# Strategies for diagnosis and treatment of children at risk for occult bacteremia: Clinical effectiveness and cost-effectiveness

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**Decision analysis was used to evaluate the probable health benefits, complications, and costs of six management strategies for febrile children at risk for occult bacteremia. The strategy that combined blood culture with empiric oral antibiotic treatment for all patients was predicted to prevent the highest number of major infections and to have the lowest cost per major infection prevented. The stragegy that combined a leukocyte count and blood culture for all patients, followed by empiric antibiotic treatment for those with leukocyte count $\geq$10,000/mm$^3$, had almost equal cost and clinical effectiveness and avoided many antibiotic complications. Culture of blood specimens from all patients and no empiric treatment constituted the third most clinically effective intervention but was the least cost-effective in this model. Giving a 2-day oral course of amoxicillin without testing had the lowest average cost per febrile patient but was the least clinically effective intervention. However, the low degree of effectiveness of empiric treatment alone was based on the assumption that oral amoxicillin therapy was only 20% effective in preventing major infections after bacteremia. At higher estimates of effectiveness, treatment alone became a more viable strategy. We conclude that approaches which combine blood culture with empiric antibiotic treatment are the most clinically effective and the most cost-effective strategies for children at risk for occult bacteremia.**
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Between 3% and 15% of children aged 3 to 36 months with temperatures $\geq$39.0 °C have bacteremic infections. However, children with bacteremia but without focal infections often appear clinically identical to children with viral illnesses.[1,2] Occult bacteremia may lead to serious focal complications including meningitis, pneumonia, and septic arthritis.[3-7] Timely diagnosis and treatment of occult bacteremia has the potential to prevent infectious sequelae but may entail the discomforts and costs of blood tests, hospitalization, and complications of antibiotic treatment.

**See related articles, pp. 11 and 67.**

No consensus exists on the optimal management of the febrile child without an obvious focus of bacterial infection. Culture of a blood specimen drawn at the initial visit does not yield results until at least 24 hours later. In the interim, children may develop focal infections or may be lost to fol-

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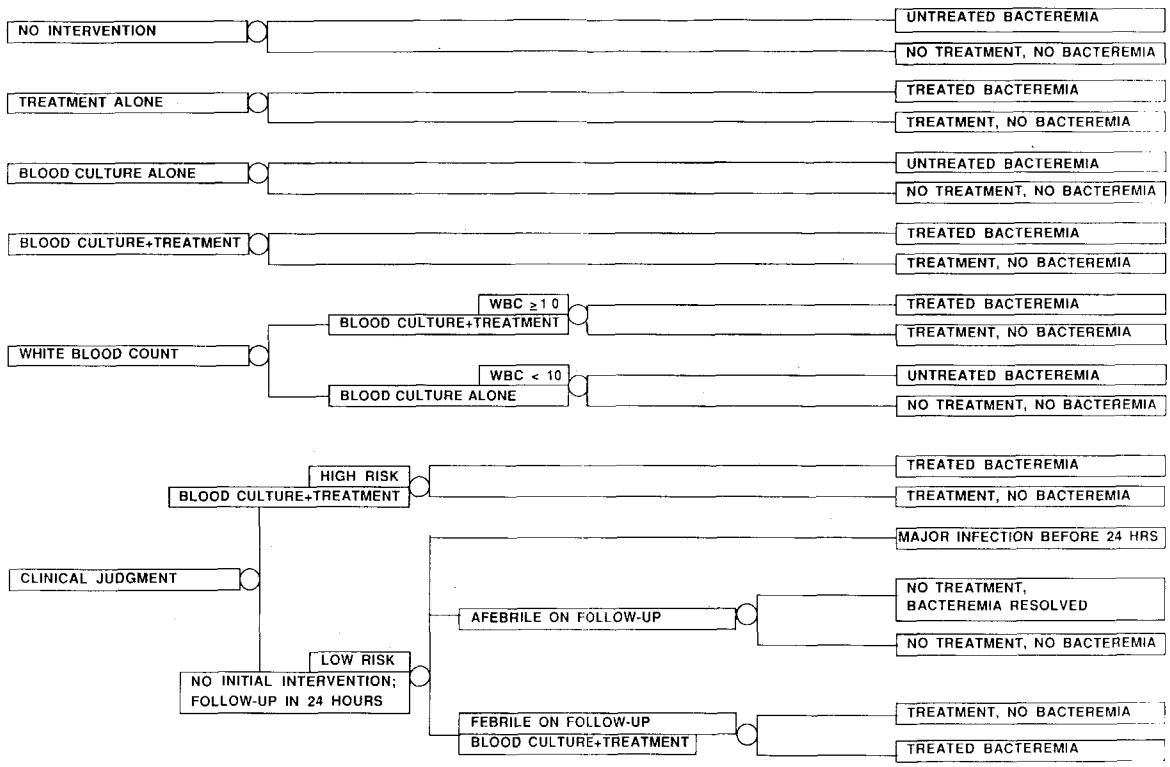


**Fig. 1.** Decision tree of alternative diagnostic and therapeutic options, resulting in intermediate patient outcomes. *LC,* Leukocyte count.

low-up.[8] Studies evaluating the empiric treatment of febrile children with intramuscular or oral antibiotic therapy have yielded mixed results,[9-11] and empiric antibiotic use exposes many children to avoidable risks of therapy. Clinical judgment or the leukocyte count may help to distinguish patients at high risk for occult bacteremia from those at low risk, but neither method can discriminate with both optimal sensitivity and optimal specificity. A previous analysis[12] evaluated the utility of obtaining blood culture specimens from children at risk for occult bacteremia, but the costs and benefits of the full spectrum of possible strategies have not been assessed in detail.

