Cautions Concerning Botox Therapy

To the Editor:
I am writing in regard to the review article about botulinum toxin (BTX) therapy by Eric S. Felber, DO,1 that appeared in the October 2006 issue of JAOA—The Journal of the American Osteopathic Association. I am a neurologist in Columbus, Ohio, and I specialize in the use of BTX to treat patients with neurologic disease. I would like to clarify and correct some comments made in Dr Felber’s article.1

In a discussion about the preparation of botulinum toxin type A (BTX-A, or Botox), Dr Felber1 states that vials of the toxin must be stored in the freezer until ready for use, and that once in solution, the toxin can be used for as long as 2 weeks if stored in a refrigerator. In fact, the manufacturer of Botox (Allergan Inc, Irvine, Calif) recommends that vials of unused toxin kept in the refrigerator be used within 4 hours.3,4 However, it is true that industry data suggests the toxin may remain viable for as long as 4 weeks.4 This is, of course, off-label information.

I also believe it is important to clarify both the on- and off-label uses of this medication, which were not presented clearly in the article. The US Food and Drug Administration (FDA) approved BTX-A in 1989 for the treatment of patients with blepharospasm, strabismus, and torticollis.2 In 2002, the toxin was approved by the FDA for the cosmetic treatment of patients with glabellar lines only.2,3 In 2004, BTX-A was approved for use in patients with axillary hyperhidrosis.5 It is important to understand that, in the United States, any other uses of BTX-A besides these conditions are considered off-label uses, even if such uses are considered the standard of care for certain conditions, including spasticity.6,7

In regard to the physiologic mechanism of BTX-A in cases of migraine, Dr Felber’s states, “Another mechanism by which BTX-A may relieve migraines is in its action on pericranial muscle spasms that pull on the skull bones and their respective sutures, causing a change in intracranial pressure and pressure on the cerebral vasculature.” I do not believe that there is any literature suggesting this particular mechanism. Rather, Dr Felber’s explanation would be only theoretical in nature, at best.

Lastly, I am concerned about the five pictures in Figure 1 that depict the sites of injection—particularly the third in this sequence.1 I believe that the use of botulinum toxin is complicated and, if not performed properly by skilled hands, it could lead to serious adverse effects. The most common adverse effects are ptosis and other problems with muscle weakness.3 The pictures in the article for frontal lines and cosmetic injections show an injection site that is clearly over the superior portion of the forehead.
levator palpebrae muscle (Figure 1 [C].)

This injection site is too low and too close to this muscle in my opinion, presenting a significant risk for ptosis in the patient. I would strongly suggest not injecting BTX-A in this region.

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References

Response
I thank Dr Taylor for his interest in my October 2006 article published in JAOA—The Journal of the American Osteopathic Association.1 To address Dr Taylor’s first point, the package insert of Botox Cosmetic (Allergan Inc, Irvine, Calif) does read, “Once opened and reconstituted, it [Botox] should be stored in a refrigerator (2°C to 8°C) and used within four hours.”2 However, there exists more than just “industry data” to indicate that botulinum toxin type A (BTX-A, or Botox), remains viable for as long as 4 weeks.3

Carruthers and Carruthers3 are famous for their pioneering discovery of the cosmetic use of BTX-A, and they remain worldwide authorities on cosmetic medical procedures. In 2005, Carruthers and Carruthers4 stated that evidence now indicates that reconstituted BTX-A can be stored refrigerated for 1 week or longer without loss of efficacy. Their evidence about the reconstitution and use of this product was derived from a double-blind, randomized controlled trial by Alam et al.5 Interestingly, Alam et al5 also concluded that reconstitution of preserved saline solution does not impair the stability of BTX-A, and administration of such a reconstituted product is less painful to patients than when the toxin is reconstituted with nonpreserved saline solution.

