Baystate
Medical Center
A Member of Baystate Health System
Springfield, Massachusetts 01199
413-794-0000

November 19, 1999

Re: **Management of Febrile Infants Age ≤ 3 months**

Dear Colleague,

Infants who present with fever in the absence of a localizing source of infection are one of the leading sources of admission to the Baystate Medical Center Children's Hospital. In recent years clinical practice guidelines have appeared in *Pediatrics* and the *Annals of Emergency Medicine* aimed at standardizing the management of these children. These guidelines recommend a comprehensive clinical evaluation and battery of simple laboratory tests to identify infants who are at low-risk of developing serious bacterial infections. When no contraindications preclude it, these low risk infants can be safely managed in the outpatient setting, and generally will not require antibiotic therapy.

Over the last several months a multidisciplinary team has met to review the care of febrile infants at Baystate Medical Center. The following guideline was developed as part of ongoing efforts to improve quality of care and represents the local adaptation of the published literature.

We will be implementing these guidelines on January 3, 2000 and will be monitoring and reporting outcomes in the months ahead. Reference materials are available upon request by contacting the Office of Clinical Practices Evaluation and Management (OCPEM) at 413-794-5763. If you have any questions or comments, please contact Donna Fisher, MD at 413-794-5379 or Richard Gabor, MD at 413-794-3233.

Sincerely,

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Clinical Practice Guideline

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Management of Infants 3 Months of Age and Younger with No Apparent Source of Fever

Key Points

- *Febrile infants 3 months of age and younger may have a life-threatening bacterial infection. (page 1.)*
- *Some very ill infants may be afebrile or hypothermic. (page 1.)*
- *In this age group, history, observation and physical exam have limitations in predicting the presence of a serious bacterial infection. (page 1.)*
- *Infants less than three months of age with a rectal temperature ≥100.4°F who are not "low risk", as defined in this guideline, require admission to the hospital and an evaluation for sepsis. (page 2.)*
- *Infants who **appear well**, who **achieve "low risk" status** upon laboratory evaluation, and who are **older than 28 days of age** **may be observed safely as an outpatient.***

Introduction

Fever in infants 3 months of age and younger, in the absence of a clinically apparent source of infection, is a common reason for admission to the Children's Hospital at Baystate Medical Center. Recent guidelines appearing in *Pediatrics, Pediatrics in Review, Opinions in Pediatrics,* and the *Annals of Emergency Medicine* provide useful perspective, and support outpatient management, without antibiotics, of selected febrile infants who are older than 28 days of age. Most authorities recommend that infants 28 days of age and younger, and all ill-appearing infants 3 months of age and younger, be admitted to the hospital, be fully evaluated for sepsis and be given empiric treatment with antibiotics[1,4-5,8,10,13-16].

Definition of Fever

A rectal temperature [obtained with a properly calibrated electronic probe left in place for three minutes] correlates highly with core body temperature. Tympanic thermometry is subject to error in placement. **A properly obtained temperature of 100.4°F (38.0°C) or greater represents a fever.**

The clinician must be aware of the limitations in homeostatic response of infants of this age to high environmental temperatures and must also consider the possibility of serious infection in an infant who appears to be ill but has no fever, or is hypothermic[15].

Evaluation

In this age group, overall, approximately 1 infant in 10 with fever without obvious source will have meningitis, bacteremia, urinary tract infection, soft tissue infection or pneumonia, most often caused by gram-negative organisms, Group B S*treptococcus*, or less commonly by *Listeria monocytogenes* and enterococci[15]. **However, recent studies have shown that a subset of infants at "low risk" for serious infection (<0.2% occurrence rate) can be identified and managed without antibiotics.**

History, observation and physical examination alone have limitations in detecting serious illness in febrile infants in this age group[15]. Nonetheless, it is important to elicit any history of antibiotics, recent contacts with illness, and to inquire as to the vigor of the infant's eating and the nature of the baby's cry.

It is important to document the history of fever at home, time of onset, method of measurement, and whether antipyretics were given.

Management

Infants ≤28 Days of Age. Because of the risk of serious bacterial infection, all infants 28 days of age and younger are to be admitted to the hospital for a full sepsis evaluation and are to receive empiric antibiotics. (Chart 1.)

Chart 1
Empiric Antibiotic Therapy

Febrile infants ≤ 28 days of age should generally receive coverage for *Listeria monocytogenes*. A reasonable combination is:
ampicillin 50 mg. per kg. of body weight per dose q. 6h. i.v. or i.m.
and
gentamicin 2.5 mg. per kg. of body weight per dose i.v. or i.m. q. 8h.

Febrile infants over 28 days of age should receive:
ceftriaxone 50-100 mg. per kg. of body weight per day i.v. or i.m. (may be divided into 2 doses).

