Born of the bacterium *Clostridium botulinum*, the botulinum neurotoxin is a protein, exerting its influence by cutting communication between nerves and muscles to immobilize its target. In its raw form, it’s one of the deadliest substances known to man, but when purified, heavily diluted, and expertly injected in tiny doses, it can harness its powers for good. The type-A toxin activating FDA-approved neurotoxins Botox Cosmetic, Dysport and Xeomin has been shown to ameliorate everything from crow’s feet and muscle spasms to chronic migraines and urinary incontinence. Fully defying its vanity-stigma, “more than half of the botulinum toxin now used in the world is for medical purposes,” says New York dermatologist Paul Jarrod Frank, MD. Aiming to add to its repertoire, Botox is currently being investigated as a treatment for depression, a host of pain disorders, even atrial fibrillation in cardiac patients—earning itself a reputation as “the product that keeps on giving,” says Chicago facial plastic surgeon Steven Dayan, MD.

Botulinum toxin first proved its medical value in the 1970s, correcting ophthalmological conditions like strabismus (crossed eyes) and blepharospasm (marked by uncontrollable blinking). In 1987, the story goes, Vancouver-based ophthalmologist Jean Carruthers, MD, wife of world-renowned dermatologist Alastair Carruthers, MD, discovered a happy side effect of treating such eye issues with toxins: a softening of the lines between patients’ brows. The drug, which came to be known as Botox, was approved for therapeutic use in 1989, and as a fix for frown lines in 2002. Since then, Botox’s myriad talents have shone in more than 500 peer-reviewed articles. And newer brands of toxin, like Dysport and Xeomin, have emerged as worthy competitors. The category as a whole has become an unrelenting tour de force, with doctors administering over 5 million neurotoxin injections worldwide in 2017, according to the International Society of Aesthetic Plastic Surgery (ISAPS).

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With a Taylor Swift-caliber fan club, Botox Cosmetic has become a household name—the Kleenex of toxins—and its manufacturer, pharmaceutical goliath Allergan, bears the bottomless pockets needed to keep the brand on the forefront of groundbreaking research. Still, the majority of injectors artfully use all three muscle relaxers in practice, appreciating their subtle differences and finessing them to beautiful effect. The doctors we spoke with also expect to welcome into their armamentarium several new neurotoxins in the near future, each poised to offer its own breakthrough advantages once greenlighted by the FDA.

Over the next few pages, we’ll share all we know about the neurotoxins of today and tomorrow—fascinating theories on how they may wrangle sadness, the science behind their ability to improve scars, refine pores, prolong blowouts, and out-contour the Kardashians, and why, despite prevailing no-big-deal notions, one should never underestimate the gravity and complexity of these “miracle poisons.”
**BEAUTY AND BEYOND: POPULAR USES FOR NEUROTOXINS**

The list of FDA-sanctioned (on-label) uses for botulinum toxins is concise, but doctors routinely inject them experimentally (off-label) to address countless other beauty and wellness concerns. (F) "Botox Cosmetic and "Botox," the therapeutic version, are the same drug vett ed in different settings.

**FINE LINES**
Botox Cosmetic.

**RARES**
Micro-sized injectable particles that target the arrector pili muscles, which control pore size.

**LARGE PORES**
Micro-sized injectable particles that target the arrector pili muscles.

**EXCESSIVE SWEATING**
The sympathetic nervous system rules our sweat glands, not our acetylcholine. When toxins block the chemical, glands can’t contract, and perspiration subsides. This is why Dopamine shores up its ability to dry up sweat glands as well. However, Dr. Matarasso says that "we've seen Botulinum toxin injectable particles that target the arrector pili muscles, which control pore size." Dr. Hartman. Relieving these muscle causes pores to shrink, up a bit and secret less oil.

**TIP FLIP**
Injecting toxin at the base of the nose releases the muscle responsible for enlarging the tip with age, and age.

**GUMMY SMILES**
Almost all areas of the face.

**SCARS**
Tension is the worst thing for a fresh scar. But when used off-label, it can help decrease inflammation.

**PAIN DISORDERS**
Neurologists are using toxins (off-label) to treat all kinds of aches, typically as part of comprehensive pain-management regimens. Other uses of botulinum in many advantages. Botulinum toxins can be safely combined with other treatments, and have very few interactions with medications. Dr. Karp, adding that some patients are even able to control their pain with toxins. In a study of botulinum toxin for the chronic pelvic pain of endometriosis, we’ve seen women decrease their daily use of anesthetics and better tolerate pelvic floor physical therapy after injections, she adds.

**THE BIG THREE:**
**WHICH WRINKLE-BUSTER IS RIGHT FOR YOU?**

While Botox Cosmetic may be the most famous of the bunch, Dysport and Xeomin contain the same type of protein, known by identical names—botulinum. The key difference: Botox requires a higher dose for the release of a chemical messenger called acetylcholine to loosen muscle contractions for three to four months in most cases. “The overall gestalt of neurotoxins is that there is not much difference in their effectiveness,” says Dr. Frank, due to slight distinctions between final formulations. Beyond an unsurpassed track record—"it is the most tried and true," says New York dermatologist Macrene Alexanders, MD—Botox Cosmetic is famous for its potency. “Patients with very strong muscles, and those wanting a complete block, tend to prefer it because it really gives a precise and powerful correction,” says Philadelphia plastic surgeon Ivena Perez, MD. ""Dysport" reportedly kicks in faster than its competitors—within a couple days opposed to a week. It also “diffuses a bit more into its surroundings, making it ideal for treating a high forehead or a long stretch of crow’s feet, or for softening the lines of the neck,” says New York dermatologist Stefani Heidt Waldorf, MD. Injectors commonly describe its effect as softer and smoother, “theoretically due to the diffusion,” notes Dr. Perce, “but the data isn’t definitive.” Xeomin is also known for its mild manner, but more so for its peerless purity, as it omits the complexing proteins present in other neurotoxins. “Which may play a role in immunogenicity,” says the fact that a small percentage of patients don’t respond well to Botox (and Dysport) after many years of use, explains Dr. Al. The purpose of the proteins is delectable, but they’re thought to help stabilize the drugs. While there’s very little evidence of immunogenicity in cosmetic doses, I have had a handful of patients—very few in more than 50,000 treatments—"who’ve become inexplicably unresponsive to Botulinum", says Dr. Dayan. In those cases, switching them to Xeomin usually remedies the problem. Still, he adds, “It’s hard to say definitively if Xeomin is successful because of the lack of a control group.”

