COVID-19 with dermatologic manifestations and implications: An unfolding conundrum

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Abstract
The novel coronavirus SARS-CoV-2 has caused Coronavirus Disease 2019, widely known as COVID-19, now a pandemic with extraordinary infectivity, mortality, and fomite adhesiveness. We delineate cutaneous manifestations of COVID-19, some of which may represent adverse cutaneous drug reactions, and skin changes associated with COVID-19 lifestyle alterations in patients and health care workers. We review COVID-19 from both a dermatologic and public health perspective.

KEYWORDS
urticaria, skin signs of systemic disease, infection—bacterial/fungal/viral, drug reaction, therapy—topical, inflammatory disorders

1 | INTRODUCTION

Coronavirus disease 2019 (COVID-19) is a viral infection caused by severe acute respiratory syndrome coronavirus type-2 (SARS-CoV-2) that was first reported from Wuhan in central China in December 2019.1-5 In a short span of 5 months, it has spread to almost all the countries around the world, resulting in the ongoing 2019-20 coronavirus pandemic.6 The World Health Organization (WHO) declared it a Public Health Emergency of International Concern on January 30, 20207 and a pandemic on March 11, 2020.6

COVID-19 is a flu-like syndrome commonly characterized by fever, cough and dyspnea. Other symptoms associated with it include malaise, myalgia, diarrhea, sore throat, abdominal pain, and loss of smell and a variety of other acute neurologic manifestations.1,8 In fact, smell dysfunction has been characterized as a biomarker for COVID-19, as one study showed 59 of 60 patients exhibited some smell dysfunction with 35 of them either anosmic or severely microsmic.8 While more than 90% of COVID-19 patients reported mild symptoms, some do require hospitalization and develop severe pneumonia and eventually multiorgan failure, meriting management in an intensive care unit.

2 | THE VIRUS AND ITS TRANSMISSION

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is the seventh coronavirus known to infect humans with SARS-CoV-1, MERS-CoV and SARS-CoV-2 capable of causing severe disease. The four others produce only mild symptoms. SARS-CoV-2 is a novel coronavirus, an RNA virus closely related to the original SARS-CoV.9 It has been proclaimed as unlikely to have been derived through laboratory manipulation of a related SARS-CoV-like coronavirus.10

SARS-CoV-2 is spread through close contact with infected individuals and by droplets released into the air during coughing, sneezing and talking. In addition, fomite spread is an important feature, which is not surprising, because it had played a central role in the SARS 2003 epidemic. However, fomites have also proven important during other outbreaks.5,10 Bed curtains, restroom fixtures, and countertops touched are good examples.

3 | CLINICAL APPROACH

COVID-19 typically takes approximately 5 days for the first symptoms to manifest, but this period can vary from 2 to 14 days.1-5 The virus is most contagious when people are symptomatic. The diagnosis is rendered usually by real-time reverse transcription polymerase chain reaction (rRT-PCR) from a nasal swab, which is generally used as a standard diagnostic method. The spread of infection can be markedly diminished by taking certain preventive measures including frequent hand washing, social distancing by maintaining physical distance from others, covering coughs and sneezes with a tissue or inner elbow and keeping unwashed hands away from the face. The use of masks when appropriate is also
believed to limit its spread and has been recommended by many countries. Current management involves symptomatic treatment, supportive care, isolation, and certain experimental therapeutic measures.

4 | PATHOPHYSIOLOGY

Lungs are the most severely affected organ by COVID-19 because the virus enters the host cells via the integral membrane protein angiotensin-converting enzyme 2 (ACE2), which is attached to cellular membranes in the lungs, arteries, heart, kidney, and intestines. It is most abundantly found in the type II alveolar cells of the lungs. The virus uses a special surface glycoprotein called a "spike" (peplomer) to connect to ACE2 and gain entry into the host cell.

