

# RAYNAUD PHENOMENON



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# WHAT IS RAYNAUD PHENOMENON?

Raynaud phenomenon is the exaggeration of the normal response to cold temperatures and emotional stress. 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 congestion in veins and 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 uncomplicated 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 the immediate attention of a physician.

# 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.

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 is yet defined. Primary Raynaud phenomenon usually starts at a young age (teenage to 20s) and improves with aging.

**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, Sjren 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 specialized thermoregulatory blood vessels in the skin. These blood vessel have a special structure and 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 2) 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 vessels are affected by a secondary disease process.



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.

Other common causes of secondary 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 identify an event. 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. Rapidly shifting from a warm to cold environment or cold-damp breezes are very common aggravating factors. 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.

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 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, then drug therapy is not needed. Non-drug therapy is very effective and 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. Treating the underlying disease process is most important (e.g., thyroid replacement if hypothyroid). 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.

Local applications of nitroglycerin preparations alone or combined with the calcium channel blocker can be helpful. Newer approaches include the use phosphodiesterase inhibitors (e.g. sildenafil, tadalafil), an angiotensin receptor inhibitor (e.g., losartan), or a serotonin uptake inhibitors (e.g., fluoxetine). Older agents like the alpha-adrenergic blocker prazosin) are rarely used.

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. Some use intermittent intravenous therapy to prevent critical digital ischemia. Oral prostaglandins are now available but more studies are needed to determine their benefit. Studies suggest

that bosentan (an inhibitor of endothelin-1) can reduce the number of new digital ulcers in patients with scleroderma and recurrent digital ulcers but it does not reduce the severity of the Raynaud events.

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 a local injection of Botox is popular; however more studies are needed to confirm their benefit.

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 now performed locally in the hand or involved fingers (digital sympathectomy) thus avoiding complications of procedures done more proximally. It improves blood flow in the digital arteries by stripping the sympathetic nerves away from the blood vessel; thus stopping sympathetic mediated vasoconstriction. However, surgical sympathectomy often provides only temporary relief and should be reserved for urgent situations and it should be coupled with continued drug therapy.

Despite ideal therapy Raynaud events may continue to occur. The goal of therapy is to reduce the severity of Raynaud's events, to improve quality of life and prevent ischemic events (e.g., ulcers or loss of a digit). Digital ulcers have a significant impact on well-being causing pain and functional impairment. Digital ulcers are best handled with regular soap and water washing 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 treatment.

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 Fredrick Wigley, M.D. for his help with this pamphlet.*

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When you become a member of the Scleroderma Foundation, you support the organization's mission of support, education and research. Your donation helps pay for programs in each of those three areas, including:



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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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**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.



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