Whats In?

Pediatric Infectious Disease (2020): 10.5005/jp-journals-10081-1263

Source: Dong Y, Mo X, Hu Y, et al. Epidemiological characteristics of 2143 pediatric patients with 2019 coronavirus disease in China. Pediatrics 2020.

The authors discuss the epidemiological characteristics and transmission patterns of pediatric patients with coronavirus disease-2019 (COVID-19) in China in a nationwide case series of 2,143 pediatric patients with COVID-19. Over 90% of all patients were asymptomatic, mild, or moderate cases. The median time from illness onset to diagnoses was 2 days (range: 0–42 days). There was a rapid increase in disease at the early stage of the epidemic, and then there was a gradual and steady decrease.

The authors conclude that children at all ages appeared susceptible to COVID-19, and there was no significant gender difference. Although clinical manifestations of children's COVID-19 cases were generally less severe than those of adults' patients, young children, particularly infants, were vulnerable to infection. The distribution of children's COVID-19 cases varied with time and space. Furthermore, this study provides strong evidence for human-to-human transmission.

Source: Emanuel E, Persad G, Upshur R, et al. Fair Allocation of scarce medical resources in the time of COVID-19. New England Journal of Medicine 2020. DOI: 10.1056/NEJMsb2005114.

Governments and policy makers must do all they can to prevent the scarcity of medical resources. However, if resources do become scarce, as discussed in the article, the six recommendations, i.e., maximize benefits; prioritize health workers; do not allocate on a first-come, first-served basis; be responsive to evidence; recognize research participation; and apply the same principles to all COVID-19 and non-COVID-19 patients; and should be used to develop guidelines that can be applied fairly and consistently across cases. Such guidelines can ensure that individual doctors are never tasked with deciding unaided which patients receive life-saving care and which do not. Ideally, the guidelines should be provided at a higher level of authority, both to alleviate physician burden and to ensure equal treatment. The described recommendations could shape the development of these guidelines.

Source: Tricou V, Sáez-Llorens X, Yu D, et al. Safety and immunogenicity of a tetravalent dengue vaccine in children aged 2–17 years: a randomised, placebo-controlled, phase 2 trial. The Lancet 2020.

Researchers here evaluated three different dose schedules of a tetravalent dengue vaccine (TAK-003) over a 48 month period for the immunogenicity and safety in children living in dengue-endemic countries. A large, phase 2, double-blind, placebo-controlled trial including healthy participants aged 2–17 years was conducted at three sites in the Dominican Republic, Panama, and the Philippines. From December 5, 2014 to Februaty 13, 2015, they randomly assigned 1,800 children to the following groups: two-dose primary series (days 1 and 91; $n = 201$), one primary dose (day 1; $n = 398$), one primary dose plus 1 year booster (days 1 and 365; $n = 1,002$), and placebo ($n = 199$). Outcomes revealed elicitation of antibody responses against all four serotypes following administration of TAK-003; these responses persisted to 48 months postvaccination, regardless of baseline serostatus. They identified no important safety risks. Vaccinees exhibited a long-term reduction in risk of symptomatic dengue virus disease. This study yields a long-term safety database and support evaluation of the vaccine in the ongoing phase 3 efficacy study.

Source: Loffredo L, Spalice A, Salvatori F, et al. Oxidative stress and gut-derived lipopolysaccharides in children affected by paediatric autoimmune neuropsychiatric disorders associated with streptococcal infections. BMC pediatrics 2020;20(1):1–6.

Pediatric autoimmune neuropsychiatric disorders associated with streptococcal infections syndrome (PANDAS) identifies patients with acute onset of obsessive–compulsive and tic disorders. The authors in this study have compared serum levels of soluble NOX2-dp (sNOX-2-dp), iso-PGF2α, and LPS in 60 consecutive subjects, including 30 children affected by PANDAS and 30 controls (CT) matched for age and gender. Serum zonulin was used as intestinal permeability assay. The results show, compared with CT, PANDAS children had significantly increased serum levels of sNOX-2-dp, 8-iso-PGF2α and LPS. Serum LPS significantly correlated with zonulin ($R_s = 0.610$; $p < 0.001$), and 8-iso-PGF2α ($R_s = 0.591$; $p = 0.001$). The authors conclude that children affected by PANDAS have high circulating levels of sNOX2-dp, isoprostanes, and of LPS that could be involved in the process of neuroinflammation.

Source: Liu J, Kozhaya L, Torres VJ, et al. Structure-based discovery of a small-molecule inhibitor of methicillin-resistant Staphylococcus aureus virulence. Journal of Biological Chemistry 2020:jbc-RA120.

The rapid emergence and dissemination of methicillin-resistant *Staphylococcus aureus* (MRSA) strains poses a major threat to public health. MRSA possesses an arsenal of secreted host-damaging virulence factors that mediate pathogenicity and blunt immune defenses. Panton-Valentine leukocidin (PVL) and α-toxin are exotoxins that create lytic pores in the host cell membrane. They are recognized as being important for the development of invasive MRSA infections and are thus potential targets for antivirulence therapies. In this article, the authors report the high-resolution X-ray crystal structures of both PVL and α-toxin in their soluble, monomeric and oligomeric membrane-inserted pore states in complex with *n*-tetradecylphosphocholine (C14PC). The structures revealed two evolutionarily

conserved phosphatidylcholine-binding mechanisms and their roles in modulating host cell attachment, oligomer assembly, and membrane perforation. It is also demonstrated that the soluble C14PC compound protects primary human immune cells *in vitro* against cytolysis by PVL and α-toxin and hence may serve as the basis for the development of an antivirulence agent for managing MRSA infections.

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