The virus also affects gastrointestinal organs as ACE2 is abundantly expressed in the glandular cells of gastric, duodenal and rectal epithelium as well as endothelial cells and enterocytes of the small intestines. It also affects the cardiovascular system, where it causes acute injury to myocardium, more commonly documented in critically ill patients. They also have a high incidence of thrombosises and venous thromboembolisms, the presence of which is associated with a poor prognosis.

4.1 | Pathology

Increasing data is becoming available about the microscopic changes occurring in various organs with COVID-19. Autopsy specimens have highlighted pulmonary involvement with a severe pneumonia showing diffuse alveolar damage with diffuse alveolar exudates, findings linked with acute respiratory distress syndrome and severe hypoxemia. Other findings include disseminated intravascular coagulation and a leukoerythroblastic reaction.

5 | DERMATOLOGICAL IMPLICATIONS

Dermatological implications fall into four main groupings: cutaneous manifestations of COVID-19, skin changes from COVID-19 lifestyle alterations, cutaneous adverse reactions to COVID-19 medications, and effects of COVID-19 and its therapy on primary skin diseases and their management. COVID-19 has been associated with suggestive skin manifestations which we classify into 6 categories with three distinct patterns: vesicular (varicella-like), vasculopathic, and chilblains-like ("COVID toes") plus three less indicative ones: dermatitic, maculopapular, and urticarial morphologies.

Cutaneous manifestations are varied, as noted in some of our COVID-19 patients, which include urticaria, varicella-like vesicles, transient livedoid eruptions, livedoid vasculopathy, purpuric eruptions, lichenoid photodermatitis, erythroderma, photo-contact dermatitis, and generalized pustular figurate erythema (Figure 1-11). Similar findings were observed by others and in about one-fifth of patients with COVID-19 at a hospital near the shores of Lake Como in northern Italy. Of the 88 hospitalized patients visited either directly or indirectly by dermatologists often involved because of a lack of general physicians, 20.4% developed skin manifestations. Eight of the 18 (44%)
had a skin eruption at onset of symptoms, and the remainder after hospitalization. Fourteen (78%) had an erythematous rash, three had widespread urticaria, and one had chickenpox-like vesicles. The most commonly affected area was the trunk. Itching was mild or absent; lesions usually healed in a few days. The skin manifestations did not usually correlate with disease severity. It was speculated that the above cutaneous findings are similar to those occurring during common viral infections. However, others from Italy have suggested the varicella-like exanthem as a rare but specific COVID-19-associated skin manifestation with scattered truncal distribution, little or no pruritus, and an onset 3 days after systemic symptoms but disappearance without

**FIGURE 4**  A and B, Livedoid vasculopathy in COVID-19 patient

**FIGURE 5**  A and B, Purpuric eruption in COVID-19 patient

**FIGURE 6**  Purpuric eruption in COVID-19 patient

**FIGURE 7**  Purpuric eruption in COVID-19 patient

**FIGURE 8**  Lichenoid photodermatitis in COVID-19 patient
scarring in 8 days. COVID-19 patients may also have cutaneous eruptions reflecting vascular considerations. Petechial and transient livedo reticularis-like eruptions are being described. A patient in a Bangkok hospital had a petechial eruption and other findings that resembled dengue fever. Seven critically ill Chinese patients from Wuhan had acro-ischemia presentations including finger/toe cyanosis, skin bulla and dry gangrene. Four of them were diagnosed with disseminated intravascular coagulation. Others with COVID-19 develop lesions resembling chilblains disease, referred to by some as "COVID toes." Changes in lifestyle, including prolonged contact to personal protective equipment, and excessive personal hygiene, may produce cutaneous findings, including pressure injury, contact dermatitis, and contact urticaria, as we have noted too (Figure 12-15). The exacerbation of preexisting skin diseases like seborrheic dermatitis, atopic dermatitis, and acne, can be anticipated. Most frontline health care workers will develop cutaneous lesions affecting the nasal bridge, hands, cheek, and forehead. As expected, frequent hand hygiene was associated with a higher incidence of hand dermatitis. There is also an enhanced risk of developing the Goldman-Fox syndrome of pseudomonas-infected green nails, with the possibility of transmitting pseudomonas to otherwise compromised patients. The use of preventive measures, including emollients, barrier creams, and moisturizers, may be desirable in ameliorating skin complications aggravated by protective measures during this pandemic. Although there are as yet no proven effective therapies for COVID-19, many medications have been suggested as efficacious. Drug interactions or adverse cutaneous drug reactions have been observed in COVID-19 positive patients being treated with experimental agents or the high-risk groups like health care workers being given possibly prophylactic anti-COVID drugs. The antimalarials, specifically chloroquine and hydroxychloroquine, are a popular option,
which can aggravate preexisting psoriasis or produce a variety of cutaneous reactions. Recent interest has focused on generalized pustular figurate erythema (Figure 11), a newly delineated potentially life-threatening severe cutaneous drug reaction previously classified as atypical acute generalized eruptive pustulosis (AGEP) or AGEP/Steven-Johnson syndrome overlap.

