Scleroderma Quebec™

HOW DOES SYSTEMIC SCLEROSIS EVOLVE

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The evolution of systemic sclerosis is variable, depending on the extent of skin thickening (limited or diffuse systemic sclerosis), the presence of specific autoantibodies in the blood and the presence of internal organ involvement.

LIMITED OR DIFFUSE SKIN INVOLVEMENT

When skin thickening is limited to the hands, forearms, feet, legs below the knees, face and/or neck, this is referred to as **limited systemic sclerosis**. This form of systemic sclerosis is usually associated with a lower risk of developing severe internal organ involvement, except for pulmonary arterial hypertension, the risk of which increases after 5 to 10 years of disease.

When skin involvement extends above the elbows and knees, affecting the skin of the upper arms, thighs, trunk and/or abdomen, this is referred to as **diffuse systemic sclerosis**. In this form of systemic sclerosis, internal organ involvement is generally more common and extensive.

Limited or diffuse skin involvement does not usually change in the same patient. Thus, a patient with the limited form does not progress to the diffuse form of the disease. However, at disease onset, it may be difficult to be certain of the limited nature of the disease. A patient may initially have limited involvement of the hands (and be classified as having limited disease), but the involvement may rapidly progress to diffuse involvement over the next few months. The presence of swelling of the fingers and hands, and the presence of autoantibodies associated with the diffuse form of systemic sclerosis (e.g., anti-topoisomerase I/Scl-70 or anti-RNA polymerase III) usually point to a possible evolution toward the diffuse form of the disease.

In the diffuse form, skin thickening generally progresses in the first 2 to 5 years of the disease, then progression halts with a tendency towards spontaneous "softening" of the skin. The skin then becomes thinner and more fragile, but less "hard" than in the initial phase. In the limited form, skin involvement is restricted to the areas defining the limited form and does not progress further.

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SYSTEMIC SCLEROSIS-SPECIFIC AUTOANTIBODIES

Anti-centromere (or anti-CENP-B) autoantibodies are usually associated with the limited form of systemic sclerosis, a slower disease course at the onset of disease and less severe involvement of internal organs, but with more pulmonary arterial hypertension later in the course of the disease.

Anti-topoisomerase I (or anti-Scl-70) autoantibodies are usually associated with the diffuse form of systemic sclerosis, a more rapidly progressive disease course at the onset of disease, and an increased frequency of pulmonary fibrosis.

Anti-RNA polymerase III autoantibodies are usually associated with the diffuse form of systemic sclerosis, a more severe disease course and a higher risk of developing scleroderma renal crisis. In these patients, blood pressure should be closely monitored and corticosteroids should be avoided.

Anti-Th/To autoantibodies are associated with the limited form of systemic sclerosis, as well as an increased risk of pulmonary fibrosis and pulmonary hypertension. Anti-fibrillarin (or anti-U3-RNP) autoantibodies are associated with diffuse systemic sclerosis and an increased risk of pulmonary fibrosis. These autoantibodies are not available in all centres, but give a "nucleolar" pattern on the antinuclear antibody (ANA) test.

INTERNAL ORGAN INVOLVEMENT

Unlike skin involvement which tends to improve over the years, internal organ involvement usually does not regress. In the case of pulmonary fibrosis, disease progression is highly variable: some patients will have a mild and relatively stable disease, some will have a disease that progresses slowly over the years, and some will progress rapidly. Patients whose thoracic CT scan shows involvement that extends beyond the lung bases are usually at higher risk of developing more progressive pulmonary fibrosis.

It is commonly said that organ involvement (skin, lungs, heart, kidneys, and others) occurs in the first 3 to 5 years of the disease, with the exception of pulmonary arterial hypertension, which occurs after 5 to 10 years of disease progression. However, more recent studies have questioned this notion. Pulmonary fibrosis frequently occurs early in the course of the disease, but can also appear later on. Inflammatory damage to the heart (myocarditis) usually occurs early in the disease, but fibrotic damage gradually progresses throughout the disease course. Digestive involvement also becomes progressively more important as the disease moves from the vascular and inflammatory phase to the more fibrotic phase of disease. The tissues of the digestive system then become weaker and unable to contract, leading to greater motility disorders and malabsorption over the course of the disease.

IN SUMMARY

The course of systemic sclerosis is highly variable. An initial assessment of skin and internal organ involvement and the search for systemic sclerosis-specific autoantibodies in the blood can help predict the course of systemic sclerosis in an individual and inform the approach to screening for internal organ involvement.