To significantly improve QoL for patients with mucosal and nonmucosal PV, complete disease clearance may be necessary. Small amounts of worsening activity have an increasingly significant impact on QoL at the lower end of the spectrum. Above mild levels of activity, increasing activity has linear but detrimental smaller effects on QoL. The findings for patients with mucosal PV further support this, likely because oral erosions are painful and impact eating. Consistent with prior findings, the Skindex-S best correlates with PDAI score in all patients.

A notable limitation of this study is that our population had milder disease, with a median PDAI of 6-75 and ABSSS of 11-75. However, we are still able to show a change in QoL as the PDAI decreases, even at lower PDAI levels. Our findings have important clinical implications in determining appropriate outcomes for therapies. Unlike dermatomyositis and systemic lupus erythematosus, in patients with PV, complete clearance should be the goal.

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Conflicts of interest: A.S.P. is a cofounder and equity holder in Cabaletta Bio, Inc., focused on targeted immunotherapy of B-cell-mediated diseases including pemphigus. She is an inventor on patents licensed by Novartis and Cabaletta Bio, Inc. for cellular immunotherapy of autoimmune diseases, and has previously served as a consultant for Syntimmune, Inc. V.P.W. has grants from Roche/Genentech and Syntimmune, Inc. She is a consultant for Roche/Genentech, Syntimmune, Janssen and Principia.

V.P.W. was involved in the development of the PDAI.

Occupational dermatoses during the COVID-19 pandemic: a multicentre audit in the UK and Ireland

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Dear Editor, During the COVID-19 pandemic, with the greater need for donning personal protective equipment (PPE) and frequent handwashing, we have noted increasing reports in the UK and abroad of high rates of irritant dermatitis in frontline healthcare workers (HCWs). In China, where the severe acute respiratory syndrome–coronavirus 2 (SARS–Cov-2) virus was first reported, up to 97% of frontline HCWs reported skin changes related to new infection control practices.1,2 A recent study of 146 HCWs from Manchester and London diagnosed irritant contact dermatitis (ICD) in 97.1%, with high rates of pressure-related facial dermatitis caused by masks and goggles.3

The British Society for Cutaneous Allergy has conducted the first UK-wide prospective audit of occupational dermatoses in HCWs during the COVID-19 pandemic. Eleven centres in the UK and Ireland set up dedicated occupational skin disease clinics to treat PPE-related dermatoses, collecting data from 337 self-referred HCWs between 1 May and 31 July 2020 (summarized in Table 1).

The presenting dermatosis was occupational in 315 (93.5%). The majority of HCWs (n = 210; 62.3%) were nurses and healthcare assistants, disciplines with dominant

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related acne or rosacea have not been demonstrated, although of 26 wearing respirators (15%) vs. one of 208 wearing a mask is more likely to present with healthcare-related occupational health. To date, preventive measures for mask-wearing HCWs requesting dermatology assessment, respirator wear is associated with facial pressure injury, and all mask wear may exacerbate or precipitate acne. The high incidence of ICD is unsurprising; it is a well-recognized manifestation of increased sweating. It is also likely due to increased occlusion or pressure from heavier, tighter-fitting PPE.

Table 1

| Diagnosis                          | n (%)       |
|------------------------------------|-------------|
| Irritant contact dermatitis         | 199 (59)    |
| Acne                               | 56 (17)     |
| Atopic eczema                      | 42 (12)     |
| Allergic contact dermatitis        | 22 (7)      |
| Facial pressure injury             | 11 (3)      |
| Urticaria                          | 11 (3)      |
| Other hand/foot eczema             | 8 (2)       |
| Psoriasis                          | 7 (2)       |
| Folliculitis                       | 6 (2)       |
| Pempholyx hand eczema              | 6 (2)       |
| Type I allergy                     | 5 (1)       |
| Dry skin                           | 4 (1)       |
| Other endogenous dermatosis        | 3 (1)       |
| Seborrheic dermatitis              | 3 (1)       |
| Othera                             | 15 (4)      |

Sixty patients had two diagnoses, so are represented twice (397 diagnoses in 337 patients). Encompassing 45 patients with acne vulgaris (13-4%) and 11 with rosacea (3-3%). Other diagnoses were herpes labialis (n = 4), hay fever (n = 2), lichen simplex (n = 1), lichen planus (n = 1), lichen amyloidosis (n = 1), pruritus (n = 1), tinea pedis (n = 1).