Another important concern is management of patients with autoimmune and chronic inflammatory disorders being treated with biologic drugs or immunosuppressants, specifically those with psoriasis, atopic dermatitis, connective tissue diseases, and hidradenitis suppurativa. European Task force Dermatology Specific Guidelines were published, suggesting continuing all immune-modulating treatments, including immunosuppressive therapy, since exacerbations of underlying diseases can have a large negative impact on patient immunity. It lamented that many conventional systemic immune-modulating agents, such as cyclosporine, may interact with the human body’s defense mechanisms against viral disease, but warned that it is not currently known how SARS-CoV-2 affects atopic dermatitis patients and specifically those on immune-modulating therapies.

6 | RISK FACTORS AND PREVENTION

Public health policy is pivotal and varied. Enclosed space air cleansing devices should be widely employed. At-home testing and monitoring for possible COVID-19 represent a solid approach to keeping these COVID-19 patients out of understaffed limited-equipment hospitals. As another measure to prevent people from being hospitalized, it might be wise to actively discourage health care workers at high-risk, no matter how well-meaning, from being present at health care facilities, given both direct and fomite COVID-19 spread. Since risk is stratified by age, with deaths concentrated at older ages, and underlying co-morbidities, recommendations by us have been made (Table 1). Calling for older health care workers to volunteer is questionable. A study of 663 COVID-19 patients from Wuhan, China stressed that patients more than 60 years old and those with chronic diseases were at enhanced risk of severe COVID-19, and more likely to die. A larger Chinese study using multivariate Cox regression analysis showed that age \( \geq 65 \) years, coronary heart disease, cerebrovascular disease, and dyspnea were independent risk factors associated with fatal outcome.

We urge that health care workers over 65 years of age be strongly encouraged to shelter at home and to telecommute unless they are immune from COVID-19, presumably after surviving an infection, assuming post-infection immunity can be proven. Appropriate precautions should be taken to minimize the risk of virus transmission to others, especially in health care settings when performing...
procedures that can generate aerosols.\textsuperscript{43} The United States Centers for Disease Control and Prevention recommends placing the COVID-19 patients in an Airborne Infection Isolation Room, in addition to standard, contact, and airborne precautions.\textsuperscript{44}

One must also recall that co-infections may occur, with emerging epidemics of pathogens such as Candida auris lurking with particular ferociousness in intensive care units.\textsuperscript{53} Like SARS-CoV-2, Candida auris may rest on fomites such as plastic and stainless steel, copper and cardboard, with viable virus and/or fungus on these surfaces.\textsuperscript{53,54} Preliminary results showed that fomite transmission of SARS-CoV-2 is plausible with this virus remaining viable on surfaces up to days.\textsuperscript{54}

Neuropsychiatric sequelae of COVID-19 should be a concern.\textsuperscript{55-61} We recommend considering the post-pandemic neuropsychiatric complications of the two major pandemics of the last century, the Spanish flu of 1917 and the Asian flu of 1957, appreciating the meticulous work of von Economo\textsuperscript{55} and of Kapila\textsuperscript{56} in what has later become known as von Economo’s disease and the Kapila syndrome.

