because I became an expert at it. When one medication trial works, the doctor assumes the medication choice was the causative factor, when in fact it could be any number of other factors, which the physician does not ask about. We now know of so many factors that feed into the syndrome we call *depression*, so perhaps the patient responded because their mother-in-law moved out, their husband became more loving after he got his raise, their anemia corrected, et cetera. If we invest our resources in detailing the specific factors at play in each individual, and correct them, most people will recover from depression fully and with less medication. As an added bonus, the chronic medical conditions that are comorbid with depression also improve. On the other hand, the current neurocentric paradigm that relies heavily on medications has high cost, low efficacy, and worsens the burden of chronic medical illnesses such as diabetes. Worst of all, we know that treatment with medications, even combinations of medications—at the very, very most—get 60% of people into recovery. Why spend more resources trying to make

predictions when there is no evidence of superiority among antidepressants?

So, in answer to your question, I am adamant that putting so much of our energies into being able to predict medication response is a very big error. I am continually struck by the fact that doctors—who are supposed to be scientists are heart, as well as healers—ignore a huge body of evidence that has identified the wide range of treatable factors involved in depression. Pills, while useful in some situations, are really overprescribed, overused, and receive way too much of the resources.

**IMCJ:** You mentioned that the psychotropic drugs have effects that extend well into the function of the rest of the body. If this is so well accepted, then why is it so hard for people to accept that conditions affecting the function of the rest of the body can also then, conversely, affect the function of the brain?

**Dr Hedaya:** I think there are 2 problems. One is “group-think,” and the other is money. We are operating within the latest in a long series of faulty paradigms. There has been a great deal of mystery about the nature of mental health, questions that go back for at least 2500 years. Check out the book of Job. The paradigm there, for Job, was that his misfortune and misery were the result of a kind of “bet” between Satan and God. For a more recent example of a faulty paradigm, we can look back to the mid-1500s. At that time, it was thought that depression was caused when one was inhabited by evil spirits. So, quite logically, exorcism was the treatment of choice. The fact is that the etiological theories of mental illness have changed in cycles lasting approximately 50 or 60 years. Often, as in our current psychopharmacological paradigm, financial gain distorts the science. At the start of a cycle, the results of the new approach are always exceptional and promising. People get very excited and hopeful, and others capitalize on that exuberance. Eventually, when the bloom is off the rose, the limitations of the methodology and treatment become apparent. Eventually a new paradigm and methodology are born.

At this point, I believe we are coming to the tail end of the psychopharmacological era and people are looking at rTMS, transcranial magnetic stimulation, as the new hope. I am not certain that it will take root, as the evidence base is already quite weak. But, we are always looking for a magic bullet, group-think takes over, and people make money from it.

A third factor is that people do not like uncertainty. It makes them anxious. In order to reach an integrative experience of a problem, one must first pass through a threatening state of tension. What if I am wrong? What if I lose? What if I fail? These and other doubts and fears flank the bridge we must cross to become holistic, integrative thinkers and problem solvers. If you look at the world, you see a tremendous amount of dualism. Just read the headlines: the Republicans and the Democrats, the

Sunnis and the Shiites, the Jews and the Arabs. They cannot come to an integrative solution. In medicine, this shows up as, “I don’t want to think about how it all works together, I will just think about the liver, or the neuron—not even the whole brain. Only neurons matter, astroglia and microglia don’t really have a clinical impact.” Either we are not trained to think integratively, or it is very, very difficult for people to think in an integrated way. It is much easier and less anxiety provoking to have a simple solution, based on good/bad, right/wrong dualities.

**IMCJ:** Depression in our society is running rampant. What are your thoughts on why this is happening and why the medical establishment is failing in its efforts to reduce its prevalence?

**Dr Hedaya:** Depression will be the second leading cause of disability, according to the World Health Organization, by 2020. Why? The answer depends on what lens you use to analyze the problem. On a molecular level, there are so many toxins and new-to-nature chemicals in the environment—for example, hormone interrupters—that they can influence people’s vulnerability to depression. We can also look at the nutritional value of foods: where they are grown, how they are processed, and even what one’s mind state is when one is eating matters. As an example, some people I treat come from Pennsylvania. They are never deficient in zinc, but many people living in Maryland are deficient in zinc. This is because of the soil, the genetics of crops, the weather, and the way they are grown.

On a macro level, we need to look at the social fabric. Community and family systems have broken down. Social networks are transient and fragile. That has an effect on a person’s mental health, because we experience this as if we are in survival mode—existentially threatened. If you are connected to a group, you have a safety net. If you are fundamentally alone, if it’s all up to you, then you walk a tight-rope. People are like giant neurons; the better connected we are, the healthier we are.

