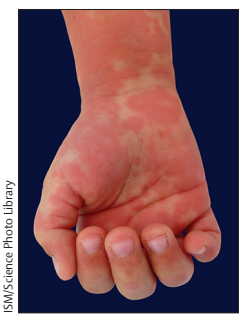
Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Kawasaki disease in the COVID-19 era: a distinct clinical phenotype?



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For more on **PIMS-TS** see https://www.rcpch.ac.uk/resources/guidance-paediatric-multisystem-inflammatory-syndrome-temporally-associated-covid-19-pims

For more on **MIS-C** see https://www.cdc.gov/mis-c/hcp

> "Tapestries are made by many artisans working together. The contributions of separate workers cannot be discerned in the completed work, and the loose and false threads have been covered over. So it is in our picture of particle physics."
>
> *Sheldon L Glashow*

Several reports have emerged from Europe and America of a surge in an inflammatory syndrome similar to Kawasaki disease[1–4] during the COVID-19 pandemic, challenging previous observations[5] that children have mostly mild disease. Children in the described cohorts have shown significant systemic inflammation, fluid-refractory shock, and cardiac abnormalities. Although features exist that are consistent with those of Kawasaki disease, the systemic inflammation appears to be more profound, resulting in sicker children. This finding has led to the creation of new terms with broader definitions—paediatric multisystem inflammatory syndrome temporally associated with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection (PIMS-TS) or multisystem inflammatory syndrome in children (MIS-C).[6]

In *The Lancet Child & Adolescent Health*, a time-series analysis by Naim Ouldali and colleagues[7] adds further insight to this new entity. The authors described clinical features of ten children diagnosed with Kawasaki disease over a month-long period in April, 2020, representing a rise of 495% as compared with baseline hospital admission rates over a 15-year period. This marked rise in the incidence of Kawasaki disease occurred 2 weeks after the peak of COVID-19 admissions in Paris, France and when SARS-CoV-2 was the major circulating respiratory virus. Indeed, one of the strengths of this study is the concurrent documentation of the load of other common respiratory viruses during this period. Additionally, the authors also found a similar peak in Kawasaki disease following the 2009 influenza A H1N1 pandemic. The temporal association described in the study supports the hypothesis that Kawasaki disease is secondary to a post-infectious trigger by a novel ribonucleic acid.[8] This finding provides further proof-of-concept evidence that SARS-CoV-2 infection has the potential to trigger a severe form of Kawasaki disease. Whether previous surges of Kawasaki disease occurred in other countries during viral pandemics would be useful to review to draw further conclusions.

The spectrum of Kawasaki disease temporally associated with COVID-19 described in the current study and an Italian cohort[1] have some notable differences to the classic presentation. Both series describe an older median age of presentation (11·6 years in the French cohort and 7·5 years in the Italian cohort) compared with when Kawasaki disease typically manifests.[9] Incomplete Kawasaki disease was common (ten [50%] of 20 children) and many children had haemodynamic instability requiring inotropic support (five [50%] of ten in the French cohort and two [20%] of ten in the Italian cohort). This finding again is not in keeping with the previously described incidence of Kawasaki disease shock syndrome at 7%.[9] Given these differences, certain investigators might consider this phenomenon under the broader umbrella of PIMS-TS or MIS-C. We argue that doing so might be more of an academic exercise because the management approach to date seems to be similar to that of severe Kawasaki disease. However, future data and clinical information will provide rich insight into the pathophysiology and increase our understanding of Kawasaki disease.

Interestingly, a surge in cases of Kawasaki disease, PIMS-TS, or MIS-C has not been reported in Asia. The annual incidence rates of Kawasaki disease in Asian countries, especially Japan and Korea, is 10–20 times higher than that in Europe and America.[10] Large paediatric cohort data from the first epicentre of the outbreak, Wuhan, China, reported that most infected children had a mild course of illness.[11] No COVID-19-related Kawasaki disease has been reported in China so far. Similarly, in Singapore, no Kawasaki disease or inflammatory syndromes were observed in 61 paediatric patients with COVID-19.[12] The reason for this discrepancy between Asian and Western counterparts remains unclear, although some postulations exist. Genomic diversity of SARS-CoV-2 has been reported,[13] which might result in the presentation of different antigens. Selected antigens might lead to the activation of the immune system resulting in a cytokine storm, whereas

others might not. Additionally, individual genetic variation in the three major histocompatibility complex (MHC) class 1 genes have been reported to affect the severity of SARS-CoV-2 infection,[14] which could also explain the manifestation of Kawasaki disease in some infected children observed in Europe and the USA who might share a different MHC class 1 gene from that of Asian children. Genetic studies in SARS-CoV-2-infected children worldwide can provide more information regarding the association of certain MHC class 1 genes with Kawasaki disease, MIS-C, or PIMS-TS.

More questions than answers emerge from our collective experience in managing children with COVID-19. Why is there a lack of description of this inflammatory clinical phenotype in the Asia-Pacific region? What is the natural history of the cardiac lesions associated with this clinical phenotype? More work remains to be done, especially in long-term follow-up of paediatric COVID-19 survivors.

We declare no competing interests. The authors would like to pay tribute to Tomisaku Kawasaki, who passed away at age 95 on June 10, 2020.

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The burden of childhood pneumonia in India and prospects for control

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Pneumonia continues to be the leading cause of mortality in children worldwide, with India accounting for 20% of those deaths and a higher burden of childhood pneumonia than any other country.[1] In *The Lancet Child & Adolescent Health,* Brian Wahl and colleagues[2] report the first comprehensive evaluation of state-specific pneumonia incidence in children in India using a risk factor-based modelling approach. By calculating the effect of temporal changes in prevalence of well-known pneumonia risk factors such as malnutrition, incomplete immunisation, and exposure to indoor air pollution on incidence, the authors estimated the change in pneumonia morbidity over time. Wahl and colleagues obtained individual-level data from the National Family Health Survey in India to model the number of children with each combination of risk factors, thereby accounting for interactions between risk factors, which is a novel aspect of the study when compared with previous models that have considered that the prevalence of