Raynaud’s Disease Among Women and Girls

By Ray W. Gifford, Jr., M.D., and Edgar A. Hines, Jr., M.D.

The diagnosis of Raynaud’s disease was suspected in 756 female patients at the Mayo Clinic from 1920 through 1945. The diagnosis was substantiated from the records of the initial examination or from the follow-up data or examination in 474. The clinical characteristics, including diagnostic criteria, clinical course, complications, and sequelae are discussed.

From January 1920 to December 1945, inclusive, Raynaud’s disease, Raynaud’s phenomenon, or questionable Raynaud’s disease was diagnosed in 756 female patients at the Mayo Clinic. Data gleaned from a critical review of the clinical records and from follow-up questionnaires constitute the basis for the present report. In 1945 Hines and Christensen, in a similar study of Raynaud’s disease among men, reported that 77 per cent of patients with Raynaud’s disease or Raynaud’s phenomenon at the Mayo Clinic were women.

Diagnosis

Since Raynaud’s original thesis, terminology relating to Raynaud’s phenomenon and Raynaud’s disease has been confused. Raynaud’s phenomenon may be defined “as an episode of constriction of the small arteries or arterioles of the extremities resulting in intermittent changes in color of the skin of the extremities, such as pallor, cyanosis or both.” Raynaud’s phenomenon is, therefore, a symptom and not a disease. Raynaud’s phenomenon may be associated with, and can be the first manifestation of numerous conditions or diseases, both local and systemic. When Raynaud’s phenomenon is primary, that is, when it exists in the absence of conditions or diseases to which it may be secondary, it is properly called “Raynaud’s disease.” Allen and Brown re-emphasized and elaborated on Raynaud’s original criteria for making a diagnosis of Raynaud’s disease. Their criteria are: (1) episodes of Raynaud’s phenomenon excited by cold or emotion; (2) bilaterality of Raynaud’s phenomenon; (3) absence of gangrene, or, if present, its limitation to minimal grades of cutaneous gangrene; (4) absence of any other primary disease that may be causal, such as occlusive arterial disease, cervical rib, or organic disease of the nervous system; and (5) symptoms for at least 2 years.

Of the 756 girls and women in this series, 127 were promptly eliminated because the available information was inadequate, or the Raynaud phenomenon was obviously secondary to existing diseases. For the remaining 629 patients, the diagnoses as revised by the Allen-Brown criteria were then further validated or invalidated by follow-up information when available. Follow-up information was obtained by sending questionnaires to the patients and by re-examination at the clinic for some. The results are shown in tables 1 and 2.

From table 1 it is evident that adherence to the criteria of Allen and Brown led to a change in the original diagnosis in almost 30 per cent of the cases. There are two reasons for this: (1) many of the records antedated the publications of Allen and Brown in 1932 in which criteria for differentiation between Raynaud’s phenomenon and Raynaud’s disease were elucidated, and (2) the diagnosis of Raynaud’s disease was changed unless the record clearly and unmistakably showed that all the criteria had been fulfilled.

Validity of Diagnosis Based on Allen-Brown Criteria. A diagnosis of Raynaud’s disease according to the criteria of Allen and Brown was made for 377 of the 629 female patients by reviewing the initial records and was substantiated in 267 of 280 (95 per cent) by follow-up information. In 13 patients, diseases had developed in the interval to which the Raynaud’s phenomenon may have been secondary.

Rheumatoid arthritis is believed to have
developed in 5 of these 13 patients 2 or more years after the onset of Raynaud's phenomenon. Although the diagnosis of rheumatoid arthritis was unequivocally confirmed by examination at the clinic for only 1, it was strongly suspected on the basis of examinations at the clinic for 2 and on the basis of rather detailed follow-up letters from 2. The latent period between the onset of Raynaud's phenomenon and the appearance of rheumatoid arthritis varied from 4 to 14 years.

In 4 of the 13 patients acrosclerosis is believed to have developed 2 or more years after the onset of Raynaud's phenomenon. Three of these 4 patients had sclerodactylia (without other evidence of scleroderma) or trophic ulcerations of the fingers or both within 5 years of the onset of Raynaud's phenomenon, but acrosclerosis was diagnosed from 14 to 26 years after the onset of Raynaud's phenomenon. For the purposes of this paper sclerodactylia is defined as sclerodermatous changes confined to the skin of the digits. As a complication of Raynaud's disease it remains localized to the acral parts in contradistinction to the progressive scleroderma that is characteristic of acrosclerosis and diffuse scleroderma.