The objective of this study was to evaluate the probable health benefits, complications, and costs of alternative management strategies in febrile children without an apparent source of infection. Our analysis included the options of performing a leukocyte count and of giving empiric antibiotic treatment on the initial visit. It also took into account the imperfect sensitivity of blood culture and the imperfect effectiveness of follow-up hospitalization in preventing the complications of occult bacteremia related to the delay inherent in obtaining blood culture results.

## METHODS

This study used decision analysis, a quantitative modeling technique that evaluates alternative management options for clinical problems. A decision tree was constructed to outline alternative decision options and chance events. The probability of each chance event was noted and an outcome measure was assigned for each branch of the tree. The value of each decision option was determined by multiplying the outcome measure for each branch by the probability of its occurrence and summing the values for all branches following from a decision point. Because some degree of uncertainty surrounds all probabilities and outcome measures, sensitivity analyses were performed to determine the effects of variation in probabilities and outcome values on alternative strategies.

**Structure of the decision model.** This analysis compared six strategies for the diagnosis and treatment of febrile children aged 3 to 36 months without an obvious focus of bacterial infection (Fig. 1):

1. *No intervention:* Patients would not receive diagnostic testing or antibiotic administration on the initial visit.
2. *Treatment alone:* All patients would receive a prescription for a 2-day course of oral amoxicillin therapy.
3. *Blood culture alone:* All patients would have a blood specimen cultured. Patients with positive blood cultures would receive follow-up management; patients with negative blood cultures would receive no further management unless a major infection developed.
4. *Blood culture plus treatment:* All patients would have

a blood specimen cultured and would receive a prescription for a 2-day oral course of amoxicillin therapy. Patients with positive blood cultures would receive follow-up management; patients with negative blood cultures would receive no further management unless a major infection developed.

5. *Leukocyte count:* All patients would have a leukocyte count performed. Patients with a count $\geq 10{,}000/mm^3$ would receive a prescription for a 2-day oral course of amoxicillin therapy. Patients with a count $<10{,}000/mm^3$ would not receive antibiotic treatment. All patients with positive blood cultures would receive follow-up management.

6. *Clinical judgment:* A clinical assessment would be performed for all patients. Patients judged at high risk for occult bacteremia would have a blood specimen drawn and would receive treatment on the initial visit. Patients judged at low risk would receive no initial intervention but would be contacted by telephone 24 to 48 hours after the initial visit. Patients who were afebrile on follow-up would have no further intervention. Patients who were persistently febrile would have a blood specimen drawn and would receive treatment on a follow-up visit. Those with positive blood cultures would receive follow-up management.

Follow-up management of patients with positive blood cultures in this model was assumed to depend on the organism causing bacteremia. *Streptococcus pneumoniae* accounts for approximately 80% of occult bacteremias.[4, 10, 13, 14] Unlike other bacteremias, pneumococcal bacteremia usually resolves without treatment or sequelae. In this model, patients with pneumococcal bacteremia who were afebrile on follow-up would not receive further testing or treatment. Patients who were febrile on follow-up would be hospitalized for intravenous ampicillin therapy and would have one or more repeat blood cultures. Patients with pneumococcal bacteremia would remain hospitalized until one blood culture was negative after 48 hours of incubation, and would then be discharged to complete a 10-day course of oral amoxicillin therapy.

Bacteremias caused by *Haemophilus influenzae* and other organisms would receive more aggressive management.[6, 7, 15] Patients with blood cultures positive for *H. influenzae* would be hospitalized for 7 days to receive intravenous ampicillin and chloramphenicol therapy. Because *Neisseria meningitidis* and *Salmonella* species account for less than 5% of all bacteremias, this model assumed that they were managed identically to *H. influenzae* bacteremia.

A single blood culture has imperfect sensitivity in the detection of bacteremia.[16, 17] In this model, patients with negative blood cultures would not receive follow-up management, but a proportion of these patients would have undetected bacteremia and would be at risk for infectious complications. Conversely, blood culture was assumed to have perfect specificity (i.e., a positive, noncontaminated blood culture always signified bacteremia).

The decision tree's terminal branches that end with bacteremia were extended to include an outcome: no sequelae or major infection. In this analysis, meningitis was used as the model of a major infection and entailed a 10-day hospitalization. Other major infections, including cellulitis, epiglottitis, and pyogenic arthritis, were treated identically to meningitis in this model, although this is a simplification of the actual situation.

