

Sick Kids Look Sick

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Emergency physicians commonly evaluate children with fever and worry about how to best detect “occult” or “early” presentations of serious bacterial infections such as meningitis or sepsis. Laboratory testing is at times used to supplement clinical examination and physician judgment; however, the merits of such screening have long been debated and substantial practice variation remains.¹⁻⁴

In this issue of *Annals*, there is a landmark study with important implications for the evaluation of the febrile child. Vaillancourt et al⁵ queried the aggregate health register for the province of Ontario, identifying 521 children, aged 30 days to 5 years, with confirmed sepsis or meningitis. Given that all province-wide emergency department (ED) visits are interlinked in this comprehensive database, they found that 22% of these children were discharged from an ED with a minor infectious diagnosis (eg, otitis media or upper respiratory tract infection) within 5 days preceding their life-threatening illness. Thus, approximately 1 in 5 children apparently received a misdiagnosis and was sent home shortly—half of children in 24 hours or less and essentially all within 72 hours—before a repeated ED visit in which sepsis or meningitis was ultimately confirmed.

Emergency physicians dread missing early presentations of sepsis or meningitis and would intuitively expect increased morbidity and mortality to result should these critical infections be missed. However, Vaillancourt et al⁵ found that the children with delayed diagnoses had no relative increase in mortality, critical care use, or length of stay compared with those receiving a correct diagnosis on the first visit. Their administrative database lacked the capability to provide more detailed clinical information than these global measures.

What should we make of this unexpected result? One interpretation posed by the authors is that of spectrum bias, ie, children receiving a correct diagnosis on the first visit might have had more aggressive disease, with an anticipated greater risk of harm in this group, offsetting the negative

consequences of delayed diagnoses in the less severely ill children. This proposed explanation, however, is speculative and cannot be confirmed by the study. Furthermore, it would appear improbable that these 2 opposing forces would so near-perfectly balance each other for all outcomes studied.

A second explanation, simpler and more plausible, is that sepsis or meningitis was not present at the initial visit. The first diagnoses of nonserious viral or bacterial infections were not in error; however, after discharge these children had the rare misfortune of an unanticipated progression of illness. We know that sepsis and meningitis are commonly preceded by a nonserious infectious illness. This initial infection may induce bacteremia that, in rare circumstances, might advance to sepsis or meningeal seeding.^{1-4,6,7}

Antibiotics are the critical curative therapy for sepsis and meningitis, with delays in administration universally believed to worsen outcomes.⁶⁻¹¹ The “missed” children in this study received a correct diagnosis a median of 25 hours later. It seems inconceivable that delays of a day or more for antimicrobial therapy would not result in any measurably greater mortality, critical care use, or length of stay, even if the sepsis or meningitis were in an early stage on the initial visits. The absence of apparent harm from late receipt of antibiotics corroborates the contention that sepsis or meningitis was not present on these first visits, but instead developed later.

The study data of Vaillancourt et al⁵ suggest that, outside of the neonatal period, sepsis and meningitis are not occult conditions and that, accordingly, “sick kids look sick.” If febrile children lack evidence of these serious illnesses after a careful examination, then at that point they would appear to not have them. After ED discharge, a more serious infection may in rare cases develop; however, the child will then look sick and be clinically identifiable. Vaillancourt et al⁵ reassure us that children identified on a second ED visit will have a similar clinical outcome.

If unanticipated progression of illness rather than misdiagnosis is a more credible explanation for the current study’s findings, then important corollaries for emergency care of the febrile child follow:

Progression of illness to sepsis or meningitis is unpredictable in normal healthy children. If sepsis and

meningitis are often preceded by nonserious, common bacterial or viral illnesses, then later rapid progression would appear unpredictable. By the time sepsis or meningitis is clinically detectable, some children will have unavoidable morbidity and mortality.

The addition of screening interventions is unwarranted. If little can be done at present to enhance the early detection of progression from minor illness to sepsis or meningitis, then attempts to implement screening in well-appearing, low-risk, febrile children with imperfect diagnostic tests (eg, WBC counts, C-reactive protein, procalcitonin, blood cultures)⁴ or clinical decision rules¹² would not appear useful. The nature and extent of screening that occurred during the current study are unknown; however, Ontario EDs are unlikely to differ substantially from those in the United States, where most children who are febrile without source receive no laboratory testing.³

Data from the current study illustrate the challenge for screening for significant bacterial infections. In this investigation, 114 of 2,397,427 ED visits, or 1 in 21,000, had meningitis or sepsis purportedly missed on the initial ED visit. If one conservatively assumes that roughly half of this total denominator of visits was due to some form of minor viral or bacterial illness and optimistically speculates that a new screening test or algorithm might reduce the frequency of misdiagnosis by half, then the number needed to benefit would be 21,000 screening tests per child with a theoretical benefit. If the screening test decreases the frequency of misdiagnosis by only 20%, then the number needed to benefit is approximately 100,000. This would represent enormous effort for a miniscule or nonexistent gain.

The alternative to diagnostic screening in healthy, well-appearing, febrile children is relying on a careful physical examination, clinical gestalt, careful parent instructions, and watchful waiting with close follow-up.

The status quo is working. Because the current study found that children receiving a diagnosis on the second ED visit experienced no additional measurable harm, whatever Ontario's emergency physicians are doing appears to be effective. There is nothing in this study to suggest physician error or a need to alter practice. The sick kids would appear to have looked sick and to have been identified as such at the earliest visit possible, whether by emergency physicians staffing larger EDs, pediatricians staffing children's hospital EDs, or family physicians staffing Ontario's smaller EDs.⁵

Sepsis and meningitis are rare. During 5 years in this populous province, only 521 occurrences of these serious illnesses were noted in 2,397,427 ED visits in children within the study's 30-day to 5-year age range, or 1 diagnosis per 4,602 ED visits. Given the low prevalence of

invasive bacterial infections in the conjugate vaccine era, individual emergency physicians treating largely healthy children may not encounter a child with either condition during decades of practice.

Revisits often involve different EDs. Another important observation from the current study is that 30% of the time, parents took their children to a different hospital for their second visit. The reasons for seeking an alternate ED are unknown and likely multifactorial, and may include distrust of the initial hospital, a preference for a fresh evaluation, or embarrassment at returning so quickly after discharge.

Careful evaluation remains the best approach. We mention medical malpractice issues last, but they will not be least in many physicians' minds. The current study provides evidence that common, nonserious, infectious illnesses often precede the rapid onset of sepsis and meningitis, and that this does not appear to reflect any failure of the health care team. "Sick kids look sick" reassures us that the children did not have sepsis or meningitis on the first visit, but developed them later. Such thinking should provide emergency physicians the confidence that they can and should continue to rely on careful examinations and their best clinical judgment. Watchful waiting is an appropriate strategy when coupled with parental education about the uncommon possibility of rapid progression of illness. Rare unfortunate outcomes will occur but appear unavoidable at present.

In summary, the study by Vaillancourt et al⁵ reassures us that although children discharged from the ED with a diagnosis of a minor infectious illness may rarely develop sepsis or meningitis, they ultimately do not have worse outcomes than if they had received the diagnosis on their original presentation. The most credible interpretation is that sepsis and meningitis were absent on the first visit and cannot be diagnosed until clinically manifest. In other words, sick kids look sick. These results encourage emergency physicians to trust the power and value of their clinical gestalt.

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CORRECTION

In the April 2015 issue, regarding the Policy Statement by Marin et al (“Point-of-Care Ultrasonography by Pediatric Emergency Physicians,” pages 472-478) the Pediatrics Point-of-Care Ultrasound Work Group author list should have been listed as:

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