Patient-facing contact that require frequent handwashing and PPE wear. The most common diagnosis was ICD (n = 199; 59.0%). A history of atopic eczema was seen in 137 (40.6%), in comparison with an estimate in the UK adult population of 8.3%, supporting previous studies showing that atopic eczema is more likely to present with healthcare-related occupational dermatitis.4,5

Fifty-six (16.6%) presented with acne or rosacea (45 acne, 11 rosacea); all wore a face mask. Workers with a previous history of acne or rosacea appeared prone to an exacerbation: 36 of 65 (55%) with previous facial skin problems had acne or rosacea vs. 20 of 100 (20%) with no such history $\chi^2$ (1 + 1 degree of freedom, 234) = 21.9994; P < 0.001. There was no significant association with mask type. It is likely that the occlusive nature of all masks provides a warm, moist environment, which traps saliva, bacteria and sebum, worsening or triggering symptoms.6 To date, preventive measures for mask-related acne or rosacea have not been demonstrated, although standard treatments such as oral tetracyclines may be beneficial.

Eleven HCWs (3%) reported facial pressure injury. This was associated with the type of mask worn, being present in four of 26 wearing respirators (15%) vs. one of 208 wearing a fluid-resistant surgical mask (0.5%) $\chi^2$ (1 + 1 degree of freedom, 234) = 24.5496; P < 0.001. This observed relationship is likely due to increased occlusion or pressure from heavier, tighter-fitting PPE.

Fifty-one (15.1%) HCWs required time off work due to skin disease, losing a total of 468.5 working days across all sites. The mean number of handwashes with soap per day in those needing time off was 23.6 [median 20, interquartile range (IQR) 12–30]. Each handwash per shift increased the expected amount of time off by 0.014 days [95% confidence interval (CI) –0.021 to 0.050; P = 0.43]. Each use of alcohol gel per shift reduced the expected number of days off by 0.03 (95% CI 0.003–0.056; P = 0.29). Use of soap or detergent and water disrupts the skin barrier, particularly with inadequate rinsing or drying, or with the immediate application of gloves.4,7 While alcohol can dissolve the protective lipid layer in the stratum corneum, previous studies have shown that alcohol-based hand cleaning products are better tolerated than detergent products.7,8 However, it is acknowledged that owing to the stinging effect of alcohol on damaged skin, people with severe dermatitis may avoid it, creating a false inverse association with time off.

The mean number of hours of PPE wear per shift was 7.1 (median 8; IQR 4.5–10). We did not find any significant association between duration of PPE wear and time required off work. However, longer PPE wear was related to the incidence of pressure injuries: 10 of the 11 (91%) patients with pressure injuries wore their PPE for ≥ 5 hours per shift.

Our data support reports of increased cutaneous morbidity in HCWs during the COVID-19 pandemic, and identify trends that may aid preventive strategies in workforce planning and skin protection measures. Predominantly patient-facing roles and past history of atopic eczema or acne are prevalent in HCWs requesting dermatology assessment, respirator wear is associated with facial pressure injury, and all mask wear may exacerbate or precipitate acne. The high incidence of ICD is unsurprising; it is a well-recognized manifestation of increased handwashing with soap, a particularly important skin hygiene measure currently.

Owing to the significant number of working days lost to occupational dermatoses, our findings support the need to identify and mitigate predisposing factors to skin injury through close team-working between dermatology and occupational health.

