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White Blood Cell Count versus Temperature as Predictors of Pediatric Bacteremia

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Abstract

Introduction: Although the prevalence of bacteremia has largely declined with the development of the Haemophilus Influenza Type b (Hib) and pneumococcal vaccines, it continues to be a leading cause of morbidity and mortality in children. Thus, it is crucial to differentiate bacteremia from other illnesses via the clinical picture and laboratory test results. **Objective:** The purpose of this research was to determine whether there is a clinically significant difference between temperature and white blood cell (WBC) count as determinants of bacteremia in the pediatric population. **Methods:** A PubMed search was conducted utilizing the following terms and filters: temperature, WBC, pediatrics, bacteremia, humans and English. The search resulted in two articles that met the parameters of the research. **Conclusion:** The data showed WBC count to be a better predictor of bacteremia as compared to temperature, but ultimately neither is exceptional. Blood cultures (BC) remain the gold standard for bacteremia identification, but the delayed results prevent an expeditious diagnosis. Recognizing a relationship between bacteremia and other laboratory tests, such as procalcitonin, may help develop more effective ways at early disease detection.

INTRODUCTION

The differential diagnosis list for infants 3-36 months with fever is quite extensive. One diagnosis that must always be considered is bacteremia due to the dire consequences of delaying treatment. However, most infants with fever have a source other than bacteremia for their fever that does not require intervention. The discovery of the H. influenzae type b (Hib) and pneumococcal vaccines has substantially decreased the prevalence of bacteremia in infants. Prior to the Hib vaccine, which was not available until 1985, the prevalence of bacteremia was 3-5% in well-appearing children with a fever of 39°C. Now, the prevalence has decreased to 1.6% in 3-36 month olds.[1] Even with the decline in bacteremia, it remains the 7th leading cause of morbidity and mortality in children under 1 year old and the 8th leading cause in children 1 - 4 years old.[2] Early recognition of bacteremia and distinction from other illnesses is key to the successful treatment of the disease. Complications of diagnosis arise when a child is able to compensate for their illness and appear less sick than expected. In addition, stable children with illnesses such as bronchiolitis can meet sepsis criteria but do not have bacteremia.[3] Specific systemic inflammatory response system (SIRS) and sepsis criteria have been adapted for children from the adult guidelines. Table 1 outlines SIRS criteria modified for children.

Table 1. Modified SIRS Criteria

A child meets SIRS criteria if they have 2 of the following, with one being an abnormal temperature or leukocyte count:
Core temperature >38.5°C or <36°C
Tachycardia greater than 2 standard deviations above average for their specific age group or for children <1 year
Bradycardia below the 10th percentile for their age group for more than ½ hour
Average respiration rate greater than 2 standard deviations above average
Elevated or depressed leukocyte count

Sepsis criteria includes meeting SIRS criteria in the presence of a suspected or confirmed infection source.[4] The decision of how to proceed in an emergency room evaluation of a febrile infant is often left up to the individual discretion of the physician or provider receiving the case. A 2015 survey of pediatric emergency room physicians demonstrated the most commonly used clinical and laboratory parameters in the diagnosis of sepsis. The most common clinical parameters included: tachycardia, abnormal temperature, altered mental status, peripheral capillary refill, and tachypnea. Laboratory studies used frequently included white blood cell count, neutrophil count and band count. Overall, clinical signs and symptoms were used more often to diagnose sepsis than laboratory measures. However, there remains a large variation between providers for which parameters they use to initially diagnose sepsis.[2]

Blood cultures are the current gold standard for definitively diagnosing bacteremia, but the results can take up to 24-48 hours. This leaves providers wanting alternative laboratory guidelines to further support the clinical diagnosis of bacteremia in the absence of blood culture data. Traditionally, WBC count and temperature have been used as objective predictors of

bacteremia and are used as guideposts to determine the necessity of further investigation and possible empiric antimicrobial treatment. In one study, 95-98% of providers stated that they obtain WBC count in febrile young infants as a screening tool for bacteremia. Temperature and WBC count measures are quick and easy to obtain, but the questionable effectiveness of these tests to predict bacteremia can potentially lead to inappropriate testing, increased cost and unnecessary or misguided treatment. The utilization of WBC count and temperature have been studied and been proven effective in older populations, but the accuracy of these criteria in young children has yet to be evaluated.[5] The purpose of this review is to determine the clinical accuracy of temperature versus white blood cell count in predicting pediatric bacteremia.