We need to also consider the value system in Western society. We place a premium on material things. There is tremendous competition and pressure to achieve material wealth, in the face of a growing population and fewer resources, on a per capita basis. We are oriented towards and are taught to value the material, not the relational, not the meaningful. Living out of the latter 2 constructs requires much strength and support, as one who adopts these values is very much like a salmon swimming upstream to its birthplace.

**IMCJ:** You have mentioned viewing a patient’s case through lenses of various power. Through whole psychiatry, how do you put your lenses metaphor into practice?

**Dr Hedaya:** What I do is fairly unique and I am fortunate to be able to do it, because I have developed my practice

this way. When I see a new patient, I spend 4 hours with them, and whenever possible a person whom they trust and who knows them well, so that I can get an outside perspective. I start by getting basic metrics—eg, BMI—and then we identify the problems the person wants help with. After expanding on these, I do my best to determine what sequence of events led up to the problems. This usually results in a few different overlapping timelines. Following this, I delve more deeply into the individual problems, so that I can understand what processes—metabolic or otherwise—might underlie the symptoms. Following this, I take a detailed 3- or 4-generation family history. While I used to believe this would shed light on genetics, it has since become clear that environment and genetics are seamlessly connected, via epigenetics. But through this exercise, I pick up important facts that give me a transgenerational perspective on the bio-psycho-social elements. This is followed by a review of the developmental personal and medical history and a physical exam. After I have gathered all of this information, we discuss hobbies, goals, and the nature of the partnership of healing. Throughout this process, I am assessing mental status and making a to-do list for the patient, to help them prepare for the next appointment. I am also educating them as to the nature of the problem—eg, I might teach them about learned helplessness, or about the connection between depression and inflammation. When I feel I have gotten all that I need to form a provisional understanding of the person, I take a few moments by myself to integrate the information. We then talk for about 30 minutes. During that time, I retell the story of the development of the problems to the present day. Because of the complexity, I do this in 2 ways. First, I discuss traditional diagnoses. Second, I tell the story back to the patient in a way that integrates the different strands. Many patients are so relieved to be understood in a manner they themselves intuited but could not articulate. Following this, I outline the work-up I recommend, the costs, and the follow-up plan. The plan is then amended, based on the person's resources, readiness to change, and ability to be a partner. One of the most important things to assess is whether one has a partner in healing and what supports they themselves have. Once we have decided on the plan, we move forward. When I have all the information back—lab tests, computer tests, et cetera—I spend 2 hours with the information and write up a plan, which I then present to the person and their support person. In follow-up meetings, I track all the parameters that we are working on.

**IMCJ:** You have discussed the volume of clinical science that links subjective and objective mental health to at least 6 metabolic processes. Through the lens of depression, will you discuss how each affects the patient?

**Dr Hedaya:** One of the things people who read this journal are aware of is the functional medicine matrix,

which is a useful tool for assessing these things. Let's start with nutrition. What we take in is essential. Are we eating enough protein, healthy fats, complex carbohydrates, fibers, et cetera? Are we eating a good balance of these macronutrients? These factors almost always play a role in mood regulation. Are we eating frequently enough, or do we have intraday mood swings? Obviously the nutritional value of what we eat, how we eat it, and what our mind state is when we eat it have important roles in our body getting the basic building blocks and resources it needs to function. This is particularly important when you are under a lot of stress. As an example, zinc is necessary for proper serotonergic signaling, for production of testosterone, and for immune regulation. Fatty acids, vitamin D, a variety of B vitamins, other amino acids—all of these nutrients and others play central roles in the neuro-immuno-endocrinology of depression.

As we move from nutrition to digestion and absorption, we become concerned with whether a person is able to extract what they need from the food, without paying too much of an "immunological cost." This is another way of saying that digestion, absorption, immune function, and depression are inseparable. Numerous studies have shown that tryptophan depletion, whether due to diet or pancreatic exocrine deficiency, causes a relapse of depression within 6 days in people who are fully responsive to SSRIs. Supplying free-form tryptophan to these same people results in complete recovery at day 6. This tells me that we humans have a 6-day reserve of serotonin, and that if a depressed person eats poorly, even if she is on an SSRI, she will have a partial response to the medication. Should she switch to a new medication, or should nutrition and digestion be assessed? In this regard, I find food sensitivity testing, a comprehensive stool analysis, and a consultation or 2 with a nutritionist to be 3 powerful tools to normalizing the gut in the vast majority of patients. All of this is also quite relevant because a large number of depressed people have significant gastrointestinal problems, such as IBS.

