The Enigma of Primary Raynaud’s Disease

Jay D. Coffman, MD

Despite many years of investigation, the pathophysiology of vasospastic attacks in primary (idiopathic) Raynaud’s disease is unknown. In secondary Raynaud’s phenomenon, it is understandable that digital arteries may close during normal sympathetic stimuli or external pressure on the fingers due to low blood pressure distal to stenoses or obstructions or thickened vessel walls or to decreased blood flow caused by increased blood viscosity or persistent vasoconstriction. Digital arterial disease occurs in the connective tissue diseases and vinyl chloride disease. Increased blood viscosity is present in cryoglobulinemia and polycythemia. Persistent vasoconstriction may be caused by drug therapy such as ergotamine preparations or β-adrenoceptor-blocking agents. However, in primary Raynaud’s disease of recent onset, there is no abnormality of the blood vessels pathologically or by angiography, and blood viscosity is probably normal. There are two theories to explain digital vasospastic attacks with normal blood vessels. The first, an overactivity of the sympathetic nervous system, is attributed to Maurice Raynaud. Supporting evidence for this theory is the demonstration that normal blood flow is attained in the hands and fingers by warming or sympathetic blockade, that there is an exaggerated digital vasoconstrictor response to postural changes, and that emotional stress produces attacks in some patients with primary Raynaud’s disease. However, normal microelectrode recordings of skin sympathetic nerve activity at rest and with various stimuli, normal vasoconstriction of the contralateral hand during cooling of one hand, and normal catecholamine levels in patients with primary Raynaud’s disease do not substantiate this theory.

Lewis9 is credited with the theory of a local fault at the digital artery level. He produced vasospastic attacks in single fingers by direct cooling, induced attacks in sympathetically denervated fingers, and showed that vasospasm of the fifth finger was unrelieved by ulnar nerve anesthetization. The local fault was considered at the digital artery level, because local warmth would only relieve a vasospastic attack if applied proximally and not distally to the finger and cold water applied to the proximal finger with the distal finger kept warm produced an attack. These studies have been criticized on the basis that they were performed on patients with probable digital artery vascular abnormalities due to advanced primary disease or secondary causes. The only other investigation to show that sympathetic blocks did not prevent vasospastic attacks is that of Halpern and coworkers. Again, it is questionable whether they were studying patients with normal digital arteries. This is the importance of the study by Freedman and coworkers appearing in this issue of Circulation. They have reproduced one of Lewis’ experiments by inducing vasospastic attacks in nerve-blocked fingers in patients with primary Raynaud’s disease. For this study to be acceptable, it must be documented that the six patients who had vasospastic attacks had primary Raynaud’s disease, normal digital arteries, and a complete sympathetic nerve block of the fingers. Documentation of primary Raynaud’s disease is adequate by present-day criteria. As a group, a maximal vasodilation test is offered as proof of a normal circulation. Because biopsies of digital arteries cannot be ethically recommended, digital vasculature magnification angiography and presentation of the individual finger blood flows for the six patients would have lent credibility. Digital nerve blocks have been found unsatisfactory by other investigators when the anesthetic is injected into the tissues outside nerve sheaths. However, Freedman and coworkers show that the reflex sympathetic digital vasoconstriction to ice on the neck was inhibited by their nerve blocks; again the data are presented for the entire group of patients and individual values are not given for the patients who had vasospastic attacks during nerve blockade. Despite these comments, it appears that vasospastic attacks can be produced in nerve-blocked fingers of patients with primary Raynaud’s disease when the studies of Lewis and Halpern and coworkers are considered together with the study of Freedman and coworkers. The local fault theory is substantiated, and Lewis’ contribution should no longer be criticized.

The opinions expressed in this editorial comment are not necessarily those of the editors or of the American Heart Association.

From Peripheral Vascular Section, Boston University School of Medicine, Massachusetts.

Address for correspondence: Dr. Jay D. Coffman, Chief, Peripheral Vascular Section, Boston University Medical Center, 88 East Newton Street, Boston, MA 02118-2393.
Although the evidence now supports an abnormality in the digital circulation as pathogenetically important for induction of vasospastic attacks in patients with primary Raynaud’s disease, we still do not know the nature of this abnormality and are, therefore, no closer to an understanding of episodic digital vasospasm. Because ice placed on the neck caused a greater vasoconstriction in cooled hands of patients with primary Raynaud’s disease than normal subjects, Jamieson and colleagues postulated that there may be an increased sensitivity to cold of the \( \alpha \)-adrenoceptors. In support of this hypothesis, one group of investigators have reported an increase in the levels of \( \alpha_2 \)-adrenoceptors of platelets by increased binding capacity and affinity in patients with primary Raynaud’s disease compared with normal subjects and patients with secondary Raynaud’s phenomenon. We have shown that the \( \alpha_2 \)-adrenoceptors are most important in the reflex digital sympathetic vasoconstriction that occurs with body cooling in normal subjects; \( \alpha_1 \)-adrenoceptors play a minor role. Sympatholytic agents have been one of the main treatment modalities for Raynaud’s phenomenon. Therefore, an increased sensitivity of the \( \alpha_2 \)-adrenoceptors to cold is a logical but unproven theory to explain vasospasm of digital arteries during cold exposure in patients with primary Raynaud’s disease. Substantiation of the pathogenesis awaits the demonstration of an increase in sensitivity of \( \alpha_2 \)-adrenoceptors at the tissue level. Detractors will point out that this explanation does not explain the production of vasospastic attacks in some patients by emotional stress. However, the few patients who have attacks during emotional upsets may have secondary digital vascular disease due to repeated episodes of ischemia. In our experience, patients develop vasospastic attacks to emotional stimuli only after a few years of attacks occurring during cold exposure. If digital artery stenoses or obstructions are present, then a normal sympathetic stimulus could induce a vasospastic attack.

References

1. Lewis T: The pathological changes in the arteries supplying the fingers in warm-handed people and in cases of so-called Raynaud’s disease. Clin Sci 1938;3:288–311
9. Lewis T: Experiments relating to the peripheral mechanism involved in spasmic arrest of circulation in fingers, a variety of Raynaud’s disease. Heart 1929;15:7–101
The enigma of primary Raynaud's disease.
J D Coffman

Circulation. 1989;80:1089-1090
doi: 10.1161/01.CIR.80.4.1089

Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1989 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on
the World Wide Web at:
http://circ.ahajournals.org/content/80/4/1089.citation

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally
published in Circulation can be obtained via RightsLink, a service of the Copyright Clearance Center, not the
Editorial Office. Once the online version of the published article for which permission is being requested is
located, click Request Permissions in the middle column of the Web page under Services. Further
information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation is online at:
http://circ.ahajournals.org//subscriptions/