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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.

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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 $>15,000/\text{mm}^3$ revealed that neither a polymorphonuclear count of $>10,000/\text{mm}^3$ ($>66\%$ segmented forms) nor a band count of $>500/\text{mm}^3$ 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 (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 6579 outpatients aged 3 to 36 months presenting to the emergency department with temperatures of 39°C or higher showed an ANC of >10,000/mm³ as more predictive of occult pneumococcal bacteremia than an elevated WBC count (>15,000/mm³) alone.⁸ Another retrospective review of more than 10,000 patients aged 3 to 36 months presenting to the emergency department used logistic regression to identify predictors of bacteremia. In this study, ANC (>9500/mm³) and WBC (>14,300/mm³) 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 (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/mm³.^{3,14}

TABLE 1

WBC markers: How good are they at predicting serious bacterial infection?^{9,18,19}

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

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/mm³ or ANC >10,000/mm³ provide support for antibiotic therapy.¹⁵ 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/mm³, they recommend a blood culture and treatment with antibiotics pending culture results.^{3,16}

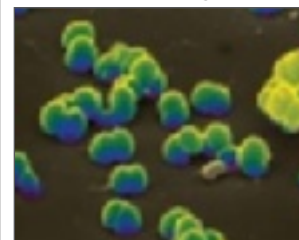
It is important to note that in the age of *Haemophilus influenzae* and *Streptococcus pneumoniae* vaccination, the rate of occult bacteremia in febrile children presenting without a source has fallen from 3% to 10% to 1% or less.¹⁷ A lower prevalence reduces the utility of routine CBC or blood culture 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 ■

References

1. Wile MJ, Homer LD, Gaehler S, Phillips S, Millan J. Manual differential cell counts help predict bacterial infection. A multivariate analysis. *Am J Clin Pathol* 2001; 115:644–649.
2. Seebach JD, Morant R, Ruegg R, Seifert B, Fehr J. The diagnostic value of the neutrophil left shift in predicting inflammatory and infectious disease. *Am J Clin Pathol* 1997; 107:582–591.

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Neisseria meningitidis



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

TABLE 2

Clinical criteria for predicting serious bacterial infection in febrile children

CRITERION	ROCHESTER CRITERIA ¹¹	BOSTON CRITERIA ¹²	PHILADELPHIA CRITERIA ¹³
Predictive value	98.9% PV– in ruling out serious bacterial infection	95% PV+ to identify serious bacterial infection	100% PV– in ruling out serious bacterial infection
Age	<60 days	1–3 mos Present to emergency dept. with fever $\geq 38.0^{\circ}\text{C}$	29–56 days Present with fever $\geq 38.2^{\circ}\text{C}$
Appearance	Well-appearing Previously healthy No evidence of infection (skin, bone, joint, soft tissue or ear)	Healthy appearing No ear, soft tissue, joint or bone infection on exam	Well-appearing
White blood cell count	WBC 5–15,000/mm ³ Bands $\leq 1,500/\text{mm}^3$	Peripheral WBC $\leq 20,000/\text{mm}^3$	WBC $\leq 15,000/\text{mm}^3$ Band-to-neutrophil ratio of ≤ 0.2
Urinalysis	≤ 10 WBC/hpf of centrifuged urine	Urinalysis ≤ 10 WBC/hpf	Urinalysis ≤ 10 WBC/hpf
Other tests	If diarrhea, ≤ 5 WBC/hpf of stool smear	CSF WBC $\leq 10/\text{hpf}$	CSF WBC $\leq 8/\text{hpf}$ with negative gram stain If watery diarrhea, few or no WBC/hpf on stool smear

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

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In this age of vaccination, the rate of occult bacteremia in febrile children presenting without a source has fallen to 1% or less

- Bonsu BK, Harper MB. Utility of the peripheral blood white blood cell count for identifying sick young infants who need lumbar puncture. *Ann Emerg Med* 2003; 41:206–214.
- Kramer MS, Tange SM, Mills EL, Ciampi A, Bernstein ML, Drummond KN. Role of the complete blood count in detecting occult focal bacterial infection in the young febrile child. *J Clin Epidemiol* 1993; 46:349–357.
- Brown L, Shaw T, Wittlake WA. Does leucocytosis identify bacterial infections in febrile neonates presenting to the emergency department? *Emerg Med J* 2005; 22:256–259.
- Garges HP, Moody MA, Cotten CM, et al. Neonatal meningitis: what is the correlation among cerebrospinal fluid cultures, blood cultures, and cerebrospinal fluid parameters? *Pediatrics* 2006; 117:1094–1100.
- Gombos MM, Bienkowski RS, Gochman RF, Billett HH. The absolute neutrophil count: is it the best indicator for occult bacteremia in infants? *Am J Clin Pathol* 1998; 109:221–225.
- Kuppermann N, Fleisher GR, Jaffe DM. Predictors of occult pneumococcal bacteremia in young febrile children. *Ann Emerg Med* 1998; 31:679–687.
- Isaacman DJ, Shults J, Gross TK, Davis PH, Harper M. Predictors of bacteremia in febrile children 3 to 36 months of age. *Pediatrics* 2000; 106:977–982.
- Cornbleet PJ. Clinical utility of the band count. *Clin Lab Med* 2002; 22:101–136.
- Dagan R, Powell KR, Hall CB, Menegus MA. Identification of infants unlikely to have serious bacterial infection although hospitalized for suspected sepsis. *J Pediatr* 1985; 107:855–860.
- Baskin MN, O'Rourke EJ, Fleisher GR. Outpatient treatment of febrile infants 28 to 89 days of age with intramuscular administration of ceftriaxone. *J Pediatr* 1992; 120:22–27.
- Baker MD, Bell LM, Avner JR. The efficacy of routine outpatient management without antibiotics of fever in selected infants. *Pediatrics* 1999; 103:627–631.
- American College of Emergency Physicians. Clinical policy for children younger than three years presenting to the emergency department with fever. *Ann Emerg Med* 2003; 42:530–545.
- Cincinnati Children's Hospital Medical Center. Evidence-based clinical practice guideline for fever of uncertain source in children in 2 to 36 months of age. Cincinnati, Ohio: Cincinnati Children's Hospital Medical Center; 2003.
- Baraff LJ, Bass JW, Fleisher GR, et al. Practice guideline for the management of infants and children 0 to 36 months of age with fever without source. *Ann Emerg Med* 1993; 22:1198–1210.
- Stoll ML, Rubin LG. Incidence of occult bacteremia among highly febrile young children in the era of the pneumococcal conjugate vaccine. *Arch Pediatr Adolesc Med* 2004; 158:671–675.
- Pulliam PN, Attia MW, Cronan KM. C-reactive protein in febrile children 1 to 36 months of age with clinically undetectable serious bacterial infection. *Pediatrics* 2001; 108:1275–1279.
- Pratt A, Attia MW. Duration of fever and markers of serious bacterial infection in young febrile children. *Pediatr Int* 2007; 49:31–35.