In influenza and recent CoV outbreaks, neuropsychiatric symptoms are often overlooked in favor of respiratory and other symptoms. During the more recent influenza epidemics and other coronavirus infections (SARS-CoV-1 epidemic and the Middle East respiratory syndrome coronavirus), neuropsychiatric sequelae have been described including narcolepsy, seizures, encephalitis, encephalopathy, and the Guillain-Barre syndrome.

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### REFERENCES

1. Hui DS, I Azhar E, Madani TA, Ntoumi F, Kock R, Dar O, Ippolito G, Mchugh TD, Memish ZA, Drosten C, Zumla A, Petersen E. The continuing 2019-nCoV epidemic threat of novel coronaviruses to global health – The latest 2019 novel coronavirus outbreak in Wuhan, China Int J Infect Dis 2020;91:264–266.

2. Jewell NP, Lewnard JA, Jewell BL. Caution warranted: using the Institute for Health Metrics and Evaluation Model for predicting the course of the COVID-19 pandemic. Ann Intern Med. 2020. https://doi.org/10.7326/M20-1565.

3. Guan WJ, Ni ZY, Hu Y, et al. Clinical characteristics of coronavirus disease 2019 in China. N Engl J Med. 2020;382:1708-1720. https://doi.org/10.1056/NEJMoa2002032.

4. Ippolito G, Hui DS, Ntoumi F, Maeurer M, Zumla A. Toning down the 2019-nCoV media hype and restoring hope. Lancet Respir Med. 2020;8(3):230-231. https://doi.org/10.1016/S2213-2600(20)30070-9.

5. Yen MY, Schwartz J, Chen SY, King CC, Yang GY, Hsueh PR. Interrupting COVID-19 transmission by implementing enhanced traffic control bundling: implications for global prevention and control efforts. J Microbiol Immunol Infect. 2020. https://doi.org/10.1016/j.jmii.2020.03.011.

6. WHO Director-General’s opening remarks at the media briefing on COVID-19. World Health Organization (WHO) (Press release); 2020. Archived from the original on March 11, 2020. Retrieved March 12, 2020.

7. Statement on the second meeting of the International Health Regulations (2005) Emergency Committee regarding the outbreak of novel coronavirus (2019-nCoV). World Health Organization (WHO). Archived from the original on January 31, 2020. Retrieved February 11, 2020.

8. Moein ST, Hashemian SMR, Mansourafrshar B, Khorram-Tousi A, Tabarsi P, Doty RL. Smell dysfunction: a biomarker for COVID-19. Int Forum Allergy Rhinol. 2020. https://doi.org/10.1002/alr.22587.

9. Anderssen KG, Rambaut A, Lipkin WI, Holmes EC, Garry RF. The proximal origin of SARS-CoV-2. Nat Med. 2020;26:450-452.

10. Letko M, Marzi A, Munster V. Functional assessment of cell entry and receptor usage for SARS-CoV-2 and other lineage B betacoronaviruses. Nat Microbiol. 2020;5:562-569.

11. Hamming I, Timens W, Bulthuis ML, Lely AT, Navis G, van Goor H. Tissue distribution of ACE2 protein, the functional receptor for SARS coronavirus. A first step in understanding SARS pathogenesis. J Pathol. 2004;203:631-637.

12. Zheng YY, Ma YT, Zhang JY, Xie X. COVID-19 and the cardiovascular system. Nat Rev Cardiol. 2020;17:259-260. https://doi.org/10.1038/s41569-020-0360-5.

13. Liang WH, Guan WJ, Li CC, et al. Clinical characteristics and outcomes of hospitalised patients with COVID-19 treated in Wuhan (Hubei, epicenter) and outside Hubei (non-epicenter): a Nationwide analysis of China. Eur Respir J. 2020;pi:2000562. https://doi.org/10.1183/13993003.00562-2020.

