CREST (calcinosis, Raynaud’s phenomenon, esophageal dysmotility, sclerodactyly, and telangiectasia) syndrome is a member of the heterogeneous group of scleroderma, and its name is an acronym for the cardinal clinical features of the syndrome. In 1910, Thibierge and Weissenbach described the first case report of what was later called CRST (calcinosis cutis, Raynaud’s phenomenon, sclerodactyly, and telangiectasia) syndrome in English by Winterbauer who, in 1964, described a series of 8 patients with the features that make up the abbreviation CRST [1,2]. Although he noted esophageal dysmotility in 4 of 8 patients, he did not include this feature in his original description of CRST syndrome. Frayha et al. [3] noted the frequent occurrence of esophageal dysmotility and suggested that the acronym CREST may be more appropriate. Velayos et al [4] reviewed 13 patients with CREST and CRST syndromes and found the syndromes equivalent.

The 1980 American College of Rheumatology Classification Criteria for Rheumatic Diseases is the most widely used system for systemic scleroderma. Because it was designed for research applications and not for clinical diagnosis, it has been criticized for its low sensitivity in identifying early disease and milder forms of systemic scleroderma such as CREST syndrome. Several authors recognized this limitation and responded by categorizing patients with scleroderma syndromes into 2 groups: those with diffuse cutaneous scleroderma and those with a limited form of scleroderma [5-7].

Others have shown that visceral involvement, poorer prognosis, and higher mortality are all more common in patients with diffuse disease [8-11]. Several new classification systems may better categorize the wide spectrum of systemic scleroderma.

In 2004, Nadashkevich et al [12] proposed the classification criteria:
1. Autoantibodies to centromere proteins, Scl-70 (topo I) and fibrillarin
2. Bibasilar pulmonary fibrosis
3. Contractures of the digital joints or the prayer sign
4. Dermal thickening proximal to the wrists
5. Calcinosus cutis
6. Raynaud’s phenomenon (at least a 2-phase color change)
7. Esophageal distal hypomotility or reflux esophagitis
8. Sclerodactyly or non-pitting digital edema
9. Telangiectasias

These can be remembered by the acronym ABCD CREST. Fulfilling 3 or more criteria indicates definite systemic scleroderma with a sensitivity and specificity as high as 99% and 100%, respectively.
Also in 2004, Maricq and Valter [13] had a complex but potentially very useful proposal for classifying the scleroderma spectrum disorders; however, in 2005, Wollheim [14] reported that without substantial independent confirmatory work, this classification system may not gain widespread acceptance in its present form. Maricq and Valter’s [13] proposed classification for scleroderma spectrum disease is as follows:

Type I – Diffuse skin involvement proximal to elbows/knees, including the trunk

Type II – Intermediate skin involvement proximal to the metacarpal phalangeal/metatarsal phalangeal joints, distal to the elbows/knees; trunk not involved

Type III – Digital sclerodactyly only (meets American College of Rheumatology minor criteria but excludes those without skin involvement)

Type IV – Scleroderma sine scleroderma (capillary pattern or pitting scars and visceral involvement; no anticentromere antibodies; no telangiectasia)

Type V – Undifferentiated connective-tissue disease with 2 of 3 of the following scleroderma features: sclerodactyly, pitting scars, or scleroderma capillary pattern; or one of these features along with one of the following: Raynaud’s phenomenon, pulmonary fibrosis, or visceral involvement (esophagus, heart, kidney); but do not meet the criteria for groups III and IV; no anticentromere antibodies; no telangiectasia

Type VI – CREST; no skin involvement, or sclerodactyly only; telangiectasia is required with one or more other acronym-satisfying criterion; or anticentromere antibodies with any 2 or more acronyms.

Telangiectasias in CREST and scleroderma

Telangiectasias are defined as visibly dilated capillaries or venules seen in the skin or mucosa. Multiple telangiectasias are particularly common in the systemic autoimmune disorder systemic sclerosis (scleroderma) where they are most commonly observed on the face and hands [15]. Their number and size tend to increase with disease duration and their occurrence is strongly correlated with the presence of the anticentromere antibody which is a frequent finding in the more benign limited variant of scleroderma (also including the CREST subtype) [16]. This limited variant is the most common form of scleroderma seen in Caucasian populations. Telangiectasia, however, are not specific for scleroderma as they are also found in other systemic rheumatic disorders, in the familial disorder hereditary hemorrhagic telangiectasia (HHT), in actinic skin damage, and occasionally in health [15].

**Pathophysiology**

Three primary pathologic features are found in scleroderma and include increased collagen deposition, perivascular mononuclear cell infiltration, and vascular abnormalities. Vascular abnormalities are also likely to be an early contributor to the pathogenesis of scleroderma. Pericytes, the smooth muscle–like mural cells of capillaries and venules, synthesize matrix components and fibroblast-activating cytokines; thus, they are potential mediators of pathological changes in scleroderma. Pericyte density is increased in the microvasculature of the peripheral zones of active disease [17]. Clinically, micro vascular changes are apparent in the nail-fold capillaries as larger tufted capillaries and areas of dropout. The vasospastic phenomenon of Raynaud’s is present in most scleroderma patients. Endothelial cell injury and dysfunction, intimal proliferation, thrombocytosis, elevated factor VIII–von Willebrand factor levels, and vasospasm are found in scleroderma patients and result in vascular compromise. Elevated levels of platelet-derived growth factor (PDGF) and increased expression of PDGF type-B receptors are found in the skin of scleroderma patients [18,19]. Ischemia is an important contributor to end organ damage in scleroderma patients. Animal models of scleroderma may help identify abnormalities in human scleroderma. An avian model, the UCD-200 chicken, develops fibrosis of the skin and internal organs and the presence of ANAs.

