

The following information resources have been selected by the National Health Library and Knowledge Service Evidence Virtual Team in response to your question. The resources are listed in our estimated order of relevance to practicing healthcare professionals confronted with this scenario in an Irish context. In respect of the evolving global situation and rapidly changing evidence base, it is advised to use hyperlinked sources in this document to ensure that the information you are disseminating to the public or applying in clinical practice is the most current, valid and accurate. For further information on the methodology used in the compilation of this document—including a complete list of sources consulted—please see our National Health Library and Knowledge Service Summary of Evidence Protocol.

#### **YOUR QUESTION**

What are the dermatological manifestations of COVID-19 and what are the implications for assessment and treatment?

#### IN A NUTSHELL

Dermatological manifestations in patients with COVID-19 are not well comprehended. There have been reports of maculopapular<sup>2,3</sup>, urticarial<sup>1,2,16</sup>, <sup>20,30</sup> and vesicular eruptions<sup>1,2,16</sup>, and transient livedo reticularis<sup>1,2,16,24,34</sup>. Reddish-purple nodules on the distal digits similar in appearance to pernio or chiblains have also been described<sup>1,2,4,11,16,26</sup>, mainly in children and young adults with documented or suspected COVID -19 although an association has not yet been clearly established<sup>2</sup>. The published data currently available to suggest a potential link between dermatologic manifestations and COVID-19 are small in size; other reports have been mainly anecdotal<sup>7</sup>.

It is uncertain whether skin lesions on COVID-19 patients are from viral infection, systemic consequences of the infection or drugs the patient may be prescribed as a result of the infection of the infection are caused by COVID-19 or as a result of drugs used to treat the infection or even as a consequence of worsening of previous dermatological injuries.

Clinical images of cutaneous manifestations are difficult to obtain because introducing a photographic device into a restricted room could pose an infection risk<sup>32</sup>. A simple and easily reproducible method involving zip-lock transparent bags made of low-density polyethylene has been put forward as a possible solution<sup>15</sup>.



The dermatologic component of the disease has been mostly observed in the trunk as opposed to the extremities <sup>1, 2, 17, 25, 32, 34</sup>. It has been suggested that lesions affecting the trunk improve over time with conservative therapy<sup>2</sup>. There is no analytical evidence at this time to draw relationships between lower-extremity lesions in otherwise asymptomatic patients, COVID-19 infections and an associated risk of SARS-Cov-2 infection transmissibility by proxy, although more research is needed<sup>2</sup>.

A possible manifestation of COVID-19 is the so-called 'COVID toe' phenomenon<sup>30</sup>, a term coined in the media as opposed to the scientific literature. Several medical papers from Spain, Belgium and Italy described a surge in complaints about painful lesions on patients' toes, Achilles' heels and soles of the feet; whether the patients were infected was not always clear, because they were otherwise healthy and testing was limited. Most cases have been reported in children, teens and young adults, and some experts say they may reflect a healthy immune response to the virus. Scientists are just beginning to study the phenomenon, but so far chilblain-like lesions appear to signal a mild or even asymptomatic infection<sup>38</sup>.



#### **POINT-OF-CARE TOOLS**

#### What does BMJ Best Practice say?

Coronavirus disease 2019 (COVID-19)1

Diagnosis: Other Diagnostic Factors

Cutaneous manifestations—erythematous or maculopapular or morbilliform rash; petechiae; urticarial; vesicles; ischaemic and ecchymotic acral lesions as a manifestation of clotting disorders; pityriasis rosea—have been reported in some patients. Chilblains, particularly on the toes or foot, are an emerging symptom, especially in younger patients without a history of chilblains, Raynaud's phenomenon or collagen vascular diseases such as systemic lupus erythematosus. A case collection survey of images and clinical data classified lesions as: maculopapular eruptions (47%); acral areas of erythema with vesicles or pustules, or pseudo-chilblain (19%); urticarial lesions (19%); other vesicular eruptions (9%); and livedo or necrosis (6%). Vesicular lesions often appear early in the course of disease before other symptoms, and the pseudo-chilblain pattern frequently appears later in the course after the appearance of other symptoms. A papulovesicular exanthem similar to varicella has been observed rarely in Italy; it typically involves the trunk, has a scattered distribution, and pruritus is mild or absent. A case of digitate papulosquamous eruption has been reported, although it is unknown whether it was caused by SARS-CoV-2 infection. Cutaneous manifestations have been reported in children. It is unclear whether skin lesions are from viral infection, systemic consequences of the infection or drugs the patient may be precribed. Further data are required to better understand skin involvement

#### What does UpToDate say?

#### Coronavirus Disease 2019 (COVID-19)<sup>2</sup>

Clinical Manifestations

Dermatologic findings in patients with COVID-19 are not well characterized. There have been reports of maculopapular, urticarial and vesicular eruptions and transient livedo reticularis. Reddish-purple nodules on the distal digits similar in appearance to pernio [chilblains] have also been described, mainly in children and young adults with documented or suspected COVID-19, although an association has not been clearly established.



#### INTERNATIONAL LITERATURE

### AHOUACH et al (2020) Cutaneous lesions in a patient with COVID-19: are they related?<sup>3</sup>

A previously healthy 57-year-old woman presented with fever [39 °C] lasting for 4 days; a dry cough and rash appeared 2 days before. Diffuse fixed erythematous blanching maculopapular lesions were present, asymptomatic over the limbs and trunk, with burning sensation over the palms. She denied any drug intake, excepting paracetamol for fever. Thorax computed tomography scan was typical of COVID-19; nasopharyngeal swab polymerase chain reaction confirmed SARS-CoV-2. Infectious enquiry was otherwise negative. Skin biopsy specimen showed slight spongiosis, basal cell vacuolation and mild perivascular lymphocytic infiltrate.

