



Ed Harris – My Story

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My Medical History

Diagnosis and Early Symptoms

I was diagnosed with CREST syndrome (old name for limited systemic scleroderma) in January of 1990, but had initial symptoms for about five years before my diagnosis. My approach from the onset has been to read everything I could find on the disease and decide on my own course of treatment. (I had to change physicians before I could find one who was willing to let me take charge of my own treatments!)

The conventional medical approach for treating this disease is to wait until symptoms develop and then try to treat the symptoms. This made no sense to me at the time of diagnosis and still does not. Even before I understood what I now do about the disease, it was obvious to me that trying to prevent the disease from progressing would potentially be “easier” than dealing with symptoms after they arose.

In 1991, I began to have severe heartburn, which is characteristic of CREST syndrome. This is because the lower esophageal sphincter loses muscle tone as part of the disease, resulting in acid reflux, i.e., the backup of stomach acid into the esophagus, which is what heartburn is. At the time I was taking Procardia (nifedipine) to treat my Raynaud’s symptoms. My physician had either not known or failed to mention to me that Procardia and all other similar medications have a side effect of reducing the lower esophageal sphincter pressure, thus increasing heartburn! I dropped the Procardia, which improved the heartburn, but my Raynaud’s got worse. By 1992, my heartburn was so bad that it was not fully controlled by large doses of Prilosec (omeprazole). Also, by late 1992 I had become chronically chilled, to the point where I was wearing sweaters in the summer and raising the heat in my car so much my family was constantly complaining about suffocating from the heat!

Search for a Potential Treatment

By late 1992, I was starting to feel increasingly hopeless as my symptoms continued to progress. My wife and I went to see the movie “Lorenzo’s Oil” and I left the movie inspired to try to find a treatment approach that perhaps my physicians didn’t know about. So, in early 1993, I began a much more thorough literature search to see if I could get a better understanding of the disease process and perhaps discover a way to either stop or delay the normal disease progression. However, you have to think about how challenging this was in 1993. There was no Internet and while I had access to a medical school library where I lived, doing a literature search meant starting with card catalogs and ultimately going through many bound volumes of multiple rheumatology

journals as a first step. This task was very slow and difficult and I was increasingly feeling that it was an insurmountable task.

Then, through an amazing “pay it forward” story, everything changed. I was the founder and CEO of a fairly large software company back then and was on an airplane trip to a trade show that we were exhibiting at. I don’t recall how this came up but I ended up talking with the person sitting next to me about my medical situation and what I was trying to accomplish in my review of the medical literature. It turns out that this gentleman was also the CEO of a software company, but in his case, his company (Silver Platter) sold Medline – the medical search catalog – to medical libraries and research facilities on CD Rom for several thousand dollars. He said “tell you what, when I get back to the office next week, I will send you a free copy of Medline so you can better do the research you are trying to do”. He followed up and about two weeks later I received his incredibly generous gift, which literally changed (and probably saved) my life! (As a side note, in 2014, I tracked him down with great difficulty and told him everything that has transpired since because of his generous gift. He told me later that he was really moved after reading my email.)

Armed with a vastly improved way to do medical research, I located some little known research studies from the Netherlands that showed a very significant finding about scleroderma that appears to have been missed by virtually all scleroderma researchers at that time. It turns out that in scleroderma patients with Raynaud’s, these researchers had discovered that the red blood cells clump together abnormally as compared to either normal people or even people with primary Raynaud’s (same symptoms, but no underlying serious disease). They were using a treatment called plasmapheresis (more correctly called therapeutic plasma exchange or TPE) to treat the Raynaud’s symptoms, and had discovered that it had significantly reduced scleroderma related Raynaud’s but no effect on primary Raynaud’s. More importantly, the TPE treatments resulted in a return to normal red blood cell aggregation that lasted for a significant amount of time (three to nine months) following a single series of just four weekly TPE treatments. I called the researchers as well as a clinician in the Netherlands and learned that they had been using it clinically there for a while with good success, especially with CREST patients.