Two of the 13 patients who were thought to have Raynaud's disease by the criteria of Allen and Brown died of protracted febrile illnesses. One died at age 24 years 1 year after the apparently valid diagnosis of Raynaud's disease was made at the clinic, and 3 years after the onset of Raynaud's phenomenon. The other died at age 29 years, 4 years after the apparently valid diagnosis of Raynaud's disease was made, and 14 years after the onset of Raynaud's phenomenon. The final diagnoses in these 2 cases are in doubt, since necropsy data are not available. Raynaud's phenomenon may have been incidental and not secondary to the fatal illnesses.

One woman died of polyarteritis nodosa when 39 years old, 1 year after an apparently valid diagnosis of Raynaud's disease was made and 8 years after the onset of Raynaud's phenomenon.

In the last of the 13 patients thought to have Raynaud's disease, a bizarre type of muscular atrophy and primary biliary cirrhosis (both confirmed at the clinic) developed 8 years after the diagnosis of Raynaud's disease was made and 13 years after the onset of Raynaud's phenomenon. Again, the relationship of Raynaud's phenomenon to the disease of muscle and liver is problematic, but for the purposes of

### Table 1.—Revised or Verified Diagnoses According to Criteria of Allen and Brown for 629 Patients Suspected of Having Raynaud's Disease

<table>
<thead>
<tr>
<th>Original diagnosis</th>
<th>Total cases</th>
<th>Revised or verified diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Raynaud's disease</td>
<td>514</td>
<td>353</td>
</tr>
<tr>
<td>Questionable Raynaud's disease...</td>
<td>115</td>
<td>24</td>
</tr>
<tr>
<td>Total</td>
<td>629</td>
<td>377</td>
</tr>
</tbody>
</table>

* Reasons for doubtful diagnosis listed in table 2.

### Table 2.—Final Diagnoses for 629 Patients Suspected of Having Raynaud's Disease

<table>
<thead>
<tr>
<th>Revised or verified diagnosis (by Allen-Brown criteria)</th>
<th>Cases</th>
<th>Final diagnosis (from follow-up data)</th>
<th>Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Raynaud's disease</td>
<td>377</td>
<td>Raynaud's disease</td>
<td>267</td>
</tr>
<tr>
<td>Duration not stated</td>
<td>56</td>
<td>Dead (see table 3)</td>
<td>37</td>
</tr>
<tr>
<td>Duration inadequate</td>
<td>138</td>
<td>Raynaud's phenomenon disappeared</td>
<td>29</td>
</tr>
<tr>
<td>Pulsations absent or not recorded</td>
<td>17</td>
<td>Rheumatoid arthritis</td>
<td>15</td>
</tr>
<tr>
<td>Unilateral</td>
<td>14</td>
<td>Acrosclerosis</td>
<td>12</td>
</tr>
<tr>
<td>Possibly secondary to other disease</td>
<td>27</td>
<td>Dermatomyositis</td>
<td>1</td>
</tr>
<tr>
<td>Raynaud's phenomenon still unilateral</td>
<td></td>
<td></td>
<td>4</td>
</tr>
<tr>
<td>No follow-up</td>
<td></td>
<td></td>
<td>44</td>
</tr>
</tbody>
</table>
Table 3.—Causes of Death in 37 Cases of Questionable Raynaud's Disease

<table>
<thead>
<tr>
<th>Cause</th>
<th>Deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unknown</td>
<td>19</td>
</tr>
<tr>
<td>Disseminated lupus erythematosus</td>
<td>6</td>
</tr>
<tr>
<td>Proved</td>
<td>2</td>
</tr>
<tr>
<td>Suspected</td>
<td>4</td>
</tr>
<tr>
<td>Carcinoma</td>
<td>3</td>
</tr>
<tr>
<td>Stomach</td>
<td>1</td>
</tr>
<tr>
<td>Breast</td>
<td>1</td>
</tr>
<tr>
<td>Uterus</td>
<td>1</td>
</tr>
<tr>
<td>Miscellaneous*</td>
<td>9</td>
</tr>
</tbody>
</table>

* Includes 1 case each of: muscular atrophy, cerebral arteriosclerosis, malignant hypertension, pneumonia, hemorrhagic diathesis, possible selenium poisoning, acute nephritis, possible Addison's disease, and possible sclerodermat.

Table 4.—Ages at Death in 37 Cases of Questionable Raynaud's Disease

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td>10-19</td>
<td>1</td>
</tr>
<tr>
<td>20-29</td>
<td>8</td>
</tr>
<tr>
<td>30-39</td>
<td>4</td>
</tr>
<tr>
<td>40-49</td>
<td>7</td>
</tr>
<tr>
<td>50-59</td>
<td>5</td>
</tr>
<tr>
<td>60-69</td>
<td>1</td>
</tr>
<tr>
<td>70 or more</td>
<td>7</td>
</tr>
<tr>
<td>Unknown</td>
<td>4</td>
</tr>
<tr>
<td>Youngest</td>
<td>14 yr.</td>
</tr>
<tr>
<td>Oldest</td>
<td>96 yr.</td>
</tr>
<tr>
<td>Average</td>
<td>47 yr.</td>
</tr>
</tbody>
</table>

this paper Raynaud's phenomenon has been presumed to be a secondary manifestation.

