

Nikolsky's Sign in Autoimmune Skin Disorders

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Autoimmune skin disorders sometimes are characterized by acantholysis, or loss of the normal epithelial cell-to-cell adhesion within the skin.¹ Clinically, these disorders present with blistering of the skin and include the pemphigus and pemphigoid groups of disorders. On visual inspection only, these skin conditions are difficult to diagnose and may be confused with other types of skin disorders. Nikolsky's sign is a well-described clinical sign that can be helpful in differentiating some of the autoimmune skin disorders and even determining their prognosis.²

HISTORICAL PERSPECTIVE

Pyotr Vasilyewich Nikolsky (1858–1940) was a Russian dermatologist who studied at the University of Kiev and published a thesis on pemphigus in 1895. He subsequently was appointed Professor and Chief of Dermatology at the University of Warsaw and authored numerous papers and books on a variety of topics, including gangrene and syphilis.³

Nikolsky first described the sign that bears his name in 1896. He related how, after rubbing the skin of patients who had pemphigus foliaceus, there was a blistering or denudation of the epidermis with a glistening, moist surface underneath.⁴ According to his explanation, the skin showed a weakening relationship and contact between the corneal (horny) and granular layers on all surfaces, even in places between lesions (eg, blisters, excoriations) on seemingly unaffected skin.⁵ Nikolsky's observations were later confirmed by Lyell in 1956, who described a Nikolsky sign in patients with toxic epidermal necrolysis.⁴

ELICITATION

There is no absolute consensus on how to elicit Nikolsky's sign. Nikolsky's original criteria for a positive sign included the ability to dislodge both affected skin (ie, skin within or immediately adjacent to pemphigus lesions) and normal skin. He asserted quite specifically that a positive sign occurred only in cases of pemphi-

NIKOLSKY'S SIGN IN PEMPHIGUS

Elicitation: Apply pressure to the affected skin (eg, where a blister is located), perilesional skin, or normal skin in patients with suspected pemphigus.

Positive Response: There is extension of the blister and/or removal of epidermis in the area immediately surrounding the blister.

gus foliaceus and not pemphigus vulgaris because, in the latter disorder, unaffected normal skin could not be removed by lateral pressure.³ However, this specificity could not be duplicated in later studies.

Many experts now agree that the sign is elicited by application of pressure on the skin that results in both the peripheral extension of a blister and the separation or removal of the epidermis.² The sign occurs when pressure is exerted on either the blister, the perilesional skin, or the adjacent normal skin (**Figure 1**). A finger or thumb is usually used to exert the pressure, although some authors have recommended using a paper clip.⁶ Nikolsky's sign is often painful.

Interestingly, although the classic Nikolsky's sign is seen on the skin, there have been 2 case reports alleging its appearance on mucous membranes of other tissues. In one instance, a Nikolsky's sign was elicited in the esophageal mucosa of a patient with pemphigus vulgaris.⁷ In the other, Nikolsky's sign was elicited in the mucosa of the uterine cervix in 13 of 16 patients with pemphigus.⁸ However, these occurrences are exceedingly rare.

PATHOPHYSIOLOGY

The mechanism of Nikolsky's sign most likely reflects the underlying pathologic disease process. The

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Figure 1. Elicitation of Nikolsky's sign. Reprinted with permission from Fitzpatrick TB, Johnson RA, Polano MK, et al. Color atlas and synopsis of clinical dermatology: common and serious diseases. 2nd ed. New York: McGraw-Hill; 1992:539.

primary histologic finding in patients with pemphigus is acantholysis with the occurrence of suprabasal epidermal/intraepidermal splits^{3,9}; these events presumably contribute to the epidermal separation characteristic of a positive Nikolsky's sign. One study corroborated these findings by demonstrating a microscopic Nikolsky's sign in patients with pemphigus in whom tangential pressure was applied to perilesional skin, resulting in the characteristic biopsy findings described above.⁹

CLINICAL UTILITY OF NIKOLSKY'S SIGN

In general, Nikolsky's sign has been considered very useful in differentiating the bullous skin diseases. Specifically, elicitation of the sign can help distinguish pemphigus vulgaris, which is strongly associated with the sign, from bullous pemphigoid, in which the sign is usually absent. One study, however, did report a positive Nikolsky's sign in 13% of patients with bullous pemphigoid.¹⁰ The authors suggested the term *pseudo-Nikolsky's sign* for these cases in which the epidermal separation was actually subepidermal instead of intraepidermal, as in pemphigus vulgaris.

There are a number of other diseases associated with a positive Nikolsky's sign. Patients with toxic epidermal necrolysis, staphylococcal scalded skin syndrome, bullous impetigo, and epidermolysis bullosa all can exhibit the sign. Moreover, Nikolsky's sign has been described anecdotally in other conditions as well, including mycosis fungoides, bullous lichen planus, and benign mucous membrane pemphigoid^{2,11,12}; the sign also allegedly occurred in a patient with systemic sclerosis who developed D-penicillamine-induced pemphigus vulgaris.¹³

Nikolsky's sign may have prognostic value in patients with bullous skin diseases. One study described 2 distinctly different versions of the sign: the so-called "wet" Nikolsky's sign, in which a moist, glistening base of eroded skin is seen after pressure is exerted on the skin; and the so-called "dry" Nikolsky's sign, in which a dry base of eroded skin is seen after pressure is exerted on the skin. In patients with active pemphigus vulgaris, a wet sign is expected, whereas the presence of the dry sign may indicate reepithelialization beneath a pemphigus blister, which could signify healing and thus be a favorable finding.²

SUMMARY

Nikolsky's sign is a well-known clinical sign classically associated with the pemphigus group of disorders but also occurring in other autoimmune dermatologic conditions. The lack of standardization regarding how exactly to elicit the sign has limited its usefulness, but it remains an interesting sign to observe and interpret. **HP**

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