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# Pernio in Pediatrics

Tamara D. Simon, MD; Jennifer B. Soep, MD; and J. Roger Hollister, MD

**ABSTRACT.** Pernio, or chilblains, is a localized inflammatory lesion of the skin resulting from an abnormal response to cold. Five cases were seen among adolescent female patients who presented to our rheumatology service in a pediatric tertiary care center in the winter of 2003 to 2004. All 5 patients were thin (BMI of <25th percentile) and had either toes or fingers that were affected. For each, laboratory evaluation results were unremarkable, including negative antinuclear antibody profile results. Symptomatic treatment, with or without medication, was recommended. Pernio most commonly occurs among young women but may occur among older individuals or among children. Because pernio develops among susceptible individuals who are exposed to non-freezing cold, the lesions usually begin in the fall or winter and disappear in the spring or early summer. Acute pernio may develop 12 to 24 hours after exposure to the cold. Single or multiple erythematous, purplish, edematous lesions appear, accompanied by intense pain, itching, or burning. Chronic pernio occurs with repeated exposure to the cold and the persistence of lesions. In an acute exacerbation, the major differential diagnosis alternative would be Raynaud's phenomenon, which consists of sharply demarcated cutaneous pallor and cyanosis, followed by erythema, of far shorter duration (hours rather than days). Frostbite is freezing of tissue, with resultant tissue necrosis. Several conditions have been described as predisposing subjects to pernio, including the presence of cryoproteins, excessive cold exposure, and anorexia nervosa among children and systemic lupus erythematosus and antiphospholipid antibodies among adults. It is important, therefore, when evaluating a patient with pernio, both to exclude an underlying diagnosis and to determine whether additional testing is necessary. The lesions of acute pernio are usually self-limited but may lead to recurrent disease. The involved limb should be cleaned and dried, and rewarming should occur. Prevention is the best form of therapy, and cold exposure should be minimized after an initial insult. The prognosis for properly treated pernio is excellent. Nifedipine, which produces vasodilation, has been demonstrated to be effective in reducing pain, facilitating healing, and preventing new lesions of pernio. We think that the 5 cases seen in our rheumatology clinic represent an increase, compared with prior years; the dermatology clinic at the University of Colorado reported a series of 8 children treated during a 10-year period. The reasons for the possible increase are likely multifactorial, with cold

climate, a vulnerable population with thin body habitus, and cold exposure all being contributing causes. Of note, the quality of cold in Colorado is quite dry; however, the winter of 2003 to 2004 was not particularly colder or drier than prior years. All patients were very thin, and thin body habitus may be associated with increased cutaneous vasoreactivity. It is also unclear how these cases of pernio may reflect that winter's fashion trends (2 patients reported wearing sandals in winter). General pediatricians, particularly those who practice in colder climates, should be aware of the presentation and treatment of pernio in childhood. *Pediatrics* 2005;116:e472-e475. URL: [www.pediatrics.org/cgi/doi/10.1542/peds.2004-2681](http://www.pediatrics.org/cgi/doi/10.1542/peds.2004-2681); *rheumatology, adolescence, chilblains, pernio, cold injury*.

ABBREVIATIONS. ANA, antinuclear antibody; CBC, complete blood cell; ESR, erythrocyte sedimentation rate.

**P**ernio, or chilblains, is a localized inflammatory lesion of the skin resulting from an abnormal response to cold. We report 5 cases of pernio seen among adolescent female patients who presented to our rheumatology service in a pediatric tertiary care center in the winter of 2003 to 2004.