This gave me a clue as to what might be going on in scleroderma. By doing significantly more literature research, I was able to convince myself that most, if not all, scleroderma symptoms could be accounted for simply by the potential long-term effects of abnormal red blood cell aggregation. Ironically, at the time I did this, the idea of progressive vascular damage as a trigger for the development of scleroderma symptoms was not widely discussed in the research literature, but in the past few years, I have noticed that this is now the generally accepted theory as to the mechanism of damage in systemic scleroderma. However, I have to this date still not seen any mention of the abnormal red blood cell aggregation as a potential “first cause”.

Therapeutic plasma exchange, by the way, is a simple but effective procedure. What is done is to insert one needle into a vein on one arm, and another needle into a vein on the other arm. A continuous flow machine removes blood from one arm, separates out the red and white blood cells and platelets from the plasma using a centrifugal separation mechanism, discards the plasma, re-mixes the red/white blood cells/platelets typically with 5% sterilized albumin, and puts the new mixture back in the other arm. It takes about one and one-half hours, is mildly uncomfortable once they get the needles in, and leaves me feeling tired for a few hours after treatment. The usual rationale for using TPE to treat and autoimmune disease is that it temporarily reduces circulating antibodies and other possible substances that might have a role in the development of disease symptoms. However, while this may be a factor in the improvements seen from using TPE with

scleroderma patients, I now believe that the research supports a different mechanism of action that may account for most of these improvements.

I put together a treatment plan that included annotated research citations, submitted it to my physicians, and after months of effort actually managed to convince my insurance company to fund a one-year trial of this treatment approach. It is worth noting that while my team of physicians agreed to try this since they had nothing else to offer that they felt would be effective in slowing down disease progression, they did not expect it to have any beneficial effects.

I began treatments in November 1993. Based on the research results from the original studies and a discussion with the clinicians trying this in the Netherlands, I decided on an initial treatment cycle that consisted of one treatment per week for four weeks, followed by a two-month layoff, then the cycle repeats, for a total of 16 treatments during this first year.

Initial Results

After one year of treatments my reflux was significantly improved and while I was still somewhat chronically chilled it was not as bad as it had been before starting the treatments. After two years of treatments my reflux was under complete control with a very low dose of Prilosec. And, I was no longer chronically cold at all. These are nice results, but they are subjective. Of much more significance is the fact that my hematocrit value (a quantitative measure of the percentage of red blood cells), which had been abnormally low for the previous 8 years, returned to a normal range following the first round of four plasmapheresis treatments. This was completely unexpected since normally with plasmapheresis treatments you may see a slight drop in hematocrit levels because of minor blood loss from the procedure. When I first saw this sudden increase of hematocrit after the first round of treatments, I speculated that the reason for this might be because the automated equipment used for doing blood counts might be counting small clumps of red blood cells as a single large red blood cell and that once the clumping was broken up, the red blood cell count would be more accurate. I was finally able to confirm in 2014 that this is exactly what happens with clumped red blood cells by talking with an engineer at the company that makes the cell counting equipment that was in use back in 1993 (Beckman-Coulter).

One other significant quantitative measure that supported the theory that the plasmapheresis treatments were stopping the progression of the disease is the results of repeated pulmonary function tests (PFT). In June 1994, I had an initial PFT that showed that while most measures, e.g., lung capacity, were normal or above normal (I exercise a lot), the gas exchange ability of my lungs had declined to about 68% of the expected value. This is common with limited scleroderma and if it continues to reduce over time, this can be very serious, ultimately leading to pulmonary hypertension, which is even now very difficult to treat. About one year later, in May 1995, I repeated the PFT. The results of this critical measure were unchanged. At that time, I considered this to be the best possible result since these changes to the lungs are normally irreversible and progressive. In August 1997 I repeated the PFT again. Again, all other measures except gas exchange were normal or above normal. However, this time my gas exchange measure had increased significantly, up to about 76% of expected. This was an unexpected result and certainly very good news. It suggested that my lungs were slowly healing. My most recent PFT was done in December 2000. This time my gas exchange measure had increased to 81% of the expected value, which is in the normal range of 80% to 120%.