Clinical Scenario:

AJ is an 18 month old, African American male presenting to the emergency room complaining of fever, lethargy, and poor feeding. His mother denies any exposure to recent illnesses. On initial observation, the child looks unwell. A temperature and complete blood cell count (CBC) are immediately obtained. Given the concern for bacteremia, it is unclear which test may offer the best diagnostic information.

PICO criteria:

Population: Pediatric patients between the ages of 3-36 months
Intervention: Temperature
Comparison: WBC count
Outcome: Correctly predict bacteremia

Clinical question: Among pediatric patients between the ages of 3-36 months, does temperature as compared to white blood cell count correctly predict bacteremia?

METHODS

An initial PubMed search was conducted in September 2015. The terms searched included temperature, WBC, pediatrics, and bacteremia. Nineteen articles matched the search criteria. When the limits "humans" and "English" were applied, the number of articles to assess was reduced to eight.

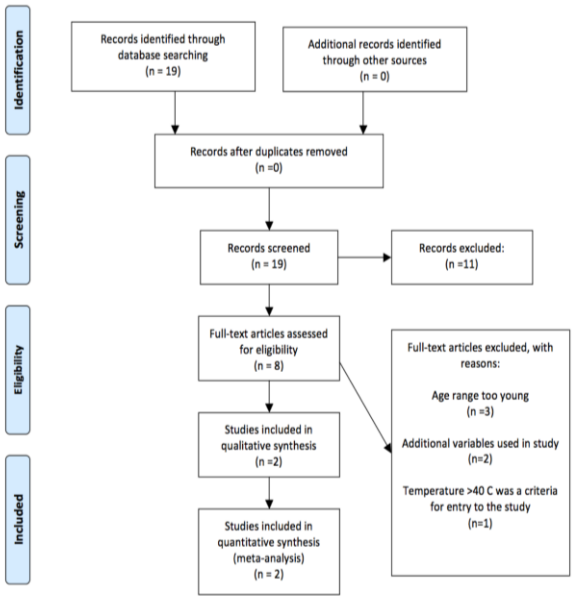
Upon evaluation of eligibility, six articles were excluded. Three articles were excluded because they involved children outside the desired age range. An additional two articles were eliminated because they focused on additional variables outside of the defined clinical question.

Lastly, one article required a temperature of 40° C for inclusion of the study, which limited the temperature variable under analysis. Thus, two qualifying articles remained and were selected to evaluate temperature versus WBC count in the detection of bacteremia in children. See Figure 1 for the PRISMA flow diagram.

Given the temperature and WBC count cut-offs, sensitivity and specificity were collected or calculated from the data in the individual papers. The sensitivity and specificity were used to construct 2x2 tables to calculate negative and positive predictive values (NPV and PPV), determine discriminate ability, and likelihood ratios (LR) for each cut-off value. Bayes' theorem

was applied to pretest probability and likelihood ratios to determine post-test probabilities of disease for defined cut-off values of temperature and WBC count. This was illustrated by the use of nomograms.[6] The defined cut-off values were established by having the highest sensitivity and specificity from each article.

Figure 1. PRISMA Flow Diagram



RESULTS

Study 1

Temperature and Total White Blood Cell Count as Indicators of Bacteremia. Jaffe and Fleisher [7]

Objective: To quantify the accuracy of rectal temperature and total white blood cell count as indicators of bacteremia.

Design:

Information was collected for a retrospective review using a previous study's data that was assessing the efficacy of oral antibiotics in the treatment of bacteremia. The patients were children between 3-36 months with a rectal temperature of greater than 39°C presenting to the emergency department of Children's Hospital of Philadelphia and the Children's Memorial Hospital in Chicago between January 1982 to July 1984 qualified for enrollment. All children who were eligible had a history and physical exam conducted by a pediatric house officer and an attending ER physician. Those who met exclusion criteria were removed from eligibility. See Table 2 for the exclusion criteria utilized.