It should be noted, however, that some studies suggest only "ill appearing," (Chart 2.) not "low risk" infants in this age group receive empiric antibiotic therapy, and further, they suggest that those infants in this age group who are not "ill appearing" and who are determined to be "low risk" (Chart 3.) may be observed without parenteral antibiotic therapy pending results of cultures[1,4,8,10,14-15]. (Evidence Grade III, Recommendation Category C)

Infants 29 - 90 days of age. Infants between the ages of 28 days and 90 days of age who are well-appearing, previously healthy, full-term infants, who have not received antibiotics, and whose basic laboratory evaluation places them at "low risk," are to be observed closely for signs of deterioration. They do not require empiric antibiotic therapy[1,4,8,10] (Evidence Grade II-1, Recommendation Category B)

Chart 2
Clinical Clues to the Ill-appearing Infant [(1.)]

Lethargy
(a level of consciousness characterized by poor or absent eye contact with persons or objects)
Signs of poor perfusion
Marked hypoventilation
Hyperventilation
Cyanosis

If a physician consenting to assume responsibility for the infant's care can be identified, and if the patient's home situation permits, outpatient manage-ment can be appropriate[8-9,13] (Evidence Grade I-2, Recommendation Category B)

If a physician willing to assume responsibility for outpatient care cannot be identified, or if the primary care physician so elects, the infant is to be admitted to the hospital.

Given the low risk of serious bacterial infection, the routine administration of antibiotics is not recommended[1-2,4,8,10,14]. (Evidence Grade I-2, Recommendation Category B)

If antibiotic usage is planned, however, a full sepsis evaluation is to be completed prior to administration of the drugs[1-2, 5, 9].

"Ill appearing" infants and well-appearing infants whose basic laboratory evaluation is *not consistent* with "low risk," are to be admitted for a full sepsis evaluation (see appended algorithm) and are to receive empiric antibiotic therapy.

Infants who are well appearing but have a history of prematurely, co-morbid illness, or recent antibiotic usage should be admitted for a full sepsis evaluation and should receive empiric antibiotic therapy.

Chart 3
Laboratory Markers of Low Risk

peripheral blood WBC count 5,000-15,000 /mm^3
and
absolute band form count ≤1,500 /mm^3
and
catheterized or suprapubic aspiration microscopic U/A ≤10 WBC per HPF on spun urine sediment **or** negative leukocyte esterase.

and, in the setting of diarrhea

≤5 WBC per HPF on examination of stool smear.

Infants who appear severely ill should receive expeditious supportive inter-vention, undergo a sepsis evaluation, and receive empiric antibiotic therapy without delay.

Baystate Health System

Clinical Practice Guideline

Management of Infants 3 Months of Age and Younger with No Apparent Source of Fever

