

Evaluation of Febrile Infants ≤ 60 days Old

An Evidence-Based Approach

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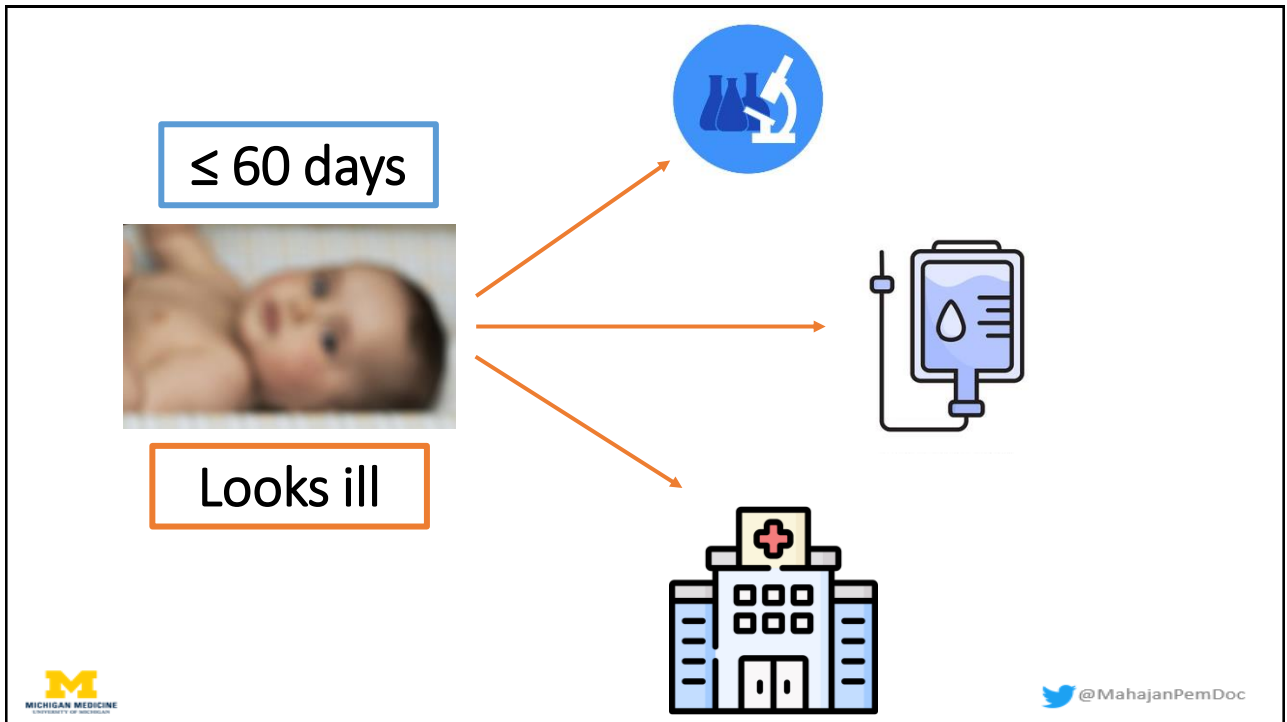


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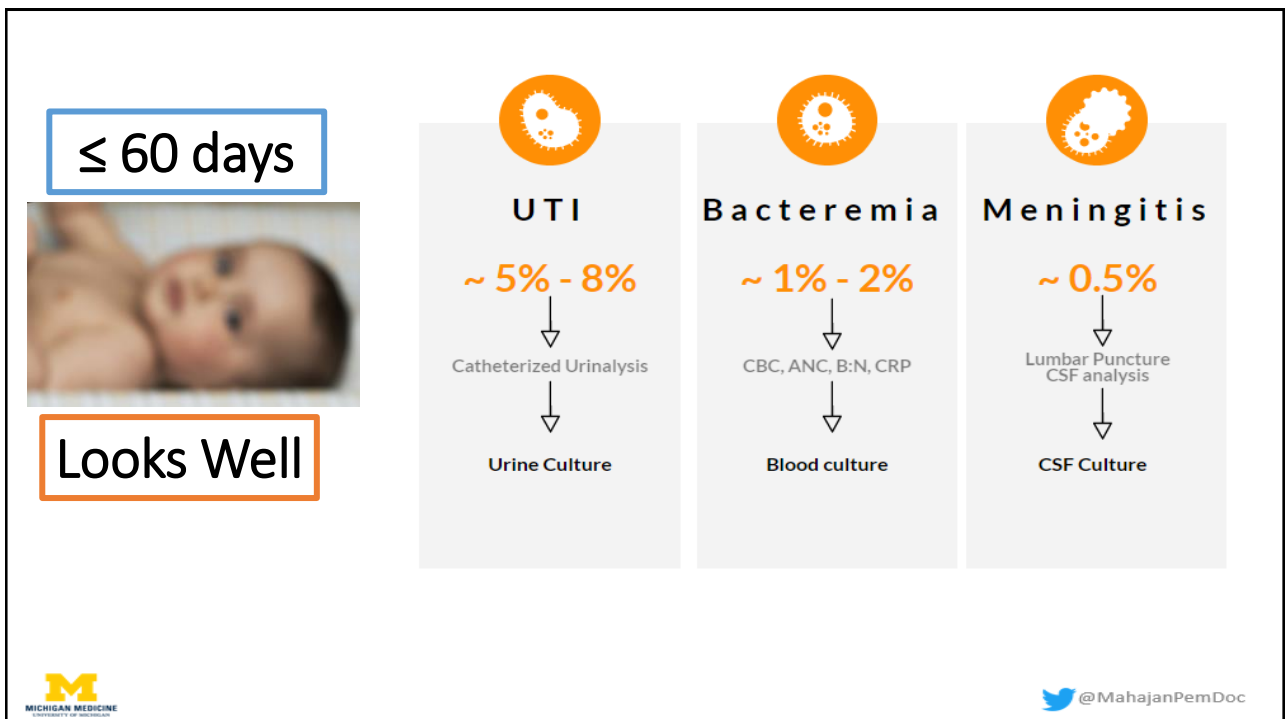
No Financial COI



