# Correspondence

**INSTRUCTIONS FOR LETTERS TO THE EDITOR**

**Editorial comment in the form of a Letter to the Editor is invited; however, it should not exceed 800 words, with a maximum of 10 references and no more than 2 figures (submitted as camera ready hard copy per Journal Guidelines) or tables and no subdivision for an Abstract, Methods, or Results. Letters should have no more than 4 authors. Full name(s) and address of the author(s) should accompany the letter as well as the telephone number, fax number, or E-mail address.**

***Contact.*** **The Managing Editor, The Journal of Rheumatology, 365 Bloor Street East, Suite 901, Toronto, ON CANADA M4W 3L4. Tel: 416-967-5155; Fax: 416-967-7556; E-mail: jrheum@jrheum.com Financial associations or other possible conflicts of interest should always be disclosed.**

## Raynaud's Phenomenon and Serotonin Reuptake Inhibitors

*To the Editor:*

Raynaud's phenomenon (RP) and the associated digital ischemic lesions are one of the main challenges in caring for patients who have scleroderma[1]. Although the precise pathophysiological mechanisms remain unclear, there is evidence that intrinsic endothelial and intimal abnormalities leading to platelet activation may play a role in its pathogenesis[2]. Activated platelets release thromboxane $A_2$ and serotonin, which are potent vasoconstrictors. Matsuura, *et al* [3] described that depressive symptoms are frequent in patients with systemic sclerosis and, in this regard, Coleiro, *et al* [4] report that selective serotonin reuptake inhibitors (SSRI) could reduce the frequency and the intensity of RP attacks. However, variability in the response to this treatment was noted, and worsening of RP with digital infarction has been described[5]. We describe our successful experience with SSRI therapy on a patient with RP and critical digital ischemic lesions associated with scleroderma and depression.

In 2001, a 58-year-old woman presented at the emergency room because of numbness and intense pain of the right 2nd, 3rd, and 5th digits. She also complained of a 4-month history of pain and pallor affecting the digits of the hands, without other symptoms. Her clinical history was unremarkable. On examination, telangiectasias and digital ischemic tip ulcerations and necrosis at the right 3rd and 5th digit were observed. Laboratory investigations including full blood cell count, hepatic and renal function, and coagulation tests were normal. Erythrocyte sedimentation rate and C-reactive protein were 29 mm/h and 8.1 mg/l (normal < 5), respectively. Antinuclear antibodies were positive, 1/1280 anticentromere. Rheumatoid factor, anti-DNA, C3, C4, anticardiolipin antibodies, cryoglobulins, and antinuclear cytoplasmic antibodies were negative or normal. Plain chest radiograph showed no abnormalities.

A diagnosis of incomplete CREST syndrome with critical digital ischemic lesions was established. Treatment with nifedipine and low molecular weight heparin, was started, without improvement, then intravenous iloprost was used, and she was discharged from hospital 17 days later. However, she developed new recurrent digit-threatening ischemic episodes, and was re-hospitalized and treated with iloprost. Three months later, due to family problems, she reported insomnia and depressed mood and a psychiatric consultation was required. A diagnosis of depression was made and paroxetine (20 mg/day) was prescribed. To our surprise, the patient improved without digital ischemic episodes, and no new hospitalizations have been required since then.

Depression increases the risk of cardiac mortality and morbidity in patients with coronary heart disease[6]. Enhanced platelet activation has been hypothesized to represent one of the mechanisms underlying this association[6,7]. Despite recent advances in our understanding of these potential mechanisms, further research is needed to determine how depression increases vascular damage. Although the precise mechanism of endothelial cell damage and platelet activation in patients with scleroderma is unclear, it is likely to be multifactorial. Also, the role of depression in the pathogenesis of RP is unknown. SSRI inhibit the reuptake of serotonin with decreased storage of 5-hydroxytryptamine in platelets, leading to symptomatic dysfunction. Our case suggests that SSRI might be of some value in these patients. We speculate that the response to SSRI may be mediated by dose, differences in serotonin metabolism, and also by an underlying depression. The antiplatelet and endothelium-protective properties of SSRI may represent an attractive additional advantage in patients with depression and scleroderma. Patients who have scleroderma should be screened for depression, and SSRI might be considered when indicated.