## ALRAMTHAN et al (2020) A case of COVID-19 presenting in clinical picture resembling chilblains disease. First report from the Middle East<sup>4</sup>

Clinical characteristics of COVID-19 disease were identified in a cohort study involving 1099 patients from China. COVID-19 most commonly present with fever, cough, fatigue and congestion. 2 out of 1099 patients were reported to have skin rash, but time of onset and clinical description of rash were missing. Another study focused primarily on cutaneous manifestations associated with COVID-19 evaluated 88 patients from Italy. 18 out of the 88 patients developed cutaneous manifestations, but only 8 patients developed skin lesions at onset of disease.

### AMATORE et al (2020) SARS-CoV-2 infection presenting as a febrile rash<sup>5</sup>

Our case report provides two important insights. Firstly, COVID-19 disease can present with a distinctive rash which is histologically similar but clinically different to classic viral exanthemata. Indeed, the annular, polycyclic and circinate appearance of the skin lesions differed from classic paraviral rashes in adults and also the papules on the palms. In addition, as distinct from viral infection-associated urticaria, the plaques were both fixed and non-pruritic. Secondly, a febrile rash may be the only clinical manifestation of COVID-19.



### <u>AVELLANA MORENO et al (2020) Cutaneous Manifestation of COVID-19 in</u> <u>Images: A Case Report<sup>6</sup></u>

Keeping COVID-19 in the differential diagnosis of a rash is the key because patients may be misdiagnosed by another entity. It will also be important to determine if the injuries are caused by COVID-19, if they are secondary to the use of drugs to treat the infection or if they are the consequence of worsening of previous dermatological injuries due to emotional stress or by frequent use of disinfectants, hand washing or permanent use of masks. In our case, the patient did not have previous medication intake; nor was she exposed to any disinfectant. Therefore, other potential diagnoses were excluded. Based on our findings and review of the current literature, cutaneous manifestations although in a low percentage are present in COVID19 positive patients without being associated with a worse prognosis. The presence of other symptoms, the epidemiological history and the PCR test will be important to establish the diagnosis and to be able to establish early preventive measures. More studies are needed confirm and better understand how COVID-19 affects the skin.

# BASATNEH et al (2020) Addressing the Question of Dermatologic Manifestations of SARS-CoV-2 Infection in the Lower Extremities: A Closer Look at the Available Data and its Implications<sup>7</sup>

Although there are many viruses that present with dermatologic manifestations in the lower extremities, the published data currently available to suggest such an association with the novel coronavirus are small in size and other reports have been mainly anecdotal across the globe. The literature available today suggests that although there may be a dermatologic component to the disease, lesions have mostly been observed in the trunk; the literature also suggests that these lesions improve over time with conservative therapy. There is no analytical evidence at this time to draw any relationships between lower-extremity lesions in otherwise asymptomatic patients, COVID-19 infections and an associated risk of SARS-CoV-2 infection transmissibility by proxy. However, any definitive statements regarding a correlation between the novel coronavirus and dermatologic manifestations in the lower extremities should be reserved until more evidence is analyzed.



### BOUAZIZ et al (2020) Vascular skin symptoms in COVID-19: a French observational study<sup>8</sup>

Skin symptoms of COVID-19 have been poorly described but may include erythematous rash, urticaria and lesions similar to chicken pox.

### <u>DARLENSKI et al (2020). .COVID-19 pandemic and the skin - What should</u> dermatologists know?<sup>9</sup>

Despite the virus not being dermatotropic, several skin conditions have emerged, mainly as a result of prolonged contact to personal protective equipment and excessive personal hygiene. Pressure injury, contact dermatitis, itch, pressure urticaria and exacerbation of pre -existing skin diseases including seborrheic dermatitis and acne have been described. We have focused on the dermatologic aspects of COVID-19 infection so that dermatologists may be aware of skin complications and preventive measures to be taken in the COVID-19 pandemic.

### <u>DIAZ-GUIMARAENS et al (2020) Petechial Skin Rash Associated With</u> <u>Severe Acute Respiratory Syndrome Coronavirus 2 Infection<sup>10</sup></u>

Viral rashes can be polymorphic. In this patient, the clinical picture resembled the periflexural petechial exanthem of parvovirus B19. Skin biopsy specimens from patients with this disease show a perivascular mononuclear inflammatory infiltrate, eosinophils, and extravasated erythrocytes; in addition, viral proteins from parvovirus B19 have been found within the endothelial cells of dermal vessels and could be implicated in the pathogenesis of purpura. We hypothesize that SARS-CoV-2 could affect the skin in a similar way. Some histologic features — mounds of parakeratosis, mild spongiosis, extravasated erythrocytes — overlap with those of pityriasis rosea, which is suspected to have a viral pathogenesis. Adverse drug reactions to supportive medications used in patients with severe viral infections are an important diagnostic consideration; however, in this case, the rash preceded the initiation of lopinavir-ritonavir and hydroxychloroguine. Sharing the images of this case may benefit physicians dealing with similar rashes in undiagnosed patients during this pandemic. We hope that, in the upcoming months, skin rashes associated with COVID-19 will be better understood.



