Hand and Foot Color Change: Diagnosis and Management

Dustin E. Fleck, MD,* Mark F. Hoeltzel, MD*

Division of Pediatric Rheumatology, Department of Pediatrics, University of Michigan, Ann Arbor, MI

Education Gap

Primary care clinicians are challenged to evaluate an array of different hand and foot color changes in kids, as treatment may range from reassurance of a benign, self-limited condition to further diagnostic evaluation and treatment with vasodilator pharmacotherapy. The most common and well-known causes of these color changes are Raynaud phenomenon, acrocyanosis, and the more rare but serious erythromelalgia. Clinicians should be aware of the clinical presentation, symptoms, etiologic origins, diagnostic evaluation, treatment, and potential complications of Raynaud phenomenon, acrocyanosis, and erythromelalgia in children.

Objectives After completing this article, readers should be able to:

1. Identify the various causes of hand and foot color change in children and adolescents.
2. Recognize the differences in signs and symptoms of acrocyanosis, erythromelalgia, and Raynaud phenomenon.
3. Recognize complications associated with acrocyanosis, erythromelalgia, and Raynaud phenomenon.
4. Describe current treatments for acrocyanosis, erythromelalgia, and Raynaud phenomenon.

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ABBREVIATIONS

ADHD	attention-deficit/hyperactivity disorder
ANA	antinuclear antibody
POTS	postural tachycardia syndrome

ACROCYANOSIS

Clinical Presentation

Acrocyanosis is a clinically benign process that is known to cause alarm in patients and their parents. Acrocyanosis typically presents as symmetrical blue and/or purple discoloration in the peripheral extremities, usually either the hands or the feet (Figs 1, 2, 3, 4). In infants, acrocyanosis also includes the perioral area but not the lips or tongue, where central cyanosis becomes a concern. It is often seen after bathing, after feeding, or in a cool environment. It is evanescent and benign. The bluish discoloration in acrocyanosis is often asymptomatic, without clear demarcation of color change. Acrocyanosis episodes can be either precipitated or

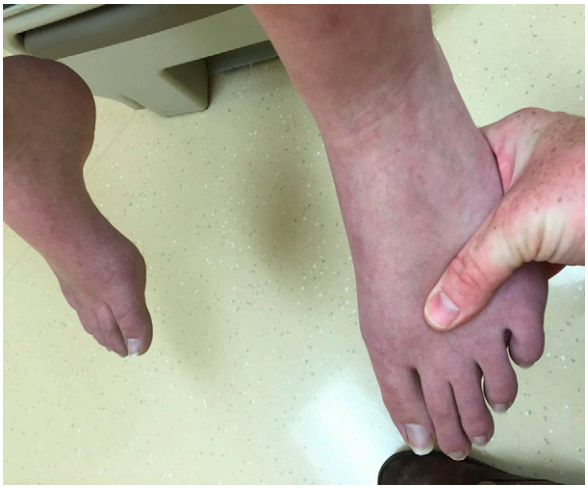

Figure 1. Teenage girl with bilateral acrocyanosis of her feet. Note the purplish discoloration, with no clear area of demarcation.

exacerbated by external factors, such as cold temperatures. Acrocyanosis may also be a process secondary to an underlying systemic disease or a side effect of certain medications.

Although sometimes confused with central cyanosis associated with hypoxemia, patients with acrocyanosis lack central features of cyanosis, such as cyanosis of the lips and tongue. Acrocyanosis is also exacerbated with the limb in a dependent position and will likely resolve when the limb is placed horizontally. The presence of acrocyanosis on the hands and feet is usually symmetrical and is often accompanied by hyperhidrosis. Acrocyanosis is common in the 2nd and 3rd decades of life, but its frequent presentation in adolescents makes this a common complaint in the pediatric clinic. (1) There are currently no clear diagnostic guidelines for acrocyanosis, and the diagnosis is usually established clinically. The true prevalence of acrocyanosis in the pediatric population is unknown, but in adults, it is found to be around 10% to 15% (2), with a female predominance. Geographic location is a major factor in prevalence, since environmental factors such as climate (cold temperature) can exacerbate this condition.

