## SARS-CoV-2 Has Not Been Detected Directly by Electron Microscopy in the Endothelium of Chilblain Lesions: reply from authors

Dear editor,

We thank Dr Brealey and Dr Miller for their interest in our paper<sup>1</sup> and their valuable comments.

We fully agree that the interpretation of electron microscopy findings can be challenging, even for experts. Differences between viral pathogens and normal subcellular organelles may be subtle, and some cellular components can masquerade as viruses. The size and shape of the particle shown in our paper fit with other descriptions of SARS-CoV-2, but there may be a bias in interpretation. As Brealey and Miller state, the location inside the cell is not typical, and the internal pattern of the nucleocapsid is absent, raising reasonable doubts whether this structure represents a clathrin-coated vesicle. As we already mentioned in our previous letter,<sup>2</sup> immune electron microscopy could be the best way to confirm the true nature of this particle, but unfortunately, we do not have remaining tissue to perform additional studies.

After the publication of our series, new evidence is rising favouring a causal role for SARS-CoV-2 in COVID chilblains. Positive immunohistochemistry for SARS-CoV has been reported by different authors in cutaneous biopsies of COVID chilblains using antibodies directed against different parts of the virus,<sup>3,4</sup> and SARS-CoV-2 RNA-positive cells have been demonstrated by RNAscope.<sup>4</sup>

We acknowledge that more cases are necessary to demonstrate the presence of coronavirus in skin lesions consistently.

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