Can you differentiate bacterial from viral pediatric infections based on the CBC?

Evidence-based answer
No—the complete blood count (CBC) alone does not have adequate sensitivity or specificity to tell bacterial from viral infections (strength of recommendation [SOR]: B, cohort studies). When used in conjunction with other clinical parameters in validated decision-making algorithms, the CBC can help detect serious bacterial infections in pediatric patients with fever (SOR: B, cohort studies).

Clinical commentary
There’s no substitute for history, physical exam, and good judgment
Viral vs bacterial—often these are surrogate terms for minor vs serious illness. This review is a great lesson in likelihood ratios. Based on the low likelihood ratio, a CBC alone does not shift our suspicion greatly for serious bacterial infections in intermediate-risk patients; however, if you combine it with a clinical decision rule, it can greatly help decision-making, as evidenced by negative predictive values of 99% and above.

In contrast, we don’t need the CBC to tell us that an adult with the sniffles has a rhino/corona/whatevervirus, nor do we need it to tell us that a febrile, lethargic child with a petechial rash has a life-threatening bacteremia. If you enjoy the muck and the mess of primary care as much as I do, this inquiry should provide you with the validation that there’s no substitute for the history, physical exam, and judgment of a good clinician.

FAST TRACK
A CBC alone does not shift our suspicion greatly for serious bacterial infections in intermediate-risk patients

Evidence summary
For acutely febrile patients, the presence of an elevated white blood cell (WBC) count with elevated band forms has dogmatically been thought of as a marker for bacterial infection.¹ Current literature, however, does not support this.²

A retrospective study of 5353 infants ages 3 to 89 days presenting to the emergency department for evaluation of fever showed that 3 of 4 infants ultimately diagnosed with bacterial meningitis would have been missed if the WBC count alone were used to predict which infants need a lumbar puncture.³ A prospective study of 2492 children ages 3 to 24 months presenting to the emergency department with acute fever and an absolute WBC count >15,000/mm³ revealed that neither a polymorphonuclear count of >10,000/mm³ (>66% segmented forms) nor a band count of >500/mm³ was associated with an increased likelihood of occult bacterial infection.⁴ Other studies
show that the WBC alone is poorly discriminatory for identifying either bacteremia or meningitis.\(^5,6\)

To improve the diagnostic utility of the CBC, other studies have examined individual components of the white blood cell differential count (\textit{Table 1}). In particular, the use of the absolute neutrophil count (ANC) has been proposed as a superior marker of serious bacterial infection.\(^7\) A review of 6,579 outpatients aged 3 to 36 months presenting to the emergency department used logistic regression to identify predictors of bacteremia. In this study, ANC (>9,500/mm\(^3\)) and WBC (>14,300/mm\(^3\)) were of equal sensitivity (75%) and specificity (75%) in identifying serious bacterial infection.\(^9\) Finally, the band count alone does not accurately predict serious bacterial infection.\(^10\)

In summary, the CBC cannot be used in isolation to differentiate bacterial from viral illness. The CBC can, however, augment clinical data from the history and physical examination to predict the likelihood of serious bacterial illness. As a result, numerous diagnostic criteria, each incorporating elements of the CBC, have been developed in an attempt to accurately differentiate bacterial from viral illness in acutely febrile patients, most typically children (\textit{Table 2}). These criteria differ by age of the patient, clinical testing recommendations, indications for antibiotic therapy, as well as WBC cutoffs.

**Recommendations from others**

The American College of Emergency Physicians recommends considering antibiotic therapy for previously healthy, well-appearing children ages 3 to 36 months who present with a fever without a clinical source and a WBC count >15,000/mm\(^3\).\(^3,14\)

- **Neisseria meningitides**
- **FAST TRACK**

3 of 4 infants diagnosed with bacterial meningitis would have been missed if the WBC count alone was used.

