

IN THE SPOTLIGHT

Researching the Regeneration of Articular Cartilage with Stem Cell Prolotherapy: An Interview with Nathan Wei, MD

Ross A. Hauser, MD & Nathan Wei, MD

Hauser: Dr. Wei, can you tell us a little bit about your educational background and why you became interested in pain management, and subsequently Prolotherapy?

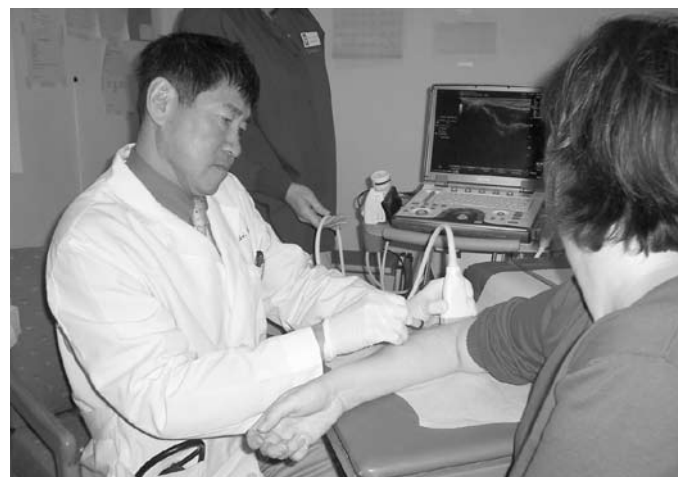
Wei: I got to this rather circuitously. Originally, out of medical school, I went to medical school in Philadelphia, at Jefferson Medical. I did my residency at University of Michigan and started out in radiology, and switched back to internal medicine. When I was done I had no idea what I wanted to do. I decided to go to the National Institutes of Health and do a two year fellowship. It just so happens that I matched with the arthritis division there. When I was done with my two years there, I still didn't know what I wanted to do. But I was eligible to take the board exams, so I took it, passed. I thought *well, you know, this is it.*

In looking back at it, a lot of fate was involved, because within a few years of starting practice, one of my sisters came down with rheumatoid arthritis. Subsequently, one of my children came down with a form of juvenile arthritis. I guess really when you look at it, I was destined to do this.

Now, the problem with conventional rheumatology training programs is that they do a pretty good job teaching us about the science of arthritis, and how to use very potent drugs to treat arthritis. But they don't really prepare us for what we'll see in private practice. And the types of things we see in private practice are common things, mostly osteoarthritis as well as rheumatoid arthritis, and these types of conditions require a much different set of tools. I've always been very procedurally oriented. I have been an arthroscopist for close to 20 years. I am the only rheumatologist elected to the Arthroscopy Association of North America. Some of the best arthroscopists in the world belong to that (society). So, in terms of using procedures to help patients feel better, that's really where I feel my strengths lie. So, with arthroscopy we've been able

to do interventions that help relieve various discomforts related to arthritis.

But more recently, within the last, I'd say three years, I've become very interested in other imaging techniques. Remember, I first started out in radiology. One of those modalities is diagnostic ultrasound. I got hooked up with Dr. Tom Clark, one of the foremost musculoskeletal ultrasonographers in the world, and he introduced me to the use of ultrasound to guide interventions. Along the way, he asked if I ever heard about Prolotherapy. I told him that I didn't really know much about it. I had heard the term, but I didn't even know what it was. So he said he would introduce me to a colleague of his. At a course, he introduced me to Dr. Dean Reeves. Dean, a very nice man, gave me the ins and outs of Prolotherapy and he knew already that I was doing PRP treatments for patients with various tendinopathies and arthritis disorders, and also doing stem cells. He said, "What you are doing right now is a type of Prolotherapy." And so my eyes were really opened at that.



Dr. Wei treating a patient for lateral epicondylitis at his clinic, Arthritis and Osteoporosis Center of Maryland.

Hauser: Dr. Wei, describe for our readers PRP and then stem cell therapies.

