

Editor's key points

- ▶ An increasing prevalence of cutaneous presentations of severe acute respiratory syndrome coronavirus 2 infection has been reported globally. The authors review the literature on cutaneous diseases associated with the global coronavirus disease 2019 (COVID-19) pandemic and provide a general approach for family physicians to diagnose and manage changing dermatologic presentations associated with COVID-19.
- ▶ Various skin conditions might be directly related to COVID-19, or indirectly related because of behavioural changes, specifically with regard to use of personal protective equipment and frequent sanitization. Topical medications and preventive strategies are suggested.
- ▶ Psychiatric stressors contribute to additional dermatologic presentations and exacerbation of pre-existing skin disease.

The COVID-19 pandemic and its skin effects

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Abstract

Objective To review the current literature on cutaneous diseases associated with the global coronavirus disease 2019 (COVID-19) pandemic, and to provide a general overview for family physicians of dermatologic presentations associated with COVID-19.

Quality of evidence Google Scholar and PubMed searches were conducted using the terms *COVID-19*, *SARS-CoV-2*, *pandemic*, *dermatology*, *livedoid*, *chilblain*, *urticaria*, *maculopapular*, *Kawasaki's*, and *related synonyms*. Additional terms were personal protective equipment (PPE), hand hygiene, and psychosocial factors affecting skin diseases. Only English-language literature was reviewed. Evidence ranged from levels I to III.

Main message Coronavirus disease 2019 is associated with a range of cutaneous presentations through direct infection with severe acute respiratory syndrome coronavirus 2, such as maculopapular, vesicular, pseudo-chilblain, livedoid, necrotic, urticarial, and Kawasaki-like rashes. Indirect presentations secondary to behavioural modifications are associated with use of personal protective equipment and sanitization procedures. Furthermore, psychosocial factors and stress associated with the pandemic also exacerbate pre-existing skin conditions.

Conclusion The COVID-19 pandemic has increased rates of dermatologic conditions through direct infection, behavioural changes, and association with psychosocial factors. As the incidence of COVID-19 increases, family physicians should be well equipped to diagnose and manage dermatologic presentations as they change within the context of the pandemic.

La pandémie de la COVID-19 et ses effets dermatologiques

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Résumé

Objectif Passer en revue les ouvrages scientifiques récents sur les maladies cutanées liées à la pandémie mondiale de la maladie à coronavirus 2019 (COVID-19), et présenter aux médecins de famille un aperçu général des manifestations dermatologiques associées à la COVID-19.

Qualité des données Une recherche documentaire a été effectuée à l'aide de Google Scholar et de PubMed à l'aide des expressions en anglais *COVID-19*, *SARS-CoV-2*, *pandemic*, *dermatology*, *livedoid*, *chilblain*, *urticaria*, *maculopapular*, *Kawasaki* et de synonymes connexes. Parmi les autres expressions utilisées, on peut mentionner l'équipement de protection individuelle (EPI), l'hygiène des mains et les facteurs psychosociaux qui affectent les maladies cutanées. Seule la documentation en anglais a fait l'objet de la revue. La qualité des données probantes était de niveaux I à III.

Message principal La maladie à coronavirus 2019 est liée à diverses manifestations cutanées à la suite d'une infection directe au coronavirus 2 du syndrome respiratoire aigu sévère, comme des éruptions maculopapuleuses, vésiculaires, livedoïdes, nécrotiques, urticariennes, des pseudo-engelures et des éruptions de type Kawasaki. Des manifestations indirectes, secondaires à des modifications comportementales, sont associées à l'utilisation de l'équipement de protection individuelle et aux procédures de désinfection. En outre, des facteurs psychosociaux et le stress associé à la pandémie exacerbent aussi des problèmes dermatologiques préexistants.

Conclusion La pandémie de la COVID-19 a augmenté les taux de problèmes dermatologiques par l'entremise d'une infection directe, de changements comportementaux et d'une association avec des facteurs psychosociaux. Au moment où s'accroît l'incidence de la COVID-19, les médecins de famille devraient être bien préparés pour diagnostiquer et prendre en charge les manifestations dermatologiques à mesure qu'elles changent dans le contexte de la pandémie.