#### <u>DUONG et al (2020) Did WhatsApp ® Reveal a New Cutaneous COVID-19</u> Manifestation?<sup>11</sup>

The French Union of Dermatologists created a text messaging group on WhatsApp to share administrative information about teledermatology as well as scientific reviews about the pandemic. In dermatology, publications related to COVID-19 mostly focused on skin damage to healthcare workers, unspecific viral skin manifestation and strategies to avoid virus transmission in dermatologists' practices, favoring teledermatology implementation. Atypical skin eruptions or lesions of suspected or confirmed COVID-19 patients were posted on the WhatsApp group which included 400 dermatologists. We performed an analysis of all 295 cases submitted in this group from its creation on March 14 until April 10, 2020. The first post was an atypical eruption of vesicles in a suspected COVID-19 patient. Then, after the first atypical hands eruption reported on March 23, an outbreak of chilblainlike lesions was reported during the third week of containment in paucisymptomatic COVID-19 patients. On the WhatsApp group, 74% (N=219) of cases were shared for the first time by the members, 4% (N=11) were reposted from a dermatologist Facebook network and 22% (N=65) from the group administrator network. Chilblains or chilblain-like lesions represented 146 posts; 149 posts included other suspected COVID-19-related skin eruptions such as urticaria, rash, chickenpox-like or pytiriasis rosea. A signal was also detected in other European physicians' networks and 36 patients submitted their testimonials through the SNDV website. The number of observed chilblain or chilblain-like lesions during this pandemic is very unusual, especially in springtime and in patients confined at home. A previous case was reported in a child in Italy. Further studies are needed to establish the role of COVID-19 in these lesions, but altered coagulation status and micro-thrombi observed in severe COVID-19 patients are consistent with the observed lesions. This alert was pointed out through the SNDV messaging group.

### EHSANI et al (2020) Pityriasis rosea as a cutaneous manifestation of COVID-19 infection<sup>12</sup>

Cutaneous manifestation has been reported in 0.2% of patients infected by COVID-19 in China and 18 out of 88 patients in Italy. The most commonly reported features are exanthomatous rash, urticaria, chickenpox-like vesicles, petechiae and acute hemorrhagic edema of infancy. Herein, we report one case of pityriasis rosea in a patient infected with COVID-19.



### ESTEBANEZ et al (2020) Cutaneous manifestations in COVID-19: a new contribution<sup>13</sup>

We report a mild COVID-19 disease case with no history of drug intake for the last 10 days. The observed skin manifestations could be related to the COVID-19 viral infection or to the immune response.

# FERNANDEZ-NIETO et al (2020) Characterization of acute acro-ischemic lesions in non-hospitalized patients: a case series of 132 patients during the COVID-19<sup>14</sup>

Blood coagulation is altered in COVID-19 patients. Elevated levels of D-dimer and prothrombin time are associated with poor prognosis. Acral, true ischemic lesions have been described in severely ill COVID-19 patients manifesting a disseminated intravascular coagulation. There is an increasing concern about clinical implications of acute acro-ischemic lesions in asymptomatic or mildly symptomatic patients. The patients in this study did not develop COVID-19 pneumonia or any other complication. The latency time between COVID-19 symptoms and skin manifestations, and the low positive rate for nasopharyngeal swabs suggest that it represents a late manifestation of SARS-CoV-2 infection. Whether they represent a coagulation disorder or a hypersensitivity reaction is not determined.

# <u>FERNÁNDEZ NIETO et al (2020) Comment On: Cutaneous Manifestations in COVID-19: A First Perspective. Safety Concerns of Clinical Images and Skin Biopsies<sup>15</sup></u>

Dermatologists and non-dermatologists who are in charge of patients with COVID-19 and skin signs are using zip-lock transparent bags to transport their mobile phones or other photographic devices. These disposable bags are made of low-density polyethylene allowing high-quality pictures trough their transparent material and permitting glove interaction with current smartphones. After the evaluation, these sealed bags are dipped in a container with a 70% ethanol solution for complete disinfection. This is a safe method to avoid unnecessary visits, attempting to reduce person-to person spread. We are also performing biopsies in these patients when indicated. The same plastic bags are used to introduce disposable instruments in order to avoid sterilization. After local anesthesia, we use a 4mm or 5mm biopsy punch to cut the skin. The skin sample is lifted with a 25g subcutaneous needle and then cut with the scalpel blade. Optionally, a silver nitrate stick is used for hemostasis and the skin is covered with liquid petroleum jelly. The biopsy recipient is also sterilized in a 70% ethanol



solution. We present an example of an urticariform rash in a 32-year-old woman with COVID-19. It appeared 6 days after the onset of symptoms. Hydroxychloroquine and azithromycin had been administered for 4 days. Histologic examination revealed a perivascular infiltrate of lymphocytes, some eosinophils and upper dermal edema. Oral antihistamines were added to her treatment with clinical and symptomatic improvement in a 5-day period.

# GALVÁN CASAS et al (2020) Classification of the cutaneous manifestations of COVID-19: a rapid prospective nationwide consensus study in Spain with 375 cases<sup>16</sup>

Background: Cutaneous manifestations of COVID-19 disease are poorly characterized. Objectives: To describe the cutaneous manifestations of COVID-19 disease and to relate them to other clinical findings Methods: Nationwide case collection survey of images and clinical data. Using a consensus, we described 5 clinical patterns. We later described the association of these patterns with patient demographics, timing in relation to symptoms of the disease, severity and prognosis. Results: Lesions may be classified as acral areas of erythema with vesicles or pustules [pseudochilblain (19%), other vesicular eruptions (9%), urticarial lesions (19%), maculopapular eruptions (47%) and livedo or necrosis (6%). Vesicular eruptions appear early in the course of the disease [15% before other symptoms]; the pseudo-chilblain pattern frequently appears late in the evolution of the COVID-19 disease [59% after other symptoms]; while the remainder tend to appear with other symptoms of COVID-19. Severity of COVID-19 shows a gradient from less severe disease in acral lesions to most severe in the latter groups. Results are similar for confirmed and suspected cases, both in terms of clinical and epidemiological findings. Alternative diagnoses are discussed but seem unlikely for the most specific patterns: pseudo-chilblain and vesicular. Conclusions: We provide a description of the cutaneous manifestations associated with COVID-19 infection. These may help clinicians approach patients with the disease and recognize paucisymptomatic cases.

## <u>GENOVESE et al (2020) Varicella-like exanthem associated with COVID-19 in an 8-year-old girl: a diagnostic clue?</u>

It has been reported that COVID-19 may be associated with a papulovesicular exanthem predominantly involving the trunk. We hereby present a case of



COVID-19-associated varicella-like exanthem in an 8-year-old girl with mild systemic symptoms.

