Dermatological examination of bullous diseases

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2 Dermatological Examination of Bullous Diseases

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Introduction & AIMS

Short Definition in Layman Terms

The vesicle or blister is the top efflorescence in the clinical reasoning chain for dermatological diagnosis. Finding only one single blister on the skin is sufficient to make the diagnosis bullous disease. The notion that a skin disease might be autoimmune emerges after a blister is found by physical examination. However, autoimune bullous diseases not always present with blisters. In this chapter the skills and knowledge is outlined of the dermatological examination.

Autoimmune bullous diseases not always present with blisters.

Learning Objectives

After reading this chapter you know the algorithm and definitions for the physical examination of skin and mucous membranes for bullous diseases.

Case Study: Part 1

A 61-year-old male presented with a widespread bullous eruption of 3 months duration. Clinically, he had numerous flaccid blisters, and a few tense bullae on both inflamed and non-erythematous skin involving primarily the scalp, face, neck, and breast. Examination of the oral mucosa revealed extensive desquamative gingivitis and three erosions on hard palate and buccal measuring up to 2 cm in diameter. Perilesional skin of an erosion exhibited a positive marginal Nikolsky's sign, the base of which was moist and exudative.

A biopsy for histopathology of the left arm revealed suprabasal blister formation with acantholysis. A biopsy for direct immunofluorescence revealed immunoglobulin G (IgG) and C5 deposition throughout the epidermis in a pattern along the cell surface. Indirect IF on monkey esophagus circulating anti-cell surface antibodies were detected. The ELISA indices of autoantibodies for desmoglein 1 was 57 and for desmoglein 3 was >150.

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Didactical Questions; Cross Section of Questions to Prime the Readers Interest

Meticulous skin examination is needed when a vesiculo-bullous disorder is suspected, since finding one vesicle is sufficient for making the diagnosis. However the absence of a vesicle does not exclude bullous disease, since several may come with only erythema, wheals, papules, nodules, erosions, or crusts. Vesicles are hard to identify on the mucous membranes. For instance, erosions on the gingiva may look like bright red erythema (enanthema), but the glistening surface betrays the lack of epithelium. How can the disease activity be scored?

Facts & Figures

Definitions and Classification

The efflorescences of vesiculo-bullous diseases as defined by the International League of Dermatological Societies are:

- Vesicle (vesicula): A circumscribed elevation ≤1 cm in diameter that contains liquid (clear, serous or hemorrhagic).
- Blister (bulla): A circumscribed elevation >1 cm in diameter that contains liquid (clear, serous or hemorrhagic).
- Pustule (pustula): A circumscribed lesion that contains purulent material.
- Crust (crusta): Dried serum, blood or pus on the surface of the skin.
- Erosion: Loss of either a portion of or the entire epidermis.

The nomenclature of efflorescences are defined by the International League of Dermatological Societies.

The distribution of vesicles may be solitary, grouped (herpetiform), or arch-like (circinate). The content of vesicles or bullae may be clear (transudate), opaque (serous), red-blue (hemorrhagic). If the blister cavity is hollow (air-filled) within the corneal layer, than in sensu strictu it does not fulfill the definition of a bulla, and might be called exfoliation or skin peeling. If the content is yellow (pustular) but yet also serous than the transitional word vesiculo-pustule is used.

Symptoms

Burning and pain are almost invariable features of blisters; pruritus is particularly associated with pemphigoid diseases, and dermatitis herpetiformis. Bullous diseases may start with erythematous lesions that can be macular, papular, urticarial, or nodular before a vesicle or blister erupts. Serous vesicles may become pustular with time as secondary efflorescence. Tense bullae are characteristic of blistering diseases with subepidermal split level such as pemphigoid, whereas slack bullae that break easily are seen in bullous diseases with intra-epidermal split, such as pemphigus. When the roof of the blister is lost, an erosion develops. When the liquid in the blister cavity is released it dries out into a crust. The color of the crust depends on the nature of the blister liquid (light yellow = exudate, blue-black = blood, gold = pus). If the blister does not have an underlying erythema, it is called monomorphic (monomorphic pemphigoid, pseudoporphyria).

Bullous diseases may come with itch, that evokes scratching, which results in excoriations. The lifetime of a vesicle may be extremely short by immediate scratching such as in dermatitis herpetiformis. Milia (horny pearls in the upper dermis) and scarring appear when the basement

membrane is interrupted, such as in epidermolysis bullosa acquisita.

The distribution pattern of the lesions may by solitary (solitary bullous mastocytosis), grouped 'en bouquet'/herpetiform (herpes simplex), circinate (linear IgA bullous disease), linear (phytophotodermatitis) or randomly (bullous pemphigoid).

Lesions may be distributed over de whole body such as in bullous pemphigoid, present in a circumscriptive area such as to head and neck in pemphigus, segmental in herpes zoster, or confined to skin folds such as in pemphigus vegetans.

The mucous membranes of body openings (eyes, nose, mouth, genitals) might be involved. Examine the eye for erythema of upper and lower conjunctiva, synechiae of conjunctival sac (symblepharon), and corneal abnormalities (pannus), inverted eyelashes (trichiasis). In the nose (blood) crusts or erosions can be found on the septum in the nasal vestibule. White patches in the mouth cavity may consist of blister roof of thickening of epithelium (leukoplakia). Other efflorescences are erosions, and intact vesicles or blisters. Erosions are intense red and differ from red epithelium by their glistering. Patients with bullous disease of the mucous membranes complain of pain or burnings sensations of the sensitive mucosa. Ask your patient for photophobia, nasal cleaning, hoarseness, dysphagia, dysuria and dyspareunia.

