

Everyday amnesia

The curious effects of a common drug

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The Pediatric Pre-Operative Unit is an anxious place. Parents wait tensely as their children play with nervous energy, many too young to fully understand or verbalize their uneasiness. Some older children sit rigidly, others become effusive and needy. An eight-year-old girl awaits involved surgery, repeatedly grabbing her father's arm with playfulness mixed with desperation.

The unit is decorated like a kindergarten classroom, replete with primary colors, Lego sets, and stuffed animals. Yet for many of the parents, the room might as well be bare. Their thoughts are elsewhere, trying to temper nightmarish scenarios with common sense and hopefulness. In some cases, a downward cycle of anxiety and apprehension forms between parent and child, the child sensing the parent's nerves and becoming anxious, making the parent all the more jittery.

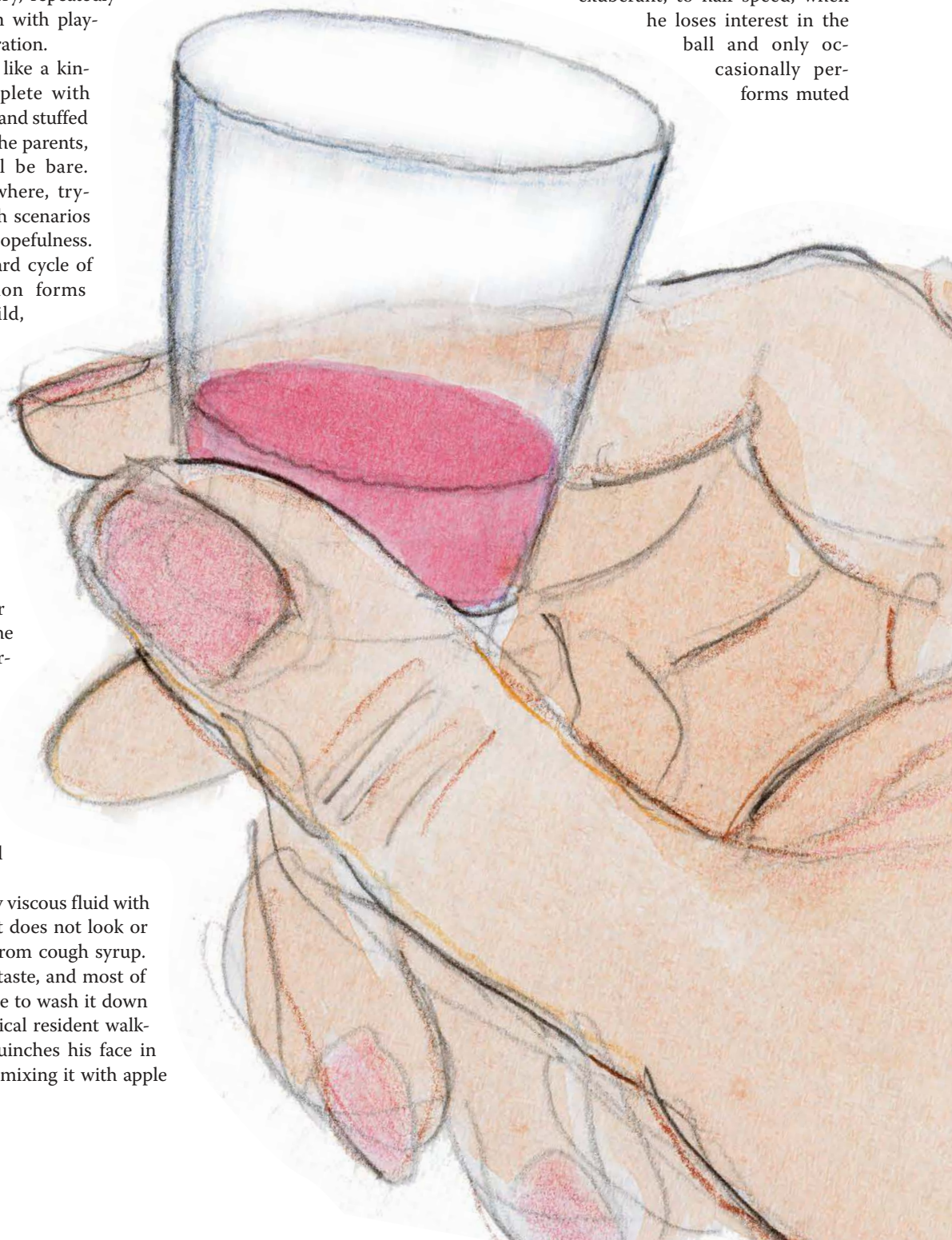
As operating rooms are prepared and surgical teams assemble, the families are informed that the time has come to leave their children in the care of the anesthesiologists and surgeons. Instead of being the climactic moment of anxiety, however, this is often a moment of deep relief, largely due to the appearance, a few minutes before, of what the nurses fondly call "happy juice."

