

# FDA Approves Botox to Treat Migraine

**N**ews for those who suffer with migraine headaches: the FDA has recently approved Botox as a treatment protocol for this condition.

We asked Dr. Charles Matthews, a board certified neurologist and Director of the North Carolina Comprehensive Headache Clinic, to explain the likely benefits of this decision.

"But first," he said, "my usual caution: Botox was FDA approved for *chronic migraine*. If you have frequent headaches, they are *likely* to be migraine, but they *may not be* migraine.

"There are many causes of chronic headache. Other types of chronic headache include chronic or paroxysmal hemicrania, hypnic headache, cluster headache, primary thunderclap headache, spontaneous intracranial hypotension, benign intracranial hypertension, trigeminal neuralgia, and others.

"Infections and inflammatory disorders like temporal arteritis also can cause chronic headache. Botox doesn't help any of these conditions. Typically in these conditions a standard MRI will be negative, so you really should have a neurologist go over these possibilities with you. The Triangle area has many outstanding neurologists who are knowledgeable about headache."

*Health & Healing: So, tell us about Botox for migraine.*

**DR. MATTHEWS:** Botox is a trademark of Allergan, the pharmaceutical company that makes onabotulinumtoxinA for medical use. Botox received FDA approval for the treatment of chronic migraines in October of 2010. So, when I say "Botox," I'm referring to that particular type of botulinum toxin.

Botulinum toxin is made by the bacterium, *Clostridium botulinum* that causes botulism. Botulism is not common now, but symptoms are very dramatic and it played an important historical role in understanding neurophysiology. The word "botulism" derives from German for sausage, as I understand it; it was described in Germany when people became ill from bad sausages.

*H&H: Why do bacteria make toxins?*

**DR. MATTHEWS:** Bacteria as a group can reproduce very rapidly. Let's say that a bacterium divides once every 12 hours. In a month, if you don't have something constraining the growth that means you will have two to the sixtieth bacteria. That's a lot of bacteria! In very short order, the surface of the earth would be covered unless something happens. The reason this doesn't happen is, partly, the bacteria run out of food, but mostly, bacteria make poisons to kill off their competitors. Sometimes the poisons cause problems for people.

Botulinum toxin is really a muscle relaxant. It has some other effects, but the one best understood is how it works to relax muscles. Nerve endings very close to the muscle surface secrete a chemical that tell the muscle to contract. The chemical is called acetylcholine, and it is released from the nerve and sticks to the muscle at sites that are called acetylcholine receptors, and that tells the muscle to contract.

Botox works at least partly as an injectible muscle relaxant. When Botox is injected into the muscle, it binds to a receptor on the muscle surface, and stays there. It blocks the signal from the brain to make the muscle contract. The binding is like hair dye; it's permanent, but after a while the roots start showing. It's the same with Botox; after awhile new receptors are made, so the Botox falls out with the receptor. There are no known permanent side effects of Botox.

The word "toxin" can be misleading. When properly injected in low doses, it doesn't make you toxic all over; it's just toxic to the acetylcholine receptor at the injection site, and then you grow new ones.

*H&H: How long does Botox last?*

**DR. MATTHEWS:** New receptors are made after about three months, about the same length of time as it takes to make new red blood cells.

It's important to realize that Botox has only been shown to work for *chronic migraine*. "Chronic" means you have migraine headaches more than half the time (more than 14 days a month).

*H&H: What if a person has migraine headaches only 13 days/month?*

**DR. MATTHEWS:** It's a complicated question, and it's under discussion among headache specialists. But basically, "chronic mi-

graine" is in important ways different from "episodic migraine." *I don't believe there is any benefit at all from using Botox for headaches that occur on fewer than 15 days a month. It isn't that Botox will one day be seen to benefit episodic migraine, or that people with episodic migraine are getting shortchanged since Botox is not covered for them. It's that it just doesn't work with episodic migraine.*

*H&H: What's special about chronic migraine?*

**DR. MATTHEWS:** Nothing definite, but this is what I think is happening. For many people, they start out having episodic migraine, maybe a few times a month, then a few times a week. What causes this transformation from episodic to chronic migraine? I personally think that classical conditioning—such as Pavlov described—plays an important role in transformation to chronic migraine, and suppressing that conditioning with Botox can convert chronic migraine back to episodic migraine, hopefully to the frequency you had migraines when you started. So, Botox may cause a *remission* of chronic migraine by keeping headaches suppressed for long periods of time.

