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Curiouser and Curiouser

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Curiouser and curiouser!” cried Alice (she was so much surprised, that for the moment she quite forgot how to speak good English).

— Lewis Carroll, *Alice’s Adventures in Wonderland*

WHEN IT COMES TO SCIENCE, we are living in strange times. Although much of the health, wealth, and power of our society derives from extraordinary achievements in physics, biochemistry, engineering, and medicine over the last 100 years, it seems curious indeed that political figures who trumpet America’s material success are launching assaults on the nature of scientific endeavor—challenging the value of expertise, positing “alternative facts,” rejecting evidence-based findings in favor of bombastic claims and personal beliefs.

It is in this context of seeming open hostility toward scientific evidence that our society considers (some would say resumes) important deliberations about how to schedule, regulate, (de)criminalize, and otherwise govern whether its citizens will have legal access to a host of molecules—some plant-derived, some synthesized—for therapeutic uses. For we palliative care clinicians, the paramount uses in question relate to reducing intractable suffering—in particular, suffering for which our available treatments are often inadequate.

As an instructive example of the current disconnect between science and policy discourse in the public square, compare the scholarly 2017 monograph on the health effects of cannabis and cannabinoids produced by the National Academy of Sciences¹—which cites good clinical-trial evidence supporting the efficacy of cannabis and cannabinoids for pain management, (including for HIV- and chemotherapy-related peripheral neuropathies)—to an assertion by the future Attorney General of the United States during his Senate confirmation hearings: that “...good people don’t smoke marijuana....”² Witness also the Attorney General’s recent rollback³ of Obama-era directives that prohibited federal law enforcers from expending their resources to enforce the antiquated and unscientific 1970s-era Drug Enforcement Agency (DEA) Controlled Substances Schedule in states with cannabis legalization statutes. In case readers need reminding, DEA still rates cannabis as a Schedule I compound (“no currently accepted medical use and high potential for abuse”). Elements of that four-decade-old assertion are simply false.

In this issue of JPM, our colleague Ira Byock, a wise and thoughtful palliative care physician who helped introduce Western readers 20 years ago to the concept of “Dying

Well,”⁴—now brings to our Journal a provocative commentary on high-quality clinical data suggesting that “psychedelic” drugs may play an important new role in managing intractable suffering. Specifically, Dr. Byock reviews recent trials of psilocybin, lysergic acid diethylamide (LSD), 3,4-methylenedioxy-methamphetamine (MDMA), and ketamine, and describes strong evidence for improvement in refractory symptoms related to end-of-life anxiety/depression in patients with cancer and other terminal illnesses (psilocybin), treatment-resistant depression in healthy individuals and end-of-life depression in cancer patients (ketamine and psilocybin), and severe post-traumatic stress disorder (MDMA).

Byock weaves a compelling narrative, summarizing the unmet needs that are all-too common in patients who face catastrophic medical illness. He integrates into his review a discussion of the reasons given by patients who have sought to utilize the Oregon “Death With Dignity” act, pointing out that most of these patients are looking to death for relief from what Byock terms “nonphysical suffering”—loss of autonomy, dignity, and the ability to enjoy life—symptoms that might, it turns out, be amenable to the therapeutic effects of psychedelics. In the face of Washington’s stubborn resistance to reclassifying anything in the Controlled Substance Act Schedule, perhaps a sense of common cause may emerge among those of us who would advocate for our palliative care patients a “right to try” psychedelics regardless of our personal positions on physician aid in dying.

If larger scale trials confirm that safe therapeutic doses of any of these agents help reduce suffering, death fears, or treatment-resistant end-of-life depression, I believe our field and our patients would welcome them as important new options. It is hard to imagine that palliative care clinicians would object to the idea that in carefully supervised trials, these old/new drugs might be offered to patients with existential concerns, intense death anxiety/fear, or treatment-resistant depression as primary drivers for their pursuit of physician aid in dying. We would welcome the potential safe relief in suffering these substances might provide, and would consider it a therapeutic success if patients experiencing benefit might choose to rescind or defer their legal pursuit of Physician Aid in Dying or Physician Assisted Death (PAD).

Why do I juxtapose a brief narrative about cannabis with the emerging data regarding psychedelics? Is there a unifying thread? Sadly, I think there is: it is the unfortunate legacy of the “drug culture” of the 1960s (cannabis, LSD, psilocybin) mixed with the legacy of the “club culture” of the 1980s

(ketamine, MDMA). The excesses of those eras, mixed with the social upheaval and challenges to authority that accompanied them and terrified “the establishment”,⁵ provide a rich topsoil of images and impressions to support reactionary resistance to the emerging evidence.

Dr. Byock is no stranger to the politics and regulatory barriers that might lie ahead; he describes them plainly in the article. And even beyond those expectable barriers, we find ourselves in a “1984” world of political suppression of scientific and public policy discourse. A painful recent example: in an early 2018 editorial in the *Annals of Internal Medicine*, a group of Emory University public health experts called attention to an effort by the White House to ban specific words from the U.S. Center for Disease Control’s 2019 annual budget request.⁶ What those words mean—“vulnerable,” “diversity,” “transgender,” “fetus,” “evidence-based,” and “science-based”—is essential in all of medicine, and particularly in the field of palliative care. Is the idea that, if we do not use those words, vulnerability, diversity, transgender people, unborn fetuses, evidence, and science will just go away?

Palliative medicine physicians are accustomed to being outside the spotlight of high-tech modern medicine, and we routinely advocate for patients who do not get first-priority attention from our medical colleagues. If clinical trials continue to demonstrate new hope from psychedelics for some of our patients’ most intractable symptoms, we may find ourselves a bit blinded by an unfamiliar spotlight, and we may feel compelled to join an advocacy effort for the “right to try” these treatments. Common sense and good science are not likely to prevail on their own.

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