I agree with Dr Taylor regarding the importance of distinguishing between on- and off-label uses of BTX-A. As indicated by Dr Taylor, the only reconstitution use of BTX-A that is approved by the US Food and Drug Administration (FDA) is the treatment of patients with glabellar wrinkles.5 To clarify the other on-label uses, BTX-A has been approved since 1989 for the treatment of patients with strabismus and blepharospasm associated with dystonia; since 2000 for patients with cervical dystonia and “associated abnormal head position and neck pain”; and since 2004 for patients with primary axillary hyperhidrosis that cannot be managed by topical agents such as prescription antiperspirants.7

Despite these limited FDA approvals, BTX-A is increasingly being used for various off-label uses with favorable results for patients. In 2002 alone, there were approximately 1.1 million to 1.6 million patients using cosmetic botulinum toxin, and many of these cases involved such off-label uses as elimination of forehead wrinkles.6,8 It is also interesting to note that only one fatal case of anaphylaxis has been recorded in the vast usage of BTX-A.2 That fatality occurred when lidocaine was used as a diluent, and, consequently, the causal agent of the fatality could not be reliably determined.2

In regard to my proposed mechanism for how BTX-A relieves migraine,1 the proposal is, indeed, theoretical considering the fact that the mechanism of migraine itself remains unknown. My rationale for proposing that BTX-A may cause changes in intracranial pressure and pressure on cerebral vasculature by acting on pericranial muscles is that many patients describe headaches, especially tension headaches, as a “tightening,” “squeezing,” or “pressing” pain. Those terms sound muscular in nature and, thus, it is logical to propose that a product like BTX-A, which causes selective muscle paralysis, might alleviate these symptoms. Furthermore, Zalvan9 states, “The exact mechanism of this action [BTX-A relief of headaches] is unknown; however, the effect appears to be mediated by both a decrease in muscular tension and a central modulation of theafferent pathways.”

I agree with Dr Taylor that ptosis is a significant risk of BTX-A administration, and that only well-trained physicians should administer BTX-A, as I stated in my JAOA article.1 The injections for a brow lift shown in the third image of Figure 1 referred to by Dr Taylor must be given to patients at least 1 cm above the superior orbital margin, starting at the midpupillary line and extending to the lateral brow. I repeatedly and strongly urged this precaution in my paragraph describing the brow lift procedure.1

Once again, I thank Dr Taylor for his interest in this fascinating field.

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References

(continued)
Repatriating DOs With MD-Affiliated Residencies

To the Editor:

I am writing in regard to the letter about osteopathic graduate medical education by George Mychaskiw II, DO,1 that appeared in the May 2006 issue of JAOA—The Journal of the American Osteopathic Association, as well as the multiple responses to Dr Mychaskiw’s communication.2-6 I am an osteopathic physician who completed a rotating internship at an osteopathic medical institution and then, like Dr Mychaskiw, chose to pursue avenues for advanced residency training at an institution that was not osteopathically affiliated. Although some people in the osteopathic medical profession refer to such institutions as “MD” or “allopathic” hospitals, I have found in more than 30 years of practice that a medical institution that is not an osteopathic hospital is usually referred to simply as “a hospital.”

I considered attempting to obtain approval from the American Osteopathic Association (AOA) for both my anesthesiology residency and my occupational medicine residency, but I concluded that these paths were too time-consuming and would lead to substantial additional expenses that would never be recouped. Although I have paid AOA dues for most of the years since graduating from my osteopathic medical school, there were a few years when I chose not to do so. My withholding of dues was prompted by the AOA’s refusal to recognize my board certifications and list me as a certified physician in the AOA Directory of Osteopathic Physicians, which I find rather insulting. There are many trained osteopathic physicians, like me, who would prefer to be more closely aligned with the AOA.

I believe that the main issue influencing decisions on where to pursue residencies is not about an osteopathic residency versus an “allopathic/MD” residency, but rather about “location, location, location”: smaller community private hospitals versus larger public institutions. Frankly, osteopathic hospitals tend to be smaller and have fewer beds than “allopathic” hospitals, and having an adequate number of beds is of vital importance in advanced specialty training. Furthermore, osteopathic hospitals may not offer training in certain important procedures. The institution in which I completed my rotating internship—despite being one of the largest osteopathic medical institutions in the United States—did not, 30 years ago, perform cardiac surgical procedures, major pediatric surgeries, radical cancer surgeries, or total joint procedures, and it rarely performed neurologic, thoracic, or vascular procedures or invasive monitoring.

I am not complaining about my internship. In fact, I was very satisfied with it and felt it prepared me well for my residency training. I remain extremely grateful for the interest and time that the osteopathic physicians provided me in my education. However, for many, there may come a time when one must pursue the opportunities afforded by a more demanding and challenging clinical setting. I believed that the needs of my anesthesiology residency could not be fulfilled at an osteopathic medical institution because these institutions lacked firm, didactic, mandatory, and ongoing formal educational programs in this area. I find this problem to be characteristic of many small private training programs in many residencies—not just residencies at osteopathic medical institutions.

