ALTHOUGH case reports of painful, red extremities date back at least to 1834, Mitchell first analyzed the symptoms in 1878 and suggested the term "erythromelalgia." During the ensuing 55 years, reports of this entity appeared so sporadically that, in 1933, Lewis considered that the term lacked precise definition and should be abandoned.

In 1938, however, Smith and Allen reported a series of patients who had elevated local skin temperatures besides the characteristic burning distress and red discoloration. They termed the condition "erythermalgia" and stated: "This condition is characterized by burning distress, involving any of the extremities, which is inseparably linked with, and entirely dependent on, elevation of the temperature of the skin of the affected parts."

They further pointed out that the condition could be either primary (idiopathic) or secondary (related to nervous, peripheral vascular, or other diseases). Since then, only sporadic mention of this syndrome has been found in the literature.

Our impression that significant clinical differences may exist between the primary and the secondary form and our experience of finding erythermalgia as an important clue to more serious disease prompted this review. Fifty-one cases of this syndrome, seen at the Mayo Clinic during the years 1951 to 1960 inclusive, were considered sufficiently informative to be included in this report.

### Table 1

<table>
<thead>
<tr>
<th>Age, years</th>
<th>Type</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Primary</td>
</tr>
<tr>
<td>0-9</td>
<td>2</td>
</tr>
<tr>
<td>10-19</td>
<td>0</td>
</tr>
<tr>
<td>20-29</td>
<td>3</td>
</tr>
<tr>
<td>30-39</td>
<td>3</td>
</tr>
<tr>
<td>40-49</td>
<td>6</td>
</tr>
<tr>
<td>50-59</td>
<td>8</td>
</tr>
<tr>
<td>60-69</td>
<td>6</td>
</tr>
<tr>
<td>70-79</td>
<td>2</td>
</tr>
<tr>
<td>Total</td>
<td>30</td>
</tr>
</tbody>
</table>

### Primary Erythermalgia

Thirty patients with erythermalgia without associated disease of the hematologic, vascular, or nervous system were classified as having primary erythermalgia. The distribution of patients according to age at onset and type of erythermalgia can be found in table 1. Two thirds of the patients had had symptoms 1 to 3 years before consultation at the Mayo Clinic, and a few had suffered for as long as 7 to 15 years. There were 20 males and 10 females in the group with primary erythermalgia.

Nearly all patients described their distress as a burning pain; in some instances, it was also described as a sharp, stabbing, or stinging pain or "as if one's toes had been hammered repeatedly." This distress tended to occur intermittently, and careful questioning revealed that the onset of the attacks was related to situations that either promoted increased heat or caused prolonged dependence of the affected part. Thus, attacks were re-
ATED TO WALKING, STANDING, EXERCISING, SLEEPING UNDER COVERS, WEARING SHOES OR GLOVES, OR PLACING THE EXTREMITIES NEAR HEATERS. SEVERAL PATIENTS HAD NOTICED AN INCREASE EITHER IN THE NUMBER OF ATTACKS OR IN THE INTENSITY OF THE ATTACKS OR IN BOTH DURING THE SUMMER.

THE DURATION OF THE ATTACKS WAS VARIABLE, BUT, IN MOST CASES, THEY LASTED FROM MINUTES TO HOURS. THE MOST COMMON DURATION WAS TWO TO THREE HOURS, BUT IN A FEW INSTANCES THE ATTACK CONTINUED ONE TO TWO DAYS.

ONLY ABOUT TWO-thirds OF THE PATIENTS HAD NOTICED INCREASED HEAT AND REDNESS IN THE AFFECTED EXTREMITY DURING THE ATTACKS; IN SOME, TEMPERATURE AND COLOR CHANGES WERE NOT NOTED BECAUSE THE EPISODES OCCURRED AT NIGHT OR WHILE THE PATIENT WAS WEARING SHOES. IN ALL PATIENTS THE CHARACTER OF THE PAIN WAS TYPICAL ENOUGH TO INCLUDE THEM IN THE SERIES.

THE DISTRESS WAS CONSIDERED AS MODERATELY SEVERE IN MOST PATIENTS, BUT IT WAS SEVERE ENOUGH IN THREE TO REQUIRE THEM TO ELEVATE OR TO COOL THEIR FEET ALMOST CONTINUOUSLY.

MOST PATIENTS HAD SOUGHT RELIEF BY LOWERING THE TEMPERATURE OF THE SKIN BY VARIOUS MEANS SUCH AS WALKING ON SNOW, ON WET SAND, ON COLD FLOORS OR BY SLEEPING WITH THE AFFECTED PART OUTSIDE THE COVERS OR WITH THE FEET ELEVATED. SOME PATIENTS USED AN ELECTRIC FAN TO COOL THE EXPOSED FEET, AND OTHERS USED COLD PACKS TO RELIEVE THE AFFECTED PART.