# <u>GIANOTTI et al (2020) Cutaneous clinico-pathological findings in three covid-19-positive patients observed in the metropolitan area of Milan, Italy<sup>18</sup></u>

We describe the clinical and histopathological features of 3 Italian patients with different cutaneous presentations of COVID-19 infection observed and followed at the University of Milan.

# GOREN et al (2020) 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<sup>19</sup>

Androgenetic alopecia (AGA), often referred to as male pattern hair loss, is the most common form of hair loss among men. The development of androgenetic alopecia is androgen mediated and is dependent on genetic variants found in the androgen receptor gene located on the X chromosome. We hypothesized that males with AGA are more likely to be hospitalized for COVID-19 complications compared to controls. To explore this potential association, we conducted a preliminary observational study of the prevalence of AGA patients among hospitalized COVID-19 patients at two Spanish tertiary hospitals between March 23 and April 6, 2020. The diagnosis of AGA was performed clinically by a dermatologist.

### HENRY et al (2020) Urticarial eruption in COVID-19 infection<sup>20</sup>

The particular interest of this case is the inaugural appearance of a cutaneous manifestation before fever or any respiratory symptom.

## HUNT et al (2020) A Case of COVID-19 Pneumonia in a Young Male with Full Body Rash as a Presenting Symptom<sup>21</sup>

We describe a case of COVID-19 pneumonia requiring hospitalization that presented with fever and extensive rash as the primary presenting symptoms. Rash has only been rarely reported in COVID-19 patients and has not been previously described.



### JOOB et al (2020) COVID-19 can present with a rash and be mistaken for dengue<sup>22</sup>

There is a possibility that a patient with COVID-19 might initially present with a skin rash that can be misdiagnosed as another common disease. In addition, some of these patients are afebrile initially.

### MAHE et al (2020) A distinctive skin rash associated with Coronavirus Disease 2019 ?<sup>23</sup>

A skin rash has been reported in 2 out of 1,099 patients presenting with COVID-19 in China and in 14 of 48 patients with the same disease in Italia, but unfortunately without further description of its semiology. We wish to report the case of a woman who presented coincidently with COVID-19 a skin rash that had an original picture.

### MANALO et al (2020) A Dermatologic Manifestation of COVID-19: Transient Livedo Reticularis<sup>24</sup>

To date, described COVID-19-associated rashes include: nondescript erythematous rash, urticaria and vesicles in Italy; and dusky acrocyanosis and dry gangrene in critical ICU patients in Wuhan, China. No photos were available for the first two reports. We present two cases of transient unilateral livedo reticularis in COVID-19-positive non-ICU subjects to bring awareness to a dermatologic manifestation.

## MARZANO et al (2020) Varicella-like exanthem as a specific COVID-19-associated skin manifestation: multicenter case series of 22 patients<sup>25</sup>

Ours is the first series on this varicella-like exanthem as a specific COVID-19-associated cutaneous picture as distinct from the non-specific cutaneous manifestations such as erythematous rash or urticaria reported by Recalcati. Its typical features are constant trunk involvement, usually scattered distribution and mild/absent pruritus, the latter being in line with most viral exanthems but dissimilar to true varicella. Lesions generally appear 3 days after systemic symptoms and disappear upon 8 days without leaving scarring. A limitation of our study was missing histology in some cases. Moreover, demonstration of SARS-CoV-2 presence by PCR in lesional skin was not possible due to specific primer unavailability. If further studies validate our findings, this early skin manifestation will represent a useful clue to suspect COVID-19 in asymptomatic/paucisymptomatic patients.



### MOREY-OLIVÉ et al (2020) Cutaneous manifestations in the current pandemic of coronavirus infection disease (COVID 2019)<sup>26</sup>

Based on the evidence published to date, the cutaneous manifestations of novel coronavirus are similar to those caused by other common viral infections. There is no evidence that the extent of cutaneous involvement is related to the severity of disease. We ought to consider that in addition to the exanthems characteristic of the acute phase of infection described in this article, there have been recent reports of acral and/or chilblain-like lesions in children and youths who are otherwise asymptomatic that could be a late manifestation of inflammatory processes or microthrombotic events in the immune phase of disease. Contrary to what we observed in our patients, all described adult patients with cutaneous manifestations also had respiratory symptoms during the course of disease and could have received treatment for them. Thus, we also need to consider the possibility of cutaneous manifestations being adverse drug reactions. Our observations reveal that it is possible for paediatric patients with COVID-19 to present with a rash that may be attributed to other common childhood diseases as the only manifestation or in association with mild symptoms.

## NIRENBERG et al (2020) Foot Manifestations in a COVID-19 Positive Patient: A Case Study<sup>27</sup>

COVID-19 is not fully understood at this time and as such the medical community must proceed cautiously when drawing conclusions. This case represents just one example of foot manifestations and gait alteration that appear to be related to COVID-19. For medical certainty, more cases and research are needed. The authors expect additional studies and research will emerge to further understand the influence of COVID on gait and the vascular, neurologic, musculoskeletal and dermatologic effects of the disease on the foot.

### PAOLINO et al (2020) Diffuse cutaneous manifestation in a new mother with COVID-19 (SARS-Cov-2)<sup>28</sup>

Our case shows a cutaneous manifestation in a new mother with COVID-19 characterized by the simultaneous presence of erythematous, maculopapular lesions and urticaria-resembling skin lesions, further highlighting the variety of the clinical features which are associated with this new disease.



### <u>PICCOLO et al (2020) Chilblain-like Lesions During COVID-19 Epidemic: A</u> <u>Preliminary Study on 63 Patients<sup>29</sup></u>

We have recently noticed an outbreak of chilblain-like lesions in Italy contemporaneous to the COVID-19 epidemic. Children presenting even with only skin manifestations potentially imputable to COVID-19 should be considered contagious until otherwise proven. Further structured molecular and serological studies are needed.

