

Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.

Table I. Nucleic acid testing on the surface of
personal protective equipment, medical facilities,
and the belongings of patients

Location	No. of tests	No. of positive results
Face shields	30	0
Protective goggles	30	0
Nurse rolling carts	15	0
Nurse station tables	5	0
Patients' water cups	10	0
Patients' mobile telephones	20	1

were collected in Hankou Hospital, Wuhan. All samples were sent to the Wuhan Dean medical laboratory center for COVID-19 nucleic acid detection, which adopted real-time polymerase chain reaction technology to detect nucleic acid sequences at 3 targets, with a sensitivity of greater than 90%.

After the medical staff removed their protective face shields and goggles and left the isolation ward, test swabs were daubed on the outer surfaces of the equipment 3 times. A total of 30 face shields and 30 sets of protective goggles were tested for SARS-Cov-2. In addition, the surfaces of a total of 20 nurse rolling carts and station tables were tested with the swabs in the same way. Surfaces of the belongings of 20 patients with confirmed disease, such as water cups and screens of mobile telephones, were also tested with swabs, and 30 samples were sent to the laboratory for nucleic acid testing for COVID-19 (Table I).

All surfaces of the face shields and protective goggles were devoid of SARS-Cov-2. Additionally, the surface test results for nurse stations and rolling carts and the water cups were negative, except for 1 positive result from the surface of a mobile telephone of a patient with COVID-19 (Table I).

It is well known that COVID-19 can be transmitted by an airborne route<sup>4</sup>; however, it was not clear whether the virus could float on surfaces in a medical environment and cause contact infection of medical staff. This study revealed that the probability that COVID-19 on surfaces can cause contact transmission is low; instead, more attention should be paid to personal isolation and protection from air transmisson. However, fomites such as patient belongings are a potential route of transmission, and therefore it is essential for hand washing and disinfection after contact with such items.<sup>5</sup>

We thank Inuk Zandvakili for revising the manuscript.

- *Qianli Jiang, MD,<sup>a</sup> Yinghua Chen, PhD,<sup>b</sup> Yingchun Dai, PhD,<sup>c</sup> Shaoxi Cai, MD,<sup>d</sup> and Guodong Hu, MD<sup>d</sup>*
- From the Department of Hematology<sup>a</sup> and Department of Respiratory and Critical Care Medicine,<sup>d</sup> Nanfang Hospital, the Guangdong Provincial Key Laboratory of Construction and Detection in Tissue Engineering, Department of Histology and Embryology, School of Basic Medical Sciences,<sup>b</sup> and the Department of Epidemiology, School of Public Health,<sup>c</sup> Southern Medical University, Guangzhou, Guangdong, China.
- *Funding sources: Supported by the Technology Planning Project of Guangdong Province* (2017A020215188).

### Conflicts of interest: None disclosed.

Correspondence to: Guodong Hu, MD, Department of Respiratory and Critical Care Medicine, Nanfang Hospital, Southern Medical University, 1838, Guangzhou North Ave, Guangzhou, Guangdong 510515, China

## E-mail: huguodong123123@126.com

### REFERENCES

- Bedford J, Enria D, Giesecke J, et al. COVID-19: towards controlling of a pandemic. *Lancet*. 2020;395(10229):1015-1018.
- Anelli F, Leoni G, Monaco R, et al. Italian doctors call for protecting healthcare workers and boosting community surveillance during COVID-19 outbreak. *BMJ*. 2020;368:m1254.
- 3. The Lancet. COVID-19: protecting health-care workers. *Lancet*. 2020;395(10228):922.
- Guan L, Zhou L, Zhang J, Peng W, Chen R. More awareness is needed for severe acute respiratory syndrome coronavirus 2019 transmission through exhaled air during non-invasive respiratory support: experience from China. *Eur Respir J.* 2020; 55(3):2000352.
- Lotfinejad N, Peters A, Pittet D. Hand hygiene and the novel coronavirus pandemic: the role of healthcare workers. *J Hosp Infect.* 2020. https://doi.org/10.1016/j.jhin.2020.03.017.

https://doi.org/10.1016/j.jaad.2020.05.150

# New insights in COVID-19–associated chilblains: A comparative study with chilblain lupus erythematosus

*To the Editor:* An unexpected outbreak of chilblains has been reported in association with COVID-19.<sup>1</sup> Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection has been shown in a few documented cases of chilblains. Chilblains may also be observed in acquired lupus and rarely as a manifestation of a familial disorder related to

