

antibodies.

**Treatment**

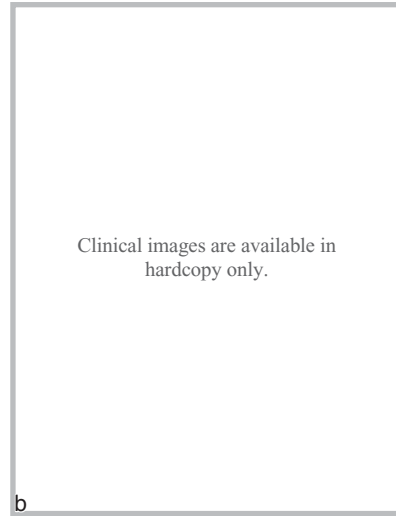
Symptomatic therapies for the eruptions and the systemic symptoms are the main treatments. A pacemaker may be implanted in patients with cardiac block.

**6. Nodular cutaneous lupus mucinosis** ★

Papules and nodules occur on the back and upper arms. Nodular cutaneous lupus mucinosis is a subtype of cutaneous LE. These lesions are caused by deposition of mucin in large amounts in the dermis, and they often accompany SLE.

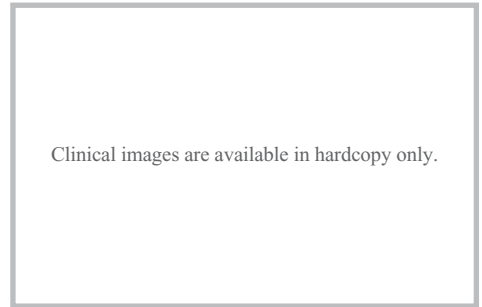
**7. Bullous lupus erythematosus** ★

Bullous lupus erythematosus is a specific subtype of cutaneous LE in which blisters form. Antinuclear antibodies in the serum and autoimmune antibodies against type VII collagen in the basement membranes are thought to cause blistering. Blisters may form on normal skin or on LE erythematous lesions (**Fig. 12.10**).



**Fig. 12.9-2 Annular erythema in neonatal lupus erythematosus.**

b: Two annular erythema on the face.



**Fig. 12.10 Bullous lupus erythematosus.**

Bullous LE in a patient with SLE. Vesicles form not only on the LE erythema but also on the normal looking skin.

## B. Scleroderma

Scleroderma is characterized by sclerosis of the skin that follows a course of edema, sclerosis and atrophy. It is divided into systemic sclerosis (SSc) and localized scleroderma. In SSc various lesions occur in the internal organs, whereas in localized scleroderma the internal organs are not involved.

**1. Systemic sclerosis (SSc)** ★★

Synonym: Progressive systemic sclerosis (PSS)

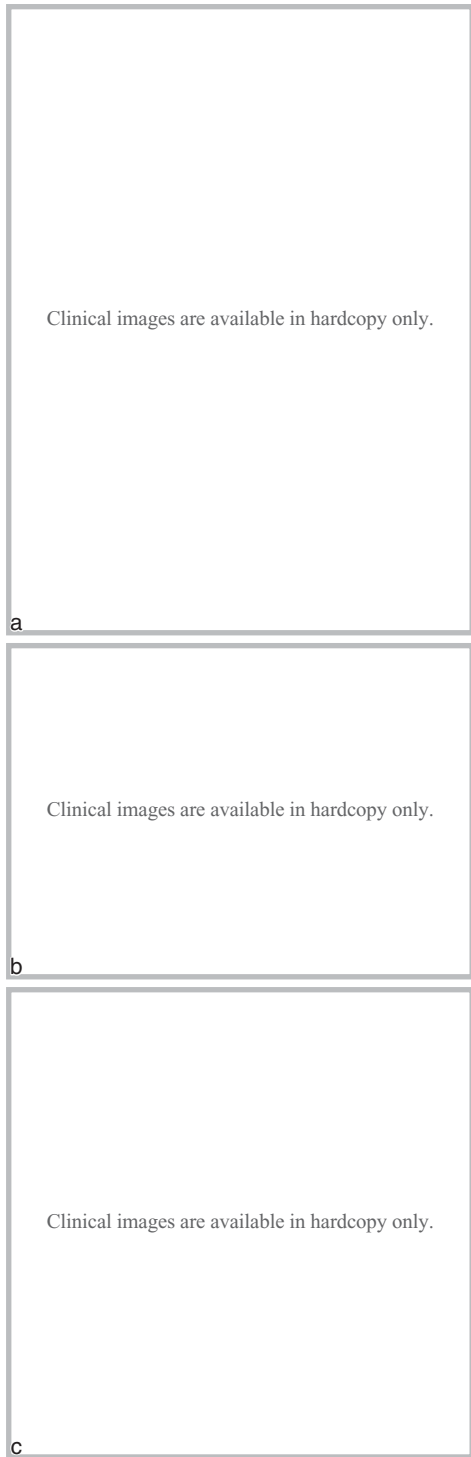
**Outline**

- Generalized cutaneous sclerosis, fibrosis in the synovium and small arteries, and Raynaud’s phenomenon are found.

