APPARENT FINGER SYSTOLIC Pressures DURING COOLING IN PATIENTS WITH RAYNAUD’S SYNDROME

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ABSTRACT Despite considerable research, the mechanisms responsible for the vasospasm associated with Raynaud’s syndrome are not well understood and there is no reliable diagnostic test. In the present studies, measurements of systolic pressure in locally cooled fingers were used to address these issues. We found that local cooling produced a marked decrease or loss of the apparent finger systolic pressure in patients with Raynaud’s syndrome in whom a standardized vasoconstriction had been induced by body cooling. Abnormal responses were encountered in 109 of 125 patients with secondary Raynaud’s syndrome, in 21 of 37 patients with primary Raynaud’s disease or the syndrome of uncertain cause, and in two of 63 subjects without symptoms of Raynaud’s. These data suggest a high accuracy of the test in patients with secondary Raynaud’s syndrome and lower accuracy in those with disease of primary or uncertain cause. We studied responses of systolic pressures to alterations in body and local temperatures in fingers with and without low pressures secondary to proximal arterial obstruction. Our data show that although local cooling has a small independent effect that increases vascular tone: (1) sympathetic vasoconstriction induced by body cooling is necessary to produce vasospasm and often produces it without local cooling, (2) high local temperature (30°C) protects from vasospasm, and (3) low finger blood pressure predisposes to it. Delayed opening of the vessels observed after sudden deflation of blood pressure cuffs suggests that abnormal responses of finger systolic pressure to cold represent combined effects of high vascular tone, delayed opening, and local blood pressure. We conclude that measurements of local systolic pressures in response to cold provide a valuable method for the study of the mechanisms of Raynaud’s syndrome, a useful diagnostic test, and may have an application to the evaluation of therapeutic interventions.


ELUCIDATION of the mechanisms responsible for the vasospasm accompanying Raynaud’s syndrome and the management of patients have been hampered by the lack of a reliable, quantitative laboratory method for the study of the vasospastic phenomena, for the follow-up of the patients, and for the evaluation of therapeutic procedures. Typical color changes associated with digital vasospasm allow a definite diagnosis. Vasospastic phenomena, however, are elusive and cannot be reproduced consistently at home, in the clinic, or in the laboratory.1 Measurements of changes in blood flow in response to a cold challenge or measurements of some index of blood flow, e.g., skin temperature, have been used extensively. They have not proven to be reliable, however, probably because various factors that influence the occurrence of vasospasm are difficult to control.1, 2 Also, since Raynaud’s attacks are thought to be associated with critical closure of the main digital arteries,3–5 measurements of blood flow, which depend mainly on the degree of vasoconstriction in the peripheral vessels of the microcirculation, may not provide information relevant to the larger digital vessels implicated in Raynaud’s syndrome.

Noninvasive measurements of local systolic pressure represent an established and valuable method for assessment of obstruction in the arteries supplying the extremities and digital pressures have been used for that purpose in the upper and lower limbs.6–9 It is known that in normal subjects and patients with a certain degree of obstruction, digital pressures are affected by the vasomotor tone.9, 10 Vasodilatation, such as may be induced by body heating, increases blood flow and results in lower systolic pressure because pressure energy is lost to a greater extent with high flow through the vessels proximal to the digits. Conversely, with vasoconstriction and low blood flow the distal pressures increase. However, Krähenbühl et al.4 and Niel-
sen and Lassen\textsuperscript{11} have reported that in certain individuals, especially those with Raynaud’s syndrome, finger pressures recorded during local cooling of the digits fell precipitously. There was often loss of measurable pressure, indicating the occurrence of critical closure in the main arteries of the fingers. Since this technique provides information concerning the response of the digital arteries to cold, it represents a potentially valuable method for the study of vasospastic phenomena and for the evaluation of treatments.

