

Q: When do Raynaud symptoms merit a workup for autoimmune rheumatic disease?

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A: Indications that Raynaud phenomenon may be the presenting manifestation of a systemic autoimmune rheumatic disease are older age at onset (ie, over age 30), male sex, asymmetric involvement, and prolonged and painful attacks that can be severe enough to cause ischemic digital ulceration or gangrene (FIGURE 1).

Hence, chronic and severe digital ischemia causing ulceration or infarction differentiates secondary from primary Raynaud phenomenon and should prompt an investigation for an autoimmune rheumatic process. When taking the history, the clinician should seek clues to an underlying autoimmune condition, such as arthralgia, heartburn, dysphagia, shortness of breath, cough, and should examine the patient for telltale signs such as puffy hands and fingers, sclerodactyly, digital pitting scars, loss of fingertip pulp tissue, telangiectasias, and calcinosis.

■ CLUES TO PRIMARY VS SECONDARY RAYNAUD PHENOMENON

A diagnostic algorithm of digital ischemia (FIGURE 2) illustrates the range of presentations and possible causes. In Raynaud phenomenon, cold temperature and emotional stress provoke reversible color changes of the fingers and toes. Intense vasospasm of the digital arteries produces three well-defined phases¹: white (pallor resulting from vasospasm), blue (dusky cyanosis due to deoxygenation of static venous blood) (FIGURE 1), and red (reactive hyperemia after the restoration of blood flow).

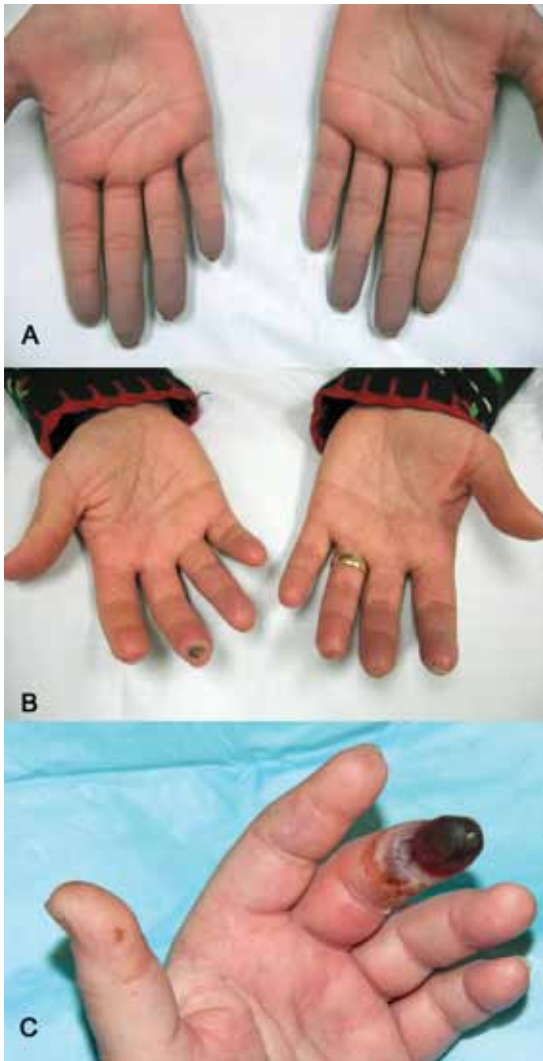


FIGURE 1. Evidence of digital ischemia in patients with systemic sclerosis: (A) cyanotic phase of Raynaud phenomenon showing blue discoloration of the fingers; (B) ischemic digital ulcers; and (C) digital gangrene.

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Ask about other clues, eg, arthralgia, heartburn, dysphagia, shortness of breath, cough

