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**COVID-19: Important Updates and Developments**  
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## COVID-19: The Italian experience

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**Abstract** Italy was among the world's earliest and most affected countries by coronavirus disease 2019 (COVID-19). We report the Italian experience with the pandemic. The dermatologic community immediately reduced any type of activities to 80% to 90% of outpatient consultations, both in public hospitals and in private offices. The Italian Society of Dermatology and Sexually Transmitted Diseases and the Italian Forensic Dermatologic Society supported the dermatologic community by reporting recommendations in newsletters (vademecum) regarding the routine management of dermatologic patients either in the hospital or private setting. We have provided an overview of the skin manifestations from the pandemic, including the consequences of the misuse of safety measures. We also have evaluated the recently developed research projects on patients treated with biologics for psoriasis, atopic dermatitis, and hidradenitis suppurativa, as well as on the registries regarding various skin diseases affected by COVID-19.

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### Introduction

After the coronavirus disease 2019 (COVID-19) outbreak in China, Italy had become—by early March 2020—one of the countries most affected by COVID-19 in the world (Figure 1). The dissemination of the virus was quite rapid in Northern Italy, especially in the Lombardy region, and on March 9, 2020, the Italian government issued a lockdown that lasted until June 3, 2020. The Italian health system was greatly challenged by this unexpected pandemic, which represented the most pressing health concern during that period. As of May 26, 2020, a total of 126 general practitioners and physicians who were on the front line died of COVID-19 infection.<sup>1</sup> As a result of the pandemic, the dermatologic community continually decreased most activities, reducing outpatient consultation by 80% to 90% in public hospitals and private practice settings.<sup>2,3</sup> Dermatology settings were

considered at serious risk for contagion for the following several reasons: the close contact required for an accurate skin evaluation, the lack of office facilities with adequate biosafety requirements, and the personal protection equipment shortage. During February 2020, an Italian dermatologist was reported to be among the first physicians who tested positive for COVID-19 and was hospitalized at the Policlinic of Milan, where he presented with changes in taste and smell and an unusual trunk eruption with varicelliform microvesicles.<sup>4,5</sup> Most public dermatology clinics postponed appointments for elective surgery and nonurgent visits as a way to discourage people from commuting and overcrowding. This restriction was in line with the legislative decree from the Italian prime minister: “I stay at home” (IoRestoA Casa), recommending the closure of any commercial establishments, with the exception of such essential services as pharmacies and grocery stores.<sup>6</sup> People were not allowed to leave their homes except for work (health workers), urgent health reasons, or the purchase of necessary goods. Fortunately, many people could work virtually.

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**Fig. 1** Acral purpuric maculopapular lesions on the right heel of a boy (14 years old) affected by COVID-19.

#### *The public and institutions support the Italian dermatologic community*

Because a dermatology consultation was considered as a medium-high risk for COVID-19 transmission, the Italian Society of Dermatology and Sexually Transmitted Diseases (Società Italiana di Dermatologia medica, chirurgica, estetica e delle Malattie Sessualmente Trasmesse [SIDeMaST]) issued a series of information papers, referred to as “vademecum,” directed toward both dermatologists and patients. This was made easily accessible and downloadable as a PDF file from the SIDeMaST official website ([www.sidemast.org](http://www.sidemast.org)) as well as from social networks, such as Facebook and LinkedIn. It has been continually updated as new epidemiologic data and indications became available from major health institutions such as the Italian Ministry of Health, the Italian Medicines Agency, the National Health Institute, and the World Health Organization.

In accordance with the regulations set forth by the Italian Ministry of Health and the National Health Institute, the vademecums addressing dermatologists published the following rules dermatologists were required to observe: (1) always wear a protective face covering; (2) limit the number of patients in the waiting room; (3) wash hands with soap and water or sanitize hands with hydroalcoholic gel before and after each patient encounter; (4) do not wear jewelry or wristwatch during encounters with patients; (5) wear disposable gloves; (6) clean and disinfect examination tables with chlorine derivatives and medical devices with 70% ethyl alcohol; (7) refrain from work in case of fever, cough, cold, and flu-like clinical manifestations; and (8) sanitize systematically all the medical instruments (manual or digital

dermatoscope or any other nondisposable tool) used after each patient encounter.