Although several reports using the above approach have appeared, there are considerable differences in the methods and reported results.\textsuperscript{12–14} Also, although vasospastic Raynaud’s attacks are known to be precipitated by cooling, the relative importance of the effect of local temperature and of sympathetic vasospastic induction by cold on the digital blood vessels has not been elucidated.\textsuperscript{1, 3, 5} The present study demonstrates the importance of sympathetic vasospastic induction in producing the spasm of the digital arteries and of its interaction with the local temperature. The effect of cold on the opening of digital arteries and of arterial obstruction on the measurements in patients with Raynaud’s syndrome were examined. Also, it was demonstrated that when a controlled state of vasospastic induction was maintained during the measurements, the method provided a useful tool for the diagnosis of Raynaud’s phenomena of various causes.

\textbf{Methods}

\textbf{Subjects.} The results are based on studies of 162 subjects with and 63 without Raynaud’s syndrome. All subjects gave informed consent and the protocol was approved by the Committee of the Faculty of Medicine, University of Manitoba, for the Use of Human Subjects in Research. Table 1 shows the numbers of subjects and characteristics of the various groups. Patients were included in the group with Raynaud’s syndrome if they gave a clear history of episodic white and/or blue discoloration of the fingers precipitated by exposure to cold.\textsuperscript{1, 3, 5, 15} Consecutive patients referred to the Vascular Laboratory for assessment of symptoms in the fingers were included, with the exception of six patients who had surgical sympathectomy or were being treated with vasodilator drugs and three in whom a maintained state of vasoconstriction was not attained despite the experimental cooling protocol. The duration of the vasospastic symptoms varied from 2 months to more than 20 years. The age ranged from 13 to 75. Patients were assessed clinically and hematologic, immunologic, and radiologic studies were carried out to determine the diagnosis of primary Raynaud’s disease or secondary vasospastic phenomena of various causes.\textsuperscript{1, 15}

Also, a subgroup of patients with short duration of symptoms (average 1.5 years, range 0.3 to 3 years) was designated as having Raynaud’s syndrome of uncertain cause, because it is known that manifestations of a connective tissue disorder may not develop for several years after the onset of vasospastic symptoms.\textsuperscript{5} The subgroup with arterial occlusive disease included six patients with arteriosclerosis and two with thromboangitis obliterans. Patients with connective tissue disorders were categorized with use of the currently used clinical and laboratory criteria\textsuperscript{15–18} and included 13 patients with systemic sclerosis, four with rheumatoid arthritis, two with systemic lupus erythematosus, and 11 with undifferentiated connective tissue disease. The other subgroups of patients with secondary Raynaud’s syndrome included those with accidental (n = 4) or occupational (n = 8) trauma, patients with a history of exposure to vibratory tools (mainly workers in the metal mines of Northern Manitoba), and patients with miscellaneous other conditions known to be associated with Raynaud’s syndrome, including frostbite (n = 3), \(\beta\)-blocker use (n = 4), hypothyroidism (n = 2), Dupuytren’s contracture (n = 2), carpal tunnel syndrome (n = 2), and thoracic outlet syndrome (n = 1).\textsuperscript{1, 19, 20}

The group without a history of Raynaud’s syndrome consisted of 46 consecutive patients referred for assessment of atypical symptoms of coldness or paresthesia and who denied a history of episodic digital discoloration, seven patients with acrocyanosis, and 10 healthy volunteers. Their ages ranged from 13 to 73 years.

\textbf{Techniques and experimental protocols.} Studies were carried out in supine subjects who had refrained from smoking and eating for at least 2 hr and had rested for not less than 30 min. Room temperature was maintained relatively constant within \(\pm 1^\circ\) C and averaged \(18^\circ\) C.

The effect of local temperature. Figure 1 shows a schematic diagram of the experimental apparatus. Systolic pressures were measured in two of the middle three fingers with 3 cm wide pneumatic cuffs placed around the middle phalanx of the digits. One of the fingers was locally cooled and is referred to as the test finger and the other served as the control digit. Changes in the local temperature of the test finger were achieved by perfusing water at the desired temperature through a double-inlet cuff applied to the middle phalanx for 6 min before the measurements. During the perfusion the circulation to the digit was arrested by inflating a tourniquet cuff to above systolic pressure on the proximal phalanx to allow equilibration of the temperature of the finger with that of the circulating water.\textsuperscript{15} After 6 min, the middle phalanx cuffs were inflated on both fingers, the proximal phalanx cuff on the test finger was deflated, and the measurements were carried out during deflation of the middle phalanx cuffs at the rate of 2 mm Hg/sec. In preliminary experiments during body cooling in 10 subjects with and four without Raynaud’s syndrome the occlusion of the circulation for 6 min before the measurements without water perfusion was found to have no significant effect on the finger pressure. The pressure

