

## Unmet Needs in Pemphigoid Diseases: An International Survey Amongst Patients, Clinicians and Researchers

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Pemphigoid diseases are subepidermal autoimmune bullous diseases, characterized by autoantibodies against structural proteins of the dermal–epidermal junction (1). Symptoms of severe pruritus, with or without tense blistering of the skin or mucosa, cause a high disease burden (2). Basic and clinical research has led to better understanding of the mechanisms of pemphigoid diseases and novel therapies have been developed (3). Nonetheless, there are gaps in our knowledge, and several disease areas are not studied yet. These unmet needs have not been well-characterized. While available time and resources are often limited in research, it is essential to address topics relevant to both patients and healthcare professionals (4). It is widely recognized now that patients play an important role in setting the research agenda (5). The aim of this study was to explore and prioritize unmet needs in pemphigoid diseases from the perspective of patients, clinicians and researchers, in order to guide future research towards important research topics. A secondary aim was to identify points of improvement in patient care.

### METHODS

A steering group was established in February 2017, consisting of a project coordinator (AL), experts on pemphigoid diseases (SAG, BH, DZ, MFJ) and a patient representative (MY; director of the International Pemphigus and Pemphigoid Foundation (IPPF)). A preliminary list of unmet needs was drawn up and discussed by the steering group in June 2017 at the IPPF conference in Lübeck, Germany. An online anonymous survey was developed using Qualtrics survey software (Table S1<sup>1</sup>), containing questions about participants' characteristics, and unmet needs in pemphigoid diseases. Seven or eight pre-listed needs composed by the steering group were provided and participants were asked whether they recognized the needs as unmet, and to designate a top 3 of the most urgent unmet needs. Moreover, participants were asked to complement the list composed by the steering group. In addition, patients were given questions about satisfaction with patient care, and their reasons for (dis)satisfaction.

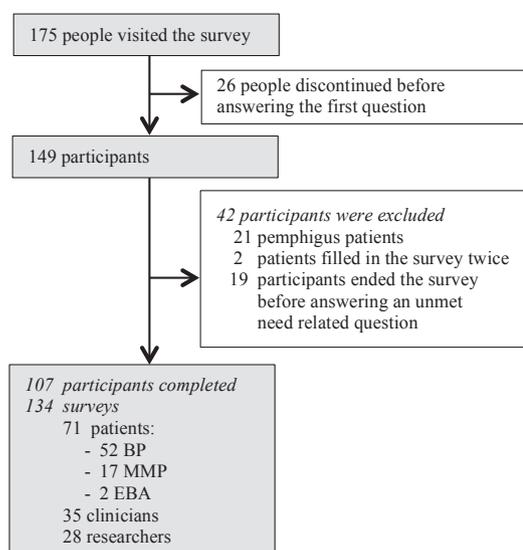
The survey was distributed internationally between October 2017 and April 2018. Patients were invited by email via the IPPF, and national German and Dutch patient organizations. Clinicians and researchers were invited by email via pemphigoid research groups, and via the European Academy of Dermatology and Venereology. Data was exported from Qualtrics directly into SPSS Statistics version 23 (IBM, Chicago, IL, USA). Descriptive and

qualitative statistics were used for data analysis. An overall ranking score was calculated by awarding 3 points every time unmet needs were ranked highest, 2 points if ranked 2<sup>nd</sup>, and 1 point if ranked 3<sup>rd</sup>.

### RESULTS

The inclusion and exclusion process is shown in **Fig. 1**. The clinicians' and researchers' response rate was 36/99 (36%). The patients' response rate is unknown. Participants characteristics and the top 3 most urgent needs are shown in **Table I**. Patients, clinicians and researchers agreed that the most urgent need was improvement in therapeutic options for pemphigoid diseases (Table I). In addition, patients frequently expressed the need for more public information ( $n=9$ ) (Table S1<sup>1</sup>).

Data on patient satisfaction showed that half of the patients were unsatisfied with patient care during the diagnostic process, mainly due to misdiagnosis and long diagnostic delay (mentioned by 88% of unsatisfied patients; Table S1<sup>1</sup>). Six patients visited more than 5 doctors before a correct diagnosis was made. Patients with epidermolysis bullosa acquisita and mucous membrane pemphigoid reported a longer diagnostic delay (mean  $90.3 \pm 127$  and  $19.7 \pm 23$  months), compared with patients with bullous pemphigoid ( $9.0 \pm 22$  months). Most patients



**Fig. 1. Flowchart of inclusion and exclusion of study participants.** BP: bullous pemphigoid; MMP: mucous membrane pemphigoid; EBA: epidermolysis bullosa acquisita.