The decision tree's terminal branches that end with antibiotic treatment were extended to include an outcome: no complications, rash, or anaphylaxis. Outpatients with an antibiotic-associated rash were assumed to require one follow-up outpatient visit. Outpatients with anaphylaxis would require an extended emergency department visit and a brief admission to the hospital. Inpatients with antibiotic complications would receive appropriate care, but the duration and cost of hospitalization would not change. The analysis did not consider long-term sequelae of meningitis (e.g., deafness or death) or anaphylaxis.

**Data and assumptions: Test performance, probabilities, and treatment effectiveness** (Table I). The model used data from the literature and from a 1987 prospective study of occult bacteremia in 955 children.[9] The probability of occult bacteremia in a febrile child aged 3 to 36 months without an obvious focus of bacterial infection was estimated at 3%. Studies using duplicate blood cultures have estimated the sensitivity of a single blood culture in detecting bacteremia as 45% to 70%.[16-18] In this analysis the sensitivity of a single blood culture was set at 70% and the specificity at 100%.

Our model used the leukocyte count's test performance characteristics from the largest available prospective study of occult bacteremia.[9] Receiver operating curve analysis suggested that a criterion of $\geq 10{,}000/mm^3$ predicts bacteremia with a sensitivity of 92% and a specificity of 43%, while classifying 42% of the febrile children as at low risk.[19]

We used an average of the estimates from two studies that evaluated the accuracy of clinical judgment to predict occult bacteremia.[20, 21] The model assumed a sensitivity of 43% and a specificity of 80% for clinical judgment. Other articles have reported a higher sensitivity for clinical scores or other assessments, but these studies included patients with focal symptoms.[22, 23]

The probabilities of major focal infection after occult bacteremia differ for *S. pneumoniae* and *H. influenzae* bacteremias, and were estimated on the basis of previous studies.[5, 6, 9, 11, 14]

Because major focal infections develop before blood culture results are available for many patients with occult bacteremia, we used a baseline figure of 50% for the applied effectiveness of antibiotics administered intravenously to prevent major focal infections after positive blood culture results are obtained.[8] The effectiveness of oral or intramus-

**Table I.** Assumptions used in calculations

| | Baseline analysis | Sensitivity analysis |
|---|---|---|
| *Initial management of febrile child* | | |
| Blood culture | | |
| Sensitivity | 0.70 | 0-1.00 |
| Specificity | 1.00 | 0-1.00 |
| Leukocyte count ≥10,000/mm³ | | |
| Sensitivity | 0.92 | 0.65* |
| Specificity | 0.43 | 0.77* |
| Clinical judgment | | |
| Sensitivity | 0.43 | 0-1.00 |
| Specificity | 0.80 | 0-1.00 |
| Prevalence of occult bacteremia | 0.03 | 0-0.10 |
| Proportion of bacteremic patients with specific organism | | |
| *S. pneumoniae* | 0.80 | |
| *H. influenzae* | 0.20 | |
| *Probabilities of further complications* | | |
| After untreated bacteremia with *S. pneumoniae* | | |
| Fever on follow-up visit | 0.50 | 0-100 |
| Major infection | 0.15 | 0-100 |
| After untreated bacteremia with *H. influenzae* | | |
| Major infection | 0.40 | 0-1.00 |
| After intravenous ampicillin | | |
| Rash | 0.06 | |
| Anaphylaxis | 0.0004 | |
| After oral amoxicillin | | |
| Rash | 0.04 | |
| Anaphylaxis | 0.00004 | |
| *Effectiveness of antibiotic treatment* | | |
| Oral amoxicillin on initial visit | 0.20 | 0-1.00 |
| Intravenous ampicillin ± chloramphenicol begun on follow-up hospitalization after positive blood culture results | 0.50 | 0-1.00 |

*Sensitivity and specificity of a leukocyte count ≥15,000/mm³.

cular antibiotic therapy given empirically at the initial outpatient visit (initial treatment) to prevent major focal complications has not been well established.[9-11] The baseline analysis for this model assumed that for all patients with bacteremia, initial treatment reduced the incidence of subsequent major infection by 20%, and in patients with pneumococcal bacteremia the initial treatment reduced the incidence of fever at the follow-up visit by 70%.