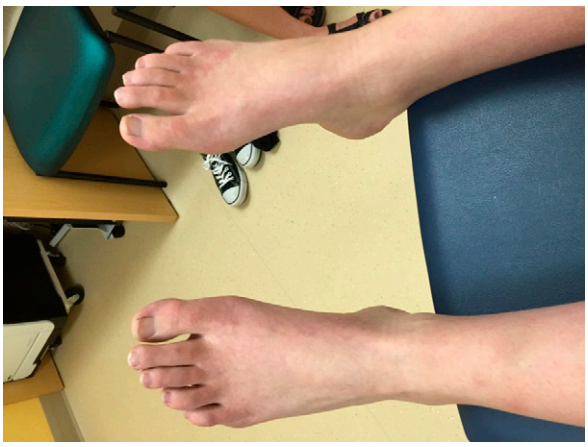

Figure 2. The same patient as in Fig 1 after elevation of her lower extremities for 2 minutes. Note the full resolution of color change.

Etiologic Origins

Primary Acrocyanosis. Acrocyanosis usually manifests as a benign condition with no associated comorbid diagnosis. This is commonly referred to as *primary acrocyanosis*. The underlying mechanism of acrocyanosis is now believed to be a result of a chronic vasospastic process of the small cutaneous arteries. This causes capillaries and postcapillary venules to compensate by dilating, which can lead to venous pooling in the distal extremities, resulting in cyanosis and hyperhidrosis. It has been postulated that chronic vasospasm of the small cutaneous arteries may be an end result of an overactive sympathetic reflex. However, attempts at local blockade of the autonomic ganglia does not markedly affect the venous pooling, as shown by persistent prolonged blanching of the cyanotic areas. Attempts at manipulation of the autonomic system do result in increase of skin temperature of the affected areas. (3) These results indicate that an abnormal autonomic response is not a sufficient explanation for the findings seen in acrocyanosis. Histologic changes for primary acrocyanosis are not specific. They include prominent dilated papillary and subpapillary vessels sometimes associated with dilated superficial capillaries, local edema, or fibrosis. (4) It is common to see an increased abundance of arteriovenous anastomoses at histologic evaluation. (5)

Secondary Acrocyanosis. Frequently, acrocyanosis can be associated with psychostimulant medications such as attention-deficit/hyperactivity disorder (ADHD) medications, which are commonly prescribed in the pediatric population. (6) On rare occasions, acrocyanosis may be a sign of a more serious process, and the physiology of secondary acrocyanosis varies, depending on the underlying cause. Acrocyanosis is known to manifest with a high prevalence in patients with anorexia nervosa, ranging from a clinician-observed 21% to 40%, (7)(8) with patient-reported (via questionnaire) prevalence of up to around 80%. (9) Acrocyanosis associated with anorexia nervosa is likely mediated by impaired thermoregulation and decreased responsiveness for vasoactive substrates, with an end result of venoconstriction. Acrocyanosis has been reported with benign and malignant neoplasms. (10) Up to 50% of patients with postural tachycardia syndrome (POTS) will have acrocyanosis. Acrocyanosis in patients with POTS is gravity dependent and pronounced, often extending much further up the affected extremity than seen with primary acrocyanosis. Patients with POTS likely have abnormal arterial vasoconstriction in conjunction with

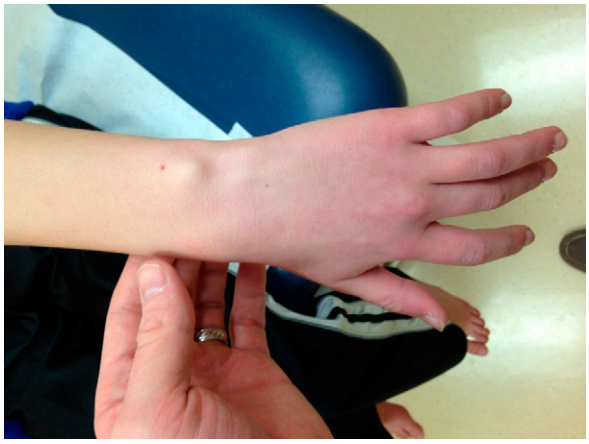

Figure 3. Acrocyanosis in the hand of a 10-year-old boy.

decreased overall blood flow in the arms and legs, likely secondary to decreased cutaneous neuronal nitric oxide production. (11) Medications used in the outpatient pediatric setting that may induce acrocyanosis include psychostimulants and tricyclic antidepressants. Acrocyanosis can also be seen in infections, disseminated intravascular coagulation, and spinal cord injury (12), as well as genetic and/or heritable conditions, such as mitochondrial diseases (13) and Ehlers-Danlos syndrome. (14)

Evaluation

Diagnosis of primary acrocyanosis is primarily based on a through clinical history and physical examination. No laboratory investigations have been shown to be helpful in the evaluation of acrocyanosis. History and physical examination will provide insight on possible secondary causes of acrocyanosis, such as medications, eating disorders, malignancy, or infection.

