Clinical Pathways

Fever and Sepsis Evaluation in the Neonate (0-28 days old)

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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

- Standardize initial work-up for neonates presenting with fever/sepsis
- Decrease unnecessary variation in patient care based on current evidence
- Provide guidelines for when to include HSV testing/treatment
- Help guide appropriate antimicrobial therapy
- Provide guidelines for a safe discharge home

Why is Pathway Necessary?

- In 2014, there was a cross sectional study done of febrile neonates (0-28 days) across 36 pediatric emergency rooms[1]
  - Recommended management only occurred in about 66.4% of patients
  - More than a 2 fold variation across the EDs in adherence to recommended management/testing/treatment
  - Significant variation in testing and treatment between admitted/discharged neonates
  - Conclusion: wide variation of care from the recommended management

Background

- Neonates are at increased risk for serious bacterial infectionsManagement, including proper diagnostic testing and empiric treatment, should be standard
- The incidence of neonatal HSV infection in the U.S. has increased in the past two decades[2]
- In newborns, HSV can manifest as disseminated (involving multiple organs with 60-70% with CNS involvement), localized CNS disease, or disease localized to skin eyes and/or mouth[2]
  - ~25% of neonates with HSV have disseminated disease, 30% have CNS disease, and 45% have SEM disease

Background – AAP Red Book 2021

- 2021 AAP Red Book Recommendations[2] for HSV included:
  - Disseminated HSV infection should be considered in those with:
    - Sepsis and negative bacterial studies
    - Severe liver dysfunction
    - Consumptive coagulopathy
    - Suspected viral pneumonia (especially hemorrhagic pneumonia)
  - Work up:
    - For diagnosis of neonatal HSV, all specimens should be obtained for each patient:
      - surface specimens for HSV culture or PCR
      - specimen of skin vesicles for HSV culture or PCR
      - CSF for PCR
      - *whole blood sample for HSV PCR*
      - Whole blood for ALT

Background – AAP CPG 2021

- 2021 AAP Clinical Practice Guideline (CPG)[3] released for *well-appearing* febrile infants 8 to 60 days old
- These recommendations were carefully reviewed by our CT Children's stakeholders in Infectious Disease and Immunology, Pediatric Hospital Medicine and the Emergency Department, and modified to meet the needs for our specific patient population.

Pantell, R., et al. *Evaluation and Management of Well-Appearing Febrile Infants 8 to 60 Days Old.* Pediatrics. August 2021, 148 (2) e2021052228; DOI: https://doi.org/10.1542/peds.2021-052228.

Background – AAP CPG 2021

AAP CPG:

- Risk stratification based on age groups due to rate/likelihood of bacteremia:
  - 8-21 days old
  - 22-28 days old
  - 29-56 days old

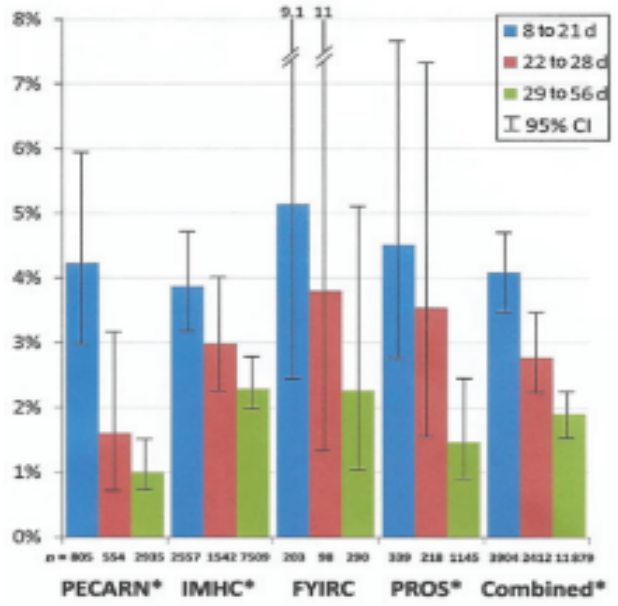

FIGURE 4 Rate of bacteremia by age groupings. * χ^2 for trend: $P < .001$. Note that the 95% CIs in the combined group do not overlap. Data were adapted from reference 61; from reference 94, with detail provided by C.L.B. (personal communication, 2020); from reference 24, with detail provided by Paul Aronson (personal communication, 2020); and from reference 17, with detail provided by Matthew Pantell (personal communication, 2020). FYIRC, Febrile Young Infants Research Collaborative; IMHC, University of Utah/Intermountain Healthcare.

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Background – AAP CPG 2021

For 8-21 days old, AAP recommended:

- HSV risk stratification to determine if HSV studies/acyclovir needed
- Initial parenteral antibiotics and observation in house
- Potential discharge within 24-36 hours.

