

Letters to the Editor

SARS-CoV-2 has not been detected directly by electron microscopy in the endothelium of chilblain lesions

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Linked Article: Colmenero et al. *Br J Dermatol* 2020; **183**:729–737.

DEAR EDITOR, We are concerned that yet another erroneous report of the electron microscopic observation of coronavirus in tissue has been published. The paper by Colmenero et al. presents a study of skin biopsies from paediatric patients presenting with chilblains during the coronavirus disease 2019 (COVID-19) pandemic.¹ Seven cases were examined by histopathological and immunohistochemical techniques, and one of these was additionally studied by transmission electron microscopy. As part of the investigation, the authors report the electron microscopic visualization of coronaviruses in endothelial cells and apply this observation as supporting evidence that the vascular lesions arising in the chilblains are a manifestation of endothelial infection by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).

The paper presents a representative electron micrograph depicting a round membrane-bound structure measuring approximately 90 nm in diameter that is interpreted as a coronavirus based on its size and the presence of external projections. However, this is incorrect; the particle depicted is a clathrin-coated vesicle – a normal subcellular organelle.² While its size is consistent with that of a coronavirus, its morphology is not characteristic of this virus.^{3–5} For example, the structure is shown in direct contact with the cytosol and not within a membrane-bound vacuole, as is observed for intracellular coronaviruses. Moreover, it lacks the characteristic speckled core that represents cross-sections of the coiled coronavirus nucleocapsids. Also, while it is studded by electron-dense material, producing a somewhat coronavirus-like appearance at its margin, the appearance is typical of several normal intracellular constituents, including clathrin-coated vesicles and circular profiles of rough endoplasmic reticulum.

Thus, the micrograph presented in this paper depicts a normal subcellular structure and not a coronavirus. Therefore, the conclusion that these structures ‘support a causal relation of the lesions with SARS-CoV-2’ cannot be supported by the electron microscopic data presented.

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SARS-CoV-2 has not been detected directly by electron microscopy in the endothelium of chilblain lesions: reply from the authors

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Linked Articles: Colmenero et al. *Br J Dermatol* 2020; **183**:729–737. Brealey and Miller. *Br J Dermatol* 2021; **184**:186. Colmenero et al. *Br J Dermatol* 2020; **183**:1170–1171.




DEAR EDITOR, We thank Dr Brealey and Dr Miller for their interest in our paper¹ and their valuable comments.²

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,³ 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.

Since the publication of our series, new evidence has arisen 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,^{4,5} and SARS-CoV-2 RNA-positive cells have been demonstrated by RNAscope.⁵

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

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News and Notices

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6th – 8th July 2021, Birmingham

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