

# VENOUS Review

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## The Microscopic Correlates of the Skin Changes of Venous Insufficiency

By Robert C. Kiser, DO, MSPH

Venous insufficiency is associated with progressive skin changes including hyperpigmentation, collagen hyperplasia (atrophe blanche and lipodermatosclerosis) and skin ulceration. This is common knowledge. This article hopes to provide a survey of what is known about the microscopic changes that cause these macroscopic, visible changes. Several theories have been advanced to explain the skin changes seen in venous insufficiency, and a brief historical overview of these theories is instructive to understand how many of the currently accepted beliefs about venous insufficiency have come into being -- and how some of these have persisted despite little or contrary evidence, and what recent research shows us. Much of this section comes from the excellent and more comprehensive article by Gschwandtner and Ehringer in *Vascular Medicine* 2001.<sup>1</sup>

### The Mechanistic View: Hypertension and Hypoxia

An early scientific hypothesis of venous insufficiency was propounded by the eminent John Homans in 1917 surmising that venous hypertension leads to capillary stasis, resulting in local tissue hypoxia and cell death. This has intuitive appeal and is at least in part correct, in that venous insufficiency does cause venous hypertension. One can still hear the mechanistic-hypoxia hypothesis oft-repeated by clinicians today, as it is a quick and intuitive way of explaining how venous insufficiency results in skin changes. The hypoxia portion of this hypothesis was largely disproven by Blalock in 1929 when higher rather than lower oxygen levels were found in varicose veins as compared to healthy, matched contralateral veins.<sup>1</sup> Although arteriovenous shunts



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# Top 10 Myths Regarding "Vein Disease"



By Sean K. Stewart, MS, MD

Despite the fact that venous insufficiency affects 30 million Americans, many misconceptions still exist. Here are 10 common myths you might hear in your own practice:



**1** **"Vein treatments are for cosmetic concerns only."**  
Often thought of as a cosmetic nuisance, varicose veins represent underlying venous disease that can lead to chronic pain, swelling and skin ulcerations.

**2** **"My parents and grandparents suffered, so it's my fate to suffer also."**  
Vein diseases and varicosities can be hereditary, but varicose veins are very common - up to 50% of Americans will develop venous insufficiency or varicose veins in their lifetime. Nowadays, office-based, minimally invasive, safe and effective treatments are readily available.

**3** **"Insurance does not cover vein treatment."**  
Because varicose veins and chronic venous disease can lead to more serious and expensive medical conditions, most insurance plans will cover treatment.

**4** **"Spider veins are benign."**  
They can be an indicator that there is underlying venous disease. Many times the changes you see on the surface are just the "tip of the iceberg," and a more thorough evaluation should be completed to determine the extent of the disease.

**5** **"You need a vascular surgeon to treat vein disease."**  
Vein stripping is now considered an outdated option for treatment of chronic venous disease. Current treatment involves minimally invasive, ultrasound-guided, catheter-based procedures. A working knowledge of bedside sonography and ultrasound-guided venous access skills are paramount.

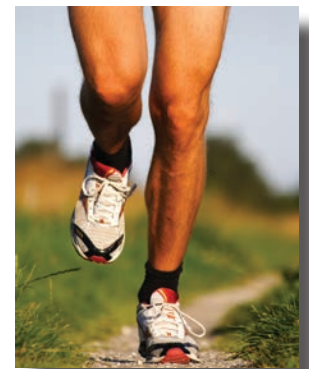
**6** **"Compression stockings cure vein disease."**  
Although compression stockings that provide graduated compression from the ankle up to the knee or thigh help to reduce pain and swelling, they only help to manage symptoms and do not provide a cure.

**7** **"Women should wait until after child-bearing years before seeking treatment."**  
With treatments being 98% successful, the new paradigm ought to be that obstetric physicians send their patients for venous insufficiency evaluation prior to their getting pregnant. This would prevent them from having the pain and discomfort so often associated with varicose veins during pregnancy.

**8** **"Men do not get varicose veins."**  
It is reported that 42% of men will suffer with CVI by the time they reach their 60s. Though men are less likely to seek varicose vein treatment, they are at risk for more severe venous diseases if they ignore the symptoms.