14. Klok FA, Kruip MJHA, van der Meer NJM, et al. Incidence of thrombotic complications in critically ill ICU patients with COVID-19. Thromb Res. 2020;191:145-147. https://doi.org/10.1016/j.thromres.2020.04.013.

15. Cui S, Chen S, Li X, Liu S, Wang F. Prevalence of venous thromboembolism in patients with severe novel coronavirus pneumonia. J Thromb Haemost. 2020;18:1421-1424. https://doi.org/10.1111/jth.14830.

16. Yao XH, Li TY, He ZC, et al. A pathological report of three COVID-19 cases by minimally invasive autopsies. Zhonghua Bing Li Xue Za Zhi (in Chinese) 2020;49:e009. https://doi.org/10.3760/cma.j.cn111251-20200312-00193.

17. Adádías-Granado I, Palma Ruiz AM, Cerro PA, Gomez-Mateo G, Gilaberte Y, Schwartz RA: Generalized pustular figurate erythema as a specific COVID-19-associated skin manifestation: multicenter case series of 22 patients. J Am Acad Dermatol. 2020. https://doi.org/10.1016/j.jaad.2020.04.044.
20. Su CJ, Lee CH. Viral exanthem in COVID-19, a clinical enigma with biological significance. J Eur Acad Dermatol Venereol. 2020. https://doi.org/10.1111/jdv.16469.

21. Henry D, Ackerman M, Sancelme E, Finon A, Esteve E. Urticarial eruption in COVID-19 infection. J Eur Acad Dermatol Venereol. 2020. https://doi.org/10.1111/jdv.16472.

22. Kanitakis J, Lesort C, Danse M, Julienne D. Childblain-like acral lesions during the COVID-19 pandemic ("COVID toes"): Histologic, immunofluorescence and immunohistochemical study of 17 cases. J Am Acad Dermatol. 2020 Jun 2;S0190-9622(20)31022-7. https://doi.org/10.1016/j.jaad.2020.05.145.

23. Beun R, Kusadasi N, Simka M, Westerink J, Huisman A. Thromboembolic events and apparent heparin resistance in patients infected with SARS-CoV-2. Int J Lab Hematol. 2020. https://doi.org/10.1111/ijlh.13230.

24. Joob B, Wiwanitkit V. Hemorrhagic problem among the patients with COVID-19: clinical summary of 41 Thai infected patients. Clin Appl Thromb Hemost. 2020;26:1076029620918308. https://doi.org/10.1177/1076029620918308.

25. Lin P, Zhu S, Huang Y, et al. Adverse skin reactions among healthcare workers during the coronavirus disease 2019 outbreak: a survey in Wuhan and its surrounding regions. Br J Dermatol. 2020. https://doi.org/10.1111/bjd.19089.

26. Joob B, Wiwanitkit V. COVID-19 can present with a rash and be mistaken for dengue. J Am Acad Dermatol. 2020;82:e177. https://doi.org/10.1016/j.jaad.2020.03.036.

27. Manalo IF, Smith MK, Cheeley J, Jacobo R. A dermatologic manifestation of COVID-19: transient livedo reticularis. J Am Acad Dermatol. 2020. https://doi.org/10.1016/j.jaad.2020.04.018.

28. Mahé A, Birckel E, Krüger S, Merklen C, Bottlaender L. A distinctive skin rash associated with coronavirus disease 2019? J Eur Acad Dermatol Venereol. 2020. https://doi.org/10.1111/jdv.16471.

29. Estébanez A, Pérez-Santiago L, Silva E, Guillén-Climent S, García-Vázquez A, Ramón MD. Cutaneous manifestations in COVID-19: a new contribution. J Eur Acad Dermatol Venereol. 2020. https://doi.org/10.1111/jdv.16474.

30. Zhang Y, Cao W, Xiao M, et al. Clinical and coagulation characteristics of 7 patients with critical COVID-19 pneumonia and acro-ischemia. Zhonghua Xue Ye Xue Za Zhi. 2020;28:418(8):E006. https://doi.org/10.3760/cma.j.issn.0253-2772.2020.0006. [Epub ahead of print]. PMID: 32220276.

