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CURESZ FOUNDATION

Newsletter

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Comprehensive Understanding via Research and Education into SchiZophrenia

Treatment Resistant Depression (Part 1 of 2)

by **Stephen Rush**, *MD*

In recent decades, as the stigma around mental health has begun to dissolve, it has become more common for people to openly talk about feeling *"depressed."* But what does that mean? What are the differences between feeling *"sad"* and feeling *"depressed?"* Sadness frequently occurs in response to loss, disappointment or when facing difficult problems. Stressful events such as the loss of a loved one, loss of a job or income, failing an exam or the breakup of a relationship often make us feel sad. This emotion stems from a triggering event or situation and usually passes with time or resolution of the stressful event.

But when sadness doesn't go away with time or the resolution of stressors and interferes with the ability to function at home, at work, or in relationships, it may be *"depression."* While sadness is a normal human emotion, depression is a psychiatric condition with emotional and physical symptoms that disrupt our ability to manage everyday life.

Many people use the word *"depression"* when describing sadness and *"clinical depression"* to describe the medical condition that requires treatment by trained experts. Other terms for *"clinical depression"* include Major Depressive Disorder and Bipolar Depression. Throughout this article, we will use the word *"depression"* to refer to a psychiatric depressive illness, diagnosed by a doctor, therapist or counselor and requiring specialized treatment.

What Is Depression?

A depressive episode occurs when an individual experiences a period of at least 2 weeks during which they have five or more of the following symptoms, with at least one of those symptoms being either depressed mood or loss of interest or ability to feel pleasure.

Symptoms include[1]:

- Depressed mood
- Loss of interest/pleasure
- Decreased appetite/weight loss or increased appetite/weight gain
- Insomnia or hypersomnia
- Psychomotor agitation or retardation
- Fatigue
- Feeling worthless or excessive/ inappropriate guilt
- Decreased concentration
- Thoughts of death/suicide

Decreased ability to function, when depressed, is often due to a lack of interest in normally enjoyable activities, decreased energy, lack of motivation and difficulty concentrating on otherwise easy tasks. When untreated, this disease can result in a decline in grades at school, poor performance at work and withdrawal from social interaction with friends and family.

A 2020 survey found 21 million people in the United States, or 8.4% of the population, had experienced a depressive episode at some time in their lives.[2] While depression can affect persons of any age, ethnicity or gender, it is usually first diagnosed in early adulthood, with 17% of people ages 18-25 experiencing at least one episode of depression. Women are almost 2 times more likely to develop depression than men and the highest prevalence of depression occurs in people of mixed ethnicity.[3]

Fortunately, depression can be successfully treated, thanks to the availability of specific medications and psychotherapies. However, it is important that treatment begins early in the course of depression, before it results in poor occupational, academic or social functioning.

The most well-known and first-line treatments for depression are medications often called *"antidepressants."* There are several classes of FDA-approved antidepressants, all of which have effects on *"neurotransmitters,"* or the chemical messengers in the brain that impact thoughts, feelings, and actions. The chemical messengers most often targeted in treating depression are serotonin, norepinephrine, and dopamine.

While all antidepressants can produce similar improvements in depression, they differ in their tolerability due to side effects and their safety concerns in certain populations. The Selective Serotonin Reuptake Inhibitors (SSRIs) are often the first type of antidepressants prescribed. Prozac, developed in 1987, was the first SSRI approved by the FDA, soon followed by others including Zoloft, Paxil, Celexa and Lexapro. Other classes of antidepressants are the Serotonin-Norepinephrine Reuptake Inhibitors (SNRIs) and the *"atypical anti-depressants"* such as Wellbutrin, a Norepinephrine-Dopamine Reuptake Inhibitor (NDRI) and Remeron, which affects serotonin and norepinephrine in unique ways.