During the time I considered having my anesthesiology residency approved by the AOA in the late 1970s, the AOA exhibited very punishing tactics toward residents like me, including invoking excessive costs and forcing physicians to wait years for approval. As I watched residents in other programs at my residency institution fall prey to these tactics, I decided this was something that I did not want my family, myself, or my pocketbook to endure. In addition, the university through which I performed my residency training had previously had other residents in my specialties proceed through the same “allopathic” programs. The occupational medicine program had even included several osteopathic residents in the past. That particular program happened to be the oldest occupational medicine residency in the world. Yet the AOA required each resident marching through that program who was an osteopathic physician to “jump through the same hoops,” including obtaining multiple additional credentials and continuing medical education credits.

In this day and age, it is cost prohibitive to invoke such demands on residents. I speak from a great deal of experience in this regard.

It is time for the AOA to revisit the issue of graduate medical education for many reasons—but primarily to repatriate many of the physicians who have completed osteopathic internship training but then proceeded to perform residencies at institutions that were not osteopathically affiliated. I hope the AOA will find the common sense and  

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resolve to repatriate osteopathic physicians who have trained outside of osteopathic institutions, instead of treating us as lesser citizens and refusing to list us as board-certified physicians in the Find a D.O. search utility on the Association’s home page (http://www.osteopathic.org/directory.cfm). The AOA should recognize that many of us continue to be very committed to the osteopathic medical philosophy.

Why punish us any more than we have already been punished by the AOA over these many years?

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Irresistible Indexes for Somatic Dysfunction

To the Editor:
I read with interest the editorial by Michael M. Patterson, PhD,1 in the January 2007 issue of JAOA—The Journal of the American Osteopathic Association. The editorial highlighted important challenges to the osteopathic medical profession regarding research protocols for osteopathic manipulative treatment (OMT).

The points raised by Dr Patterson’s editorial1 reminded me of the work by J. S. Denslow, DO,2 in which he rated the severity of tissue texture abnormality with a graded index, finding that pathologic conditions could be identified between the mild and moderate grades of the index. My own research3 has led to similar findings regarding carpal tunnel syndrome (CTS). I applied a clinimetric index rating of 0 to 5 for palpatory restriction at the carpal tunnel, with level 2 (ie, moderate restriction) representing the onset of measurable abnormality.

In my research,3 I had the luxury of being able to correlate electrophysiologic findings on nerve conduction values with palpatory findings and patients’ symptom/complaint ratings. I believe that CTS represents the ideal form of somatic dysfunction for osteopathic medical research because it embodies the essential defining components—joint, nerve, skeletal, soft tissue, and vascular dysfunctions—within the diagnosis. Therefore, by measuring electrical changes in CTS, it is possible to study this type of somatic dysfunction in relative isolation, documenting resolution of specific focal restrictions that correlate with clinical improvement.

I went on to perform a reverse double-blind study involving 10 subjects with CTS and 10 without (B. M. Sucher, DO, unpublished data). In this study, we used a device that simulates OMT (Carpal Tunnel Stretch prototype; Chattanooga Group, Hixson, Tenn), as well as a sham device, in the treatment of the subjects. Each subject received treatment with the OMT-simulation device, whereas all these conditions worsened with the sham device.

I realize that there is a greater challenge in applying the type of index used in my research2 or that of Denslow2 to more generalized medical conditions, such as chronic low back pain. Still, the appeal to do so is irresistible.

The use of indexes allows osteopathic medical researchers to achieve more quantitative ratings of somatic dysfunction. Although it may be difficult to obtain interexaminer reliability with such index ratings, I have found that such reliability is possible. In the late 1990s, I conducted a workshop with second-year osteopathic medical students at the Midwestern University/Az State University/Arizona College of Osteopathic Medicine in Glendale. We achieved approximately 80% agreement for one level (up or down) in a rating scale for CTS/wrist palpatory restriction (B. M. Sucher, DO, unpublished data). These results were accomplished with only a 40- to 50-minute demonstration-and-practice session, followed immediately by the testing session.

Imagine what might be achieved with more extensive training!