Wei: PRP, which stands for Platelet Rich Plasma, is a derivative of whole blood. In other words, what we do is draw a sample of blood from the patient, then we spin that sample down to get small amount of plasma that has a lot of platelets in it. Platelets are components of blood that contain a lot of growth and healing factors. When they go to an area of new injury, these growth and healing factors stimulate the healing response. They accelerate it and send it into work drive. So for certain conditions such as ligament injuries and tendon injuries, where we know that the problem is not really inflammation...but injury, it works to help the healing. I want to emphasize the term tendonitis should not be used. It's actually tendinopathy because the pain associated with tendon problems is related to wear and tear, and not inflammation. So, by guiding the injection of this substance called PRP, platelet rich plasma, into the area where the tendon or ligament is injured, you can actually accelerate, speed up, the healing process. Now that's one part of this whole deal.

The other, what I consider actually an even more interesting aspect, is the use of what are called mesenchymal stem cells. Mesenchymal stem cells are really baby cells. They are cells that have not really differentiated yet. They have not become any specific organ. They are just sort of sitting there waiting to be prompted and stimulated to become whatever tissue you want them to become. If you take a stem cell and give it the right environment, it will become a heart cell, a lung cell, etc. Or in the conditions that we want to treat, it can become a cartilage cell. So what we have been able to do and accomplish is take people with osteoarthritis (wear and tear arthritis, the most common type of arthritis effecting the hip, the knee, and other areas), and by introducing the stem cells, along with an environment that is conducive to their growth and multiplication, we have actually been able to stimulate cartilage growth. And that is exciting because one of the most common surgeries performed in the United States these days is joint replacement. So if we can find a procedure that can prevent or possibly delay indefinitely the need for that kind of surgery, I think that is wonderful.

Hauser: Can you explain where stem cells come from? Explain the procedure in your office.

Wei: Fortunately stem cells are present in all of us. They are actually located in the bone marrow. By going to the back of the hip, there is an area called the iliac crest, which is rich in bone marrow. By using local anesthetic and ultrasound guidance, we can actually harvest stem cells, harvest bone marrow from the iliac crest, then prepare it and concentrate a large amount of stem cells, 1.5 million, from this bone marrow aspirate. Believe it or not, this really doesn't hurt.

Hauser: What conditions does stem cell therapy work well for?

Wei: The types of things we see in our office, and again, remember I am a rheumatologist, an arthritis specialist, are osteoarthritis primarily of the hip and the knee. We are looking at other joints as well. Also (we are using it) for patients who have osteoarthritis in the shoulder and who have rotator cuff problems in the shoulder because stem cells can help heal partial tears in the rotator cuff. We have had quite a bit of success with that as well.

Hauser: You are doing a study with stem cell therapy, correct?

Wei: Yes, we are doing a study in order to get around this whole mystique. A whole lot is written about stem cells. If you go to a source like Google for instance, you get a lot of misinformation. Number one, people don't know what stem cells are, and number two, when they're told things, they're told this is the next best thing since sliced bread. They are just not true. What we are doing is taking a select group of patients who range in age from about 25-75. We made that age cut off because we know stem cells in older patients respond less well to stimulus than those coming from younger patients. What we are looking at is osteoarthritis of the knee and we are measuring different parameters, including what is called the Visual Analog Scale (VAS), which is basically what a patient tells us is happening as far as are they feeling better or worse. That is coming from the patient perspective, as well as the physician perspective. We are having patients fill out a WOMAC questionnaire, which is a standard questionnaire used in osteoarthritis studies to describe a patient's ability to perform activities of daily living (ADL's). We measure the speed of a 50 ft walk. Finally, and most importantly in order to create objective data, we are measuring the thickness of cartilage growth in the knee joint, between the knee cap and the upper leg bone.



Dr. Wei performing a PRP injection procedure, under ultrasound guidance, on a patient.

This is called the patellofemoral joint. It is the only joint that is really accessible to ultrasound measurement. We have been able to demonstrate, over a one year period of time, significant improvement in cartilage thickness in most of our patients. Not all. We have had a couple patients not respond and that is to be expected. If you see a paper, and they report 100% success, there is something wrong. I mean there is no treatment in the world that works 100% of the time. The same thing is true with stem cells. But the data that we are getting, both subjective as well as objective, is very encouraging.

Hauser: How many treatments do patients receive and how frequent are the treatments given in the study and in your private patients?

Wei: They only require one treatment. We are only doing one treatment, because we want to see what that effect is. Now, in the future we might learn the patient may require another treatment in order to get better results. The patient may not need one for five years, or may not need another one for 10 years. Because we are at the very beginning stages of this whole stem cell frontier, it is difficult to know what the best approach is.