Now, even though most practicing mental health practitioners prefer to deny it, we know the gut is intimately linked with the immune system, which in turn is linked to the brain. Even minimal peripheral immune activation via dysbiosis or even minor exposure to the lipopolysaccharide envelope of bacteria leads very quickly to elevated levels of IL-2, IL-1, IL-6, and TNF- $\alpha$ . This changes brain function within 1 hour of immune activation. All the changes are linked with depression because of reduced ability to synthesize serotonin and melatonin, and increased dopamine and glutamate, which are excitatory and in the latter case, neurotoxic. Does this mean that all depression is caused by inflammation? Not at all. However, it is usually a layer of the problem, which results in inadequate treatment response, and it can be the trigger of an affective episode, and certainly, if the research is to be believed, it increases the risk of neurodegenerative diseases. If the gut

is malfunctioning, the psychiatrist must take note. An irritable gut makes an irritable mind, and vice versa. So, in this sense, psychotherapy and pharmacotherapy function as immune modulators, and this has been a focus in the mainstream journals. Unfortunately, the recognition of the immune role in mental health and illness is followed by a simplistic call for drug development.

We have talked about nutrition, digestion, and the immune system. But of course, all 3 of these aspects of physiology are inseparable from the endocrine system. And of course hormones are also linked to one's psycho-social-spiritual status. In the case of depression, and really all psychiatric illness, we must always consider the hormonal systems. Every hormone affects brain function. As one example, adequate catecholamine signaling and melatonin receptor function require adequate activation of the thyroid receptor by free  $T_3$  in the brain. I urge clinicians to do a very thorough assessment of thyroid function using body temperature, symptoms, signs, and laboratory data. Barring medical reasons to the contrary—such as atrial fibrillation or untreated adrenal insufficiency—a patient with depression should always have a TSH below the population mean of 1.4. There is literature that indicates that hyper-metabolic doses of thyroid hormone can effectively result in recovery from depression, and I have used this approach with success at times.

Next, we should consider genetics. For example, the MTHFR SNP is very relevant. While it seems that people in the general population may have the C677T SNP anywhere from 15% to 30% of the time, a retrospective analysis of 100 patients in my practice has shown that the incidence of heterozygotes is about 60%. Homozygotes are present in about 20% of my patients. This knowledge is very important because it obviously has effects on methylation pathways and the ability to make and break down neurotransmitters and certain hormones.

Interestingly, when the genes related to bipolar disorder were recently mapped, over 100 were identified. The genes that were most closely related to bipolar disorder were those related to the metabolic syndrome, cocaine abuse, and hyperthyroidism. But there are 2 caveats when it comes to genetics. First, although we like to think that a certain SNP correlates with a clinical syndrome, that is not usually true, because a gene can always be compensated for, to some degree, by other genes and metabolic pathways, and one gene is always part of a much larger network. A gene is only a vulnerability; it is not a statement of absolute fact in terms of function. Second, and this is not well-appreciated: Genetic testing is not without errors. A woman I treated was tested at 3 different labs for a MTHFR SNP. Two were in agreement, and one was not. It took 6 months and a conference call with several experts to determine that one lab was using a technology that conferred some increased risk of error.

Of course, genetics leads to a discussion of epigenetics, which is really fascinating. I will share a case here: I treated

a 19-year-old African-American woman who was studying architecture. She was failing her classes, could not concentrate, had tremendous anxiety, and was overweight. I asked her what her diet was. Her diet was, she thought, very good. She ate a traditional African-American diet, which included high protein and high fat content. She thought eating fried chicken was healthy. We worked on her diet and did nothing else. A year and a half later she was getting straight As and doing exceptionally well.

I think that part of the issue was not only cultural, but may also have been epigenetic. African Americans needed high fat/high protein diets, for back in the days when there was slavery, people worked long days in the fields—very heavy labor. I think that her inheritance reflected the genetic adaptation to that environmental circumstance. She experienced the need for those types of foods as if she were really still working in the fields. She changed her dietary intake to reflect the current circumstance, which was difficult—but she did do it. As her food-based information washed over her genetic code, the expression of her genes changed. I think that may be an example of epigenetic as well as cultural phenomena. Certainly, current research into the etiology of bipolar disorder and psychosis is pointing to the role of epigenetics in phenotypic expression.