Table 2. Patient Exclusion Criteria

Jaffe and Fleisher Study:
Specific viral infection (i.e. varicella)
Child was known to have chronic illness or immune-deficiency
Antibiotic use within the prior 48 hours
Focal infection requiring immediate antibiotic therapy (i.e. otitis media)
"Toxic" appearing child requiring immediate admission to the hospital
DTaP vaccine within the prior 48 hours

Each enrolled child had a temperature taken and blood drawn for a CBC and BC. Other studies were conducted as indicated by the child's symptoms, such as chest x-ray, UA, urine culture, and CSF studies.

Temperature and WBC count were divided into increments. For temperature, the cut-off points were 39.5°, 40.0°, 40.5°, and 41.0°C. The cut-off points for WBC were 5 000, 10 000, 15 000, 20 000, and 25 000 /mm^3. Receiver-operating-characteristic (ROC) curves were established using the defined cut-off points for temperature and WBC, both independently and combined.

Results:

Nine hundred and fifty-five children were included and completed the study; 57% were boys and 86% were African American (A.A.). The majority of participants received medical assistance as payment for cooperation in the study. Data for WBC count was only available for 885 of the 955 participants. Averages of temperature, WBC count, and age were calculated using the entire sample and those found to have bacteremia; See Table 3 for the data. Among the sample, twenty-seven children were found to have bacteremia. The major source of bacteremia was from S. pneumoniae, with only a few sprouted from H. influenza type b and Salmonella.

The balance between high sensitivity and low false-positive rates made it impossible to determine a suitable temperature cut-off for bacteremia. With each incremental increase, sensitivity rose along with false-positive rates. For example, at a temperature cut-off of 40°C, sensitivity was 52% and false-positive rate was 36%.

On the other hand, WBC offered much more insight to the presence of bacteremia. Contrary to temperature, WBC incremental increases lowered false-positive rates more than the effect on sensitivity. For example, a WBC count of 10 000 allowed for 92% sensitivity and 57% false positive rate.

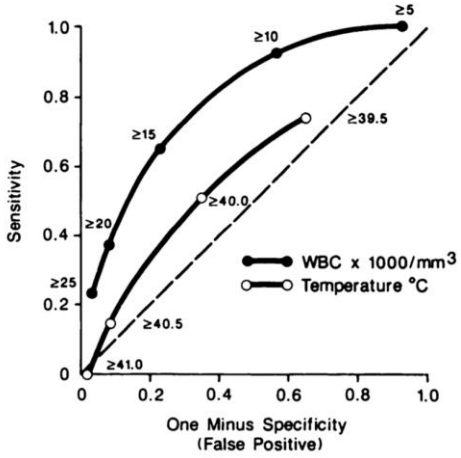


Figure 2. ROC Curves for Temperature and WBC count[7]

Thus, they concluded that with the use of ROC curves, WBC provided more accurate diagnostic information compared to temperature as predictors of bacteremia. See Figure 2 for the ROC curve of temperature and WBC count that was used in the study.

Table 3. Average Values in Total Sample and Bacteremia Positive Patients

	Mean Temperature	Mean WBC	Mean Age
Total sample	39.7°C	12 000/ mm^3	16.7 months
Bacteremia positive	39.9°C	20 488/ mm^3	18 months

Critique:

A large disadvantage to this study was the fact that only 27 out of 955 children had bacteremia. This makes it very difficult to compare data between children with and without bacteremia. The small sample of children with bacteremia makes it more difficult to determine the accuracy of the diagnostic tests utilized.

On another note, the study mentioned that WBC information was only available on 885 of the 955 participants. They failed to explain why this was the case and failed to mention whether BC data was also affected or not. There was no WBC information for one of the 27 patients with bacteremia; therefore, pertinent WBC data was not included in the bacteremia data that was analyzed. With such a small sample of children with bacteremia, this additional data would have been beneficial. Furthermore, only one temperature cut-off point was discussed and no data was provided for the remainder of the three temperature points. The lack of data was likely due to the fact the study was of a retrospective design. This type of study relies heavily on the accuracy at which the information was obtained, and therefore, a large amount of data can be missed.[8]

