CureSZ
Research | Recovery | Hope

CURESZ FOUNDATION

Newsletter

ISSUE 7
SUMMER 2019

Comprehensive Understanding via Research and Education into SchiZophrenia

Removing Barriers to Clozapine Use

Clozapine is the only effective medication for treatment resistant schizophrenia, with response rates in the range of 40%-60% compared to < 5% for other antipsychotics.[1] Despite this, clozapine is significantly underutilized with up to 8-fold variation in rates of clozapine use between states.[2] In the U.S., the main barriers to clozapine use rest on two issues: the burdens of monitoring and prescriber fear.[3]

These two issues are intertwined and relate to the association between clozapine use and serious decreases in infection fighting cells (i.e. neutrophils) in 1% of patients. Clozapine's U.S. approval (1989) came with mandatory monitoring to track neutrophil counts: weekly for 6 months, every 2 weeks for the next 6 months, and monthly thereafter. While this has nearly eliminated serious outcomes from clozapine-related neutropenia, the fear which this (and other unusual adverse effects) aroused dissuades many clinicians from using clozapine with the net result that many did not learn how to use clozapine. Although data indicate that clozapine use lowers mortality,[4] many clinicians overestimate the risks of treatment and, sadly, subject patients to multiple trials of other agents with little chance of therapeutic benefit. While mandatory monitoring has vastly improved safety, it poses a number of difficulties for patients: travel costs, time, possible need for assistance to travel, discomfort from the blood draw, concerns among some about uses of their specimen, and the impact of delays in receiving the next prescription. Clozapine dispensing is tightly tied to pharmacy notification of blood results, and the quantity dispensed matches the interval to the next blood draw. For those on weekly testing, a delay of 24 hours in going to the lab or transmitting lab results places the patient in jeopardy of running out of clozapine.

Jonathan M. Meyer, M.D.
Clinical Professor of Psychiatry – University of California, San Diego
Psychopharmacology Consultant – California Department of State Hospitals

Yet, there is hope. At the state hospital system to which I consult, a regular lecture series on clozapine increased prescribing more than 2-fold. Moreover, healthcare systems in New York and the Netherlands showed that supporting prescribers facilitates greater clozapine use. Knowledge is indeed power, and clinicians in the U.S. have two new resources to facilitate clozapine prescribing: one is a handbook that I co-authored inspired by the lack of clinically oriented published resource on clozapine;[1] the other is a web-based educational site that (importantly) also provides clinical consultations to registered users (https://smiadviser.org). This initiative is free, and is sponsored by the American Psychiatric Association and the Substance Abuse and Mental Health Services Administration.

For patients, monitoring burdens may be lessened by a newly approved point-of-care (POC) device that uses a small drop of blood from a finger stick. The first of these devices (http://athelas.com) not only provides results within minutes, the results are automatically transmitted to the monitoring system so that medication can be delivered to the patient's home within 24 hours. The discomfort is less, there is no risk of delay between obtaining the results and medication dispensing, and the patient sees exactly how their blood specimen is used. The lack of delay means that a patient can have the test done anytime, and in almost any setting with trained personnel.

The clozapine renaissance has begun.

References:
1. Meyer JM, Stahl SM. The Clozapine Handbook. New York, NY: Cambridge University Press; 2019.
2. Stroup TS, Gerhard T, Crystal S, Huang C, Olfson M. Geographic and clinical variation in clozapine use in the United States. Psychiatr Serv 2014;65:186-92.
3. Cohen D. Prescribers fear as a major side-effect of clozapine. Acta Psychiatr Scand 2014;130:154-5.
4. Vermeulen JM, van Rooijen G, van de Kerkhof MPJ, Sutterland AL, Correll CU, de Haan L. Clozapine and long-term mortality risk in patients with schizophrenia: a systematic review and meta-analysis of studies lasting 1.1–12.5 years. Schizophrenia Bulletin 2019;45:315-29.

WhatSZ IN THIS EDITION

CureSZ News

SCHIZOPHRENIA SURVIVORS

Lauren Kennedy

Living Well with Schizophrenia

Lauren Kennedy, Social worker, research assistant and graduate student studying Health Policy Research at the University of Alberta

Lauren experienced a normal childhood, free from trauma. But as a teenager, she struggled with mood problems and apathy. She also experienced thought broadcasting, believing that others could hear her thoughts. Though symptoms caused her to skip classes, she maintained decent grades. These early warning signs went unnoticed.