I'll caution here that *long-term remission of chronic migraine has not been adequately studied experimentally*. But I've administered Botox about 800 times for migraine since 1993, and in my experience there has not been a single case of continued need for Botox beyond about three years. The most common is three applications, once every three months, and then we wait and see if they are still needed.

In migraine, every time you have a headache attack, and something else happens at the same time, your brain learns to link these up. I think this is one reason (there are others) that people with migraine attacks eventually get neck pain—the neck "learns" that a migraine is coming, and starts to guard just like the dog learns to salivate when the bell rings. After awhile, the neck stays tight, and the brain learns this as a trigger for migraine. This mutual "conditioning" eventually leads to progression, with the neck pain triggering migraine, and the migraine triggering neck pain.

In general, people who have migraine usually have triggers—odors, weather, food, fatigue, menses. Sometimes they will run their lives trying to avoid all their triggers. They come to the headache clinic hoping I will help them identify all their triggers. Unfortunately, when the migraine is chronic, avoiding triggers is like arranging deck chairs on the Titanic. If you avoid one trigger, your brain will learn a new one.

So, in my view, Botox may work by suppressing chronic migraine for a sufficiently long period of time for your body to unlearn those classical conditioned responses.

*H&H: How well does Botox work to suppress chronic migraine?*

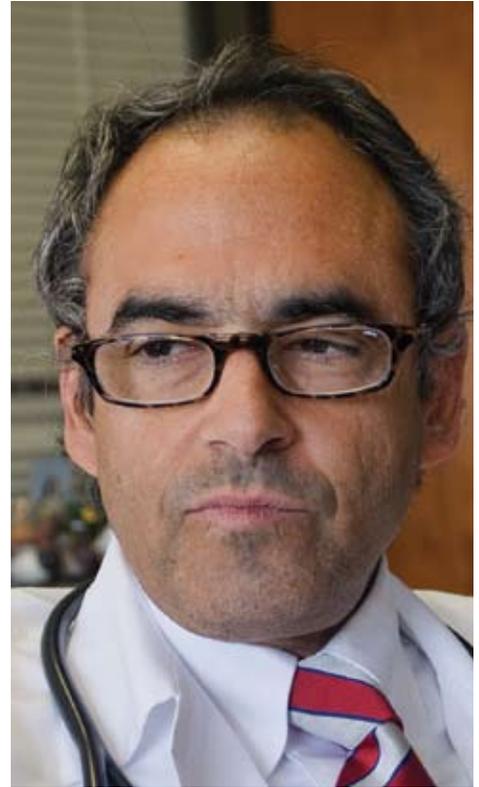
**DR. MATTHEWS:** The available studies show only a modest effect that continues to increase for about six months through the second administration. Longer outcomes haven't been studied adequately.

The studies were done in specialty headache clinics. They did not look at how well this modest effect would hold up when used outside of headache centers, and I think it won't work quite as well in the follow-up studies. So, I have some sympathy with the hesitancy of some insurers. On the other hand, combining Botox with other treatments, I expect, will work out much better than previous studies, since in my view the whole point is to suppress chronic migraine completely for months in an attempt to get a remission to episodic migraine. So, Botox for chronic migraine may work best in an overall headache program.

Combining properly chosen preventive medicines, treatment for factors that make migraines worse such as sleep disturbance and pain medication overuse, and nerve blocks when indicated, when combined have a high rate of success in inducing chronic migraine remission.

At the Headache Clinic, when treating chronic migraine we look down the road five years, sometimes 20 years. We want the patient to be *way better for the long term* than they would have been if they had not seen us.

I think treating chronic migraine with the goal of remission does people a *lot* of good. In the long term, less OTC painkillers that cause so many problems, fewer migraines, no lost days at work or with your family, hopefully few or no doctor visits for headache, better health overall. And that's what medicine is all about. **h&h**



Dr. Matthews.

**"Botulinum toxin is really a muscle relaxant. It has some other effects, but the one best understood is how it works to relax muscles."**

The North Carolina Comprehensive Headache Clinic is an outpatient neurology facility providing diagnostic evaluation and treatment for the patient with headache.

For information, contact

**NORTH CAROLINA COMPREHENSIVE HEADACHE CLINIC**

2501 Atrium Drive, Suite 400  
Raleigh, NC 27607

Telephone: (919) 781-7423  
www.ntheadache.com

For more information, please visit our website at  
www.ntheadache.com.

New patients are welcome