Nowadays, the human race is becoming more sensitive to the changes in the environment. This sensitivity may result in triggering a number of diseases, including Raynaud’s disease, which constitutes a change in the vascular functions of the human body. Conferring to the facts and figures of Raynaud, every 5 out of 100 Americans suffer from this disease. On the other hand, merely 1 out of 5 pursues treatment. Raynaud’s phenomenon most often impacts women, rather than men, exclusively in the ages from 20 to 40. Raynaud’s phenomenon can occur on its own or in relation to other medical conditions such as rheumatic diseases. Read on for an extensive explanation of Raynaud’s disease.

Introduction

Raynaud’s disease (also Raynaud, or Raynaud’s phenomenon) was illustrated for the very first time in 1862 by Auguste Raynaud. Even at a first look, the disorder appears quite obvious, owing to the fact that the patient notices the change in the color of their skin, particularly in their limbs.

At low temperatures, the skin becomes cold and pallor, owing to a spasm in the arterioles, which narrow and thus limit the blood supply in those areas. This may result in the coldness and cyanosis of the limbs as the distension of veins occurs, followed by the bluish skin color. With the rise of temperature, the skin turns warm and red as a result of the arterioles’ response to vasodilatation.

It took quite a few years of study for complete comprehension of the pathology and
physiology of Raynaud, which continues to be explained today. In 2005, Hendrik classified the causes and mechanisms of Raynaud’s phenomenon under three groups, namely:

- Vascular
- Intravascular
- Neural abnormalities

Definition of Raynaud’s Disease

Raynaud’s disease is a disorder that causes pain in the margins in the cold environment. Reduction in the size of the blood vessels, most usually in the fingers and toes, results in change of color from white to blue. Then, as the stream of blood resumes, the skin turns red.

Raynaud’s phenomenon is an ailment causing a specific sequence of color changes in the extremities when in contact with fluctuations in weather, either hot or cold, or due to stress. A great number of people with Raynaud’s disease have extreme sensitivity to cold temperature.

Classification of Raynaud’s Disease

Raynaud’s is classified to:

- Primary Raynaud’s, also known as Raynaud’s disease
- Secondary Raynaud’s, also known as Raynaud’s phenomenon

Primary Raynaud’s

Raynaud appearing all alone is termed as “Raynaud’s disease”, or more appropriately, as primary Raynaud’s phenomenon. When it appears accompanied by
Secondary Raynaud’s

Raynaud’s phenomenon is customarily a sign or symptom of different ailments, including atherosclerosis, scleroderma, lupus and rheumatoid arthritis. It can also be a result of taking assured medicines, having frostbite, smoking or using vibrating power tools for numerous years. Therefore, it is sometimes referred to as secondary Raynaud’s.

The most usual group of symptoms is disclosure to cold atmosphere. At cold temperatures, the typical response of our body is to constrict the minor vessels of blood to the skin and to expose the blood vessels to the exclusive parts of our body to keep us warm and to maintain our temperature through homeostasis. With Raynaud’s phenomenon, the body confines the flow of blood more toward the skin than to other parts where it is needed. Additional triggers may be stress related, or such that have an impact on the flow of blood, including some medicines, caffeine and smoking.

Secondary Raynaud’s is more frequent than the Raynaud’s syndrome. Also, it is more likely to occur in both genders with an almost equal ratio.

It appears that women are affected more adversely, specifically with age ranging from 20-30 years. The disorder progresses proportionally, affecting digits from both hands or feet. Over a period of time, recurrent and sustained spasms become more common.

The pathogenesis of Raynaud’s syndrome is characterized by an increased reaction of the arterioles to stimuli that are vasospastic, exclusively in situations of emotional stress or cold temperatures. This disorder can occur both in our lower and upper limbs as well as the chin, nose, lips and ears. In occasional situations, low oxygen supply can result in the occurrence of necrosis.

Pathophysiology of Raynaud’s Disease

People suffering from Raynaud’s phenomenon experience changes in the color of
their skin due to an anomalous spasm in the blood vessels, which may result in a reduced supply of blood to the localized body tissues.