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Looks well



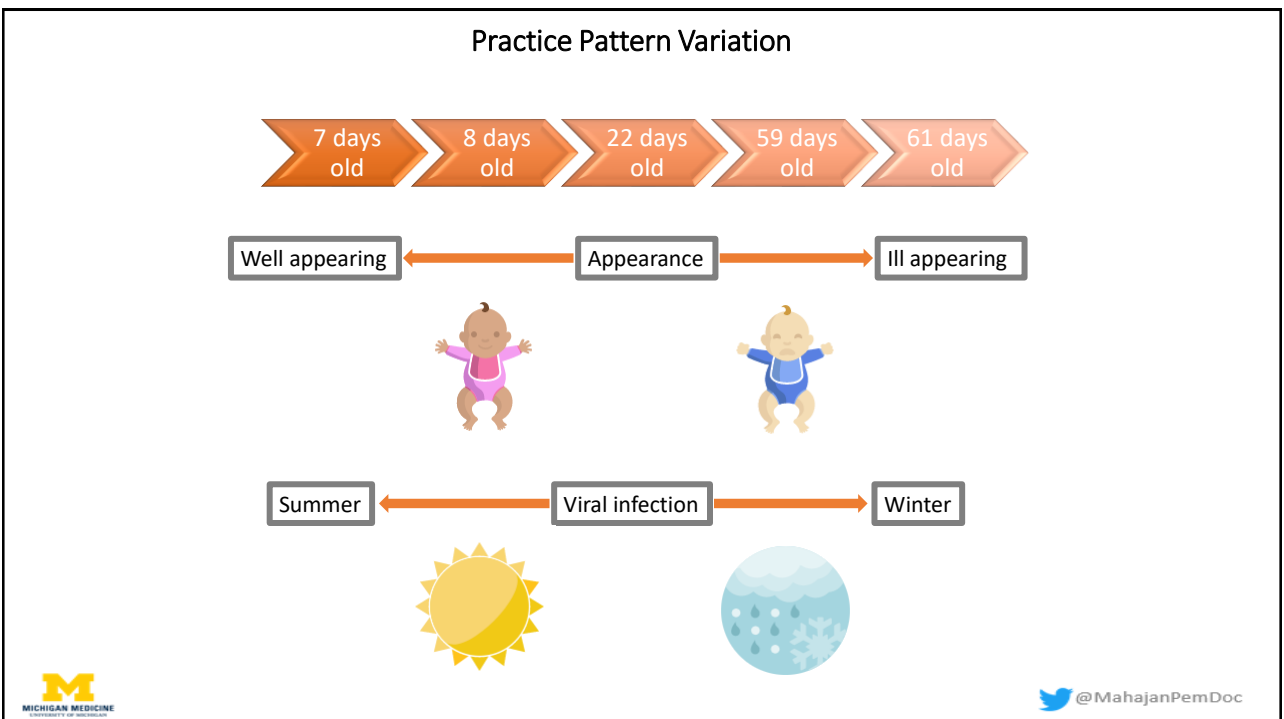





☒ 7 day old
☐ 22 day old
☐ 50 day old
 Flu +
 WBC > 15K
 UA +




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Why?



Epidemiology

History and Examination

Screening Tests are Suboptimal

Risk Prediction Models are Irrelevant

Reference Test – Culture - Suboptimal



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Blood Cultures – False Negatives



Time between collection and incubation



Volume



Organism characteristics



Prior antimicrobial therapy

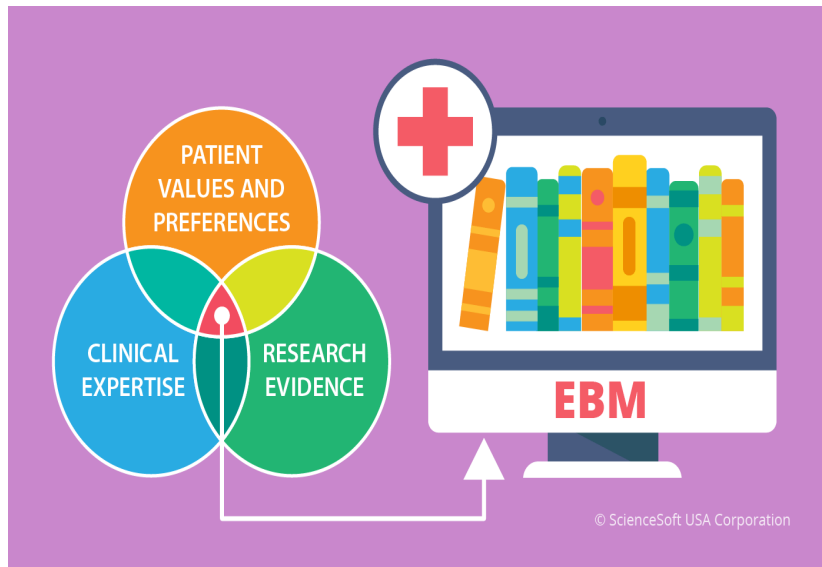


Timing: Transient or intermittent bacteremia



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JAMA Pediatrics | Original Investigation

