Disclosure

I have NO financial relationships to disclose.

NEMOURS
CHILDREN'S HEALTH

Approach to Young Febrile Infants – Things Have Changed!

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July 23rd, 2022

Learning Objectives

"We are not makers of history. We are made by history."

~ Martin Luther King, Jr.

"There is nothing permanent except change."

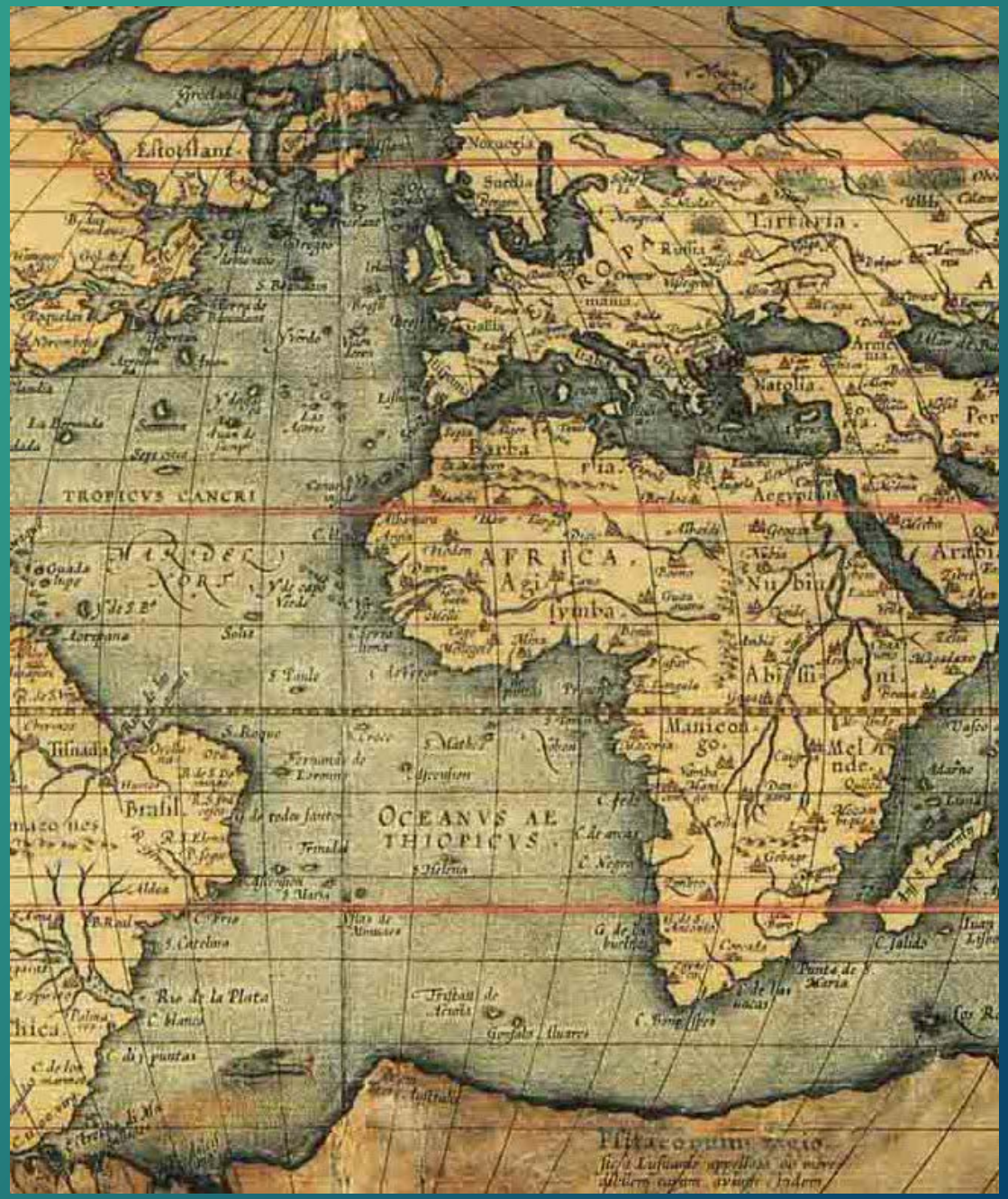
~ Heraclitus

"Do not dwell in the past, do not dream of the future, concentrate the mind on the present moment."

