

New treatments for Dupuytren contracture

D. Kay Kirkpatrick, MD, leads a roundtable discussion

Recently, the U.S. Food and Drug Administration (FDA) approved a new treatment for Dupuytren contracture—an enzyme injection (collagenase clostridium histolyticum) to soften and weaken the diseased cords of tissue that cause fingers to contract. In addition, other treatment options such as needle aponeurotomy—a minimally invasive technique that uses needles to puncture and weaken the contracting cords until they can be broken by mechanical force—are providing alternatives to surgery.

D. Kay Kirkpatrick, MD, a hand surgeon and member of the AAOS Practice Management Committee, recently conducted a roundtable discussion on these new treatments. Joining her were **Charles Eaton, MD, FACS**; **F. Thomas D. Kaplan, MD**; and **Roy A. Meals, MD**.



D. Kay Kirkpatrick, MD



Roy A. Meals, MD



*F. Thomas D. Kaplan,
MD*



*Charles Eaton, MD,
FACS*

Dr. Kirkpatrick: *Why do you think there is suddenly so much interest in new treatments when open fasciectomy has been the gold standard for so many years?*

Dr. Meals: I think it's just coincidental. Needle aponeurotomy was initially popular with rheumatologists in France, and only recently has it been practiced in the United States. Similarly, collagenase injections (Xiaflex, Auxilium Pharmaceuticals, Inc., Malvern, Pa.) have been in clinical trials for some time, but received approval from the FDA

just this year.

Dr. Eaton: I think it started with a combination of patients, surgeons, and the Internet as a vehicle for communication. The unmoderated online BioSpecifics Dupuytren patient discussion group enabled patients to spread the word about needle aponeurotomies. Patients then tried to recruit U.S. surgeons to provide this treatment. When I learned the technique, I was overwhelmed by patients who found me online.

Dr. Meals: The general trend is toward minimally invasive surgery.

Dr. Kirkpatrick: *Let's move on to collagenase injections. What are the clinical indications? What are—or are there—advantages in using collagenase injections over needle aponeurotomy?*

Dr. Kaplan: I think that the advantages of collagenase injections versus aponeurotomy are yet to be fully elucidated. So far, collagenase injections have only been looked at on their own compared to placebo injections. Aponeurotomy has been looked at and compared to total or limited fasciectomy, but collagenase injections haven't really been compared to needle aponeurotomy. That research still needs to happen.

Based on Phase I clinical trials, collagenase injections work better for metacarpophalangeal (MP) joint contractures than for proximal interphalangeal (PIP) joint contractures, and for lower severity contractures than for higher severity contractures.

Ideally, patients for collagenase injection should have a well-defined, palpable cord, ideally one that is strung away from the flexor tendon system. The worst patient is probably someone who has a small finger IP contracture that's more than 50 degrees and has been there for 5 or 10 years. Collagenase can only affect the cord itself; it won't be able to act on the secondary tissues that have changed.

Dr. Meals: One other consideration is that the collagenase injection requires two office visits—the injection on day one, and the manipulation of the finger to rupture the cord on day two. Some surgeons can perform needle aponeurotomy in their offices, but in California, the Medicare carrier will not pay for needle aponeurotomy in a nonfacility setting. That means a trip to a minor operating room, with all the associated facility and cost issues.

Dr. Eaton: I think that the primary advantage of the collagenase treatment is that it does not have as much of a learning curve as a percutaneous needle release. It is technically simple to perform, relatively quick, and much less demanding. Giving a shot is fast, but performing a needle aponeurotomy may take up to 20 minutes, depending on the severity. If multiple fingers are involved, the procedure may take closer to an hour. That can be an ordeal for the patient.

[The impact of collagenase injections can be seen in this series of photos \(PDF\)](#)

Dr. Kirkpatrick: *What about the risks of these two procedures?*

Dr. Meals: Each of these treatments has its own risk profile, different from the other. Needle aponeurotomy would be risky for the digital nerves, which the collagenase injection typically does not put at risk. On the other hand, two patients in the clinical trials did have tendon ruptures following collagenase injections.

Dr. Kaplan: Tendon rupture is also a risk of needle aponeurotomy. Another issue to consider with collagenase is that you can only inject one cord for one joint at a time, and injections must be at least a month apart because that's the way it was tested. We don't know whether giving two injections at the same time—even if in different hands—will result in worse side effects or an immunologic response.

Needle aponeurotomy can be used to treat multiple affected fingers and joints during one setting. We need to keep these parameters in mind when selecting what may be the best procedure.

Dr. Eaton: The other issue is what happens when someone has a recurrence after receiving treatment. Early on, there was concern that the collagenase would cause a gross architectural change and make surgical exploration difficult. But the few reports of patients who have had recurrences after an initial collagenase injection have been very favorable.

In contrast, the scar tissue that forms after needle aponeurotomy can be extensive and I suspect may be closer to the kind of scar tissue that forms after a fasciectomy. That in itself may be a long-term advantage in terms of the recurrence timeline between the two procedures.

Dr. Kirkpatrick: *Are the contraindications for needle aponeurotomy and collagenase injections the same or different?*

Dr. Eaton: Collagenase is contraindicated for patients who are on anticoagulation, but that is not an issue for needle aponeurotomy because the skin stops bleeding quickly after a puncture wound. Another potential limitation for collagenase would be lymphedema or prior lymph node surgery on the side being treated. A percentage of people will have a lymphatic reaction after collagenase injection. The only other issue is a patient who had previous surgery and has implants in that hand.