A diagnostic algorithm for digital ischemia

Digital ischemia

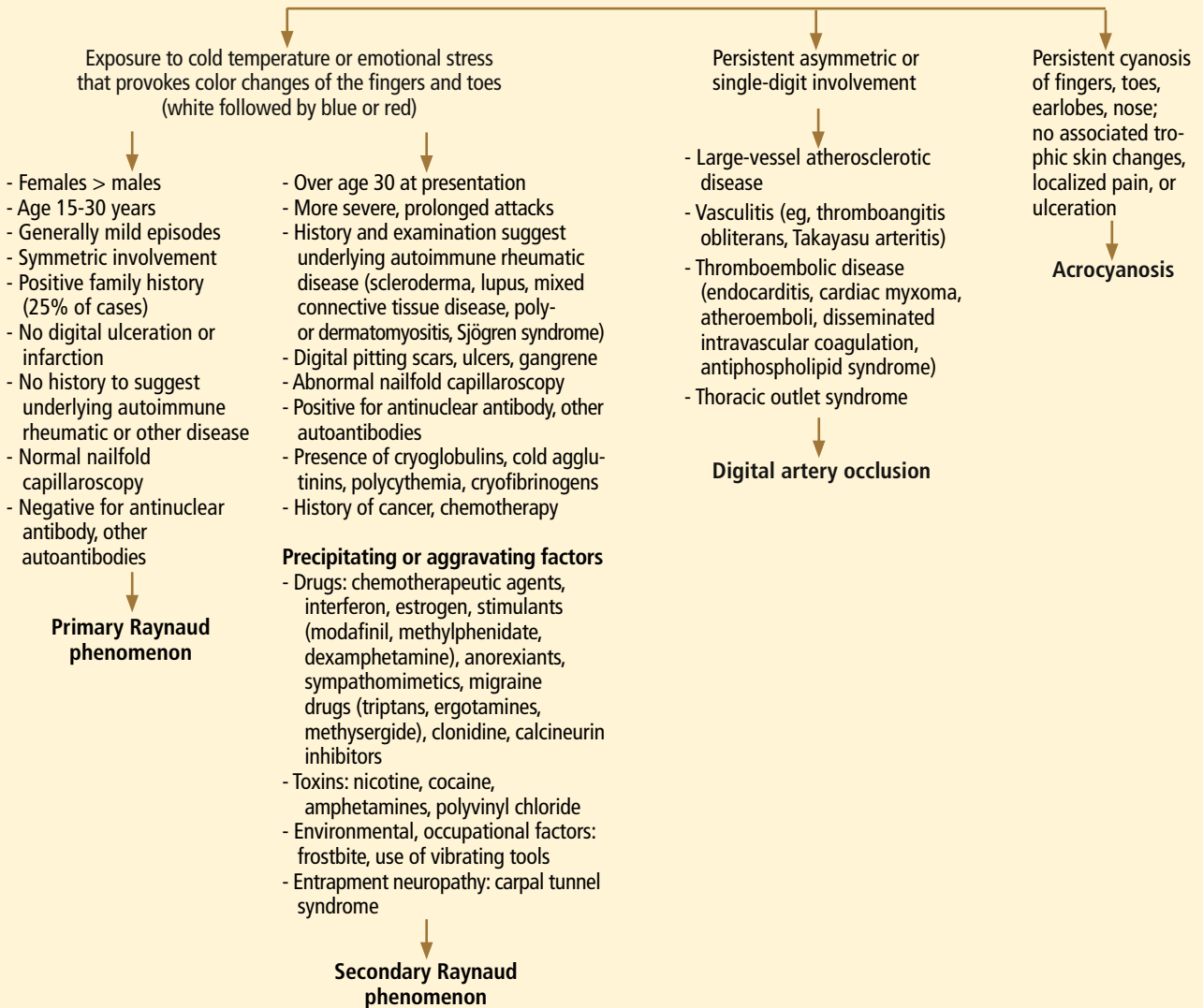


FIGURE 2

However, only about 60% of patients have all three color changes. The attacks are associated with paresthesias, an uncomfortable feeling of coldness in the fingers, and ischemic pain.

Primary Raynaud phenomenon

Primary or idiopathic Raynaud phenomenon is seen in 5% to 10% of the general population. It more commonly affects women ages 15 to 30, is generally mild, involves the digits symmetrically, and is sometimes familial. An increase in alpha-2 adrenergic responses

in the digital vessels leads to arterial vasospasm, an exaggerated physiologic response to cold temperatures.² Geographic variability in prevalence likely represents differences in mean outdoor temperatures,³ which is in part why attacks of primary Raynaud phenomenon tend to be worse in the winter months.⁴

Secondary Raynaud phenomenon

Raynaud phenomenon also often occurs in certain autoimmune rheumatic diseases (secondary Raynaud phenomenon): for example,