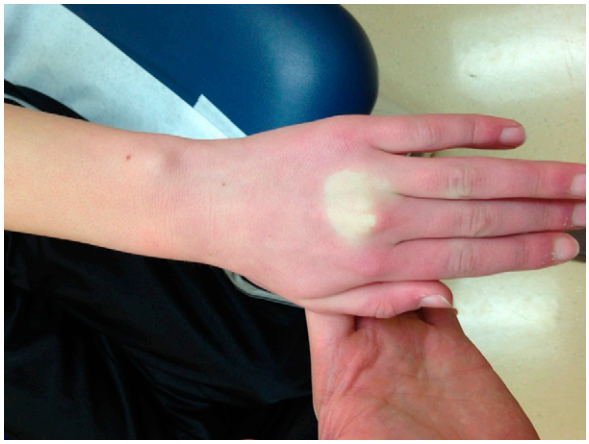

Figure 4. Five seconds after applying pressure to the hand of the same patient as in Fig 3, the blanching persists, which is consistent with the delayed capillary refill seen in acrocyanosis.

Capillaroscopy has been widely studied in the evaluation of acrocyanosis and is performed with a magnification system that ranges from ×20 to ×600 by using a dedicated capillary scope. In the primary care setting, a capillary scope may not be readily available, so an otoscope or ophthalmoscope may be used. However, owing to inadequate magnification produced with these devices (×2.5 magnification with a standard otoscope, ×15 magnification with a standard ophthalmoscope), adequate visualization of the capillary beds is not possible. Capillaroscopy can be used at the conjunctiva, lip, or tongue, but is more commonly used at the nail beds. Findings of acrocyanosis can include dilated capillary loops and/or pericapillary edema. (15) These findings are not always present in patients with acrocyanosis, nor are they specific to this disease process, as they can be seen in other connective tissue disorders.

Treatment

One of the most important aspects of treating patients with acrocyanosis is providing reassurance, since this is a benign condition with no long-term complications. Beyond reassurance, treatment for primary acrocyanosis is usually conservative, such as avoiding cold exposure and trauma and drinking adequate fluids.

If an underlying cause is associated with acrocyanosis, therapy should be directed at the primary diagnosis. If the underlying cause is thought to be secondary to medications such as ADHD medications, severity of the symptoms in combination with the benefit received from the medication will demonstrate whether the medication should be continued. Only in rare cases do symptoms impose a clinically significant burden that warrants discontinuation.

ERYTHROMELALGIA

Clinical Presentation

The term *erythromelalgia* consists of the Greek words "erythros" (red), "melos" (extremity), and "algos" (pain), which adequately describes this condition. Erythromelalgia is characterized by episodes of painful and red extremities, primarily the hands and feet (Fig 5); however, on rare occasions it can be isolated to other places, such as the ears. Duration of an attack is highly variable and can last 2 to 3 hours, or the condition may be present constantly, with no periods of relief. Erythromelalgia episodes can be induced by heat exposure and exercise and cause the affected areas to be warm or hot, both subjectively and objectively. This is different than other forms of hand color changes, such as those seen in Raynaud phenomenon and acrocyanosis. Patients with erythromelalgia will find some relief when the affected areas

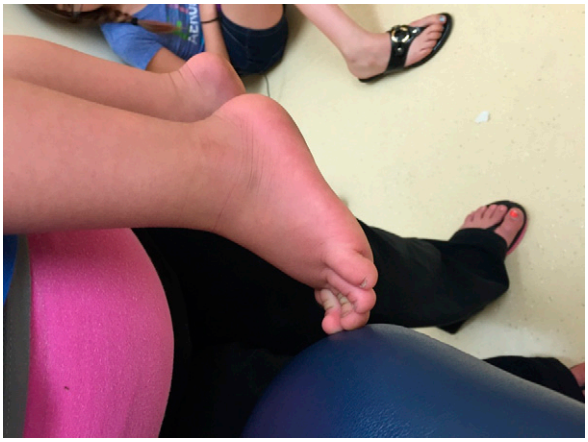

Figure 5. A 2-year-old with erythromelalgia of the feet. Note the erythema on the acral surface of the foot, with no marked involvement of the dorsum.