Evidence for Effectiveness of Treatments - Part 1

In 1997 I was forced to stop my plasmapheresis treatments against my wishes. While my internist and rheumatologist were then becoming increasingly convinced that the treatments were effective

at stopping or at least delaying the progression of my limited scleroderma, one of the physicians who was in charge of the transfusion services unit where my treatments were being done had always been hostile to the treatments, considering them a waste of time and that all of my so-called improvements were placebo effect. He convinced my physicians to stop the treatments to see what would happen. The results were very significant. About six months after my treatments were suspended, my heartburn symptoms started to return for the first time in years. This gave my main physicians enough "ammunition" to justify putting me back on the treatments. As before, it took about one year of treatments for the reflux to get under full control again. While this forced vacation from the treatments was not to my liking, it actually had a major impact on how my physicians viewed the effectiveness of the treatments.

[Technical digression... In addition to being a computer expert, I am trained as a research clinical psychologist. During my research training we learned how to correctly design research experiments. Obviously a single case study is never any more than suggestive that a treatment may be effective in the general population. However, there is a single subject research design that can be used to establish that any effects seen after a treatment is initiated is likely to be from the treatment and not just coincidence. Basically, if you take a baseline measure of a condition, add a treatment and get a change in that measure, then remove the treatment and see a return to the baseline level, and then re-introduce the treatment and get the same change in the measure, there is a very significant likelihood that the treatment caused the change. This is called an ABAB Reversal design and is well established as a valid research technique in single-subject research design. And this is exactly what happened when my treatments were removed and then reintroduced.]

Evidence for Effectiveness of Treatments - Part 2

In 2003, things were continuing to go extremely well. I had no residual symptoms other than very mild Raynaud's and slight reflux completely controlled by low doses of Prilosec (see note below). So I decided to see if I could cut back the frequency of treatments a bit. I had historically followed a treatment cycle of one one treatment per week for four weeks, followed by a lay off alternating between eight and nine weeks, so as to average a two-month gap between treatment rounds. I decided to gradually increase the interval between treatment rounds. I started by doing two treatment rounds with a nine-week gap with no problems. This was followed by two treatment rounds with a 10-week gap. This also seemed to go well so I increased the gap again, to 11 weeks. However, this time my heartburn symptoms began to re-occur again. I immediately went back to the original treatment cycle, and after two treatment cycles with an eight-week gap, my heartburn symptoms again disappeared. Since then I have stayed at the original two-month treatment gap with no other problems.

On important side note on proton pump inhibitors (PPIs) such as Prilosec (omeprazole): although I had no heartburn symptoms with fairly low doses of Prilosec, whenever I stopped the medicine I started to have heartburn symptoms again. I assumed that there was still some residual weakening of the lower esophageal sphincter even with the continued plasmapheresis treatments. However, it turns out that was not the case at all. My wife, who is a physician, developed an ulcer and had to go on Prilosec as well. As it is now known that most cases of ulcers are caused by an H. Pylori infection and that appropriate antibiotic treatments can completely cure the underlying cause of the ulcers, she received a course of treatments that completely cured her ulcers. However, she was also unable to stop Prilosec without her heartburn symptoms returning! She did some research and discovered that medicines such as Prilosec actually create their own need! Apparently, if you put healthy volunteers with no heartburn symptoms on Prilosec and then stop it, the participants in the study actually develop rebound heartburn symptoms! Armed with this knowledge, we both decided to taper off Prilosec VERY slowly over a three-month period back in 2006. This worked

and neither of us have ever needed to go back on Prilosec again. I am completely free of any heartburn problems with no medications. It is very likely that I could have stopped the Prilosec back in 1996 had I known this.

The Present Day...

As I edit this article (December 2017), I am now 70 and in excellent health with the only remaining scleroderma-related symptom being very mild Raynaud's (which is saying something because I live in Madison, WI and deal with very cold winters)! According to my internist, I am the healthiest patient in my age bracket in his entire practice, in spite of the fact that I still have a formal diagnosis of limited systemic scleroderma. I am very active (I play tennis every day and also work out on my elliptical every day as well). Medicare continues to pay for my medical treatments without any problems and the current plan is to stay on a treatment frequency of 16 treatments per year indefinitely, or until a more effective treatment becomes available. To date, I have had more than 380 TPE treatments with very few issues or problems. The only exception was one incident that arose from defective tubing that led to some blood loss that was easily dealt with. This is now a routine procedure that I go through 16 times a year. I consider this a very small price to pay for being in excellent health more than 32 years after first developing symptoms of limited systemic scleroderma.

