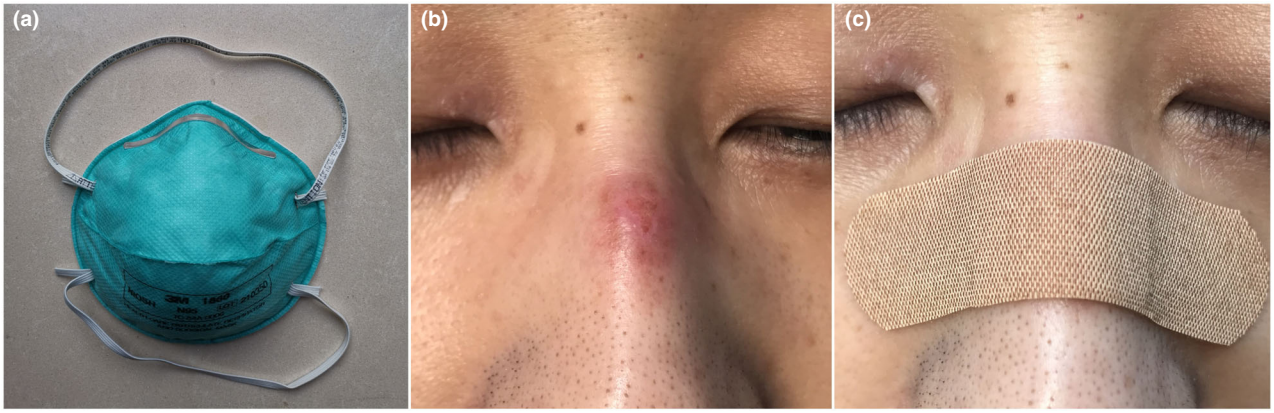

Figure 1 (a) N95 health care particulate respirator and surgical mask. (b) Pressure sore on nose bridge. (c) Application of benzalkonium chloride patch on nose bridge.

Hydrocolloid dressing is often used to prevent and cure pressure sore, which is pasted to nose bridge before wearing mask, but we found the strong stickiness of dressing would likely aggravate existent pressure sore when taking off the mask and ripping away the dressing. If pressure sore does occur, the result of wearing N95 mask and using hydrocolloid dressing every day or other day would be from bad to worse.

An improved method involving double protection that pasting benzalkonium chloride patch to the pressure sore on nose bridge firstly and using hydrocolloid dressing secondly before wearing mask (Fig. 1c). The high stickiness of both sides of benzalkonium chloride patch can keep the patch fastened to nose bridge, while the central part can protect the existent pressure sore due to decompressing effect and infection prevention and the low stickiness of central part would not make pressure sore more serious when ripping away the patch.

However, above-mentioned method is only an expedient measure, improving protective mask is a permanent solution. Although Covid-19 will eventually be controlled and even eliminated worldwide, there are liable to face new epidemic situation in the future, and any improvement on protective equipment would be meaningful and benefit global health.

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The patient in this manuscript has given written informed consent to publication of his case details.

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Should SARS-CoV-2 influence immunosuppressive therapy for autoimmune blistering diseases?

Editor

In this dramatic period where the whole world is affected by the outbreak of coronavirus disease 19 (COVID-19), scientific data relating to the causative virus SARS-CoV-2 as well as the subsequent therapeutic repercussions on the management of other diseases should be divulged in order to share as much information as possible among experts in a timely manner.

Regarding autoimmune blistering diseases, it is already widely acknowledged that physicians should search for triggers in all newly identified patients before starting any therapy, including infectious agents. But what about patients already in immunosuppressive therapy for these potentially life-threatening disorders?

Given the current lack of scientific evidence on the basis of which official recommendations with a high degree of reliability are possible, some indications have been proposed by the International Pemphigus and Pemphigoid Foundation, as the result of expertise and clinical common sense, inspired by a principle of prudence.[1] However, no clear and comprehensive data have been provided on the management of ongoing immunosuppressive therapies in these patients.

