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Beyond Cold Fingers: A Practical Approach to the Management of Raynaud's Phenomenon

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Introduction

Raynaud's phenomenon (RP) is a vasospastic condition affecting the acral and digital arteries, characterized by well-demarcated colour changes of the fingers and toes, typically progressing from pallor to cyanosis and then reactive erythema. It is commonly triggered by exposure to cold temperatures or emotional stress. First described by Maurice Raynaud in 1862, RP remains one of the most frequently encountered vascular complaints in dermatology practice.[1] RP is classified into two distinct subtypes with markedly different clinical trajectories. Primary RP is relatively common, affecting approximately 2–12% of populations worldwide, with a notable female predominance and peak onset before the age of 30.[1,2] It follows a benign, nonprogressive course without structural endovascular pathology or tissue destruction, though it may significantly impair quality of life.

Secondary RP (SRP) occurs in association with a variety of conditions, most notably autoimmune connective tissue diseases (ACTDs), particularly systemic sclerosis (SSc), in which it affects 90–95% of patients.[1,3] Unlike primary RP, SRP is accompanied by biochemical and structural abnormalities within the microvasculature, including endovascular remodelling, intimal proliferation, fibrosis, and progressive luminal narrowing. These changes induce prolonged tissue ischemia with severe clinical consequences such as digital pitting, painful ulceration, gangrene, and in severe cases, auto-amputation.[3,4] Importantly, the vasculopathy of SRP extends beyond the digital circulation. Parallel vascular involvement of the heart, lungs, kidneys, and esophagus may contribute to major systemic manifestations,

including interstitial pulmonary fibrosis, pulmonary arterial hypertension, scleroderma renal crisis, and gastroesophageal reflux disease.[1,5]

Given that RP may serve as the earliest manifestation of an evolving systemic disease, with vasospastic symptoms predating overt ACTD by up to 20 years, dermatologists are uniquely positioned to identify, risk-stratify, and intervene early.[1] Distinguishing primary from secondary RP is essential and requires a careful history, review of systems, and physical examination for features of underlying ACTD, along with nailfold capillaroscopy and targeted serologic evaluation guided by clinical findings. This review provides a practical, evidence-based approach to the management of both primary and secondary RP, progressing from foundational lifestyle modifications through pharmacologic therapy and surgical intervention **(see Figure 1)**.

Lifestyle Modifications

Lifestyle interventions remain the foundation of RP management and should be recommended for all patients irrespective of the disease subtype. For many individuals with primary RP, conservative measures alone provide adequate symptom control, and pharmacotherapy may be deferred entirely.[6]

Patients should be counselled extensively on avoidance of cold exposure and other known triggers for vasospastic attacks, such as emotional stress. Practical measures include appropriate full body covering with particular attention to protecting the hands and feet in both cold outdoor weather conditions and air-conditioned indoor environments. Counselling should emphasize wearing additional layers of clothing, hats, thick socks, and mittens, which are preferred over gloves as they offer superior insulation through reduced individual finger surface area exposure.[6,7] Patients may benefit from covering the forehead, as exposure to cold air across this region produces a vasomotor "diver's reflex" that can induce peripheral vasospasm.[8] Hand or toe warmers or other portable warming devices may also help reduce the frequency and severity of attacks.

Smoking cessation is imperative for all patients with RP. Tobacco use is strongly associated with endothelial dysfunction and impaired vasodilatation, and smokers demonstrate a higher incidence of more severe phenotypes including digital ulcers and gangrene.[9] Medications known to exacerbate RP should be identified and, where clinically feasible, discontinued. These include but are not limited to nonselective β-blockers, ergotamine-containing migraine therapies, amphetamine/dextroamphetamine, caffeine, and oral contraceptives.[6,10] Notably, a meta-analysis including over 1,000 patients found that approximately 14% of individuals receiving β-blockers developed RP.[10]

Several physical manoeuvres may help patients abort acute attacks and are generally more effective in primary RP where structural vascular disease is absent. One technique, the "Frisbee manoeuvre," involves extending the arm laterally and repeatedly performing a rapid snapping motion of the wrist, generating centripetal force to restore digital blood flow.[11] Alternatively, a windmill or swing-arm technique is performed by rotating the arm rapidly in a softball pitching motion to achieve a similar effect.[12] Biofeedback training and relaxation techniques have also demonstrated benefit, particularly in patients whose attacks are primarily triggered by emotional stress rather than cold exposure.[13]