are exposed to cold temperatures. Inheritable forms of erythromelalgia exist and make up a small portion of cases. These are associated with autosomal dominant mutations in sodium channel protein Na(V)1.7 subunit (*SCN9A*). (16) These mutations are generally not found in nonheritable cases of erythromelalgia. Erythromelalgia is the least prevalent of the hand color changes in children but has the highest associated morbidity, given the severity of symptoms in relation to its general resistance to multiple therapies. In children, erythromelalgia is extremely rare and the prevalence is unknown, but it has been found to have a female predominance and usually manifests during adolescence. (17)

Etiologic Origins

There has been some debate regarding the classification of erythromelalgia. Like acrocyanosis, it is generally categorized into primary and secondary subtypes. Many have proposed further classifications, including adult onset, childhood onset, aspirin responsive, and aspirin nonresponsive. For the purpose of this review article, we will discuss erythromelalgia in terms of primary and secondary subtypes, with focus on the primary subtype. Secondary erythromelalgia is extremely rare in children but constitutes 40% of adult-onset cases. (17)

Primary Idiopathic Erythromelalgia. Owing to the rare nature of erythromelalgia in children, data are scarce. In pediatric patients with erythromelalgia, it has been shown that most have intermittent episodes (81%), with approximately one-fifth of affected patients experiencing constant symptoms. Nearly all patients report redness, pain, and warmth. A retrospective study showed that 100% of patients have involvement of the feet, with less than 50% having symptoms proximal to the feet or in the upper extremities. The severe nature of symptoms and pain associated with erythromelalgia causes moderate to severe physical limitations in most patients. (18) This has psychological implications, with multiple reported suicides in both pediatric and adult populations. (18)(19) The pathophysiology of primary erythromelalgia is not well understood. It has been shown in children that 59% demonstrate evidence of small-fiber neuropathy on neurophysiological studies. Electromyography and nerve conduction tests have not demonstrated any large-fiber involvement. (18) Histologic evaluation of adult patients with primary erythromelalgia has shown that 81% have epidermal fiber counts less than the 5th percentile. Also, perivascular lymphocytic inflammation and smooth-muscle hyperplasia was noted in most patients. None of the patients who underwent biopsy demonstrated thrombi. (20) The pathophysiology of erythromelalgia is not well understood. Familial mutations linked to chromosomal arm 2q, leading to abnormalities in voltage-gated sodium channels, have been described. (21) Many theories have been postulated to explain nonfamilial cases, including hypersensitivity of C-fibers, (22) postganglionic sympathetic dysfunction, and arteriovenous shunting that leads to imbalances in skin perfusion. (23)

Secondary Erythromelalgia. As previously mentioned, secondary erythromelalgia is rare in children. In adults, the most common causes of secondary erythromelalgia are myeloproliferative disorders with thrombocythemia. Erythromelalgia becomes evident up to 2.5 years prior to diagnosis of the myeloproliferative disorder. Only a few cases of erythromelalgia develop after the diagnosis is established. (24) Like the primary form of disease, secondary erythromelalgia is also induced by exercise and warm exposure. In contrast to the primary form, episodes are often asymmetrical. (25) Secondary forms are more often associated with complications, such as distal digit necrosis. Histologic examination of secondary erythromelalgia, particularly thrombocythemia related, shows isolated arteriolar involvement with sparing of capillaries, nerves, and venules. Arteriole changes include endothelial swelling and vessel thickening, with or without luminal occlusion by thrombi. (26)

Evaluation

Erythromelalgia is a clinical diagnosis based on a thorough physical examination and patient history. Care should be taken to assess any other systemic symptoms or physical examination findings. Fabry disease, a genetic condition caused by mutations in α-galactosidase, can occur with similar manifestations of severe neuropathic limb pain. This disease is often associated with other manifestations, such as telangiectasia, angiokeratomas, and renal, ocular, and auditory manifestations. (27) Complete blood counts can be helpful in assessing

polycythemia or thrombocythemia that can be seen in secondary erythromelalgia, particularly in adult patients or older adolescents. Genetic testing for mutations in *SCN9A* can be considered to evaluate heritable forms. Neurophysiological and vascular studies may demonstrate abnormalities but are not diagnostic.