Another error of the study was that the sample of patients was majority African American. As a result, the sample was not diverse or likely representative of the population. Moreover, participants were compensated for participation. Unfortunately, many of those who are impoverished are also illiterate, and therefore cannot understand the risk associated with a study but are coerced by monetary gains.[9] Thus, the study took advantage of a vulnerable population and limited access to a representative sample of the population. Lastly, the study was an older study, and unfortunately, there is no recent research focusing on these parameters specifically. This is likely because new tests have been developed which have the potential to offer more information on the illness, such as c-reactive protein (CRP). [10]

Study 2

Predictors of Bacteremia in Febrile Children 3 to 36 months of Age. Isaacman et al [11]

Objective: To develop an improved model for predicting bacteremia in febrile children 3-36 months.

Design:

The study was a retrospective review of all febrile children 3-36 months old who came into the emergency room of Children's Hospital of The King's Daughters in Norfolk, VA, between December 1995 – December 1996 and had a CBC and blood culture drawn. A second set of patients was obtained from December 1996 - August 1997, in which each patient had a CBC and blood culture drawn and grew a pathogen in the culture. Two culture negative patients were randomly selected for each bacteremic patient in the second set. Table 4 outlines exclusion criteria.

Table 4. Patient Exclusion Criteria

Isaacman et al. Study:
Chronic steroid therapy
Known immunodeficiency including: sickle cell, down syndrome, immunoglobulin deficiency
Antibiotic therapy within 48 hours of presentation

Records were obtained by a monthly computer query of the hospital's

microbiology data of all blood culture ordered in the ED. Children were admitted to the hospital,l and a CBC and blood culture were obtained based on the discretion of the attending physician. Each child presenting to the emergency department had the following information collected: age, presenting temperature in centigrade, presence of focal bacterial infection, type of differential WBC count and the CBC and blood culture results. True pathogens in blood cultures included: S. Pneumoniae, H. flu, N. Meningitidis, Group A strep and Salmonella. Contaminant bacteria included: S. epidermis, P. acnes and diptheroids.

The main goal of the study was to develop a model for predicting bacteremia using a combination of different variables. The study first analyzed individual risk factors for bacteremia between the patients with and without bacteremia including: WBC count, PMN (polymorphonuclear leukocytes) %, granulocyte %, band count %, ANC (absolute neutrophil count), weight (kg), age and gender (% female). P-values for the variables were obtained by using a 2-sample Wilcoxon rank-sum test. A Wilcoxon rank-sum test is a non-parametric test used to compare two population sets. The test looks at two groups of data and calculates the difference between a set of data and analyzes the differences between the two. This test is used when data from populations does not follow a normal distribution curve[12]. The authors then proceeded to develop 2 different models for predicting bacteremia. They compared these models to individual predictors using ROC curves and the area under the curves (AUC).

The final model chosen was then tested against individual variables with a validation dataset from a different large-center study. Sensitivity and specificity of individual risk factors were compared between this study's data set and the validation set. Cut-off points for bacteremia risk factors were determined by maximizing sensitivity and specificity through a linear regression model. Odds ratios for bacteremia in high versus low values for each variable were then calculated and compared. This review will be focusing on the individual variables of temperature and white blood cell count.

Table 5. Individual Variables Significantly Associated with Bacteremia

Risk Factor	Median value in Patients with Bacteremia	Median value in patients without Bacteremia	P Value
WBC x1000 cells/mm^3	18.2	10.6	<0.0001
PMN	66.5	52.0	<0.0001
ANC x1000 cells/mm^3	13.0	6.0	<0.0001
Band count %	5.0	2.0	0.001

Results:

Six hundred and thirty-three patients met study criteria with the average age of the patient being 15.8 months with an average temperature of 39.1°C; there were 46 positive cultures. Organisms included S. pneumonia (39), N. meningitides (1), S. pyogenes (1), Salmonella (1), E. coli (1), A. baumannii and S. aureus (2). Temperature, band count, PMN, ANC, WBC and

gender were all found to be statistically significant regarding bacteremia. See Table 5 for median values for subjects with and without bacteremia and associated P-values.

