



Winter is coming: care of the febrile children in the time of COVID-19

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In the pediatric emergency department (PED), winter seems to arrive earlier each year. After the broken bones and lacerations of the summer, the winter season brings fevers and respiratory illnesses. Fever is our bread and butter—it is the most common reason for PED visits [1]. Fever phobia is ingrained in our society [2]. In the pre-vaccine era, a febrile child was cause for concern; those who were ill-appearing had high rates of bacterial meningitis, and even well-appearing children could not be rapidly discharged. Occult bacteremia was a common condition in well-appearing young febrile children and frequently required laboratory evaluation and treatment with empiric antibiotics [3].

With the introduction of the protein–polysaccharide conjugate *Haemophilus influenzae* type b vaccine in 1987, and the pneumococcal vaccine based on similar technology in 2000 (expanded in 2010), the evaluation of febrile children became a little easier for pediatricians. Rates of invasive bacterial disease declined rapidly, and while we remain vigilant in our evaluation of febrile children, most could be confidently discharged without an extensive workup, with a likely diagnosis of a viral syndrome. These PED visits for well-appearing febrile children were a constant for us. After a thorough history and physical exam, we knew how to counsel parents on the care of their child. Make sure to get plenty of rest. Encourage oral fluids. Use antipyretics for comfort. Make sure everyone at home is washing their hands well. Return to school when 24-hour fever-free. These visits were enjoyable in a way. We reassured worried parents and briefly counseled them on the difference between viral and bacterial illnesses. We comforted parents that their children

would likely recover soon, that the best medicine was the tincture of time. We counseled them on reasons to return and advised close follow-up with their pediatricians if not improving. As pediatricians, we knew what to be worried about.

This year, winter ushers in a season of uncertainty. The first case of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection changed the world. The disease (COVID-19) continues to spread globally as the world struggles with viral containment. Quarantine, isolation, and social distancing have become part of our daily vernacular. Much of the world went into lockdown and is only now just starting to emerge.

Pediatricians braced for the pandemic, but we ultimately found our units quiet. As adult emergency departments, inpatient wards, and intensive care units bulged to care for patients, children were relatively spared with children accounting for only 1–5% of infections, and generally having more mild disease with lower rates of hospitalizations and death [4]. With schools shut down and testing in short supply, febrile children in high prevalence areas like New York City were treated with the recommendation to “assume you have it and stay isolated”. As we flattened the curve, the PED saw a resurgence of common viral illnesses. We continued to reassure. Then in April, things changed again, when reports of a pediatric multi-system inflammatory syndrome began to surface. We were suddenly faced with a new pediatric disease that we knew little about. Initial reports described children with fevers, abdominal pain, and stigmata of Kawasaki disease. Laboratory evaluation was necessary and consistently showed an elevation of inflammatory markers, often coupled with abnormalities of cardiac markers. Although most children did well with available treatments, some presented in shock requiring aggressive therapy and some even had fatal outcomes [5]. Suddenly, a fever was no longer just a fever. Similar to the age of occult bacteremia, hospitals and health organizations rushed to develop guidelines outlining the screening labs for febrile children. Spurred by the media and frightened by this new mysterious disease, worried parents rushed their children to medical care.

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In the direct aftermath of the peak of cases, we realized that this new disease, now renamed multi-system inflammatory syndrome in children (MIS-C), also called pediatric inflammatory multi-system syndrome temporally associated with SARS-CoV-2 infection, is rare, but with children's lives at stake, we feel compelled to act. We assess febrile children for this disease and many undergo laboratory evaluation and subspecialty consultation. As directed, we report each potential case to local and regional Departments of Health. Unlike the evaluation of patients for invasive bacterial disease, MIS-C has no “culture” that will give us the definitive diagnosis. Instead, we are left to interpret an array of blood tests and clinical signs.

What will we do this winter? As COVID-19 cases hopefully remain low, children return to school, and our usual viral culprits such as influenza and respiratory syncytial virus return, how will we evaluate and counsel the families of our febrile children?

As we worry about a second peak of COVID-19 infections, how will we test for COVID-19? Will every fever be evaluated with a nasopharyngeal swab and are the results of those swabs trustworthy enough to allow children to return to school? Will we recommend 10 days of isolation for every febrile illness and 14 days of quarantine after every exposure? Will parents ever be able to return to work? If so, who will take care of their children? What will be the disease course for children with co-infections with COVID-19 and another viral illness?

As we look for MIS-C, the needle in the haystack, how will we decide whom to screen with laboratory tests? In those we test, how should the results even be interpreted? There are no reference values for children with viral illnesses, as these are not children we would normally evaluate with laboratory testing. Does an elevated D-dimer, erythrocyte sedimentation rate, C-reactive protein, or ferritin require repeat testing or admission for monitoring? As pediatricians, we adhere to our institutional guidelines, rely

on our clinical judgement, and depend on our subspecialists' input. We expectantly wait for evidence-based practical guidance from our professional societies to help inform our management on the front-line.

Winter is coming. What will we do with our febrile children?

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