\begin{table}[h]
\centering
\caption{Clinical data}
\begin{tabular}{llll}
\hline
\textbf{Group} & \textbf{n} & \textbf{Age (yr)*} & \textbf{Percent female} & \textbf{Percent with arterial obstruction} \\
\hline
No Raynaud’s syndrome & 63 & 32 ± 13 & 63 & 3 \\
Raynaud’s syndrome & & & & \\
Primary & 15 & 47 ± 14 & 87 & 13 \\
Uncertain & 22 & 31 ± 15 & 50 & 18 \\
Secondary & & & & \\
Miscellaneous & 14 & 45 ± 16 & 36 & 29 \\
Vibratory tools & 61 & 42 ± 11 & 0 & 30 \\
Trauma & 12 & 36 ± 7 & 8 & 100 \\
Arterial occlusive disease & 8 & 52 ± 15 & 25 & 100 \\
Connective tissue disorders & 30 & 43 ± 16 & 80 & 60 \\
\hline
\end{tabular}
\footnotesize{\textsuperscript{*}Values are mean ± SD.}
\end{table}
in the cuffs was recorded by means of a pressure transducer (Statham PM6TC) and the systolic end points were determined with photocell (Medasonics) or mercury-in-silicone rubber strain gauge (Parks Medical Electronics) plethysmography by means of sensors placed on the distal phalanx of the fingers. The systolic end points were denoted by an increase in the volume of the digits. The quality of the end points was considerably improved by rendering distal parts of the fingers relatively bloodless by the tight application of a rubber dam before the inflation of the cuffs and application of the sensors. The photocell and strain gauge sensors were found to give comparable results. The output of the pressure transducer and of the sensors was recorded on a multichannel recorder (Beckman R-611).

The effect of local cooling was studied by comparing measurements carried out after the 6 min of inflow occlusion at a local temperature of 30° C with those at lower temperatures, either by changing the temperature to 10° C or by progressive cooling by decrements of 5° or 10° C.

The effects of vasomotor tone. Measurements were carried out during sympathetic vasoconstriction induced by body cooling and during inhibition of sympathetic vasoconstrictor discharge by body heating. Body cooling and heating were carried out with a modification of the technique of Gibbon and Landis.\(^{21, 22}\) To induce body cooling a leg was immersed in water at 18° C and the subject, covered only by a light hospital gown, was exposed to room temperature. Body heating was induced by immersion of a leg in water at 43° to 44° C and by covering the trunk with a heating blanket. Skin temperatures of the finger tips were monitored with copper-constantan thermocouples. Measurements of systolic pressures during body cooling were carried out only after skin temperatures had fallen to within 3° C of room temperature and during body heating after they had stabilized at 33° C or higher.

The mechanism of the decrease or loss of measurable systolic pressure during cooling. The results of the pressure measurements with use of the deflation rate of the cuffs of 2 mm Hg/sec were compared with the time of the return of the distal inflow after the cuffs were instantaneously deflated to 0 mm Hg after the same period of cooling.

The effect of arterial obstruction. The effect of local blood pressure was assessed by comparing the results (1) in patients with Raynaud’s syndrome with and without arterial obstruction (table 1), and (2) in two fingers of the same hand with different degrees of obstruction, as indicated by differences in digital systolic pressures. The presence or absence of organic arterial obstruction was determined by measurements of finger and brachial systolic pressures and skin temperatures during body heating before the studies of the effect of exposure to cold. The criteria for the presence of arterial obstruction included one or more of the following: clearly positive Allen’s test, differences of 15 mm Hg or greater in systolic pressure among individual digits, brachial-to-finger pressure difference greater than 40 mm Hg, finger systolic pressure below 70 mm Hg, and difference in the maximal temperature among fingers of more than 2° C.\(^{8, 9, 22}\)

In all experiments brachial systolic pressures were measured by auscultation at the time of finger pressure measurements and changes in the brachial pressure were used to correct finger pressures when comparing measurements at different temperatures. Local cooling of the test finger from 30° to 10° C during body cooling was associated with a small but significant increase in the brachial pressure of 3.2 ± 1.2 (SEM) mm Hg (p < .02).