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Research

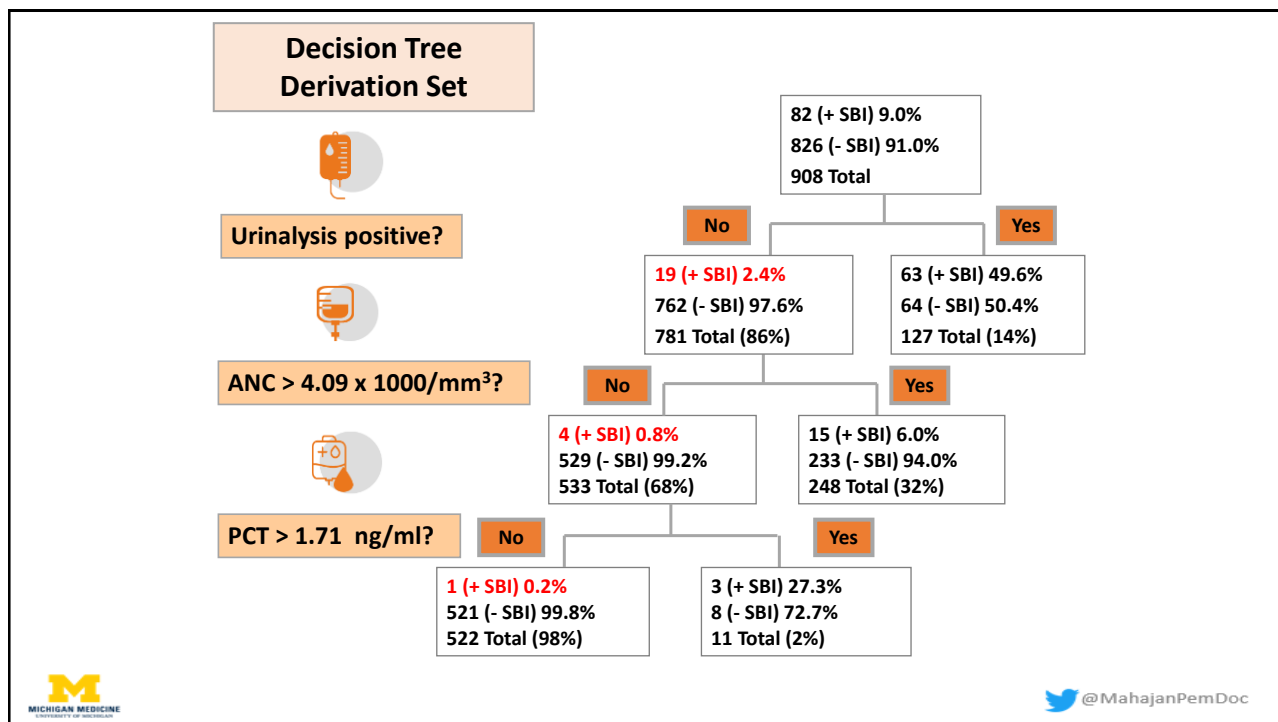
A Clinical Prediction Rule to Identify Febrile Infants 60 Days and Younger at Low Risk for Serious Bacterial Infections

Nathan Kuppermann, MD, MPH; Peter S. Dayan, MD, MS; Deborah A. Levine, MD; Melissa Vitale, MD; Leah Tzimenatos, MD; Michael G. Tunik, MD; Mary Saunders, MD; Richard M. Ruddy, MD; Genie Roosevelt, MD; Alexander J. Rogers, MD; Elizabeth C. Powell, MD, MPH; Lise E. Nigrovic, MD, MPH; Jared Muenzer, MD; James G. Linakis, MD, PhD; Kathleen Grisanti, MD; David M. Jaffe, MD; John D. Hoyle Jr, MD; Richard Greenberg, MD; Rajender Gattu, MD; Andrea T. Cruz, MD, MPH; Ellen F. Crain, MD, PhD; Daniel M. Cohen, MD; Anne Brayer, MD; Dominic Borgialli, DO, MPH; Berna Bonsu, MD; Lorin Browne, DO; Stephen Blumberg, MD; Jonathan E. Bennett, MD; Shireen M. Atabaki, MD, MPH; Jennifer Anders, MD; Elizabeth R. Alpern, MD, MSCE; Benjamin Miller, MS; T. Charles Casper, PhD; J. Michael Dean, MD, MBA; Octavio Ramilo, MD; Prashant Mahajan, MD, MPH, MBA; for the Febrile Infant Working Group of the Pediatric Emergency Care Applied Research Network (PECARN)

N ~ 8500

20 years

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Misclassification Rates						
	Derivation			Validation		
	SBI	No SBI	Total	SBI	No SBI	Total
SBI per Rule	81	305	386	86	330	416
No SBI per Rule	1	521	522	2	495	497
Total	82	826	908	88	825	913

	Derivation	Validation
Prediction rule sensitivity (95% CI)	98.8% (92.5-99.9)	97.7% (91.3-99.6)
Prediction rule specificity (95% CI)	63.1% (59.7-66.4)	60.0% (56.6-63.3)
Negative predictive value (95% CI)	99.8% (98.8-100.0)	99.6% (98.4-99.9)
Positive predictive value (95% CI)	21.0% (17.1-25.5)	20.7% (16.9-25.0)
Negative likelihood ratio (95% CI)	0.02 (0.003-0.14)	0.04 (0.01-0.15)
Positive likelihood ratio (95% CI)	2.68 (2.44 – 2.93)	2.44 (2.23-2.67)

