

RAYNAUD PHENOMENON



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WHAT IS RAYNAUD PHENOMENON?

Raynaud phenomenon is the exaggeration of the normal response to cold temperatures. The clinical manifestation of Raynaud phenomenon is caused by vasoconstriction (narrowing) of blood vessels (arteries and arterioles) that results in reduced blood flow to the skin (ischemia), while cyanosis (blue skin) is created by deoxygenation of slow-flowing blood in small blood vessels (arterioles and capillaries) in the skin. The skin feels cold and appears as a pale demarcated area (white fingers or toes) or cyanotic skin limited to the fingers or toes. Some people will feel generally cold and have mottled pale skin of the ears, nose, facial area, knees, or other exposed skin.

A Raynaud event typically starts after cold exposure or an emotionally stressful situation in one or several digits and then spreads symmetrically to all fingers of both hands. It is common for numbness, tingling and clumsiness of finger use to accompany the digital color changes.

Pain is usually not felt unless the event is severe with prolonged lack of blood flow to the digit(s). The attack usually ends with a rapid re-flow of blood into the digit. Generally an attack will last 15 minutes after leaving a cold area. The occurrence of digital ulcers (finger sores) is a sign of severe Raynaud that needs a physician's attention.

WHO GETS RAYNAUD PHENOMENON?

While studies of selected patients find that as many as 15 to 20 percent of young women have Raynaud phenomenon, population-based surveys in various ethnic groups find the prevalence to be approximately 3 to 5 percent. Geographic variation in the prevalence of Raynaud phenomenon is influenced by the region's climate. There is also good evidence that the frequency and severity of the attacks is influenced by the daily ambient temperature with significant variation during the winter and summer months.

Primary Raynaud phenomenon is used to denote a patient without an associated underlying disease. Most of the individuals with Raynaud phenomenon have

uncomplicated primary Raynaud phenomenon without any defined cause or associated systemic disease. Recent studies find that about 30 percent of people with primary Raynaud phenomenon have a first-degree relative with the same condition. This suggests there is a genetic trait associated with Raynaud phenomenon, but to date no gene or gene defect has been defined.

Secondary Raynaud phenomenon is used to describe patients with a defined secondary or associated disease. There are a number of causes of secondary Raynaud phenomenon. These include diseases that damage blood vessels, alter the nervous control of blood vessels or are associated with abnormal circulating factors.

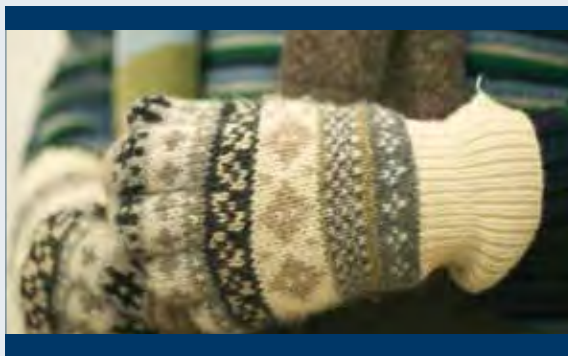
The most common diseases associated with Raynaud phenomenon are the rheumatic diseases, especially scleroderma, mixed connective tissue disease, systemic lupus erythematosus, Sjögren syndrome, and dermatomyositis. Approximately 95 percent of those diagnosed with scleroderma have Raynaud phenomenon.

WHAT CAUSES RAYNAUD PHENOMENON?

Most agree that Raynaud phenomenon is caused by a disruption in the normal regulation and responses of thermoregulatory blood vessels in the skin. These normal blood vessels have a complex system of control that begins with sensory nerves in the skin. These nerves sense the ambient temperature and relay this information to the central nervous system.

The brain then sends a signal through the sympathetic nervous system to skin blood vessels to constrict if it is cold and dilate if it is warm. Studies suggest that in patients with Raynaud phenomenon, the sympathetic receptors (alpha 2C) are overactive or overexpressed in the smooth muscle of the thermoregulatory arteries, and thus cause exaggerated responses to cold temperatures.

Studies also implicate a number of other mechanisms for causing or aggravating abnormal vascular responses in individuals with Raynaud phenomenon. These include abnormal release of vasoconstricting molecules (e.g., endothelin-1) or the underproduction of vasodilators (e.g., prostacyclin or nitric oxide) from the lining of the vessel itself.



Sensory nerves in the skin also directly release small peptides that can alter blood flow. Studies suggest that in some there is a reduced release of vasodilators from sensory nerves. Research has also found that there can be a release of vasoactive substances from cells circulating in the blood. An example of this is the release of serotonin (a vasoconstrictor) from blood platelets.

Recent studies suggest that a genetic trait that leads to altered thermoregulatory blood vessel control will be found in patients with primary Raynaud phenomenon.

Other common causes of Raynaud phenomenon include prolonged use of vibratory tools (e.g., jackhammer operators); medicines such as sympathomimetic drugs (ephedrine, epinephrine), ergots (used to treat migraine headaches), and certain chemo-therapeutic agents; peripheral nerve damage such as in carpal tunnel syndrome; and occlusive vascular disease (such as peripheral arterial disease) or metabolic diseases, including hypothyroidism.

HOW IS RAYNAUD PHENOMENON DIAGNOSED?

Raynaud phenomenon is a clinical diagnosis made by a history of cold sensitivity with the associated typical color changes (white, blue, red) of the skin.

The physician will often witness an attack during the examination or can use color photos of actual attacks to help the patient. At this time there is no blood test that identifies Raynaud phenomenon. Cold challenges (e.g., placing hand in ice water) are not necessary to make a diagnosis.