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References

Competence Levels in Musculoskeletal Medicine: A Call to Action

To the Editor:
I applaud the medical education article written by Alan R. Stockard, DO, and Thomas Wesley Allen, DO,1 in the June 2006 issue of JAOA—The Journal of the American Osteopathic Association, particularly in its effort to expose the current unfor-
tunate realities of musculoskeletal training for primary care physicians. It is alarming that musculoskeletal problems are the second most common reason that patients seek medical care, but the number of osteopathic physicians is inadequate to address the deficit. Many physicians continue to feel insufficiently prepared to care for these patients. Drs Stockard and Allen surveyed graduating medical students using a standardized basic competency examination on musculoskeletal medicine, yet theirs was not the first study to reveal this training deficit. Still, little has been done to date to address the deficit. Many physicians continue to feel impatient when patients with musculoskeletal complaints are seeking care from them—and the shortcomings of their training are realized.

There is a larger issue that the Stockard and Allen study speaks to: a void has appeared in the healthcare system that is leaving many patients desperately seeking anyone who can provide routine musculoskeletal care. For today’s primary care physicians, the vast knowledge base required to adequately manage the growing burden of cardiovascular (and related) medical conditions—confounded by the time constraints inherent in managed-care systems—has relegated complaints of pain and poor physical function to the lowest priority in a typical office visit. At the other end of the healthcare spectrum, surgical specialists have found it most productive—if not merely more professionally gratifying—to spend their time and expertise offering care for surgically amenable disease conditions.

The pool of patients left in the middle with inadequately managed musculoskeletal conditions is large and growing, as the maturation of the baby boomers has brought upon us their demands to remain physically fit and functional well into their senior years. Beyond this problem, the Centers for Disease Control and Prevention have proclaimed an upcoming “epidemic” of arthritis in the United States as the population ages. As indicated by Stockard and Allen, the front door for the majority of patients with these medical conditions is the office of the primary care physician.

I would hope to energize the call for further study on the topic. As a staff physician with two sports medicine fellowships, and as someone who is actively involved in resident teaching, I can testify to the deficit in musculoskeletal training. I have had the opportunity of exposing many senior residents who were just weeks away from private practice to the bare essentials of musculoskeletal medicine. Perhaps musculoskeletal conditions are not elevated to a higher significance in pre-doctoral studies because they are neither fatal nor easily measured by current quality-of-care standards.

Somehow it has not yet riled physicians, the public, or insurance providers that basic musculoskeletal skills are not available in many primary care offices. Thus, this currently remains a quiet problem seeking a voice—and the osteopathic medical profession has an opportunity to assume a leadership role in addressing this pressing need.

I hope to see the worthy study by Stockard and Allen lead to immediate discussion, followed by effective action, by those individuals in the osteopathic medical profession in position to influence the design of student and resident programs in family practice and internal medicine. Programs in emergency medicine and osteopathic manipulative medicine may also stand to benefit from improvements in musculoskeletal training, though I cannot speak directly to the quality of the current experiences of students in those programs. Primary care physicians trained in sports medicine are an excellent resource for our profession, qualified to assist in standardizing a curriculum that will ensure clinical competence in office-based orthopedic skills.

I call out to my colleagues and urge participation in any task force or committee able to work among the appropriate specialty boards to advance an action plan—and I welcome any invitation for the same.

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References

Response
Dr Ruane clearly points out the deficiencies in current osteopathic musculoskeletal curricula, both at the postgraduate and postdoctoral levels, brought to light by our study in the June 2006 issue of JAOA—The Journal of the American Osteopathic Association (2006;106:350-355). Those of us practicing the specialty of primary care sports medicine see these deficiencies daily when we precept students and residents in every primary care specialty.
Osteopathic medicine is keenly situated to fill this void by giving our residents in the primary care specialties (ie, family practice, emergency medicine, internal medicine, occupational and environmental medicine, osteopathic manipulative medicine, pediatrics) the basic musculoskeletal clinical skills needed to diagnose the most common musculoskeletal dysfunctions and treat and rehabilitate patients with these complaints.

The problem as I see it, after 14 years of involvement in osteopathic medical education, involves the following two points:

- Every specialty thinks the others are supplying this knowledge (or mistakenly thinks a 2- to 4-week rotation on orthopedics supplies this knowledge).
- Our residency programs have become too allopathically oriented, focusing on medical issues other than the musculoskeletal system, which is relegated to the level of triviality, as so eloquently pointed out by Dr Ruane.