Pharmacologic Treatments

When lifestyle modifications prove insufficient, pharmacotherapy is warranted. In primary RP, pharmacologic agents should be introduced for patients whose symptoms substantially impair quality of life or who develop signs of tissue compromise. In contrast, SRP often warrants early and often aggressive pharmacotherapy to prevent irreversible tissue damage, with treatment tailored to the underlying etiology and the severity of digital ischemia.[2,6]

Calcium Channel Blockers

Calcium channel blockers (CCBs) are the preferred first-line systemic agents for both subtypes. They are effective at reducing the frequency, severity, and duration of attacks in both primary and secondary disease.[14] Dihydropyridine CCBs, particularly nifedipine

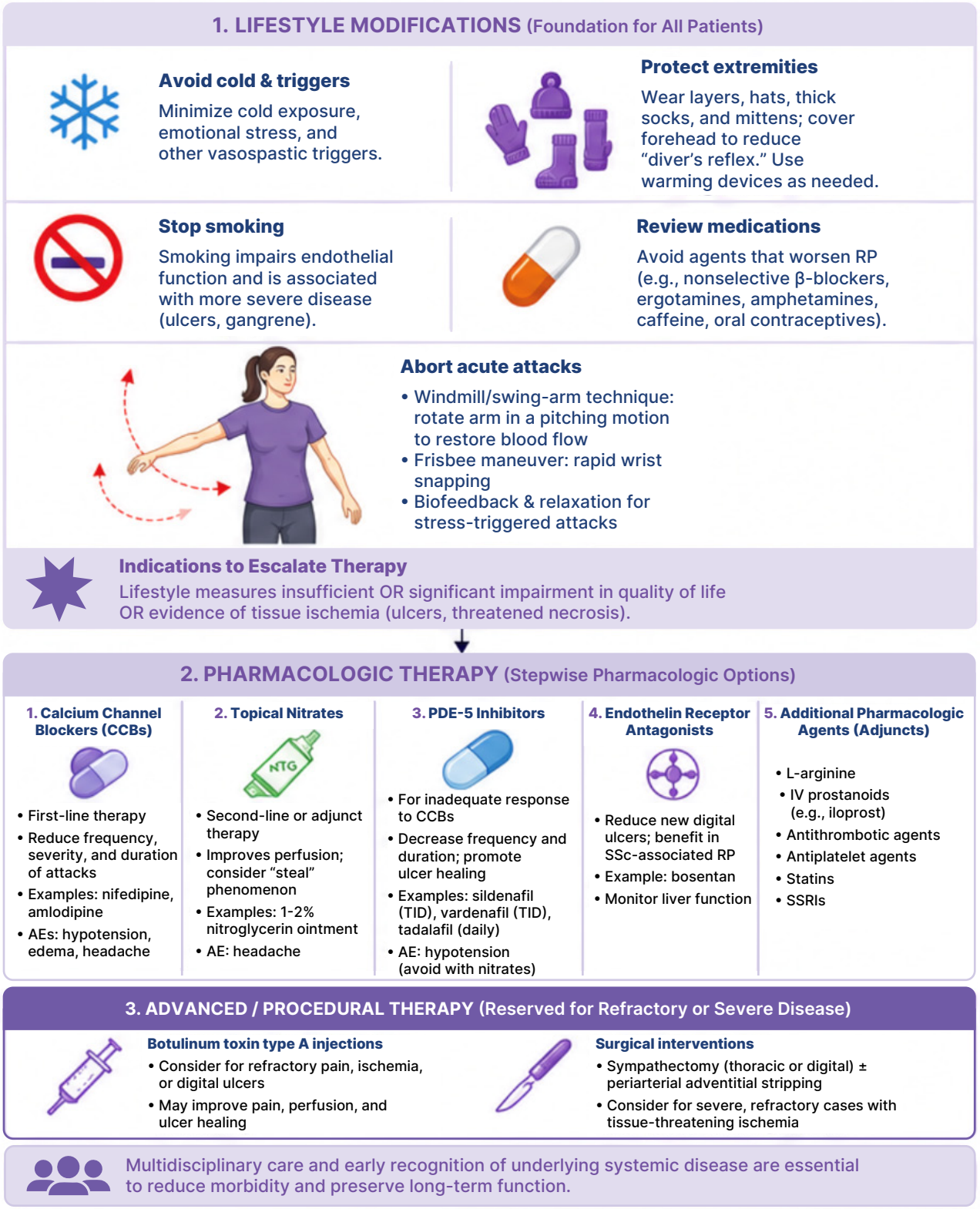

Figure 1. Approach to the Management of Raynaud's Phenomenon; *courtesy of Khalad Maliyar, MD, MScCH, FRCPC*

Abbreviation: AE: adverse effect; **CCB:** calcium channel blockers; **IV:** intravenous; **PDE-5:** Phosphodiesterase 5; **RP:** Raynaud's Phenomenon; **SSc:** systemic sclerosis; **SSRIs:** selective serotonin reuptake inhibitor; **TID:** three times daily

and amlodipine, are generally preferred over nondihydropyridine agents such as verapamil and diltiazem, as they exert more potent peripheral effects on vascular smooth muscle with less cardioselectivity. Common side effects include hypotension, peripheral edema, and headache.[14]

Topical Nitrates

Topical nitrates represent a useful second-line therapy in those with an inadequate response to CCBs, or are unable to tolerate CCB monotherapy. After application, topical nitroglycerin is metabolized to nitric oxide, providing potent exogenous vasodilation by increasing cyclic guanosine monophosphate concentrations in vascular smooth muscle. Several placebo-controlled trials have demonstrated improvements in digital artery perfusion and reducing symptom severity, and a systematic review and meta-analysis has confirmed the effectiveness of topical nitrates in both primary and secondary RP.[15] Topical nitroglycerin can be compounded as a 1–2% preparation in a hydrophilic ointment base and applied selectively to the affected digits or ischemic areas. Targeted application can help to reduce the "steal" phenomenon whereby less diseased vessels preferentially dilate and shunt blood from more severely affected digits.[6] Headache remains the most frequently reported adverse effect and limits tolerability in some patients.[15]

Phosphodiesterase-5 Inhibitors