Signs

The physician may evoke sign's to disclose epidermal dislodgement with the (hand gloved!) fingers. The most commonly used is the Nikolsky sign, however there are several other physical signs of blistering diseases. Since the broad availability of modern immunodiagnostics their relevance in the daily practice is limited (see box).

Physical Signs of Blistering Diseases

- *Nikolsky or Nikolsky's sign I* (normal or direct Nikolsky sign): ability to split the epidermis on skin areas distant from the lesions of normal appearing skin by a lateral pressure with a finger (Fig. 2.1).
- *Nikolsky or Nikolsky's sign II* (marginal or indirect Nikolsky sign): ability to split the epidermis of the skin far beyond the preexisting erosion, extending to a great distance on the normal-appearing skin, by pulling the remnant of a ruptured blister or rubbing at the periphery of existing lesions [1].
- *Pear sign*: old blisters become flaccid and acquire a pear-like shape due to weight of the exudate, resembling a rubber sack filled with fluid.
- *Sheklakov's sign* (perifocal subepidermal separation): ability to extend to a limited distance a lesion in direction of the periphery by pulling the remnant of a ruptured blister, producing erosions that are limited in size, do not have a tendency to subsequent spontaneous extension, heal fast, and may show a drop of blood.
- *Pseudo-Nikolsky sign* (epidermal peeling): ability to peel off the entire epidermis by a lateral pressure (rubbing) only on the erythematous skin areas (Fig. 2.2).
- *Asboe-Hansen's or Lutz' sign* (blister spread): ability to enlarge a blister in direction of the periphery by applying mechanical pressure on the roof of intact blister (Fig. 2.3).

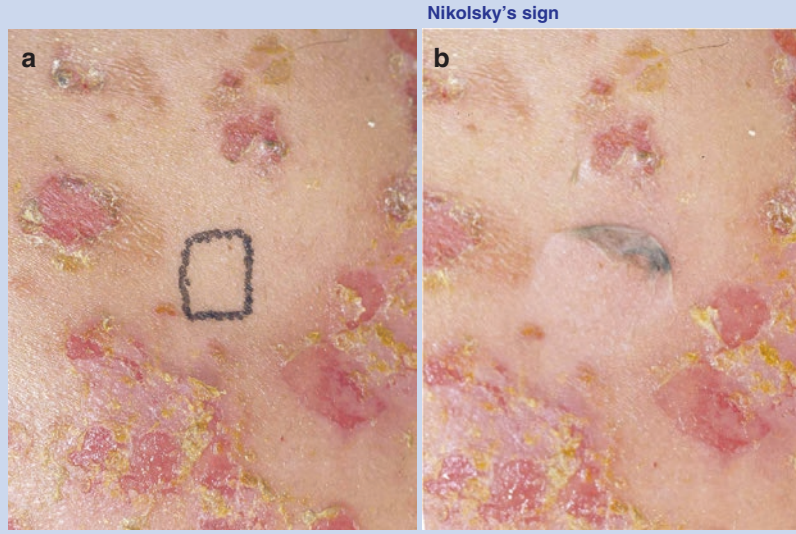

Fig. 2.1 Nikolsky sign type I procedure in pemphigus vulgaris (**a**) before and (**b**) after pressure with a finger

