

Fever Without a Source: Age 0-21 Day Pathway

Evidence Based Outcome Center

EXCLUSION CRITERIA

- Toxic appearing
- No fever
- Born < 37 weeks gestational age
- High suspicion for HSV (vesicles or seizures)
- Infants <2 weeks of age whose perinatal courses were complicated by maternal fever, infection, and/or antimicrobial use
- Documented or suspected immune compromise
- Neonatal course complicated by surgery or infection
- Congenital/chromosomal abnormality
- Medically fragile (ie, technology to sustain life)
- Received immunizations in the past 48 hrs

! ALERT

Patient Toxic/Septic Appearance
Full Sepsis Workup & treat as appropriate.
(LINK TO SEPSIS PATHWAY/GUIDELINE)

- Abnormal UA Values**
- Positive LE (leukocyte esterase)
 - Positive Nitrites
 - > 5wbc/hpf on microscopy **1**

- Abnormal CSF Values**
- ≥ 15 wbc/mm³
 - Positive Gram Stain **2**

INCLUSION CRITERIA

Non-toxic with temperature $\geq 38^{\circ}\text{C}$ (100.4°F) measured in Emergency Department OR reported measurement at home.

- Focal bacterial infection (other than otitis media) OR
- Temperature $< 36^{\circ}\text{C}$ (96.8°F) OR
- Clinical Bronchiolitis OR
- Clinically ill or concern for invasive bacterial infection

Manage OFF-PATHWAY

Order labs:

- Complete Blood Count (CBC) with differential
- Blood Culture
- Complete Metabolic Panel (CMP)
- UA
- Cerebrospinal Fluid (Hold Tube # 4)
 - Gram stain
 - Culture
 - Cell count with differential
 - Glucose
 - Protein
 - Meningitis/ Encephalitis PCR panel
- Stool culture (If patient has diarrhea)
- CRP, procalcitonin (may obtain)

Order labs:

- Herpes Simplex 1&2 Subtype by PCR of blood
- Herpes Simplex 1&2 Subtype by PCR of CSF
- Herpes Simplex 1&2 Subtype by PCR of surface cultures
 - Conjunctiva
 - Throat
 - Nasopharynx
 - Rectum
 - Vesicle (if present)

UA Positive? **1**

YES NO

Send urine culture via bladder catheterization

Herpes Simplex Virus (HSV) work-up indicated?

NO

Patient Age: 0-7 Days

1. Administer Ampicillin and Gentamicin

Patient Age: 8-21 Days

1. Administer Ceftriaxone
(Use Cefepime if contraindicated)

CSF pleocytosis, traumatic, or not interpretable? **2**

NO

ADMIT TO INPATIENT

Patient Age: 0-7 Days

Change antibiotic treatment:

1. Confirm meningitic dose of Ampicillin (Redose if needed)
2. Add Cefepime
3. Discontinue Gentamicin
4. Consider HSV workup and Acyclovir therapy

Patient Age: 8-21 Days

Change antibiotic treatment:

1. Confirm meningitic dose of Ceftriaxone (Redose if needed)
2. Add Ampicillin and confirm meningitic dosing
3. Consider HSV workup and Acyclovir therapy

Add Acyclovir

1. Treat Infection

YES

Pathogen or source identified?

NO

1. Discontinue antimicrobials and may discharge if infant is well-appearing and all culture results are negative at 24-36 hours.
2. Manage for duration of illness.