Table 6. Temperature and WBC Count Cut-off Points

Variable	Cut-point	Sensitivity	Specificity	Odd's Ratio
WBC x1000 cells/mm^3	14.3	0.76	0.75	9.50
Temp *C	39.6	0.57	0.59	1.87

Two combination models were developed through linear regression and compared to each individual predictor of bacteremia individually through a ROC curve analysis (This data is not pertinent to this review as it involves variables other than temperature and WBC count). Lab cut off points for temperature and WBC count were established based on the values that maximized sensitivity and specificity of the study data. See Table 6 for cut-off points for temperature and white blood cell count.

Study Critique:

The strengths of the paper included the use of blood cultures to confirm the presence of bacteremia in each of the study participants, as well as, the analysis of individual variables in the prediction of bacteremia. A major weakness of the paper was the non-uniformity in which the subjects for the retrospective review were acquired. It was up to individual physicians to decide to initiate a workup, which lead to variable patients with different entry criteria. The retrospective nature of the paper itself is also a major downfall. Only association with specific cut-off values for temperature and WBC can be drawn from bacteremic vs. non-bacteremic patients rather than definitive evidence that bacteremia causes WBC count and temperature to be above a certain value.

There was also variation in how the initial patients were acquired as compared to the second set of patients. Different entry criteria was used for each set. The second set of patients was acquired by selecting patients with bacteremia and then choosing two non-bacteremic patients per bacteremic patient. Thus, the sample was not randomized and included selection bias from the start of the study. Out of the 633 patients in the study, only 46 had bacteremia and that was including the validation set in which bacteremic patients were specifically picked. The data collected in the study can, therefore, not be used to predict the realistic incidence of disease in the patient population.

The paper itself does not discuss different sensitivities and specificities for temperature and WBC count at different cut-off points. They simply established a cut-off point for each that maximized the sensitivity and specificity for their data, which may or may not be applicable to the rest of the population. Finally, the main purpose of the Isaacman et al. study was not to directly compare temperature to WBC count as is the aim of this review. Many elements of the paper were omitted as a part of this analysis due to their irrelevance to the clinical question. Despite these shortcomings, the paper was included in the review due to the very low volume of recent research directly comparing temperature and WBC count.

DISCUSSION

Bacteremia in infants 3 - 36 months is a complex and difficult condition to develop concrete, objective guidelines for diagnosis. While the Hib and pneumococcal vaccines have decreased the number of cases of bacteremia per year in the U.S. since 1985, this only makes developing clear guidelines more difficult since physicians may not see bacteremia often enough to devise clear cutoffs with clinically relevant sensitivities and specificities. In addition to the decreased incidence of bacteremia, infants are especially difficult to diagnose due to the wide variation in presenting symptoms and laboratory values. A variety of laboratory tests are available to assist in the diagnosis of bacteremia including WBC count, band count and the newly investigated procalcitonin. This review will focus on comparing the use of white blood cell count to temperature in correctly predicting bacteremia and investigate the utility of the newly researched marker procalcitonin.

Table 7. Overview of Studies

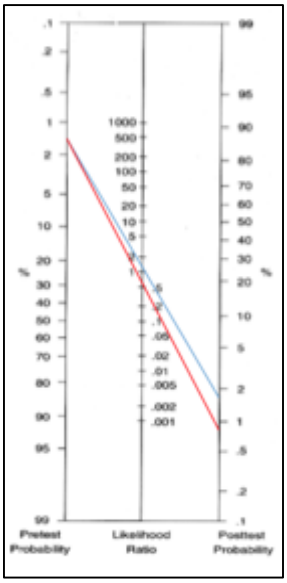
	Jaffe and Fleisher	Isaacman et al.
Sample Size	955	633
Population	• January 1982 to July 1984 • Emergency department of Children's Hospital of Philadelphia and the Children's Memorial Hospital in Chicago • Children 3-36 months old • Rectal temperature of ≥ 39°C	• December 1995 to August 1997 • Emergency department of Children's Hospital of The King's Daughters in Norfolk, VA • Children 3-36 months old • Febrile with CBC and blood culture drawn
Demographics	57% boys, 86% African American	56% male, 63% African American
Reference Standard	Blood Culture	Blood Culture
Positive Disease	27 patients with bacteremia	46 patients with bacteremia
Data	• Best WBC increment was 10,000: 92% sensitive and 57% false positive • Temperature increment of 40°C: 52% sensitive and 36% false positive rate.	• WBC cut off determined to be 14,300: 76% sensitive and 75% specific. • Temperature cut off determined to be 39.6°C: 57% sensitive and 59% specific.