Oxidative stress is, obviously, relevant to mitochondrial function and inflammation. I frequently see anxious and mildly depressed people who are stressed, and as a way of controlling their stress, overexercise. These people have high levels of oxidative stress. This type of adaptation to stress, over long periods of time, can cause fatigue via inflammation and a growing inefficiency of mitochondrial processes. This then affects microglia, astrocyte function, neuronal function, and signaling. Of course, these dysregulated processes then, if one has other vulnerabilities, will have an effect on brain function—in this case, mood and other mental illnesses. Ultimately, I think we want to be able to match genetic vulnerability with lifestyle. For example, if a child with ADD has a family history of Parkinson's disease, we might want to know the long-term effect and proper dosing of dopamine agonists, such as methylphenidate, before we use them. It is known that lower doses selectively work in the prefrontal cortex, but higher doses affect the basal ganglia, including the substantia nigra. These medications increase synaptic levels of dopamine, but intraneuronally, dopamine is converted into 3,4-dihydroxyphenylacetaldehyde, or DOPAL, which via disruption of the glutathione free radical system is neurotoxic. Could there be a risk in using them in such a situation? We do not know.

I have to say that the role of oxidative stress and free-radical biology is an area that still needs more research so that we can develop our clinical ability to assess and treat the specific downstream damage, while addressing the upstream causative factors, such as overexercise, the effect of certain medications such as dopamine agonists, et cetera.

**IMCJ:** How would circulatory and physical structural problems impact depression?

**Dr Hedaya:** Certainly structural problems can have a big impact. If you cannot sleep because you are in pain, have sleep apnea, or have arthritis, then your disrupted sleep taxes every system we are talking about. Not having adequate sleep is equivalent to having a very potent toxin in your life. It is a major, major factor. You break a bone and it changes your life. It changes your sleep. It changes your diurnal rhythms. It changes your whole pattern of functioning. If you have a chronic structural problem, you have to adapt to it, which takes time and causes stress. You *can* adapt to it though.

Circulatory problems clearly play a roll. A woman whom I was treating for migraine had certain markers that could have been indicative of hypoxia on a test of organic acids. She turned out to have a patent foramen ovale. I sent her to the cardiologist, who sent her to the surgeon, who then closed the patent foramen ovale, and her migraines went away. Just yesterday, I discovered that an 18-year-old with treatment for suicidal depression, depersonalization, OCD, babesiosis, and Lyme disease has moderately severe endocarditis, most likely from a prior staph or strep infection. Clearly, reduced oxygen perfusion caused by the structural problem, valvular vegetation, is a very likely contributor to his psychiatric problems.

On a more common level, if someone has small vessel disease, atherosclerosis, cerebral microinfarcts, or congestive heart failure, oxygen delivery to the brain is affected. One can have an infection like *Bartonella*, which causes endothelial dysfunction and consequent metabolic encephalopathy. That is both infectious and circulatory.

A long time ago, when I was early in my practice, I treated a woman who had no prior psychiatric history. When she was about 70 years old, she had a quadruple coronary artery bypass. After that surgery, she developed a suicidal depression, which she had never had before. She ended up being on lithium for the rest of her life. I think the likely cause of that was micro infarcts related to the bypass machine. In fact, there have been studies suggesting that about 50% of people at that time were having micro infarcts as a result of the problems with the bypass machine.

**IMCJ:** Is there an intervention that you can do now that is nonpharmaceutical that can address an adverse event such as that?

**Dr Hedaya:** I do not know that there are any trials that have shown evidence, but in theory, things that I would do would include recommending a strong aerobic exercise program to enhance neurogenesis, using acetyl-L-carnitine to help bring more nutrients into the mitochondria, taking CoQ10 and thiamine to assist in mitochondrial function and carbohydrate metabolism, and assuring normal iron status—as well as B<sub>12</sub> and folate. Actually, the list can be

very long. I think the optimal approach is to take a detailed history, do physical and laboratory assessments, determine the areas of physiology that need support, and design a personalized program for brain-body health. In theory, although I have no idea whether this is true, perhaps hyperbaric oxygen could be useful. I do not think that in every case these things would reverse the injury, but the brain, if one works with it over an extended period of time, and I mean a few years, is very plastic and can change for the better. Over a period of time the brain can work around these types of deficits, and even if the areas of the brain that have been damaged permanently can not be restored, other neuronal areas can be recruited to restore function.

People with strokes, over a period of years, if they really are diligent about it, can have full recovery, even from severe strokes. Therefore, I feel that if you have micro infarcts, as an example, over time, with proper nutrient and behavioral support, and management of stress and inflammation, the brain should be able to compensate eventually by finding other ways of doing what it needs to do. Now this is only one case, but I can report that I used this methodology with one woman with MS who had multiple white matter lesions on her MRI. Her symptoms and her MRI cleared completely over 18 months.

