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.

This Month In The JOURNAL of PEDIATRICS

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Early clinical evidence regarding multisystem inflammatory syndrome in children (MIS-C)

— Sarah S. Long, MD

By April 2020 physicians in the UK/France and the US recognized a unique hyperinflammatory syndrome characterized by fever, cardiovascular shock, and suspected SARS-CoV-2 infection and public health authorities published advisories concerning this entity. In the US, this has been called multisystem inflammatory syndrome in children (MIS-C). Two publications in this volume of *The Journal of Pediatrics* report data collected between April and July and results published following peer review online in early October 2020 that reflect the beginning of what would be a rapid transition from clinical experience to clinical evidence.

Dove et al performed a survey of US children's medical centers to glean 48 institution's protocols related to diagnosis and management of MIS-C. Reflecting the pandemic spread itself, institutional case counts among participating centers ranged from >25 to none, with over-representation of eastern US institutions. Definitions of MIS-C across protocols generally were similar for presence, but variable for degrees of abnormalities, for fever, organ systems involved, and laboratory markers of inflammation. Management protocols include almost universal guidance for multispecialty consultations and the use of IVIG and corticosteroids, for tiered use of additional drugs (the specifics of which varied across protocols), and for universal cardiology subspecialty follow up. Pending prospective data and controlled drug trials, shared protocols provide a starting point for providers considering management options. It is also noteworthy that although protocols could not have been in place for more than a few weeks, almost one-half had already been revised.

The report of Carlin et al from a large urban children's medical center in New York City was the result of a retrospective case–control study that attempted to find discriminating features between 44 children hospitalized for MIS-C who had treatment intervention and 181 children evaluated in acute-care outpatient visits who had common febrile illnesses. Major findings were the substantially greater odds in children with MIS-C of high fever (median 40°C), of long duration (median 5 days), and complaint of abdominal pain (OR 12.5, 95% CI 1.65–33.24) as well as several findings of the physical examination and abnormalities in laboratory test results (eg, decreased lymphocyte and platelet count and elevated C-reactive protein level). These discriminating features of children with MIS-C are useful for providers to have confidence in their re-assurances that most children evaluated have self-limited illnesses and to recognize manifestations that raise suspicion for progressive MIS-C in a few children.

Articles pages 26 and 33 ►

Can we diagnose concussion easily?

— Paul G. Fisher, MD

Concussion is generally defined as a traumatic, impulsive force transmitted to the head that results in rapid onset of transiently impaired neurological function. This straightforward definition does not result, however, in an easily reproducible diagnosis of concussion, as prior studies in *The Journal* (*J Pediatr* 2015;166;1214-20) have shown. A number of proprietary tests have been deployed

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for diagnosis, yet those all have limitations in regard to sensitivity, reliability, and expense.

Could a tennis ball, dowel, and stopwatch found in your closet or garage help remedy this problem? In this volume of *The Journal* Brown et al report a cross-sectional study of 568 clinic outpatients, some never concussed, others concussed 8 weeks or more earlier, and others concussed within 8 weeks assessed via a battery of "stick drop"—grabbing a vertically falling dowel as quickly as possible; "wall ball"—throwing a ball and catching it in the opposite hand as many times possible in 30 seconds; and "sharpened modified Romberg," an embellishment of the Romberg maneuver. The recently concussed group performed significantly worse on stick drop, wall ball, and modified Romberg, compared with never concussed and ever concussed groups. In addition, impairments were present up to 8 weeks after the concussion, suggesting that our commonly held view that most youth concussions resolve within a month of injury may be incomplete.

Although this battery was not tested to distinguish sensitivity and specificity of concussion diagnosis prospectively in single individuals, a practical approach such as this holds appeal to diagnose concussion. While pediatricians frown upon a carrot and stick approach to address many childhood problems, perhaps a ball and dowel might be useful in concussion. Deployment of this battery or any other readily available, inexpensive, and non-proprietary approach should be compared with other diagnostic, often proprietary, tools. Further study is needed.

Article page 232 ►

Analysis of temporal clusters: A new approach to unraveling the mystery of Kawasaki disease

— Jane W. Newburger, MD, MPH

Kawasaki disease is an acute vasculitis of childhood characterized by high fever, rash, bilateral nonexudative conjunctival injection, erythema of the oral mucosa, unilateral cervical lymphadenopathy, and erythema and edema of the hands and feet in the acute phase, or periungual desquamation in the subacute phase. Patients who lack full features of Kawasaki disease may have incomplete Kawasaki disease. Whereas the presenting signs of Kawasaki disease are transient, long-term morbidity and mortality may ensue because of an associated necrotizing arteritis that causes coronary artery aneurysms. Indeed, Kawasaki disease has replaced rheumatic fever as the leading cause of acquired heart disease in children in low- and middle-income countries.

There are no pathognomonic signs and no laboratory tests specific for diagnosis of Kawasaki disease. Despite almost 5 decades of research, its etiology is unknown. This has led many experts to posit that Kawasaki disease is an immune response that may be initiated by a variety of agents in genetically susceptible children. Investigators have focused on the association of temporal clusters of Kawasaki disease with environmental factors, including wind patterns, climate dynamics, and atmospheric counts of biological particles (*Sci Rep* 2011;1:152) (*PLOS ONE* 2018;13:e0191087) (*Sci Rep* 2018;8:16140).