**9** **"Ulcers only need wound care."**  
Venous skin ulcers are slow to heal and often come back if you don't take steps to prevent them. Treating the underlying vein disease has proven to increase ulcer healing rates and decrease recurrence rates.

**10** **"Varicose veins always reoccur."**  
The recurrence of varicose veins after treatment is a myth born from prior inadequate care. Treatment methods in the past, while done with best intentions, actually caused recurrence of varicose veins. Once veins are successfully treated by a qualified physician, the recurrence rates should be below 5%.



# The Microscopic Correlates of the Skin Changes of Venous Insufficiency

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have been proposed as both causes of cellular changes and the increased oxygen tension in varicose tributaries, such microshunts have not been found under experimental conditions.<sup>2</sup> Nevertheless, Homans was correct in identifying venous hypertension transmitted through the refluxing veins to the capillary level as an essential hemodynamic aberration that begins the changes leading to integumentary pathology.

## Fibrin Cuff Hypothesis

Due to several factors, the capillaries that receive venous reflux exhibit altered morphology and function. The morphological changes include enlarged interendothelial pores, which allow for increased permeability to various molecules, including fibrin. It has been hypothesized that these pericapillary fibrin cuffs prevent diffusion of nutrients and oxygen across the capillary. However it is unclear to what extent or whether the fibrin cuff creates a significant barrier to diffusion of nutrients and oxygen across the capillary.<sup>3</sup>

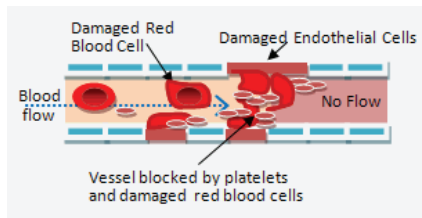
## Leukocyte Trapping, Activation and Inflammation Hypothesis

Philip Coleridge Smith, et al., have suggested, based on experimental observations of a relative "loss" of white blood cells in dependent legs with venous insufficiency, that leukocytes become trapped within capillaries via adhesion of the white cells to capillary endothelium. Such "sludged" leukocytes then are hypothesized to create a mechanical barrier to diffusion as well as expressing chemotactic factors that cause further leukocyte migration. When white blood cells are degranulated they release inflammatory mediators, proteolytic enzymes, and free radicals that result in destruction of endothelial cells. Damaged endothelium, in turn, causes increased permeability to larger molecules such as proteins and fibrin, migration of leukocytes, which then leads to a vicious circle of increased inflammation and tissue damage.<sup>3</sup> Of the various types of leukocytes, polymorphonuclear (PMNs) in particular are known to secrete proteinases such as matrix metalloproteinases (MMPs). MMPs degrade the extracellular matrix and growth factors that help to heal wounds. The net effect of leukocyte trapping and activation, therefore, is to both cause damage to existing microvascular structures and to retard the organized healing of these structures. The normalization of these processes is a postulated means by which some bioflavonoid fractions are able to help enhance wound healing.<sup>4</sup> Conversely, supplementation of platelet-derived growth factor has been shown to reduce MMP activity and is used to improve wound healing.<sup>5</sup>

## Capillary Thrombosis and Lymphatic Derangement

Bollinger used fluorescence videomicroscopy to look at capillaries downstream from venous reflux and found thrombosis preventing influx of dye within some capillaries.<sup>6</sup> Such localized small vessel thrombosis could support Coleridge-Smith's hypothesis and certainly suggests a pathway that includes endothelial disruption as well as inflammation and stasis. Laser Doppler perfusion imaging and capillary microscopy has been particularly useful in demonstrating perfusion during venous-insufficiency-associated ulcer healing. Using the two techniques together can distinguish nutritive

perfusion and subpapillary perfusion, and can demonstrate capillary density and flow in these areas. In particular, poor perfusion in the subpapillary level is associated with poorer granulation, and indeed in areas of high collagen density (scars) we see poor subpapillary perfusion with reduced but just adequate nutritive perfusion in comparison with skin or granulation tissue.<sup>7</sup> Areas in which capillary density and subpapillary perfusion is inadequate for robust granulation will instead form high-collagen scar tissue, thus prematurely ending the healing process.