The clinical judgment strategy assumed that all patients who needed follow-up received telephone contact or an outpatient visit 24 to 48 hours after the initial visit. By this time, 50% of patients with bacteremia who were destined to have major focal complications would already have acquired such infections. Of the remaining patients, 50% of those with *S. pneumoniae* bacteremia and 20% of those with *H. influenzae* bacteremia were assumed to have recovered spontaneously and become afebrile by the follow-up contact at 24 to 48 hours. The model assumed that 70% of patients with viral infections have become afebrile by the time of follow-up contact.[24]

**Cost-effectiveness analysis.** The baseline analysis used the provider's costs based on 1989 figures from the Children's Hospital of Philadelphia (CHOP). The estimated costs of blood culture ($60) and leukocyte count ($3) were based on consultations with laboratory administrators. The cost of oral amoxicillin ($5) was taken from the *Drug Topics Red Book*.[25] The costs of initial and follow-up outpatient visits ($46), and of extended emergency department visits for acute care ($210), were estimated on the basis of a fixed percentage of charges at CHOP. The estimated costs of hospitalization were based on a fixed percentage of the actual charges at CHOP for 15 cases of meningitis (average cost, $5247), 5 cases of pneumococcal bacteremia ($1096), 3 cases of *H. influenzae* bacteremia ($3029), and 2 cases of anaphylaxis ($3020). The analysis did not include the costs of long-term follow-up for patients with sequelae of meningitis or anaphylactic antibiotic reactions.

Outcomes for each strategy were expressed as the ratio of the cost of management (including outpatient visits, testing, treatment, and hospitalization) to the number of cases of major infection prevented. The numerator was expressed in terms of the dollars expended, cases of severe penicillin allergy, or hospitalizations incurred. The denominator was expressed in terms of the major infections averted. Thus cost-effectiveness ratios in this study were "cost per major infection prevented" or "rashes (or anaphylaxis cases or hospitalizations) per major infection prevented."

**Sensitivity analysis.** To assess the impact of changes in baseline assumptions, we varied selected estimates of probabilities and costs over a wide range of values. The prevalence of occult bacteremia was varied up to 10% (Table I). The probabilities of major infectious complications after bacteremia were varied up to 100%. The sensitivities of the leukocyte count and of clinical judgment in predicting a positive blood culture were varied up to 100%. The sensitivity of blood culture in predicting occult bacteremia and the effectiveness of initial treatment in preventing major infections were varied up to 100%. The costs associated with testing, initial treatment, and hospitalization were varied over a plausible range.

**Computer modeling.** The decision tree was evaluated on a microcomputer by means of the decision-making program SMLTREE. Cost-effectiveness ratios were calculated on a microcomputer with the use of the Lotus spreadsheet program.

## RESULTS

**Health benefits and complications.** Health benefits and complications of each strategy for a hypothetical cohort of

**Table II.** Health outcomes for a hypothetical cohort of 100,000 febrile children without a focus of infection

| | Blood culture +treatment | Leukocyte count | Blood culture alone | Clinical judgment | Treatment alone | No intervention |
|---|---|---|---|---|---|---|
| Complications of occult bacteremia | | | | | | |
| Patients with major infections | 312 | 320 | 390 | 400 | 480 | 600 |
| Major infections prevented | | | | | | |
| No. | 288 | 280 | 210 | 200 | 120 | 0 |
| % | 48 | 47 | 35 | 33 | 20 | 0 |
| Complications of antibiotic allergy | | | | | | |
| Patients with rash | 4049 | 2389 | 86 | 1840 | 4029 | 36 |
| Avoidable rashes* | (4013) | (2353) | (50) | (1804) | (3993) | (0) |
| Patients with anaphylaxis | 4.3 | 2.7 | 0.6 | 2.1 | 4.2 | 0.2 |
| Avoidable anaphylactic reactions* | (4.1) | (2.4) | (0.3) | (1.9) | (4.0) | (0) |
| Hospitalizations | | | | | | |
| Patients with major infection | 312 | 320 | 390 | 400 | 480 | 600 |
| Patients with *H. influenzae* bacteremia | 353 | 351 | 336 | 280 | 0 | 0 |
| Patients with *S. pneumoniae* bacteremia | 151 | 206 | 714 | 105 | 0 | 0 |
| TOTAL HOSPITALIZATIONS | 816 | 877 | 1440 | 785 | 480 | 600 |

*Antibiotic complications are potentially avoidable when patients without major focal infections are treated presumptively.

**Table III.** Cost-effectiveness ratios for each strategy under baseline assumptions

| | Strategy | | | | | |
|---|---|---|---|---|---|---|
| Cost-effectiveness ratio | Blood culture + treatment | Leukocyte count | Blood culture alone | Clinical judgment | Treatment alone | No intervention |
| Average cost per patient* ($) | 145.45 | 146.60 | 149.34 | 133.20 | 80.11 | 79.94 |
| Cost per major infection prevented ($) | 50,503 | 52,357 | 71,114 | 66,600 | 66,758 | NA |
| Rashes per major infection prevented | 14.0 | 8.5 | 0.4 | 9.2 | 33.6 | NA |
| Anaphylactic reactions per major infection prevented | 0.0150 | 0.0096 | 0.0027 | 0.0106 | 0.350 | NA |
| Hospitalizations per major infection prevented | 2.8 | 3.1 | 6.9 | 3.9 | 4.0 | NA |

*NA,* Not applicable.
*Average overall financial cost per patient, including costs of follow-up visits and hospitalizations. For example, the average cost per patient with treatment alone is only 17 cents more per patient than the no-intervention strategy because it saves the costs of 120 hospitalizations for major infections compared with the no-intervention strategy.