Points de repère du rédacteur

- ▶ Une prévalence croissante des manifestations cutanées à la suite d'une infection au coronavirus 2 du syndrome respiratoire aigu sévère a été signalée dans le monde entier. Les auteurs passent en revue les ouvrages scientifiques sur les maladies cutanées liées à la pandémie mondiale de la maladie à coronavirus 2019 (COVID-19), et proposent aux médecins de famille une approche générale pour diagnostiquer et prendre en charge les présentations dermatologiques associées à la COVID-19.
- ▶ Divers problèmes de peau peuvent être directement liés à la COVID-19, ou indirectement liés en raison de changements comportementaux, plus particulièrement en relation avec l'utilisation de l'équipement de protection individuelle et les désinfections fréquentes. Au nombre des interventions suggérées figurent des médicaments topiques et des stratégies de prévention.
- ▶ Des facteurs de stress d'ordre psychiatrique contribuent à des manifestations dermatologiques additionnelles et à l'exacerbation de maladies de la peau préexistantes.

An increasing prevalence of cutaneous presentations of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection has been reported globally.¹⁻³ Cutaneous presentations have also been associated with behavioural changes such as use of personal protective equipment (PPE) and following hand hygiene recommendations.⁴⁻⁷ Finally, acute exacerbations of chronic skin conditions have been associated with psychosocial stressors secondary to the pandemic.⁸

Data on the cutaneous presentations of SARS-CoV-2 continue to evolve.⁹ The objective of this article is to review the current literature on cutaneous diseases associated with the global coronavirus disease 2019 (COVID-19) pandemic, and to provide a general approach for family physicians to diagnose and manage changing dermatologic presentations associated with COVID-19.

Quality of evidence

A literature search was conducted using Google Scholar and PubMed on the effects of COVID-19 specifically related to skin disease and dermatology. Terms searched include permutations of *COVID-19*, *SARS-CoV-2*, *pandemic*, *dermatology*, *livedoid*, *chilblain*, *urticaria*, *maculopapular*, *Kawasaki's*, and related synonyms. Additional searches involved *skin conditions related to personal protective equipment (PPE)*, *hand hygiene*, and *psychosocial factors affecting skin diseases*. Only English-language literature was reviewed. Evidence ranged from levels I to III.

Main message

Direct cutaneous effects of SARS-CoV-2 infection. A survey of 375 Spanish patients with COVID-19 with cutaneous presentations led to 5 main clinical patterns: maculopapular eruption, vesicular eruption, pseudo-chilblain, livedo or necrosis, and urticarial lesions¹⁰ (**Box 1**).¹⁰⁻²⁶ Later cases have involved purpuric flexural lesions, herpes zoster co-infections, and Kawasaki-like syndrome.^{10,25,26} These clinical features have been included in the diagnosis of SARS-CoV-2.²⁷ Galván Casas et al have proposed that

differences within the SARS-CoV-2 virus itself, as well as host-dependent factors, contribute to the range of cutaneous presentations.¹⁰ Furthermore, some of the distribution patterns suggest co-infection with parvovirus²⁸ and herpes zoster.^{29,30} A prospective study found that more than 7% of patients testing positive for COVID-19 developed COVID-19-related skin manifestations—primarily erythematous rash and diffuse urticaria.³¹ A recent systematic review reported the prevalence of cutaneous presentations to vary from 0.19% to 20.45%.³² The relatively low prevalence of cutaneous presentations contributes to challenges in diagnosis.

Maculopapular eruption. In the Spanish study, almost half of COVID-19 patients with cutaneous findings presented with maculopapular eruptions.¹⁰ It is unclear whether this maculopapular rash is associated with severity of disease.^{10,27,33} The differential diagnoses include measles, Epstein-Barr virus, drug-induced exanthema, and graft-versus-host disease.³³ Biopsy results showed histologic features consistent with viral infection, with patterns uncharacteristic of a single virus.^{34,35} Additional investigation on skin biopsies with polymerase chain reaction (PCR) has been suggested to further differentiate these presentations.³⁴ Specific subtypes of these maculopapular rashes are listed in **Box 1**.¹⁰⁻²⁶

Vesicular eruption. Vesicular eruptions occurred most commonly before the onset of other COVID-19 symptoms and were associated with moderate disease severity.¹⁰ Distribution might be truncal with or without pruritus.³⁶ Typical lesions present as varicella-like and hemorrhagic vesicles.^{3,10} Differential diagnoses include varicella zoster virus infection and generalized exanthematic pustulosis.³³ Tzanck test, viral culture or PCR, or skin biopsy might be required to rule out other viral infections or co-infection.³⁷

