Clinical Pathways

Fever and Sepsis Evaluation in the Infant (29-60 days)

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MAGNET RECOGNIZED AMERICAN NURSES CREDENTIALING CENTER

BEST CHILDREN'S HOSPITAL WOMEN'S CHOICE AWARD 2023

What is a Clinical Pathway?

An evidence-based guideline that decreases unnecessary variation and helps promote safe, effective, and consistent patient care.

Objectives of Pathway

- Decrease variability in care for febrile infants ages 29-60 days
- Decrease unnecessary testing
- Decrease unnecessary antibiotic use
- Decrease rate of hospitalization for well-appearing infants with low risk test results
- Decrease average length of stay of patients admitted as inpatient or placed in observation

Why is Pathway Necessary?

- Fever is a very common reason for visits to ED
  - 500,000 ED visits annually children ≤ 60 days of age
  - Serious Bacterial Infection (SBI) rate: 6-10% in children ≤ 90 days of age
    - UTI 5-9%
    - Bacteremia 1.9-2.2%
    - Meningitis 0.3-0.5%
- There is great variability in care provided to patients in this age group
  - **Past** Management of febrile infants 29-60 disorder included 3 common algorithms:
    1. Philadelphia Criteria
    2. Rochester Criteria
    3. Boston Criteria

Background

- More and more evidence now exists which supports:
  - Use of clinical pathways for workup and treatment of these infants
  - Lumbar puncture not universally indicated in this age group
  - Hospitalization not necessary for all febrile infants in this age group
  - Shorter length of stay and earlier discontinuation of antibiotics if hospitalized

- Byington et al., 2012: evidence based care practice model for febrile infants 29-90 days old[1]:
  - Improved risk stratification
  - Improved rate of appropriate testing
  - Less missed SBI on initial evaluation
  - Less unnecessary antibiotics
  - Shorter hospital length of stay
  - All accomplished across multiple care sites

- Chua et al., 2015[2]
  - Showed no difference in clinical outcomes between institutions with guidelines recommending universal LP compared to institutions where LP was recommended if the patient is not “well appearing” or had high risk laboratory results

Background

- Recent literature is more relevant to our inpatient population
  - Excludes patients admitted to ICUs, with indwelling hardware, and with histories of intra-abdominal, intracranial or intrathoracic surgeries
  - Current automated technology is allowing for earlier detection
- 97% of blood cultures, 95% of urine cultures and 86% of CSF cultures treated as true pathogens were identified in ≤36 hours[3]
- Risk of positive CSF culture >24 hours is low (1.5%) and is 0% in low risk infants (well-appearing, normal laboratory values) (Fielding-Singh, 4)
- Most pathogens in blood cultures in febrile bacteremic infants ≤90 days will be identified within 24 hours of collection [5]
  - Time to positivity: 91% by 24 hours, 96% by 36 hours, 99% by 48 hours
- Newer risk stratification strategies better at predicting “Invasive Bacterial Infection (IBI)” – see next slide

Recent Literature: New Algorithms

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

Borja Gomez, MD,[a,b] Santiago Mintegi, MD, PhD,[a,b] Silvia Bressan, MD, PhD,[c] Liviana Da Dalt, MD,[d] Alain Gervaix, MD,[e] Laurence Lacroix, MD,[e] on behalf of the European Group for Validation of the Step-by-Step Approach

Original Investigation

FREE

February 18, 2019

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

Nathan Kuppermann, MD, MPH[1]; Peter S. Dayan, MD, MSc[2]; Deborah A. Levine, MD[3]; et al

» Author Affiliations | Article Information

JAMA Pediatr. 2019;173(4):342-351. doi:10.1001/jamapediatrics.2018.5501

PECARN Rule for Low Risk Febrile Infants 29-60 Days Old
Online tool

Conclusion:

- CBC not very predictive
- ANC better
- PCT most useful

*But using a combination of these is best

Recent Literature: Bacterial Meningitis with Positive UA and Use of Procalcitonin

JAMA Network | Open

Original Investigation | Pediatrics

Prevalence of Bacterial Meningitis Among Febrile Infants Aged 29-60 Days With Positive Urinalysis Results
A Systematic Review and Meta-analysis

Brett Burstein, MD, CM, PhD, MPH; Vikram Sabhaney, MD; Jeffrey N. Bone, MSc; Quynh Doan, MD, CM, PhD, MHSc; Fahad F. Mansouri, MD; Garth D. Meckler, MD, MSHS

Rate of bacterial meningitis 0.44% in patients with positive urinalysis (2703 infants) vs 0.5% in patients with a normal urinalysis (10,032)

Additional references re prevalence of meningitis with a positive UA:

- Young BR, Tran NHP, Alabaster A, Greenhow TL. The Prevalence of Bacterial Meningitis in Febrile Infants 29-60 Days With Positive Urinalysis. *Hosp Pediatr.* 2018 Aug;8(8):450-457.
- Biondi EA, Lee B, Ralston SL, et al. Prevalence of Bacteremia and Bacterial Meningitis in Febrile Neonates and Infants in the Second Month of Life: A Systematic Review and Meta-analysis. *JAMA Netw Open.* 2019 Mar 1;2(3):e190874.

RESEARCH ARTICLE

Use of Procalcitonin in a Febrile Infant Clinical Pathway and Impact on Infants Aged 29 to 60 Days

Kaitlin Widmer, MD,[a,b] Sarah Schmidt, MD, MSHI,[a,c] Leigh Anne Bakel, MD, MS,[a,b] Michael Cookson, MD, MHS,[b] Jan Leonard, MSPH,[a,c] Amy Tyler, MD, MSCS[a,b]

ABSTRACT

OBJECTIVES: Recent evidence suggests that measuring the procalcitonin level may improve identification of low-risk febrile infants who may not need intervention. We describe outcomes after the implementation of a febrile infant clinical pathway recommending measurement of the procalcitonin level for risk stratification.

METHODS: In this single-center retrospective pre-post intervention study of febrile infants aged 29 to 60 days, we used interrupted time series analyses to evaluate outcomes of lumbar puncture (LP), antibiotic administration, hospital admission, and emergency department (ED) length of stay (LOS). A multivariable logistic regression was used to evaluate the odds of LP.

RESULTS: Data were analyzed between January 2017 and December 2019 and included 740 participants. Procalcitonin use increased post–pathway implementation (PI). The proportion of low-risk infants receiving an LP decreased significantly post-PI ($P = .001$). In the adjusted interrupted time series analysis, there was no immediate level change (shift) post-PI for LP (0.98 [95% confidence interval (CI): 0.49–1.97]), antibiotics (1.17 [95% CI: 0.56–2.43]), admission (1.07 [95% CI: 0.59–1.96]), or ED LOS (1.08 [95% CI: 0.92–1.28]), and there was no slope change post-PI versus pre-PI for any measure (LP: 1.01 [95% CI: 0.94–1.08]; antibiotics: 1.00 [95% CI: 0.93–1.08]; admission: 1.03 [95% CI: 0.97–1.09]; ED LOS: 1.01 [95% CI: 0.99–1.02]). More patients were considered high risk, and fewer had incomplete laboratory test results post-PI ($P < .001$). There were no missed serious bacterial infections. A normal procalcitonin level significantly

CONCLUSIONS: Clinicians quickly adopted procalcitonin testing. Resource use for low-risk infants decreased; however, there was no change to resource use for the overall population because more infants underwent laboratory evaluation and were classified as high risk post-PI.

Recent Literature: New AAP Infant Fever Guidelines 2021!