Validity of the Diagnosis of Questionable Raynaud's Disease Based on Allen-Brown Criteria. The revised diagnosis was questionable Raynaud's disease for 252 patients. Follow-up data could not be obtained on 44 of these patients. The diagnosis of Raynaud's disease was verified by the follow-up information for 110 (53 per cent) of the 208 female patients on whom such data were available. The results of follow-up study for the remainder are shown in table 2.

Follow-up information revealed the rather startling fact that 37 patients for whom a diagnosis of questionable Raynaud's disease was made (17.8 per cent of those with follow-up data available) had died; more than half before the age of 50. The causes of death are listed in table 3, and the ages at time of death are listed in table 4. Nineteen of the 37 deaths occurred within 5 years of the time that the patients were first seen at the clinic. Twenty-eight of the patients who subsequently died had noted Raynaud's phenomenon for less than 2 years when they were seen at the clinic.

Analysis of Data from 474 Patients

The next part of this paper is devoted to the analysis of data derived from the records of the 474 women and girls for whom the final diagnosis was Raynaud's disease (table 2). The diagnosis was made according to the criteria of Allen and Brown either from the records of the initial examination or from follow-up data or examination.

Age at Onset. The age at which Raynaud's phenomenon first appeared was known for 425 of the 474 female patients with Raynaud's disease (table 5). The earliest age of onset was 4 years, the latest was 88 years, and the average age was 31 years. Seventy-eight per cent of the patients were 30 years old or less at onset.

Location of Raynaud's Phenomenon. The fingers of 467 of the 474 patients were the site of color change when they were first seen at the clinic. In 4, only the toes were involved, and in 3 the sites of involvement were not clearly stated. In 259 patients the fingers only were involved, and in 202 patients both the fingers and toes were involved. Involvement of the nose, ears, face, chest or lips also occurred in 6 cases. Initially, Raynaud's phenomenon was unilateral, involving the fingers of 1 hand in 10 cases. The longest duration of unilateral Raynaud's phenomenon at the time of the initial visit to the clinic was 5 years, and this was reported by only 1 patient; the average duration was 21/2 years. In all 10 of these patients Raynaud's phenomenon eventually occurred bilaterally.

Precipitating Factors. Exposure to cold was the only stimulus for precipitating Raynaud's phenomenon in 365 patients. Emotional reactions were the only precipitating factors in 4 patients, and 85 stated that both exposure to cold and emotional reactions were responsible. In addition to exposure to cold, tea and coffee
were implicated by 1 patient and pressure by another. Eight patients could cite no precipitating factors and 10 records were not clear on this point. Strict adherence to the first criterion of Allen and Brown would have led to discarding these 18 cases. However, the absence of any disease to which Raynaud’s phenomenon might have been secondary made it difficult to classify these cases as anything but Raynaud’s disease.

**Duration of Symptoms.** Raynaud’s phenomenon had been present for as brief a period as 1 month and for as long as 40 years when these patients were first seen at the clinic for this complaint (table 5). The average duration was 7 years. The records of 49 patients were not clear as to the exact duration, but such phrases as “many years,” “all her life” and “since girlhood,” indicated long duration for most of these. In all cases in which the duration of symptoms was in doubt or less than 2 years at the time of the initial examination, when the follow-up data were obtained Raynaud’s phenomenon had been present for at least 2 years.

**Phases of Color Change.** Although the classical description of Raynaud’s phenomenon includes a 3-phase color change from pallor to cyanosis to rubor, this was not always observed. Only 133 of the 474 records contained detailed descriptions of the color changes. Of these 133, 87 (65 per cent) described the typical 3-phase color change; 29 (22 per cent) described only a 2-phase color change and 17 (15 per cent) described only 1 phase of the color change (usually pallor, occasionally cyanosis).

**Family History.** Twenty of the 474 patients knew of 1 or more relatives who had Raynaud’s phenomenon. These consisted of a sister in 6 cases, a mother in 4 cases, a mother and father in 1 case, a sister and daughter in 1, a father in 1, a brother in 1, and a father and sister in 1. In 5 cases the relationship of the affected kin was not clearly stated.