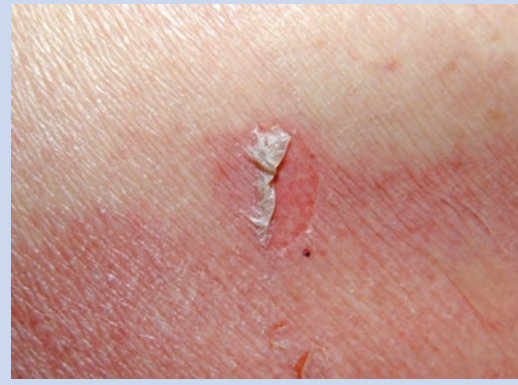

Fig. 2.2 Pseudo-Nikolsky sign in toxic epidermal necrolysis

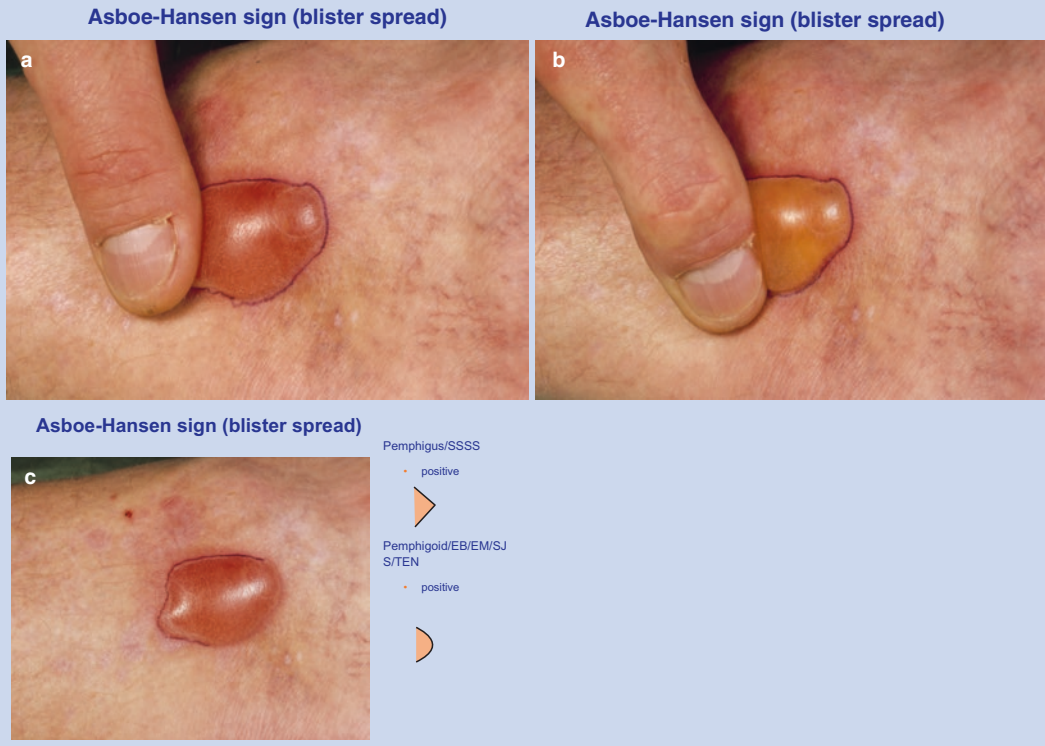

Fig. 2.3 Asboe-Hansen's (or blister spread) sign. (**a**) Draw line around the blister edge, and (**b**) press with thumb on blister. (**c**) Asboe-Hansen's sign is positive if the blister has spread beyond the line

The Nikolsky sign is positive in epidermal acantholysis such as in all forms of pemphigus and in staphylococcal scaled skin syndrome (SSSS) [2].

The pseudo-Nikolsky sign is positive in Erythema exsudativum multiforme (EEM), Stevens-Johnson syndrome (SJS) and Toxic epidermal necrolysis (TEN). Asboe-Hansen sign is positive in all bullous diseases.

Definitions and Activity Scores

Pemphigus

Definitions

The consensus definitions of the clinical milestones for pemphigus are listed [3] (Table 2.1).

Pemphigus Disease Area Index (PDAI)

The activity, extent and damage of skin and mucous membranes pemphigus can scored with PDAI [4] (Fig. 2.4 and Table 2.2).

Bullous Pemphigoid

The consensus definitions of the clinical milestones for pemphigoid are listed [5] (Fig. 2.5 and Table 2.3).

Bullous Pemphigoid Area Index (BPDAI)

The activity, extent and damage of skin and mucous membranes pemphigus can scored with BPDAI [5] (Fig. 2.6 and Table 2.4).

Table 2.1 Pemphigus definitions [3]

Early observation points	
Baseline	The day that therapy is started by a physician
Control of disease activity (disease control; beginning of consolidation phase)	The time at which new lesions cease to form and established lesions begin to heal
Time to disease control	The time interval between baseline and control
End of the consolidation phase	The time at which no new lesions have developed for a minimum of 2 wks, approximately 80% of lesions have healed, and when most clinicians start to taper steroids
Late observation end points	
Complete remission off therapy	Absence of new or established lesions while the patient is off all systemic therapy for at least 2 mo
Complete remission on therapy	The absence of new or established lesions while the patient is receiving minimal therapy
Other definitions	
Minimal therapy	Prednisone (or the equivalent) at ≤10 mg/d and/or minimal adjuvant therapy for at least 2 mo
Minimal adjuvant therapy	Half of the dose required to be defined as treatment failure
Partial remission off therapy	Presence of transient new lesions that heal within 1 wk without treatment and while the patient is off all systemic therapy for at least 2 mo
Partial remission on minimal therapy	The presence of transient new lesions that heal within 1 wk while the patient is receiving minimal therapy, including topical steroids
Relapse/flare	Appearance of ≥3 new lesions/mo that do not heal spontaneously within 1 wk, or by the extension of established lesions, in a patient who has achieved disease control

[Reprinted from: Murrell DF, Dick S, Ahmed AR, Amagai M, Barnadas MA, Borradori L, et al. Consensus statement on definitions of disease, end points, and therapeutic response for pemphigus. Journal of the American Academy of Dermatology 2008;58:1043-6, with permission from Elsevier.]

Case Study: Part 2

The patient was diagnosed with pemphigus vulgaris. At the start of therapy the PDAI score was 23 on skin and 12 on mucous membranes.

He was successfully treated with prednisone 1 mg/kg daily tapered in 4 months, and in addition 2× 1000 mg rituximab. During the induction phase, non-inflamed skin exhibited a positive direct Nikolsky's sign, beneath which was a non-exudative blister base. After 2 weeks control of disease was reached where no new lesions anymore developed. The skin improved quicker than the mouth with a PDAI at the end of the consolidation phase of 0 and 5 respectively.

Mucous Membrane Pemphigoid Area Index (MMPDAI)

The consensus definitions of the clinical milestones for mucous membrane pemphigoid are listed [6] (Table 2.5).

The activity, extent and damage of skin and mucous membranes pemphigus can scored with MMPDAI [6] (Fig. 2.7 and Table 2.6).

Case Study: Part 3

Patient reached complete remission while off therapy by 6 months that sustained during the total follow up period of 18 months. The PDAI dropped to 0.