Fever Without a Source: Age 22-28 Day Pathway

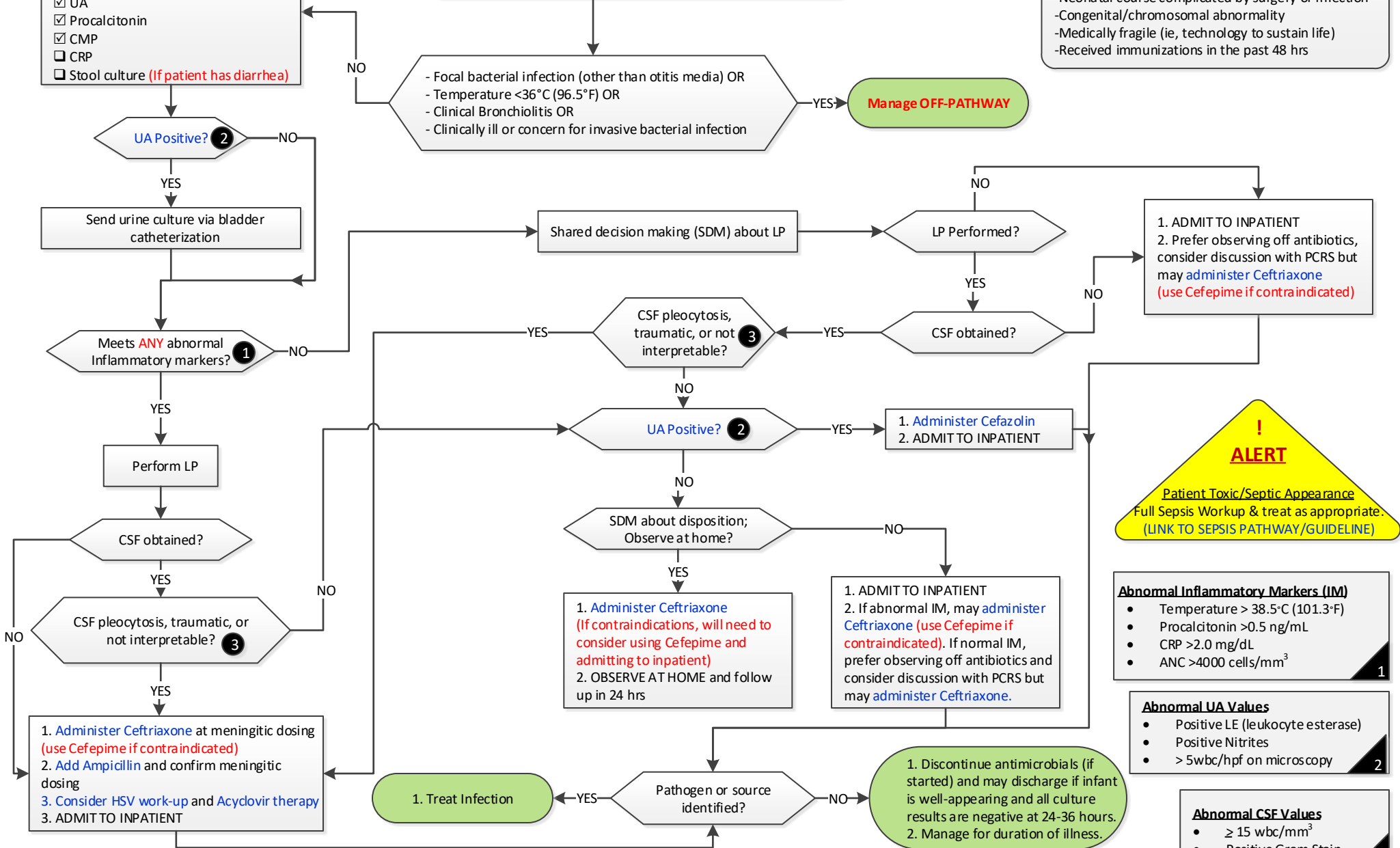
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- Order labs:**
- CBC with differential
 - Blood culture
 - UA
 - Procalcitonin
 - CMP
 - CRP
 - Stool culture (If patient has diarrhea)

INCLUSION CRITERIA

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! ALERT

Patient Toxic/Septic Appearance
Full Sepsis Workup & treat as appropriate.
(LINK TO SEPSIS PATHWAY/GUIDELINE)

- Abnormal Inflammatory Markers (IM)**
- Temperature > 38.5°C (101.3°F)
 - Procalcitonin >0.5 ng/mL
 - CRP >2.0 mg/dL
 - ANC >4000 cells/mm³

- Abnormal UA Values**
- Positive LE (leukocyte esterase)
 - Positive Nitrites
 - >5wbc/hpf on microscopy