**Associated Diagnoses.** A variety of functional complaints were commonly associated with Raynaud’s disease. One hundred seventy-nine (38 per cent) of the 474 patients in this group had one or more of the following included in the final diagnosis: Chronic nervous exhaustion in 74 cases, various types of psychoneurosis in 44, chronic constipation in 31, anxiety state in 21, irritable bowel in 11, tension state in 9, obesity in 8, dysmenorrhea in 8, pain in the chest wall in 6, and functional gastrointestinal disorder in 6. Many other similar diagnoses were made in 5 cases or less. Many other patients had similar complaints, that were not included, however, in the final diagnoses.

Migraine headache was diagnosed in 65 (14 per cent) of the 474 patients. Hypertension (blood pressure greater than 150 mm. Hg systolic and 90 mm. Hg diastolic) was present in 43 (9 per cent) of the 474. These figures include 10 cases in which hypertension and migraine headache coexisted.

**Incidence of Complications at First Examination.** At the time of the initial examination at the clinic for Raynaud’s phenomenon, 63 (13 per cent) of the 474 patients had or gave a history of having had trophic changes (ulceration, chronic paronychia, necrosis, scarring, fissuring) of one or more digits. The toes of only 4 were involved in the trophic changes. The duration of Raynaud’s phenomenon for these 63 patients varied from 1½ to 35 years, and the average duration was 8½ years.

At the time of the initial examination at the clinic for Raynaud’s phenomenon, 57 (12 per cent) had evidence of sclerodactyly involving the fingers (in only 1 patient was sclerodactyly noted in the toes also). The duration of Raynaud’s phenomenon for these 57 patients varied from 6 months to 35 years and the average duration was 8 years.

Twenty-three patients had both sclerodactyly and trophic changes of the digits when first

### Table 5.—Raynaud’s Disease among 474 Patients

<table>
<thead>
<tr>
<th>Age at onset</th>
<th>Duration of symptoms at first visit to clinic for this complaint</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>Patients</td>
</tr>
<tr>
<td>0-9</td>
<td>8</td>
</tr>
<tr>
<td>10-19</td>
<td>74</td>
</tr>
<tr>
<td>20-29</td>
<td>123</td>
</tr>
<tr>
<td>30-39</td>
<td>127</td>
</tr>
<tr>
<td>40-49</td>
<td>59</td>
</tr>
<tr>
<td>50-59</td>
<td>26</td>
</tr>
<tr>
<td>60-69</td>
<td>8</td>
</tr>
<tr>
<td>Indefinite or not stated</td>
<td>49</td>
</tr>
</tbody>
</table>
seen at the clinic, and are included in both groups.

Calciosis of the fingers was noted in only 1 patient at the time of the initial examination at the clinic. Amputations of terminal phalanges had been performed for complications of Raynaud’s disease on 2 women (0.4 per cent) of the 474 before they came to the clinic the first time. One woman lost the terminal phalanx of 1 finger while the other lost terminal phalanges of 2 toes. These amputations were performed for nonhealing, painful, infected ulcers of the tips of the digits. True gangrene had not developed. Although both these women had Raynaud’s disease by the criteria outlined, the woman who lost the terminal phalanges of 2 toes also had a more persistent mottled cyanosis of her lower extremities in addition to episodic Raynaud’s phenomenon. She probably had livedo reticularis in addition to Raynaud’s disease.

Amputation of an entire digit was performed on 1 additional patient at the time of her first admission to the clinic. The patient, a woman 68 years old, had had Raynaud’s disease for 35 years at the time of amputation. The pathologic specimen revealed an atherosclerotic process obliterating the digital arteries. For this reason the amputation was attributed to occlusive arterial disease and not to coexisting Raynaud’s disease.

**Course and Prognosis**

Of the 474 female patients with Raynaud’s disease, 397 were treated conservatively and 77 were subjected or had previously been subjected to surgical sympathetic denervation of 1 or more extremities. These latter patients will be considered in a separate communication.

Follow-up information was obtained by questionnaire or by re-examination at the clinic for 307 of the 397 treated medically. Medical treatment of this group consisted largely of reassurance and protection of the extremities from cold and trauma with or without whatever medicinal agents were in vogue at the particular time the patients were seen. The age at onset, location, duration, phases of color change, family history of Raynaud’s phenomenon, and incidence of associated diagnoses were all similar to those for the entire group. The incidences of sclerodactyly (9 per cent) and trophic changes (5 per cent) were less than those of the entire group, since many of the patients with these complications were treated surgically.

**Duration of Follow-up.** The shortest span of follow-up from the first examination at the clinic for Raynaud’s phenomenon was 1 year, the longest was 32 years, and the mean duration was 12 years. The duration of symptoms from the onset of Raynaud’s phenomenon (when known) to the end of the follow-up period varied from 3 to 46 years, and the mean duration of symptoms was 17 years for this group of 307 patients.