## <u>QUINTANA-CASTANEDO et al (2020) Urticarial exanthem as early</u> diagnostic clue for COVID-19 infection<sup>30</sup>

All professionals should recognize the possibility that a patient might have only a skin rash and consider COVID-19 infection in order to promptly prevent transmission.

#### RECALCATI et al (2020) Acral cutaneous lesions in the Time of COVID<sup>31</sup>

We report here on peculiar perniosis-like skin lesions observed in young outpatients visiting our Dermatologic Unit in the last 4 weeks of the COVID-19 pandemic. Similar cases were referred to us in the same period by paediatricians and dermatologists from Italy and other European countries.

### RECALCATI (2020) Cutaneous manifestations in COVID-19: a first perspective<sup>32</sup>

As dermatologists we tried to analyze the cutaneous involvement in COVID-19 patients hospitalized in the Lecco Hospital, Lombardy, Italy. We visited directly or indirectly [because of the high-risk of contagious and the lack of protective masks 148 positive patients and we tried where possible to record medical history. No clinical images were performed because of the high risk of infecting other patients by introducing a photographic device in a restricted room. Analyzing history of recent drug intake, we excluded 60 patients that had used any new medicine in the 15 previous days. From the collected data [88 patients], 18 patients [20.4%] developed cutaneous manifestations. 8 patients developed cutaneous involvement at the onset, 10 patients after the hospitalization. Cutaneous manifestations were erythematous rash [14 patients], widespread urticaria [3 patients] and chickenpox-like vesicles [1 patient]. Trunk was the main involved region. Itching was low or absent and usually lesions healed in a few days. Apparently there was not any correlation with disease's severity. Analysing these data, we may speculate that skin manifestations are similar to cutaneous involvement occurring during common viral infections.



### RIVERA-OYOLA et al (2020) Dermatologic findings in two patients with COVID-19<sup>33</sup>

At present, there is limited data regarding cutaneous manifestations following SARS-CoV-2 infection. Given the importance of prompt COVID-19 diagnosis during a global pandemic, it is necessary to highlight the possible dermatologic manifestations and to characterize their morphology. COVID-19 should be considered in the initial differential diagnosis for a patient with acute skin changes following ILI symptoms. Future studies are needed to further elucidate the relationship between cutaneous eruptions and SARS-CoV-2 infection.

### SACHDEVA et al (2020) Cutaneous manifestations of COVID-19: Report of three cases and a review of literature <sup>34</sup>

Various cutaneous manifestations have been observed in patients with COVID-19 infection. However, overall similarities in the clinical presentation of these dermatological manifestations have not yet been summarized. The most common cutaneous manifestation of COVID-19 was found to be maculopapular exanthem [morbilliform], presenting in 36.1% [26/72] patients. The other cutaneous manifestations included: a papulovesicular rash [34.7%, 25/72], urticaria [9.7%, 7/72], painful acral red purple papules [15.3%, 11/72] of patients, livedo reticularis lesions [2.8%, 2/72] and petechiae [1.4%, 1/72]. Majority of lesions were localized on the trunk [66.7%, 50/72], however, 19.4% [14/72] of patients experienced cutaneous manifestations in the hands and feet. Skin lesion development occurred before the onset of respiratory symptoms or COVID-19 diagnosis in 12.5% [9/72] of the patients, and lesions spontaneously healed in all patients within 10 days. The majority of studies reported no correlation between COVID-19 severity and skin lesions.

Infection with COVID-19 may result in dermatological manifestations with various clinical presentations, which may aid in the timely diagnosis of this infection.

## <u>TÜRSEN et al (2020) Cutaneous Side-Effects of the Potential Covid-19</u> Drugs<sup>35</sup>

Erythematous rash, acute hemorrhagic edema, petechiae, morbilliform rash, chickenpox-like vesicles, livedoid lesions, localized or widespread urticaria confluent erythematous-yellowish papules and plaques may be the most common manifestations in acute severe COVID-19 cases. However, it can be



difficult to distinguish the underlying cause: whether or not viral infection or newly prescribed anti-COVID-medication.

### VAN DAMME et al (2020) Acute urticaria with pyrexia as the first manifestations of a COVID-19 infection<sup>36</sup>

Based on these two case reports, we want to warn clinicians that urticaria with pyrexia in the current context of COVID-19 pandemic can be the first manifestations of this infection, even without any respiratory symptoms. These patients can unknowingly infect others and contribute to the spread of the COVID-19 infection; hence their necessary isolation. It is evident that urticaria can go with a viral infection and, due to the prevalence of COVID-19, we should consider this as a potential cause when completing our diagnosis. Therefore, we need to have rapidly more available screening tests to counter the underestimation of the number of cases.

### ZENGARINI et al (2020) Histological pattern in .COVID-19 induced viral rash<sup>37</sup>

Our report focuses on a COVID-19 related rash description and is supported by clinical images and histopathological examinations. Histological examination did not show any particular signs that can make this affection different from other rashes of viral aetiology except for extremely dilated vessels in the dermis which could represent a histological diagnostic finding. It should be kept in mind that skin manifestations associated with this virus could present in any form and at any time during the natural history of the disease and we have no data demonstrating a direct correlation with the prognosis of this illness. More studies of the physiopathology of the SARS-CoV 2 action is needed, above all regarding its interaction with endothelial cells in small vessels sites and its possible prognostic role.

#### **OTHER**

### Rabin (2020) What Is 'Covid Toe'? Maybe a Strange Sign of Coronavirus Infection<sup>38</sup>

Federal health officials do not include toe lesions in the list of coronavirus symptoms but some dermatologists are pushing for a change, saying so-called 'COVID toe' should be sufficient grounds for testing.

Several medical papers from Spain, Belgium and Italy described a surge in complaints about painful lesions on patients' toes, Achilles' heels and soles



of the feet; whether the patients were infected was not always clear, because they were otherwise healthy and testing was limited.