Patients with Raynaud phenomenon should have a complete history and physical examination to look for any underlying cause for the attacks. A careful examination of the blood vessels is important. One special test is nailfold capillaroscopy, where a doctor puts a drop of oil on the patient's skin at the base of the fingernail. The physician then examines this area under a microscope to look for any capillary changes. Enlarged, dilated or absent nailfold capillaries are noted among patients with scleroderma and other rheumatic diseases.

Blood tests are performed if the history or physical examination suggests that secondary Raynaud phenomenon is present. The specific testing done depends on the clinical situation. For example, tests for the presence of autoantibodies may be done if an autoimmune disease like scleroderma or systemic lupus erythematosus is suspected. If vascular disease is suspected, an examination of larger vessels using arterial Doppler flow studies may be conducted.

HOW IS RAYNAUD PHENOMENON TREATED?

NON-DRUG THERAPY

Treatment begins by educating the patient about the causes of the Raynaud attacks, and methods to avoid the common provoking and aggravating factors.

The avoidance of cold temperatures is the best method to prevent an episode of Raynaud phenomenon. Warming the whole body with loose fitting clothing, stockings, vests, headwear, and gloves is a key strategy. Contact with cold objects such as iced beverage containers or a cold steering wheel should be avoided by covering these objects or wearing warm gloves. Chemical warmers placed in pockets or gloves can be most helpful. Avoiding trauma to the fingers or toes is also helpful. Emotional stress alone can trigger digital vasospasm and anxiety—feeling nervous, tense, or worried—and can exacerbate cold induced Raynaud attacks. Therapies designed to reduce emotional stress are helpful.

Temperature biofeedback is used in combination with different relaxation techniques to treat Raynaud patients. However, a controlled trial found that

temperature biofeedback training did not reduce attacks significantly compared to the control procedure. Conditioning treatment, temperature biofeedback and relaxation therapy are all non-drug therapies that are still controversial.

Avoiding agents that cause vasoconstriction is also important. These drugs include over the counter cold preparations containing sympathomimetics agents (e.g., Sudafed); caffeinated drinks, clonidine, ergotamines, serotonin receptor agonists (e.g., migraine medications), narcotics, and some chemotherapeutic agents. Smoking can potentially worsen attacks, because nicotine decreases blood flow to the fingers and toes. Use of estrogens or non-selective beta blockers is reported to be associated with Raynaud phenomenon, but this is still controversial.

DRUG THERAPY

Drug therapy is not indicated in every case. If the patient has primary Raynaud phenomenon the attacks are usually mild and do not cause tissue damage. Therefore, non-drug therapy is recommended unless the attacks are intense, altering quality of life, and compromising the ability to perform daily activities.

Drug therapy is recommended in patients with secondary Raynaud phenomenon who have severe attacks or if there is evidence of tissue damage such as digital ulcerations. Digital ulcers can have a significant impact on patients, causing pain and functional impairment. Digital ulcers are best handled with regular soap and water washing, antibiotics, and good vasodilator therapy. In cases of delayed healing, or if signs and symptoms of infection (e.g., swelling, excessive pain, or drainage) develop or the digit becomes discolored, contact your physician for further evaluation.

The most common medications used for Raynaud phenomenon are vasodilators such as the calcium channel blockers (e.g. nifedipine or amlodipine). Most cases can be managed with appropriate doses of a calcium channel blocker.

Older agents used with some success include alphaadrenergic blockers (e.g., prazosin) or local applications of nitroglycerin preparations. Newer approaches include the use of angiotensin receptor

inhibitors (e.g., losartan), phosphodiesterase inhibitors (e.g., cilostazol, sildenafil), and serotonin uptake inhibitors (e.g., fluoxetine).

Intravenous prostaglandins (e.g., iloprost, epoprostenol) are used in severe cases of secondary Raynaud phenomenon with recurrent digital ulcers that are refractory to the use of oral vasodilator therapy. New studies suggest that bosentan (an inhibitor of endothelin-1) can reduce the number of new digital ulcers in patients with scleroderma and severe Raynaud phenomenon.

Other therapies include the use of statins – the drugs used to lower cholesterol. Studies suggest statins can reduce digital ulcers in patients with scleroderma. Use of anti-oxidants and local injection of Botox is also reported to be helpful.

In complex or severe cases, combinations of these agents are tried. Some are using intravenous therapy periodically to prevent new ischemic events.

If Raynaud events are severe and associated with critical tissue damage (e.g., deep tissue gangrene or digital ulcers) that is not responsive to medical therapy, then surgical sympathectomy can be done. Sympathectomy is a surgical procedure that is performed to improve blood flow in the digital arteries by destroying nerves in the sympathetic nervous system. New techniques allow this to be done at the level of the involved finger (digital sympathectomy) thus avoiding complications of procedures done more proximally. However, surgical sympathectomy often provides only temporary relief and should be reserved for urgent situations and it should be coupled with continued drug therapy.

Please note that this pamphlet is provided for educational purposes only. It is not intended to substitute for informed medical advice.

The Scleroderma Foundation thanks Frederick Wigley, M.D. for his help with this pamphlet.

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- Helping patients and their families cope with scleroderma through mutual support groups, physician referrals and the National Patient Education Conference.
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Please consider joining the Scleroderma Foundation today. A membership form is attached on the reverse side of this panel.

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Support: To help patients and their families cope with scleroderma through mutual support programs, peer counseling, physician referrals, and educational information.

Education: To promote public awareness and education through patient and health professional seminars, literature, and publicity campaigns.

Research: To stimulate and support research to improve treatment and ultimately find the cause of and cure for scleroderma and related diseases.



Rev. 2

A publication of
Scleroderma Foundation
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