## CASE REPORTS

### Patient 1

A 21-year-old, hospitalized, African, female patient was referred for evaluation of painful swollen toes and difficulty walking for 3 weeks in mid-December 2003. She denied any known triggers or associated symptoms, including extreme cold exposure. She denied recent fever, weight loss, joint symptoms, abdominal pain, diarrhea, and Raynaud's symptoms but reported a history of blanching cold fingers on exposure to cold. She was examined by members of the hematology and infectious disease services, who were concerned about vasculitis and recommended rheumatology consultation. The patient's medical history was notable for a positive purified protein derivative test result and a history of periodic fevers, possibly malaria, in August 2003, with inconclusive evaluation findings. Medications included isoniazid. The family history was noncontributory. The physical examination was notable for emaciation (weight: 35 kg; height: 150 cm; BMI: 16 kg/m<sup>2</sup> or <5th percentile<sup>1</sup>). The feet demonstrated bilateral tender edema of the second through fifth toes (left more than right). There was a tender nodule over the left fourth interphalangeal joint and tender macular lesions on the left lateral fifth toe and between the fourth and fifth toes, as well as cool toes and fingers. There were no abnormal nail-fold capillaries. Laboratory evaluations included normal complete blood cell (CBC) count, erythrocyte sedimentation rate (ESR), and C-reactive protein levels and negative antinuclear antibody (ANA) profile results. The patient began a therapeutic trial of extended release nifedipine (60 mg, every 24 hours), and symptomatic treatment, including keeping her feet warm and dry, was advised. In a follow-up examination in the clinic 9 days later, the patient demonstrated significant improvement, with only slight swelling of her right second toe and discoloration of her left second toe.

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### Patient 2

A previously healthy, 14-year-old, white, female patient was referred for outpatient rheumatology evaluation in March 2004, because of a 2-year history of intermittent pain, swelling, and coolness of her toes bilaterally. These symptoms usually lasted 1 to 2 weeks and occurred 3 or 4 times per year, always in winter. The patient denied any known triggers, including extreme cold exposure; however, the episodes occurred only in winter, and her extremities became cool to the touch. The patient denied recent fever, weight loss, diarrhea, and Raynaud's symptoms. The medical history was notable for incontinence, which was treated with oxybutynin. The physical examination revealed a slender female patient (weight: 53.4 kg; height: 173 cm; BMI: 18 kg/m<sup>2</sup> or 25th percentile<sup>1</sup>) with violaceous warm fingers with 3-second capillary refill, cool cyanotic toes with 4-second capillary refill, and normal nail-fold capillaries. Laboratory evaluations included negative ANA profile results. The patient began a therapeutic trial of extended release nifedipine (30 mg, every 24 hours as needed), and symptomatic treatment was advised. Six weeks later, the patient reported no additional episodes of pain and swelling.

### Patient 3

A previously healthy, 13-year-old, white, female patient was examined in March 2004, because of a 4-month history of toe injury. She first noticed symptoms after snowshoeing, at which time her feet were cold and wet. Her toes then became purple, swollen, and painful, and 8 weeks later the skin over her toes peeled. The patient reported subsequent cold exposure, wearing sandals to a school dance in the snow. She denied fever, recent weight loss, and Raynaud's symptoms. The medical history was unremarkable, and the patient took no medication. The physical examination revealed a slender female patient (weight: 48.8 kg; height: 174.4 cm; BMI: 16 kg/m<sup>2</sup> or 10th percentile<sup>1</sup>) with faint livedo reticularis, cool fingers with 3-second capillary refill, violaceous cool toes, particularly on the second through fifth digits of the left foot and the third through fifth digits of the right foot, and no nail-bed telangiectasia. Laboratory evaluations were notable for normal CBC count and negative ANA profile results. Symptomatic treatment was advised, and the patient's family was educated regarding medication options for the following winter season, if necessary. Four weeks after her visit, the patient reported no additional symptoms.

### Patient 4

A previously healthy, 15-year-old, white, female patient was referred for rheumatology evaluation in March 2004, because of a 3-week history of bilateral toe swelling associated with pain and purple discoloration. She reported a pattern of increasing symptoms for several days, followed by relative improvement. She denied any known triggers or associated symptoms, including cold exposure, although her father pointed out that she wore sandals on a regular basis in winter months. A review of systems was negative for fever, recent weight loss, diarrhea, and the triphasic color changes and pain associated with Raynaud's phenomenon. The medical history was unremarkable, and the patient took no medications. The physical examination revealed a slender female patient (weight: 40.8 kg; height: 166.3 cm; BMI: 15 kg/m<sup>2</sup> or <5th percentile<sup>1</sup>) with cool violaceous toes bilaterally with 4-second capillary refill and no abnormal nail-fold capillaries. The patient exhibited tenderness to palpation over the third metatarsal, with trace edema. Laboratory evaluations included normal C-reactive protein levels, ESR, and CBC count and negative ANA screen results. Symptomatic treatment, including keeping the feet warm and dry, was advised. Four weeks after her visit, the patient reported that her toes were violaceous but no longer tender.