Table I.	Clinical	and	biological	findings	in	EC and CLE	-

Variable	EC (N = 7)	CLE (N = 11)	P value
Female, n (%)	4 (57)	7 (64)	>.99
Age, y, mean (SD)	42 (10)	49 (15)	.27
Previous Raynaud phenomenon, n (%)	4 (57)	4 (36)	.63
Previous other cutaneous symptoms, n (%)	3* (43)	8 (73)	.33
Localized to feet, n (%)	7 (100)	2 (18)	<.01
COVID-19 symptoms, n (%)	5 (71)	NA	_
Potential SARS-CoV-2 contact, n (%)	4 (57)	NA	_
Positive antinuclear antibodies, n (%)	0 (0)	10 (91)	<.01
Presence of other immunologic abnormalities, n (%)	3 <sup>†</sup> (43)	9 (82)	.14

*CLE*, Chilblain lupus erythematosus; *EC*, epidemic chilblains; *NA*, not applicable; *SARS-CoV-2*, severe acute respiratory syndrome coronavirus 2; *SD*, standard deviation.

\*Two patients had acrocyanosis, and 1 patient had photosensitivity.

<sup>†</sup>Two patients had antineutrophil cytoplasmic antibodies, and 1 patient had lupus-type circulating anticoagulant.

interferonopathies. To enhance understanding of these epidemic chilblains (EC) cases and their relevance to SARS-CoV-2 infection, we studied clinical, hematoimmunologic, histopathologic, immunohistochemical, and virologic characteristics of 7 EC cases and compared them with 11 previous cases of chilblain lupus erythematosus (CLE).

Patients with EC were included between February and April 2020 and were suspected of COVID-19 because they presented with COVID-19 symptoms or were in close contact with patients with presumed/confirmed COVID-19. Exclusion criteria were patients with previous chilblains episode, cold exposure preceding chilblains occurrence, and history of known autoimmune disorder. For each patient, we collected demographic data and clinical and laboratory test results, including exhaustive hematoimmunologic screening, cutaneous histology (including immunostaining for CD123, a plasmocytoid dendritic cell marker, and MxA, a type I interferon [IFN-I]—induced protein), and virologic studies.

The clinicobiological findings of EC and CLE cases are summarized in Table I. Hands, ears, or nose localization were more frequently observed in the CLE group (82% vs 0%). Antinuclear antibodies were detected only in the CLE group (91% vs 0%). Age at onset of chilblains, sex, pre-existing Raynaud phenomenon, and other immunologic abnormalities did not differ between groups. Antineutrophil cytoplasmic antibodies (ANCAs) and lupus-type circulating anticoagulant were found in 2 and 1 patients with EC, respectively, without any clinical manifestation of ANCA vasculitis or thrombosis. No patient with EC had cryoprotein, cold agglutinin, or anticardiolipin antibodies.

Our 7 EC cases were histologically similar to CLE. High expression of CD123 and MxA were observed in both groups (Table II). SARS-CoV-2 RNA detection performed at a median delay of 23 days after symptom onset (range, 10-36 d) showed negative results in nasopharyngeal, skin biopsy, and plasma samples. Repeated SARS-CoV-2 immunoglobulin (Ig) G/IgA test results were negative for all patients, except for 1 who showed an isolated IgA positivity (time between first symptoms and serologic tests range, 21-51 d).

Active human herpes virus types 6, 7, and 8 and Epstein-Barr virus infections were excluded by reliable tests (polymerase chain reaction).

These results confirmed that chilblains may be considered as a manifestation of high production of IFN-I as observed in interferonopathies. These patients may exhibit only IFN-I associated symptoms or minor forms of COVID-19 infection. High level of IFN-I was associated with moderate cases of COVID-19.2 Interferon-induced proteins such as IFITM (interferon-induced trans-membrane) 1, 2, and 3 inhibit early replication of several enveloped RNA viruses, such as Middle East respiratory syndrome coronaviruses.<sup>3</sup> In addition, active viral replication may not be necessary to mount an efficient IFN response in SARS-CoV infection.<sup>4</sup> IFN-I may also suppress antibody responses, which might explain the negative serology test results in most patients with EC.

SARS-Cov-2 infection may induce, in some predisposed patients, a high production of IFN-I responsible for a high innate immune protective response. This hypothesis provides additional arguments to propose early IFN treatment for infected high-risk patients.