31. Magro C, Mulvey JJ, Berlin D, et al. Complement associated microvascular injury and thrombosis in the pathogenesis of severe COVID-19 infection: a report of five cases. Transl Res. 2020. https://doi.org/10.1016/j.trsl.2020.04.007.

32. Goren A, Vano-Galvan S, Wambier CG, et al. A preliminary observation: male pattern hair loss among hospitalized COVID-19 patients in Spain - a potential clue to the role of androgens in COVID-19 severity. J Cosmet Dermatol. 2020. https://doi.org/10.1111/1345-5904.13443.

33. Foo CC, Goon AT, Leow YH, Goh CL. Adverse skin reactions to personal protective equipment against severe acute respiratory syndrome—a descriptive study in Singapore. Contact Dermatitis. 2006;55(5):291-294.

34. Joob B, Wiwanitkit V. COVID-19 in medical personnel: observation from Thailand. J Hosp Infect. 2020;104:453. https://doi.org/10.1016/j.jhin.2020.02.016.

35. Elston DM. Occupational skin disease among health care workers during the coronavirus (COVID-19) epidemic. J Am Acad Dermatol. 2020;82:1085-1086.

36. Elston DM. The coronavirus (COVID-19) epidemic and patient safety. J Am Acad Dermatol. 2020;82:819-820.

37. Lan J, Song Z, Mao X. Skin damage among health care workers managing coronavirus disease-2019. J Am Acad Dermatol. 2020;82:1215-1216.

38. Schwartz RA, Reynoso-Vasquez V, Kapila R. Chloronychia: the Goldman-fox syndrome: implications for patients and health care workers. Indian J Dermatol. 2020;65:1-4.

39. Soria A, Barbad A, Assier H, et al. Francés C; FISARD (French investigators for skin adverse reaction to drugs). Cutaneous adverse drug reactions with antimarial and allergological skin tests. Dermatology. 2015;231:353-359.

40. Schwartz RA, Jannier CK. Generalized pustular figurate erythema. A newly delineated severe cutaneous drug reaction linked with hydroxychloroquine. Dermatol Ther. 2020;33(3):e13380. https://doi.org/10.1111/dth.13380.

41. Wang C, Rademaker M, Baker C, Foley P. COVID-19 and the use of immunomodulatory and biologic agents for severe cutaneous disease: an Australia/New Zealand consensus statement. Australas J Dermatol. 2020. https://doi.org/10.1111/ajd.13313.

42. Wollenberg A, Flohr C, Simon D, et al. European task force on atopic dermatitis (ETFAD) statement on severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)-infection and atopic dermatitis. J Eur Acad Dermatol Venereol. 2020. https://doi.org/10.1111/jdv.16411.

43. Cheung JC, Ho LT, Cheng JV, Cham EYK, Lam KN. Staff safety during emergency airway management for COVID-19 in Hong Kong. Lancet Respir Med. 2020;8(4):e19. https://doi.org/10.1016/S2213-2600(20)30084-9.

44. What healthcare personnel should know about caring for patients with confirmed or possible coronavirus disease 2 (PDF). CDC. March 12, 2020. https://www.cdc.gov/coronavirus/2019-ncov/hcp/caring-for-patients-h.pdf, accessed April 19, 2020.

45. Carlton PK Jr, Johanjman G, Janniger EJ, Schwartz RA: COVID-19 and the urgent need to render spaces safer. Global Policy. 2020;11(2): globalpolicyjournal.com/blog/15/05/2020-covid-19-and-urgent-need-render-spaces-safer

46. Zhang J, Wang X, Jia X, et al. Risk factors for disease severity, uncompromised, and mortality of COVID-19 patients in Wuhan, China. Clin Microbiol Infect. 2020. https://doi.org/10.1016/j.cmi.2020.04.012.