Click here for full guideline

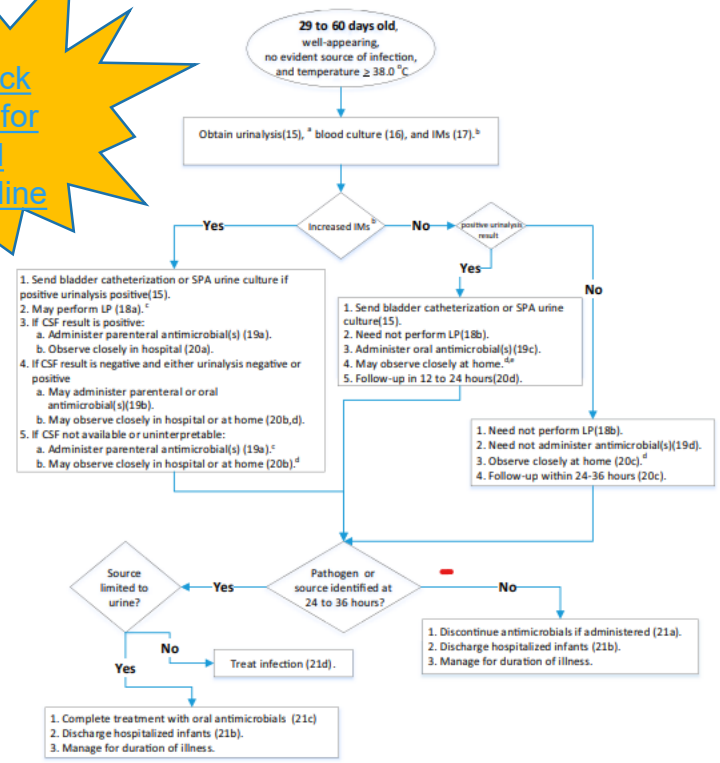


FIGURE 3 Algorithm for 29- to 60-day-old infants. [a] KAS references are shown in parentheses. [b] If available, procalcitonin should be obtained along with ANC or CRP. If procalcitonin is unavailable, both ANC and CRP should be obtained, and a temperature >38.5°C is considered abnormal. IMs are considered abnormal at the following levels: (1) temperature >38.5°C, (2) procalcitonin >0.5 ng/mL, (3) CRP >20 mg/L, (4) ANC >4000, >5200 per mm^3 (see text). [c] Send CSF for cell count, Gram stain, glucose, protein, bacterial culture, and enterovirus PCR (if available) if CSF pleocytosis is present and during periods of increased local enterovirus prevalence. Although uncommon in this age group, HSV should be considered when there is a maternal history of genital HSV lesions and in infants with vesicles, seizures, hypothermia, mucous membrane ulcers, CSF pleocytosis in the absence of a positive Gram stain result, leukopenia, thrombocytopenia, or elevated alanine aminotransferase levels. For further discussion, see the current *Red Book*. Recommended HSV studies are CSF PCR; HSV surface swabs of mouth, nasopharynx, conjunctivae, and anus for HSV culture (if available) or PCR assay; alanine aminotransferase; and blood PCR. If CSF is unobtainable or uninterpretable, there are insufficient data to make a specific recommendation. Options include the following: observe without treatment for a period of time and, depending on infant clinical condition, repeat LP and/or laboratory markers; begin empirical antimicrobial agents and reassess in 24 hours on the basis of infant response and results of blood culture; if CSF is bloody or antimicrobial agents have previously been started, analysis by multiplex PCR can add additional information; consult with local a pediatric infectious disease specialist. [d] 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. [e] Most 29- to 60-day-old infants with negative IM and urinalysis results may be observed at home. However, hospital observation is an option for infants when there are barriers to follow-up.

Support of Current Practices:

- No LP if screening inflammatory markers are normal
- Discharge of patients w/neg cultures at 24-36 hrs if well appearing, neg cultures

New Practices:

- Do NOT use WBC as inflammatory marker, but rather use ANC. However, this must be used in combination with other inflammatory markers
- Procalcitonin >0.5 is best of independent predictors, however guidelines do not recommend using in isolation for decision-making
- Positive UA alone does not count as a positive inflammatory marker
- May discharge pt from ED on oral abx if pos UA but all inflammatory markers normal – CSF included
- Discharging at 24-36 hrs should include patients with UTI since they may be managed on oral abx

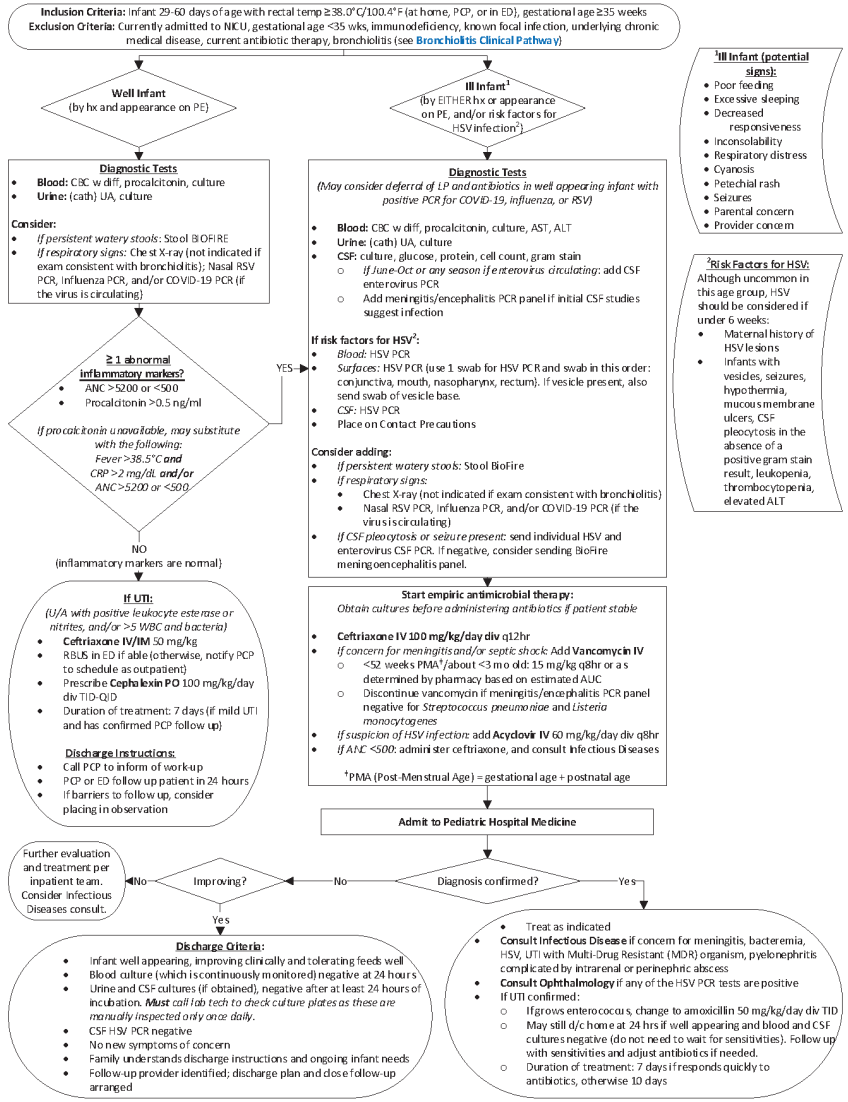
This is the Fever and Sepsis Evaluation in the Infant (29-60 days) Clinical Pathway.

We will be reviewing each component in the following slides.

CLINICAL PATHWAY:

Fever and Sepsis Evaluation in the Infant (Ages 29-60 days)

THIS PATHWAY SERVES AS A GUIDE AND DOES NOT REPLACE CLINICAL JUDGMENT.