In general, while the primary trigger for CREST syndrome is not known, a reasonable speculation is that vascular endothelial cell abnormalities incite mononuclear infiltration, and the resulting perturbations in TH1 and/or TH2 cell and cytokine balance result in abnormal fibroblast activity and increased collagen deposition.

**Frequency**

The incidence of systemic sclerosis in the U.S approximates 2.7–19.3 new cases per million adults per year. The prevalence is 253–286 cases per million persons [20]. The highest prevalence has been reported in a Choctaw Native American Group in Oklahoma (660 cases per million, based on 14 cases) [21]. The apparent increase in both incidence and prevalence over the past 50 years is most likely an artifact of better classification, earlier diagnosis, and improved survival. Some serum antibody studies suggest that CREST syndrome may account for 22-25% of all cases of systemic sclerosis; however, epidemiologic studies specifically looking at CREST syndrome are lacking [21–24].

**Race**

Both the prevalence and incidence of systemic sclerosis is higher in blacks than in whites. The prevalence of diffuse disease among black patients is nearly twice that of white patients. Survival for black
patients versus nonblack patients is marginally worse during the first 12 years after diagnosis, but, in general, survival for both groups is comparable [21]. Some Choctaw Native American and Thai populations are more likely to have diffuse disease, while some European and white Australian groups have more limited disease.

**Gender**

Females have a greater incidence of scleroderma than males. This difference appears greater during childbearing years. Mayes et al. [19] reported an overall female-to-male ratio of 4.6:1.

**Age**

The usual age of onset of scleroderma is approximately 30-65 years. Black women tend to present at an earlier age.

**Causes**

The cause of limited scleroderma is yet to be determined. Studies of genetic factors show only rare occasions of multi-case families. HLA associations are present but are not strong. These include HLA-DRB*01, HLADRB*11, HLA-A*30, and HLA-A*32 showing increased susceptibility to scleroderma and HLA-DRB*07, HLA-B*57, and HLA-Cw*14 being protective [20]. The predominance of cases occurring in women after their childbearing years and the similar clinical presentation of scleroderma to graft versus host disease has suggested the importance of fetal/maternal microchimerism in the etiology of scleroderma. Environmental factors also are likely important. Some similarities in clinical presentation occur with L-tryptophan and rapeseed oil exposure. Certain occupations have been linked to an increased risk to systemic sclerosis, including female teachers, female textile workers, and construction workers. Exposure to silica, synthetic adhesives, solvents (including chlorinated solvents, aromatic solvents, white spirit, toluene, trichloroethylene, formaldehyde, vinyl chloride, and cleaning products) have been implicated in a higher risk of developing systemic sclerosis. Interestingly, the use of vibrating tools was also found to increase the risk of systemic sclerosis [25,26].

**Treatment of Telangiectasia**

Patients with CREST/scleroderma are often in a need of psychological interventions designed to target important areas of daily living: pain, depression, and distress about disfigurement. The visible telangiectasia are an important factor in the disfigurement self conception and can be treated by a pulsed-dye laser. Pulsed-dye laser treatment has been shown to be effective for the treatment of facial telangiectasia, but this has not been specifically studied in CREST patients, until now [27]. Laser treatment of cutaneous vascular lesions has progressed significantly over the past 20 years. Based on the pioneering work of Anderson and Parrish in the early 1980s [28], several vascular-specific laser systems have been developed using principles of selective photothermolysis. Laser irradiation can selectively destroy specific targets (chromophores) within the skin by using an appropriate wavelength and pulse duration. Pulse duration must be less than or equal to the targeted thermal relaxation time of the chromophore, i.e., the time necessary for the target to cool by half of its peak temperature after laser irradiation. Because the energy deposited in the tissue is limited to targeted sites, significant thermal diffusion to adjacent skin is prevented. In addition, because wavelengths corresponding to absorption peaks for various skin chromophores are known, absorption of laser energy can be localized without damaging neighboring structures. The targeted chromophore for vascular lesions is intravascular oxyhemoglobin; thus, thermal damage is largely restricted to cutaneous blood vessels [29]. Early laser technology used continuous-wave (CW) mode lasers for treating cutaneous vascular lesions. These lasers did not restrict damage to the targeted vascular structures, and, consequently, their use resulted in a high prevalence of scarring. Pulsed laser systems, such as the 585-nm pulsed dye laser (PDL), the subject of our study, subsequently were developed, and have become the mainstays of therapy for both congenital and acquired vascular lesions [30]. These lasers offer excellent clinical improvement with a low risk of adverse sequelae. Transient purpura is the most common adverse effect of PDL treatment. However, although pulsed dye laser is considered to be the treatment of choice for skin telangiectasia, we have the impression of relatively poor treatment response in patient with CREST/scleroderma.

**References**