An overview of the studies is provided in Table 7. Both studies were retrospective reviews. The study by Jaffe and Fleisher used information gathered as part of a different clinical trial to measure the efficacy of antibiotic treatment, while the study by Isaacman et al. reviewed medical records collected over a specified period of time. Both studies had a very small number of true positives for bacteremia, but this is consistent with the low incidence of bacteremia in the U.S. with the development of the Hib vaccine. The studies were limited in their ability to be objective due to the variability of providers responsible for admission to the hospital for evaluation. Another significant drawback of the two studies in the review is their age. The study

by Jaffe and Fleisher was from 1991 and the study by Isaacman et al. was from 2000. There are many more recent articles studying newer laboratory indicators for bacteremia, such as procalcitonin but none directly comparing temperature and WBC count. Most articles use a temperature cut-off as the entry criteria and then evaluate laboratory data within that specific patient population. Although the new indicators for bacteremia are promising, there is a clear need for research of temperature and WBC count since these two measures are commonly used for first line decision-making in the diagnosis and treatment in bacteremia.

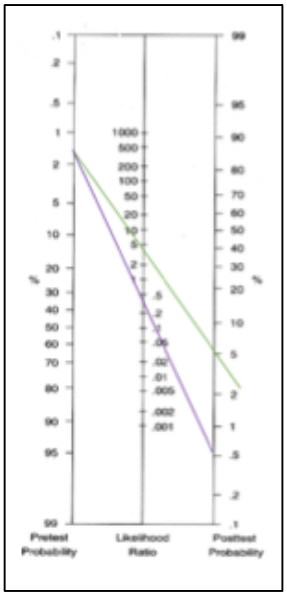
An overview of results of each study is provided in Table 8. Both studies only included data on one temperature cut-off, Jaffe, >40°C and Isaacman et al. >39.6°C. Both cut-off points show poor sensitivity and specificity with each temperature cutoff having a discriminate ability of 58%. A nomogram was created for the temperature cut-off for the Isaacman et al study and is shown in Figure 3.

Figure 3. Nomogram for Temperature cut off of 39.6°C.
Key: Blue = positive LR, Red = negative LR



The prevalence of bacteremia in children 3 - 36 months in the general population is 1.6%.[1] Using 1.6% as the pretest probability, the positive and negative likelihood ratios were plotted on a nomogram to determine the post-test probability using the 39.6°C cut-off point. The posttest probability of a patient with a fever greater than 39.6°C having bacteremia is 1.9%, raising the pretest probability by only 0.3%. The posttest probability of a patient with a fever less than 39.6°C having bacteremia is 0.9%, decreasing the pretest probability by 1.0%. Clearly, a temperature threshold of 39.6°C is not a suitable measure to determine if a pediatric patient does or does not have bacteremia, even if Isaacman et al. determined that this temperature had the best sensitivity and specificity.

Figure 4. Nomogram of using for WBC count >14,300 cells/mm^3
Key: Green = positive LR, purple = negative LR



For WBC count, Jaffe and Fleisher examined five potential cut-off values ranging from 5 000 – 25 000 WBC/mm^3. The best cut-off value was determined to be 15 000 WBC/mm^3, with a discriminative ability of 71%. As the WBC count cut-off increases past 15 000, the more false negatives are expected as the negative likelihood ratio increases. Isaacman et al. determined 14 300/mm^3 as the best cut-off with a discriminative ability of 76%. As discriminative ability is equal to area under the curve, the cut-off point of 14 300 WBC/mm^3 is the only clinically useful marker discovered in the review.

Again, using 1.6% as the pretest probability, the positive and negative likelihood ratios were plotted on a nomogram to determine the posttest probability using a WBC cut-off point of 14 300/mm^3, as determined by Isaacman et al. The posttest probability of a patient with a WBC count greater than 14 300 having bacteremia is 5%, raising the pretest probability by 3.4%. The posttest probability of a patient with a WBC count less than 14 300 having bacteremia is 0.6%,

decreasing the pretest probability by 1%. Although WBC count shows a slightly better positive and negative post-test probability, a 3.4% increase is not clinically useful in guiding treatment of a bacteremic child. The nomogram for WBC is shown in Figure 4.