**Renaming from PSS to SSc**

MEMO

Because progressive systemic sclerosis (PSS) is not necessarily progressive, the disease has come to be called systemic sclerosis (SSc).



- It affects multiple organs, with unknown etiology.
- Anti-Scl-70 antibodies and anti-centromere antibodies may be positive.
- Penicillamines and nonsteroidal anti-inflammatory drugs (NSAIDs) are the main treatments.

**Classification**

There are two classification systems for systemic sclerosis (SSc): Barnett’s, and LeRoy and Medsger’s. Classification is done according to the degree of hardening of the skin. These classifications are used to describe the severity of SSc (**Table 12.5**).

**Clinical features**

SSc frequently occurs in adults aged 30 to 50. The incidence is greater among women, with a ratio of 3 or 4 women to 1 man. The onset is Raynaud’s phenomenon or arthralgia that becomes aggravated in winter. The affected skin gradually hardens, beginning with the peripheral skin. Skin lesions demonstrate characteristic clinical features that differ according to the affected site. The course is usually edema, sclerosis and atrophy.

As SSc progresses, the skin becomes impossible to pinch, resulting in impaired finger extension. When it progresses further, the fingers become pointy or crooked, and swollen like sausages (sausage-like fingers). Small ulcers form on the finger pads from circulatory failure, which results in intractable, concave, worm-eaten scarring (**Fig. 12.11-1**). These symptoms spread from the fingers to the upper arms (proximal scleroderma).

**Table 12.5 Classification of systemic sclerosis (SSc).**

a. Barnett Classification	
Type I	Cutaneous symptoms are Raynaud’s phenomenon and hardening of the fingers.
Type II	Hardening of skin occurs on the extremities and face.
Type III	Hardening of skin spreads to the trunk.
b. Medsger & LeRoy Classification	
Limited cutaneous	Hardening of skin is seen only on areas distal from the elbows, and lesions in internal organs are mild. The prognosis is good. Most cases with anticentromere antibody-positive are classified as this type.
Diffuse cutaneous	Hardening of skin spreads to proximal sites, including the trunk and upper arms. Visceral involvement quickly progresses to conditions such as interstitial lung disease, oliguric renal failure, diffuse gastrointestinal disease, and myocardial involvement. The prognosis is poor in many cases. Cases with anti-DNA topoisomerase I (anti-Scl-70) antibody positive tend to be classified as this type.
c. Other classifications	
CREST syndrome: A subtype of SSc, it is characterized by five symptoms: calcinosis, Raynaud’s phenomenon, esophageal dysfunction, sclerodactylia and telangiectasia. Anti-centromere antibody (ACA) positive is serologically present. This syndrome may be used as a synonym for limited cutaneous SSc.	

**Fig. 12.11-1 Systemic sclerosis.**

a: There is intense sclerosis and impaired movement in the fingers. b: Sclerosis leads to impaired extension in the fingers. c: The ends of the fingers, particularly the index finger, are lost or shortened due to necrosis from blood circulation disorder.

Telangiectasia, pigmentation, depigmentation and calcium deposition are also found.

①SSc in the face (Fig. 12.11-2)

**Mask-like face:** Wrinkles on the face disappear from edematous hardening. The nose becomes characteristically pointy.

**Microstomia:** There is difficulty in opening the mouth, which makes the mouth appear small.

**Miscroglossia, tongue-tie:** The tongue is difficult to stick out.

②SSc in other organs

The main symptoms found in other organs are arthralgia (swelling), decreased esophageal peristaltic motion, dilation of the lower esophagus, lung fibrosis, cardiac symptoms (arrhythmia, conduction disturbance), maldigestion syndrome, renal symptoms (manifesting as malignant hypertension; severe cases are called sclerodermatous kidney), and chronic thyroiditis (Hashimoto’s thyroiditis).

**Pathogenesis**

The fundamental etiology is unknown. SSc rarely runs in families.

**Environmental predisposition:** Patients with silicosis are prone to SSc. SSc-like symptoms may be found in workers who handle polyvinyl chloride or epoxy resin and as a side effect of the anti-tumor drug bleomycin.

A type of SSc called human adjuvant disease occurs in half of those who have received silicon or paraffin injections or implants for cosmetic purposes. The disease appears 10 years or more after the operation. These substances are no longer in use.