**IMCJ:** How does whole psychiatry give you an advantage in addressing the cascades that eventually end up causing depression?

**Dr Hedaya:** In a broad sense, if I can help people with this approach, not only do we use less medicine and improve mental function, but at the same time we are actually improving overall health and function in the world. People have more satisfaction with life and can live into the life they envision for themselves. You improve mental health, physical health, and social functioning, and in that case you are really affecting the whole system and the systems that the person is embedded in. That is pretty significant. With this approach, less energy goes into managing the side effects of medications with other interventions, which we know cause or contribute to other chronic medical problems and the bankrupting of our medical system.

On the case-by-case level, when you are trying to treat something with a drug, if you have not addressed the underlying mechanisms necessary to allow the drug to work, the drug cannot work, or it can only work partially. For example, I treated a 60-year-old woman with psychotic depression. She had lost 50 pounds and thought her husband and son were plotting to kill her. She had been to 2 or 3 other doctors and a major university department of psychiatry, where ECT, or electroconvulsive therapy, was recommended. The family brought her to me because she had not responded to various interventions and her son did not want ECT. She walked in circles in my office for 3 hours, not saying a single word, while I collected the



history from her family. In this case, I used medication concurrent with a personalized correction of the systems we have been discussing. Within 2 months, and that is no exaggeration, she was 85% back to normal. Her system was corrected so that the medications could assist in recovery. That was a tremendous advantage because she did not have to have ECT. At the same time, I helped her body to begin functioning normally. She has been fine for 5 years, except for one moderate relapse that was the result of her decision to stop various aspects of her program. Basically, the advantage is that you can treat treatment-resistant cases with less medication and with fewer side effects. That is the bottom line.

**IMCJ:** In cases such as psychosis or conditions where people have started to lose touch with reality, how does that impact your ability to apply all the aspects of whole psychiatry, especially in collecting the history and communicating with these patients to obtain the concrete information that is key to making decisions?

**Dr Hedaya:** As in the case I just mentioned, having a very involved, organized, and committed family member is essential. It would be wonderful if there were an inpatient facility that would work in this way for those who do not have the support or ability.

**IMCJ:** What other aspects of depression need some lip service?

**Dr Hedaya:** One thing I would talk about that I think is relevant concerns the article in the *New England Journal of Medicine*, published in 2008, by Eric Turner, which talked about selective publication bias of antidepressant trials. It is really important to note that the publication of medication trials is very biased in favor of positive outcome. The article discussed the fact that about 50% of the antidepressant trials approved by the FDA were not published. It turned out that 94% of the ones that were published observed positive results. However, this was very deceptive since only the positive studies were published by the drug companies. When Turner studied all FDA approved studies, it turned out that only 51% of all the studies were positive. Clinicians were misled by the drug companies' own bias. We really need to question and be somewhat cynical about what is published in terms of medication effectiveness and science in general. I believe that there is so much competition for grant money and the desire to advance one's career, that many scientists become biased. For example, you may read an abstract in an article where the authors say, "We did this study to prove that hypothesis X is true." Really, what it should say is, "We did this study to test hypothesis X." If you say you did the study to prove the hypothesis, that means you are already invested in the outcome, and therefore you are already more biased than the inherent observer bias that has been

documented in physics. When I read an abstract with that terminology, I become biased against the conclusions of the authors because of the erosion of the scientific attitude. It affects mental health research, and to varying degrees, all research, really.

One item that is not seriously attended to, I think, is the nature of the patient's relationship with the physician. It has a huge, huge impact on healing and physiology. I could give you so many examples of this. I saw a patient today who was suicidal. He had transferred to another clinician in my office, but since he was suicidal, I wanted to see him. The other clinician could not really work with him, but because I had a long-term relationship with him, he was very amenable to what needed to be done.

A better example is a woman I have been working with for 2 years—very complex—with complex temporal lobe symptoms and severe fatigue. She was not functioning at all, and she had narcolepsy and nonpsychotic visual hallucinations. After much work, she is feeling better than she has felt in her whole life. I said to her, "What do you attribute your improvement to?" She said, "First of all, Dr Hedaya, I love you." Okay, that is not what I expected, and I felt very humbled. She didn't mean, "I am in love with you," obviously, but the relationship was so valuable because she felt she had someone in her corner who could understand her, could relate to her, was open to her perspective, and could work in partnership with her. That has tremendous value.

We cannot successfully achieve that with everyone, because to a certain degree, this is a matter of chemistry. I think we give lip service to it, but the clinicians who are more experienced and who are not working in managed care really come to appreciate that over time.