### Patient 5

A 16-year-old, white, female patient was referred for outpatient rheumatology evaluation in April 2004, because of a 10-year history of blue, warm, swollen toes and 6 months of red, swollen, tender fingers (Fig 1). She denied any known triggers or associated symptoms, including excessive cold exposure. She denied fever, recent weight loss, and diarrhea. The medical history was notable for attention-deficit disorder and pernio diagnosed 2 to 3 years previously. The patient took no medications. The physical examination revealed a slender female patient (weight: 45.2 kg; height:



Fig 1. Red, swollen, tender fingers in pernio (patient 5).

166.5 cm; BMI: 16 kg/m<sup>2</sup> or <5th percentile<sup>1</sup>) with cool violaceous fingers and toes with brisk capillary refill and no nail-fold telangiectasia. Laboratory evaluations included normal ESR, CBC count, and rheumatoid factor levels and negative ANA profile results. Symptomatic treatment was advised. Three weeks after her visit, the patient reported no additional symptoms.

## DISCUSSION

Localized inflammatory lesions of the skin resulting from abnormal responses to the cold, usually with a component of dampness, have been described in several different settings. Chilblains is an Anglo-Saxon term meaning chill and blegen (sore), whereas perniosis is a Latin word that is synonymous.<sup>2</sup> The syndrome is also called trenchfoot<sup>3</sup> and kibes when it occurs in the feet.<sup>4</sup>

Pernio occurs most commonly among young women between the ages of 15 and 30 years but may occur among older individuals or children. Historically, up to 50% of women developed pernio in wartime conditions in northern Europe. Pernio is now less common but is still seen in the temperate humid climates of northwestern Europe and in the northern United States.<sup>5</sup> The exact incidence of pernio among children is unknown; however, one study of children treated at a pediatric dermatology clinic in a tertiary care center in Denver diagnosed only 8 cases in a 10-year period.<sup>4</sup>

Pernio develops among susceptible individuals who are exposed to nonfreezing cold. Characteristically, the lesions begin in the fall or winter and disappear in the spring or early summer. There is controversy regarding whether dry cold or damp-

ness is more likely to cause pernio.<sup>3,4</sup> In advanced cases, the seasonal variation may disappear and chronic occlusive vascular disease may develop.

Acute pernio may develop 12 to 24 hours after exposure to the cold. Single or multiple erythematous, purplish, edematous lesions appear, accompanied by intense pain, itching, or burning. These lesions may have a yellowish or brownish discoloration and may be associated with some peeling. They tend to affect the toes and dorsum of the proximal phalanges.<sup>3</sup> Parts of the body that can also be affected are pinnae,<sup>6</sup> cheeks,<sup>7,8</sup> and thighs.<sup>9</sup> The arterial circulation is normal in physical examinations and in noninvasive vascular laboratory tests.<sup>10</sup> As for our patients, typically the lesions last 1 to 2 weeks.<sup>11</sup> Chronic pernio, which has been described for pediatric and adult patients,<sup>5</sup> occurs when repeated exposure to the cold results in the persistence of lesions, with subsequent scarring and atrophy.<sup>12</sup>

In the presence of an acute exacerbation, the major alternative in the differential diagnosis is Raynaud's phenomenon. Raynaud's phenomenon is an abnormal vasoconstrictive response to cold; however, spasm or closure of cutaneous arteries results in sharply demarcated cutaneous pallor and cyanosis, followed by erythema, and the response is of far shorter duration (hours rather than days).<sup>10</sup> Frostbite is distinguished from pernio in that it is freezing of tissue, with resultant tissue necrosis.<sup>3</sup> Other diseases that can cause recurrent, erythematous, nodular, and ulcerative lesions include erythema induratum, nodular vasculitis, erythema nodosum, cold panniculitis, atheromatous embolization, and thrombotic or embolic phenomena. Another entity to consider among children is microgeodic disease, consisting of chilblain-like appearance, tenderness of digits, and radiographic findings of patchy osteoporosis; radiographic evaluation may be considered to help confirm this diagnosis.<sup>13</sup>