Phosphodiesterase-5 (PDE-5) inhibitors are reserved for patients who do not respond to CCB therapy. These agents inhibit the degradation of cyclic guanosine monophosphate, thereby potentiating the effects of both endogenous and exogenous nitric oxide. Evidence from randomized controlled trials (RCTs) and meta-analyses support the efficacy of PDE-5 inhibitors in decreasing the frequency and duration of attacks in SRP.[16] The landmark SEDUCE trial, a placebo-controlled study involving 83 patients with SSc, demonstrated a statistically significant benefit of sildenafil in healing ischemic digital ulcers at 8 and 12 weeks.[17] Available PDE-5 inhibitors include sildenafil and vardenafil, which may be administered up to three times per day and tadalafil, typically administered once per day.[2] Of note, a key side effect is that co-administration of PDE-5 inhibitors and topical nitrates can lead to profound hypotension.[2]

Endothelin Receptor Antagonists

Endothelin levels are pathologically elevated in SSc and are implicated in the underlying disease processes of severe RP phenotypes. Endothelin receptor antagonists limit endothelin-mediated vasoconstriction and pathologic vascular lumen remodelling. In particular, bosentan, a dual endothelin-1 and endothelin-2 receptor antagonist, has been evaluated in two major clinical trials—RAPIDS-1 and RAPIDS-2, where it demonstrated efficacy in reducing the formation of new digital ulcers, most prominently in patients with preexisting ulceration.[18] It is commonly initiated at a dose of 62.5 mg per day.

Botulinum Toxin Type A

Botulinum toxin type A (BoNT-A) has emerged as an increasingly popular adjunctive therapy for RP. Its therapeutic effects appear to result from both vascular and neuromodulatory mechanisms including inhibition of sympathetic vasoconstriction and blockade of pain-associated neurotransmitters, such as substance P and calcitonin gene-related peptide.[4,19] Numerous studies have reported improvements in pain, perfusion, colour change, and ulcer healing following treatment.[19] There is no consensus regarding optimal dosing, dilution, or injection sites. A commonly used approach involves slowly injecting five units of BoNT-A into the bilateral interdigital web spaces at the bifurcations of the superficial digital arteries surrounding each affected digit, for a total dose of 50 units per hand.[2] Some clinicians avoid thumb injections unless symptoms are substantial. Clinical benefits can be observed within days to one week. Adverse effects are generally mild and transient, most commonly localized injection-site discomfort or temporary hand weakness.