- Abnormal CSF Values**
- ≥ 15 wbc/mm³
 - Positive Gram Stain

Fever Without a Source: Age 29-60 Day Pathway

EXCLUSION CRITERIA

- Toxic appearing
- No fever
- Born < 37 weeks gestational age
- High suspicion for HSV (vesicles or seizures)
- Documented or suspected immune compromise
- Neonatal course complicated by surgery or infection
- Congenital/chromosomal abnormality
- Medically fragile (ie, technology to sustain life)
- Received immunizations in the past 48 hrs

INCLUSION CRITERIA

Non-toxic with temperature $\geq 38^{\circ}\text{C}$ (100.4°F) measured in Emergency Department OR reported measurement at home.

Order labs:

- CBC with differential
- Blood culture
- UA
- Procalcitonin
- CMP
- CRP
- Stool culture (If patient has diarrhea)

Abnormal UA Values

- Positive LE (leukocyte esterase)
- Positive Nitrites
- > 5wbc/hpf on microscopy

1

Abnormal CSF Values

- > 9 wbc/mm³
- Positive Gram Stain

2

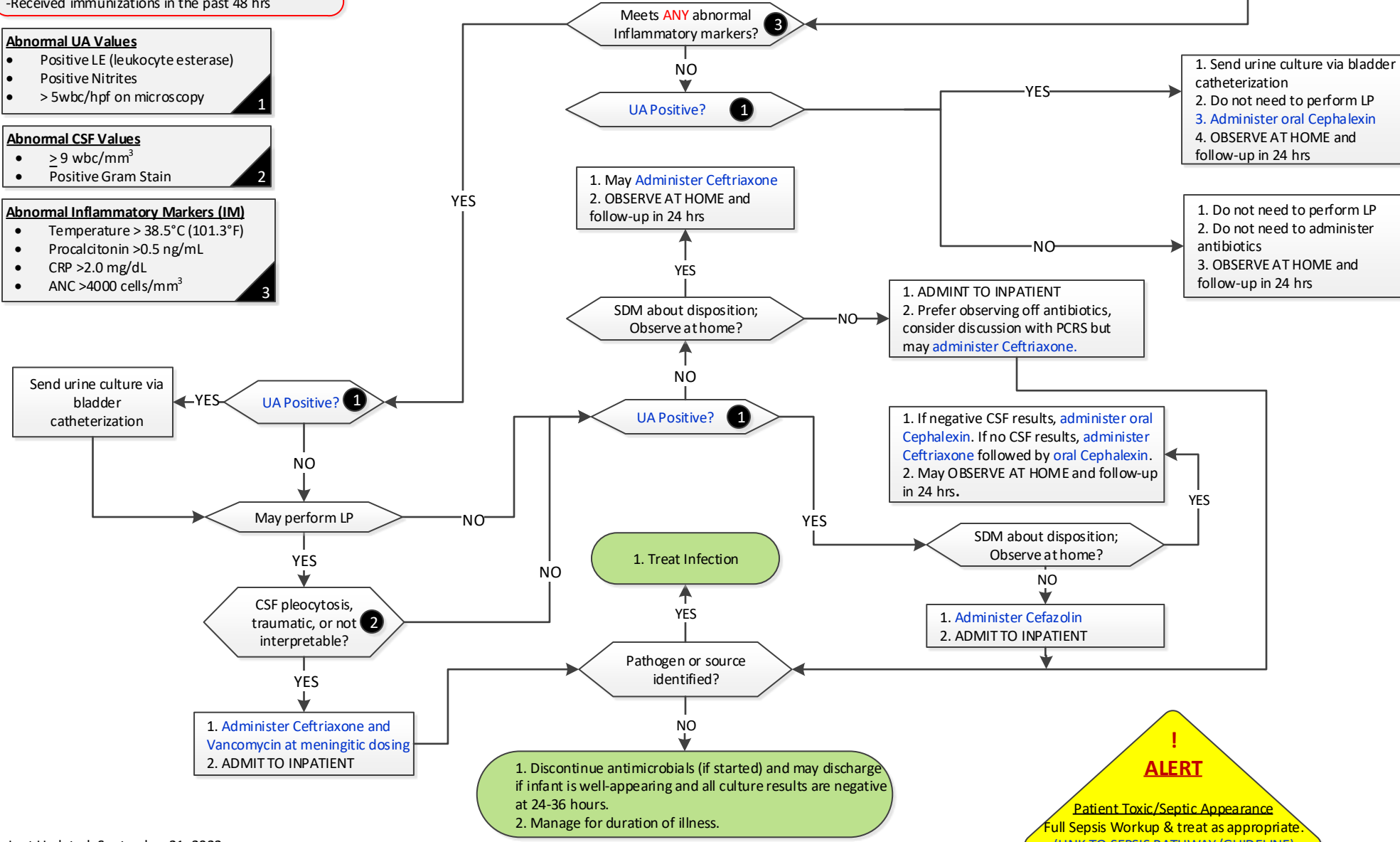
Abnormal Inflammatory Markers (IM)