A variety of conditions have been described as predisposing patients to pernio. Among children, the presence of cryoproteins, such as cold agglutinins and cryoglobulins, has been reported in association with pernio.<sup>4</sup> Excessive cold exposure<sup>3</sup> and parental neglect<sup>14</sup> have also resulted in pernio. Among adolescents, pernio has been seen in association with anorexia nervosa.<sup>15</sup> Among adults, pernio has been reported in association with systemic lupus erythematosus,<sup>7</sup> lupus anticoagulant, anticardiolipin, and antiphospholipid antibodies,<sup>14</sup> chronic myelocytic leukemia,<sup>16</sup> metastases from carcinoma of the breast,<sup>17</sup> and reaction to medication.<sup>18</sup>

It is important, therefore, to consider these conditions when evaluating a patient with pernio, both to exclude an underlying diagnosis and to determine whether additional testing is necessary. Aside from a low BMI, our patients did not have specific symptoms of an underlying medical condition. Specifically, they did not have livedo reticularis, other skin rashes, fevers, Raynaud's phenomenon, arthritis, gastrointestinal symptoms, nail-fold changes, or blood clots. All of the patients we described had negative ANA profile results, which essentially ruled out systemic lupus erythematosus. On the basis of

their reassuring histories and physical examination results, we did not screen routinely for antiphospholipid antibodies, cryoproteins, or other underlying abnormalities among our patients, because abnormal results were not anticipated to change treatment. In addition, we asked our patients to return if their symptoms did not resolve, so that we could pursue additional studies.

Cold-induced trauma is thought to result in vascular damage from tissue anoxemia, with secondary inflammatory reaction.<sup>14</sup> The primary pathologic changes include edema of the papillodermis and reticular dermis infiltrate in the perieccrine region.<sup>19</sup> Vasculitis characterized by a perivascular lymphocytic infiltration of the arterioles and venules of the dermis, thickening and edema of the blood vessel walls, fat necrosis, and chronic inflammatory reaction with giant cell formation have also been described.<sup>20</sup>

The lesions of acute pernio are usually self-limited, although they may lead to recurrent disease, as seen for patient 5. When symptoms do arise, the involved limb should be cleaned and dried, and rewarming should occur in an appropriate environment. Prevention is the best form of therapy, and cold exposure should be minimized as much as possible once an initial insult has occurred.<sup>3</sup> The prognosis for properly treated pernio is excellent; among 8 children treated with observation alone, all experienced complete resolution within 3 months (5 within 1 month), and there were no recurrences over a period of 3 years.<sup>4</sup>

Nifedipine, a calcium channel blocker that results in vasodilation, has been demonstrated to be effective in the treatment of pernio.<sup>21,22</sup> In a randomized trial, nifedipine reduced the pain, facilitated the healing process, and prevented new lesions.<sup>23</sup> Several treatments have been attempted in the past without success, including ultraviolet radiation,<sup>24</sup> vitamin D<sub>2</sub> administration,<sup>25</sup> and thymoxamine administration.<sup>26</sup> Topical fluorinated corticosteroids have yielded conflicting results<sup>27,28</sup> in the treatment of pernio.

## CONCLUSIONS

Our 5 patients with pernio in the winter of 2003 to 2004 were adolescent female subjects, had thin body habitus (BMI of <25th percentile), and had either toes or fingers that were affected. For each, laboratory evaluation results were unremarkable, including negative ANA profile results; therefore, systemic lupus erythematosus was excluded. Symptomatic treatment, with or without medication, was recommended. The duration of symptoms was critical in distinguishing pernio from Raynaud's phenomenon.

We think that the number of cases seen in our rheumatology clinic represents an increase, compared with prior years; as a comparison, the dermatology clinic at the University of Colorado reported a series of 8 children treated during a 10-year period.<sup>4</sup> The reasons for the possible increase are likely multifactorial, with cold climate, a vulnerable population with thin body habitus, and cold exposure all being contributing causes. Presumably each case resulted

from nonextreme cold exposure during the winter months in Denver, Colorado. Of note, the quality of cold in Colorado is quite dry; however, the winter of 2003 to 2004 was not particularly colder or drier than prior years. All patients were very thin, and thin body habitus may be associated with increased cutaneous vasoreactivity.<sup>29</sup> It is also unclear how these cases of pernio may reflect that winter's fashion trends (2 patients reported wearing sandals in winter). General pediatricians, particularly those who practice in colder climates, should be aware of the presentation and treatment of pernio in childhood.

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