**Course of Raynaud’s Phenomenon.** The data in table 6 were derived from the patients’ estimations of the severity and frequency of symptoms at the time of follow-up. Spread of Raynaud’s phenomenon to parts originally uninvolved is not taken into consideration in table 6, since some patients reported that the symptoms had improved or remained unchanged but that other extremities had become involved. Spread to the toes did not necessarily represent an increase in severity. Our data also fail to portray any temporary variations in severity that may have occurred. For instance, the symptoms may have become worse after the first examination at the clinic and then gradually improved, or the reverse may have occurred. Therefore, improvement or worsening does not necessarily imply that the entire course has been in one direction or the other.

All patients who reported that Raynaud’s phenomenon disappeared had had symptoms for at least 2 years before it disappeared, and an adequate diagnosis of Raynaud’s disease had been made at the clinic.

Accurate data on smoking habits were available for 278 patients. Of 203 who did not smoke,
90 (44 per cent) observed improvement or disappearance of Raynaud’s phenomenon. Of 34 who smoked an average of 10 or more cigarettes a day, 16 (47 per cent) observed improvement or disappearance of Raynaud’s phenomenon.

Twenty-five (57 per cent) of the 44 patients who moved to a warmer climate reported improvement or disappearance of Raynaud’s phenomenon.

Forty patients who had Raynaud’s phenomenon in the fingers only when first examined reported on follow-up that it also had appeared in the toes.

Course of Existing Complications. Fifteen (5 per cent) of the 307 patients had, or gave a history of trophic changes in one or more digits when they were first examined at the clinic. Six of these 15 patients also had sclerodactyly. Thirteen had no further difficulty with trophic lesions, but one later had sclerodactyly. Two continued to have trophic lesions.

Twenty-seven (9 per cent) of the 307 patients had sclerodactyly when they were first examined at the clinic. This includes the 6 who also had trophic lesions. Sclerodactyly disappeared in 19 (70 per cent), remained unchanged in 7 (in 1 of whom trophic lesions developed), and adequate follow-up was not available in 1.

Follow-up data were obtained for both women who had had amputations of terminal phalanges for complications of Raynaud’s disease before coming to the clinic for the first time. One who lost the terminal phalanx of a finger was followed for 7 years after cervicothoracic ganglionectomy, and the other who lost terminal phalanges of 2 toes was followed for 15 years of conservative treatment. Neither had any further complications of Raynaud’s disease, and both reported that Raynaud’s phenomenon had improved.

Incidence of New Complications. Two hundred seventy-one patients did not have sclerodactyly or trophic lesions of the fingers when they were first examined at the clinic, and 243 (90 per cent) of them remained free of these complications for the duration of the follow-up period. In 6 patients (2 per cent), follow-up information was inadequate. Nine patients (3.3 per cent) of those not having complications originally had sclerodactyly of the fingers during the follow-up period, 9 (3.3 per cent) first had trophic lesions of the fingers (and toes, 1 patient) in the follow-up period, and 4 (1.4 per cent) had both trophic lesions and sclerodactyly. Calcinosis developed in the fingers of 4 (1.3 per cent) of 307 patients.

No amputations were performed for complications of Raynaud’s disease during the period of follow-up among the 307 conservatively treated patients. Arteriosclerosis obliterans of the lower extremities, however, developed in a woman aged 65 years, 29 years after a valid diagnosis of Raynaud’s disease had been made at the clinic. Pulsations in the pedal arteries were not palpable when gangrene of the left second toe necessitated amputation of that digit. For this reason, Raynaud’s disease was not considered responsible for the amputation.

Correlation was good between the severity of Raynaud’s phenomenon and the development of complications during the follow-up period. Among 141 patients who reported that Raynaud’s phenomenon improved or disappeared, only 4 (3 per cent) reported that sclerodactyly or trophic changes had developed. Conversely, in 9 (18 per cent) of 50 patients who reported worsening of Raynaud’s phenomenon, sclerodactyly or trophic lesions or both developed during the period of follow-up. Most of the patients whose pre-existing sclerodactyly or trophic lesions improved or disappeared also reported concomitant improvement or disappearance of Raynaud’s phenomenon.

Causes of Death. Twelve (4 per cent) of the 307 traced patients treated conservatively died during the period of follow-up (table 7). The ages at time of death varied from 39 to 86 years; the average age was 59 years. None of the deaths could be attributed in any way to Raynaud’s disease. The course and progress of Raynaud’s disease had no influence on death rate as the 12 deaths were proportionately distributed among the 4 groups shown in table 6.