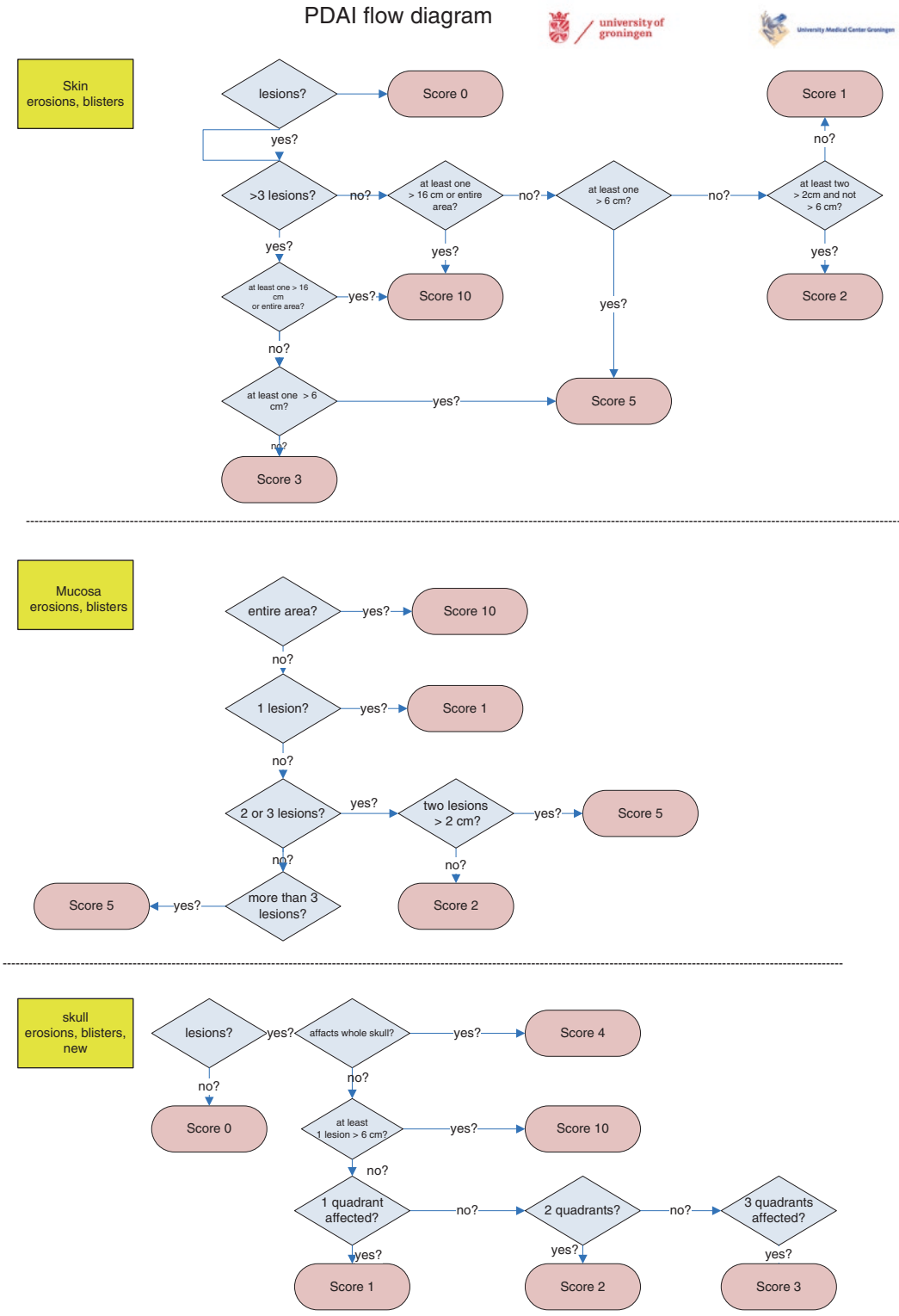

Fig. 2.4 Pemphigus Disease Area Index (PDAI) flow diagram

Table 2.2 Pemphigus Disease Area Index

PDAI	
Name:	
DOB:	
Number:	
Date:	

Treatment phase	
Baseline	Complete remission on minimal therapy
Control of disease	Partial remission off therapy
Consolidation phase	Complete remission off therapy
Partial remission on minimal therapy	Flare

Skin	**Activiity**		**Damage**
Anatomical location	**Erosions/Blisters or new erythema**		**Post-inflammatory hyperpigmentation or erythema from resolving lesion**
	0	absent	0 absent 1 present
	1	1-3 lesions, up to one lesion >2 cm in any diameter; none > 6 cm	
	2	2-3 lesions, at least two lesions > 2cm; none > 6 cm	
	3	> 3 lesions, none > 6 cm	
	5	>3 lesions; and/or at least one lesion > 6 cm	
	10	>3 lesions; and/or at least one > 16 cm or entire area	
Ears			
Nose			
Rest of the face			
Neck			
Chest			
Abdomen			
Back, buttocks			
Arms			
Hands			
Legs			
Feet			
Genitals			
Total skin scores	**/120**		**/12**

Scalp	**Erosions/Blisters or new erythema**		**Post-inflammatory hyperpigmentation or erythema from resolving lesion**
	0	absent	0 absent 1 present
	1	in 1 quadrant	
	2	in 2 quadrants	
	3	in 3 quadrants	
	4	affects whole skull	
	10	at least 1 lesion > 6 cm	
Total scalp scores	**/10**		**/1**
Total score of damage skin and scalp			**/13**

(continued)

Table 2.2 (continued)

Mucous membranes	
Anatomical location	**Erosions/Blisters**
	0 absent **1** 1 lesion **2** 2-3 lesions **5** >3 lesions of 2 lesions > 2 cm **10** entire area
Eyes	
Nose	
Buccal mucosa	
Hard palate	
Soft palate	
Upper gingiva	
Lower gingiva	
Tongue	
Floor of mouth	
Labial mucosa	
Posterior pharynx	
Anogenital	
Total Mucosa Score	**/120**
Total Activity Score Skin+Scalp+Mucosa	**/250**
Total Damage Score Skin+Scalp	**/13**

[Reprinted from: Murrell DF, Dick S, Ahmed AR, Amagai M, Barnadas MA, Borradori L, et al. Consensus statement on definitions of disease, end points, and therapeutic response for pemphigus. Journal of the American Academy of Dermatology 2008;58:1043-6, with permission from Elsevier.]