Dr. Kaplan: Anticoagulation is not actually listed as a contraindication for collagenase injection, but is a precaution. In the clinical trial, patients were excluded if on anticoagulants other than low-dose aspirin. We don't know if this will be an issue or not, but we do ask patients who are on anticoagulation drugs to stop for 5 days before receiving collagenase injections.

Dr. Kirkpatrick: *What do you think the role of open surgery is? Is it still the gold standard or the procedure of choice?*

Dr. Meals: When open surgery is done properly and the patient sees it through with therapy, the likelihood for a functionally significant recurrence of the contracture is small. Unless the contracture has a real tendency to re-form, the chances are that the patient will not need any additional treatment in that area.

Based on reported results, recurrence within several years can be expected with needle aponeurotomy. The recurrence rate on the collagenase injection is unknown. Some people prefer to have a procedure done in the office rather than in an operating room; others would prefer to have one treatment now and stay out of doctors' offices for a long time. Open surgery clearly has a role, even in previously untreated Dupuytren.

Dr. Kaplan: We really have to change our mindsets. This disease does not have a cure; what we do is manage the patient's disability and impairment as best as we can. The best treatment depends on the patient—what the risk factors are for recurrence, how many joints are affected, age, and tolerance for open surgery versus a more percutaneous or limited approach.

I would like to make one other observation. A patient who has three or four contracted joints, with one finger particularly contracted, may be happy with having the collagenase injection in that finger to let it extend as much as the adjacent fingers. This limits, but does not eliminate, the disability. A limited approach in some patients may actually allow them to recover full function without aiming for the goal of getting full extension.

Dr. Kirkpatrick: *The cost of the collagenase injection has been a huge issue in my practice. Carriers don't seem to be routinely paying for this drug, and Medicare doesn't have a specific code. Does anybody have a solution for that yet?*

Dr. Meals: As of today in Southern California, Medicare is reimbursing collagenase injections and allowing the 6 percent markup to the surgeon. In preferred provider organizations when the insurance company approves it, the company contracts with a specialty pharmacy, which delivers the drug for those insured patients. I'm reimbursed for the procedure without being involved in the purchase of the enzyme itself.

Dr. Kaplan: As far as commercial payors, several have approved collagenase injections for patients, but one still considers it experimental.

Dr. Kirkpatrick: *A lot of people are waiting to see what develops. The marketing of this product has been fairly aggressive. Does anyone have any issues with that?*

Dr. Kaplan: I attended the FDA panel review, along with several hand surgeons and rheumatologists. Interestingly, the hand surgeons were more open to allowing non-hand to surgeons administer the collagenase injections than the rheumatologists were. The FDA clearly stated that it did not want to be overly restrictive or limit patient access.

I think the most important issue with the use of this product is that you be familiar with the anatomy of Dupuytren disease, regardless of whether you are a rheumatologist, orthopaedic hand surgeon, or plastic hand surgeon.

Dr. Kirkpatrick: *Are you aware of other new treatments under development that have potential in this area?*

Dr. Eaton: At an international symposium on Dupuytren disease in Miami earlier this year, we had 47 speakers from 13 different countries with some very interesting information and some new ideas. These included the use of custom silicone rubber splints after surgery that showed progressive improvement and extension over the course of months.

A report on using an absorbable carboxy cellulose implant as a spacer at the end of a limited fasciectomy for

Dupuytren showed better early term results than not using that type of spacer. A variation of a needle release technique, using multiple superficial releases of the fascia over the entire distance of the palm, was also reported.

The most groundbreaking presentation was on the use of preoperative adjuvant tamoxifen to treat patients who had high risk for recurrence after a surgery. This randomized study showed that high-risk patients who had the preoperative treatment before limited fasciectomy for Dupuytren maintained their surgical correction to within about 10 degrees. Patients who were randomized to just the surgical treatment lost an average of 40 degrees of their initial correction.

The study used oral tamoxifen, but I'm considering a trial with topical tamoxifen. The big issues with patients who have aggressive Dupuytren are the extent of skin involvement and the dense relationship between the skin and the fascia as part of the biology. A minimal approach to straighten the fingers, followed by some sort of biologic intervention to maintain those results, would be great.

Radiation has been a commonly used approach in Germany. Radiation does have a biologic effect on nodular Dupuytren but not on the cords; it's an option for patients who have early Dupuytren with a lot of nodular involvement. The amount of radiation used in the current protocols is fairly low and the chance of side effects is low, but we have yet to see long-term results.

Dr. Kirkpatrick: I think you have done a great job in bringing us up-to-date on what's really going on, even though we may still have questions about how the various modalities are going to fit into our individual practices. Do you have any final comments?

Dr. Eaton: We need to organize large-scale studies to really look at our results. That's the only way we will continue to make progress.

Dr. Kaplan: I want to echo those remarks. It's so difficult to sort out the different techniques of needle aponeurotomy, fasciectomy, definitions of recurrent or disease extension, and patients' different biology and risk. We need multicenter prospective trials with large numbers of patients to compare all these treatment options so we can make the best decisions.

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6300 North River Road Rosemont, Illinois 60018-4262 Phone 847.823.7186 Fax 847.823.8125

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