Adequate follow-up data pertaining to Raynaud’s disease were not available for 90 patients whose Raynaud’s disease was treated conservatively. However, our attempts at follow-up disclosed that 22 of these patients were dead. Their ages at time of death varied from 35 to 77 years, and the average was 55 years.
TABLE 7.—Causes and Time of 19 Deaths among 307 Patients with Raynaud’s Disease

<table>
<thead>
<tr>
<th>Cause of death</th>
<th>Time of death</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Age (years)</td>
</tr>
<tr>
<td>Subacute bacterial endocarditis</td>
<td>39</td>
</tr>
<tr>
<td>Cirrhosis of liver and mesenteric thrombosis</td>
<td>42</td>
</tr>
<tr>
<td>Cerebral vascular accident</td>
<td>45</td>
</tr>
<tr>
<td>Carcinoma of stomach with hepatic metastasis</td>
<td>48</td>
</tr>
<tr>
<td>Accident</td>
<td>49</td>
</tr>
<tr>
<td>Carcinoma of liver</td>
<td>50</td>
</tr>
<tr>
<td>Indeterminate lesion of nervous system with paralysis</td>
<td>57</td>
</tr>
<tr>
<td>Unknown</td>
<td>57</td>
</tr>
<tr>
<td>Cerebral vascular accident</td>
<td>75</td>
</tr>
<tr>
<td>Unknown</td>
<td>76</td>
</tr>
<tr>
<td>Cerebral vascular accident</td>
<td>81</td>
</tr>
<tr>
<td>Gangrene of feet and legs†</td>
<td>86</td>
</tr>
</tbody>
</table>

* Date of onset of Raynaud’s phenomenon not clearly stated.
† Presumably owing to arteriosclerosis obliterans.

Raynaud’s phenomenon had disappeared before death.

The causes of death were known for 10 and included cirrhosis of the liver in 2, hypertensive heart disease in 2, postoperative deaths in 2, and carcinoma of the rectum, Bright’s disease, “circulatory collapse,” and accidental death in 1 each.

DISCUSSION

It is interesting that 8 patients in whom the final diagnosis was Raynaud’s disease could not implicate cold or emotional reactions as precipitating factors for Raynaud’s phenomenon. Follow-up information convinced us that all 8 had Raynaud’s disease.

It is also interesting that a few patients who were subsequently proved to have Raynaud’s disease, first noted unilateral Raynaud’s phenomenon for several years before it became bilateral. Hines and Christensen1 reported the occurrence of unilateral Raynaud’s phenomenon in several men for whom the diagnosis of Raynaud’s disease seemed adequate otherwise.

Raynaud’s phenomenon may be a manifestation of serious and disabling diseases. Follow-up studies revealed that of 208 female patients who had Raynaud’s phenomenon, but for whom the diagnosis of Raynaud’s disease could not be confirmed by the criteria of Allen and Brown at the time of revision or on follow-up, 37 (17.8 per cent) had died. The causes of death were not learned for more than half of these patients, but the fact that 13 of the 37 deaths occurred before the patients were 40 years of age is certainly indicative that in many of the cases Raynaud’s phenomenon was a secondary manifestation of serious underlying disease.

The most common and least serious cause of Raynaud’s phenomenon is Raynaud’s disease. When this diagnosis can be verified, the physician has every right to reassure the afflicted patient. Raynaud’s disease was not implicated in any of the deaths that occurred among this group of patients, and indeed, if there is a mortality rate for Raynaud’s disease, it is negligible. In this series, the average age at death for those patients who succumbed during the period of follow-up was less than 60 years, but this figure is not significant, since 96 per cent of the patients were still living when the study was completed. It is our present impression that Raynaud’s disease is not incompatible with a normal span of life.

Uncomplicated Raynaud’s disease may be responsible for inconvenience in that the extremities must be protected from cold and trauma, but it is usually not disabling. Whereas 46 per cent reported that their symptoms improved or disappeared, only 16 per cent of conservatively treated patients reported increase in the severity or frequency of Raynaud’s phenomenon during the follow-up period. Sympathectomy might have been helpful for some of the latter, but for various reasons was not performed. Blain, Coller, and Carver6 have reported that 31 per cent of their patients with Raynaud’s disease noted moderate or severe progression of symptoms. The discrepancy is easily explained by the fact that Blain and his colleagues were reporting on patients treated surgically as well as nonsurgically.
whereas we have confined the follow-up data in
this report to patients not treated surgically.
It is only natural that patients with the more
severe and progressive disease should be se-
lected for surgical treatment. It must be
emphasized, however, that many of our con-
servatively treated patients were advised to
have sympathectomy but refused it.