~ Buddha

"In the middle of a difficulty lies opportunity."

~ Einstein



History
(Fifty Decades)

- 1970s: Group B *Streptococcus* (GBS)
- 1980s: First guidelines, risks, and costs
- 1980s-1990s: Attempts to develop and validate prediction models
- 2000s: Lots more studies…

Clinical Trial > N Engl J Med. 1993 Nov 11;329(20):1437-41.
doi: 10.1056/NEJM199311113292001.

Outpatient management without antibiotics of fever in selected infants

M D Baker [1], L M Bell, J R Avner

Affiliations + expand

PMID: 8413453 DOI: 10.1056/NEJM199311113292001

Free article

Abstract

Background: In many academic centers it is standard practice to hospitalize all febrile infants younger than two months of age, whereas in community settings such infants are often cared for as outpatients.

Methods: We conducted a controlled study of 747 consecutive infants 29 through 56 days of age who had temperatures of at least 38.2 degrees C. After a complete history taking, physical examination, and sepsis workup, the 460 infants with laboratory or clinical findings suggestive of serious bacterial illness were hospitalized and treated with antibiotics. The screening criteria for serious bacterial illness included a white-cell count of at least 15,000 per cubic millimeter, a spun urine specimen that had 10 or more white cells per high-power field or that was positive on bright-field microscopy, cerebrospinal fluid with a white-cell count of 8 or more per cubic millimeter or a positive Gram's stain, or a chest film showing an infiltrate. The 287 infants who had unremarkable examinations and normal laboratory results were assigned to either inpatient observation without antibiotics (n = 148) or outpatient care without antibiotics but with reexaminations after 24 and 48 hours (n = 139).

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Why Change?

- Changing bacteriology
- Cost of unnecessary care
- Advances in testing
  - Inflammatory markers
  - Pathogen identification
  - Viral testing
  - Emerging technologies
- Opportunities to improve the care of hospitalized infants
- Evolving research strategies

AND there is evidence to support the change…

Evidence for Age-Based Risk Stratification

JAMA. 2004 Mar 10;291(10):1203-12. doi: 10.1001/jama.291.10.1203.

Management and outcomes of care of fever in early infancy

Robert H Pantell [1], Thomas B Newman, Jane Bernzweig, David A Bergman, John I Takayama, Mark Segal, Stacia A Finch, Richard C Wasserman

Affiliations + expand

PMID: 15010441 DOI: 10.1001/jama.291.10.1203

Results: The PROS clinicians hospitalized 36% of the infants, performed laboratory testing in 75%, and initially treated 57% with antibiotics. The majority (64%) were treated exclusively outside of the hospital. Bacteremia was detected in 1.8% of infants (2.4% of those tested) and bacterial meningitis in 0.5%. Well-appearing infants aged 25 days or older with fever of less than 38.6 degrees C had a rate of 0.4% for bacteremia/bacterial meningitis. Frequency of other illnesses included urinary tract infection, 5.4%; otitis media, 12.2%; upper respiratory tract infection, 25.6%; bronchiolitis, 7.8%; and gastroenteritis, 7.2%. Practitioners followed current guidelines in 42% of episodes. However, in the initial visit, they treated 61 of the 63 cases of bacteremia/bacterial meningitis with antibiotics. Neither current guidelines nor the model developed in this study performed with greater accuracy than observed practitioner management.

Evidence for Age-Based Risk Stratification

Observational Study > Ann Emerg Med. 2018 Feb;71(2):211-216.
doi: 10.1016/j.annemergmed.2017.07.488. Epub 2017 Oct 6.