The vademecum for patients reminded them that the most effective preventive measures are wearing a protective face covering, frequent hand washing, and use of alcohol-based and gel hand sanitizer before and after entering the medical office. This vademecum included the following additional patient information for specific dermatologic situations: (1) nonurgent skin consultations should be avoided in case of fever, cough, cold, or flu-like clinical manifestations; (2) priority for dermatologic consultations and investigations at public institutions is generally established by general practitioners and the dermatologists; (3) no accompanying person, unless a parent or tutor (for minors) or a caregiver (for non-self-sufficient patients), is allowed during the visit or in the waiting room and all attending subjects must comply with interpersonal distance requirements and temperature checks by infrared remote thermometer; (4) surgery for a suspected skin cancer (melanoma, squamous, and basal cell carcinomas) is usually warranted and scheduled according to the availability of operating rooms.

An additional challenge concerned dermatologic patients requiring systemic treatment, particularly those with impaired immunologic status.<sup>7</sup> According to the SIDeMaST recommendation, patients receiving topical steroids, calcineurin inhibitors, or oral isotretinoin are not exposed to a higher risk of COVID-19; therefore, they should not discontinue treatment, unless on the advice of their dermatologist. SIDeMaST also released eight vademecums related to specific dermatoses, such as chronic inflammatory (psoriasis and psoriatic arthropathy, atopic dermatitis, hidradenitis suppurativa), neoplastic (melanoma, squamous cell carcinoma, basal cell carcinoma, primary cutaneous lymphoma), and bullous and autoimmune disorders, treated with traditional systemic drugs or with biologic agents.

These vademecums confirm that ending the treatment with biologics or traditional drugs for these disorders is unnecessary, especially if there are no clinical and laboratory signs of COVID-19, as there is no evidence that treatment discontinuation protects against an infection. In addition, any interruption in therapy might result in a loss of response when treatment is reintroduced. These recommendations were later adopted by several international societies, such as those representing rheumatologists, gastroenterologists, and dermatology societies, including the American Academy of Dermatology.<sup>8</sup>

SIDeMaST also updated physicians and patients on the regulatory statement issued March 11, 2020, by the Italian Medicines Agency regarding a 90-day validity extension of all treatment plans for biologic agents, expiring in March and April, aimed to control the turnover of patients in dermatologic departments and clinics to limit potential virus spread. This extraordinary extension implied, however, that the prescribing physician would check in with the patient by telephone or e-mail regarding the occurrence of any adverse events or any clinical changes that may require an immediate

consultation. In addition, the civil protection agency established a drug delivery service throughout the country for oncologic and immunosuppressed patients and for those treated with biologics.

Finally, SIDeMaST encouraged all dermatologists to consider creating a network with patients and other physicians by using innovative communication methods such as e-learning and teledermatology. The latter could provide images of isolated patients' skin lesions, thus reducing the number of patients visiting hospitals and clinics or the need for bedside consultations. Also, teledermatology may allow therapeutic continuity through periodic check-ins with the patient.<sup>9</sup>

During the pandemic, another challenge was the need to prevent negative COVID-19 patients with advanced skin cancer from being exposed to viral infection. Another consideration was the prevention of accidental transmission to health professionals or other patients by persons with COVID-19. To address this problem, the Skin-Multidisciplinary Tumor Board of the University Hospital Foundation A. Gemelli (Rome, Italy) established a dedicated working group to define a detailed internal management plan approved by representatives of the Institutional Comprehensive Cancer Center (Rome, Italy). The frequency of internal medical staff meetings and the number of attending physicians were reduced and limited to essential meetings and staff only, adopting strategies for social distancing. The Skin-Multidisciplinary Tumor Board prioritized advanced skin tumors and classified them according to their biologic aggressiveness, into three main categories (melanoma, squamous cell carcinoma, and basal cell carcinoma) labeled through a "triage" system using various colors (red, yellow, green, and white). The Skin-Multidisciplinary Tumor Board also introduced a risk ladder, which was useful for prioritizing the management of both oncologic and COVID-19 risk patients.