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## Dr. Matsuura, *et al* reply

*To the Editor:*

Dr. Garcia-Porrua and colleagues report an interesting case of CREST syndrome in which selective serotonin reuptake inhibitor (SSRI) was effective



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for severe Raynaud's phenomenon (RP) and digital ulcerations. We have shown that depressive symptoms are frequent (46%) in scleroderma patients[1]. Although we did not describe the details of the drugs that were used, antidepressants were prescribed only in a few cases, but SSRI were used in none. In our study, 90% of patients had RP, and digital ulcerations or necrosis were seen in 14%. However, there was no significant association between the peripheral vascular damage and depression (Beck Depression Inventory score; r = –0.024, nonsignificant). Depression score was found to be significantly correlated with helplessness, low sense of coherence, pain, low working ability, and low social activity, but not with skin thickness or internal organ involvement, indicating that depression in scleroderma patients may be derived from the lack of truly effective drugs, the chronic expression of the disease, and various complications, but not directly from the RP disease itself. Thus, the mechanism of developing depression in patients with scleroderma may be heterogeneous. Also, the pathomechanism of RP and peripheral vascular damage is likely to be multifactorial, although platelet activation and endothelial cell injuries are thought to be predominantly involved. At present, there seems to be no evidence of pathognomonic relationships between depression and peripheral vascular changes in scleroderma.

SSRI are generally used for the therapy of depression and depressive symptoms that are relatively frequent and may be overlooked in patients with scleroderma as described. There is an increasing number of reports[2,3] that SSRI can improve RP and peripheral vascular lesions. In these reports, SSRI were thought to improve platelet dysfunction (platelet activation/aggregation) by depleting platelet serotonin. However, the worsening of preexisting RP with use of SSRI was also reported, indicating that some SSRI might instead exacerbate the symptoms[4]. Although large placebo-controlled trials are required to further assess clinical efficacy and tolerability of SSRI for RP, SSRI may be a suitable drug for scleroderma patients with severe drug-resistant peripheral vascular disease, especially those also having depressive symptoms.

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## Erectile Dysfunction and Scleroderma

*To the Editor:*

We read with interest the article by Hong, *et al* evaluating erectile dysfunction (ED) in patients with scleroderma compared to patients with rheumatoid arthritis[1]. The authors review the literature showing an association between severe Raynaud's phenomenon (RP) and ED[2-4]. We have described a patient with limited scleroderma who experienced worsening of his RP when treated with yohimbine for his ED[5].

Apart from a letter describing the utility of topical nitropaste in a scleroderma patient, ours was the first report to review the topic and describe ED responsiveness to application of topical nitroglycerin paste to the penis or chest[4,5]. If applied to the penis, the patient should be counseled to use a condom prior to sexual intercourse. This should protect the sexual partner from the adverse effects of nitroglycerin paste, such as hypotension and headache. Scleroderma patients may also benefit from nitropaste or nitropatch on the chest, due to the systemic vasodilatory effects of the nitroglycerin.

We would be interested to know if other clinicians have found this intervention useful for ED in the scleroderma population.

SINDHU R. JOHNSON, MD, FRCPC, Division of Rheumatology, University Health Network, Toronto Western Hospital, Edith Cavell Wing 5-028, 399 Bathurst Street, Toronto, Ontario M5T 2S8, E-mail: sjohnson4681@rogers.com; CATHARINE DEWAR, PhD, MD, FRCPC, Division of Rheumatology, Lions Gate Hospital, North Vancouver, British Columbia, Canada. E-mail: c.dewar@telus.net

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## Drs. Pope and Ouimet reply

*To the Editor:*

We read the case report describing a man with limited scleroderma whose Raynaud's phenomenon worsened when taking yohimbine for his erectile dysfunction (ED)[1]. Topical nitropaste was used in this patient to improve penile blood flow and ED. We have no experience with this treatment. Even in the treatment of Raynaud's, nitropaste/nitropatches have not been well studied or utilized, and although studies have reported a physiological response to topical nitroglycerin, the evidence of a clinically significant effect remains unclear[2-4]. We agree that the potential for topical nitroglycerine to treat ED secondary to scleroderma is an interesting topic for future research. However, this therapy should be used only with caution until better understood. Additionally, your observation does highlight the common occurrence of ED in scleroderma, as we have reported compared to rheumatoid arthritis[5].

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