Most cases have been reported in children, teens and young adults, and some experts say they may reflect a healthy immune response to the virus. Scientists are just beginning to study the phenomenon, but so far chilblain-like lesions appear to signal a mild or even asymptomatic infection. They may also develop several weeks after the acute phase of an infection is over.

### <u>Ducharme (2020) From 'COVID Toes' to Hives, These Are the Skin</u> Conditions Dermatologists Think Could Be Signs of Coronavirus<sup>39</sup>

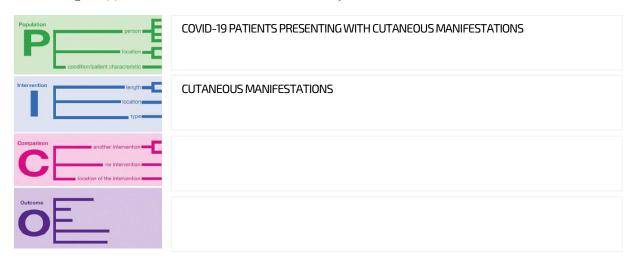
Dermatologists around the world are gathering data on what may be largely overlooked symptoms of COVID-19: skin conditions ranging from rashes to 'pseudo-frostbite.'

Many viral illnesses—including chickenpox, measles and mononucleosis are accompanied by skin rashes, often a result of the body's heightened inflammatory response while fighting off infection. Though more research is needed, a growing number of case reports and preliminary studies suggest SARS-CoV-2, the virus that causes COVID-19, can also affect the skin. In late March, an Italian physician submitted a letter to the editor of the Journal of the European Academy of Dermatology and Venereology, describing skin conditions that affected about 20% of 88 COVID-19 patients analyzed in the Lombardy region of Italy. Most of them developed a red rash on their torsos, while a few suffered hives or blisters resembling chickenpox. Then, in early April, a dermatology organization representing more than 400 French dermatologists issued a statement noting that among probable COVID-19 patients they had seen skin symptoms including hives, red rashes and frostbite-like lesions on the extremities. And finally, in mid-April, in a letter to the editor of the Journal of the American Academy of Dermatology, a group of Italian physicians described a chickenpox-like rash as a rare but specific COVID-19-associated skin manifestation. In the U.S., the 'pseudo-frostbite' condition described by French dermatologists in their statement has been nicknamed 'COVID toes.' More than 100 cases of the condition—characterized by purple, bruise-like bumps and swelling—have been recorded in a COVID-19 symptom registry kept by the American Academy of Dermatology.

National Health Library and Knowledge Service | Evidence Team Summary of Evidence: COVID-19 CURRENT AS AT 12 MAY 2020 VERSION 1.0

Produced by the members of the National Health Library and Knowledge Service Evidence Team<sup>†</sup>. Current as at 12 May 2020. This evidence summary collates the best available evidence at the time of writing and **does not replace clinical judgement or guidance**. Emerging literature or subsequent developments in respect of COVID-19 may require amendment to the information or sources listed in the document. Although all reasonable care has been taken in the compilation of content, the National Health Library and Knowledge Service Evidence Team makes no representations or warranties expressed or implied as to the accuracy or suitability of the information or sources listed in the document. This evidence summary is the property of the National Health Library and Knowledge Service and subsequent re-use or distribution in whole or in part should include acknowledgement of the service.

The following PICO(T) was used as a basis for the evidence summary:



The following search strategy was used:

"COVID-19" OR CORONAVIRUS OR "WUHAN VIRUS" OR "2019-NCOV" OR "SEVERE ACUTE RESPIRATORY SYNDROME CORONAVIRUS 2" OR "2019 NOVEL CORONAVIRUS" OR "2019 NEW CORONAVIRUS"

AND

 ${\sf DERMATOLOGIC^*OR\,SKIN\,OR\,CUTANEOUS\,OR\,RASH\,OR\,RASHES\,OR\,TOE^*}$ 

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<sup>&</sup>lt;sup>1</sup> BMJ Best Practice. Coronavirus disease 2019 (COVID-19). <a href="https://bestpractice.bmj.com/topics/en-gb/3000168">https://bestpractice.bmj.com/topics/en-gb/3000168</a>. [Accessed 05 May 2020].

<sup>&</sup>lt;sup>2</sup> UpToDate. Coronavirus disease 2019 (COVID-19): Epidemiology, virology, clinical features, diagnosis, and prevention. <a href="https://www.uptodate.com/contents/coronavirus-disease-2019-covid-19-epidemiology-virology-clinical-features-diagnosis-and-prevention">https://www.uptodate.com/contents/coronavirus-disease-2019-covid-19-epidemiology-virology-clinical-features-diagnosis-and-prevention</a>. [Accessed 05 May 2020].

<sup>&</sup>lt;sup>3</sup> Ahouach B, Harant S, Ullmer A, et al. Cutaneous lesions in a patient with COVID-19: are they related? [published online ahead of print, 2020 Apr 30]. *Br J Dermatol*. 2020;10.1111/bjd.19168. doi:10.1111/bjd.19168

<sup>&</sup>lt;sup>4</sup> Alramthan A, Aldaraji W. A case of COVID-19 presenting in clinical picture resembling chilblains disease. First report from the Middle East [published online ahead of print, 2020 Apr 17]. *Clin Exp Dermatol*. 2020;10.1111/ced.14243. doi:10.1111/ced.14243

<sup>&</sup>lt;sup>5</sup> Amatore F, Macagno N, Mailhe M, et al. SARS-CoV-2 infection presenting as a febrile rash [published online ahead of print, 2020 Apr 24]. *J Eur Acad Dermatol Venereol*. 2020;10.1111/jdv.16528. doi:10.1111/jdv.16528