THE DISTRIBUTION OF PATIENTS ACCORDING TO SITE OF INVOLVEMENT AND TYPE OF ERYTHEMALGIA MAY BE NOTED IN TABLE 2. THE INVOLVEMENT WAS BILATERAL IN 28 OF THE 30 CASES. THE EXTENT TO WHICH THE EXTREMITIES WAS INVOLVED VARIED WIDELY. IN ABOUT 50 PER CENT OF THE PATIENTS WHO HAD THE LOWER EXTREMITIES AFFECTED, THE DISTRESS WAS CONFINED TO THE SOLES OF THE FEET. IN SOME, ONLY THE TOES OR FINGERS WERE AFFECTED WHILE, IN OTHERS, THE ENTIRE HAND OR FOOT WAS AFFECTED. IN TWO PATIENTS, SYMPTOMS EXTENDED FROM THE FEET TO THE KNEES.


ROENTGENOLOGIC STUDIES WERE DONE ON THE FEET OF FIVE PATIENTS. NO ABNORMALITY WAS DEMONSTRATED IN TWO. ONE PATIENT WITH BILATERAL SYMPTOMS HAD OSTEOPOROSIS OF THE RIGHT FOOT ONLY. ANOTHER PATIENT HAD BILATERAL OSTEOPOROSIS AS WELL AS BILATERAL SYMPTOMS. HYPERTROPHIC OSSOUS CHANGES OF BOTH FEET WERE DEMONSTRATED IN ONE PATIENT. IN THE LATTER PATIENT, THE DISTRESS WAS BILATERAL AND EXTREMELY SEVERE; THE TYPICAL TRIAD OF BURNING DISTRESS, REDNESS, AND INCREASED WARMTH DISAPPEARED WHEN THE PATIENT IMMERSED HIS FEET IN COLD WATER. THE DISTRESS OCCURRED USUALLY AT NIGHT WHEN THERE WAS NO WEIGHT-BEARING, AND SOME RELATION TO EMOTIONAL FACTORS WAS NOTED. CALCIFICATION OF THIS PATIENT'S PEDAL ARTERIES WAS NOTED, BUT THE PERIPHERAL PULSATIONS WERE NORMAL. NO ARTERIAL CALCIFICATION WAS FOUND FROM ROENTGENOGRAPHIC STUDIES IN THE OTHER FOUR CASES.

SECONDARY ERYTHEMALGIA

TWENTY-ONE PATIENTS WITH ERYTHEMALGIA...
were included in this group because of the presence of disease which might be causative of the syndrome. Eleven were females and 10 were males. The distribution of patients with secondary erythermalgia according to age at onset is summarized in table 1 and compared to that of the patients with primary erythermalgia. It may be seen that all patients with secondary erythermalgia were 40 years old or older, while only about two thirds of those with the primary type were of this age. The character of distress and the factors that increased or relieved the symptoms were, in general, similar to the ones described for the patients with the primary type, although the pain seemed to be less intense. Fifteen patients had symptoms in both upper, in both lower, or in all four extremities (table 2). Six had symptoms with asymmetric distribution; in five of these, only one lower extremity was involved. Asymmetric involvement is more frequent in the secondary type.

The distribution of patients according to diseases that were associated with secondary erythermalgia can be noted in table 3. Erythermalgia was most frequently associated with one of the myeloproliferative disorders, particularly polycythemia vera. Since the criteria currently in use for the diagnosis of polycythemia vera are more rigid than those used during the earlier years represented by our study, not all of the patients could be positively diagnosed retrospectively as having primary polycythemia. However, in five of the nine patients polycythemia could be diagnosed with certainty, while, in the other four, it could be considered as a highly probable diagnosis. One patient was found to have splenomegaly and an increased number of megakaryocytes in the bone marrow. His condition was later diagnosed elsewhere as myeloid metaplasia and apparently was confirmed at necropsy. An outstanding feature is that in eight of the nine patients with polycythemia and in the one with myeloid metaplasia, erythermalgia was the initial complaint and preceded the full-blown myeloproliferative disorder by as long as 12 years. Detailed report of these cases will be made elsewhere.9

Eleven patients had hypertension, although in only three was this the only associated condition. None of these 11 patients had diastolic pressures greater than 110 mm. of mercury, and all of them were in groups 1 or 2 of the Keith-Wagener-Barker classification10 of eye ground changes. The relation of erythermalgia to hypertension has been described previously,1 but, in the present series, the number of patients who had hypertension as the only associated factor is too small to permit any reliable conclusions regarding the significance of this association. The association of erythermalgia with diabetes mellitus and with rheumatoid arthritis may be coincidental, but since arterial disease and peripheral neuropathy may occur in both diseases, the three patients with these conditions were considered as having secondary erythermalgia. Acute systemic lupus erythematosus developed in one patient five months after the appearance of typical erythermalgia. This occurrence has not been previously described.