Treatment

Most patients with secondary erythromelalgia associated with thrombocythemia will respond to aspirin therapy and have substantially reduced morbidity. Primary idiopathic erythromelalgia has no universally effective therapy. Topical lidocaine can be one of the most useful therapies and has been found to be effective in 55% of adult patients. (28) Mexiletine, a nonselective voltage-gated sodium channel blocker, has also been reported to be effective in children with primary erythromelalgia. (29) In a retrospective review of pediatric primary erythromelalgia, aspirin was found to be helpful in only 7% of patients. The medications that seem most beneficial include antidepressants and gabapentin. However, these were only found to have any benefit in 40% and 33% of patients, respectively. (18) Therapies that have been found to be relatively ineffective in most patients include anti-inflammatories (glucocorticoids, nonsteroidal anti-inflammatory drugs), antihistamines, vasodilators, biofeedback, anticonvulsants, homeopathic agents, and sympathectomy. (18)

Most patients have symptomatic relief with exposure to cold, and the use of cooling gloves can be helpful. Complications such as frostbite and immersion injuries can arise when patients seek relief from soaking and cold exposure. There have been reported cases of self-induced near-fatal hypothermia, (30) as well the death of a patient secondary to infection caused by prolonged soaking of the extremities. (18)

RAYNAUD PHENOMENON

Clinical Presentation

Raynaud phenomenon is a well-known vasospastic disorder, primarily of the distal extremities—particularly the fingers and toes—but it has also been known to involve other areas of the body, including the ears, nose, and nipples. Much like the other causes of hand and foot color change, Raynaud phenomenon is categorized as primary and secondary. Primary Raynaud phenomenon is considered idiopathic. Secondary Raynaud phenomenon is often associated with connective tissue disorders and rheumatologic processes, such as lupus, scleroderma, and mixed connective tissue disorders. Raynaud phenomenon is characterized by episodic color change, including pallor, cyanosis (Fig 6, 7), and/or rubor. The color changes are classified as monophasic, biphasic, or triphasic in relation to how many phases of color changes take place during an episode. In children, mono-, bi- and triphasic variants of Raynaud phenomenon occur with nearly equal frequency, with a slight propensity for monophasic color change. (31) In contrast to acrocyanosis, the color changes seen with Raynaud phenomenon have a clear area of demarcation. Most patients with both primary and secondary Raynaud phenomenon experience pain, discomfort, or numbness in the affected areas during an episode. However, some patients may be asymptomatic. Episodes can range from minutes to hours. The frequency is highly variable and ranges from seldom to multiple times per day. Attacks can be precipitated by environmental factors, such as exposure to cold or physical trauma. Smoking, heavy alcohol consumption, caffeine, or vasoactive medications can precipitate episodes. Certain medications, such as ADHD medications, can

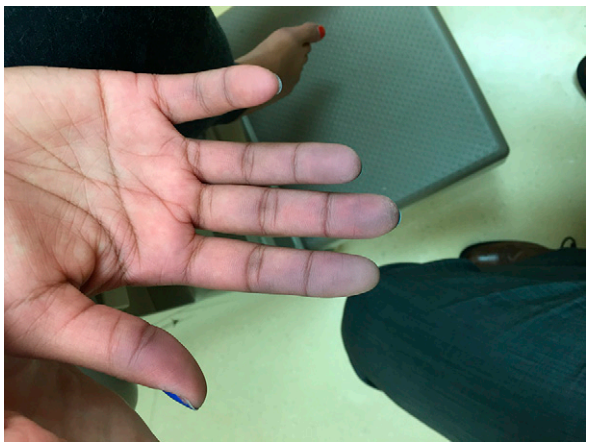

Figure 6. Teenage girl with secondary Raynaud phenomenon (cyanotic phase). Note that the color change is distal to the metacarpophalangeal joints, and there is evidence of skin breakdown in the tip of the third digit.