100,000 children with a temperature of ≥39.0° C and no obvious focus of bacterial infection are shown in Table II. The benefits are expressed as the number of major infections prevented. The complications are expressed as the total and avoidable number of reactions to antibiotics and the total number of hospitalizations. The following strategies are discussed in descending order of expected clinical effectiveness:

*Blood culture plus treatment* prevents the most major infections but also leads to 14 cases of antibiotic rash and 0.015 case of anaphylaxis for each major infection prevented. More than 95% of these antibiotic complications are avoidable (i.e., result from empiric treatment of patients who did not have bacteremia).

*Leukocyte count* prevents nearly as many major infections as blood culture plus treatment. When a leukocyte count is used, only patients at high risk for occult bacteremia receive treatment, and therefore 40% of the antibiotic complications incurred with the blood-culture-plus-treatment strategy are averted.

*Blood culture alone* prevents fewer major infections than do strategies that combine blood culture with empiric treatment, but leads to the fewest cases of antibiotic complications.

*Clinical judgment* prevents only 33% of all potential major infections. It leads to fewer antibiotic complications than do the strategies that use empiric treatment.

*Treatment alone* prevents the fewest cases—only 20% of

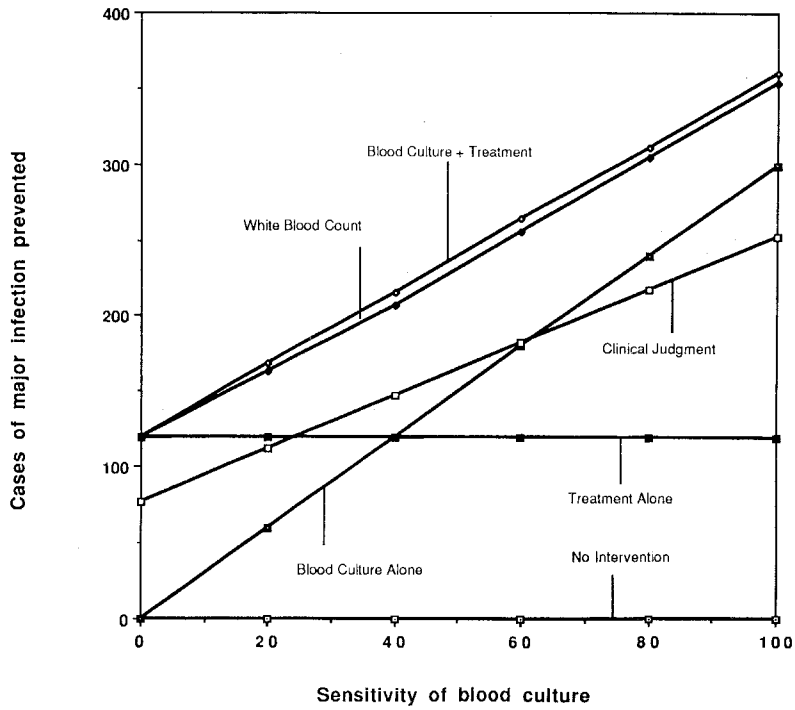


**Fig. 2.** Prevention of bacteremic complications at varying estimates of blood culture sensitivity.

the 600 potential major infections. The advantage of treatment alone is that it leads to the fewest cases of avoidable hospitalization of any intervention.

*No intervention* leads to the highest rate of major infections (600/100,000 febrile children). This strategy also has the lowest rate of antibiotic complications, with an expected 36 cases of rash and 0.2 case of anaphylaxis caused by intravenous ampicillin therapy.

Death from antibiotic allergy is rare, occurring only once in 5 million patients when all patients are treated empirically with oral amoxicillin therapy and less than once in 12 million patients when any other strategy is used.

**Cost-effectiveness of testing and treatment.** *Blood culture plus treatment* and *leukocyte count* have the lowest basic cost per disease case prevented (Table III). These strategies are approximately equal in terms of average cost per patient and cost-effectiveness.

*Clinical judgment* costs an average of $12 less for each febrile child compared with blood culture plus treatment. However, clinical judgment is a less cost-effective strategy than are the strategies that combine blood culture and empiric antibiotics because it prevents fewer major infections.

*Treatment alone* is the second least cost-effective strategy and incurs the highest proportion of antibiotic complications per major infection prevented. Its only advantage is that it is the cheapest intervention, with an average cost per patient of only 17 cents more than the no-intervention strategy. This occurs because although initial treatment costs $5, it saves the costs of 120 hospitalizations for major infections compared with the no-intervention strategy.

*Blood culture alone* is the least cost-effective intervention because of the large number of patients hospitalized with pneumococcal bacteremia, but it incurs the fewest antibiotic complications per major infection prevented.