<sup>&</sup>lt;sup>6</sup> Avellana Moreno R, Villa E, Avellana Moreno V, Estela Villa C, Aparicio M, Fontanella A. Cutaneous manifestation of COVID-19 in images: A case report [published online ahead of print, 2020 Apr 24]. *J Eur Acad Dermatol Venereol.* 2020;10.1111/jdv.16531. doi:10.1111/jdv.16531

<sup>&</sup>lt;sup>7</sup> Basatneh R, Vlahovic TC. Addressing the Question of Dermatologic Manifestations of SARS-CoV-2 Infection in the Lower Extremities: A Closer Look at the Available Data and its Implications [published online ahead of print, 2020 Apr 20]. *J Am Podiatr Med Assoc*. 2020;10.7547/20-074. doi:10.7547/20-074

<sup>&</sup>lt;sup>8</sup> Bouaziz JD, Duong T, Jachiet M, et al. Vascular skin symptoms in COVID-19: a french observational study [published online ahead of print, 2020 Apr 27]. *J Eur Acad Dermatol Venereol*. 2020;10.1111/jdv.16544. doi:10.1111/jdv.16544

<sup>&</sup>lt;sup>9</sup> Darlenski, R et al (2020). .COVID-19 pandemic and the skin - What should dermatologists know? https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7102542/. [Accessed 05 May 2020].

<sup>&</sup>lt;sup>10</sup> Diaz-Guimaraens B, Dominguez-Santas M, Suarez-Valle A, et al. Petechial Skin Rash Associated With Severe Acute Respiratory Syndrome Coronavirus 2 Infection [published online ahead of print, 2020 Apr 30]. *JAMA Dermatol.* 2020;10.1001/jamadermatol.20 20.1741. doi:10.1001/jamadermatol.2020.1741

<sup>&</sup>lt;sup>11</sup> Duong TA, Velter C, Rybojad M, et al. Did Whatsapp® reveal a new cutaneous COVID-19 manifestation? [published online ahead of print, 2020 Apr 24]. *J Eur Acad Dermatol Venereol*. 2020;10.1111/jdv.16534. doi:10.1111/jdv.16534

<sup>&</sup>lt;sup>12</sup> Ehsani AH, Nasimi M, Bigdelo Z. Pityriasis rosea as a cutaneous manifestation of COVID-19 infection [published online ahead of print, 2020 May 2]. *J Eur Acad Dermatol Venereol*. 2020;10.1111/jdv.16579. doi:10.1111/jdv.16579

<sup>&</sup>lt;sup>13</sup> Estébanez A, Pérez-Santiago L, Silva E, Guillen-Climent S, García-Vázquez A, Ramón MD. Cutaneous manifestations in COVID-19: a new contribution [published online ahead of print, 2020 Apr 15]. *J Eur Acad Dermatol Venereol*. 2020;10.1111/jdv.16474. doi:10.1111/jdv.16474

<sup>&</sup>lt;sup>14</sup> Fernandez-Nieto D, Jimenez-Cauhe J, Suarez-Valle A, et al. Characterization of acute acroischemic lesions in non-hospitalized patients: a case series of 132 patients during the COVID-19 outbreak [published online ahead of print, 2020 Apr 24]. *J Am Acad Dermatol*. 2020;S0190-9622(20)30709-X. doi:10.1016/j.jaad.2020.04.093

<sup>&</sup>lt;sup>15</sup> Fernandez-Nieto D, Ortega-Quijano D, Segurado-Miravalles G, Pindado-Ortega C, Prieto-Barrios M, Jimenez-Cauhe J. Comment on: Cutaneous manifestations in COVID-19: a first perspective. Safety concerns of clinical images and skin biopsies [published online ahead of print, 2020 Apr 15]. *J Eur Acad Dermatol Venereol.* 2020;10.1111/jdv.16470. doi:10.1111/jdv.16470

<sup>&</sup>lt;sup>16</sup> Galván Casas C, Català A, Carretero Hernández G, et al. Classification of the cutaneous manifestations of COVID-19: a rapid prospective nationwide consensus study in Spain with 375 cases [published online ahead of print, 2020 Apr 29]. *Br J Dermatol*. 2020;10.1111/bjd.19163. doi:10.1111/bjd.19163