Epidemiology of Bacteremia in Febrile Infants Aged 60 Days and Younger

Elizabeth C Powell [1], Prashant V Mahajan [2], Genie Roosevelt [3], John D Hoyle Jr [4], Rajender Gattu [5], Andrea T Cruz [6], Alexander J Rogers [2], Shireen M Atabaki [7], David M Jaffe [8], T Charles Casper [9], Octavio Ramilo [10], Nathan Kuppermann [11],
Febrile Infant Working Group of the Pediatric Emergency Care Applied Research Network (PECARN)

Collaborators, Affiliations + expand

PMID: 28988964 PMCID: PMC5815881 DOI: 10.1016/j.annemergmed.2017.07.488

Results: Of 7,335 screened infants, 4,778 (65.1%) had blood cultures and were enrolled. Of these patients, 84 had bacteremia (1.8%; 95% confidence interval [CI] 1.4% to 2.2%). The prevalence of bacteremia in infants aged 28 days or younger (47/1,515) was 3.1% (95% CI 2.3% to 4.1%); in infants aged 29 to 60 days (37/3,246), 1.1% (95% CI 0.8% to 1.6%). Prevalence differed by week of age for infants 28 days of age and younger (0 to 7 days: 4/156, 2.6%; 8 to 14 days: 19/356, 5.3%; 15 to 21 days: 15/449, 3.3%; and 22 to 28 days: 9/554, 1.6%). The most common pathogens were Escherichia coli (39.3%; 95% CI 29.5% to 50.0%) and group B streptococcus (23.8%; 95% CI 16.0% to 33.9%). Bacterial meningitis occurred in 19 of 1,515 infants 28 days of age and younger (1.3%; 95% CI 0.8% to 2.0%) and 5 of 3,246 infants aged 29 to 60 days (0.2%; 95% CI 0.1% to 0.4%). Of 84 infants with bacteremia, 36 (42.9%; 95% CI 32.8% to 53.5%) had urinary tract infections (E coli 83%); 11 (13.1%; 95% CI 7.5% to 21.9%) had bacterial meningitis.

Evidence for Age-Based Risk Stratification

Comparative Study > Pediatrics. 2016 Aug;138(2):e20154381. doi: 10.1542/peds.2015-4381. Epub 2016 Jul 5.

Validation of the "Step-by-Step" Approach in the Management of Young Febrile Infants

Borja Gomez [1], Santiago Mintegi [2], Silvia Bressan [3], Liviana Da Dalt [4], Alain Gervaix [5], Laurence Lacroix [5], European Group for Validation of the Step-by-Step Approach

Affiliations + expand

PMID: 27382134 DOI: 10.1542/peds.2015-4381

Conclusions: We validated the Step by Step as a valuable tool for the management of infants with fever without source in the emergency department and confirmed its superior accuracy in identifying patients at low risk of IBI, compared with the Rochester criteria and the Lab-score.

Evidence for Age-Based Risk Stratification

Pediatrics. 2019 Jul;144(1):e20183604. doi: 10.1542/peds.2018-3604. Epub 2019 Jun 5.

A Prediction Model to Identify Febrile Infants ≤60 Days at Low Risk of Invasive Bacterial Infection

Paul L Aronson [1 2], Veronika Shabanova [3], Eugene D Shapiro [3 4], Marie E Wang [5], Lise E Nigrovic [6], Christopher M Pruitt [7], Adrienne G DePorre [8], Rianna C Leazer [9], Sanyukta Desai [10], Laura F Sartori [11], Richard D Marble [12], Sahar N Rooholamini [13], Russell J McCulloh [8], Christopher Woll [3 2], Fran Balamuth [14 15], Elizabeth R Alpern [12], Samir S Shah [10 16], Derek J Williams [17], Whitney L Browning [17], Nipam Shah [7], Mark I Neuman [6], Febrile Young Infant Research Collaborative

Objectives: To derive and internally validate a prediction model for the identification of febrile infants ≤60 days old at low probability of invasive bacterial infection (IBI).

