by ROGER L. HIATT, M.D.

Botulism:

A SEVERE DISEASE TURNED TO THE GOOD OF MAN

SINCE WE IN MEDICINE are faced with so much adversity, perhaps during these times it is beneficial for us to meditate upon the positive things that we can attain. Let us consider a recent triumph that has occurred in the face of these tribulations. One of the most exciting accomplishments that American ingenuity has yielded during this decade has been developed from an unexpected area: botulism, a serious type of food poisoning. A potentially fatal disease has been turned to the good use of man.

• I would like to address this achievement by discussing how it has been explored in ophthalmology and also by honoring a colleague who persevered in developing a treatment that is an inspiration in American medicine today.

ILLUSTRATIONS BY

Henrik Drescher

during this six-month interval.[7] The therapy also enhances the opportunity for corrective surgery if it is needed, making the surgical procedure less complicated because of decreased contracture and deviation.

A second indication is blepharospasm. So many people are affected with this problem that there is even a club organized in this country called the "Essential Blepharospasm Club." The patients who suffer from this malady experience involuntary muscle spasm that causes their eyes literally to "clamp down." The disease is sometimes so debilitating that they can not drive a car. Rather than performing a major surgical procedure, the physician now has the option of injecting the orbicularis muscle with the drug and suppressing this muscle spasm from three to five months.[8]

A third use for the drug Occulinum is treatment for comitant strabismus in infants. An ophthalmologist can treat infants with crossed eyes by injecting their inner muscles (in esotropia) under general anesthesia (or, in careful hands, under office anesthesia) and straighten their eyes.

OUR EXPERIENCE

Our interest has been primarily in VI and other cranial nerve palsies. We have treated 27 patients with the drug. Each patient was evaluated with a complete eye exam including a history. The procedure was explained, informed consent was obtained, and photographs were taken of the patient. The Occulinum was stored in a refrigerator undiluted. Before use, it was warmed to room temperature and rehydrated according to the concentration required.[9] Topical anesthesia both by local drops and by subconjunctival injection was used. After the patient was placed in the supine position, the limbus of the eye was grasped with fixation forceps for injection of the muscle with the needle. Audioelectromyography was used to guide the needle to the proper muscle location. The surgeon listened for the signal indicating when the proper muscle was located. Of course, if the muscle was missed, there was little effect obtained. The injection can occur in the wrong location, such as the globe, which has been reported on a few occasions. The injection was performed almost blindly except for the electromyographic needle signal to aid the experience of the surgeon.

CASE REPORT

The following is a typical case report. The patient was a 37-year-old black male with a bilateral VI cranial nerve palsy that had been present for two months. He was crossed 45 diopters in the primary position and 60 diopters to the right and left, meaning he could not turn his eyes to the right or left very well. Only one week after injection of 2.5 units of botulinum into each medial rectus muscle, he was zero straight ahead. Six months after the injection, he was straight in all directions of gaze left and right and up and down.

SIX MONTHS AFTER THE INJECTION, THE PATIENT WAS STRAIGHT IN ALL DIRECTIONS OF GAZE LEFT AND RIGHT AND UP AND DOWN.

CASE STUDIES

Of the 27 patients in the clinical trials conducted over the past months, 25 decided to have the botulinum injection. Their results were followed for an average of four and a half months following the injection. Seventeen treatments were considered successes. For four patients requiring surgery, the operation was less difficult, because they did not experience the severe contracture of the opposing muscle. Two of the patients were lost to follow up, and two were injected too recently to fully realize the effect of the drug, but the prognosis is favorable. The bilateral nerve palsy cases did not respond to the treatment as well as the unilateral cases.

Other cases included a patient with thyroid eye disease whose condition improved but required surgery. Another patient with III cranial nerve palsy definitely improved after the injection. There was one patient with hypertrophia and three with hypotropia and exotropia, all of whom resolved. The complication in our series included ptosis in 29 percent, lasting from a few days to three months. Most of the patients who have ptosis as a side effect experience it because the levator muscle is extremely sensitive to the drug. About a third of the patients experienced a drooped lid. However, this side effect disappeared in about three months in all reported cases.[6]

OTHER USES

The botulinum toxin is being used for many other conditions, including oramandibular dystonia, focal dystonias of the hand, spasmodic torticollis, vestibilo-ocular abnormalities, and cranio cervical dystonia.[10]

CONCLUSION

The results obtained in our trials are similar to those that have been reported by others around the country and the world.[6,11,12] We are excited about the benefit in cranial nerve palsies in particular, as this has been our main indication for its use. The spontaneous recovery rate for untreated cranial nerve palsy is about 30 percent, but botulinum therapy improves that percentage considerably. Even if a cure does not result, the patients are greatly improved, as there is less contracture of opposing muscles. In those patients who require surgery, it is made less difficult with a better result. In our opinion, this is a wonderful addition to the armamentarium of physicians—the ophthalmologist in particular—and to those who treat peculiar muscle anomalies that require denervation.

One of the principle objectives in the fight against disease is to expose the weakest link in the chain of infection and break it. Alan Scott did the unusual; he did not break the link but instead used it for the benefit of man. He had the vision to take a severe disease, realize that symptomatically it caused paresis of the eye muscles and double vision, and then, using these known facts, have enough patience with the FDA, the pharmaceutical companies, critics, and colleagues to make this therapy available. His efforts culminated in having the purified and standardized drug produced by a pharmaceutical company for the benefit of man. We in ophthalmology should be proud of Alan Scott, for what he has done is an inspiration to the scientists in this country who work to find ways to turn things that can harm us into those that can help us.

POSTSCRIPT

A NIH conference cosponsored by the National Institute of Neurological Disorders and Stroke, the NIH Office of Medical Applications of Research, the National Institute of Deafness and Other Communication Disorders, and the FDA was held November 12–14, 1989, in Bethesda, Maryland. This conference resulted in the recommendation that the FDA, in December 1989, approve the use of Occulinum, botulinum toxin.[13]

NOTES

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