Older antidepressants, the Tricyclic Antidepressants (TCAs) and Monoamine Oxidase Inhibitors (MAOIs), are less tolerable due to more severe side effects and less favorable safety profiles. As a result, TCAs and MAOIs are typically reserved for depression that has failed to respond to at least two or three of the newer medications: SSRIs, SNRIs or atypical antidepressants.[4]

Research also shows that psychotherapy, or counseling, is as effective in treating depression as antidepressants, both acutely and long-term. Many different types of psychotherapy can treat depression, including Cognitive Behavioral Therapy and Interpersonal Therapy, amongst others. These approaches involve identifying life events, distorted ways of thinking and unhelpful behaviors that contribute to depression, followed by developing specific skills that help with management of the symptoms of depression. Most importantly, the success of psychotherapy depends on a positive relationship between the therapist and the patient. In fact, a positive therapeutic relationship can be the number one predictor of successful treatment.[5]

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WhatSZ IN THIS EDITION

CureSZ News

SCHIZOPHRENIA SURVIVORS

Sarah Marzen, PhD

Today, my life is filled with love and support and kindness from strangers – even if they only ever know about me as the biophysicist who invented an opinion dynamics model out of psychosis.

~ Sarah Marzen

I grew up with a silver spoon in my mouth. I was advantaged by being in one of the best school systems in the country. I started out in AP Calculus BC in 9th grade – unusual for the school, but not unheard of.

But something was wrong. In 11th grade, I stopped trying as hard as I used to. I wasn't top 24 in the United States in Physics like I seemingly was in 10th grade anymore – only top 200. Overall, none of my teachers thought that my 11th grade performance was dismal. However, my mom was dismayed.

At that time, I started having bizarre dreams and experiencing visual hallucinations. I thought I was Ariel, the Little Mermaid, in dreams, and in real life, I thought I could make a vase wobble with my mind, like Matilda. But I graduated, and off to Caltech I went.

Despite the brokenness of my brain, I was quite social, active, and successful. I then chose to pursue a PhD in physics at the University of California, Berkeley, where things really started to go wrong with my mind. At first, things seemed to be going great. I was happily dating a new guy, one of the members of the Redwood Center for Theoretical Neuroscience, learning computer science and math from him. But my mood fluctuated. Some days I wrote songs about how poorly he treated me, and other days I felt we were deeply in love.

Love is love, but there was an actual problem in my life. The social ringleader of Redwood started insulting me at times for no reason that I could decipher while insisting that he loved me. I decided to leave Redwood and never go back, only to find out a year later that there were other women who didn't want to join the Redwood Center either because of him. We complained to faculty, and again, I felt incredibly guilty.

This was when my psychotic break first happened. I was sure that a powerful secretive organization had been infiltrated by people (mostly hackers). I was sure they had made up an entire email that I just didn't write.

I was so sad about this conspiracy, which I believed had ruined my reputation, that I decided to kill myself with aspirin. That day, I was taken to the hospital where they pumped my stomach, and eventually sent me to a psych ward. I was then medicated for paranoid schizophrenia.

Nothing worked medically. Finally, they let me out of the psych ward. I was zonked on Haldol and exhausted, but I still believed the hackers were following me. I stopped taking my medicine as soon as I could. I thought I didn't need it, and that I was just fine. But the symptoms got worse. The voices talked to me on and on. I was sure they were human and related to the organization.

Soon after, while my boyfriend was away, I swallowed 98 pills of meds that I hadn't taken, and washed them down with bourbon. The voices told me to call 911, and I did.

When I woke up, there was a tube in my throat to enable me to breathe. My then-boyfriend was there, working on a paper. But he couldn't take it anymore.

Somehow, throughout it all, the voices made me work. They insisted. Sometimes, they tried to block my thinking, but they always wanted me to publish paper after paper. So I was quite accomplished-looking by the end of my Ph.D., even getting an award for excellence. I had managed to nab a fancy MIT postdoctoral fellowship, which was probably a good thing, because then I lived with my little sister.

My first year at MIT, I published ten papers . At the same time, I was completely out of it. I never came into work. I constantly talked to the voices like they were people. Sometimes, I couldn't see my credit card, and then it would reappear in the same location just a day later.

My next psych ward stay was different than previous psych ward stays because for the first time ever, I tried Latuda, and it did something. All my voices collapsed into one. My brain, being trained in physics, was logical enough. If the voices were people, they wouldn't have collapsed into one. Therefore, the voices were voices. This was a disease.