Additional Pharmacologic Agents

Several adjunctive therapies with a more limited evidence base warrant consideration in select patients. L-arginine, an amino acid and nitric oxide precursor, is particularly useful for patients

who cannot tolerate conventional vasodilators due to low systemic blood pressure.[20] Intravenous prostanoids, notably iloprost, have shown efficacy in SSC-related SRP, with a Cochrane meta-analysis of seven RCTs reporting improvements in attack frequency and severity as well as digital ulcer healing and prevention.[2] In patients with SRP associated with underlying hypercoagulable states, such as antiphospholipid syndrome, consideration may be given to antithrombotic therapy, including anticoagulants (e.g., low-molecular-weight heparin) and antiplatelet agents such as aspirin.[2] Losartan has also shown superiority to nifedipine in one RCT for reducing RP attack severity and frequency, making angiotensin II receptor blockers a reasonable adjunct.[2] Statins may also improve endothelial dysfunction in SSc through pleiotropic effects. Finally, selective serotonin reuptake inhibitors remain an option in patients with concurrent low blood pressure, although higher quality evidence is needed before their routine use can be recommended.[2]

Surgical Interventions

Surgical intervention is generally reserved for patients with severe refractory SRP who have failed medical therapy or who develop threatened digital viability, including impending digital necrosis or progressive ischemic ulceration. Historically, sympathectomy procedures involved the ligation of sympathetic fibers at the thoracic level and were used to reduce vasospastic activity. Contemporary use of this procedure is increasingly performed using minimally invasive endoscopic techniques in order to minimize surgical morbidity, although long-term recurrence remains a concern.[2] Peripheral digital sympathectomy with periarterial adventitial stripping is another method used to improve blood flow and help with ulcer healing in severe cases. This approach aims to restore vascular compliance and address the fixed obstructive component of advanced SRP that pharmacotherapy alone cannot overcome.[2]

Conclusion

RP is far more than a benign inconvenient reaction to cold exposure or a cosmetic concern; particularly in its secondary form, it can be associated with substantial morbidity. Early distinction between primary and secondary disease is paramount, as SRP may herald serious systemic pathology that extends well beyond the digital vasculature. Effective management requires a stepwise approach guided by disease subtype, severity, and associated comorbidities. This approach begins with comprehensive lifestyle modifications, progressing through evidence-based pharmacotherapy, and incorporating procedural or surgical interventions when necessary. Given their role in early recognition of connective tissue disease and cutaneous vasculopathy, dermatologists are uniquely positioned to identify, risk-stratify, and longitudinally manage patients with RP. A comprehensive and multidisciplinary treatment strategy addressing both vascular dysfunction and systemic disease remains central to reducing morbidity and preserving long-term function and quality of life.

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References

1. Curtiss P, Svigos K, Schwager Z, Lo Sicco K, Franks AG Jr. Part I: Epidemiology, pathophysiology, and clinical considerations of primary and secondary Raynaud's phenomenon. J Am Acad Dermatol. 2024;90(2):223-234. doi:10.1016/j.jaad.2022.06.1199
2. Curtiss P, Svigos K, Schwager Z, Lo Sicco K, Franks AG Jr. Part II: The treatment of primary and secondary Raynaud's phenomenon. J Am Acad Dermatol. 2024;90(2):237-248. doi:10.1016/j.jaad.2022.05.067
3. Flavahan NA. A vascular mechanistic approach to understanding Raynaud phenomenon. Nat Rev Rheumatol. 2015;11(3):146-158. doi:10.1038/nrrheum.2014.195
4. Matucci-Cerinic M, Kahaleh B, Wigley FM. Review: evidence that systemic sclerosis is a vascular disease. Arthritis Rheum. 2013;65(8):1953-1962.

