



**Figure 1** Generalized maculopapular confluent exanthema with targetoid lesions.

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## Iatrogenic dermatitis in times of COVID-19: a pandemic within a pandemic

### Editor

The pandemic of the 21st century COVID-19 emerged in Wuhan, China, and swiftly became a global phenomenon. The frontline barriers for preventing spread are hand hygiene and personal protective equipment (PPE). The amplified hygiene practices and PPE as recommended have brought in its wake a second pandemic – a pandemic of dermatitis!<sup>1</sup>

We reviewed the most prevalent types of iatrogenic skin damage among healthcare workers (HCWs), notably irritant, and allergic contact dermatitis (ACD) to PPE and hand hygiene

measures, as well as face mask induced pressure-related skin damage.<sup>2–4</sup> The prevalence of occupational skin disease among HCWs in earlier studies (pre-COVID era) has been estimated to range from 20 to 50%.<sup>5</sup> However, in two recent studies from Hubei, China, a staggeringly higher number of HCWs (97%,  $n = 526/542$  and 71%,  $n = 234/330$ ) HCWs engaged in the care of COVID-19 patients reported self-perceived skin barrier damage.<sup>2,6</sup> Majority experienced skin dryness/tightness (70.3%) and desquamation (62.2%) commonly occurring on the nasal bridge (83.1%) (Fig. 1).<sup>2</sup> Skin damage was more prevalent among HCWs wearing N95 masks and goggles for more than 6 h a day, whereas the face shield produced no such effect on prolonged wearing. Goggles were reported as the commonest (51.92%) culprit among PPE and about a fifth of patients reported work absenteeism because of dermatitis.<sup>3</sup> Face mask and headgear worn tightly for prolonged hours result in ACD, ICD, pressure urticaria, friction dermatitis, abrasions and aggravation of pre-existing dermatoses.<sup>6</sup> N95 respirators may contain formaldehyde, a known allergen.<sup>7</sup> Retro-auricular skin is vulnerable to frictional dermatitis due to ear loops of the facemasks.<sup>4</sup> Frequent



**Figure 1** Iatrogenic dermatitis during COVID-19 pandemic. (a) Contact dermatitis to hand cleanser in a patient, present distinctly over the dorsum of metacarpophalangeal joints and web spaces (highlighted with “\*\*”). (b) Irritant contact dermatitis to chlorhexidine gluconate (savlon) over the volar aspect of forearm of a patient. (c) Contact dermatitis to latex gloves in a patient, showing sharp cut-off at wrist. (d) Irritant contact dermatitis secondary to prolonged use of powdered gloves in a health care worker (Courtesy of Dr. Ahmed Nassar, Assistant lecturer of Dermatology, Ain Shams University, Cairo, Egypt). (e) Angioedema over hand after contact with latex gloves in a patient. (f) Pressure injury over the forehead and malar areas (highlighted with “\*\*”) occurring as a result of tight fitting helmet and N95 mask in a health care worker (Courtesy of Dr. Abhigyan Mukherjee, Consulting dermatologist, Dr Mukherjee’s Skin, Hair and Laser Clinic, Pune, India).