Morbidty, in the form of trophic lesions of
the digits or sclerodactyia or both, had oc-
curred at or prior to the first examination at
the clinic for 20 per cent of our 474 patients with
Raynaud’s disease. For many, the symptoms
were mild and not incapacitating; amputa-
tions of terminal phalanges for Raynaud’s disease had
been necessary on only 2 patients (0.4 per cent)
before their first examinations at the clinic.
These figures are representative, since they
include all patients regardless of subsequent
treatment. For the 307 patients who were
treated conservatively, follow-up data revealed
that only 8 per cent of those initially free of
these complications subsequently had sclerodac-
tyia or trophic lesions or both, which did not
lead to amputation in a single instance. Among
this same group, trophic lesions or sclerodac-
tyia or both disappeared during the period of
follow-up in most patients. This may indicate
that sclerodactyia is a reversible process, but
we are hesitant to state this definitely because
most of this information was obtained from
follow-up questionnaires without benefit of re-
examinations. Some patients are not aware of
minimal sclerodactyia and may have given an
erroneously negative reply to the question,
“Is there any thickening of the skin on your
fingers?” If present, however, sclerodactyia
was certainly not incapacitating.

Raynaud’s disease was not responsible for
extensive gangrene or major amputations in
any patient. By Raynaud’s original definition
and by the subsequent criteria of Allen and
Brown, Raynaud’s disease cannot cause
extensive gangrene. In this study we did not
discard any case solely on the basis of this one
criterion. When the other criteria for diagnosis
were satisfied, Raynaud’s disease did not pro-
duce extensive gangrene. When massive gan-
grene does occur, other causes for Raynaud’s
phenomenon can usually be found, as demon-
strated by Allen and Brown for some of Ray-
naud’s cases and others in the literature.

In all major respects, the results of this study
are in agreement with those of Hines and
Christensen in their study of Raynaud’s disease
in men. Emotional reactions play a greater role
in precipitating the vasospastic episodes in the
females and the classical 3-phase color changes
were observed more frequently among the
females. Neither study produced any evidence
that use of tobacco influenced the course of the
disease. In approximately 10 per cent of both
groups, Raynaud’s phenomenon disappeared
during the period of follow-up. No cause for
Raynaud’s phenomenon was evident; it, there-
fore, seems that these cases represent true
Raynaud’s disease in which spontaneous “cure”
or remission has occurred.

It is interesting that the symptoms of 6
women improved or disappeared during or fol-
lowing the menopause and in 3 improved dur-
ing pregnancy. None stated that menopause
or pregnancy aggravated their symptoms. Mi-
graine headache or hypertension or both had no
influence on the subsequent course of Ray-
naud’s disease in our patients.

Like Blain, Coller, and Carver, we are
impressed that Raynaud’s disease is less likely
to be severe and progressive if the onset occurs
early or late in life. None of our patients who
first noted symptoms before age 10 years or
after age 55 years had serious or disabling
complications.

Blain and his group stated that the disease
tended to be more severe when emotional fac-
tors precipitated the vasospastic episodes. This
was not true in our group of conservatively
treated patients.

Although our data are not suitable for deter-
mining accurately the interval between the
onset of Raynaud’s phenomenon and the oc-
currence of complications when present, it is
certain that the incidence of sclerodactyia and
trophic changes does not increase appreciably
after the first decade of the disease and we are
inclined to agree with the findings of Blain and
associates that in the majority of cases progress
to the severe state will occur within 1 to 7 years
of the onset of the disease.

Our findings again confirm the relative
benignity of Raynaud’s disease as originally defined by Raynaud\textsuperscript{2-7} and as emphasized by other follow-up studies.\textsuperscript{1,6} Nevertheless, Raynaud’s disease continues to have sinister connotations for many patients and physicians.

**Summary**

From 1920 through 1945, the diagnosis of Raynaud’s disease was made or suspected for 756 women and girls at the Mayo Clinic. When the diagnoses were revised according to the criteria of Allen and Brown, the original diagnosis of Raynaud’s disease was considered incorrect for 127 patients and was considered questionable for 252. Follow-up information was available from 208 of the 252 patients with a questionable diagnosis. This revealed that 52.9 per cent did have Raynaud’s disease. In 13.5 per cent, diseases with which Raynaud’s phenomenon is commonly associated (rheumatoid arthritis, acrosclerosis, and dermatomyositis) developed. The Raynaud phenomenon subsequently disappeared in 13.9 per cent and remained unilateral in 1.9 per cent. The remaining 17.8 per cent were dead. Six patients were known or were presumed to have died of disseminated lupus erythematosus with which Raynaud’s phenomenon is commonly associated. Although the causes of death were not known for 19 patients, the young age at which many of them died suggests that their Raynaud’s phenomenon may have been secondary to a serious disease.