Conclusions: Infants ≤60 days old with fever by history only, a normal urinalysis result, and an absolute neutrophil count <5185 cells per µL have a low probability of IBI.

Evidence for Age-Based Risk Stratification

› Arch Dis Child. 2019 Sep;104(9):874-878. doi: 10.1136/archdischild-2018-316191. Epub 2019 May 30.

Risk of invasive bacterial infections by week of age in infants: prospective national surveillance, England, 2010–2017

Shamez N Ladhani [1 2], Katherine L Henderson [3], Berit Muller-Pebody [3], Mary E Ramsay [1], Andrew Riordan [4]

Affiliations + expand

PMID: 31147318 DOI: 10.1136/archdischild-2018-316191

Results: There were 22 075 IBI episodes between 2010/2011 and 2016/2017. The lowest annual cases were in 2011/2012 (n=2 799; incidence, 412/100 000 population), increasing year-on-year to 3 698 cases in 2016/2017 (incidence, 552/100 000 population). The incidence was highest in the first week of life and then declined rapidly. In 2016/2017, compared with the first week of life, weekly IBI incidence was 92% lower at 8 weeks (IRR 0.08; 95% CI 0.06 to 0.10) and 96% lower at 16 weeks of age (IRR 0.04; 95% CI 0.03 to 0.06). In 2016/2017, *Escherichia coli* was the most prevalent pathogen responsible for IBI (n=592, 16.0%), followed by group B *Streptococci* (n=493, 13.3%), *Staphylococcus aureus* (n=400, 10.8%) and *Enterococci* (n=304, 8.2%). The other pathogens were individually responsible for <5% of total cases. There were differences in age distribution of the pathogens with increasing age.

