Paradigm shift:

A timely treatment for depression and suicide

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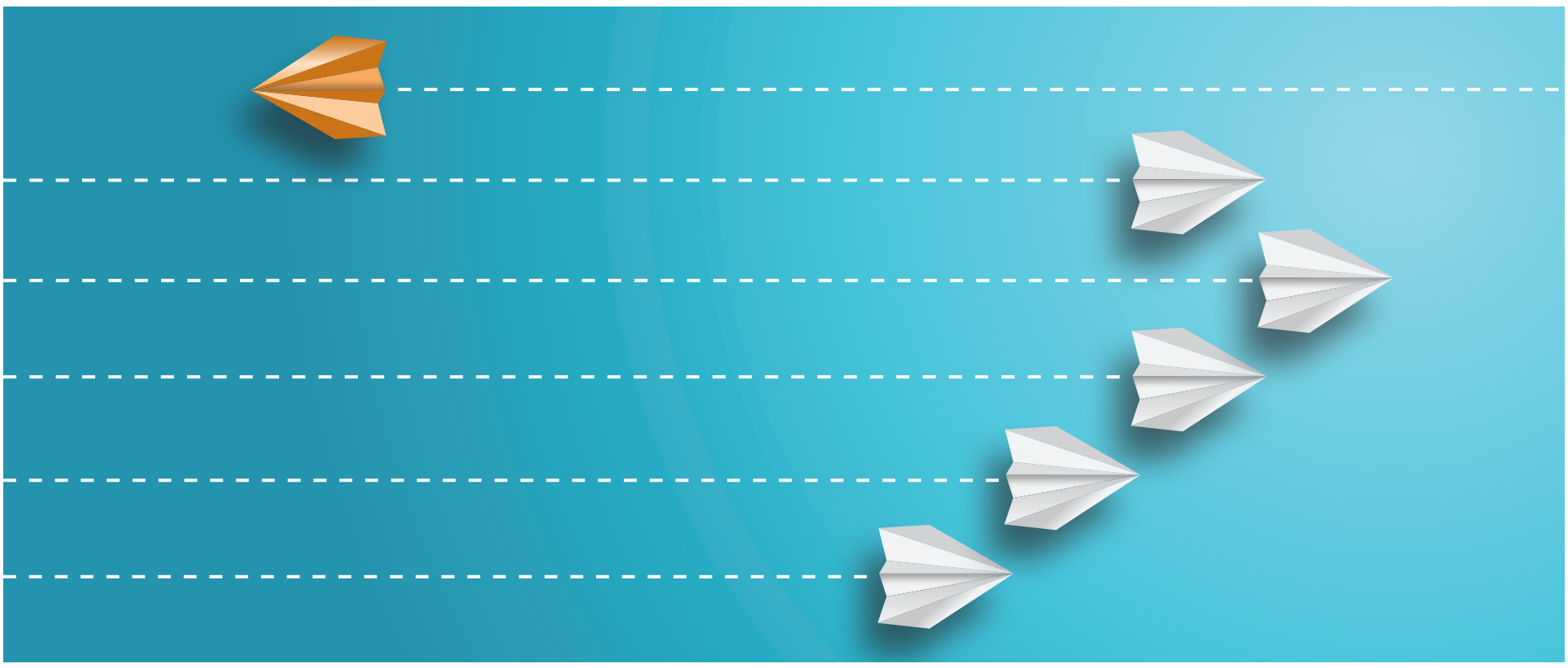

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In 2019, more than 16 million adults in the United States suffered from Major Depression Disorder – and that was before the COVID-19 pandemic started. Things have only gotten worse; recent data from the U.S. Census Bureau shows that approximately 36 percent of adults reported symptoms of anxiety or depression during the week preceding the survey.

Doctors are at even greater risk. Studies have suggested that suicide rates for male physicians is 40 percent higher than among men in the general population, and that rate skyrockets to 130 percent for female physicians.

Nearly 25 million adults have been taking antidepressants for at least two years, up 60 percent in the past decade. Furthermore, commonly used medications take at least two weeks to reduce symptoms.

Fortunately, an old drug is being used as a new treatment with robust results, when we need it most.

Receiving little fanfare in the times of COVID-19, a national recession and an impending presidential election, the FDA recently approved esketamine (Spravato) nasal spray to treat patients suffering from MDD with acute suicidal ideation or behavior. Multiple studies have shown that ketamine infusions in subanesthestic doses can decrease suicidal symptoms within hours, with effects reaching six weeks of decreased suicidal thoughts from a single 40-minute infusion.

Twenty years ago, Yale University published the first ketamine study that showed a rapid decrease of depression symptoms within hours to days, as opposed to weeks or months with more conventional oral antidepressant medications. While not completely understood mechanistically, ketamine is both an NMDA receptor blocker and an AMPA receptor agonist. National Institutes of Mental Health research has shown that treatment with ketamine infusions has increased glutamate levels and decreased GABA levels in the amygdala, the emotional center of the brain.

This novel approach to this neurobiochemistry of treating depression has also resulted in increased activity of G proteins in the neurons that result in increasing the dendritic spines amongst the neurons, effectively increasing interaction and signaling among the adjacent nerves.

The results are nothing shy of the foundation to a transformative paradigm shift as to how we approach MDD, mood disorders and suicidal thoughts and actions. We're moving from a "talk to someone" approach to a neurobiochemical medicinal approach to rapidly treat the disease process at the molecular level.

These results have shown approximately 70 percent response and 37.5 percent rate of long-term remission, versus placebo, with six infusions of IV ketamine, which is approaching 99 percent bioavailability. When combined with an oral antidepressant, esketamine nasal spray, with approximately 48 percent bioavailability, showed a 37 percent increase in symptom remission above oral antidepressant alone.

Esketamine nasal spray requires eight treatments in the first month, then weekly treatments for the next several months. Alternatively, after initial infusion protocols, booster infusions of ketamine are necessary only on an as-needed basis, with a mode of 30 days.

In 2017, the American Psychiatric Association published a consensus statement on the use of ketamine in the treatment of mood disorders. A year later, Johnson & Johnson's Janssen Pharmaceutica received FDA approval for Spravato to treat MDD, defined as failing two trials of oral antidepressant medication of adequate dosage and duration. On July 31 of this year, the FDA added a second indication for treating MDD with suicidal ideation or behaviors.

Administration of Spravato must be performed under a physician's care in an office or medical facility. Unfortunately, as of this printing, neither Medicare nor Medicaid covers this treatment or its administration. Nor do most commercial insurance companies.

This paradigm shift is timely, as our psychiatric resources are taxed as never before. The nine inpatient psychiatric units in Virginia hospitals have been operating at greater than 90 percent capacity over the past four years and have often been at more than 100 percent capacity. This leads to patients being held in crowded emergency departments around the Commonwealth, awaiting transfer and admission while not getting the care and attention they need. Unfortunately, neither esketamine nasal spray nor ketamine infusions are presently administered in any of these facilities.

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Given the stresses of life in 2020, it is imperative that we consider this new and promising therapy for improving our treatment of MDD, mood disorders and acute suicidal ideation-afflicted patients. R

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