**Incremental costs.** Incremental costs compare the extra cost incurred with the extra benefit gained when a more expensive but more effective strategy is used in place of a cheaper, less effective strategy. In this analysis the treatment-alone strategy is the intervention with the lowest average cost per febrile child. When the treatment-alone strategy is used, the basic cost of preventing one case of meningitis is $66,758. When blood culture is added to empiric antibiotic treatment (the blood-culture-plus-treatment strategy), 168 additional disease cases are prevented at an incremental cost of $38,892 per additional case prevented. When the leukocyte-count strategy is added to empiric treatment alone, 160 additional disease cases are prevented at an incremental cost of $41,556 per case. The cost of preventing additional disease cases by using the more expensive testing strategies is lower than the basic cost of preventing disease by using the cheapest strategy, treatment alone. Thus strategies that combine empiric antibiotic

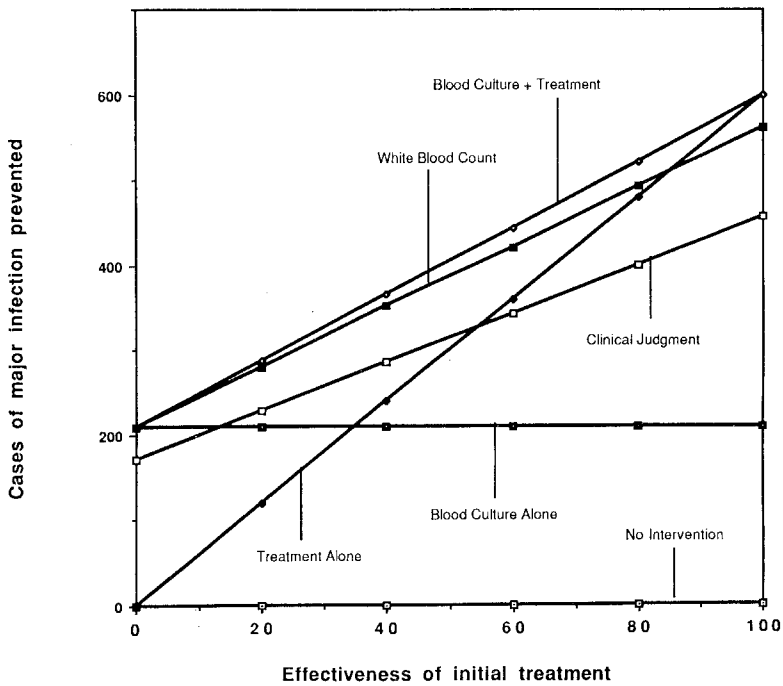


**Fig. 3.** Prevention of bacteremic complications at varying estimates of effectiveness of initial treatment.

treatment with testing (blood culture with or without leukocyte count) are incrementally cost-effective.

**Sensitivity of the analysis to critical assumptions**

*Blood culture performance characteristics.* At all estimates of blood culture sensitivity, leukocyte count and blood culture plus treatment prevent the greatest morbidity and are approximately equal in clinical effectiveness (Fig. 2).

If blood culture is assumed to be less than 100% specific, strategies that use blood culture result in unnecessary hospitalization and become somewhat less cost-effective. For example, if blood culture has a specificity of 99%, there will by 970 false-positive blood cultures for every 100,000 febrile patients. At follow-up, 291 (30%) of these patients are expected to be febrile and will be hospitalized for 2 days. This adds $1303 (approximately 3%) to the cost of preventing each case of meningitis with the blood-culture-plus-treatment strategy. If blood culture is assumed to be only 95% specific, 1455 patients will be hospitalized needlessly, adding $6517 (approximately 13%) to the cost of each case of meningitis prevented.

*Leukocyte count performance characteristics.* When a criterion of $\geq 15{,}000/mm^3$ is used for a high leukocyte count, the sensitivity of the leukocyte count falls to 65% and the specificity rises to 77%.[19] This has two main effects compared with using a criterion of $\geq 10{,}000/mm^3$: (1) the number of cases of major infection is reduced by 6% to 262, and (2) the average cost per patient drops by 30 cents.

*Sensitivity of clinical judgment.* When clinical judgment has a sensitivity of 50% or more, it prevents more major infections than does blood culture alone. However, it is not as effective as the leukocyte count until clinical judgment has a sensitivity of 95% or more.

*Effectiveness of initial treatment.* The strategy of blood culture plus treatment prevents the most cases of disease at all estimates of initial treatment effectiveness (Fig. 3). When initial treatment is ≥85% effective, treatment alone surpasses the leukocyte count in clinical effectiveness.

*Prevalence and complication rates.* The order of effectiveness of the six strategies remains unchanged because the prevalence of bacteremia and the rates of major infectious complications after bacteremia vary.

*Cost assumptions.* The relative cost-effectiveness ratios of the strategies vary depending on the cost of initial treatment (Fig. 4). When initial treatment costs $18 or more, the leukocyte count becomes more cost-effective than blood culture plus treatment. The cost analysis is also sensitive to estimates of the costs of the leukocyte count and hospitalization for pneumococcal bacteremia.