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Enhanced expression of angiotensin-converting enzyme 2 in psoriatic skin and its upregulation in keratinocytes by interferon-γ: implication of inflammatory milieu in skin tropism of SARS-CoV-2

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Dear Editor, The novel coronavirus disease (COVID-19) pandemic, caused by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), is a challenging situation globally due to its contagious nature. SARS-CoV-2 enters the host cell by the receptor-binding domain of its spike protein interacting with the angiotensin-converting enzyme 2 (ACE2) receptor present on the host cell surface. Host proteases, mainly transmembrane protease, serine 2 (TMPRSS2), play a vital role in cleaving the SARS-CoV-2 spike protein, thereby enabling the virus to enter the host cell by endocytosis. SARS-CoV-2 mainly affects the respiratory system of the infected host; however, its manifestation in other organs has also been reported. A functional ACE2 receptor and TMPRSS2 protease in a particular cell type in a tissue microenvironment are the major determinants in virus tissue tropism. No concrete evidence is available about skin tropism of SARS-CoV-2 and its implications in inflammatory dermatological conditions, but skin-associated changes have been reported in patients with COVID-19. However, it is inconclusive whether these skin-specific changes are primarily due to SARS-CoV-2 infection or develop as a result of adverse reactions to drugs used in COVID-19 management.

The status of SARS-CoV-2 determinants in inflammatory skin diseases like psoriasis is not known. Furthermore, interferons are considered the major antiviral host response, and a recent study has shown that ACE2 is the interferon-stimulated gene. Interferons are the prominent proinflammatory cytokines and play a major role in psoriasis pathogenesis. Increased expression of interferon-γ (IFN-γ) is reported in psoriatic lesions. It may be possible that enhanced expression of interferons such as IFN-γ in psoriatic lesions increases the ACE2 expression that may be exploited by SARS-CoV-2 towards skin manifestation. Therefore, to address this hypothesis, we determined the status of major determinants of SARS-CoV-2 infection (i.e. ACE2 and TMPRSS2) in the peripheral blood and skin of people with psoriasis.

We recruited 40 patients with psoriasis (30 male and 10 female) and 40 controls (30 male and 10 female), and blood samples were collected from both groups. Skin biopsy samples were collected from lesional skin of patients with psoriasis (n = 40) and the control group (n = 30; all male). Informed consent was obtained and the study was approved by the institutional ethics committee. Total RNA was isolated from peripheral blood mononuclear cells and skin homogenates using Trizol reagent. Transcripts levels of ACE2 and TMPRSS2 were determined by quantitative polymerase chain reaction using β-actin as the endogenous control, as described previously, and data are represented as 2^{-ΔΔCt}. Transcript levels of ACE2 were significantly increased in peripheral blood (P = 0.023) and lesional skin (P = 0.013) of patients with psoriasis compared with controls, but no significant difference was observed for TMPRSS2 (P > 0.05) (Figure 1a, b).

Expression of ACE2 and TMPRSS2 proteins (Abcam, Cambridge, UK) was determined in tissue lysates of psoriatic and control skin by Western blotting using β-actin as loading control, as described previously. Blot intensities quantified by densitometry analysis revealed significantly increased expression of ACE2 (P = 0.009) in lesional skin compared with control skin, but no significant difference was observed for TMPRSS2 (P = 0.19) (Figure 1c).

Next, we performed in vitro studies using primary adult human epidermal keratinocytes (HEKa cells) maintained in keratinocyte growth medium-2 (PromoCell, Heidelberg, Germany) supplemented with optimized growth factors (HiMedia Laboratories, Mumbai, India), antibiotics and antimycotics (Sigma-Aldrich, St Louis, MO, USA) in 5% humidified CO2 at 37 °C. HEKa cells were treated with 0.1 µg mL⁻¹ polyinosinic–polycytidylic acid [poly(I:C)] (Sigma-Aldrich) alone, or a combination of poly(I:C) and recombinant human IFN-γ (rhIFN-γ, 1 ng mL⁻¹; R&D Systems Inc., Minneapolis, MN, USA) for 24 h. Poly(I:C) mimics viral dsRNA and acts as a

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