Hauser: From doing searches on the web, I would say the average patient who goes to a private practitioner generally has the notion that cartilage cells cannot reproduce, or that cartilage thickness cannot improve. Most patients are under the impression that cartilage cells cannot replicate, so if you have degenerative osteoarthritis, you are always going to have it and just wait for a knee replacement. What would you say to that?

Wei: (laughs) That is the kind of opinion and notion we are trying to hopefully change. Because you are right, that has been pretty much the mindset and the message given to patients when they see either their primary care providers or orthopedists—that the cartilage is gone, bide your time and we will replace your joint. The thing is, if the patient still has viable cartilage left, meaning that it is living, that there is still some there, and there is hope that the cartilage can be prompted to grow. That is the promise of stem cells. The best approach for using stem cells in a situation like this, we are still searching for.

A really, really fine stem cell scientist at University of Pittsburgh, Dr. Rocky Tuan, is working with what is called nanofibers. He is doing animal models. These nanofibers provide a really nice framework for stem cells to stick to and help growth. We are also using a matrix as well. I think one of the big problems is people who try to do stem cell therapy, often times just think it is just injecting stem cells into the joint. Far from it. Because cartilage does not have nerves and that is why just the process of wear and tear of cartilage should not cause pain. The pain is actually coming from irritation of the joint capsule. Every joint is a capsule, it is lined by what is called synovial tissue. The pain from osteoarthritis is due to irritation of this capsule and that can come about for a lot of different reasons. But when you treat somebody with stem cell therapy for osteoarthritis, you need to treat the entire region. Not just stick stem cells inside the joint. In addition, you need to give the stem cells some bulk, some framework to stick to so they are not just crushed and washed out of the way with joint movement. There are not only techniques that we are exploring right now, we are constantly improving the process. But I think in a few years this whole approach is going to get better and better.

Hauser: Do you have a post PRP Prolotherapy or stem cell Prolotherapy protocol that you have patients follow? Do you have patients resume normal activity and/or begin special exercises, range of motion, or anything?

Wei: Absolutely. Following a stem cell procedure, or a PRP procedure for that matter, it is important that the patient initially rest for a few days. Then after that, we begin the patient with a graded program of progressive stretching and strengthening of the affected area, trying to avoid any types of things that would reduce inflammation because we are trying to do the opposite of what we have been taught in traditional arthritis. With traditional arthritis,

we use the anti-inflammatory drugs and things that block inflammation. With PRP and stem cells, we are trying to do just the opposite. We are trying to use inflammation as the subsequent healing cycle to actually create new tissue. A lot of the patients come from far distances, so we really have to outline to the physical therapist that they will be seeing at home that you cannot treat this patient like you would ordinarily treat a patient you have seen in the past. You must avoid ultrasound. You must avoid ice. You must avoid all the things that ordinarily you would use to reduce inflammation. You want to concentrate more on range of motion and strengthening. Those are the things that will eventually get the patient back to full activity.

Hauser: What do you foresee for the future of Prolotherapy and what would you like to see happen as it relates to the care of osteoarthritis in the United States?

Wei: I personally would like to see Prolotherapy used much more often. The reason is that a lot of the medications we use in traditional arthritis therapy carry with them a

significant number of potential side effects. These side effects not only cause patients to have problems that are life threatening, but they also can cause problems that lead to death. I think we can use a type of treatment like Prolotherapy, that has been around for thousands of years, to try to regenerate lost tissue to speed up the healing process using a much more natural approach. Because that is what Prolotherapy and stem cell therapies are. I mean these are as natural as you can get. PRP is derived from the patient's own blood. Stem cells come from the patients themselves. To me, it makes much more sense to approach the conditions that we see using these new types of tools as opposed to using a lot of the dangerous chemicals that we have used in the past.

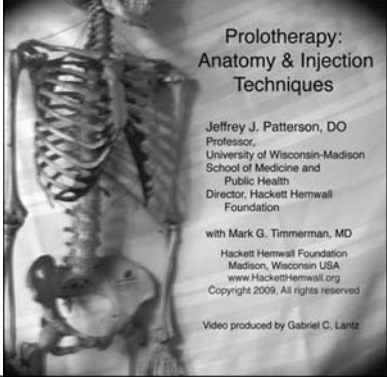
Hauser: Dr. Wei, thank you so much. I so much appreciate your time, and as a Prolotherapist, I would like to thank you for the work that you are doing.


Wei: Thank you. It has been a real honor to be in on this interview. ■

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