I recommend that a task force be formed to address this important issue, including representatives from the colleges of osteopathic medicine, program directors from each of the primary care specialties, and representatives from the American Osteopathic Academy of Sports Medicine (AOASM). I mention AOASM because this group understands how to bring all these elements together; we currently bring them together in our American Osteopathic Association-approved sports medicine fellowship programs. Although achieving that level of musculoskeletal expertise would be impossible to impart in the general knowledge base of the primary care specialties, at least a framework could be developed to augment the basic musculoskeletal knowledge in our existing residency programs.

I, for one, would volunteer for such a task force in a heartbeat—but medical educators need to identify this issue as one that could unify and strengthen our profession, which was founded on the principle of “extra education in the musculoskeletal system.” In medicine, knowledge without application is useless. We can know all the genetic markers of a disease, for example, but unless that knowledge is converted into diagnostic or treatment protocols, what good is it?

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Step Forward to Stop Bird Flu

To the Editor:
The editorial by Michael M. Patterson, PhD,1 in the November 2005 issue of JAOA—The Journal of the American Osteopathic Association reflects the important role that the osteopathic medical profession has to play in addressing the potential influenza pandemic resulting from the spread of the avian influenza virus, H5N1. To quote Dr Patterson1 in his concluding sentence, “The osteopathic medical profession [must remember]...the lessons of its heritage and [have] the courage to prepare itself to teach those lessons to others.”

Now is the time for the osteopathic medical profession to step forward and provide leadership. Dr Patterson’s editorial mentions that mortality rates from influenza during the 1917-1918 pandemic were reduced from a national average of 6% to an average of 0.25% for patients treated with muscular relaxation and osteopathic manipulative treatment (OMT), and that mortality rates from pneumonia during that pandemic were cut from as high as 75% nationally to 10% for osteopathically treated patients.1,2 If these dramatic statistics are indeed true, then does not the osteopathic medical profession have a societal obligation to train its allopathic colleagues, other care givers, and families in these life-saving techniques?

As Dr Patterson1 indicates, the use of OMT in the treatment of patients with influenza would likely result in the following benefits:

- reduced hospitalizations
- minimal reliance on medications
- improved patient immunity and defense mechanisms
- improved “self-care” regimens through the involvement of patients’ family members
- additional clinical experience for osteopathic medical students

I reiterate, the time is now—before the pandemic begins—for the osteopathic medical profession to provide leadership on the problem of avian influenza and to share its knowledge about OMT with the rest of the world.

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References

Promoting an Osteopathic Medical Research Culture

To the Editor:
I was interested to read the original contribution by Sarah J. Breese McCoy, PhD, and colleagues1 in the April 2006 issue of JAOA—The Journal of the American Osteopathic Association on risk factors for postpartum depression. I am pleased to see reports appearing in the JAOA of original research emanating from our osteopathic medical institutions, such as the Oklahoma State University College of Osteopathic Medicine in Tulsa, which was the site of the Breese McCoy et al study.

Letters

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This study corroborated results of previous allopathic studies.\textsuperscript{2-8} My hope is that the larger study recommended by Breese McCoy et al\textsuperscript{1} will include original findings focusing on osteopathic manipulative treatment (OMT) for postpartum depression. It is well known to those of us who regularly perform OMT that patients with postpartum depression respond well to manipulation of the sacrum.

In an osteopathic medical institution, such research would be an excellent opportunity for the housestaff to perform uniquely osteopathic physical examinations and to note the effects of OMT on patients in the medical record. Of course, it would also be a good exercise in any medical institution.

I suggest promoting the operational rules and regulations of the Osteopathic Postdoctoral Training Institutions,\textsuperscript{9} as well as to advance an osteopathic medical research culture at the same time.

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References

Response
I would like to thank Dr Lee for his interest in the research described in our April 2006 original contribution to JAOA—The Journal of the American Osteopathic Association.\textsuperscript{1}

My colleagues and I have recently completed a follow-up study that is similarly designed, but more scientifically rigorous, than our JAOA report. It is currently in press with the Journal of Reproductive Medicine.\textsuperscript{2} Although we have not yet formally investigated osteopathic manipulative treatment (OMT) in the management of postpartum depression, we concur with Dr Lee that such a study would be interesting and worthwhile. In fact, such a study is currently in the early planning stage in the Department of Obstetrics and Gynecology at the Oklahoma State University Center for Health Sciences and College of Osteopathic Medicine in Tulsa.

Our attending obstetricians frequently use OMT, as needed, with both pregnant and postpartum patients. We would point out, however, that properly designing a scientifically rigorous study of this nature presents some difficult challenges as a result of the need for a sham treatment resembling OMT to serve as a control.

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