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Rule validation stratified by age group

	Population	N	Sensitivity (95% CI)	Specificity (95% CI)	NPV	PPV
SBI	Total	127/1363 (9.3%)	97.6 (92.7, 99.4)	61.1 (58.3, 63.8)	99.6 (98.7, 99.9)	20.5 (17.4, 24.0)
	<29 days	42/446 (9.4%)	97.6 (85.9, 99.9)	56.4 (51.4, 61.3)	99.6 (97.2, 100.0)	18.9 (14.0, 24.9)
	29-60 days	85/917 (9.3%)	97.6 (91.0, 99.6)	63.3 (60.0, 66.6)	99.6 (98.5, 99.9)	21.4 (17.5, 25.9)
IBI	Total	25/1363 (1.8%)	92.0 (72.5, 98.6)	56.5 (53.8, 59.2)	99.7 (98.9, 100.0)	3.8 (2.5, 5.7)
	<29 days	12/446 (2.7%)	91.7 (59.8, 99.6)	52.5 (47.7, 57.3)	99.6 (97.2, 100.0)	5.1 (2.7, 9.1)
	29-60 days	13/917 (1.4%)	92.3 (62.1, 99.6)	58.4 (55.1, 61.6)	99.8 (98.8, 100.0)	3.1 (1.7, 5.5)

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What?



The
Initiative

So What?



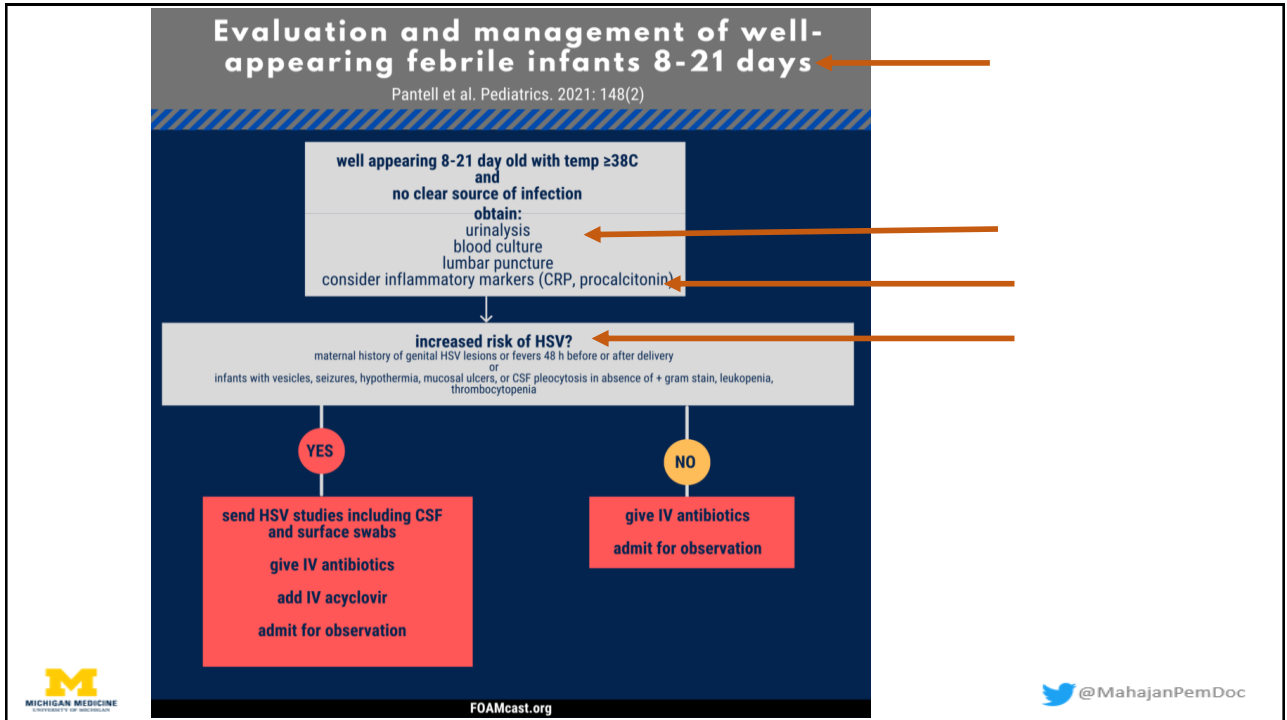
Its
Significance

Now What?