Bollinger has also used fluorescein to visualize lymphatic channels in lower extremities with venous

insufficiency and has found that in the gaiter region the lymphatic channels become hyperpermeable, refluxive from deeper to superficial channels, and that portions of the lymphatic network can be completely obliterated.<sup>8</sup> Although lymphatic derangement is generally considered a consequence, rather than a cause of venous insufficiency, the causal sequence has not yet been absolutely clarified experimentally. As the lymphatic system provides a parallel means of transporting fluids and leukocytes, the derangement of lymphatic channels seems likely to produce a further worsening of skin integrity which continues a vicious circle as damage to surrounding structures increases.

## Summary

The microscopic changes associated with the skin changes in venous insufficiency are numerous and consist of complex interactions between anatomical tissue (skin, blood, capillaries, lymphatic vessels), physics (flow rate, gravity, pressure), and molecules (fibrin, MMPs, growth factors, free radicals, O<sub>2</sub>). The cascade of events that result from venous insufficiency worsen skin integrity, and on a macroscopic level tissue destruction is favored over tissue healing and scarring is favored over healthy skin tissue regeneration. The process continues down hill until intervention is made. Useful interventions include compression, including "complex decongestive therapy" and surgical ablation of refluxing veins (to address fluid dynamics, hypertension and stasis), nutraceuticals and pharmaceuticals to address inflammatory mediators, free-radicals, and reduce early degradation of growth factors. One goal of every consultation with a specialist in venous and lymphatic medicine is to improve skin integrity by a nuanced, multimodal, and frequently multidisciplinary approach to correcting the underlying abnormalities in the patient's venous and lymphatic return systems at each affected level.



Example of Fibrin Cuff

### Footnote:

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4. Serra, R., et al., Effects of a new nutraceutical substance on clinical and molecular parameters in patients with chronic venous ulceration. *Int Wound J*, 2014.
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7. Ambrozy, E., et al., Microcirculation in mixed arterial/venous ulcers and the surrounding skin: clinical study using a laser Doppler perfusion imager and capillary microscopy. *Wound Repair Regen*, 2009. 17(1): p. 19-24.
8. Bollinger, A., et al., Fluorescence microlymphography in chronic venous incompetence. *Int Angiol*, 1989. 8(4 Suppl): p. 23-6.

CVR is one of the few vein practices that have a multimodality approach to treating complex venous conditions. We routinely use radiofrequency ablation, laser ablation, and ultrasound-guided foam sclerotherapy. These procedures, as well as extensive microphlebotomies which result in minimal or no scarring, are all performed on an outpatient, ambulatory basis in our specially equipped offices.

CVR also has an active internal and external peer review process to assure appropriate, state of the art, treatment is performed.

- 1 Venous insufficiency is a serious health issue consuming 1-3% of the health care budget in industrialized countries.
- 2 Venous disease has common symptoms and reduces the quality of life. Restless legs, swelling, heaviness, tingling, itching, pain, visible varicosities, telangiectasias, discoloration, and thickening of the skin may all be symptoms of super filial venous insufficiency

# 5

## Things We Should Have Learned In Medical School But Didn't

- 3 Venous disease may impair mobility and is associated with depression and social isolation.
- 4 Most vascular labs will NOT evaluate a patient for superficial venous disease unless a specific request is made. Because of this the majority of patients will not be correctly and promptly diagnosed.
- 5 Early identification and treatment has the potential to REDUCE overall medical costs, reduce the incidence of ulceration and improve a patient's well being

By Henry Meilman, MD

- 1 Reevaluate patients with leg complaints who have had "negative" evaluations for DVT and arterial occlusive disease by sending them for a consultation at CVR. A careful evaluation for venous insufficiency will be performed by a specially trained sonographer.
- 2 Refer any patient who as an active or healed venous ulcer for a complete evaluation and consultation.

# 5

## Things You Can Do To Improve Patient Outcomes And Satisfaction

- 3 Refer any patient with "chronic venous stasis changes" of the legs.
- 4 Refer any patient with restless legs, nocturnal cramping, leg heaviness or unexplained edema.
- 5 Refer patients who have had incomplete symptom relief or recurrent symptoms following prior venous surgery or ablations.