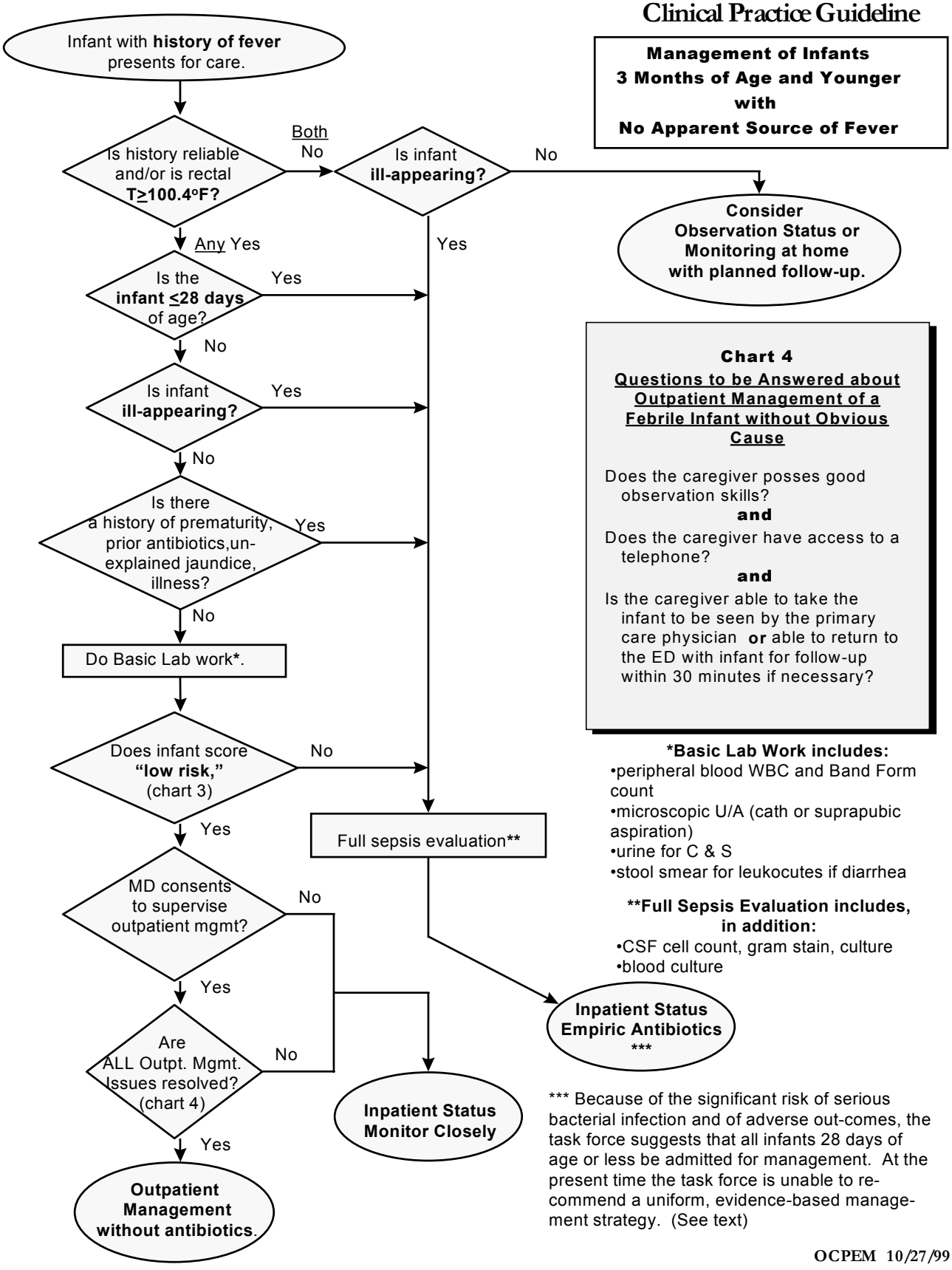

Chart 4

Questions to be Answered about Outpatient Management of a Febrile Infant without Obvious Cause

Does the caregiver posses good observation skills?

and

Does the caregiver have access to a telephone?

and

Is the caregiver able to take the infant to be seen by the primary care physician **or** able to return to the ED with infant for follow-up within 30 minutes if necessary?

***Basic Lab Work includes:**

- peripheral blood WBC and Band Form count
- microscopic U/A (cath or suprapubic aspiration)
- urine for C & S
- stool smear for leukocutes if diarrhea

****Full Sepsis Evaluation includes, in addition:**

- CSF cell count, gram stain, culture
- blood culture

*** Because of the significant risk of serious bacterial infection and of adverse out-comes, the task force suggests that all infants 28 days of age or less be admitted for management. At the present time the task force is unable to re-commend a uniform, evidence-based manage-ment strategy. (See text)

OCPEM 10/27/99

Table 1. Evidence Grading Criteria and Recommendation Grading

Evidence Grading Criteria

Best Level of Evidence Forming the basis for Recommendations

Level	Definition
I-1	**Evidence from at least one properly designed (usually large) randomized controlled trial** in which the lower limit of the confidence interval for the treatment effect exceeds the minimal clinically important benefit, **or results from a meta-analysis of randomized controlled trials** in which the treatment effects from the individual studies have the lower limit of the confidence interval exceeding the minimal clinically important benefit. Data should have low false-positive (alpha) or high false-negative errors.
I-2	Evidence from at least one randomized (usually small) controlled trial or from a meta-analysis of randomized control trials in which the confidence interval for the treatment effect overlaps the minimal clinically important benefit. Data may have high false positive (alpha) or high false-negative errors.
II-1	Evidence obtained from at least **one well-designed controlled trial without randomization** from **cohort studies** performed on contemporaneous populations, or **cross-sectional studies** or **case-controlled analytic studies** (preferably from more than one center).
II-2	Evidence obtained from multiple time-series studies, historic cohort comparisons, or from dramatic results in uncontrolled experiments.
III	Evidence from opinions of respected authorities, based on clinical experience, or from descriptive studies, well-designed non-experimental studies such as comparative, - or case series without controls, or reports of expert committees.

Categories Reflecting the Strength of Each Recommendation

Category	Definition
A	Both strong evidence and substantial clinical benefit support a recommendation for use. Generally supported by Level **I**-1 evidence.
B	Moderate evidence - or strong evidence for only limited benefit - supports a recommendation for use. Generally supported by Level **I**-2, **II**-1 or **II**-2 evidence.
C	Poor evidence supports a recommendation for or against use. Generally supported by Level **III** evidence.
D	Moderate evidence supports a recommendation against use. Generally supported by Level **II**-01 or **II**-2 evidence.
E	Good evidence supports a recommendation against use. Generally supported by Level **I**-1 or Level **I**-2 evidence.

Modified from: *Annals of Internal Medicine, 1996; 124. 349.* and *Chest, 1995; 108 (Supplement 4). 227s.*

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