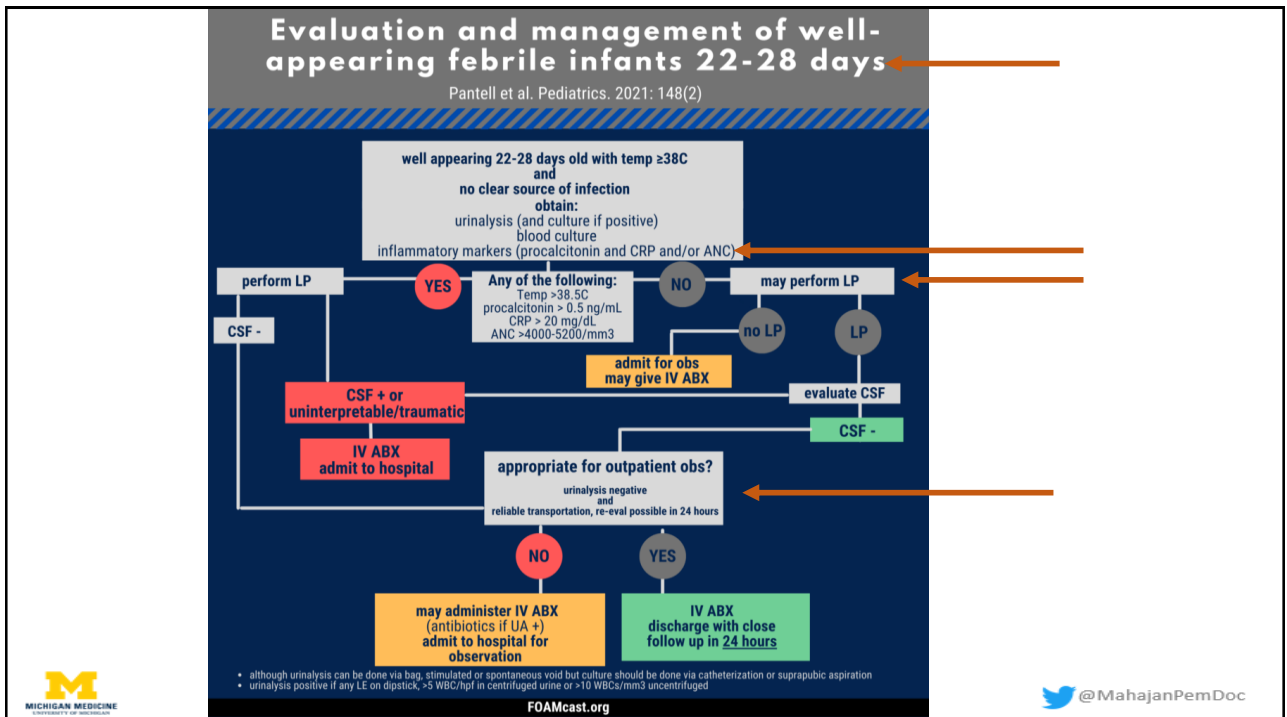


Next
Steps

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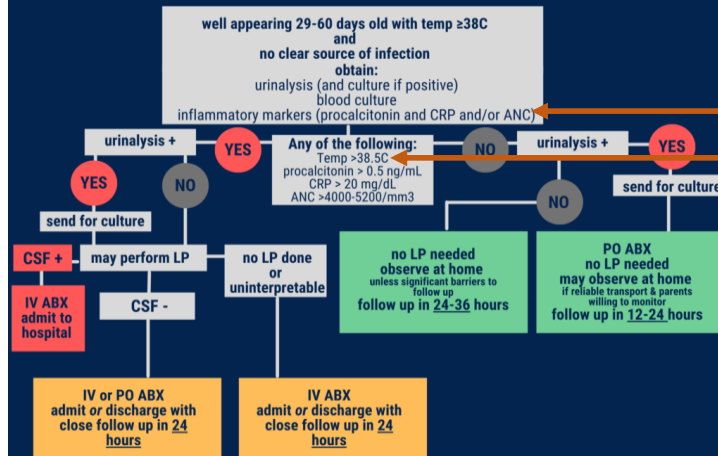
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Evaluation and management of well-appearing febrile infants 29-60 days

Pantell et al. Pediatrics. 2021; 148(2)



• although urinalysis can be done via bag, stimulated or spontaneous void but culture should be done via catheterization or suprapubic aspiration
• urinalysis positive if any LE on dipstick, ≥ 5 WBC/hpf in centrifuged urine or > 10 WBCs/mm³ uncentrifuged

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Which Well-Appearing Febrile Infants 8-60 days old Need a Lumbar Puncture?

Pantell et al. Pediatrics. 2021; 148(2)

Need a lumbar puncture

All infants ages 8-21 days

Infants 22-28 days who have any abnormal inflammatory marker
Temp $> 38.5^{\circ}\text{C}$, ANC > 4000 or 5200 , CRP $> 20 \text{ mg/L}$, procalcitonin $> 0.5 \text{ mg/mL}$