The cost-effectiveness rankings of the strategies do not change when the costs of blood culture, outpatient and emergency department visits, and hospitalization for men-

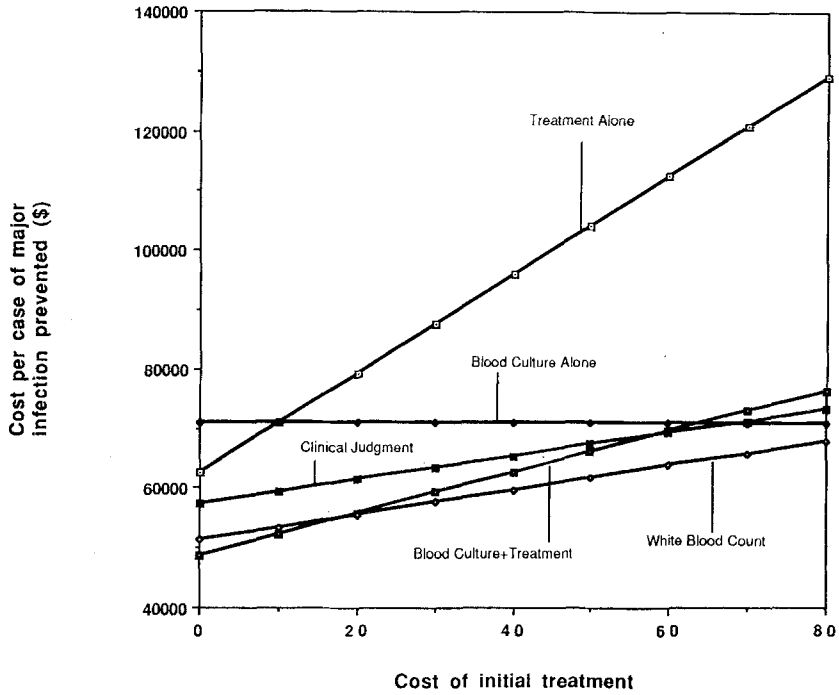


**Fig. 4.** Cost-effectiveness at varying estimates of cost of initial treatment. Effectiveness of initial treatment is held constant at 20%.

ingitis, *H. influenzae* bacteremia, and anaphylaxis are varied over appropriate ranges.

## DISCUSSION

The value of diagnostic testing or empiric treatment of young febrile children without an apparent focus of bacterial infection remains controversial. A previous analysis suggested that the preferred option was not to obtain blood cultures routinely; a second alternative was to obtain cultures for selected patients at high risk for bacteremia.[12]

Our analysis found that the two strategies that employ both testing and empiric antibiotic treatment are the most clinically effective and cost-effective of the six options considered. The strategy in which all patients receive blood culture and initial treatment prevents the most major infections and has the lowest cost per disease case prevented under a wide variety of assumptions. The leukocyte-count strategy has roughly equal clinical and cost effectiveness and has the advantage of averting many antibiotic complications. However, the leukocyte-count strategy may be unwieldy if laboratory facilities are not readily available or if time is at a premium, as in the emergency department setting.

The rate of major focal infections can be halved to 0.3% by the most effective testing and treatment strategy, but this result requires that, for each major infection prevented, 347 patients undergo venipuncture, 14 patients acquire a rash, 2.8 patients be hospitalized, and the provider pay approximately $50,000. Are the effort, discomfort, and money expended on children at risk for occult bacteremia worth the relatively infrequent complications prevented? Some physicians and parents may think not, as Kramer et al.[26] demonstrated by eliciting opinions from physicians and parents on the disutilities (drawbacks) of venipuncture, minor infection, major infection, and hospitalization.[26]

Our analysis supports the suggestion of Kramer et al.[12] that new approaches to the management of patients with occult bacteremia are needed. Our study and conclusions differ from their analysis in several important respects. First, we include the option of treating patients empirically at the initial visit with oral antibiotic therapy. Second, in the analysis of Kramer et al., children with pneumococcal bacteremia and persistent fever at follow-up are hospitalized for 10 days. In our analysis, these children are hospitalized only until one blood culture is negative at 48 hours, usually only 2 or 3 days. This is consistent with current practice in the United States and has the effect of imposing less disutility on strategies that use blood culture. Third, although we agree with Kramer et al. that obtaining only a blood culture for all patients is rarely a promising strategy,

selecting patients at high risk for bacteremia by using the leukocyte count and combining empiric treatment with blood culture are both cost-effective strategies.

Our model did not include the long-term sequelae of meningitis (e.g., deafness or death) or anaphylaxis. Our conclusions agree in part with a similar decision analysis that used quality-adjusted life-years as outcomes and suggested that empiric antibiotic treatment is the preferred option.[27] Extending our model to include long-term outcomes would make the options that prevent the most meningitis cases even more preferable.

The values placed on preventing pain and suffering caused by venipuncture, antibiotic allergy, hospitalization, and meningitis are subjective and vary among individual physicians and patients. We have not attempted to quantify the intangible costs of emotional distress, nor have we included indirect costs such as lost wages and follow-up care. Instead of presenting a prescriptive recommendation, this analysis elucidates the benefits and drawbacks of several possible options. Physicians and policymakers can integrate this study's results with their own clinical situations and values to select a rational approach to the febrile child at risk for occult bacteremia.