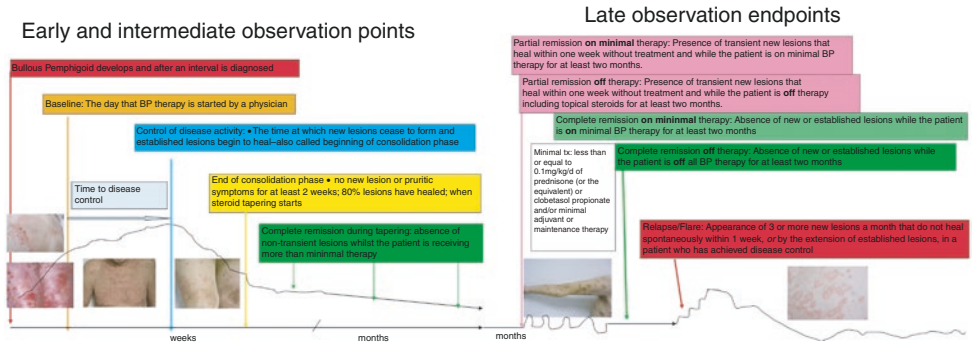

Fig. 2.5 Pictorial depiction of end points in bullous pemphigoid

Table 2.3 Definitions for Bullous Pemphigoid

Early observation points	
Baseline	Day that BP therapy is started by physician
Control of disease activity	Time at which new lesions cease to form and established lesions begin to heal or pruritic symptoms start to abate
Time to control of disease activity (disease control; beginning of consolidation phase)	The time interval between baseline and control of disease activity
End of the consolidation phase	Time at which no new lesions have developed for minimum of 2 wk and approximately 80% of lesions have healed and pruritic symptoms are minimal
Intermediate observation end points	
Transient lesions	New lesions that heal within 1 wk or pruritus lasting <1 wk and clearing without treatment
Nontransient lesions	New lesions that do not heal within 1 wk or pruritus continuing >1 wk with or without treatment
Complete remission during tapering	Absence of nontransient lesions while patient is receiving more than minimal therapy
Late observation end points	
Minimal therapy	≤0.1 mg/kg/d of prednisone (or equivalent) or 20 g/wk of clobetasol propionate and/or minimal adjuvant or maintenance therapy
Minimal adjuvant therapy and/or maintenance therapy	Following doses or less: methotrexate 5 mg/wk; azathioprine 0.7 mg/kg/d (with normal thiopurine s-methyltransferase level); mycophenolate mofetil 500 mg/d; mycophenolic acid 360 mg/d; or dapsone 50 mg/d
Partial remission on minimal therapy	Presence of transient new lesions that heal within 1 wk while patient is receiving minimal therapy for at least 2 mo
Complete remission on minimal therapy	Absence of new or established lesions or pruritus while patient is receiving minimal therapy for at least 2 mo
Partial remission off therapy	Presence of transient new lesions that heal within 1 wk without treatment while patient is off all BP therapy for at least 2 mo
Complete remission off therapy	Absence of new or established lesions or pruritus while patient is off all BP therapy for at least 2 mo
Mild new activity	<3 Lesions/mo (blisters, eczematous lesions, or urticarial plaques) that do not heal within 1 wk, or extension of established lesions or pruritus once/wk but less than daily in patient who has achieved disease control; these lesions have to heal within 2 wk
Relapse/flare	Appearance of ≥ 3 new lesions/mo (blisters, eczematous lesions, or urticarial plaques) or at least one large ([10 cm diameter) eczematous lesion or urticarial plaques that do not heal within 1 wk, or extension of established lesions or daily pruritus in patient who has achieved disease control
Failure of therapy for initial control	Development of new nontransient lesions or continued extension of old lesions, or failure of established lesions to begin to heal or continued pruritus despite: Clobetasol propionate 40 g/d for 4 wk; or Prednisone 0.75 mg/kg/d equivalent for minimum of 3 wk with or without drugs used for maintenance therapy; or A tetracycline on full dosing for 4 wk; or Dapsone 1.5 mg/kg/d for 4 wk; or Methotrexate 15 mg/wk (if [60 kg and no major renal impairment) for 4 wk; or Azathioprine 2.5 mg/kg/d for 4 wk (if thiopurine s-methyltransferase level is normal); or Mycophenolate mofetil 40 mg/kg/d (if normal renal function, otherwise according to age/creatinine clearance) for 4 wk

[Reprinted from: Murrell DF, Daniel BS, Joly P, Borradori L, Amagai M, Hashimoto T, et al. Definitions and outcome measures for bullous pemphigoid: recommendations by an international panel of experts. J Am Acad Dermatol 2012;66:479–485, with permission from Elsevier.]