May have a lumbar puncture performed

Infants 22-28 days who have NORMAL inflammatory markers

Infants 29-60 days who have ABNORMAL inflammatory markers

Do *NOT* need a lumbar puncture

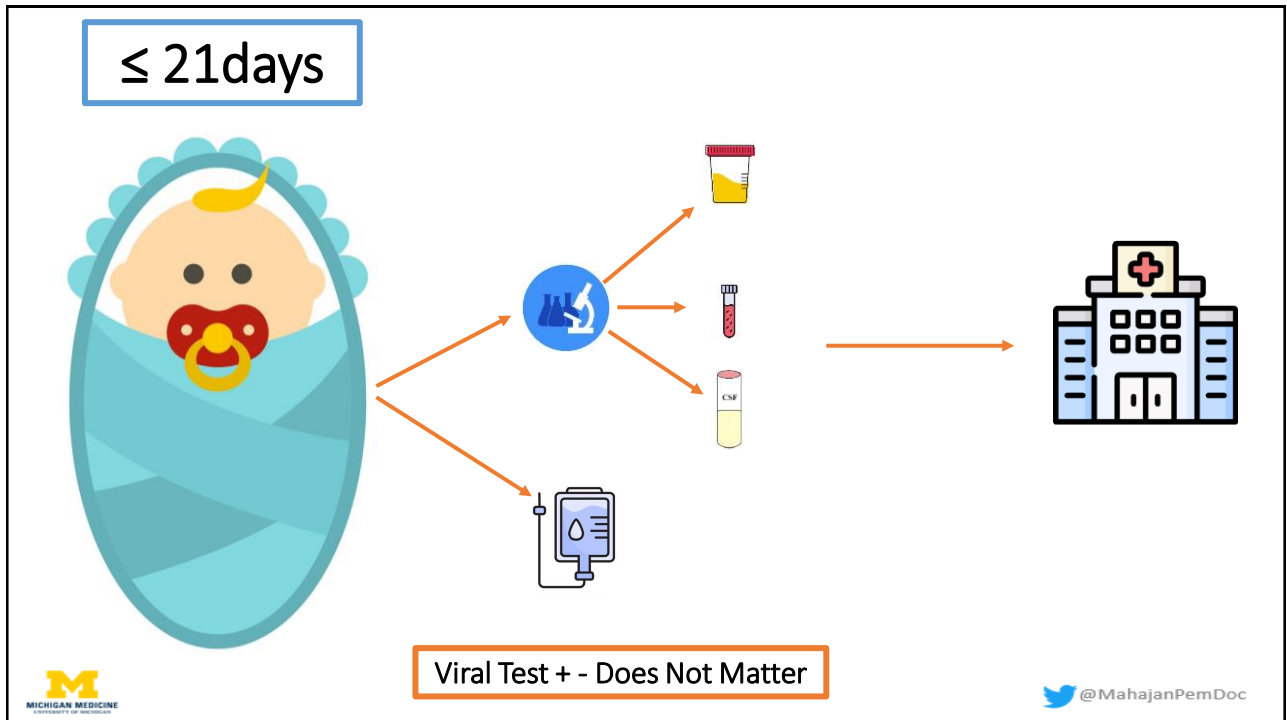
Infants 29-60 days who have NORMAL inflammatory markers

Note: not all inflammatory markers must be obtained. These recommendations refer to whether those markers that are obtained are normal or abnormal

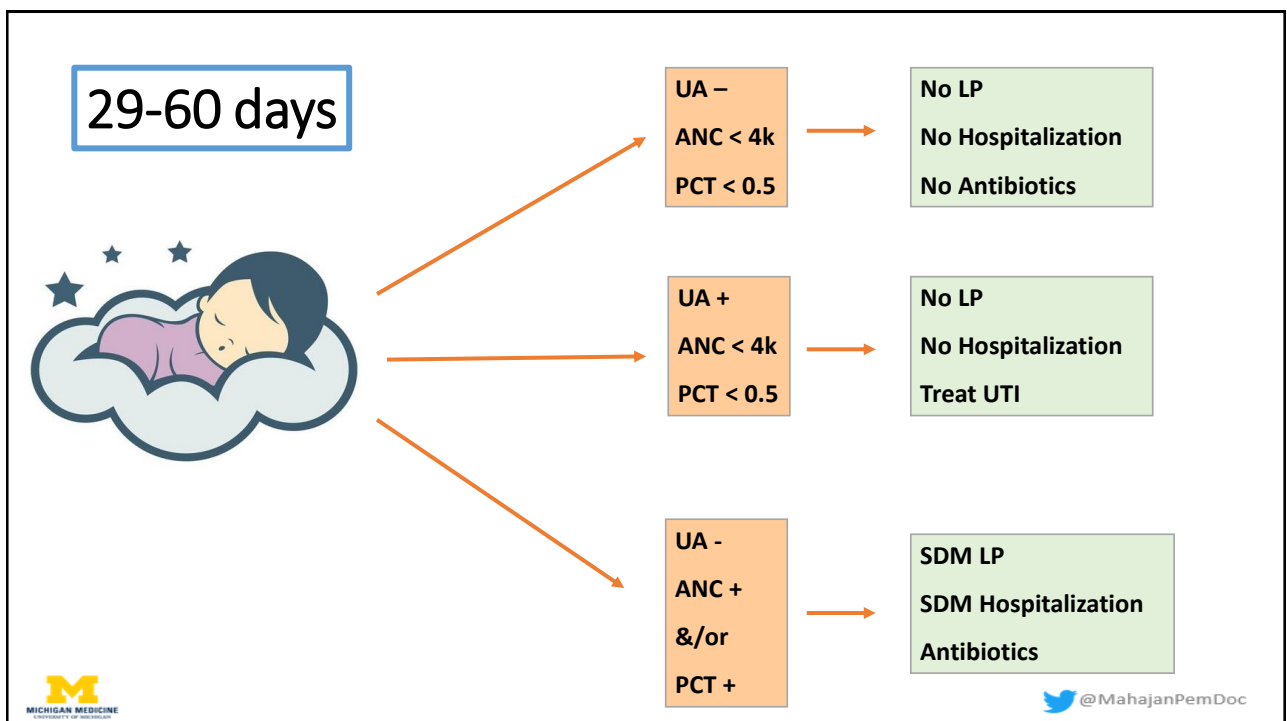
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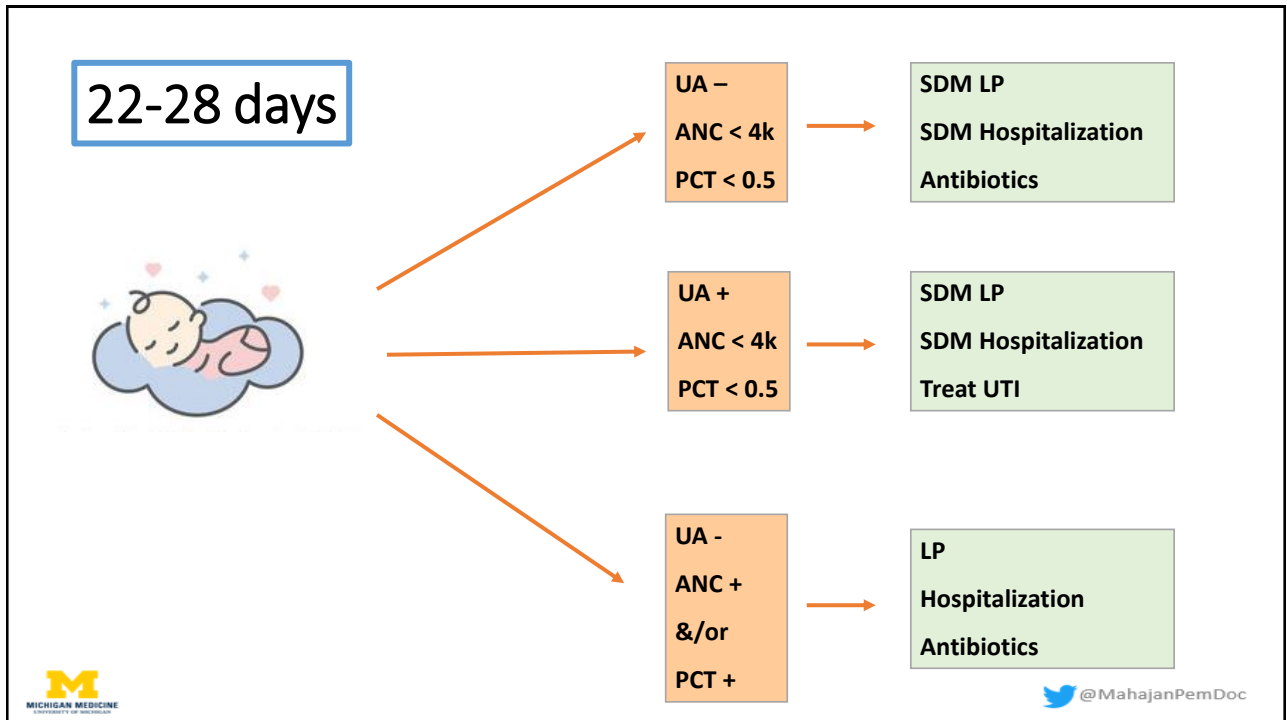
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ORIGINAL ARTICLES