In one patient with secondary erythermalgia, dorsalis pedis pulses were absent bilaterally and symptoms were confined to the soles of his feet. In another patient, diminished pulsations of the left popliteal, dorsalis pedis, and posterior tibial arteries were noted, while his distress was equal in both feet. In a third
patient, whose erythermalgia was limited to three toes on the right foot, the dorsalis pedis pulsations were absent on the left. Of seven patients who underwent radiologic study of the extremity affected by erythermalgia, only two showed arterial calcification in the foot. Dorsalis pedis pulsations were normal bilaterally in one and absent in the other.

Temperature Studies
Temperature studies were performed on 31 patients to determine the possible relation of distress to elevation of skin temperature. Nineteen of these patients had primary and 12 had secondary erythermalgia. These studies were conducted in the vascular laboratory of the Mayo Clinic, and skin temperatures were measured by thermocouples applied to the digits of all extremities. The patient was placed in a room in which the temperature was 25 C. and kept there until his skin temperature became stable. He was then moved to an adjoining room in which the temperature was 31 to 33 C., and from this room he was moved again to a room in which the temperature was 19 to 20 C. Enough time was allowed in each room for the skin temperature to become stable; both the changes in skin temperature and the patient's subjective complaints were recorded. A positive result diagnostic of erythermalgia was achieved when the increase in skin temperature induced the distress and the return to colder temperature made the distress disappear. The temperature of the affected extremities was usually higher than in the unaffected ones.

A critical point has been described to indicate the temperature at which the distress occurs, and this critical point usually lies within a range of 32 to 36 C. In the present series the results of the temperature studies were positive in 26 of 31 patients. The symptoms in the remaining five patients (two with primary and three with secondary erythermalgia) were typical enough to warrant including these patients in the series, particularly since only two were subjected to temperatures of more than 33 C. and it is possible that their critical point was never reached.

Discussion
The pathogenesis of erythermalgia remains unknown in spite of the interesting observations of Lewis and Lewis and Hess, who believed that the skin of patients with this condition is unusually sensitive to warmth. They called this the "susceptible state" and believed that increased heat susceptibility was due to damage to the skin. That the skin of these patients is more susceptible to warmth is evident from the fact that temperatures that do not provoke any discomfort in normal individuals may cause distress in patients with erythermalgia.

Allen, Barker, and Hines reported that vasodilatation is the direct cause of the spontaneous attacks of burning distress but that increased blood flow is "not an integral part of the mechanism causing the distress." The symptoms that are induced in these patients by increasing the temperature above their critical point remain unchanged even when the blood flow is interrupted by a proximal pressure cuff. Also attributable to the role that vasodilatation plays in the syndrome are the increased elimination of heat and the increased content of oxygen in the venous blood coming from the affected extremities of these patients.

Mufson believed that the distress was due to increased blood pressure in the minute skin vessels. The role of the associated myeloproliferative disorders in the pathogenesis of erythermalgia is unknown. It is also unknown whether the pathogenesis of the secondary type of erythermalgia is similar to that of the primary type.

An interesting observation by Smith and Allen was that a single dose of 650 mg. of aspirin relieved the symptoms in some patients for as long as four days. In our series, 11 of 17 patients with primary erythermalgia and 14 of 18 with secondary erythermalgia, or 70 per cent of the total who used aspirin, responded well to this small dose. Some patients who received aspirin preceding their skin temperature studies may have had false negative results. The response to aspirin is
characteristic enough to constitute a valuable diagnostic clue. The reason for this prolonged symptomatic relief is unclear, since aspirin's antipyretic effect is thought to be due to increased cutaneous blood flow, and more than 50 per cent of a single dose is excreted in 24 hours.\textsuperscript{13}

We are only slightly familiar with other reported modes of treatment, although one of our patients had relief from Kutapressin injections. Epinephrine,\textsuperscript{5} heat desensitization,\textsuperscript{12} vaccines,\textsuperscript{14} sublingual isoproterenol (Isuprel),\textsuperscript{8} nitroglycerin ointment (Nitrol),\textsuperscript{8} and phenoxybenzamine hydrochloride (Dibenzyline)\textsuperscript{15} have all been advocated in the symptomatic treatment of this condition. Patients with severe erythermalgia not responsive to conservative measures have been subjected to lumbar ganglionectomy\textsuperscript{6} or to blocking, crushing, or dividing of the peripheral nerves.\textsuperscript{1,4} Only three patients had alcohol blocks of the lumbar sympathetic chain, and two had blocks of the posterior tibial nerve. None of the five was helped by these procedures, and one of those subjected to lumbar block complained of increased distress after this procedure.

