

Clinical care of children and adolescents with COVID-19: recommendations from the National COVID-19 Clinical Evidence Taskforce

TO THE EDITOR: Fraile Navarro and colleagues¹ recently published 20 recommendations for the treatment of coronavirus disease 2019 (COVID-19) in children and adolescents from the National COVID-19 Clinical Evidence Taskforce.

For the paediatric inflammatory multisystem syndrome (PIMS-TS) recommendations, the Taskforce convened an expert advisory group.¹ In the absence of clinical trials, the panel considered peer-reviewed guidelines and cohort studies to formulate consensus recommendations.¹ However, they deferred providing any guidance to help clinicians prevent thromboembolism. We suggest the Taskforce consider the same approach for paediatric anticoagulation guidance.

COVID-19 is associated with marked coagulation activation and hypercoagulability in children.^{2,3} Life-threatening pulmonary embolus requiring thrombolysis has been encountered in Australian adolescents hospitalised with COVID-19.

A retrospective cohort study published in 2021 found that 2.1% of children hospitalised with symptomatic COVID-19 infection and 6.5% of those with PIMS-TS developed thrombosis.⁴ Thrombosis occurred more frequently in children aged 12 years and over who had central lines, PIMS-TS, or an underlying oncological diagnosis. A D-dimer of

more than five times the upper limit of normal was significantly associated with thrombosis.⁴

The authors refer to “paediatric guidelines published in the US”, which are published on behalf of the Pediatric/ Neonatal Hemostasis and Thrombosis Subcommittee of the International Society of Thrombosis and Haemostasis; these adapt current consensus prophylaxis guidelines to include COVID-19-specific features.⁵

In deferring making specific recommendations, the authors suggested using existing local thromboprophylaxis guidelines. The Royal Children’s Hospital, Melbourne and the Sydney Children’s Hospital, Randwick have both independently developed COVID-19-specific thromboprophylaxis guidelines (that are very closely aligned),^{6,7} as have many other centres globally because previous local thromboprophylaxis guidelines are inadequate for COVID-19-associated thrombotic coagulopathy. The Melbourne/Sydney guidelines advise baseline coagulation testing in hospitalised children with COVID-19, incorporating D-dimer to assist risk assessment, twice-daily enoxaparin and anti-Xa monitoring/dose titration.^{6,7} These could be provided as supplemental material in these living guidelines.

The COVID-19 anticoagulation in Children–Thromboprophylaxis (COVAC-TP) trial — a phase 2 single-arm study looking at 40 children who will receive monitored, low dose, twice-daily enoxaparin (ClinicalTrials.gov Identifier NCT04354155) — will not change the level of evidence, so waiting for completion of this trial does not seem appropriate.

Gemma L Crighton¹ 
Anthea Greenway^{1,2}
Susan Russell³

¹ Royal Children’s Hospital Melbourne, Melbourne, VIC.
² Murdoch Children’s Research Institute, Melbourne, VIC.
³ Kids Cancer Centre, Sydney Children’s Hospital, Randwick, Sydney, NSW.

gemma.crighton@rch.org.au

Acknowledgements: We thank Professor Paul Monagle for his scientific advice and critical review of this letter.

Competing interests: No relevant disclosures. ■

doi: 10.5694/mja2.51511

© 2022 AMPCo Pty Ltd.

- 1 Fraile Navarro D, Tendal B, Tingay D, et al. Clinical care of children and adolescents with COVID-19: recommendations from the National COVID-19 Clinical Evidence Taskforce. *Med J Aust* 2022; 216: 255–263. <https://www.mja.com.au/journal/2022/216/5/clinical-care-children-and-adolescents-covid-19-recommendations-national-covid>
- 2 Chima M, Williams D, Thomas NJ, Krawiec C. COVID-19-associated pulmonary embolism in pediatric patients. *Hosp Pediatr* 2021; 11: e90–e94.
- 3 Mitchell WB, Davila J, Keenan J, et al. Children and young adults hospitalized for severe COVID-19 exhibit thrombotic coagulopathy. *Pediatr Blood Cancer* 2021; 68: e28975.
- 4 Whitworth H, Sartain SE, Kumar R, et al. Rate of thrombosis in children and adolescents hospitalized with COVID-19 or MIS-C. *Blood* 2021; 138: 190–198.
- 5 Goldenberg NA, Sochet A, Albisetti M, et al. Consensus-based clinical recommendations and research priorities for anticoagulant thromboprophylaxis in children hospitalized for COVID-19-related illness. *J Thromb Haemost* 2020; 18: 3099–3105.
- 6 Royal Children’s Hospital Melbourne. Clinical Practice Guidelines. COVID clinical management guidelines package (RCH). https://www.rch.org.au/uploadedFiles/Main/Content/clinicalguide/guideline_index/RCH-COVID-clinical-management-guidelines-package.pdf (viewed Apr 2022).
- 7 Sydney Children’s Hospital. Thromboprophylaxis — children with COVID-19 infection and multi-inflammatory syndrome (MIS-C). https://www.schn.health.nsw.gov.au/files/attachments/s128v1_thromboprophylaxis_children_with_covid19_infection_and_mis-c.pdf (viewed Apr 2022). ■