Table 8. Overview of Results

	Sensitivity (95% CI)	**Specificity (95% CI)**	**+LR**	**-LR**	**PPV**	**NPV**	**Study**
Temperature:							
>40°C	52%	64%	1.44	0.75	0.042	0.98	**Jaffe**
> 39.6 °C	57%	59%	1.39	0.73	0.098	0.95	**Isaacman et al**
WBC count:							
>5,000	100%	7%	1.08	0	0.032	1	**Jaffe**
>10,000	92%	43%	1.61	0.19	0.047	0.99	
>15,000	65%	77%	2.83	0.45	0.079	0.99	
>20,000	38%	92%	4.75	0.67	0.127	0.98	
>25,000	23%	97%	7.67	0.79	0.188	0.98	
>14,300	76%	76%	3.17	0.32	0.20	0.98	**Isaacman et al**

A major factor impacting the results of this review was the small sample of bacteremia positive patients and the very low prevalence of bacteremia in the population of infants 3-36 months old. Prevalence greatly impacted the positive and negative predictive values of WBC count and temperature in both studies. The highest positive predictive value obtained for WBC count was 20% and 9.8% for temperature. Therefore, the probability of bacteremia for each cut-off value was 20% and 9.8%, respectively. Negative predictive values were similarly impacted with each cut-off value of temperature and WBC count, having a NPV of over 95%. Essentially, both tests are better at correctly predicting the absence of bacteremia, rather than it's presence.

A promising new area of research for laboratory indicators of bacteremia in children 3-36 months is procalcitonin (PCT). Procalcitonin is normally produced exclusively by C-cells in the thyroid during normal body function at a very low level, <20pg/mL. Soon after the initiation of a bacterial infection, several cytokines are released that stimulate the production of PCT in tissues throughout the body. This causes an exponential increase in serum PCT within the first four hours of a bacterial infection and up to a 10,000 times increase in the first 24 hours. PCT levels have been shown to positively correlate to severity of illness in adults.[13]

A recent meta-analysis of eight studies investigating the use of PCT, CRP, and WBC count in febrile infants less than 36 months showed promising results for the use of

procalcitonin. Using a cut off value of greater than 0.5 ng/mL, a sensitivity of 83% and specificity of 69% were achieved in predicting a serious bacterial infection such as bacteremia. The authors note that further research needs to be done to see how to best combine PCT with other indicators of serious bacterial illness to increase accuracy of diagnosis.[14]

APPLICATION TO THE PATIENT

Fortunately for the provider in our case, the child presented with a fever and appeared ill which would immediately make a practitioner suspicious of bacteremia. However, many children are brought to an ER for a complaint of fever and appear well. The difficulty bestowed on the provider is determining whether the child has bacteremia or another illness. Unfortunately, the gold standard for diagnosing bacteremia is a blood culture which takes 24-48 hours to complete; thus, practitioners are pressed for another method of diagnosing the illness. There is no consensus on the best approach to this issue, and it is largely provider preference. This can cause large variations in diagnosis and empiric treatment of the disease. The lack of protocol needs to be addressed, and one should be established to allow for more accurate diagnosis and treatment of the disease, especially given its life-threatening complications.

On another note, it is important to consider cost. In some situations, it may be more effective to empirically treat based on a clinical presentation and wait for blood culture results, rather than order an impractical wide-range list of tests.

CONCLUSION

Among pediatric patients between the ages of 3-36 months, does temperature as compared to white blood cell count correctly predict bacteremia?