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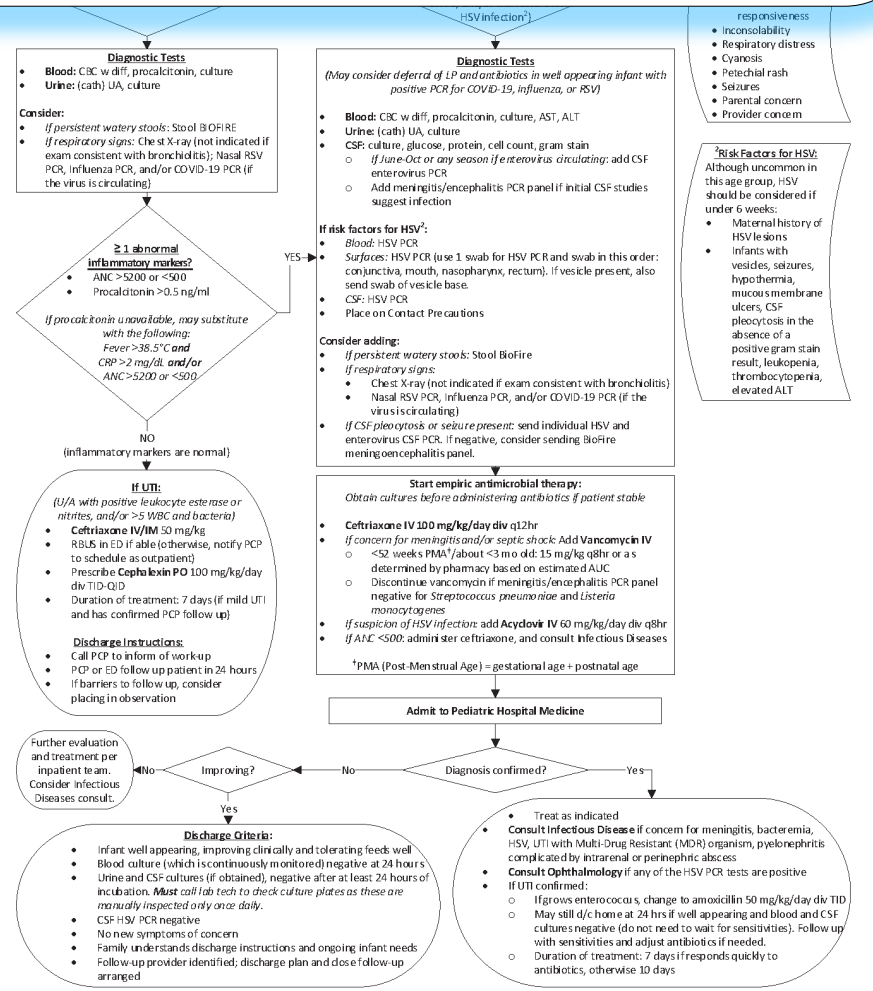
Inclusion Criteria: Infant 29-60 days of age with rectal temp ≥38.0°C/100.4°F (at home, PCP, or in ED), gestational age ≥35 weeks
Exclusion Criteria: Currently admitted to NICU, gestational age <35 wks, immunodeficiency, known focal infection, underlying chronic medical disease, current antibiotic therapy, bronchiolitis (see **Bronchiolitis Clinical Pathway**)

All infants that are 29-60 days old and ≥35 weeks gestational age with a rectal temp ≥38ºC should be included on the pathway, unless specific exclusion criteria exist.

Of note, this pathway is NOT meant for use for infants who are admitted to the NICU.



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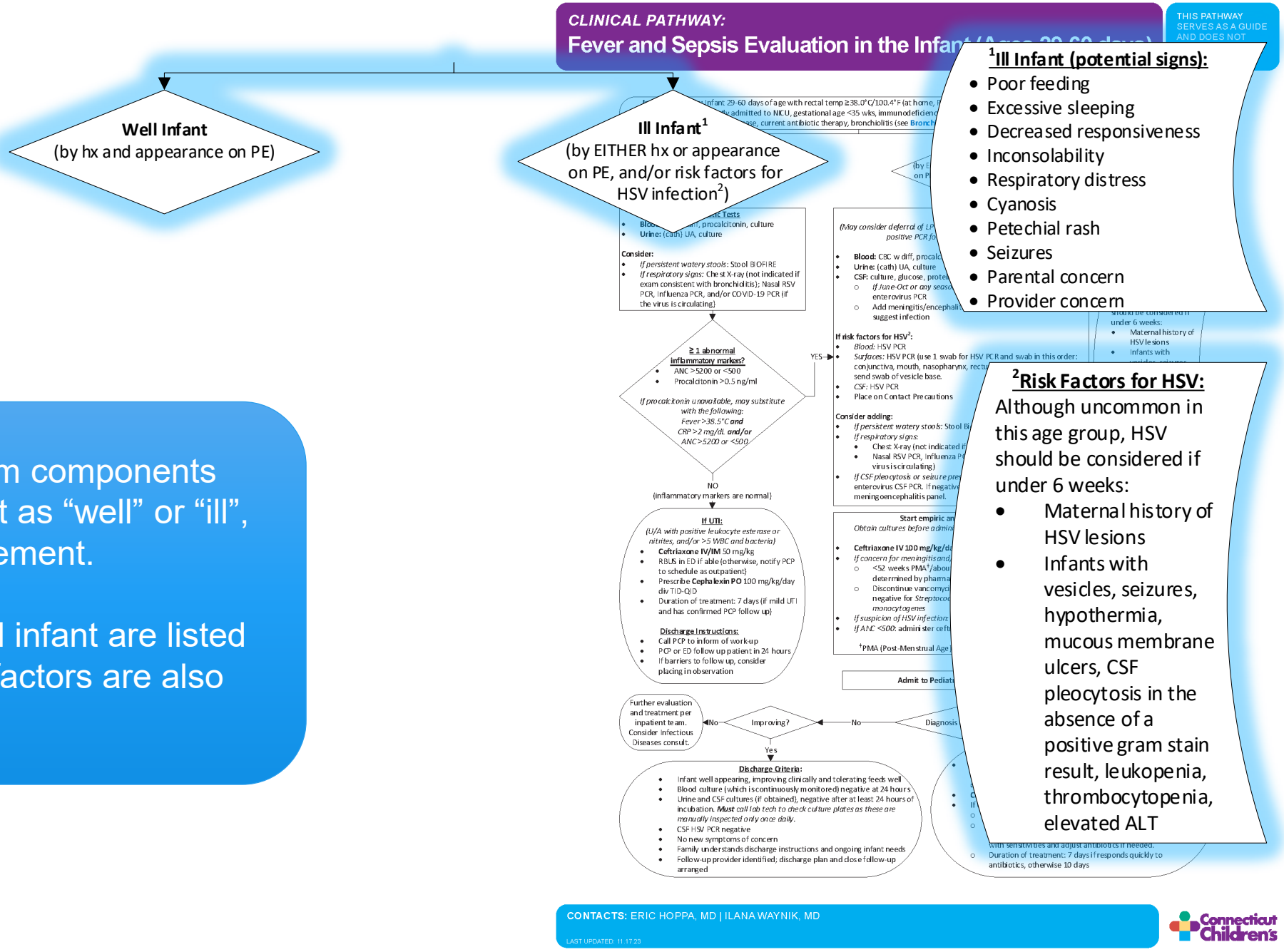
History and physical exam components are used to classify infant as “well” or “ill”, which will dictate management.

- Potential signs of an ill infant are listed
- Infants with HSV risk factors are also considered ill



Well Infant:

- Based upon recent literature, screening labs for well appearing infants are to include a CBC (to obtain ANC), procalcitonin, and urinalysis.
- These screening labs will help determine if management needs to be escalated as the infant would be at higher risk for serious bacterial illness.
- An LP is not recommended as part of the initial work up.

- If there is no procalcitonin available, should obtain a CRP.

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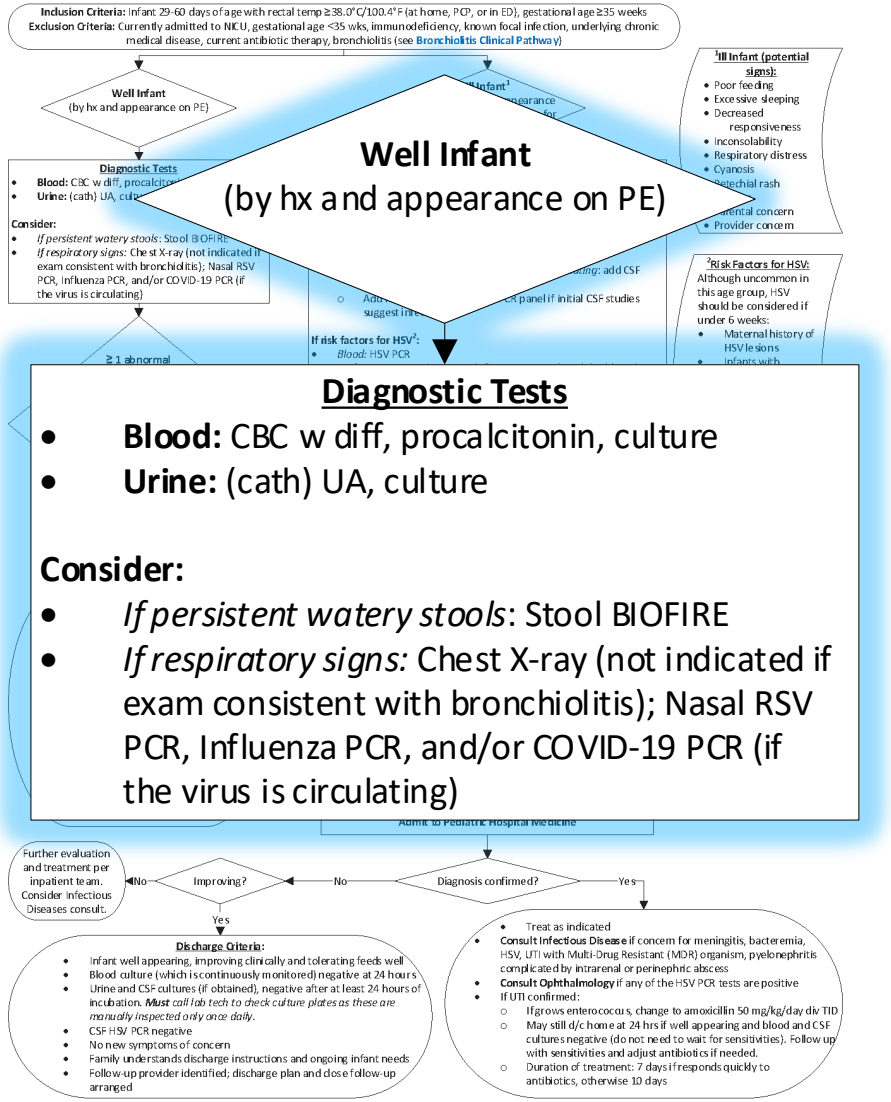