**Table 1** Potential allergens and irritants in the personal protective equipment and hand hygiene measures

Masks	Purpose	Allergens	Irritants
Standard surgical mask or fluid resistant surgical mask	<ul style="list-style-type: none"> <li>• Single use mask</li> <li>• Loose fitting</li> <li>• Prevents large particles (&gt; 5 microns) expelled by the wearer from reaching the environment.</li> <li>• Fluid resistant</li> <li>• Protects against large droplets and splashes</li> </ul>	<ul style="list-style-type: none"> <li>• Thiuram (in elastic ear strap);</li> <li>• Methylidibromo glutaronitrile;</li> <li>• Cocopropylenediamine-guanidinium diacetate (preservative in disinfectant for cleaning mask);</li> <li>• Dibromodicyanobutane (in adhesive used in mask)</li> </ul>	Friction and humidity
N95 respirator or filtering face piece (FFP)	<ul style="list-style-type: none"> <li>• Fit tightly</li> <li>• Fluid resistant</li> </ul>	<ul style="list-style-type: none"> <li>• Formaldehyde</li> <li>• Ethylene urea melamine formaldehyde</li> </ul>	Friction, mechanical pressure
FFP 1	<ul style="list-style-type: none"> <li>• Protects against very small air borne particles, body fluids and splashes</li> </ul>	<ul style="list-style-type: none"> <li>• Quaternium-15 (formaldehyde releasing preservative)</li> </ul>	
FFP 2			
FFP 3 (highest level of protection)	<ul style="list-style-type: none"> <li>• Has a filtration efficiency of 95% against particulate aerosols of size 300 nm and above</li> </ul>	<ul style="list-style-type: none"> <li>• Aluminium (in the nose clip)</li> </ul>	
Home-made (cloth or paper masks)	<ul style="list-style-type: none"> <li>• Loose fitting</li> <li>• Not fluid resistant</li> <li>• Prevents large particles expelled by the wearer from reaching the environment</li> </ul>	<ul style="list-style-type: none"> <li>• Formaldehyde textile resins (melamine formaldehyde, urea formaldehyde);</li> <li>• Formaldehyde releasers (quaternium-15, imidazolidinyl urea);</li> <li>• Disperse dyes, p-aminobenzene,</li> <li>• Paraphenylenediamine,</li> <li>• Naphthol AS, 'Black rubber mix'</li> <li>• Lanolin</li> </ul>	Friction, humidity
Gloves	Additional information	Allergens	Irritants
Natural rubber latex (NRL) gloves (powdered or unpowdered)	<ul style="list-style-type: none"> <li>• Users can be sensitive to either NRL or chemical additives or both.</li> <li>• Can worsen existing hand dermatitis from occlusion and maceration</li> </ul>	<ul style="list-style-type: none"> <li>• Rubber accelerators (thiuram, carba mix/ carbamates, mercaptobenzothiazole, diphenylguanidine)</li> <li>• Antioxidants (diaminodiphenylmethane, paraphenylenediamine, black rubber mix)</li> <li>• Immediate hypersensitivity to latex</li> </ul>	<p>Glove powder- cornstarch based</p> <p>Sterilization of gloves by gamma irradiation can increase bacterial endotoxin level, which is water soluble and can be absorbed onto glove powder leading to irritation</p>
Synthetic rubber gloves-	<ul style="list-style-type: none"> <li>• Manufactured similarly to latex gloves, including use of vulcanization accelerators</li> </ul>	<ul style="list-style-type: none"> <li>• Rubber accelerators (carba mix, carbamates, thiuram mix, 1,3-diphenylguanidine, benzothiazoles, thioureas)</li> </ul>	Cetylpyridinium chloride
Nitrile gloves			
Vinyl gloves			
Neoprene gloves			
Hand hygiene products	Components	Allergens	Irritants
Alcohol-based hand rub (liquid, gel or foam)	<ul style="list-style-type: none"> <li>• Contain one or more types of alcohol, humectants, other active ingredients with excipients</li> </ul>	<ul style="list-style-type: none"> <li>• Alcohols - ethanol, isopropanol</li> <li>• Fragrances</li> <li>• Acrylates</li> <li>• Preservative</li> <li>• Benzyl alcohol</li> <li>• Stearyl or isostearyl alcohol</li> <li>• Quaternium ammonium chloride (QAC)</li> <li>• Iodine or iodophors</li> <li>• Chlorhexidine</li> <li>• Triclosan</li> <li>• Chloroxylenol</li> <li>• Phenoxyethanol</li> <li>• Myristyl alcohol</li> <li>• Propylene glycol</li> <li>• Parabens</li> <li>• Benzalkonium chloride</li> </ul>	Ethanol, n-propranolol, isopropanol, chlorhexidine, chloroxylenol, triclosan