CT Children's recommends:

- Continuing HSV work up and acyclovir for all under 21 days old, regardless of risk
- Initial parenteral antibiotics and observation in house
- Potential discharge at 24 hours

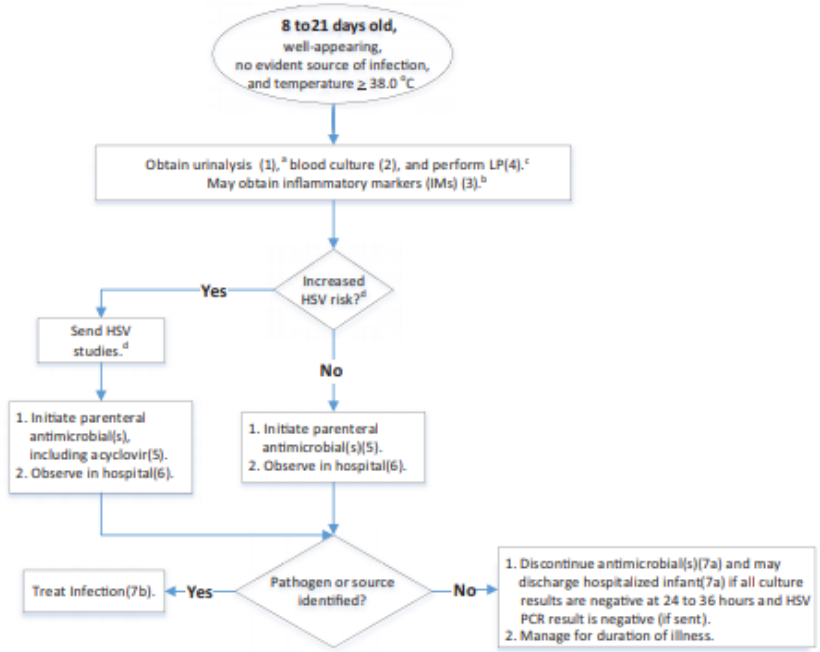

FIGURE 1 Algorithm for 8- to 21-day-old infants. [a] KAS references are shown in parentheses. [b] Laboratory values of inflammation are considered elevated at the following levels: (1) procalcitonin >0.5 ng/mL, (2) CRP >20 mg/L, and (3) ANC >4000 to 5200 per mm^3. Although we recommend all infants in this age group have a complete sepsis workup, receive parenteral antimicrobial agents, and be monitored in a hospital, knowing IM results can potentially guide ongoing clinical decisions. [c] Send CSF for cell count, Gram stain, glucose, protein, bacterial culture, and enterovirus PCR (if available) if pleocytosis is present and during periods of increased local enterovirus prevalence. [d] HSV should be considered when there is a maternal history of genital HSV lesions or fevers from 48 hours before to 48 hours after delivery 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 the mouth, nasopharynx, conjunctivae, and anus for an HSV culture (if available) or PCR assay; alanine aminotransferase; and blood PCR.

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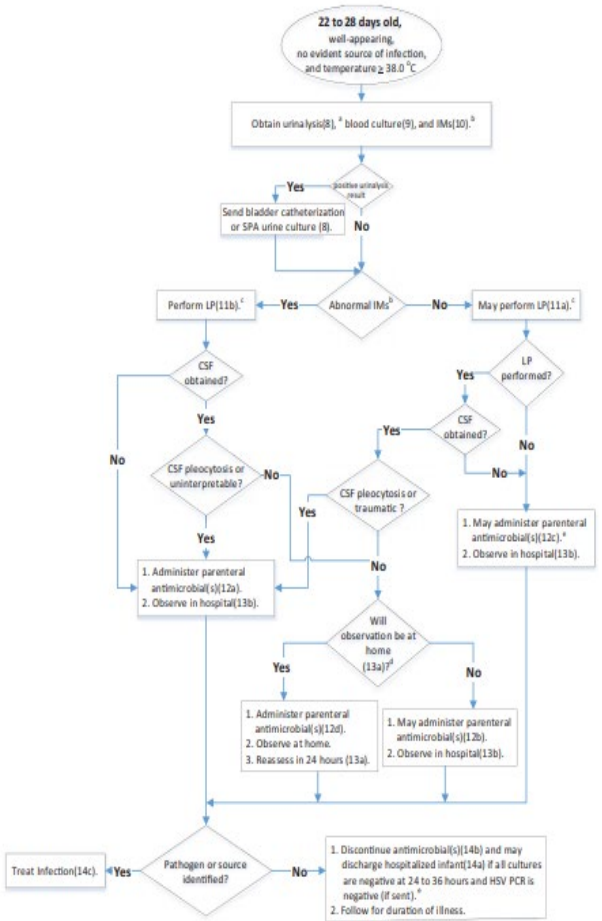
Background – AAP CPG 2021

For well-appearing 22-28 days old, AAP recommended:

- Performing LP if certain inflammatory markers were abnormal
- Adding HSV studies and acyclovir if risk factors present
- Ceftriaxone q24 hr if no source of infection found

CT Children's recommends:

- Obtaining LP for all with consideration of deferment only if certain clinical criteria met
- Adding HSV studies and acyclovir if risk factors present
- Ceftriaxone q24 hr if well appearing and concern for UTI only



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Background – Pathway History