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Well Infant:

The screening inflammatory markers will help determine if the infant can be safely discharged, or if they need further work up and management.

Abnormal inflammatory markers are:

- ANC >5200 or <500
- Procalcitonin >0.5 ng/ml

If procalcitonin is not available, the following criteria can determine abnormal inflammatory markers:

- Fever >38.5 C **and**
- CRP >2 mg/dL **and/or**
- ANC >5200 or <500

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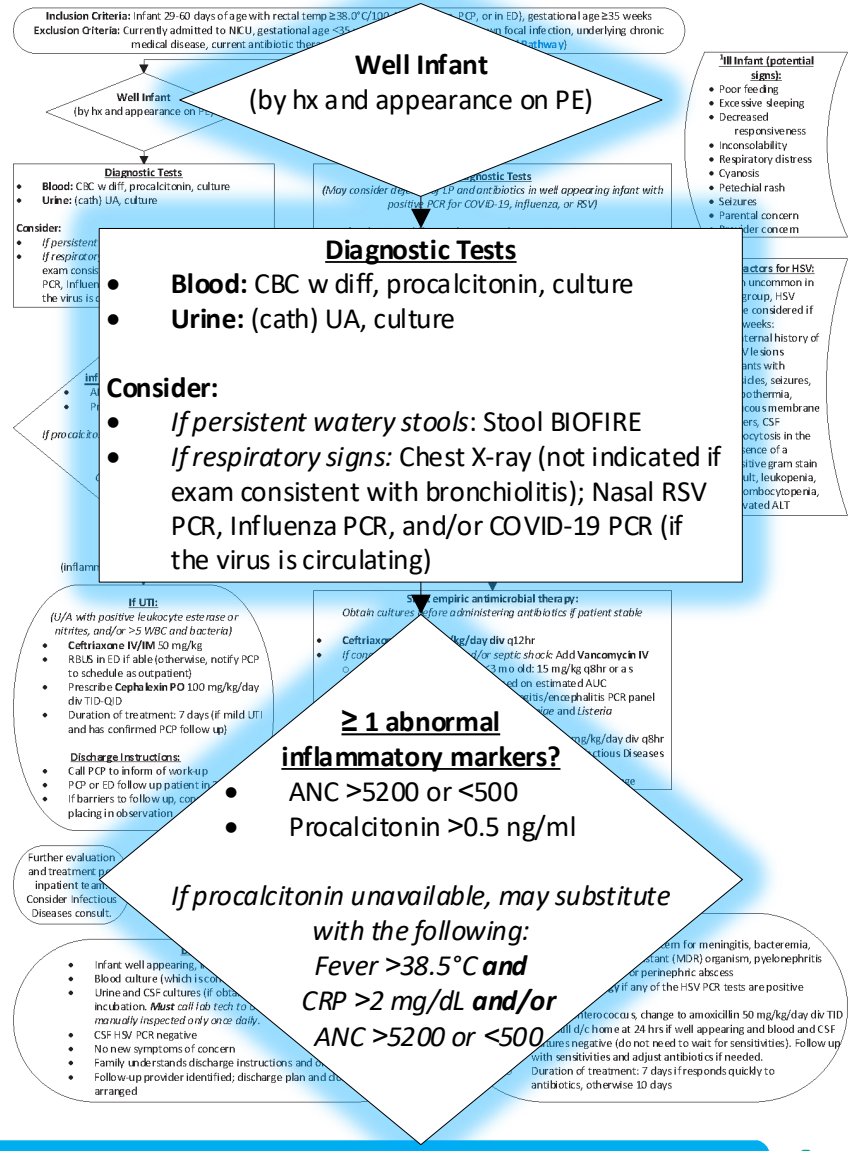

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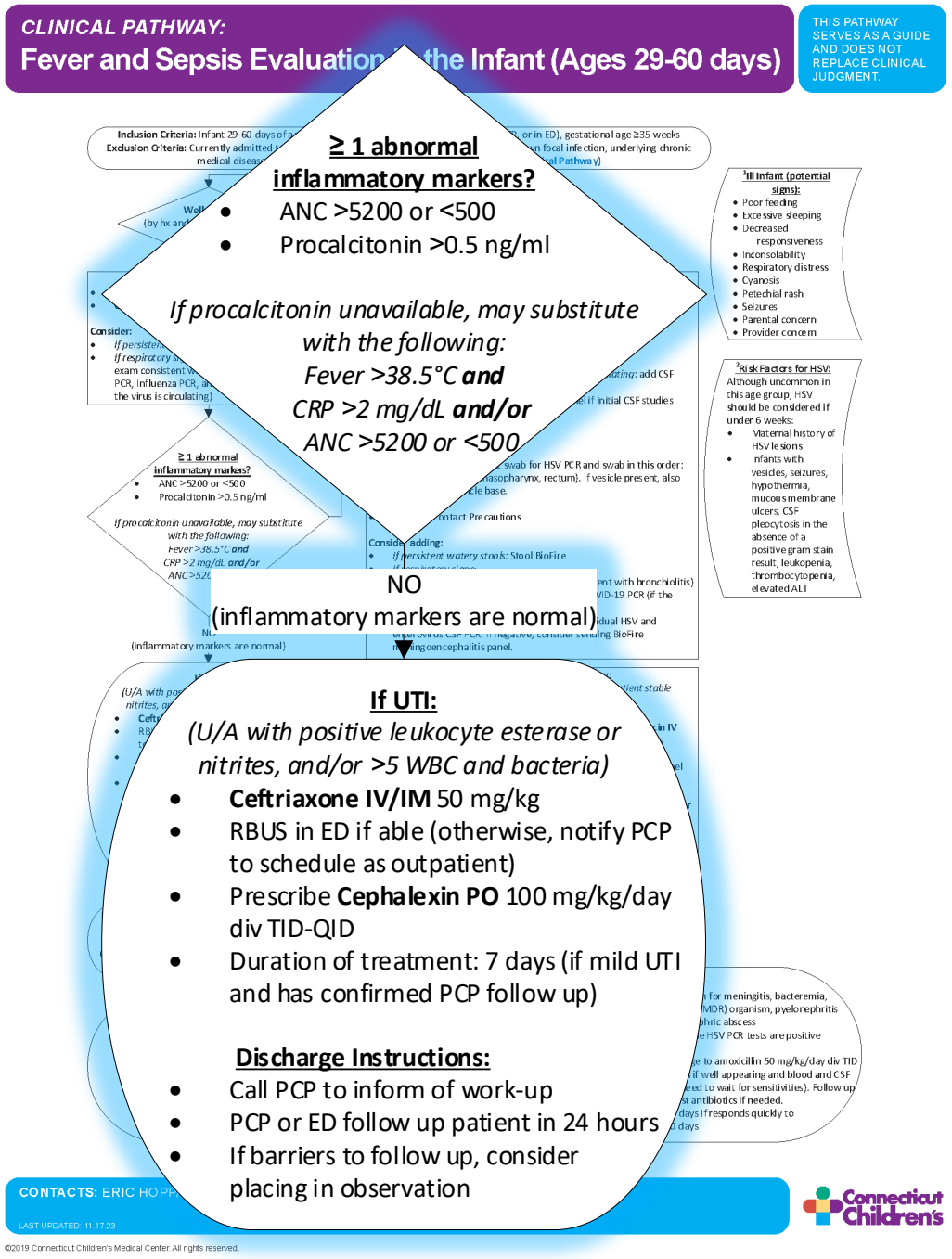
Well Infant:

If the screening labs are normal, the well-appearing infant can be safely discharged home with follow up at the pediatrician's (or ED) in 24 hours.