The triage system instituted the following color hierarchy:

1. Red: When the COVID-19 risk is higher than the oncologic risk, the patient visit or treatment must be postponed.
2. Yellow: When the COVID-19 risk is high for both patient and health care professionals and the final decision depends on the feasibility of required procedures, oncologic risk, and patient's age and comorbidities, the consultation may be postponed, and the therapeutic intervention may be delayed or replaced with alternative options on a patient-by-patient basis.
3. Green: When the COVID-19 risk is lower than the oncologic risk (ie, a patient with a clear-cut melanoma or with advanced skin cancer under systemic treatment or radiotherapy), treatment initiation or prosecution should be performed with no delay.
4. White: When the COVID-19 risk is low and treatment changes or delays do not considerably affect the prognosis, physicians may discuss alternative therapeutic approaches with the patient and schedule a time for

these approaches, which may represent a better option during the pandemic.

Finally, detailed recommendations for the management of patients affected by melanoma, squamous cell carcinoma, or advanced basal cell carcinoma have been presented elsewhere in three explanatory tables.<sup>10</sup>

### *COVID and the skin*

The correlation between COVID-19 and skin findings is strongly supported by the temporal relationship with the pandemic, the rapid outbreak and clustering of unusual cutaneous manifestations, the occurrence of familial cases attributable to being restricted at home, and the multiple reports of similar cases from other geographic areas in parallel with pandemic diffusion. Whether cutaneous manifestations are a secondary consequence of infection or represent a primary infection of the skin itself continues to be debated, and it is likely that a combination of both may occur.<sup>11,12</sup> Young age, absence of other clinical manifestations, and swab negativity appear to be common features.<sup>13</sup> This last finding could be explained by the disappearance of detectable viral presence after a brief asymptomatic course. According to this hypothesis, skin lesions would represent late manifestations of COVID-19 infection in young healthy subjects, possibly attributable to an immunologic response targeting the cutaneous vessels. The absence of similar signs in acute COVID-19–positive patients of older age would corroborate this theory. Children could be facilitators of viral spread at an early stage before skin involvement. The serology, demonstrating antibody response to COVID-19 virus, could validate this hypothesis.<sup>14,15</sup> Additional histopathologic studies and polymerase chain reaction investigations of skin biopsies are necessary to clarify the close relationship between skin manifestations and COVID-19 infection.<sup>5</sup>

Italy was among the first countries to report skin involvement in COVID-19 patients. In an Italian study of 148 COVID-19–positive hospitalized patients at Lecco Hospital in Lombardy, 18 (20.4%) presented with different cutaneous manifestations either at the onset or during the course of the infection—a total of 14 subjects presented with an erythematous rash, three with widespread urticaria, and one with a chickenpox-like vesicular eruption. Apparently, there was no correlation with COVID-19 severity, and a potential drug eruption was excluded.<sup>14,15</sup>

Other skin manifestations in Italian patients with COVID-19, other than urticaria and varicella-like papulovesicular exanthems,<sup>16</sup> included maculopapular eruptions suggestive of Grover disease, purpuric maculopapulo-vesicular eruptions, herpetiform lesions, morbilliform lesions, macular hemorrhagic eruption, widespread lesions on an erythematous-edematous base with scattered pinhead-sized pustules, and scales. Generally, a common feature was the sparing of the face, palmoplantar areas, and mucous membranes; the presence of mild pruritus; and a negative history