- Temperature > 38.5°C (101.3°F)
- Procalcitonin >0.5 ng/mL
- CRP >2.0 mg/dL
- ANC >4000 cells/mm³

3

Manage OFF-PATHWAY

Send urine culture via bladder catheterization

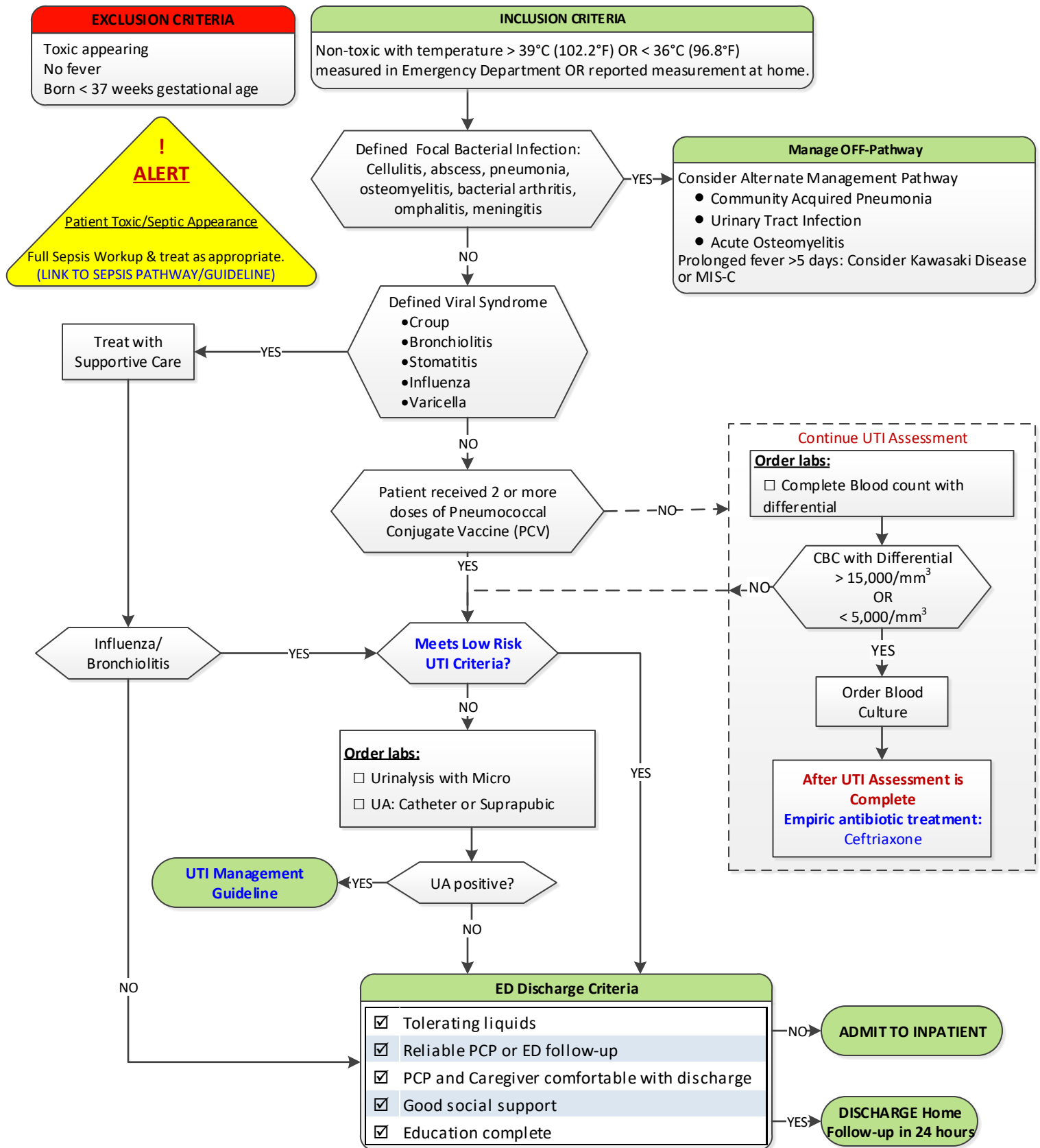


ALERT

Patient Toxic/Septic Appearance
Full Sepsis Workup & treat as appropriate.
(LINK TO SEPSIS PATHWAY/GUIDELINE)

Fever Without a Source: Age 2-6 Months Pathway

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> 2 months – Not Toilet Trained

Probability of UTI > 1%:

2 or more risk factors

Female Risk Factors*

- Non-black
- T ≥ 39°C
- Fever ≥ 2 days
- No apparent source of fever
- Age < 12 months

*Recommend screening if prior history of UTI, fever ≥ 2 days

Probability of UTI > 1%:

Uncircumcised

OR

Circumcised with 3 or more Risk Factors

Male Risk Factors*

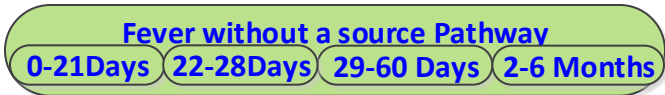
- Non-black
- T ≥ 39°C
- Fever ≥ 2 days
- No apparent source of fever
- Age < 6 months

Toilet Trained – 18 years

All Patients

- Symptoms referable to urinary tract
- Prior history of UTI, fever ≥ 2 days
- Prolonged fever (≥ 5 days)

Recommend screening for any of the above factors



DCMC Positive Urinalysis (UA) Definition: The presence of Leukocyte Esterase or Nitrites or microscopic analysis results positive for leukocytes or bacteria is suggestive of an active UTI. When more than one of these findings is present at the same time, the sensitivity and specificity increase significantly.