The approach to treatment of febrile children at risk for occult bacteremia remains controversial. We conclude that approaches which combine blood culture and treatment have the greatest clinical and cost effectiveness, even in the baseline model in which the effectiveness of initial treatment is assumed to be very low. This analysis also suggests that future gains in preventing complications of occult bacteremia may be made by focusing on ways to improve the effectiveness of initial treatment.

## REFERENCES

1. McGowan JE, Bratton L, Klein JO, Finland M. Bacteremia in febrile children seen in a "walk-in" pediatric clinic. N Engl J Med 1973;288:1309-12.
2. Teele DW, Pelton SI, Grant MJ, et al. Bacteremia in febrile children under 2 years of age: results of cultures of blood of 600 consecutive febrile children seen in a "walk-in" clinic. J PEDIATR 1975;87:227-30.
3. McCarthy PL, Grundy GW, Spiesel SZ, Dolan TF. Bacteremia in children: an outpatient clinical review. Pediatrics 1976;57:861-8.
4. McCarthy PL, Jekel JF, Dolan TF. Temperature greater than or equal to 40° C in children less than 24 months of age: a prospective study. Pediatrics 1977;59:663-8.
5. Bratton L, Teele DW, Klein JO. Outcome of unsuspected pneumococcemia in children not initially admitted to the hospital. J PEDIATR 1977;90:703-6.
6. Marshall R, Teele DW, Klein JO. Unsuspected bacteremia due to *Haemophilus influenzae:* outcome in children not initially admitted to hospital. J PEDIATR 1979;95:690-5.
7. Dashefsky B, Teele DW, Klein JO. Unsuspected meningococcemia. J PEDIATR 1983;102:69-72.
8. Alario AJ, Nelson EW, Shapiro ED. Blood cultures in the management of febrile outpatients later found to have bacteremia. J PEDIATR 1989;115:195-9.
9. Jaffe DM, Tanz RR, Davis AT, Henretig F, Fleisher G. Antibiotic administration to treat possible occult bacteremia in febrile children. N Engl J Med 1987;317:1175-80.
10. Carroll WL, Farrell MK, Singer JI, Jackson MA, Lobel JS, Lewis ED. Treatment of occult baccteremia: a prospective randomized clinical trial. Pediatrics 1983;72:608-12.
11. Baron MA, Fink HD, Cicchetti DV. Blood cultures in private pediatric practice: an eleven-year experience. Pediatr Infect Dis J 1989;8:2-7.
12. Kramer MS, Lane DA, Mills EL. Should blood cultures be obtained in the evaluation of young febrile children without evident focus of bacterial infection? a decision analysis of diagnostic management strategies. Pediatrics 1989;84:18-27.
13. Dershewitz RA, Wigder HN, Wigder CM, Nadelman DH. A comparative study of the prevalence, outcome, and prediction of bacteremia in children. J PEDIATR 1983;103:352-8.
14. Baron MA, Fink HD. Bacteremia in private pediatric practice. Pediatrics 1980;66:171-5.
15. Myers MG, Wright PF, Smith AL, Smith DH. Complications of occult pneumococcal bacteremia in children. J PEDIATR 1974;84:656-60.
16. Isaacman DJ, Karasic RB. Are two blood cultures better than one? Abstract presented to the American Academy of Pediatrics, 1989.
17. Carey RB. Clinical comparison of the Isolator 1.5 microbial tube and the Bactec radiometric system for detection of bacteremia in children. J Clin Microbiol 1984;19:634-8.
18. Aronson MD, Bor DH. Blood cultures. Ann Intern Med 1987; 106:246-53.
19. Jaffe DM, Fleisher GR. Temperature and white blood cell count as indicators of bacteremia. Pediatrics (in press).
20. Baker RC, Tiller T, Bausher JC, et al. Severity of disease correlated with fever reduction in febrile infants. Pediatrics 1989;83:1016-9.
21. Waskerwitz S, Berkelhamer JE. Outpatient bacteremia: clinical findings in children under two years with initial temperatures of 39.5° C or higher. J PEDIATR 1981;99:231-3.
22. McCarthy PL, Sharpe MR, Spiesel SZ, et al. Observation scales to identify serious illness in febrile children. Pediatrics 1982;70:802-9.
23. Nelson KG. An index of severity for acute pediatric illness. Am J Public Health 1980;70:804-7.
24. Putto A, Ruuskanen O, Meurman O. Fever in respiratory virus infections. Am J Dis Child 1986;140:1159-63.
25. Drug Topics Red Book 1989 and July Update.
26. Kramer MS, Maclellan AM, Leduc DG. Parents' vs. physicians' utilities for clinical outcomes in potentially bacteremic children [Abstract]. Am J Dis Child 1989;143:436.
27. Downs SM, Margolis P, McNutt R. A decision analytic approach to the management of febrile infants without apparent focus of bacterial infection [Abstract]. Med Decis Making 1989;9:320.