Table 1 Continued

Hand hygiene products	Components	Allergens	Irritants
Waterless/bar soaps	<ul style="list-style-type: none"> <li>• With or without added antiseptic agents</li> </ul>	<ul style="list-style-type: none"> <li>• Fragrances, tocopherol</li> <li>• Polyethylene glycol</li> <li>• Ethylhexylglycerin</li> <li>• Fragrances</li> <li>• Methylchloroisothiazolinone/methylisothiazolinone (MCI/MI)</li> <li>• Quaternium-15</li> <li>• Sodium benzoate</li> <li>• Phenoxyethanol</li> <li>• DMDM hydantoin</li> <li>• Iodopropynyl butylcarbamate</li> <li>• Alkyl glucosides</li> <li>• Chloroxylonol</li> <li>• Polyethylene glycol</li> <li>• Cocamidopropyl betaine</li> <li>• Triclosan</li> </ul>	SLS – sodium lauryl sulphate
Water-based/liquid soaps		<ul style="list-style-type: none"> <li>• Chloroxylonol, terpineol</li> <li>• Chlorhexidine gluconate, benzyl benzoate, cetrimide, isopropyl alcohol, terpineol</li> </ul>	Chloroxylonol, alcohol Cetrimide, chlorhexidine, gluconolactone Sodium hydroxide
Antiseptic agents	<ul style="list-style-type: none"> <li>• Dettol (chloroxylonol B.P. 4.8%w/v)</li> <li>• Savlon(cetrimide 3.0% w/v, chlorhexidine gluconate 0.3% w/v)</li> </ul>	<ul style="list-style-type: none"> <li>• Methylchloroisothiazolinone/methylisothiazolinone (MCI/MI)</li> <li>• Propylene glycol</li> <li>• Fragrances</li> <li>• Benzalkonium chloride.</li> </ul>	
Antiseptic hand wipe	<ul style="list-style-type: none"> <li>• Fabric or paper pre-wetted with an antiseptic agent. Not as effective as antiseptic agents or alcohol-based hand rubs</li> </ul>		

hand washing (>10 times daily) increased the risk of skin damage more than prolonged wearing of gloves.

Hand hygiene-associated dermatitis usually manifests on the knuckles and web spaces, where these irritants and allergens accumulate. Occasionally, both ICD and ACD can coexist. ACD to gloves presents with erythematous itchy plaques on convexities of dorsal surface of hands with a clear demarcation of erythema at wrists (Fig. 1).<sup>6</sup>

Contact dermatitis to various PPEs and hand hygiene measures can occur due to a variety of factors involving irritants and allergens in these agents, compounded by moisture, occlusion, friction, cold dry weather and atopic predisposition of an individual. These exposures lead to ICD and ACD through changes involving the skin barrier, cells and cytokines. Excessive hand hygiene depletes skin commensals that play an important role in Th1, Th2 and Th17 balance.<sup>8</sup>

Patch test is the gold standard for diagnosis of ACD. The battery of allergens includes standard series, textile series, fragrance series, masks, gloves and hand cleansers used by the patients. Some allergens relevant to SARS-CoV-2 pandemic viz 1,3 diphenyl guanidine, DMDM hydantoin, propylene glycol, formaldehyde and formaldehyde releasers may not be present in a single series. ACD to glove allergens also is commonly reported (Table 1).<sup>7</sup>

Healthcare workers education about hand hygiene measures combined with liberal moisturizing for skin barrier repair, avoidance of suspected allergens, ergonomic workplace interventions and emphasizing the need for redesigning PPE is vital in

tackling this iatrogenic health hazard. Alteration in the frequency of hand washing, use of correct fitting PPE and barrier creams are important. Fragrance-free emollients avoid the risk of further sensitization. If avoidance of allergen is not possible, protective measures like clothing, cotton lining latex or vinyl gloves and two-layered gauze-lined masks may be helpful.<sup>6,9</sup>

Further, the base of topical medicaments (corticosteroids and calcineurin inhibitors) to treat the dermatitis should be free from potential allergens. Correct use of PPEs and hand hygiene measures can protect HCWs from acquiring COVID-19 infection. However, iatrogenic problems because of these measures may prevent their proper use, putting HCWs at risk. There is an urgent need to sensitize the larger health fraternity about these issues.<sup>1,4,6</sup>

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## Urticarial vasculitis in COVID-19 infection: a vasculopathy-related symptom?