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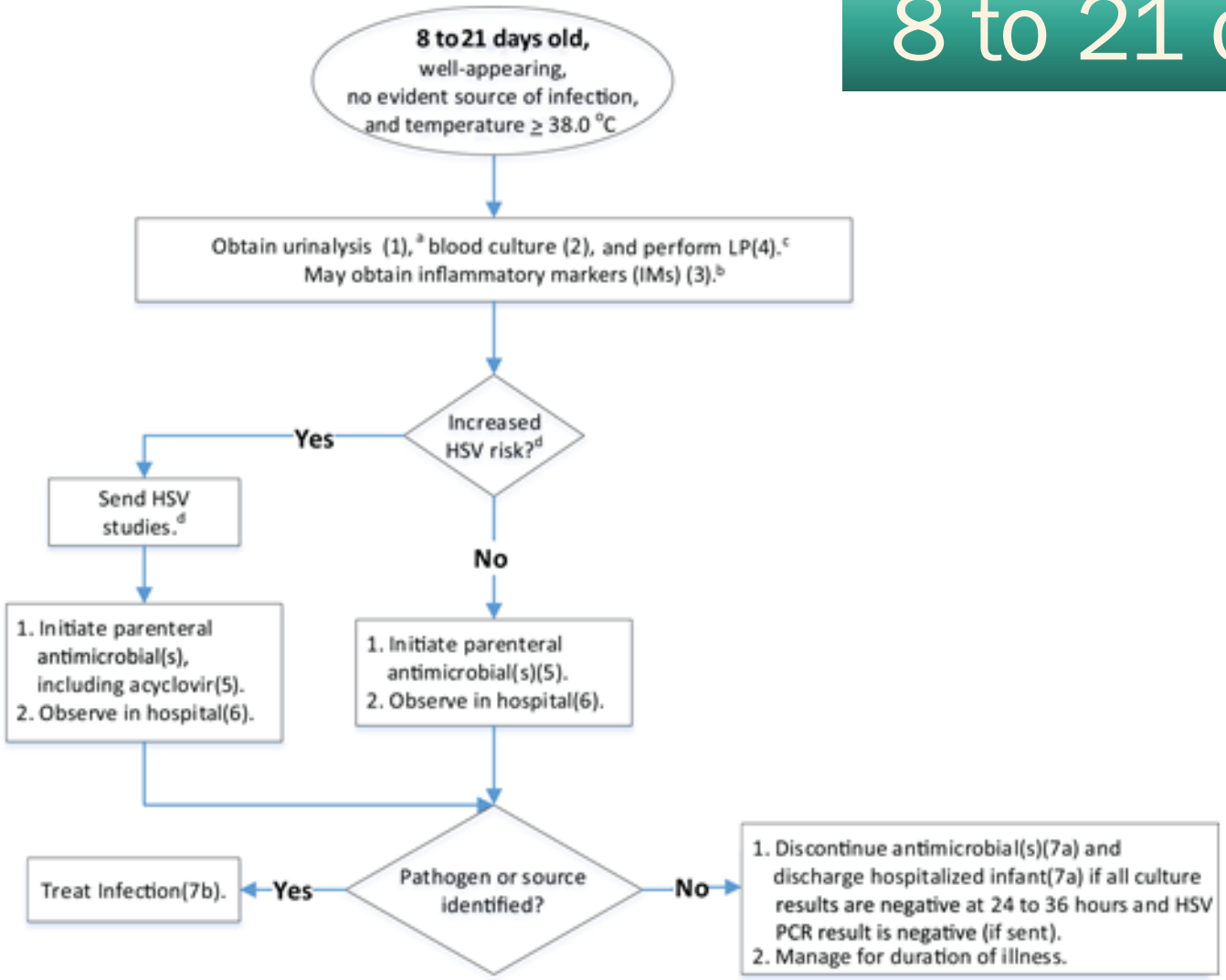