Management of secondary erythermalgia is dependent on the treatment of the primary disorder. This is particularly true in the erythermalgia that is secondary to polycythemia. Three patients experienced relief of their erythermalgia after appropriate treatment of the polycythemia, and recurrence of the erythermalgia followed recurrence of the polycythemia.

Certain data may be valuable in differentiating the primary from the secondary type (table 4). An older patient with asymmetric erythermalgia would be more likely to have the secondary type, and, thus, the possibility that he has an associated disease should be carefully considered. The distress in the primary type may be more intense, involve a greater portion of the extremities, and is more often symmetric.

Our finding that erythermalgia may precede the classic manifestations of the myeloproliferative disorders as well as of systemic lupus erythematosus for as long as 12 years makes it imperative to exclude these diseases before the erythermalgia can be considered primary. Even if no associated disease is found, one may become apparent at a later date.

Erythermalgia should be differentiated from distress relating to numerous conditions that can cause hand and, particularly, foot pain. These conditions include rheumatoid and degenerative joint disease, metatarsalgia, March fractures, plantar neuritis, plantar fascitis, peripheral neuropathies, and occlusive arterial disease.\textsuperscript{16} The majority of these conditions are aggravated by weight-bearing, whereas erythermalgia occurs not only with weight-bearing but also with mere dependency of the extremities.

In many instances the history of the peculiar and variegated modes of seeking relief that these patients offer spontaneously may alert the clinician to the diagnosis of this condition, and, furthermore, it may be a valuable clue to the early diagnosis of more serious disease.

**Summary**

The syndrome of erythermalgia is characterized by a burning distress of the extremities that is accompanied by redness and increased temperature of the skin. These symptoms are initiated or exacerbated by an increase in environmental temperature and diminished by measures that cool the skin. Of 51 patients with this clinical syndrome seen at the Mayo Clinic during the years

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**Table 4**

Differential Features of Primary and Secondary Erythermalgia (51 Patients)

<table>
<thead>
<tr>
<th>Features</th>
<th>Primary type (30 cases)</th>
<th>Secondary type (21 cases)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>20</td>
<td>10</td>
</tr>
<tr>
<td>Female</td>
<td>10</td>
<td>11</td>
</tr>
<tr>
<td>Age at onset &lt;40 yr.,</td>
<td></td>
<td></td>
</tr>
<tr>
<td>patients</td>
<td>8</td>
<td>0</td>
</tr>
<tr>
<td>Severity of distress</td>
<td>Greater</td>
<td>Lesser</td>
</tr>
<tr>
<td>Extent of involvement</td>
<td>Feet to</td>
<td>Feet to</td>
</tr>
<tr>
<td>of lower extremities</td>
<td>knees</td>
<td>ankles</td>
</tr>
<tr>
<td>Associated diseases</td>
<td>No</td>
<td>Yes</td>
</tr>
</tbody>
</table>

(See table 3)
1951 to 1960 inclusive, 30 were considered as having primary erythermalgia because of the absence of demonstrable associated conditions, and the rest were classified as having secondary erythermalgia because the condition was associated with various diseases. Particularly significant was the relation of erythermalgia to the myeloproliferative disorders as evidenced in 10 cases. In some of these cases, erythermalgia preceded other manifestations of the myeloproliferative disorder by as long as 12 years. The primary type was found to occur in younger individuals and to be more often bilateral, to produce pain of greater intensity, and to involve larger areas of the affected extremities. The pathologic physiology of this syndrome remains unknown.

References
2. MITCHELL, S. W.: On a rare vaso-motor neurosis of the extremities, and on the maladies with which it may be confounded. Am. J. M. Sc. 76: 2, 1878.
3. LEWIS, T.: Clinical observations and experiments relating to burning pain in the extremities, and to so-called “erythromelalgia” in particular. Clin. Sc. 1: 175, 1933.

Dissecting Aneurysm

Dissecting aneurysm, as found in the body of George II, was described in 1760 by Frank Nicholls (1699-1778), whose experiments had shown that the two inner coats of arteries can be ruptured while the external coat remains intact. The name “dissecting” was first used by Maunoir in 1802; Laennec gave a careful description of a case and Peacock, Bostrom, and Adami made collections of the known cases.—Sir HUMPHRY DAVY ROLLESTON. The Harveian Oration. Great Britain, Cambridge University Press, 1928, p. 58.

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RICHARD R. BABB, DONATO ALARCON-SEGOVIA and JOHN F. FAIRBAIRN

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