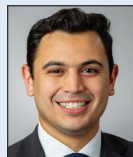


# Dx ACROSS THE SKIN COLOR SPECTRUM



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## Break the Itch-Scratch Cycle to Treat Prurigo Nodularis

### THE COMPARISON

- A** A 45-year-old Hispanic man with prurigo nodularis presented with hyperpigmented lesions on the leg due to frequent scratching.
- B** A 60-year-old Black woman with prurigo nodularis presented with hyperpigmented lesions on the hand, arm, and thigh due to frequent scratching.

**P**runigo nodularis (PN) is a chronic inflammatory skin condition characterized by firm hyperkeratotic nodules that develop when patients persistently scratch or rub intensely itchy areas of the skin. This potent itch-scratch cycle can be traced back to a dysfunctional interplay between cutaneous nerve fibers and the local immune environment.<sup>1-3</sup> Pruritis lasting at least 6 weeks is a hallmark symptom of PN and can be accompanied by pain and/or a burning sensation.<sup>4</sup> The lesions are symmetrically distributed in areas that are easy to scratch (eg, arms, legs, trunk), typically sparing the face, palms, and soles; however, facial lesions have been reported in pediatric patients with PN, who also are more likely to have back, hand, and foot involvement.<sup>5,6</sup>

Prurigo nodularis can greatly affect patients' quality of life, leading to increased rates of depression and anxiety.<sup>7-9</sup> Patients with severe symptoms also report increased sleep disturbance, distraction from work, self-consciousness leading to social isolation, and missed days of work/school.<sup>9</sup> In one study, patients with PN reported missing at least 1 day of work, school, training, or learning; giving up a leisure activity or sport; or refusing an invitation to dinner or a party in the past 3 months due to the disease.<sup>10</sup>

### Epidemiology

Prurigo nodularis has a prevalence of 72 per 100,000 individuals in the United States,<sup>11</sup> most commonly affecting adults aged 51 to 65 years and disproportionately affecting African American and female patients.<sup>12,13</sup> Most patients with PN experience a 2-year delay in diagnosis after initial onset of symptoms.<sup>10</sup> Adults with PN have an increased likelihood of having other dermatologic conditions, including atopic dermatitis (AD) and psoriasis.<sup>11</sup> Nearly two-thirds of pediatric patients with PN present with AD, and those with AD showed more resistance to first-line treatment options.<sup>5</sup>

### Key Clinical Features

Compared to White patients, who typically present with lesions that appear erythematous or pink, patients with darker skin tones may present with hyperpigmented nodules that are larger and darker.<sup>12</sup> The pruritic nodules often show signs of scratching or picking (eg, excoriations, lichenification, and angulated erosions).<sup>4</sup>

Drs. Adawi and Usatine report no conflict of interest. Dr. Heath has served as a consultant, researcher, and/or speaker for Arcutis, Apogee, CorEvitas, Dermavant, Eli Lilly and Company, Janssen, Johnson and Johnson, Kenvue, L'Oreal, Nutrafol, Pfizer, Sanofi, Tower 28, and WebMD. Dr. Heath also is the recipient of a Skin of Color Society Career Development Award and the Robert A. Winn Diversity in Clinical Trials Award.

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## Worth Noting

Diagnosis of PN is made clinically, but skin biopsy may be helpful to rule out alternative diseases. Histologically, the hairy palm sign may be present in addition to other histologic features commonly associated with excessive scratching or rubbing of the skin.

Patients with PN have a high risk for HIV, which is not surprising considering HIV is a known systemic cause of generalized chronic pruritus. Other associations include type 2 diabetes mellitus and thyroid, kidney, and liver disease.<sup>11,13</sup> Work-up for patients with PN should include a complete blood count with differential; liver and renal function testing; and testing for C-reactive protein, thyroid-stimulating hormone, and lactate dehydrogenase.<sup>4,14</sup> Hemoglobin A1c and HIV testing as well as a hepatitis panel also should be considered when appropriate. Because generalized pruritus may be a sign of malignancy, chest radiography and lymph node and abdominal ultrasonography should be performed in patients who have experienced itch for less than 1 year along with B symptoms (fever, night sweats,  $\geq 10\%$  weight loss over 6 months, fatigue).<sup>14</sup> Frequent scratching can disrupt the skin barrier, contributing to the increased risk for skin infections.<sup>13</sup> All patients with a suspected PN diagnosis also should undergo screening for depression and anxiety, as patients with PN are at an increased risk for these conditions.<sup>4</sup>

Treatment of PN starts with breaking the itch-scratch cycle by addressing the underlying cause of the pruritus. Therapies are focused on addressing the immunologic and neural components of the disease. Topical treatments include moderate to strong corticosteroids, calcineurin inhibitors (tacrolimus or pimecrolimus), capsaicin, and antipruritic emollients. Systemic agents include phototherapy (narrow-band UVB or excimer laser), gabapentin, pregabalin, paroxetine, and amitriptyline to address the neural component of itch. Methotrexate or cyclosporine can be used to address the immunologic component of PN and diminish the itch. That said, methotrexate and cyclosporine often are inadequate to control pruritus.<sup>10</sup> Of note, sedating antihistamines are not effective in treating itch in PN but can be used as an adjuvant therapy for sleep disturbances in these patients.<sup>15</sup>

The only drugs currently approved by the US Food and Drug Administration to treat PN are the biologics dupilumab (targeting the IL-4 receptor) approved in 2022 and nemolizumab (targeting the IL-31 receptor) approved in 2024.<sup>16-18</sup> The evidence that these injectable biologics work is heartening in a condition that has historically been very challenging to treat.<sup>16,18</sup> It should be noted that the high cost of these 2 medications can restrict access to care for patients who are uninsured or underinsured.

Resolution of a prurigo nodule may result in a hyperpigmented macule taking months to years to fade.

## Health Disparity Highlight

Patients with PN have a considerable comorbidity burden, negative impact on quality of life, and increased health care utilization rates.<sup>12</sup> Prurigo nodularis is 3.4 times more common in Black patients than White patients.<sup>13</sup> Black

patients with PN have increased mortality, higher health care utilization rates, and increased systemic inflammation compared to White patients.<sup>12,19,20</sup>

Social drivers of health (eg, socioeconomic challenges, education, access to high-quality health care) likely contribute to PN. Historically, there has been a paucity of research on PN, as with most conditions that disproportionately affect patients with skin of color. Several PN clinical trials currently are underway to explore additional therapeutic options.<sup>11</sup>

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