of the intake of new medications.<sup>5,16-24</sup> Skin signs related to acral ischemia (vascular acrosyndromes) have also been reported.<sup>13,22,24-27</sup> The largest study included 18 children and young adult outpatients with peculiar (perniosis-like) skin lesions (pseudochilblain) consisting of an acral eruption of erythematous-violaceous papules and macules, with possible bullous evolution, or digital swelling localized on the feet, hands, or both.<sup>14,15,28</sup> Livedoid, purpuric or petechial, and leukocytoclastic vasculitis presenting with a hemorrhagic bullous eruption were also reported.<sup>29</sup> Last, among possible cutaneous manifestations,<sup>30</sup> iatrogenic eruptions from drugs prescribed for the treatment of COVID-19, such as diffuse acute generalized exanthematous pustulosis or generalized pustular figurate erythema attributable to hydroxychloroquine, were described.<sup>3,31</sup>

Finally, another emerging problem with the application of these safety procedures has been the occurrence of skin damage among health workers, including dermatologists, either attributable to repeated or incorrect and frequent cleansing or to prolonged contact with protective devices such as clothing, gloves, face masks, eyeglasses, and visors.<sup>32</sup> The number of consultations for acute and chronic irritant and allergic contact dermatitis has increased.<sup>3</sup> Incorrect hand washing with harsh soaps and inadequate rinsing may cause skin barrier damage and dryness, resulting in itching, burning, stinging, and scaling. In addition to the hands, other frequently involved skin areas are the nasal bridge, the forehead, the cheeks, and the periocular and perioral regions. Although these manifestations are often mild and potentially self-healing, they often persist for a long time.<sup>32</sup> If the skin or mucous surfaces are damaged, contamination with secondary infections and possible aggravation of preexisting dermatoses may also occur.<sup>3</sup> The resulting skin discomfort may prompt affected individuals to inadvertently touch the mask or other potentially contaminated surfaces, enhancing the risk of acquiring COVID-19 infection.<sup>32</sup>

### Projects and registries

Because the course of COVID-19 in patients with immune-mediated dermatoses treated with various systemic therapies was completely unknown, SIDeMaST developed several research projects and registries involving dermatologists from accredited Italian centers for the prescription of biologics drugs for psoriasis (PSO-BIO-COVID), atopic dermatitis (DA-COVID), and hidradenitis suppurativa (HS-ada-COVID19). Other independent projects (SKIN-COVID-19 and PED-COVID-19) evaluated the presence of skin manifestations in COVID-19-positive patients.

The PSO-BIO-COVID is a national observational study to evaluate the management of patients on biologic therapy during the current pandemic and to track the potential development of COVID-19 in this category of patients. In particular, a 6-month study was planned from February 20, 2020, through September 30, 2020. The following monthly data will also be collected:

1. Data on the medical management of psoriatic patients and actions put in place by dermatologists.
2. The incidence of COVID-19 in these patients and their subsequent course.
3. The collection of the data (eg, age, comorbidities, etc.), the incidence of symptomatic or asymptomatic COVID-19; their correlation with age, sex, ongoing therapy, comedications or comorbidities; and close contact with SARS-CoV-2-positive subjects.<sup>33</sup>

The DA-COVID-19 registry is an observational multicenter, national, retrospective, and prospective, not-for-profit study established during the pandemic, which is designed to describe the management of adult patients with moderate or severe atopic dermatitis treated with traditional systemic immunosuppressive drugs, biologics, and phototherapy and to track the development of COVID-19 infections in these populations by the administration of interviews and questionnaires. The data were collected from February 2020 through December 2020. The data will be analyzed according to age, comorbidity, and concurrent medications, etc. to identify specific groups of patients at higher risk for adverse events.

The HS-ada-COVID-19 is a multicenter, observational study of patients with suppurative hidradenitis who are treated with adalimumab. The study's goal is to estimate the prevalence and incidence of COVID-19 in these patients and to evaluate the safety and the possible impact of adalimumab on COVID-19 course.