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**Table I. Participants characteristics (n = 107) and top 3 ranking of unmet needs in pemphigoid diseases**

	Patients (n = 71)	Clinicians (n = 35)	Researchers (n = 28)	
Mean age, years (range)	66.6 (34–94) Mean diagnostic delay: 14.1 months (1 day–15 years) Mean disease duration: 4.7 years (0–20)	51.9 (28–65) Setting: Academic 34 (97%) Peripheral 1 (3%) Consider yourself AIBD expert? Yes: 35 (100%)	51.6 (28–65) Research experience: >10 years: 20 (71%) AIBD main research topic? Yes: 21 (75%), No: 7 (25%)	
Continent of origin, n (%)				
Europe	22 (31)	21 (60)	18 (64)	
North America	48 (68)	7 (20)	6 (21)	
Asia	1 (1)	4 (11)	4 (14)	
			Unmet need recognized?	
			Yes n (%)	No n (%)
Overall top 3 ranking of unmet needs			Missing n (%)	Ranking score*
Patients (n = 71)				
1. Need for better treatment options			48 (68)	5 (7)
2. Need for quicker diagnosis			18 (25)	92
3. Need for more disease awareness			47 (66)	9 (13)
Clinicians (n = 35)				
1. Need for labelling of new drugs for the indication pemphigoid (anti-CD20, anti-complement, anti-FcRn, anti-neutrophil activating pathways)			15 (21)	84
2. Need for easy laboratory tests to diagnose pemphigoid diseases			46 (65)	8 (11)
3. Need for better recognition of non-bullous pemphigoid			30 (86)	4 (11)
Researchers (n = 28)				
1. Need for more head-to-head randomized controlled trials comparing the effectiveness and safety of current treatments			1 (3)	53
2. Need for understanding of the pathophysiology of pemphigoid for drug development			27 (77)	5 (14)
3. Need for understanding trigger mechanism (e.g. infections, drugs) in addition to genetic predisposition			30 (86)	3 (9)
			2 (7)	37
			27 (96)	0 (0)
			27 (96)	0 (0)

\*Ranking score was calculated by awarding 3 points for every time an unmet needs was ranked highest, 2 points if ranked 2<sup>nd</sup> highest and 1 point if ranked 3<sup>rd</sup> highest. AIBD: autoimmune blistering diseases.

(76%) were satisfied with current patient care, especially in the case of successful treatment (mentioned by 41% of satisfied patients), and treatment in centres of expertise (mentioned by 37% of satisfied patients) (Table SIII<sup>1</sup>). Treatment side-effects, insurance issues, and poor knowledge of the disease among doctors were the main reasons for unsatisfactory current patient care.

## DISCUSSION

This survey confirmed that a long diagnostic delay and suboptimal treatment are important concerns in pemphigoid diseases. This study is the first to explore patients' priorities in the field of pemphigoid diseases. The method used has some resemblance to the James Lind Alliance (JLA) methodology of prioritization of research topics (5). The greatest difference is the lack of a finalization workshop, in which patients and health professionals discuss the final prioritization of uncertainties face-to-face. Instead, we choose prioritization by survey, considering that pemphigoid diseases are rare, and therefore a low attendance and a high geographical selection bias would be expected. Still, the risk of selection bias was not completely prevented, as participants from only 3 continents were included. Other limitations of this study include a relatively low sample size and missing values.

Geographical differences might have caused small deviations in the ranked needs (Tables SIII–SV<sup>1</sup>). Patients from North America ranked the need for better treatment availability 4<sup>th</sup>, in contrast to European patients, who rated the urgency of this need 7<sup>th</sup>. This might be explained by the lower availability of healthcare in North America than in Europe (Table SIII<sup>1</sup>). Another interesting finding is the

higher need for easy diagnostic laboratory tests expressed by clinicians in North America and Asia, in comparison with European clinicians (Table SIV<sup>1</sup>). Whether this difference is caused by approachability, laboratory equipment, or by the use of different diagnostic techniques cannot be concluded based on our survey data.

In conclusion, further research is needed in order to improve and widen the currently available treatment options for pemphigoid diseases. Patients report a high need for shortening the diagnostic delay. Therefore, greater awareness of pemphigoid diseases should be promoted. We found that after a correct diagnosis was established, patients were most satisfied with care in centres of expertise. Focus group sessions might help to provide further information on interventions that can improve patient care.

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