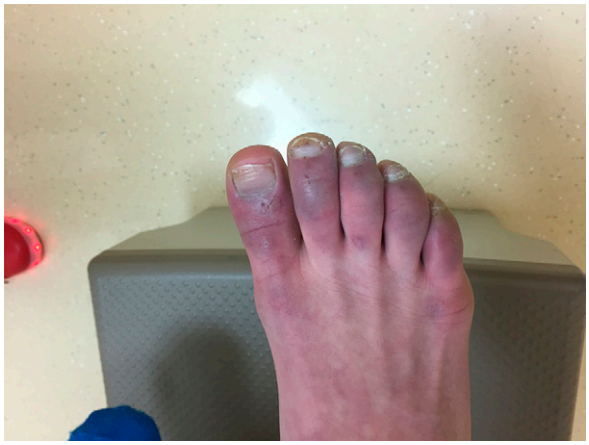

Figure 7. Raynaud phenomenon in the toes of a 16-year-old female. Note that the color change is distal to the metatarsophalangeal joints, with clear area of skin demarcation. Some area of skin breakdown is evident around the nail bed of the first digit.

predispose individuals to Raynaud phenomenon. Attempts have been made to estimate the prevalence of Raynaud phenomenon in pediatric patients. A self-reported questionnaire among children 12 to 15 years of age demonstrated a total prevalence of 15%, with a female predominance; there was a prevalence of 18% for girls versus 12% for boys. (32)

Etiologic Origins

Primary Raynaud Phenomenon. Primary Raynaud phenomenon is an isolated process not in association with any other disease process. Primary Raynaud phenomenon constitutes most cases of Raynaud phenomenon, in both children and adults. Primary Raynaud phenomenon generally follows a more benign course than its secondary form. To date, the pathophysiology behind the process is not clearly understood, but it is believed to have many possible causes, such as autonomic dysregulation, abnormal regulation of vasomotor response, and intravascular abnormalities that may predispose individuals to attacks. Regulation of blood flow and vascular tone is the end result of a delicate equilibrium of vasoconstriction and vasodilation. In individuals who are predisposed to Raynaud phenomenon, disruption of this balance by things such as trauma, temperature, or stress lead to an exaggerated vascular response. The female predominance seen in Raynaud phenomenon is likely mediated by the effects of estrogen on the vascular tone. (33) Exposure to cold is the classical trigger for Raynaud phenomenon attacks.

The abnormal vascular response takes place in multiple areas of the circulatory system, including pre- and postcapillary venules, arterioles, and arteries. Vasoconstriction of all elements leads to poor blood perfusion to the affected area, which creates the color phase of pallor (white). The hypoxic tissue responds by vasodilating the precapillary venules, leading to the accumulation of desaturated blood, which gives way to the cyanotic phase of Raynaud phenomenon. In the third phase of erythema and/or rubor, all elements—including pre- and postcapillary venules—dilate, which can lead to hyperperfusion and hyperemia of the affected area. (34)

Secondary Raynaud Phenomenon. The manifestation of secondary Raynaud phenomenon is similar to that of primary Raynaud phenomenon, but the difference lies in its severity and complications. Attacks of secondary Raynaud phenomenon are generally more severe and frequent and can be found in an asymmetrical pattern. Secondary Raynaud phenomenon is more often associated with complications such as skin breakdown, digital ulcerations, and, sometimes, ischemic self-amputation. The most common conditions associated with secondary Raynaud phenomenon are systemic autoimmune disease, such as systemic lupus erythematous, juvenile dermatomyositis, scleroderma, mixed connective tissue disease, Sjogren syndrome, and undifferentiated connective tissue diseases. It can also be present in various forms of vasculitis.

The more aggressive course of secondary Raynaud phenomenon is both explained and reflected in the pathophysiology, as well as the histology. In secondary Raynaud phenomenon associated with connective tissue disorders, endothelial injury is the likely contributing factor, which leads to structural vessel changes and disruption in vasoactive regulation. Histologic evaluations have shown infiltration of lymphocytes and monocytes. In addition, vessel fibrosis and intimal thickening are seen on the basis of abnormal synthesis of the extracellular matrix. These changes lead to obliteration of the lumen of blood vessels, which explains the higher incidence of ischemic-related injuries when compared to primary Raynaud phenomenon. (35) Vascular wall damage seen in connective tissue –related secondary Raynaud phenomenon leads to subendothelial collagen exposure with subsequent platelet activation. (36)