Temperature and WBC counts are easy, quick to obtain, and are associated with little to no risk. They help to offer practitioners guidance on the diagnosis of bacteremia, while blood culture results are pending. Ultimately, WBC is a better tool than temperature in predicting bacteremia. However, neither temperature nor WBC is very good at predicting the disease. More research needs to be done to determine alternative tests that may offer better sensitivity and specificity at detecting the life-threatening infection. Laboratory tests that hold potential to identify bacteremia include CRP, procalcitonin, and stool studies. For instance, the organism responsible for being the second most common cause of pediatric bacteremia is Salmonella, and stool studies are a suitable method for its identification.[10] The critical element is the turn around time on these tests and accuracy of diagnosing bacteremia. Moreover, one test alone will likely never offer much benefit, but rather an algorithm combining clinical picture and multiple labs will assist in a proper diagnosis. Furthermore, unless further research is conducted, bacteremia will continue to be a leading cause of morbidity and mortality among the pediatric population.

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References

1. Lee G, Harper M. Risk of bacteremia for febrile young children in the Post–Haemophilus influenzae type b era. *Archives of Pediatric Adolescent Medicine*. 1998;152:6240628. http://archpedi.jamanetwork.com/article.aspx?articleid=189702.
2. Ten leading causes of death and injury. Centers for Disease Control and Prevention Web site. http://www.cdc.gov/injury/wisqars/leadingcauses.html. Updated 2013.
3. Thompson GC, Macias CG. Recognition and management of sepsis in children in the ED. *Journal of Emergency Medicine*. 2015;49(4):391-399. http://www.medscape.com/viewarticle/853837?nlid=91855_2561&src=wnl_edit_medp_emed&uac=114398FT&spon=45&impID=900110&faf=1.
4. Goldstein, Giroir, Randolph. International pediatric sepsis consensus conference: Definitions for sepsis and organ dysfunction in pediatrics. *Pediatric Critical Care Medicine*. 2005;6(1):2-8. http://content.wkhealth.com/linkback/openurl?sid=WKPTLP:landingpage&an=00130478-200501000-00002.
5. Bonsu, Bema K; ChB, MB; Harper, Marvin B. Identifying febrile young infants with bacteremia: Is the peripheral white blood cell count an accurate screen? *Annals of Emergency Medicine*. 2003;42(2):216-225. http://www.sciencedirect.com/science/article/pii/S0196064403004414.
6. Riegelman RK. *Studying A study and testing a test: Reading evidence-based health research.* 6th ed. Philadelphia, PA: Wolters Kluwer/Lippincott Williams & Wilkins; 2013.
7. Jaffe DM, Fleisher GR. Temperature and total white blood cell count as indicators of bacteremia. *PEDIATRICS*. 1991;87(5):670-674. http://www.ncbi.nlm.nih.gov/pubmed/2020512.
8. Anthonisen NR. Retrospective studies. Canadian Respiratory Journal : Journal of the Canadian Thoracic Society Web site. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2734436/. Updated 2009. Accessed February 11, 2016.
9. Pandya M, Desai C. Compensation in clinical research: The debate continues. Perspectives in Clinical Research Web site. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3601710/. Updated 2013. Accessed January 31, 2016.
10. Bennett NJ, Domachowske J, Holland BJ. Bacteremia workup: Laboratory studies, imaging studies, procedures. Medscape Web site. http://emedicine.medscape.com/article/961169-workup. Updated 2015. Accessed November 15, 2015.
11. 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(5):977-982.

http://www.ncbi.nlm.nih.gov/pubmed/11061763.
12. Wilcoxon test definition. Investopedia Web site. http://www.investopedia.com/terms/w/wilcoxon-test.asp. Accessed March 10, 2016
13. Pierce, Bigham, Giuliano. Use of procalcitonin for the prediction and treatment of acute bacterial infection in children. *Current Opinion in Pediatrics*. 2014;26(3):292-298. http://content.wkhealth.com/linkback/openurl?sid=WKPTLP:landingpage&an=00008480-201406000-00006.
14. Yo, Hsieh, Lee, et al. Comparison of the test characteristics of procalcitonin to C-reactive protein and leukocytosis for the detection of serious bacterial infections in children presenting with fever without source: A systematic review and meta-analysis. *Annals of Emergency Medicine*. 2012;60(5):591-600. http://linkinghub.elsevier.com/retrieve/pii/S0196064412005203http://api.elsevier.com/content/article/PII:S0196064412005203?httpAccept=text/xmlhttp://api.elsevier.com/content/article/PII:S0196064412005203?httpAccept=text/plain.