*For further reading and source material for some of the above: Bergan et al, New England Journal of Medicine, 355;5, August 3, 2006; Varicose Veins in the legs, National Institute for Health and Care Excellence, July 2013.*

## CME Courses & Events

Have you attended one of our CME events? Our CMEs on venous insufficiency are conducted by Center for Vein Restoration physicians and staff. When you first join us you'll notice a difference from other

sessions you may have attended. First, we respect your busy schedules, so we tend to hold our CMEs in the evenings. We start with a nice dinner and networking and follow that with

information on the diagnosis and treatment of patients with venous insufficiency. We discuss classification of VI, the use of duplex ultrasound to screen patients, the use of modern ablation techniques like radiofrequency and laser, visual sclerotherapy and more as part of a full spectrum of care available to your patients.

Our attendees give us high marks for their experience – in fact, our recent event in Tysons Corner, Va. hosted by our Virginia staff, was one of our best-ever attended, with 74 physicians. It was a rewarding, interactive event, with many questions from the audience for our panel of seven presenting CVR physicians.

Each CME course is valued at 3.0 credits. We look forward to seeing you or a colleague at one of these events soon.

*For more information, please contact Matt McMahon, Regional Sales Director [matt.mcmahon@centerforvein.com, (312) 498-1565.]*



# Q & A

In each issue of the *Venous Review*, members of our medical team answer questions we've received from referring physicians.

This issue's guest Q & A Editors are



*Michelle Nguyen, MD*



*Anuj Shah, MD*



*Gautam Shrikhande, MD*



*Theresa Soto, MD*



**Q:** *Do you do full Doppler ultrasound at your facility? Are they available at all your locations?*

**A:** At our Center for Vein Restoration facilities, full Doppler ultrasounds are performed. Our expert vascular technicians perform a detailed and thorough ultrasound examination. Initially, the deep veins of the lower extremities are examined for evidence of any deep venous thrombosis (DVT). These include the common femoral vein, femoral vein, popliteal vein, and posterior tibial veins. Additional scanning is also performed to assess for other deep veins if present. All of the above veins are measured with Doppler flow to assess for any venous insufficiency. The vascular technician will then evaluate the superficial lower leg veins for any evidence of venous reflux. These include the sapheno-femoral junction (SFJ), the great saphenous vein, the sapheno-popliteal junction (SPJ), the small saphenous vein, accessory veins, perforator veins, and tributary veins. All of our locations can perform full Doppler ultrasounds, in addition to free limited venous scans.

**Q:** *My patient is normally on her feet a lot at work. How long would she have to be off work following a vein procedure?*

**A:** After we perform our procedures, we prefer that our patients walk as much as possible. Our recommendation is to walk for 1-2 miles after a procedure. We do not give our patients any intravenous medication or sedation, and therefore after a brief period in a recliner, patients are able to walk out of the office and drive themselves home or to work. As a matter of fact, many of our patients, including teachers and nurses, have their procedures early in the morning and go straight to their routine lives and occupations.

**Q:** *Why do my older patients seem to be more susceptible to varicose veins?*

**A:** We are all victims of the ravages of aging. Our life exposures/experiences place us at risk for varicose veins: long periods of standing or sitting over years of employment add up, pregnancy and perimenopause related hormonal, weight and volume changes are cumulative with regards to the venous system. As one ages, medical problems emerge (i.e. COPD, CHF), medications are taken, surgeries/extremity trauma happen, and DVT may occur. All of the changes in our body over the course of our lives impact our

circulation. With time and insult, veins can lose elasticity, valves become faulty and venous insufficiency with chronic venous hypertension occurs. With extended periods of exposure to the elevated pressures, veins will dilate to become visible varicosities.

**Q:** *How much does insurance cover for most procedures?*

**A:** A concern for many patients is the cost of venous ablation procedures. Fortunately, insurance companies realize that treating venous insufficiency is a medical necessity for improving our patients' quality of life. As a result, most major carriers will provide coverage for our procedures. Our staff is also very knowledgeable about the different requirements that the insurance companies mandate and are able to inform our patients at their visit regarding coverage. CVR will perform all the necessary pre-certification. In addition, we offer payment plans for those patients who



are self-pay or have large deductibles. At CVR, we understand the importance of treating venous insufficiency and will do all we can to help provide this service to our patients.