**Table 1**

<table>
<thead>
<tr>
<th>VARIABLE</th>
<th>CUTOFF</th>
<th>SENSITIVITY</th>
<th>SPECIFICITY</th>
<th>LR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>White blood cell count</td>
<td>15,000/mm(^3)</td>
<td>64%–82%</td>
<td>67%–75%</td>
<td>1.9–2.7 (1.1–3.8)</td>
</tr>
<tr>
<td>Absolute neutrophil count</td>
<td>10,000/mm(^3)</td>
<td>64%–76%</td>
<td>76%–81%</td>
<td>3.0–3.3 (1.6–6.2)</td>
</tr>
</tbody>
</table>

LR, likelihood ratio; CI, confidence interval.

The University of Cincinnati Evidence-Based Clinical Practice Guidelines for fever of uncertain source in children ages 2 to 36 months recommends obtaining a CBC for any child who is ill-appearing or at high risk for bacteremia (determined by the clinicians' judgment). A WBC of ≥15,000/mm\(^3\) or ANC >10,000/mm\(^3\) provide support for antibiotic therapy.\(^11\) The 1993 American Academy of Pediatrics guidelines for fever ≥39°C without a source in children ages 3 months to 3 years recommends a CBC; if the WBC count ≥15,000/mm\(^3\), they recommend a blood culture and treatment with antibiotics pending culture results.\(^3,16\)

It is important to note that in the age of \textit{Haemophilus influenza} and \textit{Streptococcus pneumonia} vaccination, the rate of occult bacteremia in febrile children presenting without a source has fallen from 3% to 10% to 1% or less.\(^17\) A lower prevalence reduces the utility of routine CBC or blood culture in the evaluation of immunized, febrile children. Parameters such as procalcitonin, interleukin-6, interleukin-8, interleukin-1 receptor antagonist and C-reactive protein show future promise as biochemical markers for identifying serious bacterial infections.\(^18\)
### TABLE 2

**Clinical criteria for predicting serious bacterial infection in febrile children**

<table>
<thead>
<tr>
<th>CRITERION</th>
<th>ROCHESTER CRITERIA&lt;sup&gt;11&lt;/sup&gt;</th>
<th>BOSTON CRITERIA&lt;sup&gt;12&lt;/sup&gt;</th>
<th>PHILADELPHIA CRITERIA&lt;sup&gt;13&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Predictive value</td>
<td>98.9% PV– in ruling out serious bacterial infection</td>
<td>95% PV+ to identify serious bacterial infection</td>
<td>100% PV– in ruling out serious bacterial infection</td>
</tr>
<tr>
<td>Age</td>
<td>&lt;60 days</td>
<td>1–3 mos Present to emergency dept. with fever ≥38.0°C</td>
<td>29–56 days Present with fever ≥38.2°C</td>
</tr>
<tr>
<td>Appearance</td>
<td>Well-appearing</td>
<td>Healthy appearing</td>
<td>Well-appearing</td>
</tr>
<tr>
<td></td>
<td>Previously healthy</td>
<td>No ear, soft tissue, joint or bone infection on exam</td>
<td></td>
</tr>
<tr>
<td>White blood cell count</td>
<td>WBC 5–15,000/mm&lt;sup&gt;3&lt;/sup&gt;</td>
<td>Peripheral WBC ≤20,000/mm&lt;sup&gt;3&lt;/sup&gt;</td>
<td>WBC ≤15,000/mm&lt;sup&gt;3&lt;/sup&gt; Band-to-neutrophil ratio of ≤0.2</td>
</tr>
<tr>
<td>Urinalysis</td>
<td>≤10 WBC/hpf of centrifuged urine</td>
<td>Urinalysis ≤10 WBC/hpf</td>
<td>Urinalysis ≤10 WBC/hpf</td>
</tr>
<tr>
<td>Other tests</td>
<td>If diarrhea, ≤5 WBC/hpf of stool smear</td>
<td>CSF WBC ≤10/hpf</td>
<td>CSF WBC ≤8/hpf with negative gram stain If watery diarrhea, few or no WBC/hpf on stool smear</td>
</tr>
</tbody>
</table>

WBC, white blood cell count; hpf, high-powered field; CSF, cerebrospinal fluid; PV, predictive value

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15. Cincinnati Children’s Hospital Medical Center. Evidence-based clinical practice guideline for fever of uncertain source in children 2 to 36 months of age. Cincinnati, Ohio: Cincinnati Children’s Hospital Medical Center; 2003.