Dell Children's and Seton Family of Hospitals does not currently perform an enhanced urinalysis on urine specimens routinely. The following criteria are guide in diagnosing a UTI in young children using the standard method of collection and processing.

Diagnostic	Interpretation
Nitrites	<ul style="list-style-type: none"> Poor sensitivity: Conversion of nitrates to nitrites by bacteria takes approximately 4 hours and not all bacteria reduce nitrate levels combined with frequency of infants voiding. Helpful when positive. Few false positives and high specificity.
Leukocyte Esterase	<ul style="list-style-type: none"> Positive leukocyte esterase is suggestive of a UTI. However, children may have WBC present in their urine in conditions other than a UTI (e.g. Kawasaki Disease)
White Blood Cells (WBC) - Pyuria	Positive if: <ul style="list-style-type: none"> ≥ 5 WBC per HBF via standard method Pyuria is absent in approximately 10% of children with a UTI
Bacteriuria	Presence of bacteriuria alone in the absence of other findings does not define a UTI.

Culture			
Method	Definite*	Indeterminant†	Contaminant
Suprapubic	Any growth		Growth of non-pathogens, Mixed culture
Catheter	≥ 50,000 CFU/ML	≥ 10,000 CFU/ML	Growth of non-pathogens, Mixed culture, < 10,000 CFU/ml

* If also with presence of pyuria or bacteriuria

† Consider obtaining repeat specimen

Mixed Culture = uropathogen + non-pathogen or two uropathogens

Bag UA specimens should never be sent for urine culture. Only catheter or suprapubic methods are appropriate for culture collection in this age.

