



REVIEW ARTICLE

Current management of occult bacteremia in infants[☆]



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KEYWORDS

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Abstract

Objectives: To summarize the main clinical entities associated with fever without source (FWS) in infants, as well as the clinical management of children with occult bacteremia, emphasizing laboratory tests and empirical antibiotics.

Sources: A non-systematic review was conducted in the following databases – PubMed, EMBASE, and SciELO, between 2006 and 2015.

Summary of the findings: The prevalence of occult bacteremia has been decreasing dramatically in the past few years, due to conjugated vaccination against *Streptococcus pneumoniae* and *Neisseria meningitidis*. Additionally, fewer requests for complete blood count and blood cultures have been made for children older than 3 months presenting with FWS. Urinary tract infection is the most prevalent bacterial infection in children with FWS. Some known algorithms, such as Boston and Rochester, can guide the initial risk stratification for occult bacteremia in febrile infants younger than 3 months.

Conclusions: There is no single algorithm to estimate the risk of occult bacteremia in febrile infants, but pediatricians should strongly consider outpatient management in fully vaccinated infants older than 3 months with FWS and good general status. Updated data about the incidence of occult bacteremia in this environment after conjugated vaccination are needed.

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PALAVRAS-CHAVE

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Manejo atual da bacteremia oculta do lactente**Resumo**

Objetivos: Listar as principais entidades clínicas associadas a quadros de febre sem sinais localizatórios (FSSL) em lactentes, bem como o manejo dos casos de bacteremia oculta com ênfase na avaliação laboratorial e na antibioticoterapia empírica.

Fonte dos dados: Foi realizada revisão não sistemática da literatura nas bases de dados PubMed, EMBASE e Scielo no período de 2006 a 2015.

Síntese dos dados: A ocorrência de bacteremia oculta vem diminuindo sensivelmente em lactentes com FSSL, principalmente devido à introdução da vacinação conjugada contra *Streptococcus pneumoniae* e *Neisseria meningitidis* nos últimos anos. Juntamente disso, uma redução constante na solicitação de hemogramas e hemoculturas em lactentes febris acima de 3 meses vem sendo observada. A infecção do trato urinário é a infecção bacteriana mais prevalente no paciente febril. Algoritmos consagrados, como o de Boston e Rochester, podem guiar a decisão clínica inicial para estimar o risco de bacteremia em lactentes entre um e 3 meses de vida.

Conclusões: Não há esquema padronizado para a estimativa do risco de bacteremia oculta em lactentes febris, porém deve-se considerar fortemente o manejo ambulatorial de lactentes acima de 3 meses com FSSL em bom estado geral e com esquema vacinal completo. São necessários dados atualizados sobre a incidência de bacteremia oculta em crianças vacinadas em nosso meio.

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Introduction

Fever without source (FWS) is one of the major diagnostic challenges for the emergency service pediatrician. Approximately 20% of febrile children do not have an initially-established etiological diagnosis, and around 20% of emergency consultations in children between 2 and 24 months of age are due to fever.^{1,2} In this scenario, it is essential to perform a rapid diagnosis of children with possible severe bacterial infection (SBI), who require immediate antibiotic therapy. SBIs include sepsis/septic shock, occult bacteremia (OB), bacterial meningitis, pneumonia, urinary tract infection, bacterial gastroenteritis, osteomyelitis, and septic arthritis.³

The evaluation of febrile infants is even more of a concern considering the relative immaturity of the immune system in the first 3 months of life. Factors that may increase the risk of SBI in infants include reduced macrophage and opsonization activity, in addition to lower neutrophil activity.⁴ While it is a consensus that early introduction of antibiotics leads to a favorable outcome in children with FWS in poor general status and with toxemia, the management of children in good general status is still a matter of much discussion, in whom the risk of SBI, particularly OB, is very low.⁵

Although several authors have studied the combination of clinical and laboratory parameters for risk stratification of SBI in febrile infants, to date there is no single test or set of tests that is able to detect infants with SBI with optimal sensitivity.⁶ This article aimed to describe the main clinical conditions associated with FWS in infants and to analyze the methods of laboratory evaluation of fever in this age group.

Main entities associated with FWS**Viral infections**

Viral infections are common causes of FWS in infants, and many patients are treated with antibiotics in this situation, despite the lack of evidence for bacterial infections. Viruses and bacteria interact with different pattern-recognition receptors in circulating leukocytes, triggering different specific immune responses.⁷ In a study involving 75 children with FWS,⁸ one or more viruses were detected by polymerase chain reaction in 76% of the cases; among children with fever and a probable defined infection source, this percentage was 40%, and among the afebrile children in the control group, in 35% of cases. The most often identified viruses were adenovirus, herpes virus type 6, enteroviruses, and parechovirus.

Occult bacteremia

OB is defined as a positive blood culture in a patient with FWS.⁶ The prevalence of OB has dramatically decreased in recent years, on account of conjugate bacterial vaccines. In the pre-vaccine era, the prevalence of OB was 2.4–11.6% in children with FWS, and pneumococcus was the main disease-causing agent (50–90% of cases).^{9,10} At the age of 1 week to 3 months of age, *Escherichia coli* represents 56% of bacteremia cases, with group B *Streptococcus* as the second most prevalent agent, representing 21% of cases.¹¹

A recent retrospective cohort study¹² evaluated 201 episodes of pneumococcal OB in infants with a median age of 20.5 months. The cases due to PCV7 serotype decreased from 82.2% to 19.5% after vaccination, with most

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