At first, the fingers or toes involved can turn whitish in color because of the decreased blood supply. Afterwards, these extremities will turn bluish due to the persistent deficiency of oxygen. As a final point, the blood vessels will open themselves again, resulting in localized “flushing” occurrence, which in turn causes the extremities to reappear red in color. Hence, this three-phase color system (whitish, to blue, to red) occurs more frequently upon contact with cold temperatures and is a significant characteristic of Raynaud’s phenomenon.

Particular parts of the body are more often vulnerable to cold injury. A perfect mark of distinction is present among the unaffected and ischemic parts of the body.

The impacts are reversible, and they should be distinguished from the non-reversible origins of low blood supply, including thrombosis or vasculitis. Necrosis of the tissues does not usually appear from a distal end of the particularly affected vessel. It most commonly appears at the periphery or margins of the affected vasculature. The impact on the fingers is most common, although the ears, toes and nose—in some cases even the tongue—can also be affected.

The primary Raynaud’s does not correlate to underlying medical conditions. In comparison, the secondary Raynaud’s phenomenon further reveals fundamental micro-vascular anomalies.

Vascular abnormalities

A deficit of vasodilation mediators, mainly nitric oxide, has been connected to the cause of Raynaud’s phenomenon. Moreover, effective vasoconstrictors generally present in our endothelium (known as endothelin-1) have been observed to be flowing in elevated levels in people suffering from the secondary Raynaud’s disease.

Discharge of the vasoconstrictor endothelin-1 is elicited by stimuli of vasoactivation, which comprise of transforming growth factor beta (TGF-beta), vasopressin and angiotensin. In contrast, consequences concerning the levels of endothelin-1 in people suffering from primary Raynaud’s disease are renowned.

Angiotensin has both pro-fibrotic and vasoconstrictive impacts. The research by Kawaguchi et al disclosed that increased levels of angiotensin II in people suffering from Raynaud have been observed, along with embedded cutaneous systemic sclerosis.

In people suffering from systemic sclerosis, fundamental anomalies allied with vasculature fibrotic proliferation result in decreased blood flow toward the digits. This is a usual characteristic difference from the primary Raynaud’s disease.

Neural abnormalities

Scientists discovered that originally, both the people suffering from Raynaud and those who are hale and hearty reacted to sound stimuli, along with vasoconstriction in the extremities and vasodilation in the muscles of the forearm.

Compromised vasodilation can also be part of Raynaud’s phenomenon. Calcitonin, an essential, gene-related neuropeptide, which is an intoxicating vasodilator, is released by nerves supplying the blood vessels. A lower amount of calcitonin-secreting neurons has been observed in a biopsy of skin samples of people suffering from systemic sclerosis and
Elevated vasoconstriction in Raynaud’s phenomenon can lead to increased activity of α2C-adrenoreceptors; vasoconstriction of the blood vessels has been known to be cold-induced by these adrenoreceptors. There is research about such phenomena conducted by Furspan et al. It points out the fact that there is an increased contractile reaction to α2-adrenergic agonists, along with cooling, in people having the primary Raynaud’s phenomenon. This is thought to be related to improving the activity of protein tyrosine kinase.

Intravascular abnormalities

Raynaud’s phenomenon is found to be linked with the below-mentioned intravascular abnormalities:

- In systemic sclerosis and primary Raynaud, enhanced activation and accumulation of platelets have been revealed.
- An improved synthesis of thromboxane A2 platelet, which is actually an extremely prevailing vasoconstrictor, has been seen in people with Raynaud’s phenomenon.
- Patients with systemic sclerosis have been observed to have a weakened fibrinolytic scheme, perhaps leading to obstruction in vessels.

Differential Diagnosis of Raynaud’s Disease

Autoimmune diseases

- Sjogren’s syndrome
- Dermatomyositis and polymyositis
- Lupus erythematosus
- Rheumatoid arthritis
- Scleroderma
- Primary pulmonary hypertension
- Vasculitis

Infectious diseases

- Hepatitis C
- Hepatitis B
- Infections of the mycoplasma

Neoplastic diseases

- Type-1 cryoglobulinemia
- Myeloma
- Leukemia
- Polycythemia
- Waldenstrom macroglobulinaemia
- Lymphoma
- Paraneoplastic syndromes
- Lung adenocarcinoma
Endocrinological and metabolic diseases