Oral Versed is a slightly viscous fluid with a deep pinkish-red hue. It does not look or taste markedly different from cough syrup. It does have a bitter aftertaste, and most of the kids in the unit choose to wash it down with a little water. A surgical resident walking by as a youngster squinches his face in disapproval recommends mixing it with apple

juice to neutralize the bitterness.

Prior to gulping down a thimbleful of happy juice, a two-year-old boy has been terrorizing the unit, madly throwing balls and performing jump kicks. Oral Versed takes roughly fifteen minutes to reach full effect. The little boy follows this timeline like clockwork. His energy level declines almost linearly over those fifteen minutes, from full speed to three-quarter speed,

when his throws become less aimed and exuberant, to half speed, when he loses interest in the ball and only occasionally performs muted



versions of his previously vicious jump kicks, to one-quarter speed, when even running around seems like a chore. The drug achieves its full effect when the child plops down for a light nap on his mom's lap.

Like most kids on Versed, the little boy leaves his parents uneventfully, without fear or agitation. He looks a little sleepy on the gurney, but smiles gently as if in the middle of a pleasant thought. As his eyes scan lazily across the unit and around the operating room minutes later, it is reassuring to know that his last memory will probably be of playing with a ball or lying in his mom's lap. Everyone around him also seems relaxed. His parents appear less jumpy and almost calm at the time the boy is wheeled off for surgery, and the doctors and nurses involved are undoubtedly relieved that everything has gone smoothly. Everyone appears happy, or at least as happy as could reasonably be expected. Versed has lived up to its billing.^{1,2}

One of the benzos . . .

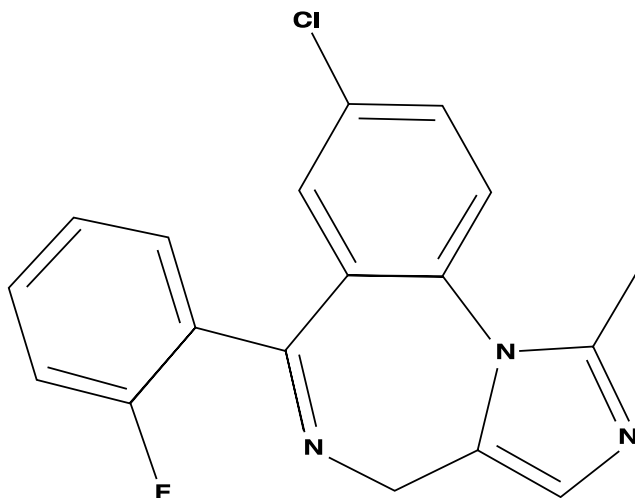


Versed (midazolam) belongs to a class of drugs called the benzodiazepines, well known for their sedative, anti-anxiety, and memory-blocking effects. This constellation of effects contributes to a condition aptly termed "conscious sedation." Anxiety and inhibition are diminished, while consciousness is dimmed but preserved. Depending on the dosage administered, a child will fall somewhere on a spectrum of less energetic than normal to very drowsy. Because kids' behaviors are not markedly different (kids become more fun-loving if anything), the drug is pleasant to work with in the clinical setting and parents are relatively undisturbed by its effects. Occasionally, however, Versed will produce a level of disinhibition that can render a child more difficult to manage. Furthermore, the serious side effect of respiratory depression must be carefully guarded against with appropriate monitoring.^{1,2}