The Rest of My Story

The Scleroderma Education Project

In 1995, as the Internet was in its infancy, I searched and discovered that there was essentially no information available online for scleroderma patients that could be readily understood by someone without a medical background. I was able to obtain an update to the Medline CD ROM library that I had originally received in 1993, reviewed all new scleroderma-related studies since 1993, and wrote and published online the first edition of a patient education document on scleroderma titled the *Scleroderma FAQ*. It won two patient education awards and was translated into Spanish over the next few years. The last major update to the *Scleroderma FAQ* was done in 2009 since good patient education information was finally becoming available from a number of sources including the Scleroderma Foundation, the Mayo Clinic, and Johns Hopkins University.

In October 2013, I decided to do an update to the *Scleroderma FAQ* as a prequel to updating the Wikipedia article on scleroderma. After reviewing the major scleroderma educational websites, I realized that there was a huge amount of important information that was not being included on any existing website. A lot of this information was fairly technical but also important for people that wanted to learn as much about the disease as possible in order to work more effectively with their doctors. I decided to completely rewrite the *Scleroderma FAQ* in order to try to produce a comprehensive document that would bridge the gap between technical and medical jargon found in research papers by explaining everything in a way that patients without a medical background could understand.

The first draft of the completely rewritten *Scleroderma FAQ* was completed in late 2013 after about 200 hours of research and writing. This initial draft of the updated *FAQ* was 34 pages long (the existing version was about eight pages long). Over the next seven months the *FAQ* went through many revisions based on excellent feedback from the Scleroderma Foundation and several physicians, including one well-respected scleroderma expert/researcher.

In April 2014 I researched and wrote a companion document to the *FAQ* titled the *Guide for New and Future Patients*. I also realized at this point that in addition to these initial two documents, there were a number of other articles that I wanted to write, including additional patient education documents but also a series of Technical Articles that would cover certain topics in more detail and include selective research citations. Some of these technical articles would be targeted at physicians and researchers in addition to more sophisticated patients. As a result, in May 2014, I made the decision to launch a complete new website called the Scleroderma Education Project which would house all of these documents. The new website, located at SclerodermaInfo.org, was launched in July 2014.

The Scleroderma Education Project website is *not* meant to replace or compete with excellent websites provided by the Scleroderma Foundation, the Mayo Clinic, Johns Hopkins, etc. It provides additional and more detailed information about a variety of topics that are usually not covered on these websites, for example, detailed discussions on ANA and antibody testing, information on the new 2013 Guidelines for scleroderma diagnosis, etc., always written at a level that people without medical training can understand. My belief is that educated patients are better able to work with their team of physicians to make the best possible decisions about their own health care.

In March 2018, we launched a completely updated website. In addition to a much cleaner and more usable design, we added a section for clinicians who are not trained in systemic sclerosis and also a new section that is focused on research. More on that in a bit...

Note: The Scleroderma Education Project Ltd is a 501(c)(3) tax exempt organization. This means that any donations are now tax deductible in the US.

Scleroderma Patient Advocate

Once the original version of the Scleroderma *FAQ* was published online in 1996, I almost immediately began to receive occasional emails with follow-up questions about scleroderma from patients around the world (my email address was included in the *FAQ*). For the most part, these types of queries were limited to a few times a month prior to the launch of the new website.

After the new Scleroderma Education Project website was launched in July 2014, I joined and became a very active member of about 12 scleroderma-related patient support groups on Facebook as well as the Inspire group run by the Scleroderma Foundation. As a result, over the last year and a half my patient support activities have increased significantly and I now spend at least a couple of hours each day working with patients both through support forums as well as on an individual basis. I always make sure that patients know that I am not a physician and cannot offer medical advice. However, I am often able to provide information to scleroderma patients that can be useful in helping them to work more effectively with their team of physicians in getting quickly and accurately diagnosed as well as to make better, more informed decisions on their own individual health care.