After high school, Lauren began studying political science and psychology part time at the University of Alberta. A few months into college, at age 19, her boyfriend noticed something was wrong, and convinced her to see a family doctor. She was diagnosed with depression. At that time, she also experienced highs which led to higher productivity, and she embarked upon *"adventures,"* such as traveling and running in the mountains. For years, she never discussed these elevated moods with her doctor.

In 2011 Lauren decided to pursue a career in social work and transferred to the University of Waterloo in Ontario in order to complete her Bachelor of Arts degree in Social Development Studies. She won several scholarships and awards, and successfully graduated in 2013.

At age 22, Lauren decided to pursue a second bachelor's degree in social work. However, at this time, she began to experience her first thoughts of suicide and sought counseling at the university. Her diagnosis was changed to bipolar disorder, type two.

A few months later, in winter of 2014, she overdosed, which lead to her first hospitalization. On her release, she experienced hallucinations, hearing someone in the distance saying her name. She also sensed terrible smells, which were olfactory hallucinations.

A year after her first hospitalization, Lauren overdosed again. This was a more serious attempt and she was placed on life support for several days.

After her release from the hospital, Lauren returned to full time school at the University of Waterloo and seemed to be doing well. However, shortly after her release, at age 24, she experienced her first full blown psychotic episode. She struggled to sleep, and was full of *"paranoid energy."* Her new psychiatrist changed her diagnosis again to bipolar one with psychotic features. After her discharge from the hospital, she graduated with her second bachelor's degree in spring of 2016.

After the completion of her social work bachelor's degree, Lauren landed her dream job as a researcher for Cancer Care Ontario in Toronto. But unfortunately, her hallucinations had never fully gone away. Believing that her medication was poisoned, and outside forces were controlling her mind, she discontinued all medication. Off medication, she experienced her second full blown psychotic episode. This time, Lauren's diagnosis was changed to schizoaffective disorder. She was 25 years old.

"Lauren remembers her diagnosis as a relief. It finally provided an explanation for what was happening."

Lauren remembers her diagnosis as a relief. It finally provided an explanation for what was happening inside of her mind. She spent a difficult month in an Alberta psychiatric hospital but finally regained stability on a newer injectable medication.

Following her final hospitalization, Lauren began looking for her *"new normal."* She found it especially hard to deal with the stigma of schizoaffective disorder. Lauren benefitted from the Schizophrenia Society of Alberta, where she met others who were thriving despite a psychiatric diagnosis.

Today, Lauren is a successful student in her Public Health graduate program and once again enjoys working as a research assistant. She lives a meaningful and productive life and has not been hospitalized since October of 2016.

Lauren maintains a YouTube channel about her recovery called ***"Living Well with Schizophrenia."*** She shares the message that there is no shame in having severe mental illness, and that with medication and treatment, it can be overcome or managed. Although her road to recovery was at times very challenging, today she is thriving. Lauren is living proof that recovery is possible.

TARDIVE DYSKINESIA

MORE THAN A SIDE EFFECT

Dr. Craig Chepke, *Private Practice Psychiatrist, and Adjunct Assistant Professor of Psychiatry, University of North Carolina School of Medicine*

Tardive Dyskinesia (TD) was first described in the early 1960s, but we don't have a clear understanding of why it happens despite nearly 60 years of research. TD does seem to have a clear relationship with dopamine, which regulates a vast number of functions in our bodies, including attention, pleasure-seeking, and motor function. Some psychiatric disorders, including disturbances of mood, sensory perception, and thought process are believed to be associated with an excess of dopamine stimulation in certain pathways, or *"circuits"* of the brain.

We often use antipsychotic medications for these symptoms because they are dopamine receptor blockers (DRBs), and thus prevent dopamine from completing the circuit. In hyperactive dopamine circuits, this normalizes function, but DRBs are unable to discriminate between overactive and normal dopamine pathways. Sometimes blocking dopamine can reduce function in pathways it should not, and cause unintended consequences.

The basal ganglia is the part of the brain that is responsible for controlling movements, and is also dependent on dopamine to conduct its signaling. Prolonged use of DRBs can stimulate the basal ganglia to produce too many highly sensitive dopamine receptors. In an attempt to rebalance its diminished dopamine signals, the process may overcompensate for some. The motor system becomes hypersensitive, and dopamine now overstimulates it, resulting in the involuntary movements, or *"dyskinesia"* that give TD its name. *"Tardive"* comes from the French word for *"late"* because it generally takes months or years of exposure to a DRB before the symptoms develop.