Regarding other inflammatory diseases, the indications of the major scientific Societies of Dermatologists, Rheumatologists and Gastroenterologists in Italy,[2–4] but also the American Academy of Dermatology Association,[5] suggest that if the patient is stable or in good health, the stop of the ongoing biologic therapy is not reasonable/indicated, as the risk of reactivation of the underlying pathology could add an additional risk factor to infections, including COVID-19.

Here, we report our experience of around 380 patients suffering from autoimmune bullous diseases and in treatment with immunosuppressive drugs currently referring to our Bullous Diseases Outpatient Service, Sant'Orsola-Malpighi University Hospital, Bologna, Italy. About 20 patients are visited per week in the space of one day. Since 9 March 2020, in accordance with the Sant'Orsola-Malpighi Hospital directives made following the last Decree of the President of the Council of Ministers of March 9, 2020 (GU Serie Generale n.62 del 09-03-2020), all the outpatient services, of any priority, first visits or control visits, have been temporary suspended and in place telephone calls have been made to all patients who were scheduled to be visited in our Outpatient Service in the following weeks to prevent them from leaving their home and crowding the hospital, given that social distancing is one of the most effective safeguards in order to limit the spread of the virus. We therefore held a telephone consultation, checking the health of patients over the last month. In particular, we asked whether patients in immunosuppressive therapy (systemic prednisone or methylprednisone, azathioprine, mycophenolate mophetile, previous rituximab infusions, previous intravenous immunoglobulins, methotrexate, cyclosporine) had suffered from flu-like symptoms. We interviewed 83 patients (30 males, 53 females; average age 58.6 years). Of these patients under immunosuppressive therapy, 18 reported having had fever, sore throat, non-productive cough, myalgia, shortness of breath, dyspnoea, anosmia, ageusia and/or gastrointestinal symptoms (nausea, vomiting, diarrhoea) in the last month. However, 10 out of 18 patients admitted that they had not had a flu vaccination. Only one of the patients interviewed told us that he had performed the swab for SARS-CoV-2, and had resulted positive. He is a 53-year-old male, in therapy with azathioprine 100 mg/die and systemic prednisone 4 mg/die, living in the northeast part of Emilia-Romagna, one of the hardest-hit areas of Italy, Since then, he stopped both immunosuppressive therapies. We advised him to restart the immunosuppressive treatment as soon as clinical healing is completely achieved, confirmed by a negative swab result. The clinical condition of the other 17 patients with flu-like symptoms was such as to not require further investigation to identify COVID-19.

Among possible trigger factors of autoimmune blistering diseases, immunization and viral infections are mentioned in the literature, although the underlying immunological mechanism is still unclear.[6–8] The most acceptable hypothesis involves the possible molecular mimicry existing between viral and epidermal proteins, and over activation of the immune system as a consequence of the viral attack.[8] Indeed, in autoimmune blistering disorders, once the autoantibodies bind to their targets, namely self-structural proteins, several pathways are activated, including complement activation and deposition, and neutrophilic chemotaxis, with the release of proteases and elastases that lead to blister formation and of cytokines such as IL-6 and IL-8, which recruit additional immune cells.[9]

To the best of our knowledge, no studies regarding previous viral outbreaks and the effects of these viruses on autoimmune blistering disease patients have been reported in the literature so far. Moreover, the pathogenesis of SARS-CoV-2 infection in humans is still unclear, although massive and prolonged chemokine response known as 'cytokine storm' correlating with high morbidity and mortality has been observed in these patients.[10]

We hypothesize that the interruption of immunosuppressive therapy in autoimmune blistering disease patients may determine a dysregulation of inflammatory cytokines that not only exacerbates the bullous disease itself but may also be involved in the pathogenesis of the viral infection. Therefore, it is likely that the management of the inflammatory processes guaranteed by immunosuppressive therapies not only controls blistering, but also contributes to a less aggressive organic response to SARS-CoV-2.