Whereas earlier studies have examined the environmental factors associated with clusters of Kawasaki disease cases, Burns et al analyze differences in the patterns of clinical and laboratory findings in patients within temporal clusters in the current volume of *The Journal*. Clusters can occur by chance alone, so the authors use sophisticated epidemiological and statistical techniques to compare the features of cases within and across clusters, as well as those occurring outside of clusters. Cases occurring within a cluster had demographic, clinical, and laboratory features that were more similar to each other than would be expected by chance. The authors suggest that the similarity of within-cluster patient characteristics could reflect different etiologies in disease clusters, for example, varying triggers for Kawasaki disease or different intensity of exposures. Future investigation of patients within clusters, for example through their antibody responses or unique environmental exposures, may reveal a range of etiologies for this still-mysterious disease.

Article page 48 ►

Kawasaki disease in African American children

— Stephen R. Daniels, MD, PhD

It is well known that Kawasaki disease has racial and ethnic variations in prevalence, response to intravenous gamma globulin, and outcomes. However, relatively little is known about African American children. In this volume of *The Journal*, Padilla et al report on comparisons between African American and white children with respect to Kawasaki Disease outcomes. They found that African American children were more likely to be refractory to IVIG treatment, have more severe inflammation, and had a greater proportion of persistent coronary artery abnormalities at follow-up compared with white children.

One important issue in understanding this comparison is whether there are health system disparities that could account for the observed differences between African American and white children. Padilla et al found no difference related to time to admission to the hospital or IVIG treatment compared to disease onset. There was also no significant difference in coronary artery abnormality at the time of admission. These finding suggest that the health care system disparities are not the likely explanation for the findings.

Article page 54 ►

A long road to go: Rural inpatient mental health research

— Michael D. Cabana, MD, MPH

In the United States, it is estimated that approximately 1 in 10 children will require mental health services; however, there is also a shortage in the supply of pediatric mental health care providers in the country. This shortage is further exacerbated in rural areas, which forces families and patients to travel even greater distances for needed mental health care.

In this volume of *The Journal*, Bettenhausen et al report the results of a retrospective cohort of rural children in the United States with a mental health hospitalization.

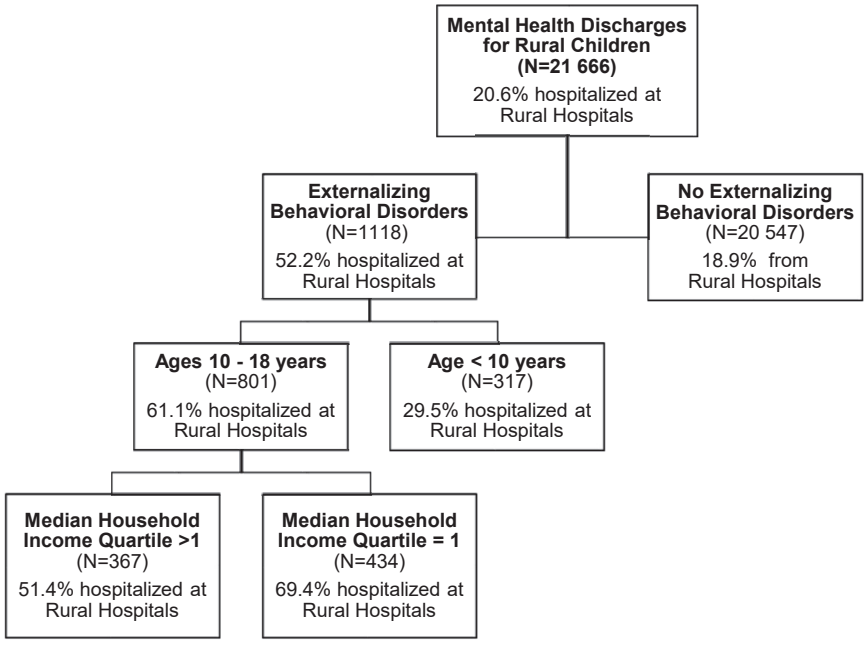

Figure. CART analysis describing characteristics of rural children hospitalized at rural hospitals with a primary mental health condition. The outcomes are calculated from weighted national estimates from the NRD. Data within the NRD are aggregated from 21 geographically diverse states representing 49% of the US population. All terminal nodes had a minimum of 100 unweighted observations, and splits were significant at $P < .05$.

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There are few studies that focus on pediatric rural mental health issues. Bettenhausen et al document where children are receiving such inpatient care, as well as explore differences in outcomes based on the hospital location and type (children's hospital, metropolitan non-children's hospital, and rural hospital) (**Figure**). They found that only 1 in 5 children in rural areas who had a mental health hospitalization received care in a rural hospital. In addition, the authors found that the length of stay was higher at non-rural hospitals compared with rural hospitals; however, the 30-day readmission frequency was much lower at these non-rural hospitals.

This is a descriptive study that has limitations, but it describes a potential gap in mental health care, based on readmission rates, provided by rural hospitals. Further work is needed to determine the reasons for such variation in outcomes, as well as develop and test new interventions. However, given the recent acceleration in the uptake of telemedicine, it may be possible to bridge geographic issues for isolated rural hospitals to mitigate differences in access to pediatric mental health professionals. More work needs to be done and this study in just one step in a long road ahead.

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