*Gilles Battesti, MD,<sup>a</sup> Jihane El Khalifa, MD,<sup>b</sup> Nour Abdelhedi, MD,<sup>b</sup> Valentine Ferre, PharmD,<sup>c</sup> Fabrice Bouscarat, MD,<sup>b</sup> Catherine Picard-Da han, MD,<sup>b</sup> Florence Brunet-Possenti, MD,<sup>b</sup> Gilles* 

# Table II. Histologic and immunohistochemical comparison between EC and CLE

Variable	EC (N = 7)	CLE (N = 11)	P value
Epidermis, n (%)	·		
Lymphocyte exocytosis	3 (43)	7 (64)	.63
Confluent necrosis	1 (14)	0 (0)	.39
Apoptotic keratinocytes	2 (29)	4 (36)	>.99
Vacuolized basement membrane zone	1 (14)	8 (73)	.049
Papillary dermis			
Edema, n (%)	4 (57)	2 (18)	.14
Lymphocyte infiltrate intensity score,* median (range)	2 (1-3)	2 (1-3)	.34
Lymphocyte infiltrate localization, n (%)			
Perivascular localization	7 (100)	11 (100)	>.99
Interstitial localization	3 (43)	8 (73)	.33
Other inflammatory cell infiltrate, n (%)	2 (29)	3 (27)	>.99
Lymphocytic vasculitis, n (%)	5 (71)	1 (9)	.01
Congestive vessels, n (%)	2 (29)	0 (0)	.13
Red blood cell extravasation, n (%)	4 (57)	1 (9)	.047
Reticular and deep dermis			
Lymphocyte infiltrate intensity score,* median (range)	2 (1-3)	2 (0-3)	.77
Lymphocyte infiltrate localization, n (%)			
Perivascular	7 (100)	10 (91)	>.99
Interstitial	0 (0)	0 (0)	>.99
Perieccrine	6 (86)	7/10 (70) <sup>†</sup>	.60
Perineural	4 (57)	7/9 (78) <sup>‡</sup>	.59
Other inflammatory cell infiltrate, n (%)	2 (29)	3 (27)	>.99
Lymphocytic vasculitis, n (%)	4 (57)	7 (64)	>.99
Leukocytoclastic vasculitis, n (%)	1 (14)	1 (9)	>.99
Congestive vessels, n (%)	3 (43)	1 (9)	.24
Neural section, median (range)	5 (2-9)	3 (0-4)	.008
Hypodermis <sup>§</sup>			
Perivascular lymphocyte infiltrate, n (%)	2/2 (100)	0/2 (0)	.33
Immunohistochemical features			
Case with $MxA^+$ cells, n (%)	7 (100)	10/10 (100)	>.99
MxA expression, median (range)	180 (105-280)	270 (120-300)	.28
Case with CD123 <sup>+</sup> cells, n (%)	6 (86)	9/10 (90)	>.99
CD123 expression, median (range)	50 (0-60)	15 (0-100)	.32
Positive cutaneous DIF, n (%)	0/3 (0)	1/2 (50) <sup>#</sup>	.4

Bold values are statistically significant.

*CLE,* Chilblain lupus erythematosus; *DIF,* direct immunofluorescence; *EC,* epidemic chilblains; *MxA,* myxovirus resistance protein A; *SD,* standard deviation.

\*Intensity was scored as follow: 0, absence; 1, rare; 2, moderated; 3, intense.

<sup>†</sup>One CLE biopsy sample did not show the eccrine gland.

<sup>‡</sup>Two of CLE biopsy samples did not show the nerve.

<sup>§</sup>Hypodermis was observed in 2 biopsy samples in each groups.

One CLE did not have immunohistochemistry analysis.

<sup>¶</sup>Three DIF analyses were performed in the EC group.

<sup>#</sup>Two DIF analyses were performed in the CLE group.

Collin,<sup>c</sup> Justine Lavaud, MD,<sup>b</sup> Patrick Le Bozec, MD,<sup>b</sup> Marion Rousselot, MD,<sup>b</sup> Amélie Tournier, MD,<sup>b</sup> Coralie Lbeure, MD,<sup>b</sup> Anne Couvelard, MD, PbD,<sup>a</sup> Salima Hacein-Bey-Abina, PharmD, PhD,<sup>d,e</sup> Amine M. Abina, MD, PhD,<sup>d,f</sup> Charlotte Charpentier, PharmD, PbD,<sup>c</sup> Sabine Mignot, PharmD, PhD,<sup>g</sup> Pascale Nicaise, PharmD, PhD,<sup>g</sup> Diane Descamps, MD, PhD,<sup>c</sup> Lydia Deschamps, MD,<sup>a</sup> and Vincent Descamps, MD, PhD<sup>b</sup>

From the Department of Pathology, Bichat Hospital, Paris, France<sup>a</sup>; Department of Dermatology, Bichat Hospital, Paris, France<sup>b</sup>; Department of Virology, Bichat Hospital, Paris, France<sup>c</sup>; Unité des Technologies Chimiques et Biologiques Pour la Santé, Centre National de la Recherche Scientifique, Unité Mixte de Recherche (UTCBS CNRS UMR) 8258, Institut National de la Santé et de la Recherche Médicale (INSERM) U1267, Faculté de Pharmacie de Paris, Université de

