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**DERMATOLOGY
IN THE TIME OF COVID-19**

in collaboration with

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*Dedico questo libro ai miei figli,
ai miei specializzandi e a tutti i miei cari colleghi*

TABLE OF CONTENTS

11 *Introduction*

CHAPTER I

SCIENTIFIC ARTICLES

- 19 1. COVID-19: Clinical Experiences In Pulmonology Units
- 27 2. The legislative framework during COVID-19 emergency and in Italy
- 39 3. Female Genital Mucosal Lesions Associated With COVID-19 Vaccination: A Brief Review of The Literature
- 45 4. Transverse orange nail lesions following SARS-CoV-2 infection
- 51 5. Local reactions to the second dose of the BNT162 COVID-19 vaccine
- 57 6. Bullous dermatosis on the hands following SARS-CoV-2 infection
- 63 7. Oral And Genital Mucosa Lesions In Patients With COVID-19: A Multicentric Case Series

- 69 8. Treatment of nasal bridge ulceration related to protective measures for the COVID-19 epidemic
- 75 9. Cutaneous long COVID
- 79 10. Local skin reaction to the AZD1222 vaccine in a patient who survived COVID-19
- 83 11. Hair and nail manifestations of COVID-19
- 101 12. Cutaneous Endothelial Dysfunction and Complement Deposition in COVID-19
- 107 13. A case of dermatitis artefacta during a pandemic
- 113 14. Severe palmar hyperkeratosis and hematochezia in COVID-19
- 119 15. Cutaneous Reactions to COVID-19 Vaccines in a Monocentric Study: A Case Series
- 135 16. Papular skin reaction after the administration of the Ad26Cov2-S vaccine
- 141 17. COPD influences survival in patients affected by COVID-19, comparison between subjects admitted to an internal medicine unit, and subjects admitted to an intensive care unit: An Italian experience
- 145 18. SARS-CoV-2 pneumonia and concurrent myelodysplasia complicated by *Pseudomonas aeruginosa* over-infection
- 155 19. Varicella-Zoster virus reactivation following severe acute respiratory syndrome coronavirus 2 vaccination or infection: New insight
- 177 20. Acral skin lesions during SARS-CoV-2 infection: a case series from a multicenter experience

CHAPTER II
**PHOTOGRAPHIC ATLAS:
CUTANEOUS MANIFESTATION OF COVID-19**

188	1. Multisystem Inflammatory Syndrome in Children (MIS-C)
200	2. Erythema Pernio (Chilblain-Like Lesions)
204	3. Morbilliform Rash
207	4. Urticaria
211	5. Vesicular Eruption
214	6. Maculopapular Rash
216	7. Hair Loss (Telogen Effluvium)
222	8. Mucosal Lesion
230	9. Mask-related acne during COVID-19 pandemic
232	10. Cutaneous manifestations following COVID-19 vaccination or infection
247	<i>Art During the COVID-19 Pandemic</i>
265	<i>Aknwoledgments</i>
267	<i>The Authors</i>

INTRODUCTION

The users of this book are undoubtedly familiar with the basics of dermatology, so a notionistic introduction to the subject seems superfluous to us.

Instead, this preface aims to introduce the topic the entire manuscript is about, namely, skin with telltale signs of ongoing systemic disease.

We want to report, specifically, our real-life experience with dermatologic manifestations related to the acute and subacute infection states during the COVID-19 pandemic.

The different areas of interest in dermatology include inflammatory diseases, autoimmune diseases, tumors, malformations, cosmetic disorders, and skin infections. In this text, dermatological manifestations related to the COVID-19 infection, or vaccination against the virus, peculiar to various areas of dermatology have been analyzed.

The skin is the largest organ in the human body and can be affected by various endogenous and exogenous factors. Some skin diseases may be a telltale sign of other diseases affecting other organs or systems, such as the immune system, endocrine system, nervous system, or gastrointestinal system. Some examples of skin diseases that may indicate other pathologies are:

Dermatitis herpetiformis, is a form of itchy dermatitis that is associated with celiac disease, a gluten intolerance; Scabies, an infectious disease caused by a mite that causes intense itching. It can be a sign of

immunodeficiency or HIV/AIDS²³; Acne, an inflammatory disease of the sebaceous follicles that can be related to hormonal imbalances, stress, diet, or medications. Psoriasis, is a chronic skin disease that causes red, scaly plaques. It may be associated with psoriatic arthritis, cardiovascular disease, diabetes, or depression. Therefore, we find it interesting to delve into the skin manifestations related to COVID-19 disease.

COVID-19 is a respiratory infectious disease caused by the SARS-CoV-2 virus, a member of the Coronavirus family. Most people infected with the virus experience mild or moderate symptoms and recover without the need for special treatment. However, some people may develop severe forms and require medical attention. The virus is mainly transmitted airborne, through respiratory droplets. To prevent infection, it is important to keep a safe distance, wear a mask, wash hands often and ventilate enclosed rooms.

COVID-19 was first detected in China in December 2019 and has since spread worldwide, causing a pandemic. As of Feb. 26, 2024, there have been 26,718,411 confirmed cases and 196,309 deaths in Italy, with an average positivity rate of 1 percent in the last week.