I spent the next two years of my postdoctoral fellowship trying to do more normal things – coming into work, finding a new boyfriend (who is now my fiancée), reading the newspaper, eating breakfast. Interestingly, I was far less productive scientifically. To this day, I am unsure why. But my record was good enough that I was competitive for faculty positions all over the U.S. I eventually got a competitive job at the W. M. Keck Science Department at the Claremont Colleges.

But then, everything started – the paranoia flared up in every way. The voices wouldn't stop talking in my mind. Somehow, out of the crazy came some of my best work. My best science, my best writing, my best songs. I can't hate it completely. At the same time, the psychosis comes with suffering.

But when the voices clear up enough to allow me to live, my life is fantastic. I'm lucky enough to have friends and family that love me and take care of me as best they can, a fulfilling and intellectually demanding job that loves me as much as a job can love a person, and a fiancée who doesn't care that I'm 100 pounds overweight from antipsychotics and depressed binge eating and drinking.

So in a way, everything is okay. But in another sense, I am so far away from the carefree child with the silver spoon in her mouth that I wonder what will happen to my child, when I have one.

With new medications – for me, Latuda and Seroquel – and continuous therapy and psychiatric treatment, my life keeps on getting better.

The Reality of Having Schizophrenia: A Medical Student's Opinion

Alvin Mantey, *MD-MPH Candidate, MS4*
University of Cincinnati College of Medicine

My name is Alvin Mantey. I'm currently in my 4th year of a 5-year dual-degree medicine and master's in public health program at the University of Cincinnati. My family moved from Ghana to the United States when I was 14 years old, and that's where my journey in academia began. From pursuing show choir and soccer at the high school level, to majoring in biology with concentrations in biomedical studies in college, my journey through the U.S. system has been exhilarating to say the least.

But I'm not just an academic – my interests outside school lie in church activities, playing intramural soccer, and dancing on social media to over 1.6 million followers with my identical twin brother. When I'm not doing these things, I spend my time on Instagram educating people on all things mental health. This work is important to me as I find quite the gap between what I know in medicine and what people know about their own mental health. I do this work to help them live fuller lives in love, power and a sound mind.

My journey in psychiatry began with a dream – a dream to live in a world where all people are able to live to their fullest potentials. The catalyst for this dream was my own lived experience in Accra, Ghana, where I lived before I moved with my family. The people I saw, and the lives missed stirred in me an unquenchable fire, that I now, somewhat ironically, seek to put out. This is a calling for me, and with residency coming up for me soon, I welcome what comes next.

I hope to share with you another perspective: one which I hope captures my lived experience as well as the lived experiences of over 500,000 people with severe mental illness in Ghana.

Imagine this. It's a lovely Sunday morning in Pokuase, a community in rural Accra, Ghana. The air is filled with the smells and yells of street vendors as they sell delicious baked goods with an ungodly amount of sugar, and the sound of old engines rattling on. Children run across the unpaved streets as cars slowly navigate an army of water-soaked potholes from yesterday's rain. The colors and aromas of neatly dressed church members and deacons fill your eyes – men in suits, kaftans and traditional wear, and women in long, flowy dresses with luxurious jewelry and headgear. It is just another Sunday.

But amidst the natural chaos something sticks out. No, *someone*. She is dressed in tattered clothes and covered with earth. Her hair is brown and her skin dark from heavy sun exposure. Her face tells you all you need to know – lips chapped, feet bare, chest bony and her demeanor, determined? Apathetic? You cannot tell. Her eyes are sunken, and she carries on, step by step. Is she hungry, can she afford a meal? Where did she sleep, because it rained yesterday. Is she alone, where is her family? You ask these questions, but not to her. She makes eye contact with you, and mutters something under her breath, and you drive away. It is just another Sunday.

Demon-possessed "mad people." That's what we called them back home in West Africa. They were paying for sins they had committed or were victims of some shaman's curse. And she is not alone. There are thousands like her across the country, all abandoned, all ostracized.