# Connecting with the Community in New York



More than 30 million Americans are affected by venous insufficiency, the often undiagnosed condition behind varicose veins and spider veins. But, many patients suffer needlessly because they don't know the basics about their condition, how it's diagnosed, or which options they have for treatment. That's why we're committed at Center for Vein Restoration to a range of programs to help everyday people understand vein health and how they can look better, feel better and live better. Among our commitments is going into local communities to give presentations and free screenings at health fairs, senior centers and more. We did just that recently with a pair of events in New York:

First, we participated in the Member Appreciation Day at the The Westport Weston Family Y in Westport. The Y's mission is to develop youth, promote healthy living and foster social responsibility, so this event provided a great platform for CVR to help create awareness around vein disease. Our CVR representatives, Jessica Ronco, RVS and Julianne DeSimone, Community Outreach Coordinator from

the Center for Vein clinic in Stamford, CT provided free vascular ultrasound demos and discussed vein health with Y's members.

Second, we exhibited at the Awaken Wellness Fair in Tarrytown. The fair, one of six in the northeast, was a combination of presentations, demonstrations, on-site treatments and exhibits designed to help people find alternative ideas and methods for healthy living – ranging from ancient and alternative wellness practices to the most modern health technologies.

Center for Vein Restoration discussed vein screening and vein health with participants – messages that were well received in a venue where many attendees simply were looking to be enlightened in various ways, whether through mind, body, and/or soul. The CVR team included Chaunita Orellana, Practice Administrator and Julianne DeSimone, both representing our CVR/Scarsdale clinic, also felt enlightened and healed after being a vendor at this event – some of whom even making holistic appointments after attending.

We continue to be proud of our community outreach efforts and look forward to more opportunities to interact with local patients and educate them on the basics of vein health.

## New Clinic: Hackensack, NJ

Center for Vein Restoration is proud to announce the opening of our newest clinic in Hackensack, New Jersey. The clinic is now open and taking referrals.

The Hackensack clinic is located at 211 Essex Street Suite 403, and can be contacted at 1-855-840-8346. As with all our locations, the Hackensack clinic is under the supervision of our senior medical team: Sanjiv Lakhnopal, MD, CVR President and CEO; and Khan Nguyen, DO, CVR corporate medical officer.



Our New Jersey medical team leader is Shubha Varma, M.D.. Dr. Varma has been chief of vascular surgery at Palisades Medical Center in New Jersey for the past 10 years. Formerly Dr. Varma was Assistant Professor, Department of Surgery at Columbia University in New York, and was a Clinical Instructor at the New Jersey Medical School in Newark. She attended Maulana Azad Medical College at the University of Delhi, and served a general

surgery residency at the New York Hospital in Queens; she did a vascular fellowship at the University of Medicine and Dentistry of New Jersey.

We look forward to serving patients in Hackensack!





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## VENOUS Review

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In your practice, like ours, you're likely to hear "old wives tales" about health conditions. Some beliefs may have a basis in fact, while the source of others, even if widely held, can be a mystery. Regardless, medical myths often find their way into common discourse with patients and the same goes with venous insufficiency. In this issue of Venous Review we tackle 10 of these myths, things you might already have heard in your own practice, to set the record straight.

Additionally, we also take a look at a different side of venous insufficiency, examining the microscopic correlates of VI-related skin changes as well as an historical look at the origin of several skin-change theories.

Meanwhile, we're happy to report that our community outreach continues; in this edition we highlight our recent appearances at community health and wellness events in Westport and Tarrytown, New York. We've also scheduled more of our popular CME courses, taught by our own physicians and staff, over the summer.

And, as always our physicians respond to your questions about all aspects of venous care in our Q&A section.

We hope this information is useful to you and your practice. We look forward to discussing vein health further with you and your patients soon.

Yours in good health,

Robert C. Kiser, DO, MSPH

Editor