- Myxedema
- Acromegaly
- Pheochromocytoma
- Diabetes mellitus

Hematological diseases

- Polycythemia
- Cryofibrinogenaemia
- Paroxysmal nocturnal hemoglobinuria

Diseases related to occupation

- Frostbites
- Exposure to lead
- Vibration
- Exposure to arsenic
- Polyvinyl-chloride exposure

Adverse reaction to drugs

- Bromocriptine
- Alpha-interferon
- Oral contraceptives
- Cyclosporine
- Beta-adrenergic
- Ergot alkaloids

Clinical Features of Raynaud’s Disease

During an occurrence of Raynaud, the body withholds the flow of blood from the feet and hands, which causes them to feel numb and cold, thus turning them white or pallor. As the blood flow returns, and the digits of the toes and fingers become hot and warm, they begin to turn red. This is followed by pounding and pain. On occasion, Raynaud can also affect the ears or nose.

The condition may manifest more frequently but last for short periods of time. Nevertheless, in some situations, it may occur long-term, ranging from one hour or more.

Diagnosis and Investigations of Raynaud’s Disease
Diagnostic criteria for the primary Raynaud's disease are mentioned below:

- Occurrences activated by disclosure to stress or cold
- Lack of necrosis
- Symmetrical bilateral involvement
- Lack of a noticeable essential pathogenesis
- Normal laboratory findings for inflammation
- Normal findings of capillaroscopy
- Lack of antinuclear factors
Because of the nature of Raynaud, analysis and diagnosis can be moderately acquired by asking the patient a sequence of questions. These questions are expected to contain an explanation of the signs and symptoms and some overall facts about habits, diet and hobbies.

The subsequent challenge is to discriminate among primary and secondary causes of the ailment. For this, the physician can take a sample of the patient's skin from the base of a fingernail to inspect it underneath a compound microscope. This technique is known as capillaroscopy. The physician will look for inflamed or abnormal capillaries, which could be a signal of the secondary illness.

A blood test might be essential, in order to see and examine the antinuclear antibodies and to assess the sedimentation rate of RBC’s. They both can expose problems related to autoimmune system or connective tissues disorders.

Treatment of Raynaud’s Disease

General measures to be taken

1. Patients should avoid trauma to the affected area.
2. Protect the patient’s body from the cold atmosphere.
3. Urgent treatment of any injury to the limbs.
4. Moisturizing lotions and creams should be used.
5. Quitting smoking is important.
6. Emotional stress should be avoided.
7. Eating fish, which is highly enriched in omega-3 fatty acids, is recommended.

Medications and drugs

1. Angiotensin II antagonist
2. Vasodilators, such as Calcium channel blockers
3. Inhibitors of angiotensin altering enzyme, such as ACEIs and ARBS

Surgical treatment

Sympathectomy is necessary when the illness obstructs the patient’s daily activities. Thoracic and cervical sympathectomy give a short-term aid; on the other hand, lumbar sympathectomy is highly preferred as it gives an intense wide-ranging relief for a much longer duration.

Prognosis of Raynaud’s Disease

The prospects for patients suffering from primary Raynaud’s disease usually are pretty good, with little morbidity and no mortality rate. In very rare situations, however, low oxygen supply in the affected part of the body can result in necrosis.

The prognosis for patients suffering from secondary Raynaud’s phenomenon is closely correlated to the underlying cause and disease. The prognosis for the patient’s digits depends on the extremity of the low oxygen supply and the efficiency of movements to reestablish the flow of blood.
Review Questions

The correct answers can be found below the references.

1. A 20-year-old woman complains about extreme sensitivity to the cold atmosphere with pallor color of the skin for few minutes. Capillaroscopy is showing inflamed vessels. What could be the possible diagnosis?

   A. Myasthenia Gravis  
   B. Neuropathy  
   C. Myopathy  
   D. Raynaud’s Disease

2. A smoker suffering from rheumatoid arthritis complains of discoloration of the periphery of the digits. What could be the most likely diagnosis?

   A. Raynaud’s disease  
   B. Raynaud’s phenomenon  
   C. Sjogren’s syndrome  
   D. Acromegaly

3. Which of the following are the diagnostic criteria for primary Raynaud’s?

   A. Lack of necrosis  
   B. Nephropathy  
   C. Hypertension  
   D. Renal Failure

References


Correct answers: 1D, 2B, 3A

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