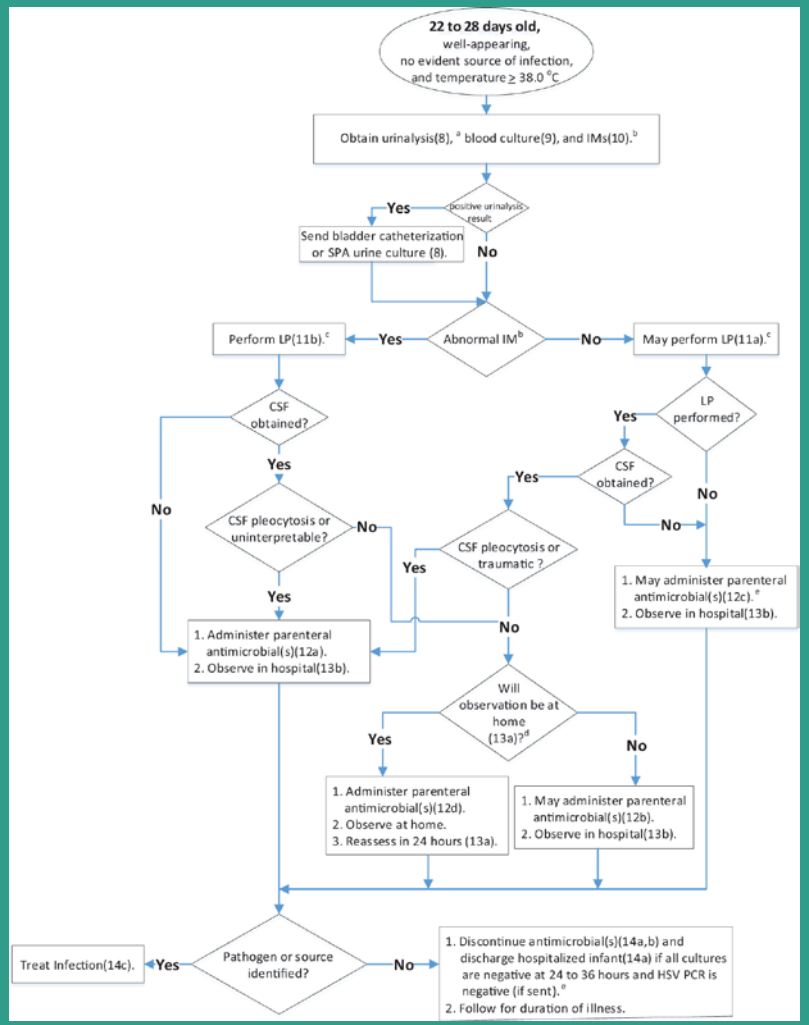
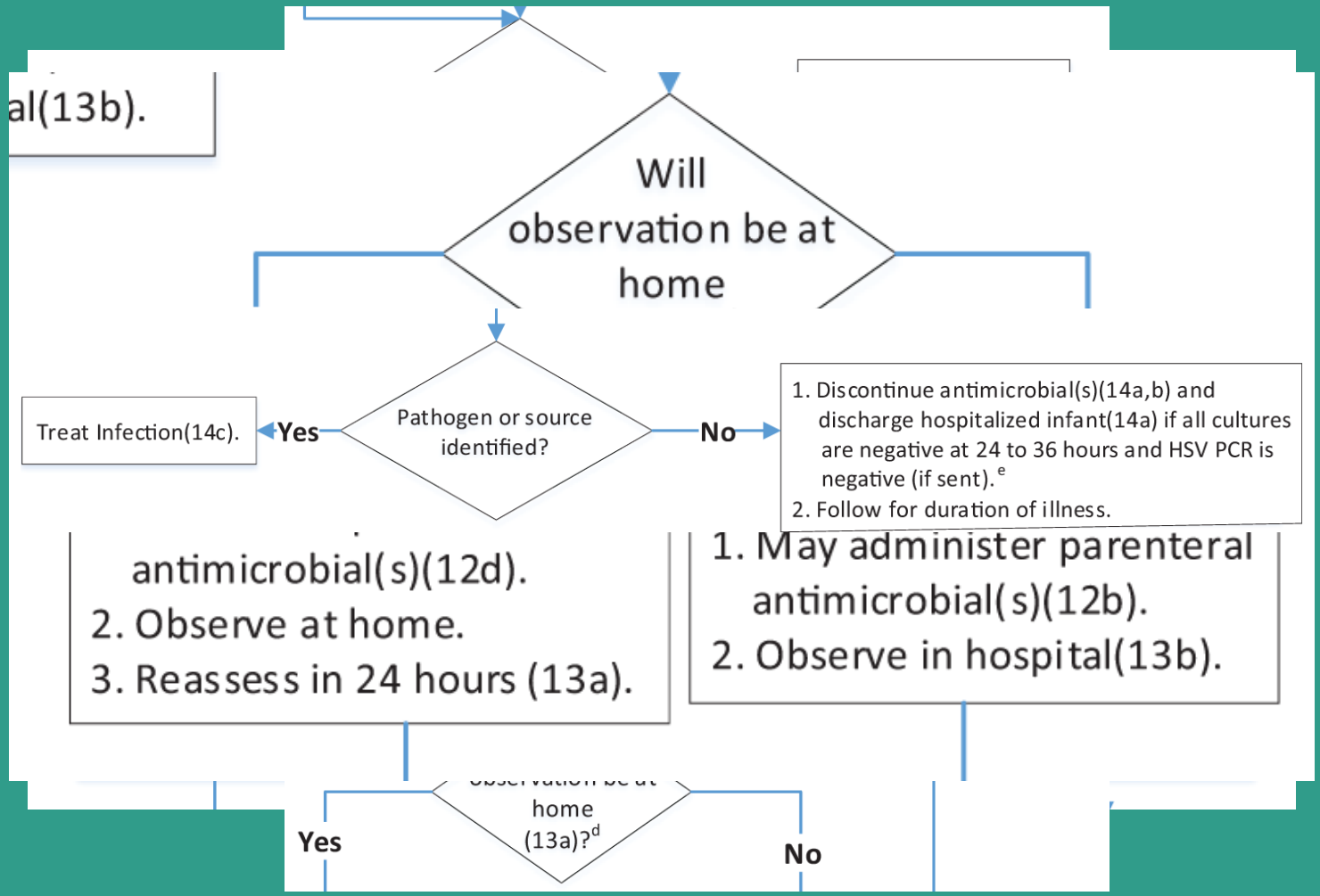
8 to 21 days old