If the infant was found to have a UTI, then a dose of ceftriaxone can be given and cephalexin prescribed for home.



Well Infant:

- If the has *abnormal* screening inflammatory markers, they will be treated like an infant who is “ill”.

****Any abnormal inflammatory marker should lead to further workup (UNLESS there is a clear source for the fever)****

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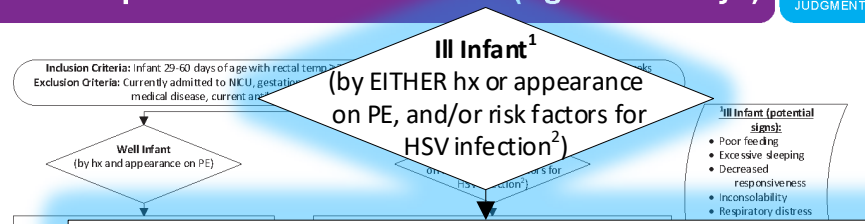

≥ 1 abnormal inflammatory markers?

- ANC >5200 or <500
- Procalcitonin >0.5 ng/ml

If procalcitonin unavailable, may substitute with the following:
*Fever >38.5°C **and***
*CRP >2 mg/dL **and/or***
ANC >5200 or <500

YES →

Diagnostic Tests

(May consider deferral of LP and antibiotics in well appearing infant with positive PCR for COVID-19, influenza, or RSV)

- **Blood:** CBC w diff, procalcitonin, culture, AST, ALT
- **Urine:** (cath) UA, culture
- **CSF:** culture, glucose, protein, cell count, gram stain
  - *If June-Oct or any season if enterovirus circulating*: add CSF enterovirus PCR
  - Add meningitis/encephalitis PCR panel if initial CSF studies suggest infection

If risk factors for HSV[2]:

- *Blood:* HSV PCR
- *Surfaces:* HSV PCR (use 1 swab for HSV PCR and swab in this order: conjunctiva, mouth, nasopharynx, rectum). If vesicle present, also send swab of vesicle base.
- *CSF:* HSV PCR
- Place on Contact Precautions

Consider adding:

- *If persistent watery stools:* Stool BioFire
- *If respiratory signs:*
  - Chest X-ray (not indicated if exam consistent with bronchiolitis)
  - Nasal RSV PCR, Influenza PCR, and/or COVID-19 PCR (if the virus is circulating)
- *If CSF pleocytosis or seizure present:* send individual HSV and enterovirus CSF PCR. If negative, consider sending BioFire meningoencephalitis panel.

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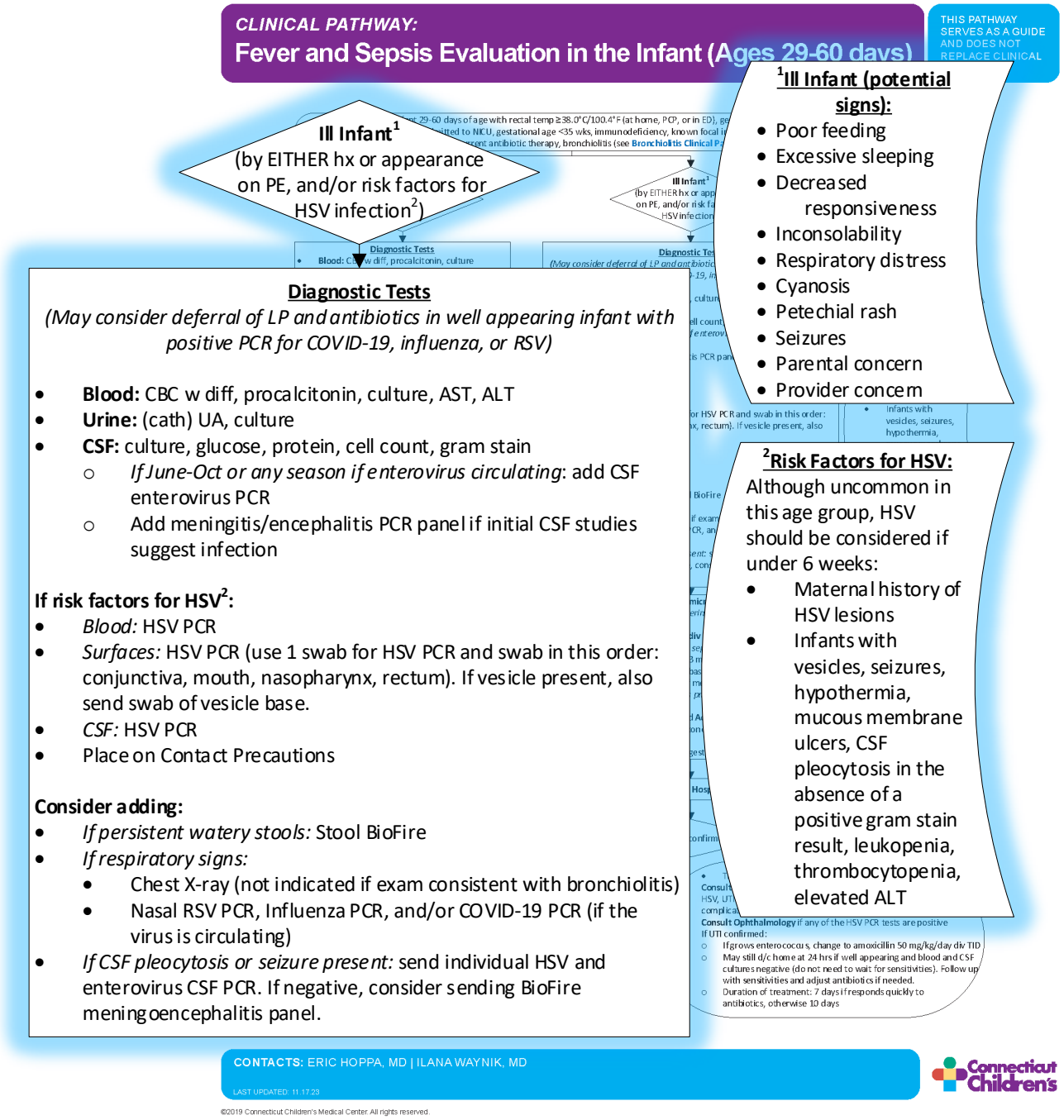
Ill Infant and/or well infants with abnormal inflammatory markers:

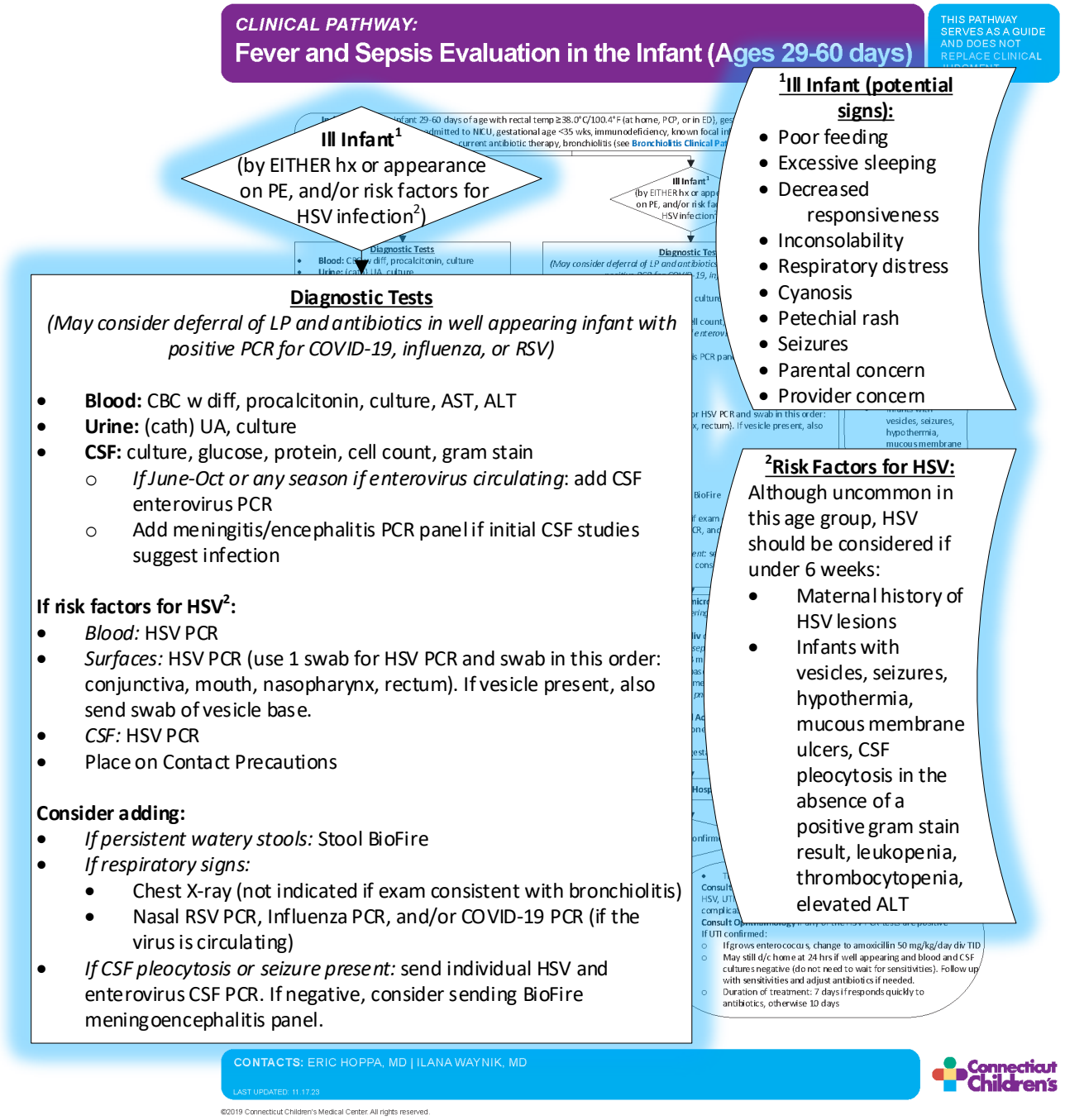
- Ill infants are those who appear ill by history, PE, or have risk factors for HSV infection
- Well infants who have abnormal inflammatory screening markers will also be managed the same
- A complete evaluation including blood, urine *and CSF* studies are recommended.

NEW 2023: *May consider deferral of LP and antibiotics in well appearing infant with positive PCR for COVID-19, influenza, or RSV*



Ill Infant and/or well infants with abnormal inflammatory markers:

- Addition of additional viral studies are listed here.



III Infant and/or well infants with abnormal inflammatory markers:

- Begin immediate empiric antimicrobials (ideally after cultures are obtained, if the patient is stable enough):
  - Ceftriaxone IV/IM
  - Vancomycin, if concern for meningitis
  - Acyclovir if risk factors for HSV

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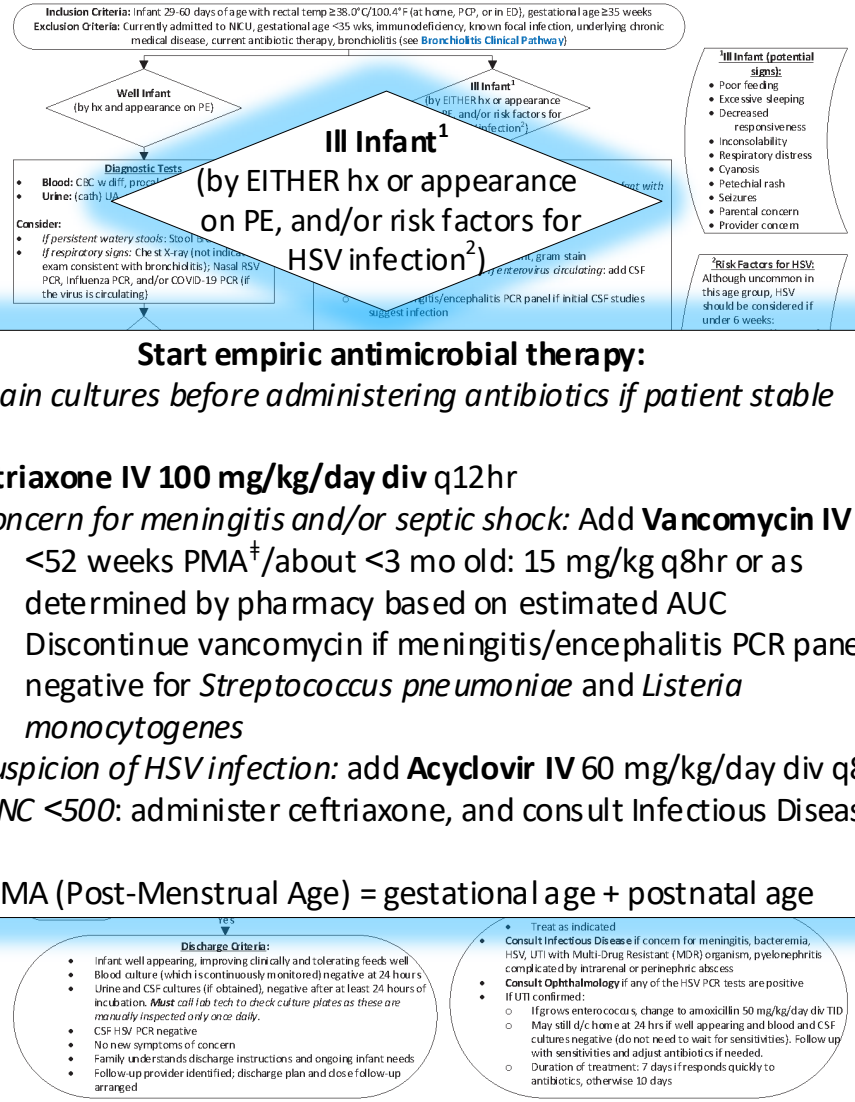

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Ill Infant and/or well infants with abnormal inflammatory markers:

- If a patient had an ANC <500, start ceftriaxone and consult Infectious Diseases.
-
- Vancomycin can be discontinued if cultures or meningitis/encephalitis panel was negative for *Streptococcus pneumoniae* and *Listeria monocytogenes.*