Versed is widely and commonly used in pediatrics. The types of procedures for which it is employed cut across many medical specialties. With a few exceptions, Versed has been used for all medical procedures more invasive and uncomfortable than an IV placement, and in certain cases for IV placements as well. For example, Versed is used for diagnostic procedures such as lumbar punctures, bone marrow biopsies, and bronchoscopies; for imaging studies such as CT or MRI scans, for which a child must lie unnaturally still for an extended period of time; for orthopedic procedures such as the resetting of a broken leg; for injections of medicine involving frightening needles; and in continuous infusion for ICU sedation, for which a child must lie still, sometimes for days, amid an intricate web of apparatus. Older people are also soothed and calmed by Versed, which is used for a similar laundry list of indications in adult medicine, though typically administered intravenously.

While Versed's anxiolytic effect is arguably its most clinically useful attribute, the amnesia it produces is its most striking feature. Many doctors who routinely use Versed have a

Chemical structure of Versed (midazolam)



favorite amnesia story. Perhaps it is about a teenager who has visited a clinic numerous times for a certain procedure, but astonishingly does not have even a faint recollection of his or her doctor. Or perhaps it is about a cantankerous man who refuses to believe he has received the medical attention he desires and accuses his doctor of lying.



Trip to amnesia

Under the influence of Versed, a patient can appear normal, and even engage in conversation that is entirely coherent and ordinary. But many patients will have no recollection of what took place during an interval that might last a couple of minutes or a few hours depending on the individual and dosage administered. The experience will simply vanish. This amnesia can seem dramatic and even difficult to believe for someone unaccustomed to Versed. The first time I witnessed the effect of the drug was as a first-year medical student, when I watched a man have his ankle reset. One moment he was writhing and sweating profusely. No more than fifteen minutes later, he was relaxed and oblivious to the discomfort he had just experienced. He had no recollection of the procedure. The precious, central faculty of memory had simply been turned off, a mundane and unremarkable moment for those who have worked for years with Versed. For the unseasoned observer, however, the moment lingers. That a person can experience an event, particularly an emotionally charged one, and emerge minutes later without a trace of recall is unsettling. It prompts one to reflect on the notion of memory.

Memory is the scaffolding upon which consciousness hangs. It is the reference point for everything we do, helping to define our every move and syllable, bounding our perceptions, crafting our personalities, assembling our identities from myriad scraps and fragments. Without it, we would find ourselves in an unimaginable void.

Having said this, it seems remarkable that more attention has not been paid to the role of amnestic agents in modern medicine. Memory is clearly a profound faculty, and simply “turning it off” for a period of time is likewise a profound undertaking. What exactly has been turned off, and what is still getting through? With respect to the typical patient on Versed, there are no definitive answers to these questions.



“Did that really happen?”

A textbook will tell you that Versed, like all benzodiazepines, achieves its anxiolytic and amnestic effect by facilitating the action of the inhibitory neurotransmitter GABA through

increased frequency of chloride channel opening. Further, there are studies and statistics addressing such things as the duration and degree of impaired recall; compared to other benzodiazepines, Versed has a higher potency and shorter duration of action.² Yet one must rely primarily on anecdotes for some of the more complex and qualitative issues surrounding the use of Versed. Are amnestic patients affected by the procedures they undergo? Do they retain anything from their experiences? Are there emotional consequences?

Take, for example, the case of HM, one of the most famous and thoroughly studied of all amnestic patients. To treat his epilepsy, surgeons in 1953 removed large portions of the medial temporal lobe on both sides of HM's brain. Since the surgery, HM has not been able to encode any new memories. It is as if he has been on Versed for the last five decades. People will have lengthy conversations with HM, leave for a moment and return to find that he has no recollection of who they are or what they were talking about.