Uropathogens		
Gram Negative	Gram Positive	Non-pathogens
Escherichia coli (~80%)	Staphylococcus saprophyticus	Lactobacillus
Klebsiella	Enterococcus	Coagulase-negative Staph
Proteus	Staphylococcus aureus	Corynebacterium
Enterobacter		
Citrobacter		

Fever without a source Pathways

0-21Days
22-28Days
29-60 Days
2-6 Months

Patients with any of the following conditions should be considered for a Herpes Simplex Virus work up and empiric treatment:

Historical and Clinical Features

Severe illness / Hypothermia / Lethargy

Seizures

Hepatosplenomegaly

Postnatal HSV contact

Vesicular rash

Conjunctivitis

Interstitial pneumonitis

Laboratory Findings

Thrombocytopenia

CSF pleocytosis

without clear bacterial infection

Transaminitis

Herpes Simplex Virus work-up consist of the following labs:

- Herpes Simplex 1&2 Subtype by PCR of blood
- Herpes Simplex 1&2 Subtype by PCR of CSF
- Herpes Simplex 1&2 Subtype by PCR of surface cultures
 - Conjunctiva
 - Throat
 - Nasopharynx
 - Rectum
 - Vesicle (if present)

Fever without a source Pathway

0-21Days 22-28Days 29-60 Days 2-6 Months

Contraindications for Ceftriaxone in patients < 28 days of age:

Gestational age < 37 weeks

Postnatal age < 7 days

Patient expected to or receiving calcium containing IV products

Total bilirubin > 10mg/dL (See risk factors for hyperbilirubinemia)

Risk factors for hyperbilirubinemia	
ABO incompatibility	Albumin < 3g/dL
HDN	Dehydration
Lethargy	Weight loss
Temperature instability	Poor feeding
Sepsis	Irritability
Acidosis	Jaundice

Fever without a source Pathway

0-21Days
22-28Days
29-60 Days
2-6 Months

Fever Without a Source Antimicrobial and Antiviral Dose Recommendations

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Recommended Doses for Antimicrobials		
Drug ^{a,b,c,d,e,f}	Dose	Duration ^e (for rule out period) ^f
Ampicillin	NON-MENINGITIC 0-7 days of age: 50 mg/kg/DOSE IV or IM q8h	5 doses
	MENINGITIC 0-7 days of age: 100 mg/kg/DOSE IV q8h	5 doses
	MENINGITIC > 7-28 days of age: 75 mg/kg/DOSE IV q6h	6 doses
Cefepime ^b	0-28 days of age: 50 mg/kg/DOSE IV or IM q12h	3 doses
	> 28 days of age: 50 mg/kg/DOSE IV or IM q8h	5 doses
Ceftriaxone ^c	NON-MENINGITIC > 7 days of age: 75 mg/kg/DOSE IV or IM QDay	2 doses
	MENINGITIC > 7 days of age: 50 mg/kg/DOSE IV q12h	3 doses
	MENINGITIC (ED ONLY) > 7 days of age: 100 mg/kg/DOSE IV ^g X 1	1 dose
Gentamicin ^d	0-7 days of age: 4 mg/kg/DOSE IV or IM q24h	2 doses
Vancomycin ^d	MENINGITIC > 28 days of age: 15 mg/kg/DOSE IV q6h	6 doses
Recommended Dose for UTI (Uncomplicated Cystitis)		
Drug	Dose	Duration
Cefazolin	UTI without BACTEREMIA: 17 mg/kg/DOSE IV or IM q8h	Total duration IV + PO = 10 days
	UTI with BACTEREMIA: 33 mg/kg/DOSE IV or IM q8h	
Cephalexin	17 mg/kg/DOSE PO TID	
Recommended Dose for Antiviral		
Drug	Dose	Duration
Acyclovir	20 mg/kg/DOSE IV q8h (0-3 months)	5 doses OR until HSV surface cultures AND PCR Blood & CSF negative (contact Infectious Disease if not resulted within 5 doses) Exceptions: Seizures, lethargy, or ongoing fever

^aDosing in this table is for patients with normal renal function. Please contact the pharmacy for assistance with dosing in renal insufficiency.