In conclusion, to date, there is a lack of direct scientific evidence to support the continuation of immunosuppressive therapies in patients infected with SARS-CoV-2. Therefore, it will be crucial for our community to learn of more cases of autoimmune bullous disease patients under immunosuppressive treatment who have developed COVID-19, in order to better quantify the risk of infection under immunosuppressive therapy. Moreover, now more than ever, research into autoimmune blistering diseases should focus attention on emerging safer therapeutic options that decrease the rate of mortality and morbidity as well as the risks connected to the therapy itself.

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Skin reactions to non-glove personal protective equipment: an emerging issue in the COVID-19 pandemic

To Editor

Protecting healthcare workers (HCWs) is crucial during Corona Virus Disease 2019 pandemic and requires wearing personal protective equipment (PPE).[1] While most of the studies have focused on the skin reactions caused by gloves, other PPE such as gowns, respirator masks, face shields and goggles are also worn by HCWs for long hours during the current epidemic and skin irritations caused by these equipment may cause discouragement of health workers from using them.[2] In this letter, we have focused on the reaction caused by non-glove PPE.

The N95 respirator masks are made of polypropylene fabric processed by a non-woven technology and should fit tightly to the face to be effective.[3] The study by Foo *et al.* revealed that 35.5% of the staff who used N95 masks regularly experienced acne, facial dermatitis and pigmentation of nasal bridge, cheeks and chin. In this study, acne was one of the most prevalent skin reactions related to the use of N95 respirator masks.[3] The dermatitis that often presented with pruritic skin lesions was mostly irritant type but allergic contact dermatitis (ACD) due to adhesives or other parts of the respirator masks such as rubber straps and metal clips was also reported.[3] Several factors including humidity, warm environment and occlusion due to local pressures could explain the exacerbation of these conditions.[3] In another study by Donovan *et al.*,[4] on the possible N95 mask reactions during the SARS epidemic in Toronto, urticarial facial eruption was reported in three patients, dermatitis in five patients and acute respiratory symptoms without skin lesions in two patients. Pressure effect on the nose has also been reported as one of the 15 delphi measures that discouraged HCWs to use N95 respirator masks.[5]

Goggles have been used routinely to protect HCWs against highly infectious diseases related to exposure to contaminated body fluids.[6] Heat and dehydration were major complications of both goggles and face shields application during the Ebola outbreak.[7] Other dermatologic side-effects such as pressure injury, contact dermatitis, urticaria, xerosis and aggravation of underlying dermatosis might occur due to the impairment of the skin integrity during mechanical trauma of goggles.[8] A study by Lan *et al.*,[2] revealed that 87.9% of HCWs, who were wearing goggles for more than 6 h, developed skin reactions on their nasal bridge. Skin reactions such as acne, ACD and irritant contact dermatitis (ICD) were mentioned following the use of goggles in HCWs. Occlusion and friction were mentioned as the underlying mechanism.[6]

Wearing gowns and coveralls may cause heat stress and dehydration.[7] Skin reactions due to the clothing, which are made of natural and synthetic untreated fabrics, are rare.[9] However, additive chemicals and dye fibres might be the main reason of ICD and ACD.[9] Skin dermatoses are mostly developed where the gowns adhere tightly to the skin.[10] Friction, moisture and warmth of those regions might increase the risk of ACD.[10] In the study by Foo *et al.*,[3] four (1.6%) out of 258 cases developed adverse skin reactions related to the repetitive wearing of disposable gowns for average time of 6.2 h during a mean period of 8.8 months in the SARS epidemic in Singapore. Itching and wrist rashes were the most frequent reactions, while pruritus without skin lesions was also observed in one case.[3] In Toronto SARS epidemic, there were reports of developing ACD due to the reaction to formaldehyde textiles and resin in gowns.[10] Avoiding over-tight gowns and sufficient ingestion of liquids are of paramount importance for HCWs to preserve a balance between self-protection and the ability to care for patients efficiently, while wearing PPE. Skin reactions to personal protective equipment and management strategies are depicted in Fig. 1.

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