Number of experimental studies. The measurements during local and body cooling and during body heating to assess the presence of organic obstruction were carried out in all subjects and patients. To further elucidate the mechanisms involved in the observed responses, additional studies were carried out on smaller subsets of consecutive subjects who consented to additional experimental measurements. The effect of local cooling during body heating was studied in 11 subjects without and 17 with Raynaud’s syndrome, and the effects of instantaneous deflation of the blood pressure cuffs was studied in 15 and those of different degrees of obstruction in two fingers of the same hand in 12 patients with Raynaud’s syndrome.

Statistical analysis. The data are reported as the mean ± SEM, except where otherwise indicated. Analysis was carried out as appropriate by SPSS and one-way analysis of variance (ANOVA), Duncan’s multiple-range test, and the two tailed t test for paired or unpaired differences or chi-square test according to Snedecor.\(^{23}\)

Results

The effect of vasomotor tone and local temperature. Figures 2 to 5 illustrate the responses to cooling and tables...
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FIGURE 2. Apparent systolic pressures in response to combined local and body cooling in 36 subjects without Raynaud’s syndrome.

2 to 4 give the group results in all studied subjects and patients. There were no significant differences in the responses to cooling among the three subsets of subjects without Raynaud’s symptoms or among subsets of patients with different types of connective tissue disorders and therefore the results of these subsets were combined.

The effect of local and body cooling. Figures 2 and 3 illustrate the effect of local cooling on the apparent

FIGURE 3. Apparent systolic pressures in response to combined local and body cooling in 36 subjects with Raynaud’s syndrome. VIBR = vibratory; CON. = connective; 2ry = secondary.

FIGURE 4. Apparent systolic pressures during body cooling with and without local application of temperature of 30°C in the same 36 patients whose results appear in figure 3. T.F. = test finger; C.F. = control finger. Other abbreviations as in figure 3.

FIGURE 5. Apparent systolic pressures in response to local cooling during body heating in patients with Raynaud’s syndrome. Abbreviations as in figure 3.
systolic pressure of the test finger during body cooling in subjects without and with Raynaud’s syndrome, respectively. For the sake of clarity, only the results in 36 subjects are shown in each figure. Figure 2 shows the results of the 10 healthy volunteers, seven patients with acrocyanosis, and the first 19 patients referred for assessment of atypical symptoms, and figure 3 the responses in the first 36 patients referred with Raynaud’s syndrome. Local cooling resulted in a relatively small decrease in the finger pressure in most subjects without Raynaud’s syndrome, but in two healthy female subjects pressure fell by more than 70 mm Hg (figure 2). By contrast, in the majority of patients with Raynaud’s syndrome there was a large fall, with many of these showing complete loss of measurable pressure (figure 3). In two patients with Raynaud’s syndrome (figure 3) and in a total of six among all who were studied, body cooling resulted in the loss of measurable pressure despite a local temperature of 30° C. Local cooling from 30° to 10° C resulted in a significant decrease in apparent systolic pressure of the test finger in the groups without and with Raynaud’s syndrome, but the decrease was significantly greater in those with Raynaud’s syndrome (table 2). Table 3 shows that local cooling from 30° to 10° C also resulted in significant decreases in apparent systolic pressure in all subgroups with Raynaud’s syndrome and these were all significantly greater than the decrease in the group without the syndrome. The effects in the subgroups with secondary disease were significantly greater than effects in patients with primary Raynaud’s syndrome.