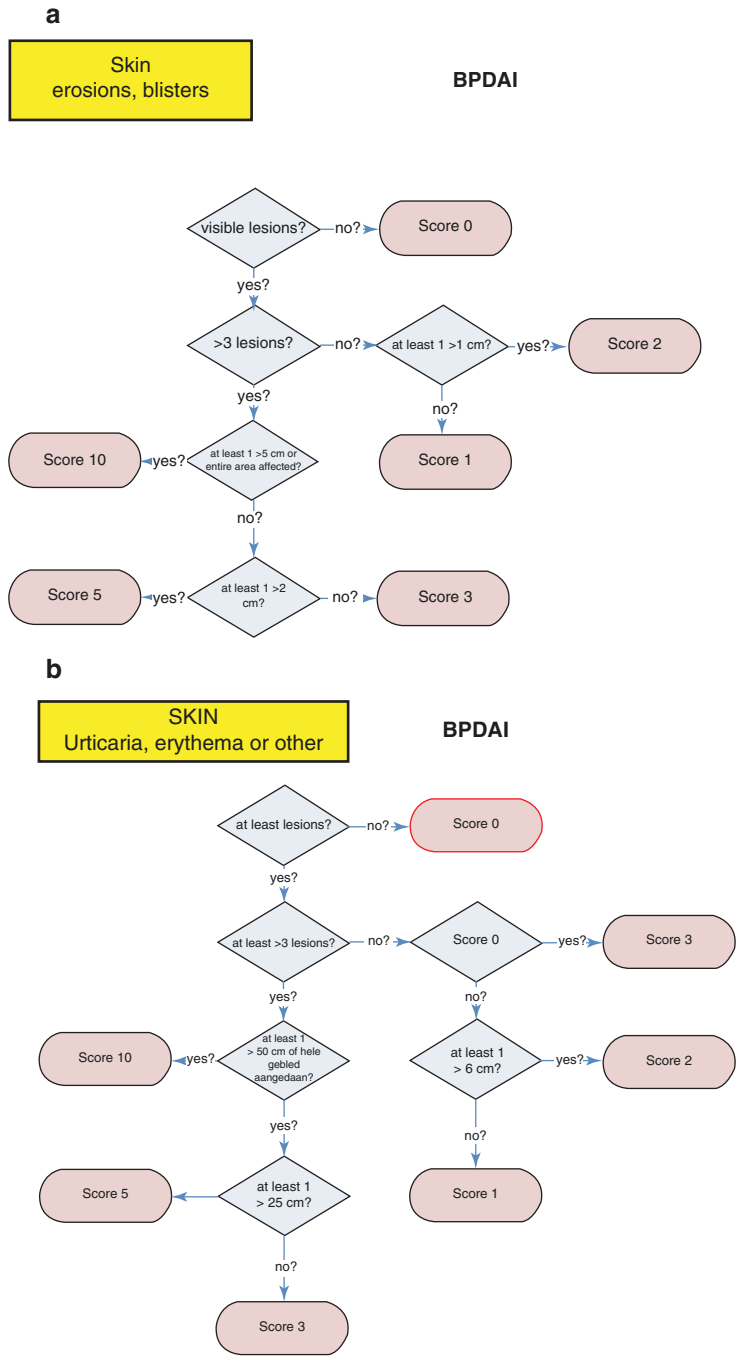

Fig. 2.6 Bullous Pemphigoid Area Index (BPDAI) flow diagram for assessment of (**a**) skin blistesr and erosions, (**b**) skin erythema and other lesions, (**c**) mucous membrane blisters and erosions

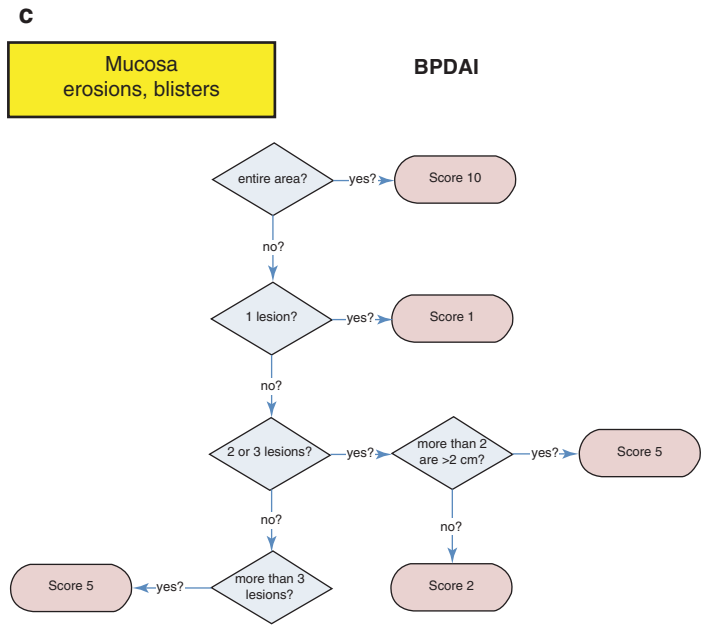

Fig. 2.6 (continued)

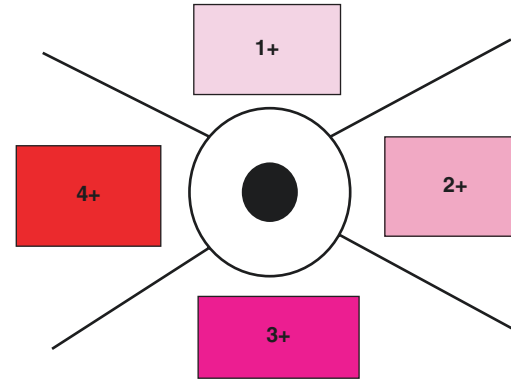

Fig. 2.7 Eye quadrants for Mucous Membrane Pemphigoid Area Index (MMPDAI). Diagram to illustrate how erythema is to be scored in different quadrants of each eye for the mucosal component of the Mucous Membrane Pemphigoid Disease Area Index. The degree of pinkness represents how high to score this parameter

