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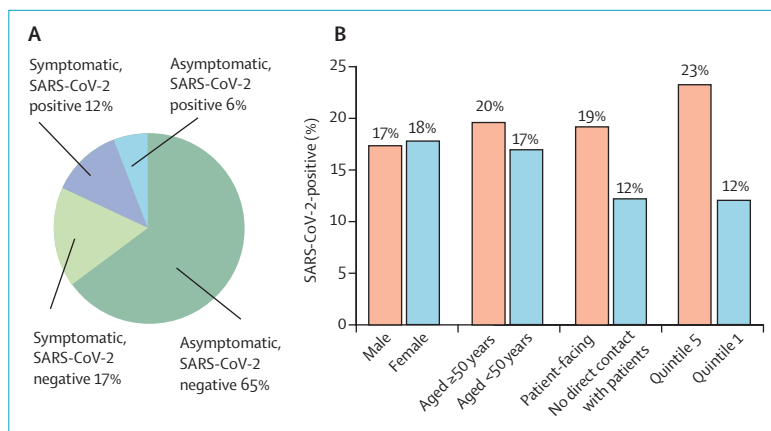
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Published Online  
May 18, 2020

[https://doi.org/10.1016/S1473-3099\(20\)30402-3](https://doi.org/10.1016/S1473-3099(20)30402-3)

For the **IMD Postcode search tool** see <https://tools.npeu.ox.ac.uk/imd>



**Figure: SARS-CoV-2 test results of 266 health-care workers at a London maternity hospital**  
Test results by symptom status (A) and characteristics (B). The IMD quintile was derived from postcode data using the IMD Postcode search tool, where quintile 1 (least deprived) corresponds to an IDM score  $\leq 8.49$  and quintile 5 (most deprived) corresponds to an IDM score  $\geq 34.18$ . IMD=index of multiple deprivation. SARS-CoV-2=severe acute respiratory syndrome coronavirus 2.

health-care workers not been tested, they would have been obliged to self-isolate for 7 days or more, and their household members for 14 days.

Regular testing also allows asymptomatic SARS-CoV-2-positive health-care workers to be identified and isolated early, thus reducing nosocomial transmission to potentially susceptible patients and other staff, and from the hospital to the community.<sup>3,4</sup> Reducing transmission is particularly relevant when personal protective equipment might be scarce. Health-care workers at our hospital are regularly reminded to self-isolate when symptomatic, and their body temperature is checked daily and they are assessed with structured questionnaires when swabbed. Our finding, however, that 16 (34%) of 47 health-care workers who tested positive for SARS-CoV-2 were asymptomatic, and that 45 (59%) of 76 symptomatic health-care workers tested negative for SARS-CoV-2, highlights a crucial need for the routine testing of all health-care workers, including those who do not have direct contact with patients.

During this pandemic, shortages of health-care staff have been a major challenge. Redeployment of health-care workers has depleted some

specialties and has led to staff working in unfamiliar environments. Training and research have been suspended, and annual leave has been postponed. The UK Health Secretary's promise to reach a target of 100 000 tests per day by the end of April, 2020, was achieved. Therefore, universal testing of health-care workers is feasible, potentially ameliorating the current workforce depletion and reducing the risk of asymptomatic spread of SARS-CoV-2.

RH is the Medical Director of The Portland Hospital for Women and Children (London, UK). KP is a current employee of The Portland Hospital for Women and Children. All other authors declare no competing interests.

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## Silent COVID-19: what your skin can reveal

Clinical manifestations of coronavirus disease 2019 (COVID-19) are rare or absent in children and adolescents;<sup>1,2</sup> hence, early clinical detection is fundamental to prevent further spreading. We report three young patients presenting with chilblain-like lesions who were diagnosed with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection. Two of them were asymptomatic and potentially contagious. Skin lesions, such as erythematous rashes, urticaria, and chicken pox-like vesicles, were reported in 18 (20.4%) of 88 patients with COVID-19 in a previous study.<sup>3</sup> These symptoms developed at the onset of SARS-CoV-2 infection or during hospital stay and did not correlate with disease severity.<sup>3</sup> In our cases, lesions involved the acral sites, especially the dorsum of the digits of the feet, beginning as erythematous-violaceous patches that slowly evolved to purpuric lesions and then to blisters and ulceronecrotic lesions, with final complete return to normal. Burning and itching were also present with some of the lesions. Informed consent was obtained from the parents of



**Figure: Chilblain-like lesions on patient 1's left foot**

patients 1 and 2 and from patient 3 himself.