Imagine you're listening to music with a friend, and you think the volume level is normal, but it's too loud for him. He gets out ear plugs, but puts them in your ears as well as his. Now you can't hear the music at all, and you find the ear plugs won't come out, so you turn the volume way up to compensate. Eventually the ear plugs may malfunction and fall out, and the music sounds unbearably loud. Unfortunately, you find that the volume button is broken, and you can't turn it down.

The real problem with TD isn't that it's delayed after the start of a DRB, it's that it's generally irreversible. Not everyone taking a DRB gets TD, but those who do can't get rid of it by stopping the medication. While some risk factors are known, we don't yet have a very good way of predicting who is going to get it before it happens. Or in the terms of the analogy above, we don't know whose earplugs are going to malfunction.

Therefore, we shouldn't consider TD a *"side effect"* of DRBs, because side effects go away if you remove the medication that cause them. Rather, we should think of TD as its own syndrome that is cause by exposure to DRBs in vulnerable people. Just like cigarette smoking causes lung cancer in some people – those who get cancer don't go into remission just because they stop smoking. Improving Tardive Dyskinesia at that point requires its own additional treatment, which I'll discuss in my next column.

CureSZ Brain Facts

by Henry A. Nasrallah, MD
CureSZ VP and Scientific Director

Brain Regions Involved in Schizophrenia

Part 2: The Hippocampus

The hippocampus is one of the most critical components of the human brain. It is involved in multiple psychiatric disorders and its volume is smaller due to atrophy in depression, PTSD, Alzheimer's Disease, and chronic alcoholism but is developmentally hypoplastic (smaller) in schizophrenia. Its functions include:

- Neurogenesis: the dentate gyrus within the hippocampus is a *"neurogenic region"* where progenitor cells (stem cells) are created throughout adult life, and replenish the brain. In young adults, the hippocampus generates 250,000 baby neurons/month!
- Memory: the hippocampus is the *"grand central station"* of auto-biographical, spatial and episodic memory in the brain. Hippocampal injury can lead to serious amnesia and poor navigation skills. Chronic stress is toxic to the hippocampus and shrinks it.
- Learning: the acquisition and retention of new information.
- Emotions: the hippocampus is a component of the *"limbic system"* which is associated with emotional regulation, and a dysfunctional hippocampus can disrupt emotional stability.

(Next issue, Part 3: The Cerebellum)

CureSZ

visit us at CureSZ.org

LONG-ACTING INJECTABLE MEDICATIONS

Long Acting Injectables (LAIs) are an intramuscular formulation of antipsychotic medications which are already available in pill form. These injections were first developed in the United States in the 1970s to ensure continuous delivery of the antipsychotic medication to the brain of a person with schizophrenia who often is unable to take their oral medication regularly, and ends up relapsing and getting re-hospitalized.

There are several reasons why nonadherence with medications is common in schizophrenia:

1) Over 80% are unaware that they are sick and refuse treatment because they believe they do not need it.
2) Memory is impaired in most individuals with schizophrenia, so they actually forget to take their tablets.
3) The paranoid thoughts make them think they are being poisoned if they have a side effect.
4) Alcohol and substance abuse is very common among persons with schizophrenia living in the community, and that interferes with taking prescription medications. Relapse is serious because psychotic recurrence destroys hundreds of millions of brain cells, eventually leading to brain atrophy and permanent disability.

In addition to being very useful in preventing relapse, LAIs are a convenient option because they eliminate the need to take pills every day. Today, several newer antipsychotic medications are available as LAIs that can be given by injection every 4, 6, 8 or even 12 weeks.

VIDEO HIGHLIGHT

Dr. Henry Nasrallah and Bethany discuss LAIs in this four-part video series.

Please consider making a donation to the CureSZ Foundation online at CURESZ.org

Your contribution will help provide education and referrals to persons with schizophrenia, their families, and those who work with the seriously mentally ill. CURESZ informs the general public to better understand this serious brain illness, and to provide scientific advances showing that there is hope for recovery, and a return to a fulfilling and normal life. The CURESZ Foundation is a 501(c)(3) nonprofit organization. All contributions are tax deductible.

"We are committed to helping individuals to cope with and recover from schizophrenia."

You can now also support the CURESZ Foundation by signing up with Kroger Community Rewards and Amazon Smile.

kroger community rewards

amazonsmile
You shop. Amazon gives.