Over the last several years, few developments in the aesthetic pipeline have generated more buzz than topical toxins. Given the theoretical promise of these much-anticipated agents, it’s easy to see why. The notion of achieving results on par with injectable toxins without any injection could be enticing for many prospective patients, even for the most cosmetic-resistant individuals. However, the somewhat erratic frequency of reporting on the development of topical toxins prompted questions about the usefulness of these agents in real-time practice.

With several developers recently stepping up efforts to position their products for eventual approval, it is important to weigh a variety of factors as physicians consider the potential value of these agents. Ahead, Mark Rubin, MD takes stock of recent developments and attempts to make sense of what we know right now about topical toxins and the impact they may have on aesthetic medicine.

How would you assess the current state of toxin treatments, and how would you situate topical toxins?

Despite the oftentimes rancorous debate among manufacturers of various injectable toxin products, Dr. Rubin has previously noted that the differences among the available agents may not be so significant. (Read Dr. Rubin’s article in the January 2013 edition of Practical Dermatology, available at www.practicaldermatology.com). But, he points out, “there is always something new to learn, like the use of zytase zinc supplements, which could increase the efficacy and longevity of neurotoxins.”

With relatively few changes in the current clinical uses of neurotoxins, anticipation has swelled over the new delivery vehicle for neuromodulation procedures that topical toxins potentially present. According to Dr. Rubin, one company that has been especially active in recent years is the California-based Revance, whose topical toxin product, currently dubbed “RT001,” is being studied for lateral canthal lines. “They presented some recent data from a trial in Mexico showing longevity that was twice as long as Botox in the treatment of glabellar furrows,” notes Dr. Rubin. If these studies are verified and this agent comes to market, Dr. Rubin believes that it could be “game-changer.”

**If topical toxins do eventually come to market, in what ways will they change the toxin landscape?**

There are several possibilities for how topical toxins may influence the spectrum of aesthetics, according to Dr. Rubin. From a more pragmatic standpoint, a non-injectable form of delivery of toxin treatment can open doors to new patients. “New patients who are needle-phobic may consider seeing a
doctor for toxin therapy now,” says Dr. Rubin. “In addition, patients on blood thinners who bruise easily would prefer a non-injected treatment.”

Beyond potentially opening up the patient field, topical toxins may also give physicians more latitude to treat different areas. “There are perhaps new clinical uses of toxin in areas like under the eyes, the neck, and the décolletage area, where small amounts of toxin could be applied to large areas to create a uniform softening effect without too much muscle weakness,” says Dr. Rubin. In addition, these agents may have benefits in non-cosmetic settings that are worth exploring, as well, such as to “reduce erythema, reduce pore size and oiliness, increase hair growth in male pattern alopecia, or even for hyperhidrosis in other areas besides the axilla,” Dr. Rubin notes.

If topical toxins ever make it to market, Dr. Rubin points out that a majority of toxin procedures will still be performed via injection. “Many patients will opt for injections due to the speed of treatment and the ability to inject in so many areas versus just the crow’s feet for topical toxins,” Dr. Rubin observes. But no matter which option patients choose, Dr. Rubin believes that the sheer presence of new agents will increase the relevance of toxins. “If nothing else, a new toxin story will get patients interested in toxins again.”

Can you explain how topical toxins would work, and how they would be incorporated into practice?

“Basically there is a carrier molecule that allows the large toxin molecule to penetrate the skin,” says Dr. Rubin. “Once the toxin molecule gets to the neuromuscular junction, its mechanism of action is the same as with injectable toxins. The novel compound is not the toxin but the carrier.” Clinical trial data is somewhat limited at the moment, but is nonetheless promising. “The data that has been released by Revance shows similar efficacy to injectable toxin,” says Dr. Rubin. Another agent that’s been developed by Anterios, Inc. (ANT-1207), which, in addition to being under investigation for crow’s feet and hyperhidrosis, is also being evaluated in the treatment of acne. However, in a strictly cosmetic setting, both ANT-1207 and RT100 are only being investigated for crow’s feet. “At this point, it doesn’t appear that topical toxins penetrate as well as injectable toxins except in areas of very thin skin. So, these products may be good for crow’s feet, but they don’t appear to be very nearly as effective in the glabellar area where the skin is thicker and the muscle is deeper below the surface,” he says.

Aside from clinical limitations, there are practical points to consider about these agents, as well. Although the novelty of topical toxins will no doubt prove beneficial if these agents come to market, the specific details on how they will be incorporated into practice are less obvious, according to Dr. Rubin. “The logistics are a bit more of a challenge, since it appears that these products would need to be applied in a doctor’s office, where a measured amount is applied to a specific sized area and then left in place for 30-40 minutes,” he says. This could translate to exam rooms being occupied for longer periods of time than for injectable toxin patients, where an injection takes no more than five minutes. “So, in a very busy practice, this could be considered a detriment to office efficiency,” Dr. Rubin says.

How would you situate topical toxins within the spectrum of investigational non-invasive aesthetic procedures, and are there other modalities that you think may play a role in the trend toward non-invasive interventions?

“These products seem to be in the regulatory home stretch with possible clinical use within the next two years,” says Dr. Rubin. “There is a strong trend toward non-invasive treatments in aesthetic medicine, but most non-invasive therapies are far less effective than invasive.” Other non-invasive treatments may be more ‘less’ invasive than ‘non’ invasive, says Dr. Rubin, such as treatments including microneedling and superficial fractional laser followed by the application of active topical products like growth factors, platelet rich plasma, etc. Within that spectrum, Dr. Rubin surmises, “Topical toxin for crow’s feet would be unique in its ability to give similar results to invasive toxin injections.” But despite rising excitement levels, it’s important for physicians to consider both the limitations and implications of the availability of topical products. “These products look interesting with the potential to have some new benefits, but the off label possibilities may be far more interesting than the on label.”

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