Evaluation

Diagnosis of Raynaud phenomenon is primarily centered on history and physical examination findings. There have been multiple proposed classification criteria for Raynaud phenomenon. However, none has been universally accepted or validated for pediatric patients. Given the intermittent nature of Raynaud phenomenon episodes, it is common for them to go unwitnessed during a clinical visit. This necessitates a descriptive history of the episode from the patient. Readily available cameras on smartphones have made photographing episodes easy, and many patients may provide pictures during their visit. Asking patients and their families to take pictures of future episodes and then either sending them to your office or bringing them to a future clinic visit can help provide a more objective picture of the patient's episodes. Physical examination should emphasize examination of the affected areas and assessment of the evidence of chronic or ischemic changes, such as skin ulceration or disrupted skin integrity. Capillaroscopy is a very important component in the evaluation of Raynaud disease. In primary Raynaud disease, capillaroscopic findings are likely to be normal. Abnormal findings can include capillary enlargement, decreased overall number of capillaries, and telangiectasias. Patients with these abnormal findings are more likely to develop a connective tissue disorder. (37)

Evaluation for autoantibodies can be helpful in differentiating primary from secondary Raynaud phenomenon. Positive antinuclear antibody (ANA) results does not necessarily indicate secondary Raynaud phenomenon, since there is a high rate of false-positive findings for ANA testing

in healthy children. (38) Laboratory investigation is useful in screening for and assessing the underlying causes of Raynaud phenomenon, but results should be interpreted along with the clinical status of the patient. Autoantibody evaluation becomes more necessary in the context of severe Raynaud phenomenon or associated chronic changes at examination, such as skin breakdown or periungual capillary change. One retrospective study in the pediatric population of children with Raynaud phenomenon demonstrated a positive ANA finding in 25% of primary Raynaud phenomenon cases and in 85% of secondary Raynaud phenomenon cases. Overall, ANA titers associated with primary Raynaud phenomenon were lower than those associated with the secondary form. (18) It remains unknown whether autoantibodies have a direct pathophysiological link to Raynaud disease, but it has been found that anti-Scl-70 seen in patients with scleroderma can induce endothelial apoptosis, possibly contributing to Raynaud phenomenon. (39) Autoantibodies may also interact with vasoactive intestinal peptide. (40) A higher incidence of antiphospholipid antibodies has been found in patients with Raynaud phenomenon, but the significance of this is not yet clear. (18) Other advanced methods are used in assessing Raynaud phenomenon, such as laser Doppler imaging, angiography, and thermal imaging, but these are not predictive of severity or responsiveness to treatment. For that reason, they have no real clinical utility at this time and are reserved for research-related uses.

Treatment

The aim of therapy is the reduction of ischemic episodes. This is generally accomplished by therapies aimed at counteracting and preventing the vasoconstrictive process. This is more readily accomplished in treating primary Raynaud phenomenon than secondary Raynaud phenomenon (particularly associated with scleroderma). Secondary forms have a tendency to be refractory to therapy, which are likely related to the extensive vascular remodeling that takes place, which already compromises vascular flow to the digits—even in the absence of external stimuli that lead to vasoconstriction.

Typically, first-line therapy for primary Raynaud phenomenon is conservative. This consists of avoiding cold temperatures and emotional and physical stress. In terms of exposure to cold, emphasis is placed on adequately protecting the affected areas, such as wearing gloves and multiple layers of socks. Individuals should also focus on keeping their core temperature warm to prevent peripheral vasoconstriction. Avoidance of offending agents, such as cigarette smoke, alcohol, and vasoconstrictive medications, is important.

If conservative measures fail, second-line therapy (first-line pharmacotherapy) for primary and secondary Raynaud phenomenon is dihydropyridine calcium channel blockers, such as amlodipine and nifedipine. (41) These have been effective in decreasing the frequency and severity of flares. For patients who fail to respond to calcium channel blockers, multiple other agents exist. These include iloprost (synthetic analogue of prostaglandin I2) and phosphodiesterase inhibitors, such as sildenafil and tadalafil. (42) Another option includes topical nitroglycerin. However, this is associated with a high side-effect profile of hypotension and headaches, which makes its use limited. These agents all work by actively dilating the peripheral blood vessels, increasing blood flow, and decreasing episodes of ischemia. Iloprost is very effective for secondary Raynaud phenomenon associated with scleroderma; it decreases both the severity and incidence of digital ulcerations. (43) In general, treating the underlying disease with immunosuppressive medications can help decrease secondary Raynaud phenomenon associated with autoimmune and/or connective tissue disease. This applies more to lupus, vasculitis, and other systemic diseases. Scleroderma and mixed connective tissue diseases that have associated Raynaud phenomenon are generally not responsive to treatment of the underlying condition.