Pseudo-chilblain. Coronavirus disease 2019 contributes to vascular disease leading to abnormal clotting and increased vasoconstriction.^{38,39} Pseudo-chilblain lesions (“COVID-toes”) might be a result of this vasoconstriction, with acral ischemia leading to swollen, erythematous, and painful digits⁴⁰ (**Figure 1**). The differential diagnoses include chilblain and chilblain lupus erythematosus.³³ Pseudo-chilblain lesions occur later in the COVID-19 disease course and have been associated with milder disease. Pseudo-chilblain lesions improve without scarring on average 2 weeks from initial onset.¹⁰ While more common in younger patients—a preliminary study⁴¹ of 63 patients reported the median age of patients with pseudo-chilblain to be 14—individual cases in older patients up to age 91 have also been reported.⁴² More than 90% of patients with pseudo-chilblain in a French study had negative results on either reverse transcriptase PCR or serology for SARS-CoV-2.⁴³ In a

Box 1. Cutaneous presentations in patients with coronavirus disease 2019

Skin condition

- Maculopapular eruption
 - Pityriasis rosea-like^{11,12}
 - Perifollicular eruption¹⁰
 - Erythema multiforme-like¹³
 - Purpuric eruptions¹⁴
 - Morbilliform eruptions^{15,16}
 - Palmar erythema¹⁷
- Vesicular eruption¹⁸
- Pseudo-chilblains¹⁹⁻²¹
- Livedoid or necrotic lesions²²
- Urticarial lesions^{23,24}
- Kawasaki-like syndrome^{25,26}

Figure 1. Clinical presentation of pseudo-chilblain lesions in a 19-year-old male patient



different study of 318 patients with pseudo-chilblain, 7% (23 of 318) had positive COVID-19 test results.⁴⁴ Delays with laboratory confirmatory testing might have affected the prevalence of patients with COVID-19 who had pseudo-chilblain lesions.

Livedoid or necrotic lesions. Similar to pseudo-chilblain phenomena, it is hypothesized that livedo reticularis is the result of the effects of COVID-19 on cutaneous microvasculature, with thromboses effectively reducing blood flow.²² Differential diagnosis of livedoid lesions includes all forms of livedoid vasculopathy and vasculitis.²³ Although other viruses have been reported as secondary causes of livedo reticularis,⁴⁵ it is unclear whether livedoid lesions might be primary to SARS-CoV-2 infection, or if they could reflect other vascular occlusion complications of COVID-19.²³ These livedoid lesions were unilateral, nonpruritic, blanching, and transient in nature.⁴⁶ Necrotic lesions were more common in adults with a severe course of COVID-19, indicating such lesions might be useful as a prognostic indicator.^{10,22}

Urticarial lesions. Urticarial rash presented before or concurrently with other typical COVID-19 symptoms, and improved when treated with oral antihistamines.^{10,24,47} Urticarial lesions were associated with severe disease and were pruritic in almost all patients in one study.¹⁰ Acute idiopathic urticaria and urticarial drug-induced rash are among the differential diagnoses.³³

Kawasaki-like syndrome. Pediatric cases of COVID-19 have been noted,^{48,49} with up to 2.0% prevalence in a study based in the United Kingdom.⁵⁰ Kawasaki-like syndrome in this population has been associated with COVID-19.^{51,52} While the exact cause of Kawasaki disease is unclear, evidence suggests an immune cascade triggered by an infectious agent.⁵³ There is some evidence to support the

role of human coronaviruses as a causative infectious agent in Kawasaki disease.⁵⁴ The immune cascade triggered produces an acute vasculitis of medium-calibre vessels causing a polymorphous exanthem, oral mucosal changes, and perineal accentuation.^{55,56} Clinical and laboratory features in patients with COVID-19 differed slightly from those of typical Kawasaki disease, therefore the term *Kawasaki-like* has been used to distinguish these patients.⁵²

Indirect cutaneous findings due to behavioural changes. Indirect effects of the COVID-19 pandemic are precipitated through behavioural changes—specifically with regard to PPE use and frequent sanitization (Table 1).⁵⁷⁻⁶⁰ A large proportion of both health care workers and the general population reported adverse skin reactions,^{6,61,62} such as hand dermatitis secondary to hand hygiene recommendations.^{60,63} Increased use of masks and goggles has been associated with pressure injury, facial dermatitis, xerosis, and aggravation of pre-existing skin conditions.⁶⁴ The use of hand emollients or detergents with moisturizing ingredients immediately after hand hygiene, appropriately fitted gloves and masks, as well as appropriate nasal and oral mucosa protection, are beneficial.⁶⁴ Contact dermatitis can be treated with topical corticosteroids and emollients.