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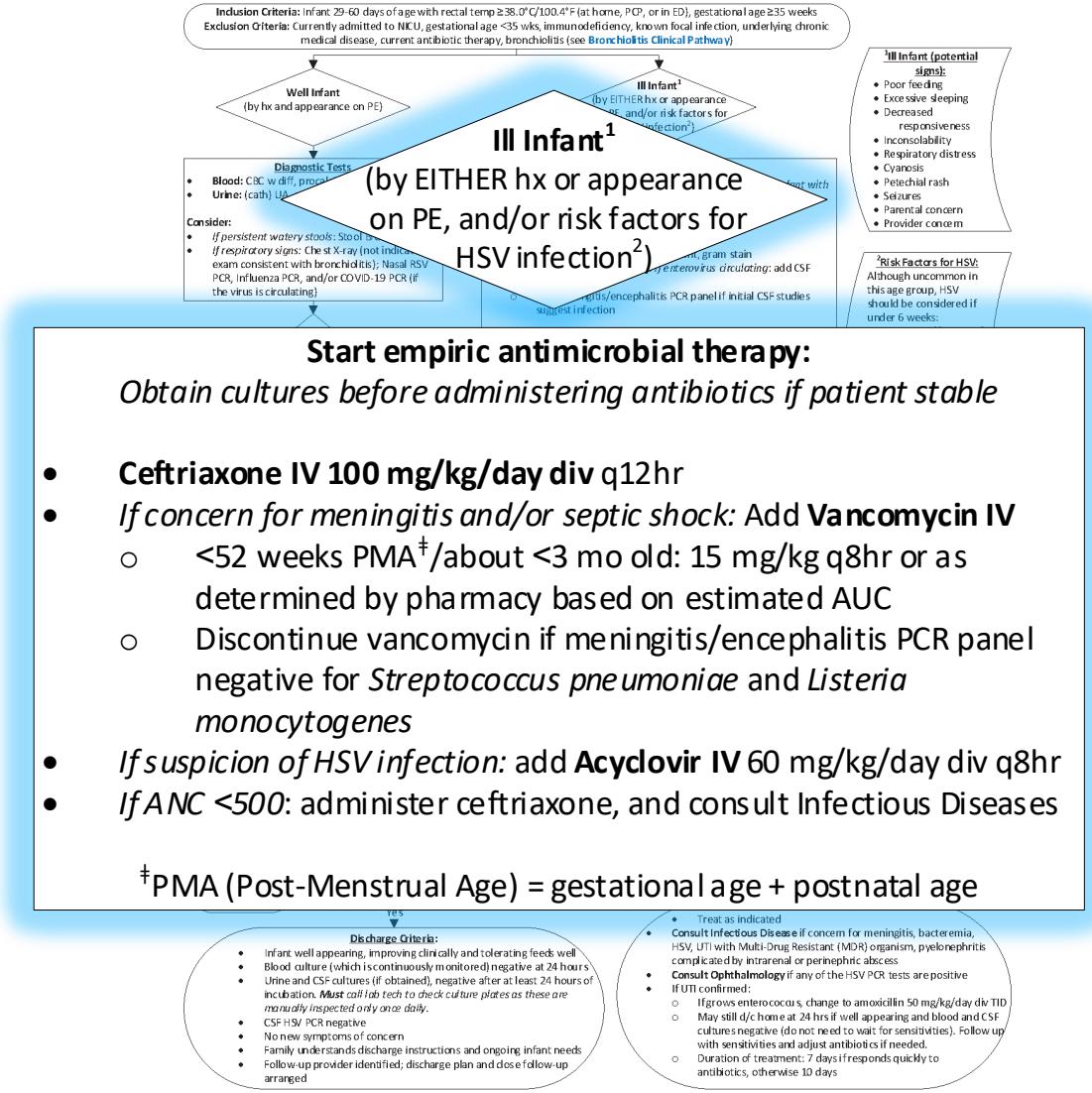

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III Infant and/or well infants with abnormal inflammatory markers or risk factors for HSV:

- If a focal infection is identified, treat appropriately and consult Infectious Diseases as needed.
- Make sure to consult ophthalmology if HSV tests are positive, to assess for ocular involvement.
- If UTI identified, may still d/c home at 24 hrs of negative blood and CSF cultures if well appearing (do not need to wait for sensitivities)

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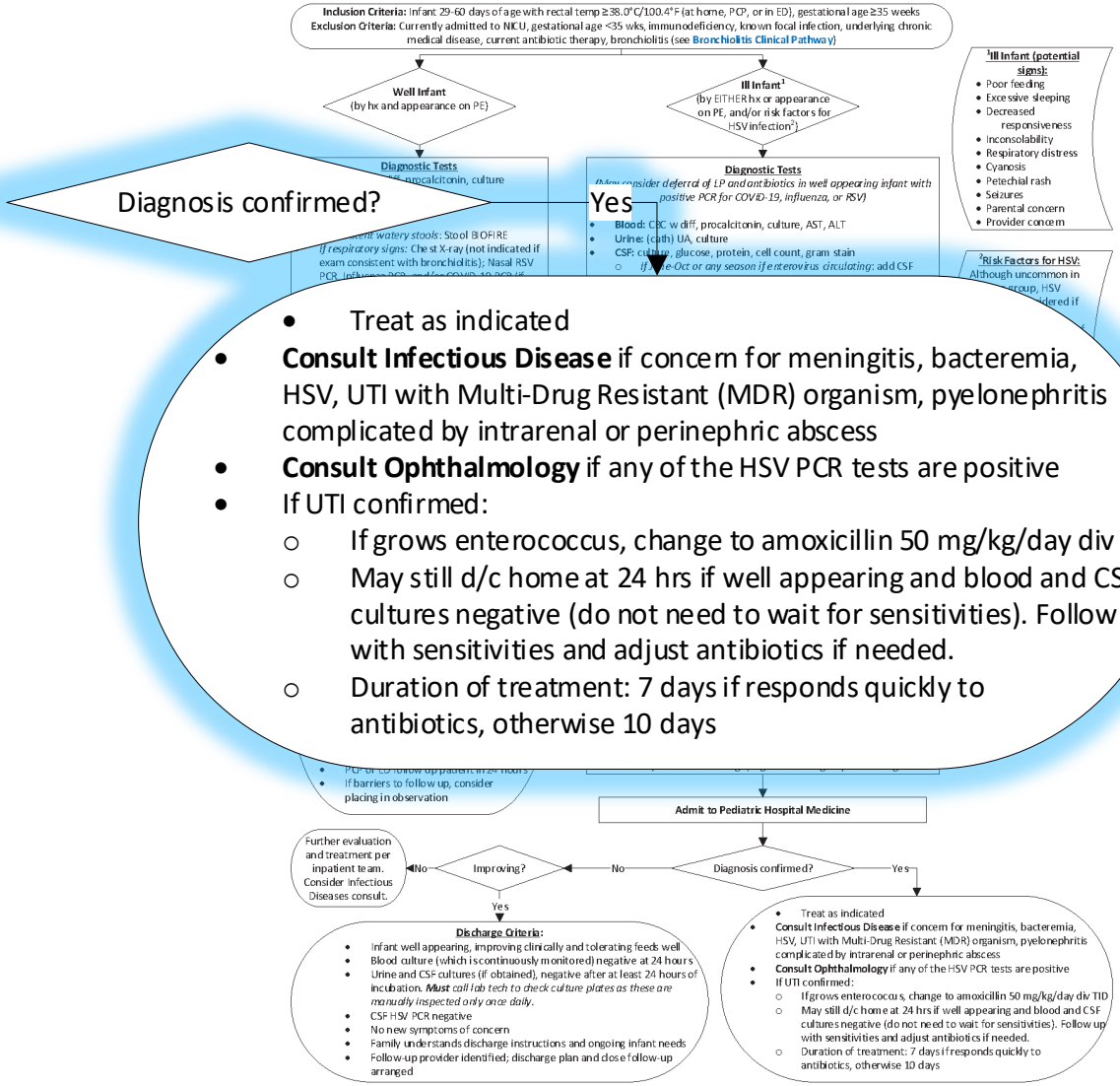

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III Infant and/or well infants with abnormal inflammatory markers or risk factors for HSV:

- If no focal infection is identified, but the patient is not improving on empiric antimicrobials, further evaluation is needed