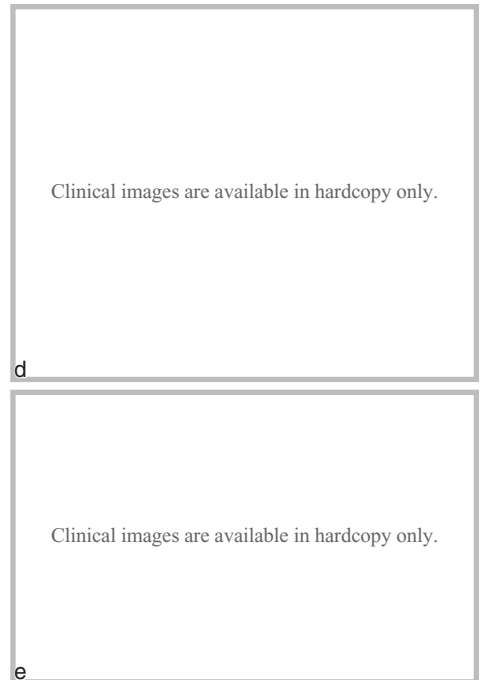
**Pathology**

In the early stages of SSc, collagen fibrils are swollen in the middle to lower layer of the dermis. Interstitial edema, hardening and lymphocytic infiltration are present. As the lesions progress, atrophy in the epidermis and appendages, deposition of collagen fibers parallel to the epidermis, and deposition of acid mucopolysaccharide (the major component is dermatan sulfate) are observed. Unlike in SLE, the deposition of immunoglobulins and complements is negative in many cases.

**Laboratory findings**

Anti-Sc1-70 antibodies are frequently seen in diffuse cutaneous SSc. Anti-centromere antibodies are frequently seen in limited cutaneous SSc and CREST syndrome.

SSc findings are similar to those of other collagen diseases: Rheumatoid factor is positive, there is biological false positive serological reaction for syphilis, and antinuclear antibody is positive (macular or nucleolar). Nonetheless, unlike in SLE, the patient tests negative for LE cells and anti-DNA antibodies, and the serum complement titer is normal.

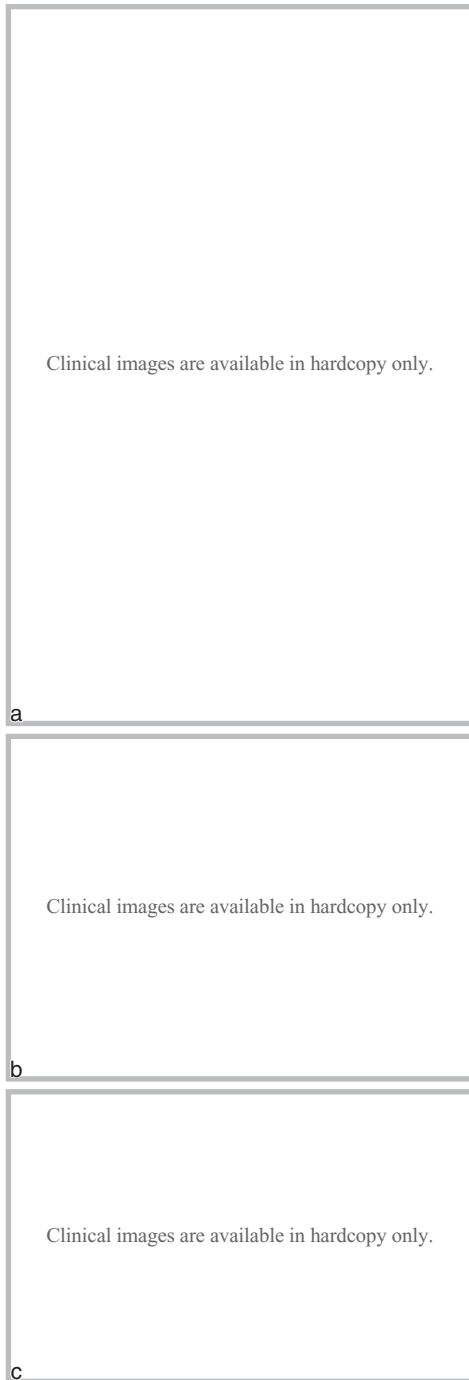


**Fig. 12.11-2 Systemic sclerosis.**  
d: Mask-like face. e: Microglossia.

**Table 12.6 Preliminary criteria for classification of systemic sclerosis (SSc).**

Major criterion
Proximal diffuse (truncal) sclerosis (skin tightness, skin thickening, non-pitting induration)
Minor criteria
1) Sclerodactyly (only of the digits)
2) Digital pitting scars or loss of substance of the digital finger pads (pulp loss)
3) Bibasilar pulmonary fibrosis
The diagnosis is given when the patient meets the major criterion or two of the three minor criteria.