Table 2.4 Bullous Pemphigoid Disease Area Index (BPDAI)

Name:	
DOB:	
#:	
Date:	

Diagnosis:	
Treatment phase:	
Number of weeks after baseline:	
Current medication:	
Baseline	Complete remission on minimal therapy
Control of disease	Partial remission off therapy
Consolidation phase	Complete remission off therapy
Partial remission on minimal therapy	Flare

[Reprinted from: Murrell DF, Daniel BS, Joly P, Borradori L, Amagai M, Hashimoto T, et al. Definitions and outcome measures for bullous pemphigoid: recommendations by an international panel of experts. J Am Acad Dermatol 2012;66:479-485, with permission from Elsevier.]

BPDAI skin	Activity		Activity		Damage
Anatomical location	**Erosions/Blisters**		**Urticaria/Erythema/Other**		**Pigmentation/ Other**
	0	absent	0	absent	0 absent 1 present
	1	1-3 lesions; none > 1 cm	1	1-3 lesions; none > 6 cm	
	2	1-3 lesions, at least 1 lesion >1 cm	2	1-3 lesions, at least 1 lesion > 6 cm	
	3	>3 lesions, none >2 cm	3	>3 lesions, at least 1 lesion > 10 cm	
	5	>3 lesions, and at least 1 lesion >2 cm	5	>3 lesions, at least 1 lesion > 25 cm	
	10	>3 lesions, and at least 1 lesion >5 cm or entire area	10	>3 lesions, at least 1 lesion > 50 cm or entire area	
Head					
Neck					
Chest					
Left arm					
Right arm					
Hands					
Abdomen					
Genitals					
Back/Buttocks					
Left leg					
Right leg					
Feet					
Total skin score	**/120**		**/120**	**/12**	
MUCOSA	**Erosions/Blisters**				0
	0 Absent				
	2 2-3 lesions				
	5 3>lesions, of 2 > 2 cm				
	10 Entire area				
Eyes					
Nose					
Buccal mucosa					
Hard palate					
Soft palate					
Upper gingiva					
Lower gingiva					
Tongue					
Floor of mouth					
Labial mucosa					
Posterior pharynx					
Anogenitaal					
Total score mucosa		**/120**			
Total activity score skin (blist./ urtic.) + mucosa		**/360**	**Total damage score skin**	**/12**	

Table 2.5 Definitions for Mucous Membrane Pemphigoid

Early observation points	
Baseline	The day that MMP therapy is started by a physician
Control of disease	The time at which new inflammatory lesions cease to form and established lesions begin to heal
Time to control disease activity (disease control; beginning of consolidation phase)	The time interval from baseline to the control of disease activity
Control of scarring	The time needed to control scarring progression
End of the consolidation phase	The time at which no new lesions have developed for minimum of 4 wk, and approximately 80% of inflammatory lesions have healed
Intermediate observation end points	
Transient lesions	New lesions that heal within 1 wk or clear without treatment
Nontransient lesions	New lesions that do not heal within 1 wk
Complete remission during tapering	The absence of nontransient lesions while the patient is receiving more than minimal therapy
Minimal therapy	Dapsone ≤ 1.0 mg/kg/d; ≤ 0.1 mg/kg/d of prednisone (or the equivalent); minocycline ≤ 100 mg/d; doxycycline 100 mg/d; lymecycline 300 mg/d; topical corticosteroids once a day including fluticasone propionate suspension 400 g/once a day; colchicine 500 g/d; Salazopyrin 1 g/d; sulfapyridine 500 mg/d; sulfamethoxypyridazine 500 mg/d; nicotinamide 500 mg/d
Minimal adjuvant therapy (and/or maintenance therapy)	The following doses or less: azathioprine (1 mg/kg/d) with normal thiopurine S-methyltransferase level; mycophenolate mofetil 500 mg/d; mycophenolic acid 360 mg/d; methotrexate 5 mg/wk; cyclosporine 1 mg/kg/d
Long-term biological therapy	Refers to therapies given intermittently, for example, when rituximab is used for MMP, or IVIG monthly
Late observation end points	
Partial remission on minimal therapy	Presence of transient new lesions that heal without scarring within 1 wk while patient is receiving minimal therapy for at least 2 mo
Complete remission on minimal therapy	The absence of new or established lesions or pruritus while patient is receiving minimal therapy for at least 2 mo
Partial remission off therapy	Presence of transient new lesions that heal within 1 wk without treatment while patient is off all MMP therapy for at least 2 mo
Complete remission off therapy	Absence of new or established lesions or pruritus while patient is off all MMP therapy for at least 2 mo
Relapse/flare	Appearance of ≥ 3 new lesions a month (blisters, erosions) that do not heal within 1 wk, or extension of established lesions in patient who has achieved disease control

IVIG Intravenous immunoglobulin, *MMP* mucous membrane pemphigoid

[Reprinted from: Murrell DF, Marinovic B, Caux F, Prost C, Ahmed R, Wozniak K, et al. Definitions and outcome measures for mucous membrane pemphigoid: Recommendations of an international panel of experts. J Am Acad Dermatol 2015;72:168–174., with permission from Elsevier.]