J Am Acad Dermatol October 2020

Paris, Paris, France<sup>d</sup>; Clinical Immunology Laboratory, Groupe Hospitalier Universitaire Paris-Sud, Hôpital Kremlin-Bicêtre, Assistance Publique-Hôpitaux de Paris, Le-Kremlin-Bicêtre, France<sup>e</sup>; Cerba Healthcare, Cerballiance-Ile-de-France Ouest, Hôpital Privé de l'Ouest Parisien, Trappes, France<sup>f</sup>; and Department of Immunology, Bichat Hospital, Paris, France.<sup>g</sup>

## Funding sources: None.

## Conflicts of interest: None disclosed.

- *IRB approval status: Reviewed and approved by the IRB of Hôpitaux Universitaires Paris Nord Val de Seine (HUPNVS), Paris 7 University, Assistance Publique Hôpitaux de Paris (AP-HP) (IRB* 00006477).
- Reprint requests: Vincent Descamps, MD, PhD, Department of Dermatology, Bichat Hospital, 46 rue Henri Huchard, 75877 Paris, France

## E-mail: vincent.descamps@aphp.fr

### REFERENCES

- 1. de Masson A, Bouaziz J-D, Sulimovic L, et al. Chilblains are a common cutaneous finding during the COVID-19 pandemic: a retrospective nationwide study from France. *J Am Acad Dermatol.* 2020;83:667-670.
- Hadjadj J, Yatim N, Barnabei L, et al. Impaired type I interferon activity and exacerbated inflammatory responses in severe Covid-19 patients. *MedR*<sub>\(\chi\)</sub> iv. 2020. https://www.medrxiv.org/ content/10.1101/2020.04.19.20068015v1. Accessed May 14, 2020.
- Wrensch F, Winkler M, Pöhlmann S. IFITM proteins inhibit entry driven by the MERS-coronavirus spike protein: evidence for cholesterol-independent mechanisms. *Viruses*. 2014;6(9): 3683-3698.
- 4. de Lang A, Baas T, Smits SL, Katze MG, Osterhaus AD, Haagmans BL. Unraveling the complexities of the interferon response during SARS-CoV infection. *Future Virol*. 2009;4(1):71-78.
- Fallet B, Narr K, Ertuna YI, et al. Interferon-driven deletion of antiviral B cells at the onset of chronic infection. *Sci Immunol*. 2016;1(4):eaah6817.

https://doi.org/10.1016/j.jaad.2020.06.1018

# Multidisciplinary care of epidermolysis bullosa during the COVID-19 pandemic—Consensus: Recommendations by an international panel of experts



*To the Editor:* The 2019 novel coronavirus (COVID-19) pandemic became apparent in China during the International Congress on Epidermolysis Bullosa (EB) in London, in January 2020. Many patients with EB have medical problems that make them a vulnerable population of patients.<sup>1</sup> We developed an international consensus to suggest the best management of patients with EB during the pandemic.

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) virus enters host cells using its spike protein binding to the cell receptor angiotensin converting enzyme 2 (ACE2), which is expressed in several tissues. Mucosae have high ACE2 expression, particularly the nasal epithelium. ACE2 is also expressed in the basal layer of keratinocytes and sebaceous glands of normal skin as well as in vascular endothelial cells, but its expression in wounded EB skin has not been studied.<sup>2</sup>

A questionnaire was drafted by an author (D.M.) into a table of suggested modifications to the management of EB during the COVID-19 pandemic. Fifty-seven well-known experts on EB were selected based on membership of the international Clin-et group or clinical expertise in EB, or both, demonstrated at International EB Congress participation. Responses and reasons for each response were requested individually to the lead author based on an ideal scenario, rather than what actually may happen in some centers with financial constraints. A priori, consensus was considered to be the agreement of more than 70% of respondents with the suggestion. Questionnaires were returned by 44 of the 57 EB experts, representing several areas of clinical expertise in EB (dermatology, pediatrics, internal medicine, and surgery) from 5 continents. After addition and revision of some items and 3 cycles of revoting, consensus was achieved for all items, which are summarized in Supplementary Table I (available via Mendeley at https://data. mendeley.com/datasets/zmpncb6zpr/2).

The main change in usual practice was the introduction of photographs from the patient/family and teledermatology as the primary visit for patients with less severe EB, with dressing supplies sent to the patients directly. For those patients with EB with significant internal disease, monitoring tests (blood and urine) must continue but can be obtained by local laboratories or family doctors close to home.<sup>3</sup> If telehealth images are insufficient to assess lesions, assessments should be conducted at the EB center.<sup>4</sup>

One of the greatest fears of families caring for patients with severe forms of EB is how they will be perceived on admission to hospitals, especially institutions with limited resources, including ventilators. Because patients with EB often appear frail and emaciated, health care workers unfamiliar with the condition may underestimate their resilience and incorrectly assume that they have a low likelihood of survival.<sup>5</sup> If a patient with EB required