Abnormal responses in the locally cooled test finger, defined as a decrease in apparent systolic pressure of at least 50%, 50 mm Hg, or both from the pressure measured at 30° C were encountered in only two healthy volunteers (women less than 25 years of age) and in a

TABLE 2
Comparison of the effect of cooling on apparent finger systolic pressure in subjects with and without Raynaud’s syndrome

<table>
<thead>
<tr>
<th>Group</th>
<th>Test finger</th>
<th>Control finger</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Difference (mm Hg)</td>
<td>Percent</td>
</tr>
<tr>
<td></td>
<td>30° vs 10° C</td>
<td>Abnormal response</td>
</tr>
<tr>
<td>No Raynaud’s syndrome</td>
<td>21 ± 2°C</td>
<td>3</td>
</tr>
<tr>
<td>Raynaud’s syndrome</td>
<td>75 ± 3°D</td>
<td>80</td>
</tr>
</tbody>
</table>

"Plus or minus" values are mean ± SEM.

aDefined as a decrease of at least 50 mm Hg and/or 50% from the pressure measured at 30° C.

bDefined as apparent systolic pressure below 40 mm Hg.

cp < .01; dp < .01 for difference from the group without Raynaud’s syndrome.

dDefined as a decrease of at least 50 mm Hg and/or 50% from the pressure measured at 30° C.

TABLE 3
The effect of cooling on apparent finger systolic pressure in groups of patients with Raynaud’s syndrome of different causes

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>Test finger</th>
<th>Control finger</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Difference (mm Hg)</td>
<td>Percent</td>
</tr>
<tr>
<td></td>
<td>30° vs 10° C</td>
<td>Abnormal response</td>
</tr>
<tr>
<td>Primary</td>
<td>51 ± 8°C</td>
<td>53</td>
</tr>
<tr>
<td>Undetermined</td>
<td>65 ± 7°C</td>
<td>59</td>
</tr>
<tr>
<td>Secondary</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Miscellaneous</td>
<td>76 ± 13°D</td>
<td>71</td>
</tr>
<tr>
<td>Vibratory tools</td>
<td>80 ± 4°D</td>
<td>83</td>
</tr>
<tr>
<td>Trauma</td>
<td>76 ± 7°D</td>
<td>92</td>
</tr>
<tr>
<td>Arterial occlusive disease</td>
<td>90 ± 12°D</td>
<td>100</td>
</tr>
<tr>
<td>Connective tissue disease</td>
<td>78 ± 5°D</td>
<td>97</td>
</tr>
</tbody>
</table>

"Plus or minus" values are mean ± SEM. All differences in column 1 are significant (p < .01). In column 4, all differences except those designated “NS” are significant at (p < .025 to .01).

aDefined as a decrease of at least 50 mm Hg and/or 50% from the pressure measured at 30° C.

bDefined as apparent systolic pressure below 40 mm Hg.

cp < .05 for difference from the group without Raynaud’s syndrome shown in table 2.

dp < .05 for difference from the group with primary Raynaud’s syndrome.
large proportion of patients with Raynaud’s syndrome (table 2). The responses were abnormal in 87% of patients with secondary Raynaud’s syndrome (table 3). In patients without a definite secondary cause of disease there were fewer abnormal responses, indicating relatively lower sensitivity to cooling. In some of these latter patients the symptoms were mild and infrequent. Loss of measurable pressure (closure) occurred in 54% of patients with Raynaud’s syndrome and was more frequent in those with Raynaud’s syndrome secondary to trauma, arterial occlusive process, or connective tissue disease (tables 2 and 3).