When Raynaud’s phenomenon occurs, the prognosis is uncertain until a diagnosis of Raynaud’s disease can be validated by the criteria of Allen and Brown. This study has shown that the diagnosis of Raynaud’s disease by these criteria will be accurate in at least 95 per cent of the cases.

Review of the records of 474 women and girls who had Raynaud’s disease and follow-up information obtained from 307 who were treated conservatively confirms the benignity of this disease. There were no deaths attributed to it, and very little disability. Amputations of terminal phalanges for complications of Raynaud’s disease were necessary for 0.4 per cent of the patients before coming to the clinic and for none during the follow-up period. Raynaud’s phenomenon became less troublesome or disappeared in 46 per cent. Trophic lesions of the fingers and sclerodactyly improved or disappeared in the majority of women who had these complications. No major amputations were necessary and gangrene did not occur in any case.

Raynaud’s phenomenon can be a manifestation of many conditions and diseases of which Raynaud’s disease is the most common and least serious.

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**Summario in Interlingua**

Ab 1920 usque al fin de 1945, le diagnosto de morbo de Raynaud esseva facite o suspicite al Clinica Mayo in 756 feminas e pueras. Le revision del diagnosces secundo le criterios de Allen e Brown resultava in le conclusion que le constatation original de morbo de Raynaud esseva incorrecte in 127 patientes e questionabile in 252. Informaciones ulterior esseva disponibile pro 208 del 252 patientes con diagnosces questionabile. Iste informaciones ulterior revelava que 52,9 pro cento del patientes in iste gruppo hava de facto morbo de Raynaund. In 13,5 pro cento, morbos se disvelopava con que le phenomeno de Raynaud es communmente associate (i.e. arthritis rheumatoide, acrosclerosis, e dermatomyositis). Le phenomeno de Raynaud dispareva subsequentemente in 13,9 pro cento del casos e remaneva unilateral in 1,9 pro cento. Le remanente 17,8 pro cento del patientes esseva morte. Sex patientes hava morite certe– o presumite ab disseminate lupus erythematoso con que le phenomeno de Raynaud es communmente associate. Ben que le causa de morte non esseva cognoscite in 19 casos, le juvene etate a que multes de iste patientes moriva suggere que lor phenomeno de Raynaud esseva possibilemente secundari a un serie morbo.

Quando le phenomeno de Raynaud occurre, le prognose es incerte usque le diagnose de
morbo de Raynaud pote esser corroborate secundo le criterios de Allen e Brown. Le presente studio ha monstrate que le diagnose de morbo de Raynaud secundo le criterios de Allen e Brown es accurate in al minus 95 pro cento del casos.

Le examine del protocollos de 474 feminas e pueras con morbo de Raynaud, insimul con informaciones ulterior pro 307 de illas in qui le tractamento usate esseva de character conservator, confirma le benignitate de iste morbo. Nulle morte esseva attribuite a illo e pauchissime invaliditate. Amputation de phalanges terminal a causae de complicaciones de morbo de Raynaud esseva necessari in 0,4 pro cento del patientes ante lor arrivata a iste Clinica e in nulle durante le periodo ulterior. Le pheneomeno de Raynaud deveniva minus incommo- dante o dispareva in 46 pro cento del casos. Lesiones trophic del digitos e sclerodactylya se meliorava o dispareva in le majoritate del feminas qui havaa iste complicaciones. Nulle amputationes major esseva necessari, e nulle gangrena occurreva in ulle del casos. Le pheneomeno de Raynaud pote esser un mani festation de numeuros conditiones e morbos. Inter illos, morbo de Raynaud es le plus common e le minus serie.

REFERENCES


The danger of sudden abolition of the carotid sinus reflex does not seem to be generally appre- ciated. Bucy pointed out in 1936 that section of 1 glossopharyngeal nerve could cause elevation of blood pressure. In 4 of 5 patients the blood pressure rose promptly after sectioning and remained elevated for 5 to 12 days. In the 49-year-old man described by the author, blood pressure rose from 120/80 to 240/140 mm. Hg while the patient was still on the surgical table. He never recovered consciousness and died 24 hours after operation. There was increased cerebrospinal fluid pressure and 40 red cells per mm.3 in the spinal fluid. Multiple cerebral hemorrhages were discovered at autopsy. The author suggests that irradiation might have advantage as treatment by reducing hyperactivity slowly. He also suggests vigilant control of blood pressure with hypotensive agents at the time of surgery.

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