(Adapted from; Subcommittee for Scleroderma Criteria of the American Rheumatism Association Diagnostic and Therapeutic Criteria Committee. Preliminary criteria for the classification of systemic sclerosis (scleroderma). *Arthritis Rheum* 1980; 23: 581-90).



**Fig. 12.12 Localized scleroderma morphea.**  
 a: A sclerotic plaque of 10 cm in diameter on the extensor surface of the forearm. The center of the lesion appears ivory-colored and glossy. A lilac ring and erythema of light color are present around the lesion. b, c: Morphea on the precordial region.

### Diagnosis, Differential diagnosis

Various diagnostic criteria are consulted. In cases with typical symptoms, the cutaneous symptoms are sufficient for conclusive diagnosis. Otherwise, skin biopsies and the characteristic auto-antibodies are used for diagnosis. SSc in the edematous period should be carefully differentiated from mixed connective tissue disease (MCTD) and overlap syndrome. The diagnostic criteria established by the American College of Rheumatology (1980) are shown in **Table 12.6**.

### Treatment

Moderate doses of oral steroids are administered against hardening of skin at the early stages. NSAIDs are used for arthralgia. Various vasodilators (e.g., calcium antagonists, prostaglandin E1) are applied for Raynaud's phenomenon. For patients with severe systemic symptoms, immunosuppressants and hematopoietic stem-cell transplantation are also used. Bed rest, and warming and massaging of the extremities are effective against cutaneous lesions.

### Prognosis

SSc tends to be chronic. Hardening of skin usually progresses gradually. The prognosis depends on the severity of lesions in the kidneys and lungs. Infection may be caused during treatment, and it is fatal in some cases. Sudden death may be caused by heart failure.

## 2. Localized scleroderma



### Definition

Localized scleroderma is sclerosis of the dermis, which occurs only on the skin. Unlike in systemic sclerosis, there is neither Raynaud's phenomenon nor lesions of internal organs.

### Clinical features

Localized scleroderma occurs most frequently in adults aged 20 to 40 and sometimes in children. The proportion of male to female patients is 1 to 3. Raynaud's phenomenon is not present. Systemic symptoms are mild, if any. Localized scleroderma includes variety of conditions.

#### ①Morphea (circumscribed plaques)

Localized round or oval indurated lesions that are silvery at the center occur on the trunk (**Fig. 12.12**). These may be surrounded by a purplish-red halo called a lilac ring. Morphea is further classified by the size and number of eruptions as localized, guttate or generalized. Generalized morphea is multiple morphea or morphea accompanied by other localized sclerodermatous lesions.

#### ②Linear scleroderma (linear morphea)

This may be accompanied by facial hemiatrophy. Linear or band-like indurated lesions resembling morphea occur on the

body. When the forehead is affected, it is called sclérodermie en coup de sabre; this spreads to the scalp, leading to alopecia (Fig. 12.13). Linear scleroderma generally penetrates to deep sites. Lilac rings are rarely seen.

### Pathogenesis

The pathogenesis is unknown. The disorder may be induced by external injury. Involvement of *Borrelia* infection has been reported recently.

### Pathology, Laboratory findings

Localized scleroderma has a histopathology similar to that of SSc. The abnormal laboratory findings that are seen in SSc are not usually found in localized scleroderma. Rheumatoid factors and antinuclear antibodies may be present in generalized morphea.

### Treatment

Steroids are topically applied or locally injected. Oral steroids may be administered for severe cases. If no spreading tendency is observed for a certain period of time, surgery may be considered.

### Prognosis

Patients with localized scleroderma have a good life expectancy; however, the condition is usually chronic. Indurated patches gradually shrink, and abnormal pigmentation appears.

Clinical images are available in hardcopy only.

Clinical images are available in hardcopy only.

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**Fig. 12.13 Linear scleroderma with facial hemiatrophy.**

Alopecia and sclerosis on the head. It resembles the slash of a sword. Atrophy occurs in the hypodermic scalp.

## C. Other collagen diseases

### 1. Dermatomyositis (DM) ★ ★

#### Outline

- Heliotrope rash, Gottron's sign and unique erythema and poikiloderma appear, and there is telangiectasia in the perionychia.
- Muscle weakness begins in the proximal muscles. Elevated levels of CPK, aldolase and urinary creatine reflect myositis.
- Malignant tumor commonly develops as a complication.
- Interstitial pneumonia may aggravate rapidly. The prognosis is poor.