The height of the Cold War, Vietnam, Michael Jackson, the Smurfs, hot pants, cell phones—HM has been spared it all. His memory of events prior to 1953 is still intact, so in many ways he is like a time traveler set down in our modern world, interpreting things through an outmoded filter, but with logic and intelligence. When HM is confronted with a modern word and asked about its meaning, he guesses by breaking the word into its component parts and applying common sense, just as any high schooler is taught to do for the SAT. “Software” might be construed as some new line of padded clothing, “Watergate” as a contraption used by a hydroelectric dam.

While HM is unable to acquire new knowledge in an explicit fashion, such as developing an updated vocabulary, he does remain capable of certain forms of learning. He retains the ability to be unconsciously influenced and educated by experiences, as do most amnestic patients. This domain of memory is often referred to as “procedural memory,” as it cannot be accessed directly, only demonstrated by performance. An amnestic patient could learn to ride a bike, but would retain no recollection of when or how the skill was acquired.



Messed-up memory circuits

Another example of the presence and influence of implicit memory is the often-related anecdote about a researcher who shook an amnestic patient's hand while holding a small, sharp object. The patient withdrew his hand in surprise, but quickly forgot the event as the researcher left the room. When the researcher returned later and offered to shake the patient's hand again, the patient refused to do so, but could not explain his asocial behavior. At some level below the surface of awareness, memory circuits that allow an amnestic patient to

record events—events that slip past the grips of conscious memory—are intact and functioning.³⁻⁵

Just as the pathologically amnesic patient refused to shake the doctor's hand a second time, a patient on Versed who is temporarily amnesic for a procedure during which he or she is uncomfortable might be subconsciously driven to behave antagonistically toward the doctor involved. Such patients have been reported in the literature. Though their conscious memory banks may be vacant after an event, implicit or subconscious channels can have a substantial effect on these patients, influencing their thoughts and dispositions, informing their behaviors.^{6,7}

The subtext to this discussion of the subconscious of amnesic patients is that taking Versed constitutes a tremendous act of trust on the part of the patient. Patients allow themselves to become powerless and vulnerable. They are in a state of diminished inhibition and judgment. And they are not likely to remember much, if anything, about their experiences while on Versed.

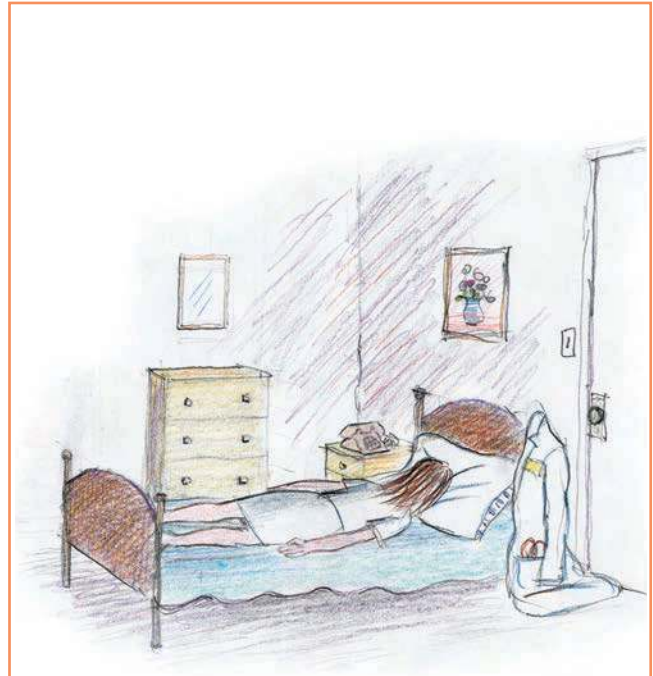
While Versed may indeed render patients strikingly vulnerable and potentially leave imprints invisible to the conscious mind, its utility in the clinical setting is undeniable, its effects clearly beneficial. Used properly, Versed can help to dissolve the tension and discomfort of hospital visits for all parties involved and contribute to the efficiency and ease of modern medicine.

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Desire

*To bed
I said
With lascivious sigh

With lust
For just
Some hours shuteye

Warm toes
Cold nose
And pillows piled high

To sleep
Dark deep
Until morning is nigh*

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