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The systematic review by Mark et al of published cases of the clinical manifestations of SARS-CoV-2 infection in infants younger than 3 months of age provides a preview, a snapshot of knowledge at this moment in time. Clinical data of the 63 patients' included were collected predominantly from single case reports, with all of the expected bias toward publication of unusual cases, ie, that struck the attending clinicians as unexpected according to the medical conversation at the time, and struck reviewers and editors as sufficiently novel and well documented to warrant publication. One cannot even guess whether the manifestations depicted by just 63 cases will with subsequent unbiased study be found to be common or uncommon, typical or atypical, unique to this age group or ageless. Why then collate? Why publish?

The compilation of cases corrects missteps in the medical and lay conversations about SARS-CoV-2 infection in children. First, the mere collectability of the cases in very young infants documents that this group is not always asymptomatic or only mildly affected when infected with SARS-CoV-2. Second, the broad spectrum of clinical manifestation and dysfunction of multiple organ systems uncovered by just 63 patients are evidence of what “can happen” when young infants are infected, and provide an investigative framework for clinicians evaluating any acute illness in this age group.

What can cohorts 50 years apart tell us about obesity?

— Stephen R. Daniels, MD, PhD

There are different approaches used in science to elucidated important relationships and work to better understand cause and effect. The cohort study is one of the strongest observational study designs because it can be used to understand temporal relationships between exposures and outcomes. However, cohort studies also have a temporal limitation as they usually unfold over a relatively short period of time in a static environment.

In this volume of The Journal, Robinson et al evaluated data from 2 cohorts examining the relationships between early life factors and socioeconomic status (SES) with BMI later in childhood. These cohorts were 50 years apart and the participants were exposed to different environments, as well as different sociocultural factors, even though the studies were done in the same geographic region. They found that although previous cohorts exposed to lower SES experienced a higher risk of growth restriction, the modern cohort exposed to lower SES had higher risk of obesity. Rapid growth in infancy was a stronger correlate of later obesity in the modern cohort. This suggests important environmental factors at work in modern infants and children.

(Continues on next page)
Predictive accuracy of transcutaneous bilirubin assessments
— Richard A. Polin, MD

The American Academy of Pediatrics recommends that a “screening” total serum bilirubin (TSB) or transcutaneous (TcB) bilirubin measurement should be obtained prior to discharge in infants ≥35 weeks’ gestation and used with an assessment of clinical risk factors to predict which infants are at risk to develop severe hyperbilirubinemia (Pediatrics 2004;129:1193-8) (J Perinatol 2009;29:612-7). The TcB and TSB values should be plotted on an hour specific bilirubin nomogram and the risk zone for hyperbilirubinemia determined on the basis of the infant’s age in hours. Transcutaneous measurements are widely used as a screening tool to decide which infants need a total serum bilirubin measurement. Transcutaneous assessment of bilirubin may underestimate or overestimate the total serum bilirubin concentration by a small amount depending on the range of serum bilirubin concentrations, the measurement device used and the infant’s ethnic background (Pediatrics 2004;113:1628-35).

In this volume of The Journal Konana et al from Intermountain Healthcare completed a quality improvement project in infants ≥35-weeks’ gestation to quantify the risk that TcB screening (>85th percentile on the Utah algorithm) would fail to identify the need for a confirmatory TSB when TSB screening alone would have revealed that phototherapy was indicated. Out of 727 paired specimens, the TcB indicated “no phototherapy” in just one infant when the TSB measurement indicated that phototherapy was indicated.

Four points are worth emphasizing from this study. First, TcB is fairly accurate but cannot replace the gold standard TSB (Figure). Second, the authors used the BiliChek device; other measurement devices (JM 103/105) may yield different results. Third, the population in Utah (77% Caucasian) may not be representative of other populations around the country. Finally, use of TcB as a screening tool will result in a high number of false positive values. In the study by Konana et al, 18.2% of values exceeded the 95th percentile (suggesting a need for phototherapy). However, 78% of the corresponding TSB values did not exceed the 95th percentile indicating a high false positive rate. If only the TcB is followed that will lead to excessive use of phototherapy. Phototherapy has recently been shown to be associated with an increase the risk of seizures (Pediatrics 2018;142:e201800648) (Epilepsy Res 2016;124:67-72). The quality improvement study by the Utah investigators is well designed and offers reassurance on the safety and relative accuracy of TcB measurements. However, TcB should not replace a TSB in deciding management.

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Figure. Bland-Altman plot showing relationship between the difference in TcB and TSB and the average of the 2.
The time is “now” for rapid PCR testing for influenza in clinical practice
— Sarah S. Long, MD

E l Feghaly et al at Children’s Mercy Kansas City presented a brief survey to providers in their emergency department and urgent care centers who placed an order for influenza RT-PCR test, asking their estimation of probability of the patient having influenza and their intentions to manage, including therapy. They also captured actual management once the results were available.

Overall, about one-half of tests were positive. Clinical suspicion was not a predictor of test results, the positivity rate being 40% if suspicion was low and 57% if high. Test results changed clinicians’ management (eg, for further tests/imaging, antibiotic/antiviral therapy) in 44% of influenza PCR-positive cases and in 93% of PCR-negative cases. The net cost savings in avoiding antiviral therapy alone offset the cost of PCR testing compared with rapid antigen testing for influenza.

It’s a new world. With PCR testing for influenza being the first highly sensitive and specific test, we can accurately discern the etiology of the patient’s illness. As the flu season looms, not only are there ramifications of testing for optimizing treatment for influenza and saving resources, but because of pandemic SARS-CoV-2 there is an urgent need to know who has what. With clinical ability to diagnose influenza as shown in this study to be no better than a coin toss, and with most SARS-CoV-2 infections in children not discernible by clinical manifestations, we face a nightmare that includes managing families and teachers and school children, if there is concurrent community activity of both viruses.

Can we tamp down the nightmare? Absolutely. 1) Promote, insist, and ensure influenza vaccination (unless a valid contraindication exists) of every person 6 months of age or older – both to reduce illness as well as the seasonal burden of influenza. In another study published in this volume and conducted across 6 countries, Goldman et al showed that there may be increased opportunity. Questioning ~2400 parents bringing a child to an emergency department earlier in the COVID-19 pandemic about their plan to have their child immunized against influenza in the Fall, almost 30% who had not done so last year planned to do so in 2020. We must capitalize on the moment, offer, and facilitate vaccinations. 2) Continue optimal behaviors to reduce SARS-CoC-2 transmission and acquisition. 3) Sort out the logistics to be able to use the powerful technology of PCR testing in everyday clinical practice in order to accurately determine etiology of respiratory illness at least for these 2 viruses.

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