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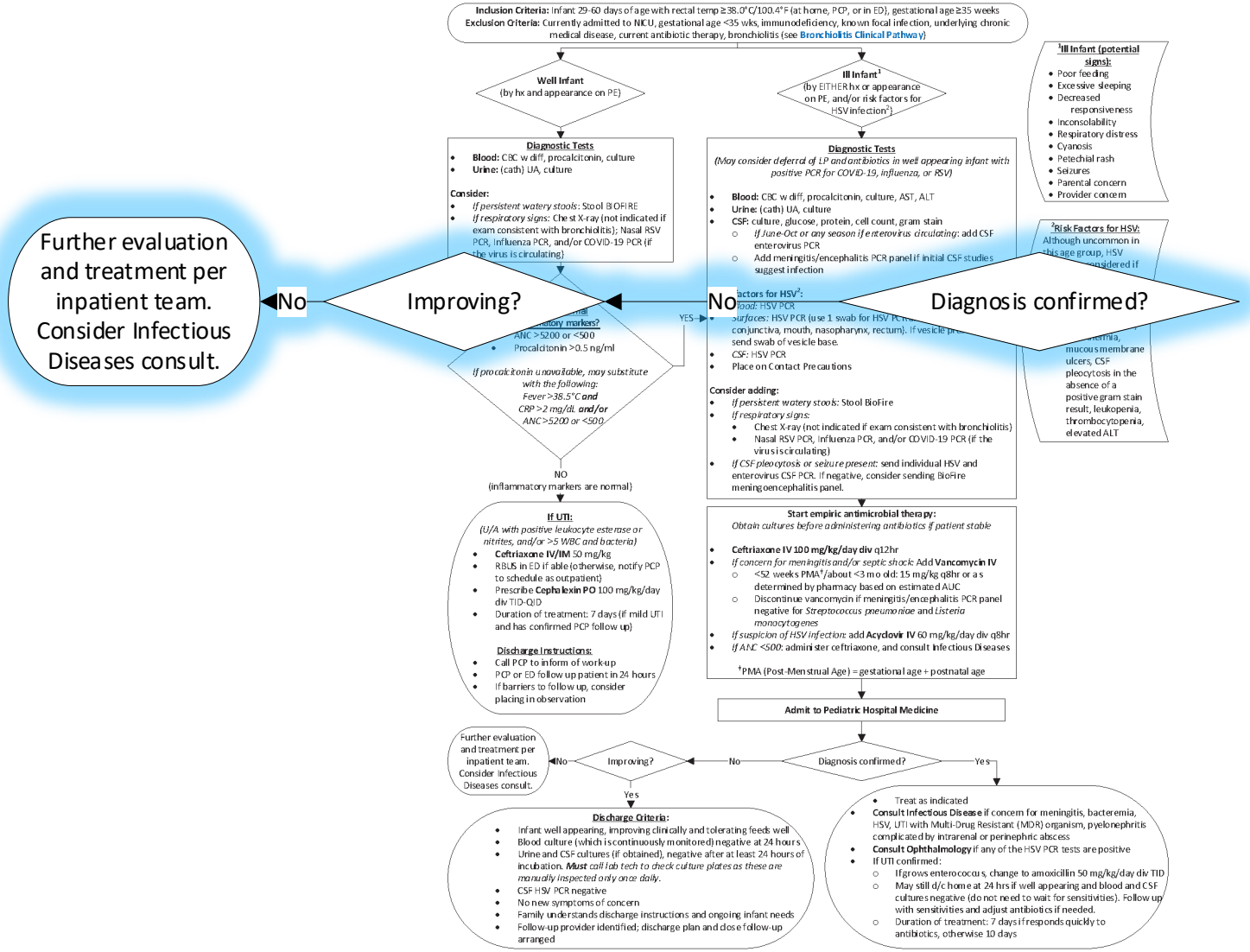

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Discharge Criteria:

- If there is no focal infection and the patient is improving on empiric antimicrobials, the patient can be discharged when cultures are negative for **24** hours and CSF HSV PCR is negative (if obtained).

- Blood cultures are monitored continuously. However, urine and CSF cultures (if obtained) are only manually inspected once daily. Providers **must** call the lab tech at 24 hours to check culture plates.

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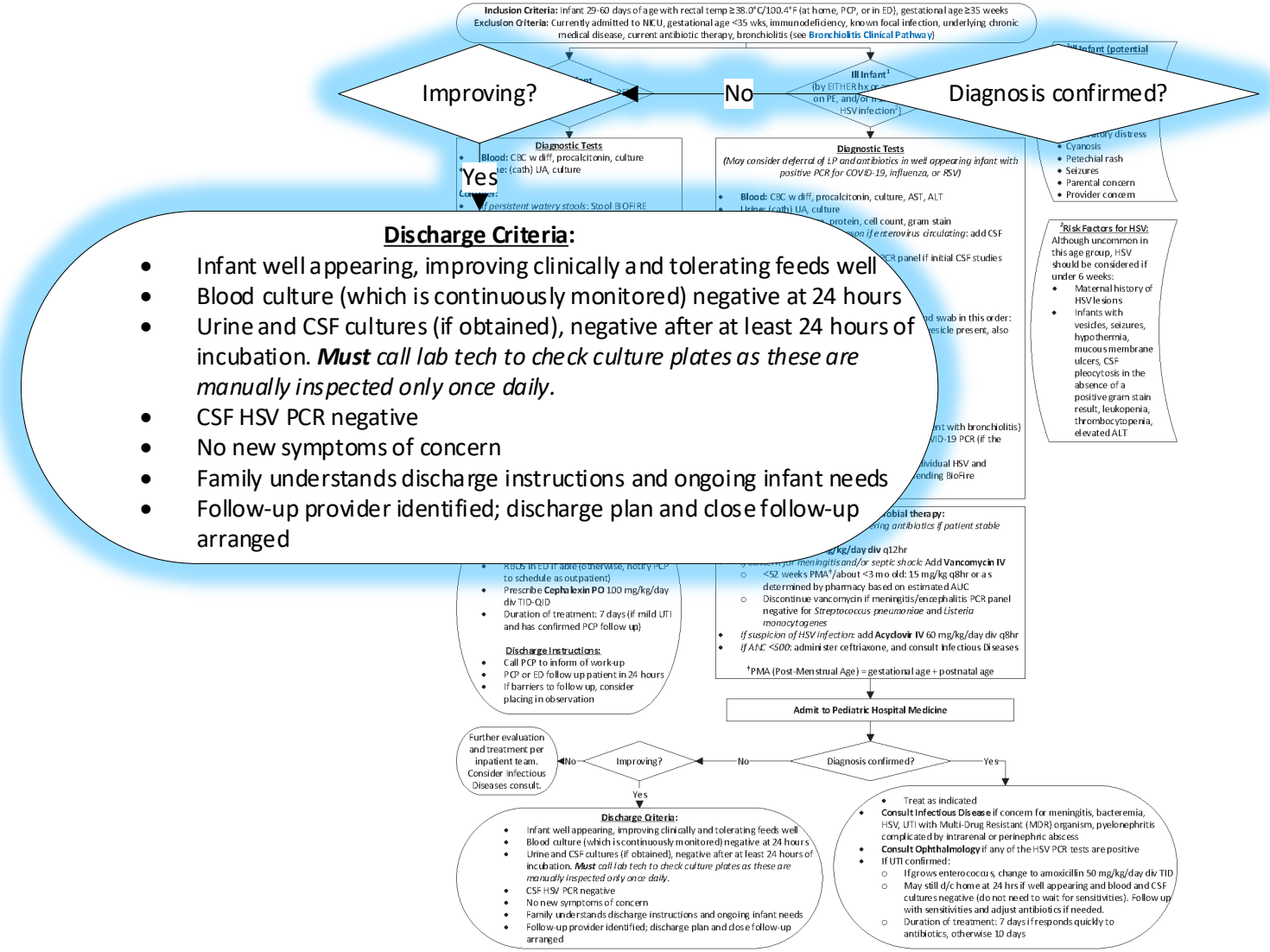

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Review of Key Points

- Clinical pathways helps standardize work up and treatment for this age group
- Workup and treatment is based on history, physical and risk stratification
- Using a group of more sensitive and specific inflammatory markers can help identify those patients at higher risk for bacterial infection
- Lumbar punctures are not universally indicated in this age group
- Newer literature shows isolated UTI with normal inflammatory markers in a well appearing infant is *not* a high risk condition that necessarily warrants hospitalization or proceeding with LP
- Shorter length of stay and earlier discontinuation of antibiotics (for hospitalized infants) is supported

Quality Metrics*

- Percentage of eligible patients treated per pathway
- Percentage of patients with order set usage
- Percentage of patients for whom recommendations for lumbar puncture followed
- Percentage of patients for whom recommendations regarding antimicrobials followed
- Average length of stay for ED patients
- Average length of stay for inpatient and observation patients (excluding those with positive cultures)
- Returns to ED within 2 days due to a positive culture
- Readmissions within 2 days due to a positive culture

**Stratifying all metrics into 2 groups: positive and negative viral testing (for influenza, RSV, COVID-19)*

Pathway Contacts

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  - Connecticut Children's Pediatric Hospital Medicine
- Eric Hoppa, MD
  - Connecticut Children's Emergency Department

References

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Thank You!

About Connecticut Children's Pathways Program

Clinical pathways guide the management of patients to optimize consistent use of evidence-based practice. Clinical pathways have been shown to improve guideline adherence and quality outcomes, while decreasing length of stay and cost. Here at Connecticut Children's, our Clinical Pathways Program aims to deliver evidence-based, high value care to the greatest number of children in a diversity of patient settings. These pathways serve as a guide for providers and do not replace clinical judgment.