SKIN-COVID-19 is a multicenter, observational study regarding the skin events associated with COVID-19. The goal of this study is to assess the incidence of skin events and their prevalence as well as to disclose their pathogenetic mechanisms. A preliminary report on 22 patients from this registry collected by eight dermatology centers has suggested that dermatologist awareness of the skin manifestations potentially related to COVID-19 may be useful in the diagnosis of patients with early infection.<sup>16</sup>

The PED-COVID-19 is a noninterventive multicenter, retrospective, and prospective project proposed by an Italian Pediatric Dermatology Group to evaluate the epidemiologic, clinical, and laboratory characteristics of the skin findings, such as perniosis-like erythema or vasculitis-like skin lesions, in pediatric patients during COVID-19. A WhatsApp group was created to share and discuss the images of patients observed by local dermatologists involved in the project.

As there were no clear-cut administrative indications for reopening private dermatologic offices after COVID-19,<sup>34</sup> SIDeMaST and the Italian Forensic Dermatologic Society (Società Italiana di Dermatologia Legale e Forense; [www.sidelf.it](http://www.sidelf.it)) released specific recommendations on the following issues:

1. Booking an appointment: A preliminary telephone screening should prioritize dermatologic management and recommend the postponement of nonurgent medical consultations for older patients with comorbidities

who are at a high risk for COVID-19. Telephone contact is also recommended for questioning the patient about suspected COVID-19 clinical manifestations before the scheduled medical consultation, so that they may be referred to a general practitioner in case of a positive response. It may be useful to advise patients regarding simple precautions, such as attending the visit alone (unless not self-sufficient), being on time (to avoid patient overlap in the waiting rooms), and bringing a face mask to wear at all times.

2. Organizing the dermatologic office: In the dermatologic office and waiting rooms, visits should be scheduled to avoid overcrowding and chairs should be spaced to prevent close contact among patients and caregivers. Hand sanitizer and disposable masks should always be in stock and readily available. Ensure that the following items are properly sanitized: office furniture (including chairs, examination beds, tabletops, and keyboards), appliances (including light switches, buttons, and handles), and medical instruments (including the dermatoscope, video microscope, wood lamp, and ultraviolet booth). Items should be sanitized after each patient visit and at the end of the working day. Frequent air renewal and regular checks on and sanitization of air conditioning systems are advisable.
3. Questioning patients: Patients should be required to fill out and sign a questionnaire stating they have no COVID-19-related clinical manifestations and report recent contacts with infected individuals. Patients should also undergo a temperature check by an infrared remote thermometer and sanitize hands before entering the waiting room.
4. Providing recommendations for health care workers: Health care workers should frequently clean their hands with soap and water or with alcohol-based hand sanitizer, wear appropriate personal protective equipment, and conduct proper sanitization with chlorine-based or alcohol-based products of furniture and medical office equipment on a regular basis. Medical gloves (latex, vinyl, powder-free rubber examination gloves) should be worn by all office staff members. Staff should wash hands for at least 60 seconds before wearing gloves, change them after each patient encounter, and properly dispose of them after each use. Eye, face, and head protection with special reusable equipment (glasses, visors, or face shields) should be used to avoid contamination by aerosols and respiratory droplets, blood, body fluids, or excretions. Finally, it is important to ensure there is an adequate supply of personal protection equipment for the next working day.<sup>34</sup>

## Conclusions

The COVID-19 pandemic is still far from over. Learning about the Italian experience may be significant for the

development of preventive and therapeutic measures in other countries.

## Conflict of interest

Maria Letizia Musumeci, MD, PhD, is an advisory board member and consultant, has received fees and speaker's honoraria, or has participated in clinical trials for the following: Abbvie, Almirall, Biogen, Eli-Lilly, Janssen-Cilag, Leo Pharma, and Novartis. Maria Rita Nasca, MD, PhD, and Giuseppe Micali, MD, have no conflict of interest to disclose.

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