- <sup>17</sup> Genovese G, Colonna C, Marzano AV. Varicella-like exanthem associated with COVID-19 in an 8-year-old girl: A diagnostic clue? [published online ahead of print, 2020 Apr 21]. *Pediatr Dermatol*. 2020;10.1111/pde.14201. doi:10.1111/pde.14201
- <sup>18</sup> Gianotti R, Veraldi S, Recalcati S, et al. Cutaneous Clinico-Pathological Findings in three COVID-19-Positive Patients Observed in the Metropolitan Area of Milan, Italy [published online ahead of print, 2020 Apr 21]. *Acta Derm Venereol*. 2020;10.2340/00015555-3490. doi:10.2340/00015555-3490 <sup>19</sup> Goren A, Vaño-Galván 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 [published online ahead of print, 2020 Apr 16]. *J Cosmet Dermatol*. 2020;10.1111/jocd.13443. doi:10.1111/jocd.13443
- <sup>20</sup> Henry D, Ackerman M, Sancelme E, Finon A, Esteve E. Urticarial eruption in COVID-19 infection [published online ahead of print, 2020 Apr 15]. *J Eur Acad Dermatol Venereol*. 2020;10.1111/jdv.16472. doi:10.1111/jdv.16472
- <sup>21</sup> Hunt M, Koziatek C. A Case of COVID-19 Pneumonia in a Young Male with Full Body Rash as a Presenting Symptom [published online ahead of print, 2020 Mar 28]. *Clin Pract Cases Emerg Med.* 2020;10.5811/cpcem.2020.3.47349. doi:10.5811/cpcem.2020.3.47349
- <sup>22</sup> Joob B, Wiwanitkit V. COVID-19 can present with a rash and be mistaken for dengue. *J Am Acad Dermatol.* 2020;82(5):e177. doi:10.1016/j.jaad.2020.03.036
- <sup>23</sup> Mahé A, Birckel E, Krieger S, Merklen C, Bottlaender L. A distinctive skin rash associated with Coronavirus Disease 2019 ? [published online ahead of print, 2020 Apr 15]. *J Eur Acad Dermatol Venereol.* 2020;10.1111/jdv.16471. doi:10.1111/jdv.16471
- <sup>24</sup> Manalo IF, Smith MK, Cheeley J, Jacobs R. A Dermatologic Manifestation of COVID-19: Transient Livedo Reticularis [published online ahead of print, 2020 Apr 10]. *J Am Acad Dermatol*. 2020;S0190-9622(20)30558-2. doi:10.1016/j.jaad.2020.04.018
- <sup>25</sup> Marzano AV, Genovese G, Fabbrocini G, et al. Varicella-like exanthem as a specific COVID-19-associated skin manifestation: multicenter case series of 22 patients [published online ahead of print, 2020 Apr 16]. *J Am Acad Dermatol.* 2020;S0190-9622(20)30657-5. doi:10.1016/j.jaad.2020.04.044
- <sup>26</sup> Morey-Olivé M, Espiau M, Mercadal-Hally M, Lera-Carballo E, García-Patos V. Cutaneous manifestations in the current pandemic of coronavirus infection disease (COVID 2019) [published online ahead of print, 2020 Apr 27]. *An Pediatr (Engl Ed)*. 2020;10.1016/j.anpede.2020.04.002. doi:10.1016/j.anpede.2020.04.002
- <sup>27</sup> Nirenberg MS, Del Mar Ruiz Herrera M. Foot Manifestations in a COVID-19 Positive Patient: A Case Study [published online ahead of print, 2020 May 4]. *J Am Podiatr Med Assoc*. 2020;10.7547/20-088. doi:10.7547/20-088
- <sup>28</sup> Paolino G, Canti V, Raffaele Mercuri S, Rovere Querini P, Candiani M, Pasi F. Diffuse cutaneous manifestation in a new mother with COVID-19 (SARS-Cov-2) [published online ahead of print, 2020 May 2]. *Int J Dermatol.* 2020;10.1111/ijd.14919. doi:10.1111/ijd.14919
- <sup>29</sup> Piccolo V, Neri I, Filippeschi C, et al. Chilblain-like lesions during COVID-19 epidemic: a preliminary study on 63 patients [published online ahead of print, 2020 Apr 24]. *J Eur Acad Dermatol Venereol.* 2020;10.1111/jdv.16526. doi:10.1111/jdv.16526
- <sup>30</sup> Quintana-Castanedo L, Feito-Rodríguez M, Valero-López I, Chiloeches-Fernández C, Sendagorta-Cudós E, Herranz-Pinto P. Urticarial exanthem as early diagnostic clue for COVID-19 infection [published online ahead of print, 2020 Apr 29]. *JAAD Case Rep.* 2020;10.1016/j.jdcr.2020.04.026. doi:10.1016/j.jdcr.2020.04.026
- <sup>31</sup> Recalcati S, Barbagallo T, Frasin LA, et al. Acral cutaneous lesions in the Time of COVID-19 [published online ahead of print, 2020 Apr 24]. *J Eur Acad Dermatol Venereol*. 2020;10.1111/jdv.16533. doi:10.1111/jdv.16533
- <sup>32</sup> Recalcati S. Cutaneous manifestations in COVID-19: a first perspective [published online ahead of print, 2020 Mar 26]. *J Eur Acad Dermatol Venereol*. 2020;10.1111/jdv.16387. doi:10.1111/jdv.16387 <sup>33</sup> Rivera-Oyola R, Koschitzky M, Printy R, et al. Dermatologic findings in two patients with COVID-19 [published online ahead of print, 2020 Apr 28]. *JAAD Case Rep*. 2020;10.1016/j.jdcr.2020.04.027. doi:10.1016/j.jdcr.2020.04.027





<sup>&</sup>lt;sup>34</sup> Sachdeva, M et al. (2020). Cutaneous manifestations of COVID-19: Report of three cases and a review of literature. <a href="https://www.sciencedirect.com/science/article/abs/pii/S0923181120301493">https://www.sciencedirect.com/science/article/abs/pii/S0923181120301493</a>. [Accessed 05 May 2020].

Rabin. (2020). What Is 'Covid Toe'? Maybe a Strange Sign of Coronavirus Infection.
 <a href="https://www.nytimes.com/2020/05/01/health/coronavirus-covid-toe.html">https://www.nytimes.com/2020/05/01/health/coronavirus-covid-toe.html</a>. [Accessed 05 May 2020].
 Ducharme. (2020). From 'COVID Toes' to Hives, These Are the Skin Conditions Dermatologists Think Could Be Signs of Coronavirus. <a href="https://time.com/5827912/coronavirus-skin-rashes/">https://time.com/5827912/coronavirus-skin-rashes/</a>[Accessed 05 May 2020].

<sup>&</sup>lt;sup>35</sup> Türsen Ü, Türsen B, Lotti T. Cutaneous Side-Effects of the Potential Covid-19 Drugs [published online ahead of print, 2020 May 1]. *Dermatol Ther.* 2020;e13476. doi:10.1111/dth.13476 <sup>36</sup> van Damme C, Berlingin E, Saussez S, Accaputo O. Acute urticaria with pyrexia as the first manifestations of a COVID-19 infection [published online ahead of print, 2020 Apr 24]. *J Eur Acad Dermatol Venereol.* 2020;10.1111/jdv.16523. doi:10.1111/jdv.16523

<sup>&</sup>lt;sup>37</sup> Zengarini C, Orioni G, Cascavilla A, et al. Histological pattern in .COVID-19 induced viral rash [published online ahead of print, 2020 May 2]. *J Eur Acad Dermatol Venereol*. 2020;10.1111/jdv.16569. doi:10.1111/jdv.16569