The effect of body cooling alone. Figure 4 compares systolic pressure in the test finger at a local temperature of 30°C with the lowest pressure recorded during body cooling in the control finger, which was not locally cooled. Data from the first 36 patients with Raynaud’s syndrome who were tested are shown in the figure; the group results for all subjects with and without the syndrome are provided in tables 2 and 3. In subjects without Raynaud’s syndrome body cooling resulted only in minor changes in the pressure in the control finger, which remained above 50 mm Hg in all cases, although the mean pressure in the control finger was significantly lower than in the test finger at 30°C (table 2). However, in the majority of patients with Raynaud’s syndrome the pressure in the control finger was lower. The difference between the pressure in the test finger at 30°C and the minimum pressure in the control finger was significantly greater in the group with than in that without Raynaud’s syndrome (table 2) and significantly greater in the three largest subgroups with secondary Raynaud’s syndrome (table 3). The pressure in the control finger fell to less than 40 mm Hg in 63% of patients with connective tissue disorders, in 20% to 25% of those in other subgroups with Raynaud’s syndrome, and in no subject without Raynaud’s syndrome (tables 2 and 3). Loss of measurable pressure in the control finger occurred in 24% of all patients with Raynaud’s syndrome and was more frequent in those with connective tissue disease.

The effect of local cooling during body heating. The group results are shown in table 4 and the responses in patients with Raynaud’s syndrome are illustrated in figure 5. Local cooling from 30°C to 10°C during body heating did not result in a significant change in finger systolic pressure in subjects without Raynaud’s syndrome (nine volunteers and two patients with atypical symptoms). However, in the group with Raynaud’s syndrome there was a relatively small but significant decrease. The group of 17 patients with Raynaud’s syndrome who were studied in this manner included 13 who exhibited a complete loss of measurable pressure when local cooling had been applied during body cooling. The decreases during body heating were 35 mm Hg or less in all but one patient and the systolic pressure remained above 40 mm Hg in 14 of 17 cases. In one patient with severe arterial obstruction the pressure was less than 30 mm Hg both at 30°C and 10°C.

Reopening time of the finger arteries. The apparent finger systolic pressures measured during body and local cooling were related to the opening time of the finger arteries in the same digits after instantaneous deflation of the blood pressure cuffs in a subset of 15 patients with Raynaud’s syndrome (table 5). Measurements were carried out in 15 control digits and in 14 fingers that were locally cooled to 10°C for 6 min both before the determination of the apparent systolic pressure and before the instantaneous deflation of the cuffs. The opening time denoted by the return of the pulse and/or increase in the volume of the distal phalanx was prolonged in those fingers in which cooling was associated with large decreases in apparent systolic pressure (table 5). In 15 of 16 fingers in which the pressure was 60 mm Hg or higher despite cooling, the return of flow to the distal phalanx occurred within less than 1 sec after instantaneous deflation. However, the opening time was significantly prolonged and exceeded 2 sec in 12 of 13 digits in which the pressure fell to less than 60 mm Hg with cooling, including 11 digits that exhibited loss of measurable pressure with cooling.

The effect of local blood pressure. Among 66 patients with Raynaud’s syndrome who had evidence of arterial obstruction and thus lower finger pressures, 64% dem-
shown loss of measurable pressure with local cooling compared with 39% of 96 patients with Raynaud’s syndrome without obstruction (p < .01).

Figure 6 shows the results of experiments in 12 patients with Raynaud’s syndrome. The effect of local cooling to 10°C during body cooling is compared in pairs of fingers of the same hand but with different degrees of obstruction. The differences in the degree of obstruction were evidenced by differences of at least 15 mm Hg between the pressures of the two fingers when measured previously during body heating. During cooling, the pressures fell to lower levels or became unmeasurable in the fingers that had lower pressures during body heating, except in three patients in whom there was loss of measurable pressure in both digits. The mean difference between the decreases in systolic pressure in the two fingers with local cooling was 30 ± 10 mm Hg (p < .02).

Discussion

Physiologic considerations. The mechanism of the decrease or loss of the finger systolic pressure in response to cooling is thought to be related to increased tone of the smooth muscle of the digital arteries. The increased tone and thus increased force of contraction in the wall of the vessels leads to critical closure and complete loss of measurable pressure in many cases. In others, the measured pressure is considerably reduced because high wall tension and cuff pressure are additive and thus closing and opening of the vessel will occur when pressure in the encircling cuff is lower than intravascular blood pressure. Another factor contributing to a lower measured pressure may be prolonged contraction or delayed relaxation of vascular smooth muscle after deflation of the cuffs. Also, increase in the stiffness of the wall of cooled digital arteries may be involved in the delayed opening because of the associated change in viscoelasticity. Our experiments with sudden deflation of the cuffs, consistent with the above hypothesis, showed that the return of the flow may be considerably delayed. These phenomena must contribute to the lowering of the measured finger systolic pressure during cooling by producing a phase shift between cuff pressure and vessel opening. Thus, it appears that digital systolic pressures measured during cooling reflect combined effects of high wall tension, delayed opening, viscoelasticity of the vessels, and the local blood pressure rather than true systolic pressure. Therefore, it is more appropriate to refer to such measurements as apparent systolic pressures.