doi:10.1002/art.37988
5. Campbell PM, LeRoy EC. Pathogenesis of systemic sclerosis: a vascular hypothesis. Semin Arthritis Rheum. 1975;4(4):351-368. doi:10.1016/0049-0172(75)90017-7
6. Bakst R, Merola JF, Franks AG Jr, Sanchez M. Raynaud's phenomenon: pathogenesis and management. J Am Acad Dermatol. 2008;59(4):633-653. doi:10.1016/j.jaad.2008.06.004
7. Dolez PI, Vu-Khanh T. Gloves for protection from cold weather. In: Williams JT, ed. Textiles for Cold Weather Apparel. Cambridge: Woodhead Publishing; 2009. p.374-398.
8. Hayward JM, Holmes WF, Gooden BA. Cardiovascular responses in man to a stream of cold air. Cardiovasc Res. 1976;10(6):691-696. doi:10.1093/cvr/10.6.691
9. Hudson M, Lo E, Lu Y, Hercz D, Baron M, Steele R, et al. Cigarette smoking in patients with systemic sclerosis. Arthritis Rheum. 2011;63(1):230-238. doi:10.1002/art.30071
10. Mohokum M, Hartmann P, Schlattmann P. The association of Raynaud syndrome with β-blockers: a meta-analysis. Angiology. 2012;63(7):535-540. doi:10.1177/000331971142861
11. Curtiss P, Cobos G, Lo Sicco K, Franks AG Jr. The Frisbee maneuver: a novel method to abort acute attacks of the Raynaud phenomenon. J Am Acad Dermatol. 2018;78(3):e61. doi:10.1016/j.jaad.2017.09.066
12. McIntyre DR. A maneuver to reverse Raynaud's phenomenon of the fingers. JAMA. 1978;240(25):2760.
13. Freedman RR, Ianni P, Wenig P. Behavioral treatment of Raynaud's disease. J Consult Clin Psychol. 1983;51(4):539-549. doi:10.1037/0022-006X.51.4.539
14. Rirash F, Tingey PC, Harding SE, Maxwell LJ, Tanjong Ghogomu E, Wells GA, et al. Calcium channel blockers for primary and secondary Raynaud's phenomenon. Cochrane Database Syst Rev. 2017;12(12):CD000467. doi:10.1002/14651858.CD000467.pub2
15. Curtiss P, Schwager Z, Cobos G, Lo Sicco K, Franks AG Jr. A systematic review and meta-analysis of the effects of topical nitrates in the treatment of primary and secondary Raynaud's phenomenon. J Am Acad Dermatol. 2018;78(6):1110-1118.e3. doi:10.1016/j.jaad.2018.01.043
16. Roustit M, Blaise S, Allanore Y, Carpentier PH, Caglayan E, Cracowski JL. Phosphodiesterase-5 inhibitors for the treatment of secondary Raynaud's phenomenon: systematic review and meta-analysis of randomised trials. Ann Rheum Dis. 2013;72(10):1696-1699. doi:10.1136/annrheumdis-2012-202836
17. Hachulla E, Hatron PY, Carpentier P, Agard C, Chatelus E, Jego P, et al. Efficacy of sildenafil on ischaemic digital ulcer healing in systemic sclerosis: the placebo-controlled SEDUCE study. Ann Rheum Dis. 2016;75(6):1009-1015. doi:10.1136/annrheumdis-2014-207001
18. Matucci-Cerinic M, Denton CP, Furst DE, Mayes MD, Hsu VM, Carpentier P, et al. Bosentan treatment of digital ulcers related to systemic sclerosis: results from the RAPIDS-2 randomised, double-blind, placebo-controlled trial. Ann Rheum Dis. 2011;70(1):32-38. doi:10.1136/ard.2010.130658
19. Jenkins SN, Neyman KM, Veledar E, Chen SC. A pilot study evaluating the efficacy of botulinum toxin A in the treatment of Raynaud phenomenon. J Am Acad Dermatol. 2013;69(5):834-835. doi:10.1016/j.jaad.2013.06.029
20. Curtiss P, Schwager Z, Lo Sicco K, Franks AG Jr. The clinical effects of L-arginine and asymmetric dimethylarginine: implications for treatment in secondary Raynaud's phenomenon. J Eur Acad Dermatol Venereol. 2019;33(3):497-503. doi:10.1111/jdv.15180