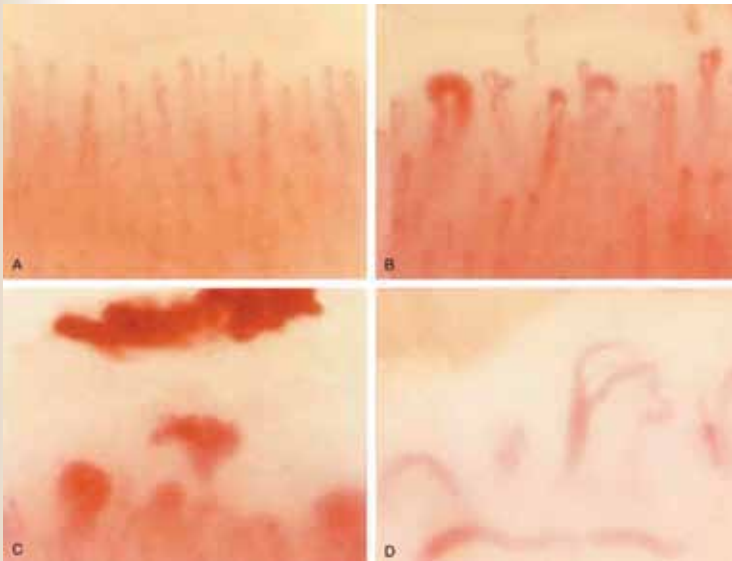


FIGURE 3. (A) Normal nailfold pattern on nailfold capillaroscopy (magnification $\times 200$). (B) In the early stages of scleroderma, capillaroscopy shows well-preserved capillary architecture and density, as well as dilated and giant capillaries. (C) In active scleroderma, it shows numerous giant capillaries and hemorrhages, a moderate loss of capillaries, and disorganized capillary architecture. (D) In late scleroderma, the capillary architecture is severely disorganized, with “dropouts,” arborized capillaries, and the absence of giant capillaries.

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it is seen in scleroderma (90% to 95% of patients), mixed connective tissue disease (85%), systemic lupus erythematosus (40%), antisynthetase syndrome (40%), and sometimes in patients with other autoimmune rheumatic diseases. It may also be seen in hematologic disorders (cryoglobulinemia, cryofibrinogenemia, paraproteinemias, cold agglutinin disease, and polycythemia rubra vera), and it can also result from environmental and occupational exposures (frostbite, use of vibrating tools) and from exposure to certain drugs and toxins, such as polyvinyl chloride (FIGURE 2).

Acrocyanosis, a benign neurohormonal condition, should be included in the differential diagnosis for Raynaud phenomenon. Raynaud phenomenon is episodic, whereas acrocyanosis leads to persistent cyanosis of the acral body parts (fingers, toes) that is exacerbated by cold temperatures. However, the

trophic skin changes, localized pain, and ulceration are not seen in acrocyanosis.

■ NAILFOLD CAPILLAROSCOPY: A KEY PART OF THE WORKUP

Nailfold capillaroscopy should be part of the evaluation of patients with Raynaud phenomenon (FIGURE 3), as it is one of the most reliable tests for distinguishing between primary and secondary Raynaud phenomenon.⁵ The sensitivity of the American College of Rheumatology classification criteria for systemic sclerosis increases significantly with the addition of nailfold capillary abnormalities.^{6,7}

A stereomicroscope or videocapillaroscope is usually recommended to evaluate nailfold capillary morphology,⁵ but if such equipment is not available, a regular ophthalmoscope (with the lens set at 20 diopters or higher for better resolution) can serve the purpose at the bedside.⁸ A drop of mineral oil is placed on the nailfold to improve the image resolution, as it makes the horny layer of the cuticle transparent.

Abnormal patterns include dilated and enlarged capillary loops, disorganized capillaries, “dropouts” (avascular areas), microhemorrhages, and arborized capillaries (FIGURE 3).⁵ At no additional cost, the presence of these microvascular changes would add to the suspicion of secondary Raynaud phenomenon (negative predictive value of 93%).⁹ In addition, evolving capillaroscopic changes can be seen during follow-up visits, indicating the progressive nature of the microvasculopathy seen in these autoimmune rheumatic diseases.¹⁰

■ ADDITIONAL TESTING

If an underlying autoimmune rheumatic disease is suspected, laboratory testing should include a complete blood cell count, an erythrocyte sedimentation rate, and an antinuclear antibody (ANA) assay. If the ANA assay is negative, no further testing is usually necessary; however, a positive test should alert the clinician to consider an underlying autoimmune rheumatic process (negative predictive value of 93%).⁹ In a patient presenting with Raynaud phenomenon, a positive ANA test

(even in the absence of other symptoms) warrants more frequent follow-up, urinalysis, and perhaps referral to a rheumatologist.

In the case of a positive ANA test, before ordering additional autoantibody tests, it is useful to consider the relevant non-Raynaud clinical manifestations. Indiscriminate ordering of a battery of autoantibodies should be avoided because of significant added cost and because it is not likely to provide additional

information to guide management.

On the other hand, these more specific antibody tests may be of value in confirming the diagnosis suggested by the clinical profile of specific autoimmune rheumatic diseases, eg, anti-double-stranded DNA¹¹ and anti-Smith¹² antibodies for lupus, anti-topoisomerase I (Scl-70) and anti-centromere antibodies for scleroderma,¹³ and anti-synthetase (eg, anti-Jo-1) antibodies for autoimmune myositis.^{14,15} ■

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