Table 2.6 Mucous Membrane Pemphigoid Disease Area Index (MMPDAI)

Name:	
DOB:	
# :	
Date:	

Treatment phase	
Baseline	Complete remission on minimal therapy
Control of disease	Partial remission off therapy
Consolidation phase	Complete remission off therapy
Partial remission on minimal therapy	Flare

[Reprinted from: Murrell DF, Marinovic B, Caux F, Prost C, Ahmed R, Wozniak K, et al. Definitions and outcome measures for mucous membrane pemphigoid: Recommendations of an international panel of experts. J Am Acad Dermatol 2015;72:168-174., with permission from Elsevier.]

Skin	**Activity**		**Damage**
Anatomical location	**Erosions/Blisters or new erythema**		**Post-inflammatory hyperpigmentation or erythema from resolving lesion or scarring**
	0	absent	0 absent 1 present
	1	1-3 lesions, up to one >2 cm in any diameter, none > 6 cm	
	2	2-3 lesions, at least two > 2 cm diameter, none > 6cm	
	3	>3 lesions, none > 6 cm diameter	
	5	>3 lesions, and/or at least one >6 cm	
	10	>3 lesions, and/or at least one lesion >16 cm diameter or entire area	
Ears			
Forehead			
Rest of the face			
Neck			
Chest			
Abdomen			
Shoulders, Back			
Buttocks			
Arms & hands			
Legs& feet			
Anal			
Genitals			
Total skin scores	**/120**		**/12**

Scalp	**Erosion/Blisters/active erythema**		**Post-inflammatory hyperpigmentation or erythema from resolving lesion or scarring**
	0	absent	0 absent 1 present
	1	in 1 quadrant	
	2	in 2 quadrants	
	3	in 3 quadrants	
	4	affects whole scalp	
	10	at least 1 lesion > 6 cm	
Total scalp	**/10**		**/1**

Mucous membranes	**Activity**	**Damage**
Anatomical location	**Erosion/Blisters/active erythema**	**Post-inflammatory hyperpigmentation or erythema from resolving lesion or scarring**

Mucous membranes	Activity	Damage
Eyes (quadrants upper, lower, medial and lateral)	**0** No erythema **1** Light pink **2** Moderate pink **3** Dark pink **4** Bright red add up quadrants	0 absent 1 present
Left eye (0-16) × 0.625		
Right eye (0-16) × 0.625		
	0 absent **1** 1 lesion, or 1 quadrant eye **2** 2-3 lesions, or 2 quadrants eye **5** > 3 lesions or two lesions > 2 cm, or three quadrants eye **10** entire area, or four quadrants eye	0 absent 1 present
Nose		
Buccal mucosa		
Palate		
Upper gingiva		
Lower gingiva		
Tongue/Floor of mouth		
Labia		
Posterior pharynx		
Anus		
Genitals		
Total mucosa scores	**/120**	**/12**
Total scores skin + scalp + mucosa	**/250**	**/25**

Review Questions

1. A vesicle is a circumscribed elevation
   a. ≥ 1 cm in diameter that contains clear liquid
   b. ≤ 1 cm in diameter that contains serous liquid
   c. ≥ 1 cm in diameter that contains purulent material
   d. Is a bulla
2. The liquid contents of a serous vesicle is
   a. Transparent
   b. Opaque
   c. Purulent
   d. Leaking
3. The Nikolsky sign is positive, except
   a. Pemphigus vulgaris
   b. Staphylococcal scaled skin syndrome (SSSS)
   c. Pemphigus foliaceus
   d. Bullous pemphigoid
4. Which is NOT an severity scores in autoimmune blistering diseases?
   a. PASI
   b. BPDAI
   c. PDAI
   d. MMPDAI
5. The beginning of the consolidation phase in BP is the moment when reached
   a. Control of disease activity
   b. Partial remission on minimal therapy
   c. Partial remission off therapy
   d. Complete remission on minimal therapy

Answers

1. b
2. b
3. d
4. a
5. a

On the web

International Pemphigus and Pemphigoid Foundation www.pemphigus.org

Supplement 2.1 ILDS – Nomenclature for description of cutaneous lesions (attached)

References

1. Grando SA, Grando AA, Glukhenky BT, Doguzov V, Nguyen VT, Holubar K. History and clinical significance of mechanical symptoms in blistering dermatoses: a reappraisal. J Am Acad Dermatol. 2003;48:86–92.
2. Mignogna MD, Fortuna G, Leuci S, Ruoppo E, Marasca F, Matarasso S. Nikolsky's sign on the gingival mucosa: a clinical tool for oral health practitioners. J Periodontol. 2008;79:2241–6.
3. Murrell DF, Dick S, Ahmed AR, Amagai M, Barnadas MA, Borradori L, et al. Consensus statement on definitions of disease, end points, and therapeutic response for pemphigus. J Am Acad Dermatol. 2008;58:1043–6.
4. Rosenbach M, Murrell DF, Bystryn JC, Dulay S, Dick S, Fakharzadeh S, et al. Reliability and convergent validity of two outcome instruments for pemphigus. J Invest Dermatol. 2009;129:2404–10.
5. Murrell DF, Daniel BS, Joly P, Borradori L, Amagai M, Hashimoto T, et al. Definitions and outcome measures for bullous pemphigoid: recommendations by an international panel of experts. J Am Acad Dermatol. 2012;66:479–85.
6. Murrell DF, Marinovic B, Caux F, Prost C, Ahmed R, Wozniak K, et al. Definitions and outcome measures for mucous membrane pemphigoid: Recommendations of an international panel of experts. J Am Acad Dermatol. 2015;72:168–74.

Additional Reading

Powell AM, Black M. A stepwise approach to the diagnosis of blisters in the clinic. Clin Dermatol. 2001;19:598–606.