What’s Up Doc?

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Questions and answers about scleroderma and your family

The Scleroderma Foundation receives questions on a daily basis from patients seeking answers to various health issues. Although scleroderma is a highly individualized disease, we have found that some concerns are very common among those affected. We hope this forum is helpful to you, our members.

We understand, however, that individual circumstances are unique and ask that you always seek the guidance of your health care professional to obtain the treatment plan that best suits your specific health situation.

Q: What role do genetics play in the likelihood of getting scleroderma?

A: Scleroderma (systemic sclerosis) is caused by an insult, such as an infection or toxic exposure, that triggers the immune system in a genetically predisposed patient and causes the features of scleroderma that occur in most people living with the disease – vascular problems, scarring (fibrosis) of the skin and other connective tissues and autoantibodies.

Genetics do play a role in scleroderma. The largest risk of developing scleroderma is a family history of scleroderma, but the genes are multiple. Scleroderma still is rare within families. However, in families of scleroderma patients, there also is a predisposition to other diseases such as lupus, Sjögren Syndrome, multiple sclerosis and juvenile arthritis.

Different populations have had variable genotypes, so it is likely that many different genes can lead to the scleroderma phenotype. There is research on genome-wide scans for scleroderma patients in North America, which has led to some novel genes being identified.
Q: Recently, I’ve read some articles that mention biomarkers. What are biomarkers, and how do they relate to scleroderma?

A: Biomarkers are markers within a patient, such as serum or skin samples, that change with disease activity. A biomarker is a biologic substance that may be an indicator of a state (active disease, severe organ involvement, inactive state, etc.) Biomarkers can help determine changes when testing a novel therapy, which also coincide with early improvement in the disease. We use several biomarkers in scleroderma:

- A low diffusing capacity represents potential pulmonary hypertension of lung disease because it represents impaired gas exchange.
- Skin biopsies may be used for disease modifying drug trials.
- Serum brain naturetic peptide (BNP) is being studied as an early biomarker in pulmonary arterial hypertension in systemic sclerosis (SSc) is being studied.

Q: What are the most promising advances that you’ve seen in the field of scleroderma research over the past couple of years?

A: Years ago, when I began a career in scleroderma research, there were very few trials. Now, there are many organ-specific trials that have made progress in the treatment of several areas. These areas include pulmonary arterial hypertension, interstitial lung disease (pulmonary fibrosis), Raynaud Phenomenon and digital ulcers.

We have had advances in clinical trial design, measuring outcomes that are sensitive to change, and determining the minimally important difference in some outcomes. We also expect new classification criteria – (supported jointly by the American College of Rheumatology (ACR) and European League Against Rheumatism (EULAR) – that can allow more patients to be included in scleroderma studies.

In parallel to clinical trial advances, there are several large cohorts in scleroderma, such as the Canadian Scleroderma Research Group (CSRG) and EULAR Scleroderma Trials and Research (EUSTAR), which allow for large observational studies of many features in scleroderma.

There have been basic science research advances that have increased our understanding of the control of fibrosis including pathways that can be switched on and off, which regulate collagen (over)production. This research will provide more potential treatment for people suffering with scleroderma.

Q: Today, is it easier to diagnose scleroderma even though it remains rare?
A: Most family practitioners will never see a patient with scleroderma. So, it is unlikely that primary care doctors will diagnose this rare disease (affecting at most 2 in 10,000 people).

However, early signs often include Raynaud Phenomenon (hands changing colors in the cold, such as turning white, then blue or red), which occurs in at least three percent of the general population and other features such as swollen puffy fingers, tight skin, problems swallowing because food sticks around the level of the sternum (breast bone), and round vascular dots (telangiectasia). Of course, some of these features may occur in other conditions, but the earlier diagnosis of scleroderma has been advanced by the availability of antibody tests that are positive in scleroderma and rare in the general population, such as anti-centromere antibody and anti-topoisomerase I antibody. Also, most people with early scleroderma have dilated capillaries visible at their nail beds.

There are prediction models – such as the new onset Raynaud Phenomenon after age 40, and the presence of dilated nail-fold capillaries, or anti-centromere antibody – that help doctors to suspect a higher likelihood of future diagnosis of scleroderma, where one in three patients will have scleroderma in the next five years.

Scleroderma incidence may be increasing, or it may be that the diagnosis is increasing, especially for patients with mild cases of scleroderma. The severity of scleroderma can be highly variable, but there may be an overall lessening of scleroderma renal crisis compared with what has occurred in the past.