The marked decrease or loss of apparent finger systolic pressure with cooling is the physiologic counterpart of the vasostrictive Raynaud’s attacks that patients experience. Indeed, when finger pressure falls to very low levels during measurements, the fingers display marked pallor and/or cyanosis characteristic of Raynaud attacks.

The excessive vasoconstriction and spasm in response to cold could result from increased sympathetic vasoconstriction, as suggested originally by Raynaud, or be due to a “local fault” in the walls of the arteries as proposed by Lewis. The relative importance of the central and local mechanisms has not been clearly elucidated, in part because various studies did not examine the responses of the main digital arteries. The results of the present study provide information about the excessive reactivity of the finger arteries whose spasm is implicated in Raynaud attacks. We found that a large decrease or complete loss of the apparent finger systolic pressure occurred in 80% of 162 patients with Raynaud’s syndrome when local cooling was combined with body cooling and the associated increase in sympathetic tone and body cooling alone resulted in a marked increase in the digital artery tone or complete closure in 30%. Keeping local temperature at 30°C during body cooling prevented the occurrence of vasospasm in 96% of the patients. Local cooling to 10°C during body heating did not result in large changes in the digital artery tone and systolic pressures remained above 40 mm Hg in 14 of 17 patients studied during body heating, although a significant but small mean decrease in systolic pressure indicated that local cooling had an independent effect.

Raynaud’s syndrome is known to occur in some patients with arterial obstruction due to atherosclerosis, thromboangiitis obliterans, or trauma. Although
it has been postulated that in the presence of proximal obstruction lower blood pressure in the digital arteries could lead to closure of the vessels without an abnormal increase in the tone of the vascular smooth muscle,¹ Nielsen et al.²⁶ reported that patients with secondary Raynaud’s syndrome associated with proximal arterial obstruction were less sensitive to local cooling than those with primary Raynaud’s disease without obstruction. Our results, and especially the experiments in which we compared the responses of the fingers with different degrees of obstruction in the same hands, showed that lower pressure resulted in a greater incidence of vasospasm.

The results of these studies indicate that, although local cooling has a small independent effect that increases vascular tone in subjects with Raynaud’s syndrome: (1) body cooling associated with sympathetic α-adrenoceptor–mediated vasoconstriction is necessary to produce the excessive digital artery tone and spasm of Raynaud attacks and often is sufficient to induce vasospasm without specific local cooling, (2) high local temperature (30° C) prevents the attacks despite adrenergic stimulation, and (3) occurrence of vasospasm is increased by low digital blood pressure associated with arterial obstruction. It appears that a combination of sympathetic stimulation and local cold provides the trigger that results in vasospastic episodes in the presence of some underlying abnormalities of the peripheral vasculature. Even minor changes in the delicate balance between constrictor and dilator mechanisms might then make the vessels vulnerable to the episodes of vasospasm.², ⁵