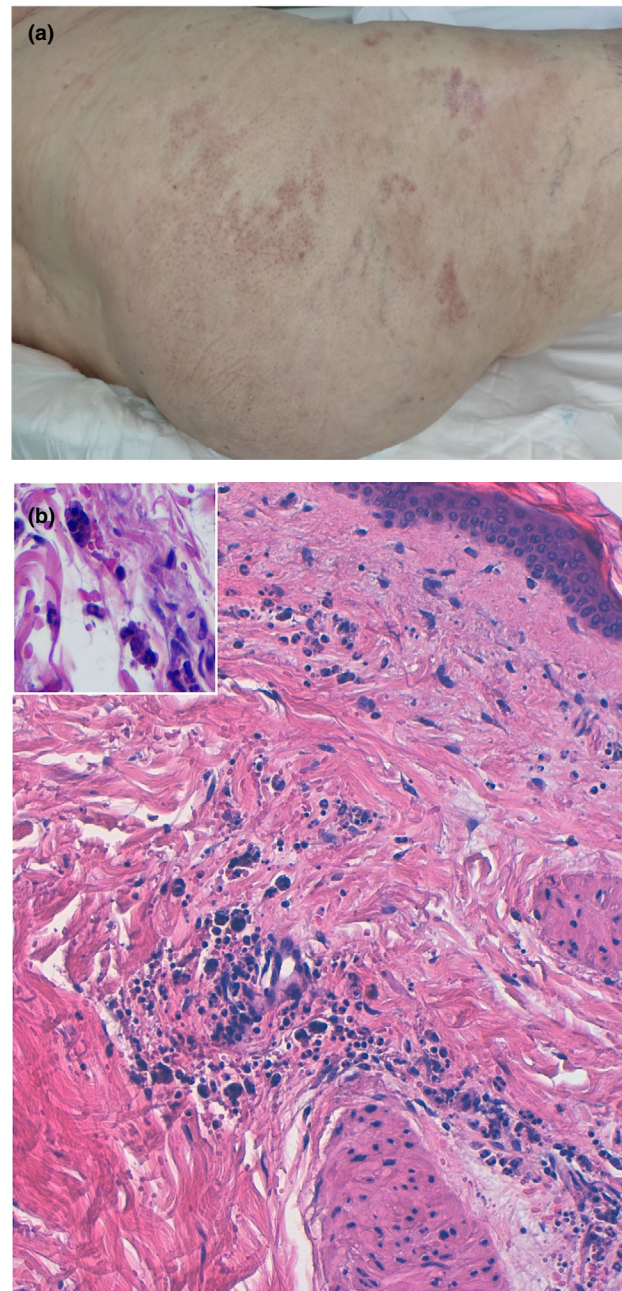
Editor,

The novel coronavirus disease (COVID-19) outbreak has been recently declared a pandemic by the World Health Organization (WHO), being Italy and Spain the worst-hit European countries. Although the main clinical picture consists of fever and respiratory symptoms, an increasing number of studies have reported associated skin manifestations. Herein, we present two patients with urticarial vasculitis arising in the context of COVID-19 infection.

The first case is an elderly woman who was admitted to the hospital with bilateral pneumonia testing positive for COVID-19. She had been receiving treatment with hydroxychloroquine, lopinavir/ritonavir and azithromycin for 5 days. The Dermatology Department was consulted for the appearance of painful erythematous patches on her trunk and hips, which left residual purpura when fading (Fig. 1a). A cutaneous biopsy was performed, revealing histologic changes characteristic of small-vessel vasculitis (Fig. 1b). A sudden worsening of her respiratory

condition led to the patient's death, and therefore, no treatment could be prescribed.

Our second case is a middle-aged man who presented to the Emergency Department with a 2-week history of fever, cough and



**Figure 1** First patient. (a) Clinical lesions on the buttocks and hips. Some erythematous patches are observed, along with other purpuric ones. (b) Histopathological images (H/E  $\times$  20) revealing blood extravasation and neutrophilic perivascular inflammation with prominent karyorrhexis. There are some macrophages with a cytoplasm full of nuclear debris (inset: H/E  $\times$  40).