SUMMARY

1. On the basis of primarily consensus, owing to lack of relevant clinical studies at this time, there are no universally accepted diagnostic criteria for acrocyanosis, erythromelalgia, and Raynaud phenomenon.
2. On the basis of primarily consensus, owing to lack of relevant clinical studies at this time, providing reassurance is generally sufficient, along with conservative measures of hydration and avoidance of cold in the treatment of acrocyanosis.
3. On the basis of some evidence, topical lidocaine, (28) mexiletine, (29) gabapentin, and antidepressants (18) have been found to be effective in some patients in the treatment of erythromelalgia.
4. On the basis of primarily consensus, owing to lack of relevant clinical studies at this time, mild Raynaud phenomenon can initially be treated with conservative measures, such as avoiding exposure to cold and vasoconstrictive substances.
5. On the basis of strong research evidence and consensus, first-line pharmacotherapy for treatment of Raynaud phenomenon consists of calcium channel blockers, such as amlodipine and nifedipine. (41) Phosphodiesterase inhibitors (42) and iloprost (43) have also been found to be effective in treating Raynaud phenomenon.

References for this article are at http://pedsinreview.aappublications.org/content/38/11/511.

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1. A previously healthy 14-year-old presents to the office with her mother in January due to a concern with her feet turning blue when she goes outside. She and her mother have not noted any color change of her face. She otherwise feels well. When she comes back inside and lays down the color of her feet returns to normal. She has not noted any other rashes. She is not on any medications. Her menstrual periods have been normal. She has not had a significant weight gain or weight loss and her BMI is at the 75th percentile. Her physical exam in the office is unremarkable. Which of the following is the most likely diagnosis?

   A. Primary acrocyanosis.
   B. Primary idiopathic erythromelalgia.
   C. Secondary erythromelalgia.
   D. Secondary Raynaud's.
   E. Systemic lupus erythematosus.

2. For the same 14-year-old girl in the previous question which of the following is the most appropriate laboratory testing?

   A. Antinuclear antibody.
   B. Complete blood count and serum electrolyes.
   C. Erythrocyte sedimentation rate.
   D. Genetic testing for SCN9A mutation.
   E. Laboratory testing not indicated.

3. A previously healthy 17-year-old boy presents to the office with a 4-week history of his feet becoming red and warm when he exercises. He has associated pain. He gets relief by taking his shoes and socks off and applying an ice pack. He has photos which show redness of the soles of his feet and plantar aspects of the toes but the dorsal aspects of his feet appear normal. His physical examination findings in the office are normal. Which of the following is the most likely diagnosis?

   A. Fabry disease.
   B. Myeloproliferative disorder with thrombocythemia.
   C. Primary idiopathic erythromelalgia.
   D. Secondary acrocyanosis.
   E. Secondary Raynaud phenomenon.

4. A 16-year-old girl presents to the office in February with a 5-week history of her fingers turning white when she goes outside in cold weather. She has photos that show a clear area of demarcation. She has associated pain and numbness of the area. The episodes last 15 to 20 minutes. She has not noted any other rashes, fatigue, or weakness. Her physical examination findings are normal. A complete blood count, serum electrolyte levels, alanine aminotransferase level, aspartate aminotransferase level, blood urea nitrogen level, and creatinine level are normal. Erythrocyte sedimentation rate is 6 mm/hour. An antinuclear antibody test is positive at 1:40, and the double-stranded DNA antibody result is negative. Capillaroscopy findings are normal. Which of the following is the most appropriate next step in diagnosis?

   A. Angiography.
   B. Antiphospholipid antibodies.
   C. No further testing indicated.
   D. Rheumatoid factor.
   E. Thermal imaging.

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5. For the same 16-year-old girl as in the previous question, which of the following is the most appropriate initial treatment?

   A. Nifedipine.
   B. No treatment indicated unless the episodes become more severe.
   C. Sildenafil.
   D. Topical nitroglycerin.
   E. Wearing gloves in cold weather.

Parent Resources from the AAP at HealthyChildren.org

- Common Conditions in Newborns: https://www.healthychildren.org/English/ages-stages/baby/Pages/Common-Conditions-in-Newborns.aspx
- Apgar Scores: https://www.healthychildren.org/English/ages-stages/prenatal/delivery-beyond/pages/Apgar-Scores.aspx

For a comprehensive library of AAP parent handouts, please go to the *Pediatric Patient Education* site at http://patiented.aap.org.

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