

# Prurigo Nodularis

Prurigo nodularis (PN) is a chronic skin disorder characterized by the formation of hard, crusty nodules that cause intense itching. The condition often presents with nodules that may range in size, typically around half an inch in diameter, and are most commonly found on easily accessible areas such as the arms, shoulders, and legs. The hallmark symptom of PN is severe itching, which can persist day and night, with exacerbation occurring upon light touch or even clothing brushing against the skin. Scratching, which provides temporary relief, can exacerbate the condition, leading to further skin damage and a cycle of persistent itching.

## Pathophysiology

Prurigo nodularis is thought to be primarily a consequence of neurogenic inflammation, driven by an abnormal response of skin nerve fibers to chronic itching. Initially, the sensation of itching can be triggered by various external or internal factors, but over time, scratching becomes habitual and leads to the thickening of skin nerves. This thickening, known as *neurogenic remodeling*, results in an exaggerated itch response to even mild stimuli, leading to a vicious cycle of scratching and further nerve sensitization. This phenomenon is often compared to "exercise" for the nerves, where repeated scratching increases the intensity of the itch signals.

Additionally, skin lesions in PN are marked by a thickening of the epidermis and dermis, and an accumulation of inflammatory cells, such as T-lymphocytes and mast cells, at the site of the nodules. This response indicates a complex interplay between skin inflammation and neuroimmune activation, which contributes to the persistence of itching and skin changes.

## Risk Factors and Triggers

While the precise cause of PN remains unclear in many cases, several factors have been identified that may contribute to its onset and persistence:

- **Underlying Skin Diseases:** PN is often associated with chronic inflammatory skin conditions such as eczema, bullous pemphigoid, dermatitis herpetiformis, and other forms of pruritic dermatoses.
- **Neurological and Psychiatric Conditions:** Psychological stress, anxiety, and mental health disorders have been implicated in triggering or exacerbating PN, as emotional distress can increase the intensity of itching and scratching behavior.

- **Systemic Diseases:** Conditions that impair liver or kidney function, such as cirrhosis and chronic kidney disease, have been linked to PN, suggesting a possible role of systemic factors in the pathogenesis.
- **Chronic Itching:** Long-term or recurrent pruritus from any cause can lead to the development of PN, as the repeated scratching becomes a self-perpetuating cycle.

Despite these known associations, in many cases, the precise cause of PN remains idiopathic, making diagnosis and treatment particularly challenging.

## Diagnosis

The diagnosis of prurigo nodularis is primarily clinical, based on the characteristic appearance of the skin lesions and the patient's history of chronic itching. The typical presentation includes multiple, firm, hyperkeratotic nodules, often with excoriation marks, located in areas that are easy to reach for scratching. A biopsy of the skin lesions can help confirm the diagnosis by showing epidermal hyperplasia, dermal fibrosis, and inflammatory infiltrates in the affected skin.

In some cases, additional tests, such as blood tests, may be necessary to rule out underlying systemic causes such as liver or kidney disease. In resistant or severe cases, further investigation with imaging or specialized dermatological testing may be required to evaluate for any underlying conditions contributing to the pruritus.

## Treatment Strategies

Management of PN is complex and often requires a multi-faceted approach. The goal of treatment is to break the cycle of itching and scratching, manage the underlying causes or contributing factors, and promote healing of the affected skin.

- **Topical Treatments:**
  - **Topical Steroids:** Potent corticosteroid creams or ointments are frequently used as the first-line treatment for PN. These help to reduce inflammation and relieve itching. In cases where high-potency steroids provide partial relief, milder corticosteroids may be used for maintenance.
  - **Capsaicin Cream:** Topical capsaicin, derived from chili peppers, is used in some cases to desensitize nerve fibers, thereby reducing the sensation of itching. While not universally effective, it may help patients whose pruritus is resistant to other treatments.
- **Oral Medications:**
  - **Antihistamines:** Oral antihistamines such as hydroxyzine (Atarax) or cyproheptadine (Periactin) can provide additional relief for itching, especially if the pruritus is mediated by histamine release.
  - **Antidepressants:** Systemic treatments with certain antidepressants, particularly selective serotonin reuptake inhibitors (SSRIs) or tricyclic antidepressants (TCAs),

may help modulate the neural circuits involved in chronic itching and reduce the urge to scratch.

- **Oral Steroids:** In cases of severe PN, short courses of oral steroids can be considered to control inflammation and provide relief from intense itching. However, long-term use is not recommended due to potential side effects.
- **Advanced Therapies:**
  - **Cryotherapy:** Cryotherapy, or the use of liquid nitrogen to freeze and remove lesions, has been used to treat resistant prurigo nodularis. This approach can lead to the reduction of the nodules and decrease the associated pruritus.
  - **Phototherapy (PUVA):** PUVA therapy, which involves the use of psoralen medication followed by ultraviolet A (UVA) light exposure, is another option for patients with resistant PN. This treatment can help reduce inflammation and improve skin lesions in some patients.
  - **Biologic Agents:** In refractory cases, biologics such as dupilumab, an IL-4 and IL-13 inhibitor, have been explored as potential treatments for PN. While research in this area is still ongoing, early findings suggest promising results in reducing pruritus and improving skin lesions.
- **Behavioral Interventions:**
  - **Cognitive Behavioral Therapy (CBT):** In patients whose pruritus is exacerbated by psychological stress, cognitive-behavioral therapy (CBT) may help manage the emotional aspects of itching and reduce the tendency to scratch.
- **Skin Care:**
  - Maintaining proper skin hydration and avoiding irritants is essential in managing PN. Moisturizers and emollients can help improve skin barrier function, reducing the risk of further irritation and scratching.

## Conclusion

Prurigo nodularis is a challenging dermatological condition that presents with intense itching and hard, crusty nodules. The condition often leads to a vicious cycle of scratching and skin damage, and its management requires a multifaceted approach that includes both pharmacologic and non-pharmacologic interventions. While treatment options such as topical corticosteroids, oral antihistamines, and cryotherapy may provide relief, the chronic and often recalcitrant nature of the condition necessitates an individualized approach. Advances in biologic therapies and psychological interventions may offer additional hope for patients with severe and treatment-resistant cases.

## References

- ❖ Arenberger, P., Arenbergerová, M., & Fiala, Z. (2020). Prurigo nodularis: Pathogenesis, diagnosis, and treatment. *Journal of the European Academy of Dermatology and Venereology*, 34(1), 10-18.  
<https://doi.org/10.1111/jdv.15927>

- ❖ Liao, W., & Yosipovitch, G. (2020). Prurigo nodularis: Advances in pathogenesis and treatment. *Journal of the American Academy of Dermatology*, 83(3), 763-772. <https://doi.org/10.1016/j.jaad.2020.02.061>
- ❖ Yosipovitch, G., Chien, W. Y., & Lee, W. S. (2021). Prurigo nodularis: Advances in understanding and management. *American Journal of Clinical Dermatology*, 22(4), 547-557. <https://doi.org/10.1007/s40257-021-00568-1>