Growing up, this was normal for me, and like most people, I paid no attention, neither did I worry or bother. Everything changed with my migration to the United States with my family when I was 14 years old. I looked for *mad people* everywhere, but they were nowhere to be seen. I thought, perhaps the United States doesn't have them like we do, or perhaps they are too good at hiding it. Or **they found a way to help them.** And I was right. Years later in medical school, I would uncover that the demons that plagued these people, were mental disorders, and the solution, anti-psychotics. Now antipsychotics are not a cure, neither are they benign. But they return the soul to the body, the mind to the person, and the person to their family. They're a game changer, and I'm not sure why I never heard of them being used back at home.

I recently took a trip back home, and surely enough, not much has changed. There were still many *mad people* walking around, and knowing what I know now, that there's treatment for them, made things even harder to wrap my head around. I know one day things will change, and with better medications on the market now, rapidly too. I hope to share the good news I've found, to *mad people* and their families, and to help people understand that there is hope – that they are not lost. That they too can put on suits and kaftans and long flowy dresses and partake in the natural chaos of a Sunday morning.

Alvin Mantey

For persons with schizophrenia, understanding and learning about the illness itself is vital. Therefore, consider investing some time learning about the biology and clinical aspects of the disease, and ask your psychiatrist and treatment team all the questions you can think of.

Click here to read the Treatment Checklist.

visit us at CureSZ.org

Treatment Resistant Depression

(continued from page 1)

What Happens When Treatment Isn't Working?

For 30-50% of depressed patients, standard treatments are not effective to adequately treat depression. Depressed patients who have not improved after at least 2 trials of antidepressant medications are often considered to have *"treatment resistant depression"* or TRD. A *"trial"* requires the medication be taken for 8-10 weeks at an effective dose, or an inability to tolerate the side effects of these medications at lesser doses.

TRD – The Need for Treatment

Having TRD increases the chances that a depressive episode will become severe or chronic, lasting 12 months or longer. TRD increases the toll that depression takes on an individual's level of functioning such that people with this refractory form of depression have a significantly lower quality of life as well as higher impairments in social and occupational function.

The economic burden of TRD is a shocking $43.8 billion annually. This is 47% of the economic burden and 50% of the total cost of care for all patients with any form of depression.[6]

Patients with TRD are more likely to have suicidal ideation (38% vs. 24%) and previous suicide attempts (14% vs. 10%) when compared to patients who respond to early treatments.[7] These statistics highlight the importance of early diagnosis and treatment.

It's Not Simple

There are psychiatric illnesses that result in symptoms that are also seen in depression. Post-traumatic stress disorder, personality disorders, anxiety disorders and even attention deficit disorder can result in the same symptoms seen in depression. In such cases, treatment of the primary illness can improve symptoms of depression, often using treatments different than those used to treat depressive disorders.

Further, other psychiatric illnesses can occur at the same time as depression and require more complex treatment. The most common comorbid psychiatric illnesses in patients with depression are anxiety disorders (Generalized Anxiety Disorder, Panic Disorder, Obsessive Compulsive Disorder), Post-traumatic Stress Disorder, Substance Use Disorders (Alcohol abuse/dependence) and certain personality disorders. Effective treatment, here, involves addressing both depression and any other psychiatric illnesses also present. Unfortunately, the presence of comorbid psychiatric illnesses increases the risk of developing TRD.

Additionally, there are medical diseases that can result in symptoms of depression including thyroid disease, heart disease (especially heart attacks), stroke, anemia, or diabetes. In other cases, the treatment of medical illness can cause depression including certain therapies for autoimmune diseases, liver disease, high blood pressure, inflammation and even acne.

Finally, there are also situations in which depression appears resistant to treatment but may be the result of preventable factors that decrease response to treatment. These include poor compliance with prescribed medications, insufficient doses of antidepressant medications and inadequate duration of treatment. If these conditions have not been met, lack of response to treatment does not indicate true TRD and appropriate trials of medications should be considered.[8]

Next time, we will review treatment options for those with Treatment Resistant Depression.

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