Clinical applications. Raynaud’s syndrome is defined as the occurrence of episodic white or blue discoloration of the digits and therefore the diagnosis of Raynaud’s syndrome can only be made by direct observation of an attack or on the basis of the classic history of episodic digital discoloration. However, because the vasospastic attacks cannot be precipitated consistently in the office or in the laboratory despite a cold challenge and because there is no reliable objective test available for Raynaud’s syndrome,¹ ¹, ² potential diagnostic modalities are evaluated by comparing subjects with and without the classic history of symptoms of the disease.¹, ², ¹, ², ¹²–¹⁴, ²⁷–³⁰ A history of the characteristic, well-demarcated, episodic digital discoloration leaves little doubt that the condition is present in such cases. Diagnostic accuracy of any test, however, depends on several factors, including the incidence of the disease in the population and sample being tested,³¹ and therefore an accuracy calculated from the results of one study may not be directly applicable to other studies. However, our results suggest that measurements of apparent finger systolic pressure in response to the cold challenge should have useful clinical applications. The test, with an apparent accuracy of 90%, may provide a reliable diagnostic method in patients with secondary Raynaud’s syndrome and may be of special importance in patients with occupational disease (because of implications for compensation) and in patients without a typical history.

The results in several previous reports using similar techniques showed considerable differences. In some studies there was a good separation between normal subjects and those with Raynaud’s syndrome,¹², ²⁷, ³⁰ whereas in others more than 20% of patients with Raynaud’s syndrome did not show an abnormal response.¹³, ²⁹, ³⁰ These differences may be related to differences in the methods. In some studies only local cooling of the digit was carried out,¹³, ²⁶, ²⁷ whereas in others the body was cooled as well.¹², ¹⁴, ²⁸ Different methods of body cooling may also be responsible for different results.¹², ¹⁴, ²⁸ Despite body cooling procedures, sympathetic vasoconstriction has not be standardized. The presence of relatively high skin temperatures²⁶ suggests that at times it may not occur. Standardization of the vasomotor tone is needed rather than an application of a cooling procedure for an arbitrary period of time. The presence of sympathetic vasoconstriction and the adequacy of body cooling can be confirmed by the demonstration of a decrease in skin temperature of the finger tips to within a few degrees of the environmental temperature of 17° to 20° C and maintenance of the temperature in that range during measurements, as was done in our study. These procedures resulted in a high incidence of abnormal responses in the groups with secondary Raynaud’s syndrome. The reason for a lower incidence in those with primary Raynaud’s disease and others without definite evidence of an underlying disorder is not clear, but it may be due in part to the inclusion of some patients with mild and infrequent episodes of vasospasm.

To our knowledge, the finding that body cooling alone resulted in the loss or a marked decrease of measurable pressure in the control finger of many patients with Raynaud’s syndrome has not been reported previously. It suggests the presence of a marked sensitivity to cold and the value of such a finding in the clinical assessment should be further explored. Also, our results indicate that the use of the difference in the pressure between a locally cooled test finger and a control digit, which is frequently applied in assessment of cold sensitivity,¹²–¹⁴, ²⁷, ²⁹, ³⁰ will in such cases lead to the underestimation of the degree of sensitivity.
It may be more reliable to use the difference between the pressure in the test finger measured at a local temperature of 30°C and that obtained at a lower temperature, such as 10°C.

The demonstration of the effect of lower finger pressure resulting from proximal arterial obstruction on the measurements indicates that the presence or absence of an obstruction must be considered in the assessment of the response of the apparent finger systolic pressure to a cold challenge. Obstruction in the arterial supply to the fingers can be assessed by measurement of local systolic pressures during inhibition of vasomotor tone by body heating.

The results of this study indicate that assessment of patients for vasospastic disorders is improved by determination of the presence or absence of arterial obstruction and standardization of the physiologic state during cooling procedures. Such techniques may also provide an objective measure of the efficacy of various therapeutic agents, as suggested by recent studies.

We thank Dr. T. H. Hassard, Director, Biostatistical Consulting Unit, Faculty of Medicine, University of Manitoba, for assistance with the data analysis and helpful discussions, and the staff of the Vascular Laboratory, St. Boniface General Hospital, for their excellent work.

References

3. Lewis T: Experiments relating to peripheral mechanism involved in spasmodic arrest of circulation in fingers, variety of Raynaud's disease. Heart 15: 7, 1929
Apparent finger systolic pressures during cooling in patients with Raynaud's syndrome.

S A Carter, E Dean and E A Kroeger

*Circulation*. 1988;77:988-996
doi: 10.1161/01.CIR.77.5.988

*Circulation* is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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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/77/5/988

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