**Aiming to improve the look of fine lines and wrinkles across this 47-year-old patient's upper face, Birmingham, AL, dermatologist Corey L. Hartman, MD, treated the forehead, glabella (between the brows), temporal lines, brow lines, and crow’s feet with Xeomin, tailoring the dose to maintain the patient’s ability to make expressions. The “after” photo was taken two weeks post-treatment.

New York facial plastic surgeon Jennifer Levine, MD addressed this 65-year-old patient’s platymyal bands and neck lines by injecting 100 units of Dysport. “The platysma is a depressor of the lower face, so when a neurotoxin causes lifting, the muscle contracts and attenuates over time; neurotoxins help soften bands, lines and wrinkles,” she says. The “after” photo was taken two weeks later.

Botox Cosmetic is approved to treat crow’s-feet and forehead wrinkles. The “after” photo was taken two weeks post-treatment. Aiming to improve the look of fine lines and wrinkles across this 47-year-old patient’s upper face, Birmingham, AL, dermatologist Corey L. Hartman, MD, treated the forehead, glabella (between the brows), temporal lines, brow lines, and crow’s feet with Xeomin, tailoring the dose to maintain the patient’s ability to make expressions. The “after” photo was taken two weeks post-treatment. New York facial plastic surgeon Jennifer Levine, MD addressed this 65-year-old patient’s platysmal bands and neck lines by injecting 100 units of Dysport. “The platysma is a depressor of the lower face, so when a neurotoxin causes lifting, the muscle contracts and attenuates over time; neurotoxins help soften bands, lines and wrinkles,” she says. The “after” photo was taken two weeks later.

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**BEAUTY AND BEYOND:**

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New Toxins in the Pipeline

Coming soon to a doctor’s office near you? A squad of new botulinum toxins, each with its own design appeal. For the die-hard or top-notch looking for a test run, there’s an innovative botulinum toxin type E from Allergan that works on demand (within 24 hours) and wears off in two to four weeks. The drug has been in clinical trials for Migraine and is looking promising for Migraine. But even patients are being investigated for its psoriasis and psoriatic arthritis. Botox is also being investigated for its psoriasis and psoriatic arthritis. It’s been shown to be effective for up to six months in studies, but more research is needed before it can be approved for use. Botox may also be effective for the treatment of chronic migraines, but further studies are needed to confirm its effectiveness.

New Toxins

Current FDA-Approved Treatments

Myth: Botox will make you lose your eyebrows. Fact: Botox is not a permanent treatment. The toxin works by temporarily paralyzing the muscles that cause wrinkles, allowing the skin to relax and smooth out. Over time, the skin can improve in texture and appearance.

Myth: Botox can prevent or reverse aging. Fact: Botox can help smooth out wrinkles and improve the appearance of the skin, but it cannot prevent or reverse the signs of aging. It is important to discuss your expectations with your doctor before undergoing Botox treatment.

Myth: Botox is painful. Fact: While some patients may experience mild discomfort during the treatment, the majority report minimal pain. The procedure is usually quick and can be performed in a doctor’s office or a clinic.

Myth: Botox is addictive. Fact: There is no evidence to suggest that Botox is addictive. However, some patients may experience an increased desire for Botox treatments due to its effectiveness in treating wrinkles and improving skin appearance.

Botox Xenon FSA Approval for Major Depressive Disorder

Since the mid-aughts, researchers have been testing Botox as an antidepressant, starting in a cache of small mental health studies, and turning up more recently to results a 50 to 60 percent response rate, in 33 percent reduction in depression symptoms, and a remission rate of approximately one third, notes Chaya Cheza, MD, dermatologist Eric Finzi, MD, PhD, in an article published in Dermatologic Surgery in 2018.

“People diagnosed with depression are reporting improvements in mood following treatment of facial wrinkling with botulinum toxin,” says Philadelphia psychologist David Barter, PhD. “These studies have captured the attention of both the doctors who offer these injections, as well as mental health professionals seeking alternative therapies for depression.”

Botox will soon be entering phase three clinical trials for major depressive disorder, yet scientists haven’t said how far the drug works to combat the disease. “We do know that improvement in mood is not related to improvements in wrinkles, because we treat someone young, who has no lines at rest, their depression doesn’t improve,” says Dr. Finzi. The most probable explanation for the drug’s psychological success, he adds, is the facial feedback hypothesis, or the idea that our expressions can influence our emotions. “Many studies have shown that people who are frowning leads subjects to have a more negative appraisal of whatever they’re evaluating—a story, a cartoon, a photograph. Subjects have also reported feeling sadder right after frowning, “says Dr. Finzi.

The facial feedback hypothesis, or the idea that our expressions can influence our emotions, has been studied extensively. “Many studies have shown that people who are frowning leads subjects to have a more negative appraisal of whatever they’re evaluating—a story, a cartoon, a photograph. Subjects have also reported feeling sadder right after frowning, “says Dr. Finzi.

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