Patient 1 was a 14-year-old boy who presented to the hospital with erythematous-violaceous lesions involving the dorsum of all digits of both feet. After 7 days, a few red macules and papules appeared on the lateral and plantar aspect of both feet and a small ulcer developed on the fifth digit of the left foot (figure). Because a family member had tested positive for SARS-CoV-2, the patient underwent nasopharyngeal swab and was found positive for SARS-CoV-2 on RT-PCR. The lesions disappeared in the following 7 days.

Patient 2 was a 14-year-old boy with no known contact with COVID-19 cases who had been asymptomatic since the beginning of the skin disease, for which his parents requested a teledermatology consultation. Manifestations consisted of small erythematous-violaceous lesions on the dorsum of almost all digits of the feet, some of which were characterised by necrotic aspects with blackish crusts (appendix). The lesions lasted 20 days, with complete healing. Nasopharyngeal swab taken by the family's paediatrician 2 days after the skin manifestations appeared was positive for SARS-CoV-2.

Patient 3 was an 18-year-old boy whose grandfather had COVID-19 pneumonia. After 2 days with fever (38.5°C), the boy reported the appearance of chilblain-like lesions involving the distal part of all digits of the feet (appendix). Skin manifestations remained unchanged for 10 days, suddenly disappearing without treatment. Nasopharyngeal swab taken 4 days after the skin manifestations appeared was positive. The patient was otherwise asymptomatic.

Acute acro-ischæmic manifestations along the course of SARS-CoV-2 infection seem to be different from classic acrocyanosis, erythema pernio, and vasculitis; however, they could represent a cutaneous expression of the

typical thrombotic pattern of COVID-19 due to hyperinflammation<sup>4</sup> and altered coagulation and endothelial damage.<sup>5</sup>

During this time, children and adolescents with chilblain-like lesions who are otherwise asymptomatic should undergo SARS-CoV-2 testing, which could help early detection of silent carriers.

We declare no competing interests.

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## Prevention of the cytokine storm in COVID-19

The Comment by Marc Feldman and colleagues,<sup>1</sup> published recently in *The Lancet*, discussed the potential of anti-tumor necrosis factor (TNF) therapy to inhibit development of a cytokine storm in patients with coronavirus disease 2019

(COVID-19). Following this Comment, I write to propose that the opioid, meptazinol, might be a possible alternative or addition to anti-TNF therapy, particularly in the UK, where meptazinol is a licensed drug (current licenced supplier Almirall, Barcelona, Spain) and thus could be easily prescribed.

The basis of this suggestion is a study I led with Bayu Teklu and colleagues,<sup>2</sup> in which we studied the Jarisch-Herxheimer (JH) reaction in louse-borne relapsing fever. The JH reaction appeared to be a transient manifestation of a cytokine storm, induced by treatment of relapsing fever with antibiotics, and only lasting for around 2 h after a single curative injection of tetracycline.<sup>3</sup> Notably, concentrations of interleukins 6 and 8 and TNF are increased during this reaction. Meptazinol, an opioid antagonist-agonist or sometimes termed a partial opioid agonist, but not naloxone, suppressed the JH reaction,<sup>2</sup> similar to the effect of anti-TNF.<sup>4</sup> Meptazinol reduced high temperature, pulse rate, and breathing rate during the JH reaction. An effect of the JH reaction is exacerbation of any local lesions (in this case, the lungs). The theoretical basis of the action of opioid antagonists was elucidated in an animal model of relapsing fever and described in detail previously.<sup>5</sup> However, a disadvantage of meptazinol is that it is short acting (half-life of about 2 h) and causes nausea and occasional vomiting.

A trial of meptazinol for COVID-19 in patients presenting with a cytokine storm and in those without, to provide proof of effectiveness, might indicate its efficacy in ameliorating symptoms. The results of such a trial might prove especially useful, given that antipyretics, such as paracetamol and aspirin, have become less favoured by clinicians. Building on this approach, a range of opioids should be tested, particularly in the context of the COVID-19 cytokine storm, to establish if a longer acting and more palatable opioid than meptazinol

See Online for appendix



Published Online  
May 7, 2020  
[https://doi.org/10.1016/S1473-3099\(20\)30376-5](https://doi.org/10.1016/S1473-3099(20)30376-5)