To counter COVID-19, several vaccines have been developed and proven to be effective and safe. The vaccination campaign in Italy began on December 27, 2023, and involves the free and voluntary administration of the vaccines to the entire population. At present, 118,456,789 people, or 30.5 percent of the population, have been vaccinated.

Dermatologic manifestations of COVID-19 are varied and may be associated with different stages of infection. Some of the most common are:

- morbilliform eruptions: these are red spots that spread throughout the body, often accompanied by fever and respiratory symptoms. They are more common in patients with mild or moderate forms of COVID-19 and tend to disappear in a few days.
- vesicular eruptions: these are fluid-filled blisters that form on the skin, especially on the trunk and extremities. They can be painful or itchy and resemble herpes or chickenpox. They are more common in elderly patients or those with severe forms of COVID-19 and may persist for weeks.

- acral lesions are alterations in blood circulation affecting the fingers and toes, causing cyanosis (bluish discoloration), chilblains, ulceration, or necrosis. They are more common in children and adolescents, often asymptomatic or with mild forms of COVID-19, and may appear even after healing.
- urticarial lesions: these are red, raised pomphi that cause intense itching and are located on various parts of the body. They may be due to an allergic reaction to the virus or to drugs used for treatment. They are more common in women and in patients with mild or moderate forms of COVID-19.
- livedo-reticularis or necrosis: these are signs of vascular obstruction manifested by purplish or blackish discoloration of the skin, sometimes with areas of necrosis. They are more common in patients with severe or critical forms of COVID-19 and may be associated with thrombotic or embolic complications.

This handbook is intended for general practitioners, dermatologists, infectivologists, and all those in the field. The authors sincerely hope that this can be a reference and working tool in daily clinical practice.

To all those who will adopt it to further their studies, in addition to our thanks, we extend an invitation to share further experiences with the scientific community in order to advance medical knowledge.

CHAPTER I

SCIENTIFIC ARTICLES

In this chapter, we have compiled scientific articles to which we have contributed, focusing on dermatological reactions associated with COVID-19. These articles provide a comprehensive overview of the various skin manifestations observed in patients with COVID-19, exploring their prevalence, clinical features, and potential underlying mechanisms. By examining these studies, we aim to enhance understanding of the dermatological impact of the virus and contribute to the broader medical knowledge surrounding COVID-19.

1. COVID-19: CLINICAL EXPERIENCES IN PULMONOLOGY UNITS

My experience in the care and treatment of patients with SARS-Cov2 infection has been very extensive and specifically refers to the period 2020-2021.

We know that a wide range of clinical manifestations are attributed to COVID-19 infection [1]. Symptoms range from very frequent fever with high temperatures, to cough, dyspnea, fatigue, from chest pain to sputum. Neurological manifestations were also present as well as dermatological manifestations up to 20% of patients. Other frequent symptoms were rhinitis, headache and diarrhea. The patients who were referred to our COVID pulmonology unit of Sant'Andrea hospital (Sapienza – University of Rome) all presented with mild or moderate interstitial pneumonia that were found at computerized tomography scan, by software analysis [2].

Tracking the evolution of the pandemic over time required analysis of genetic variants of the virus to target vaccine research. Our laboratories would search for genetic variants of the virus to better highlight its characteristics [3].

All patients had comorbidities such as diabetes and hypertension, and the mean age initially was 51 years at the beginning of the pandemic. although most of them were non-elderly adults, the patients had different levels of severity, showing that age was not the only cause of clinical evolution [4].

Various comorbidities were present such as hypertension, diabetes, COPD. The latter is a factor determinant affecting survival in subjects regardless of care setting [5].

Patients often had cardiovascular involvement or sometimes skin manifestations and required antiviral treatment [6]. The latter were often caused by destruction of both endothelial and immune system leading to a systemic vasculopathy.

All were performing chest CT scans, examination used to look for the degree of parenchyma impairment. The interstitial involvement was frequent (Figure 1).

The pictures often evolved to bacterial pneumonia with or without pleural effusion especially in case of alteration of the immune-hematological system [7].

Patients at the diagnostic level performed oro-nasal swabs with RT-PCR method for extraction of genetic material [8].

An involvement of the cardio-vascular system was very common. It depended on S-protein binding to transmembrane angiotensin-converting enzyme 2 that allows the virus to enter pneumocytes, macrophages, perivascular pericytes, and cardiomyocytes [9]. It leads to endothelial dysfunction, microvascular dysfunction, pericardial dysfunction, inducing a cytokine storm response.

The association between smoke and COVID-19 was interesting and controversial [10]. Tobacco smoking appears to hinder the entry of the virus, but at the same time results in a more severe clinical picture once the disease is contracted.

Vitamin D deficiency was often observed in chemistry detection, and it was correlated with a different severity of the disease and with the duration of virus positivity.

In our populations patients sometimes presented evidence of suspected lung tumors, which were identified in the early or late stage (Figures 2, 3) During the pandemic many cancers were diagnosed frequently in advanced stage [12].

Patients who developed ARDS reported a type I or type II respiratory failure early on. Upon PaO₂ response patients were classified into three groups: mild (PaO₂/FiO₂ > 200), moderate (PaO₂/FiO₂ 101–200), and severe (PaO₂/FiO₂ ≤ 100) [13]. The clinical-radiological