47. Chen R, Liang W, Jiang M, Guan W, Zhan C, Wang T, Tang C, Sang L, Liu J, Ni Z, Hu Y, Liu L, Shan H, Lei C, Peng Y, Wei L, Liu Y, Hu Y, Peng P, Wang J, Liu J, Chen Z, Li G, Zheng Z, Qiu S, Luo J, Ye C, Zhu S, Liu X, Cheng L, Ye F, Zheng J, Zhang N, Li Y, He J, Li S, Zhang N; Medical treatment expert group for COVID-19. Risk factors of fatal outcome in hospitalized subjects with coronavirus disease 2019 from a nationwide analysis in China. Chest. 2020. doi: https://doi.org/10.1016/j.chest.2020.04.010.

48. Geographic differences in COVID-19 cases, deaths, and incidence – United States, February 12–April 7, 2020. CDC COVID-19 response team. MMWR Morb Mortal Wkly Rep. 2020;69(15):465-471. https://doi.org/10.15585/mmwr.mm6915e4.

49. CDC COVID-19 Response Team. Severe outcomes among patients infected with SARS-CoV-2 admitted to ICUs of the Lombardy Region, United States, February 12–March 16, 2020. MMWR Morb Mortal Wkly Rep. 2020;69:343-346.

50. Dowd JB, Andriano L, Brazel DM, et al. Demographic science aids in understanding the spread and fatality rates of COVID-19. Proc Natl Acad Sci U S A. 2020;117:9496-9498. https://doi.org/10.1073/pnas.2004911117.

51. Grasselli G, Zaninelli A, Zanella A, et al. COVID-19 Lombardy ICU investigators for skin adverse reaction to drugs). Cutaneous adverse drug reactions with antimarial and allergological skin tests. Dermatology. 2015;231:353-359.

52. Glauser W. Proposed protocol to keep COVID-19 out of hospitals. CMAJ. 2020;192(10):E264-E265. https://doi.org/10.1503/cmaj.1095852.
53. Schwartz RA, Kapila R. Cutaneous manifestations of a 21st century worldwide fungal epidemic possibly complicating the COVID-19 pandemic to jointly menace mankind. *Dermatol Ther*. 2020;33(4):e13380.

54. van Doremalen N, Bushmaker T, Morris DH, et al. Aerosol and surface stability of SARS-CoV-2 as compared with SARS-CoV-1. *N Engl J Med*. 2020;382(16):1564-1567. https://doi.org/10.1056/NEJMc2004973.

55. von Economo C. Encephalitis lethargica. *Wien Klin Wochenschr*. 1917; 30:581-585.

56. Kapila CC, Kaul S, Kapur SC, Kalayanam TS, Banerjee D. Neurological and hepatic disorders associated with influenza. *Br Med J*. 1958;2:1311-1314.

57. Poyiadji N, Shahin G, Noujaim D, Stone M, Patel S, Griffith B. COVID-19-associated acute Hemorrhagic necrotizing encephalopathy: CT and MRI features. *Radiology*. 2020;201187. https://doi.org/10.1148/radiol.2020201187.

58. Bailey HE. Acute necrotizing encephalopathy associated with influenza a. *Neurodiagn J*. 2020;60:41-49.

59. Troyer EA, Kohn JN, Hong S. Are we facing a crashing wave of neuropsychiatric sequelae of COVID-19? Neuropsychiatric symptoms and potential immunologic mechanisms. *Brain Behav Immun*. 2020. https://doi.org/10.1016/j.bbi.2020.04.027.

60. Kapila R, Schwartz RA: Post-pandemic neuropsychiatric complications: von Economo’s disease, the Kapila syndrome and more: linkages in view of the new Covid-19 pandemic. *Indian J Med Sci* (in press).

61. Wu Y, Xu X, Chen Z, et al. Nervous system involvement after infection with COVID-19 and other coronaviruses. *Brain Behav Immun*. 2020. https://doi.org/10.1016/j.bbi.2020.03.031.

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