^bCefotaxime is no longer formulary at DCMC due to supply instability. In the instance cefotaxime should be available, cefotaxime could be substituted for cefepime, using the following doses:

0 to 7 days of age: 50 mg/kg/dose IV or IM q8h
> 7 days: 50 mg/kg/dose IV or IM q6h

^cCeftriaxone is contraindicated with calcium containing IV products or hyperbilirubinemia. Meningitic dosing of ceftriaxone is 80-100 mg/kg/day divided every 12-24 hours but CSF concentrations are optimal when dosed at 50mg/kg/dose IV q12h; once daily dosing should be reserved for patients to be discharged from the ED. IM dosing is inappropriate for meningitic coverage.

^dFor gentamicin or vancomycin, serum drug levels are not necessary unless treatment is anticipated or continued for more than 2 doses, SCr is increased more than 0.3 mg/dL from normal value for age, or UOP less than 1 ml/kg/hr.

^eDuration includes any doses given in the emergency department.

^fIf cultures become positive at any time, treat specific condition, narrow agent, and lengthen antibiotic duration as appropriate.

^gCeftriaxone 100 mg/kg IV X 1 for any ill appearing neonate, with the first inpatient dose starting 12-24 hours after initial dose.

DCMC Specific Antibiotic Selection and Dosing for Neonatal Fever

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Suspected Source of Infection	0-7 Days	8-21 Days	22-28 Days	29-60 Days
UTI w/o bacteremia			Cefazolin (17 mg/kg/DOSE) IV or IM q8h	Cefazolin (17 mg/kg/DOSE) IV or IM q8h
UTI w/ bacteremia			Cefazolin (33 mg/kg/DOSE) IV or IM q8h	Cefazolin (33 mg/kg/DOSE) IV or IM q8h
No Focus Identified	Ampicillin (50 mg/kg/DOSE) IV or IM q8h + Gentamicin (4 mg/kg/DOSE) IV or IM q24hr	Ceftriaxone (75 mg/kg/DOSE) IV or IM qDay or Cefepime (50 mg/kg/DOSE) IV or IM q12h <small>(when ceftriaxone contraindicated)</small>	Ceftriaxone (75 mg/kg/DOSE) IV or IM qDay or Cefepime (50 mg/kg/DOSE) IV or IM q12h <small>(when ceftriaxone contraindicated)</small>	Ceftriaxone (75 mg/kg/DOSE) IV or IM qDay
Meningitis	Ampicillin (100 mg/kg/DOSE) IV q8h + Cefepime (50 mg/kg/DOSE) IV q12h +/- Acyclovir (20 mg/kg/DOSE) IV q8h <small>(if clinical concerns of HSV)</small>	Ampicillin (75 mg/kg/DOSE) IV q6h + Ceftriaxone (50 mg/kg/DOSE) IV q12h or Cefepime (50 mg/kg/DOSE) IV q12h <small>(when ceftriaxone contraindicated)</small> +/- Acyclovir (20 mg/kg/DOSE) IV q8h <small>(if clinical concerns of HSV)</small>	Ampicillin (75 mg/kg/DOSE) IV q6h + Ceftriaxone (50 mg/kg/DOSE) IV q12h or Cefepime (50 mg/kg/DOSE) IV q12h <small>(when ceftriaxone contraindicated)</small> +/- Acyclovir (20 mg/kg/DOSE) IV q8h <small>(if clinical concerns of HSV)</small>	Ceftriaxone (50 mg/kg/DOSE) IV q12h + Vancomycin (15 mg/kg/DOSE) IV q6h +/- Acyclovir (20 mg/kg/DOSE) IV q8h <small>(if clinical concerns of HSV)</small>

NOTE: This table replicates the information in the table above.

Physician Champion: Lynsey Vaughan

Revision History

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Next Review Date: September 2026

Revision History: Updates to algorithms were made to align with the AAP VIP Network – REVISE II Project

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