Scleroderma Researcher

In early 1993, after reviewing all of the research literature on scleroderma that I could find, I developed a new hypothesis that scleroderma symptoms may develop beginning with damage to the vascular system that is a direct consequence of red blood cells being abnormally clumped together (hyperaggregation). If this hypothesis is correct (and it can easily be tested by research), then ANY treatment that can break apart the clumped red blood cells and keep them disaggregated should prevent any future symptom development and allow the body to partially or fully heal over

time, to the extent that this is possible. Obviously, if started late in the disease process, complete reversal of damage will not be possible. TPE treatments have been shown in a number of research studies to be effective in disaggregating red blood cells and returning overall blood viscosity to normal levels in scleroderma patients. There are also several drugs that may have potential as well, but have not yet been tested as a treatment for scleroderma. The Research section of the new Scleroderma Education Project website includes detailed discussions on both TPE and the research on abnormal blood rheology that is well documented in systemic scleroderma.

I am now working with a group of researchers on a series of research papers and grant proposals designed to test out this potential new disease model and treatment approach. The first research paper, a report on my own very long term (22 year) experience as a scleroderma patient receiving regular plasmapheresis treatments, was presented as a poster at a medical conference in October 2015 (I did the presentation) and the abstract is published in the September 2015 special issue of the research journal *Transfusion*. The full case report titled "Successful Long-Term (22 Year) Treatment of Limited Scleroderma Using Therapeutic Plasma Exchange: Is Blood Rheology the Key?" is published in the research journal *Clinical Hemorheology and Microcirculation*. The manuscript version of this case report can be freely downloaded here: <http://www.sclerodermainfo.org/pdf/CHM-Case-Report-Manuscript-US.pdf>.

I presented a second poster – a review of the published research literature on the use of therapeutic plasma exchange as a treatment for systemic scleroderma - at the American Society for Apheresis 2016 annual conference in May 2016. The abstract of this poster is published in the *Journal of Clinical Apheresis*. In November 2016, I presented a follow-up research poster titled "Therapeutic Plasma Exchange for the Treatment of Raynaud's and Digital Ulcers in Systemic Sclerosis: A Systematic Review" at the American College of Rheumatology meeting in Washington, DC. The abstract of that presentation is published in *Arthritis and Rheumatology*. The information in the two research posters was combined into a single paper titled "Therapeutic that was recently published in the *Journal of Scleroderma and Related Disorders*. This review, titled "Therapeutic Plasma Exchange for the Treatment of Systemic Sclerosis: A Comprehensive Review and Analysis" is published Open Access and be freely downloaded from the publisher's website: <http://journals.sagepub.com/doi/abs/10.1177/2397198318758606>.

The next paper in the series, tentatively titled "Scleroderma Blood Rheology: Implications for Treatment and Research", will be an expanded version of the blood rheology article in the Research section of the Scleroderma Education Project website. It will examine all the research that discusses abnormal blood rheology in scleroderma patients, including red blood cell hyperaggregation, and look at how this might lead to the development of scleroderma symptoms as well as exploring potential options for new treatments if this disease model is proven to be correct by suitable research. This will be submitted for publication in 2018.

As a non-physician, it has been a major challenge for me to get accepted as someone who may be able to help to advance scleroderma education and research. I am now fortunate enough to be working closely with a team of researchers who believe in the disease model that I originally proposed back in 1993. Because of the work that I have been doing over the past few years, I recently received a formal appointment as an Honorary Associate (fellowship) in the Dept. of Medicine, Division of Rheumatology at the University of Wisconsin in Madison. This new appointment has made it much easier for me to connect with scleroderma researchers around the world and may lead to collaborations on scleroderma research projects in the future.

The bottom line is this: if my proposed disease models turns out to be wrong, then worst case, some research money will have been wasted (which happens all the time). However, if it turns out to be correct, it may quickly lead to new treatment approaches for systemic scleroderma that are likely to be more effective and less toxic than current, largely ineffective, treatment approaches that are heavily focused on using immunosuppression.

About Me

A few years ago, I “retired” from a long career as a computer software developer (since 1964) and successful serial entrepreneur. I am also trained as a research clinical psychologist. I am married to a physician (which has been critical in my journey from patient to researcher). I am a skilled amateur musician (clarinet and bassoon) and play in a local community orchestra. My main hobbies are tennis (I play at least once a day), cooking, and, most important, eating high quality Belgian chocolate every day.

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