Laboratory values of inflammation are considered elevated at the following levels: (1) procalcitonin >0.5 ng/mL, (2) CRP >20 mg/L, and (3) ANC >4000, >5200 per mm^3

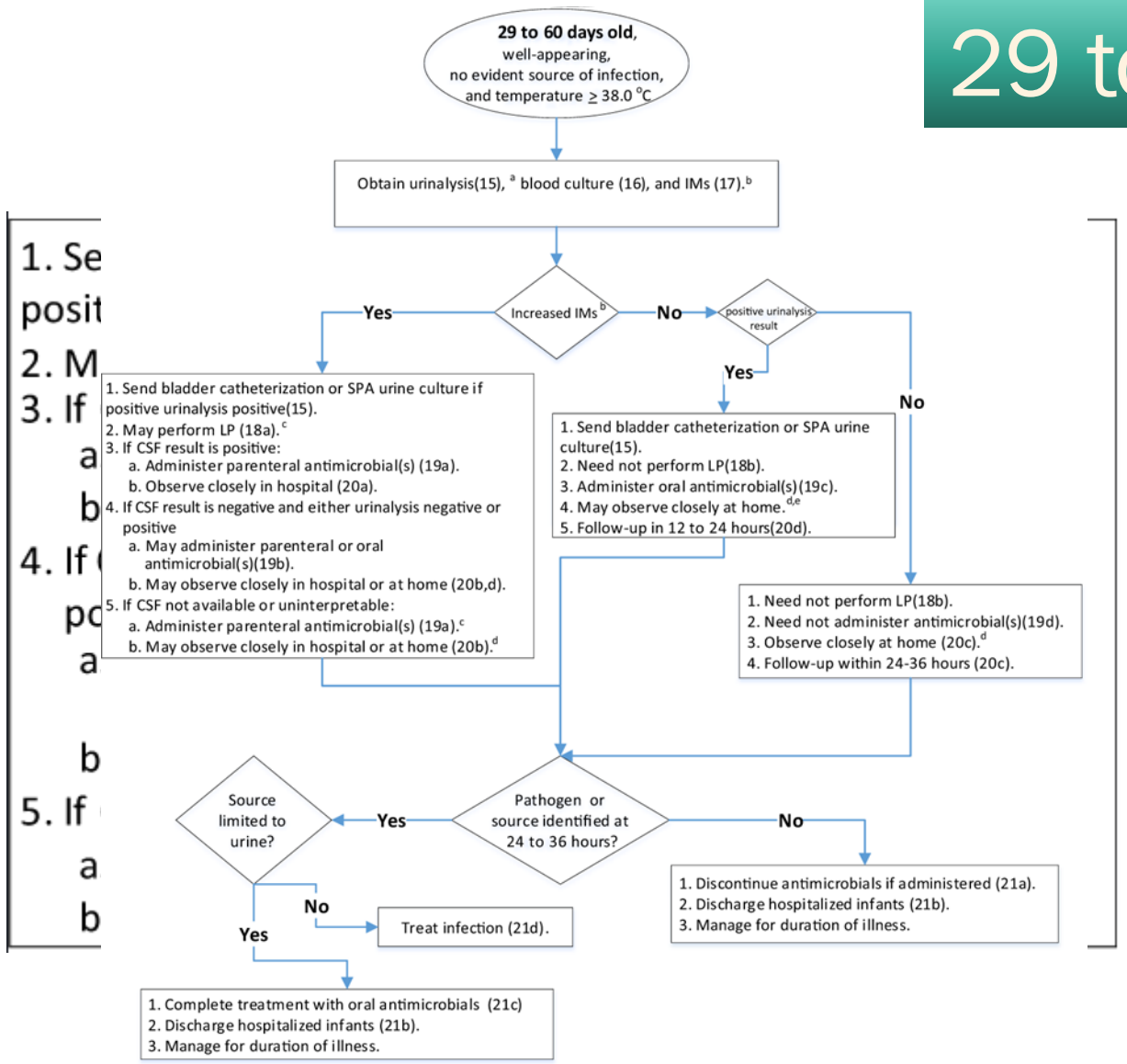
22 to 28 days old





Infant may be managed at home if parent and clinician agree that the following are present: reliable phone and transportation, parent willingness to observe and communicate changes in condition, and agreement to the infant being reevaluated in 24 hours.