Worsening of pre-existing skin conditions. The association between cutaneous disease and psychiatric conditions such as acute stress, depression, and anxiety has been discussed⁶⁵ (Box 2).^{33,66-76} Health care workers are an especially at-risk population during the COVID-19 pandemic.⁷⁷ Chronic psychosocial stressors secondary to restrictive measures of the pandemic might be associated with stress-responsive skin conditions such as alopecia, psoriasis, urticaria, chronic urticaria, and atopic dermatitis⁷⁸; however, further studies are required to clarify the complex neuroendocrine and inflammatory mechanisms.^{78,79} Counseling for patients on immunomodulatory medications (such as biologics for psoriasis and atopic dermatitis) is important to prevent abrupt discontinuation of treatment and acute exacerbation of disease, especially as there is some limited evidence that patients taking these medications are not more susceptible to COVID-19.^{80,81} Chronic skin disease follow-up and education is essential to prevent disease progression or exacerbation.⁸

Conclusion

Patients with COVID-19 can present with myriad clinical features or secondarily owing to adverse drug reaction or co-infection. Other public health measures such as PPE, hand hygiene, and psychiatric stressors contribute to additional dermatologic presentations and exacerbation of pre-existing skin disease. Patient education on prevention and further research into dermatologic presentations of SARS-CoV-2 are recommended. 🌿

Table 1. Indirect cutaneous effects of the COVID-19 pandemic

SKIN CONDITION	FIRST-LINE TOPICAL THERAPIES	METHODS OF PROTECTION
PPE use ⁵⁷⁻⁵⁹		
• Acne	BPO, retinoids, active-ingredient wash	
• Rosacea	Ivermectin, metronidazole	• Ensure proper mask fit
• Facial pressure injuries	Mild TCS, TCI	• Barrier creams*
• Atopic dermatitis	Mild TCS, TCI, PDE4i	• Protective coatings
• Seborrheic dermatitis	Antifungals, mild TCS	• PPE breaks
Frequent hand-washing or use of alcohol-based sanitizer ⁶⁰		
• Irritant contact dermatitis	Mild TCS, TCI, PDE4i	• Barrier creams*
		• Emollients*

BPO—benzoyl peroxide, COVID-19—coronavirus disease 2019, PDE4i—phosphodiesterase-4 inhibitor, PPE—personal protective equipment, TCI—topical calcineurin inhibitor, TCS—topical corticosteroid.
 *Creams and emollients suited for protection against these conditions are noncomedogenic, pH balanced, and fragrance free.

Box 2. Skin conditions associated with psychosocial factors

Hair loss

- Telogen effluvium⁶⁶
- Trichotillomania⁶⁷
- Androgenic alopecia^{33,68-70}
- Alopecia areata^{71,72}

Psoriasis

- Drug-induced flare⁷³
- Cessation of systemic therapy⁷⁴

Dermatitis

- Hand eczema⁷⁵
- Atopic dermatitis⁷⁶
- Generalized pruritus

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Contributors

Anthony Zara contributed to conceptualization, reviewing the literature, manuscript preparation, and editing. **Drs Patrick Fleming, Kyle Lee, and Charles Lynde** contributed to conceptualization and editing. All authors approved the final submission.

Competing interests

Anthony Zara has no competing interests to declare. **Dr Kyle Lee** has received honoraria, consulting fees, or advisory board fees from Bausch Health, Eli Lilly, Elvium, Eisai, and Pfizer. **Dr Patrick Fleming** has received honoraria or consulting, advisory board, or speaking fees from AbbVie, Altius, Aralez, Bausch Health, Cipher, Galderma, Eli Lilly, Galderma, Genentech, Glenmark, GlaxoSmithKline, Innovaderm, Janssen, Kyowa, L'Oréal, LEO Pharma, Merck, Medexus, Mylan, Novartis, PEDIAPHARM, Pfizer, Procter and Gamble, Roche, Sandoz, Sanofi Aventis, Sanofi Genzyme, Stiefel, Teva, and Valeant.

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