Risk of Bacterial Coinfections in Febrile Infants 60 Days Old and Younger with Documented Viral Infections

Prashant Mahajan, MD, MPH, MBA^{1,*}, Lorin R. Browne, DO², Deborah A. Levine, MD³, Daniel M. Cohen, MD⁴, Rajender Gattu, MD⁵, James G. Linakis, MD, PhD⁶, Jennifer Anders, MD⁷, Dominic Borgialli, DO, MPH⁸, Melissa Vitale, MD⁹,

Table IV. Rate of SBI stratified by age among febrile infants with and without documented viral infections

Variables	Virus positive	Virus negative	Age-specific RR
SBI			
≤28 d	4.2% (2.4%-6.7%)	16.9% (14.2%-19.8%)	4.0 (2.4-6.6)
>28 d	3.4% (2.3%-4.9%)	9.9% (8.1%-11.9%)	2.9 (1.9-4.3)
UTI			
≤28 d	2.6% (1.3%-4.8%)	13.3% (10.9%-16.1%)	5.1 (2.7-9.6)
>28 d	2.8% (1.8%-4.2%)	8.8% (7.2%-10.7%)	3.1 (2.0-4.9)
Bacteremia			
≤28 d	1.1% (0.3%-2.7%)	4.4% (3.0%-6.1%)	4.1 (1.5-11.6)
>28 d	0.6% (0.2%-1.4%)	1.8% (1.1%-2.9%)	3.0 (1.1-8.1)
Meningitis			
≤28 d	0.8% (0.2%-2.3%)	1.7% (0.9%-2.9%)	2.1 (0.6-7.5)
>28 d	0.2% (0.0%-0.9%)	0.2% (0.0%-0.7%)	0.8 (0.1-5.6)