29 to 60 days old



IMs are considered abnormal at the following levels: (1) temperature >38.5°C, (2) procalcitonin >0.5 ng/mL, (3) CRP >20 mg/L, and (4) ANC >4000, >5200 per mm^3

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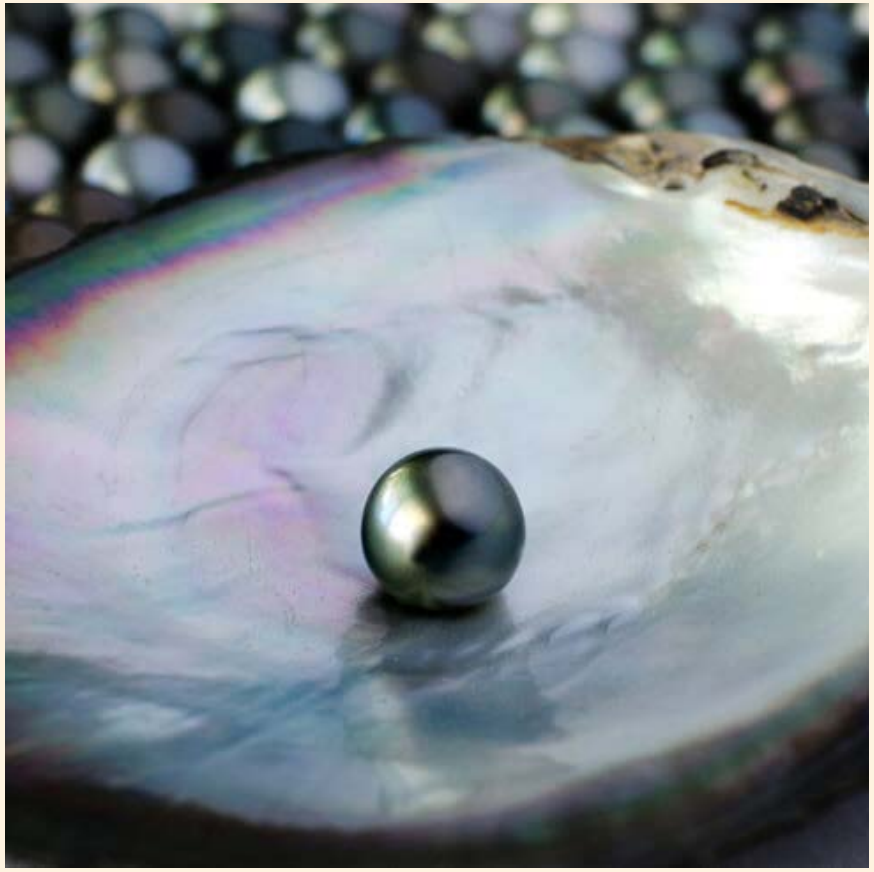
Challenges

- No infants < 7 days old
- UTIs distort prediction models
- Meningitis – uncommon – small sample size
- Epidemiology of IBIs changing
- Clinical appearance is subjective
- Clinicians work in different settings
- Variable access to newer diagnostic test and timely results
- Families with a spectrum of knowledge and skills

Take Home Pearls



Inflammatory Markers are Your Friend!

(Especially for the 22–28-day old range)

E Coli is the MOST COMMON Pathogen

(Followed by Group B Strep)

New Guidelines are for WELL Appearing Infants

(Make wise choices)

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Questions?