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No PCT

CRP but no PCT

No CRP No PCT

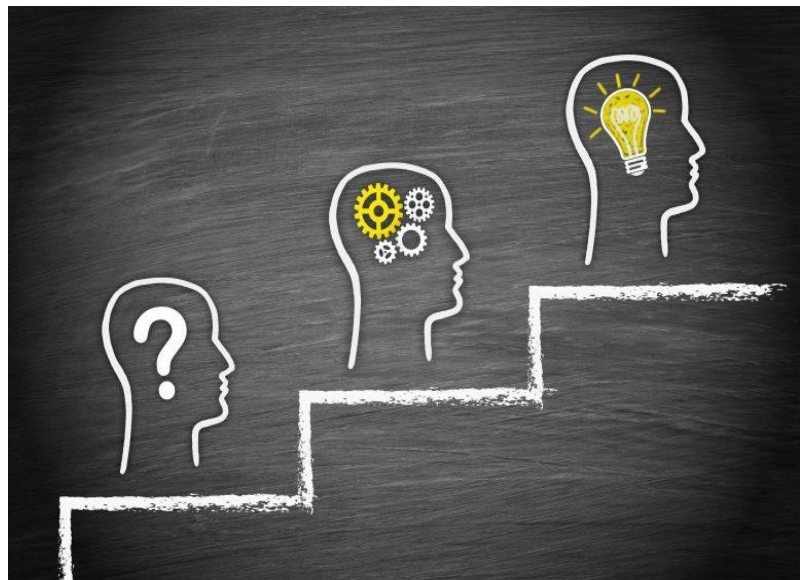
Leukopenia

61 days

Traumatic LP

Hyperpyrexia

Hypothermia





Reference Tests

JAMA 2016 Mahajan et al



Research

JAMA | Preliminary Communication | INNOVATIONS IN HEALTH CARE DELIVERY

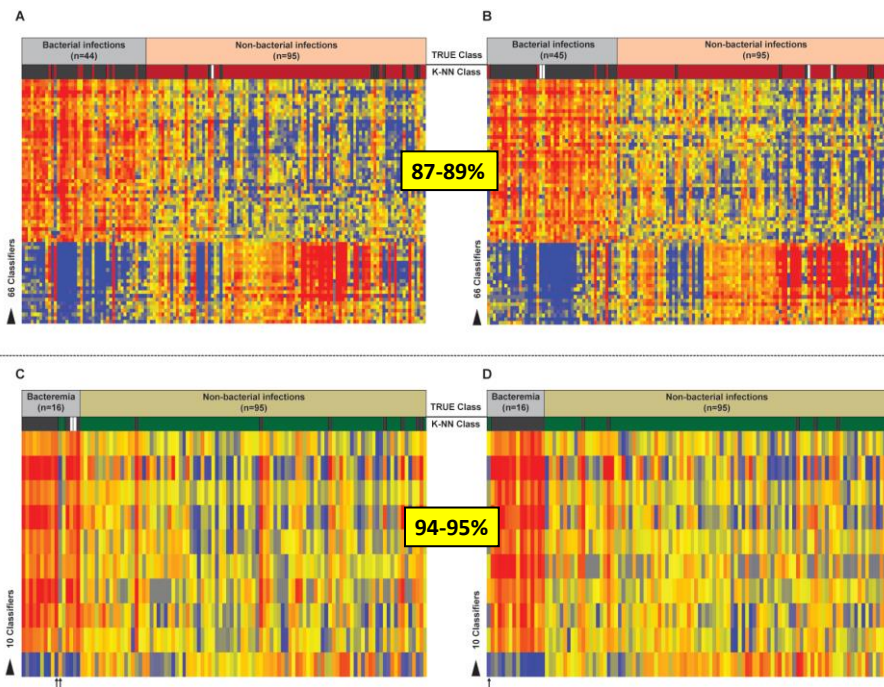
Association of RNA Biosignatures With Bacterial Infections in Febrile Infants Aged 60 Days or Younger

Prashant Mahajan, MD, MPH, MBA; Nathan Kuppermann, MD, MPH; Asuncion Mejias, MD, PhD; Nicolas Suarez, PhD; Damien Chaussabel, PhD; T. Charles Casper, PhD; Bennett Smith, BS; Elizabeth R. Alpern, MD, MSCE; Jennifer Anders, MD; Shireen M. Atabaki, MD, MPH; Jonathan E. Bennett, MD; Stephen Blumberg, MD; Bema Bonsu, MD; Dominic Borgialli, DO, MPH; Anne Brayer, MD; Lorin Browne, DO; Daniel M. Cohen, MD; Ellen F. Crain, MD, PhD; Andrea T. Cruz, MD, MPH; Peter S. Dayan, MD, MSCE; Rajender Gattu, MD; Richard Greenberg, MD; John D. Hoyle Jr, MD; David M. Jaffe, MD; Deborah A. Levine, MD; Kathleen Lillis, MD; James G. Linakis, MD, PhD; Jared Muenzer, MD; Lise E. Nigrovic, MD, MPH; Elizabeth C. Powell, MD, MPH; Alexander J. Rogers, MD; Genie Roosevelt, MD; Richard M. Ruddy, MD; Mary Saunders, MD; Michael G. Tunik, MD; Leah Tzimenatos, MD; Melissa Vitale, MD; J. Michael Dean, MD, MBA; Octavio Ramilo, MD; for the Pediatric Emergency Care Applied Research Network (PECARN)



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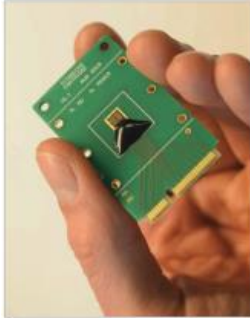
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RESEARCH LETTER

Translation of a Host Blood RNA Signature Distinguishing Bacterial From Viral Infection Into a Platform Suitable for Development as a Point-of-Care Test

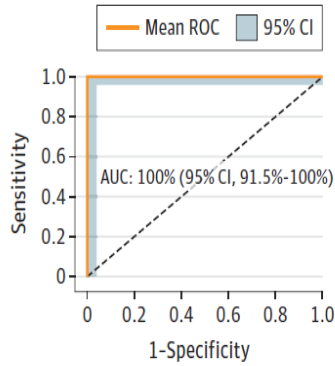
Figure 1. A Handheld Point-of-Care Test



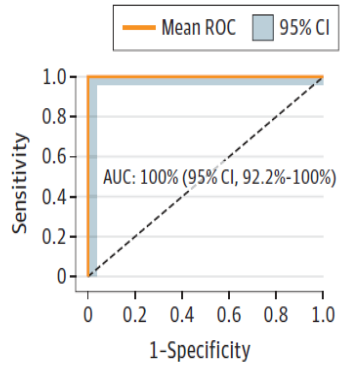
Disposable diagnostic cartridge containing a complementary metal oxide semiconductor ion-sensitive field-effect transistor array for on-chip nucleic acid amplification.



C Microarray ROC curve



D RT-eLAMP ROC curve



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