- Pathway first went live in 2013
  - 2016: data found that 36 hours of inpatient observation on empiric antibiotics was safe
  - 2018: cefotaxime shortage changed our empiric antibiotic recommendations
  - 2019: new HSV testing guidelines and suggestions added
  - 2020: consideration of MIS-C and link to MIS-C pathway added
  - 2021: procalcitonin added; consideration for deferring LP with specific criteria
  - 2022: significant changes in inclusion/exclusion criteria, work up, risk factors for HSV, antimicrobial regimens, consultation recommendations and discharge considerations

Pathway Updates 2023

- Updates have been made and will be highlighted in the following slides
- Minor clarifications were made in:
  - Inclusion Criteria
  - Work Up
  - Risk factors for HSV
  - Antimicrobial regimens
  - Consultation recommendations
  - Discharge considerations
- Newly added appendix that clarifies neonatal infection treatment considerations

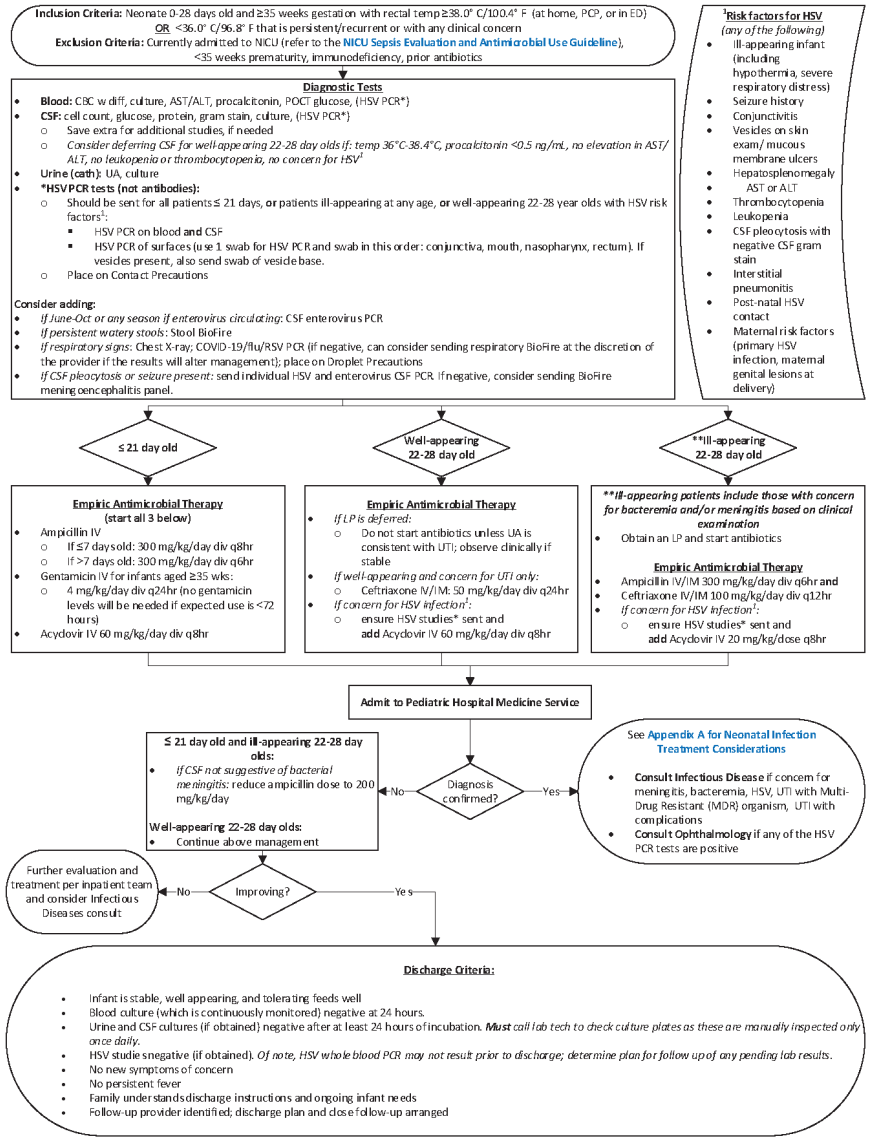
This is the Fever and Sepsis in the Neonate (0-28 days) Clinical Pathway.

We will be reviewing each component in the following slides.

CLINICAL PATHWAY:

Fever and Sepsis Evaluation in the Neonate (0-28 days)

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



CONTACTS: MELISSA HELD, MD | GRACE HONG, APRN | ANAND SEKARAN, MD

LAST UPDATED: 11.17.23

Inclusion Criteria: Neonate 0-28 days old and ≥35 weeks gestation with rectal temp ≥38.0° C/100.4° F (at home, PCP, or in ED) **OR** <36.0° C/96.8° F that is persistent/recurrent or with any clinical concern

Exclusion Criteria: Currently admitted to NICU (refer to the **NICU Sepsis Evaluation and Antimicrobial Use Guideline**), <35 weeks prematurity, immunodeficiency, prior antibiotics

Inclusion Criteria:

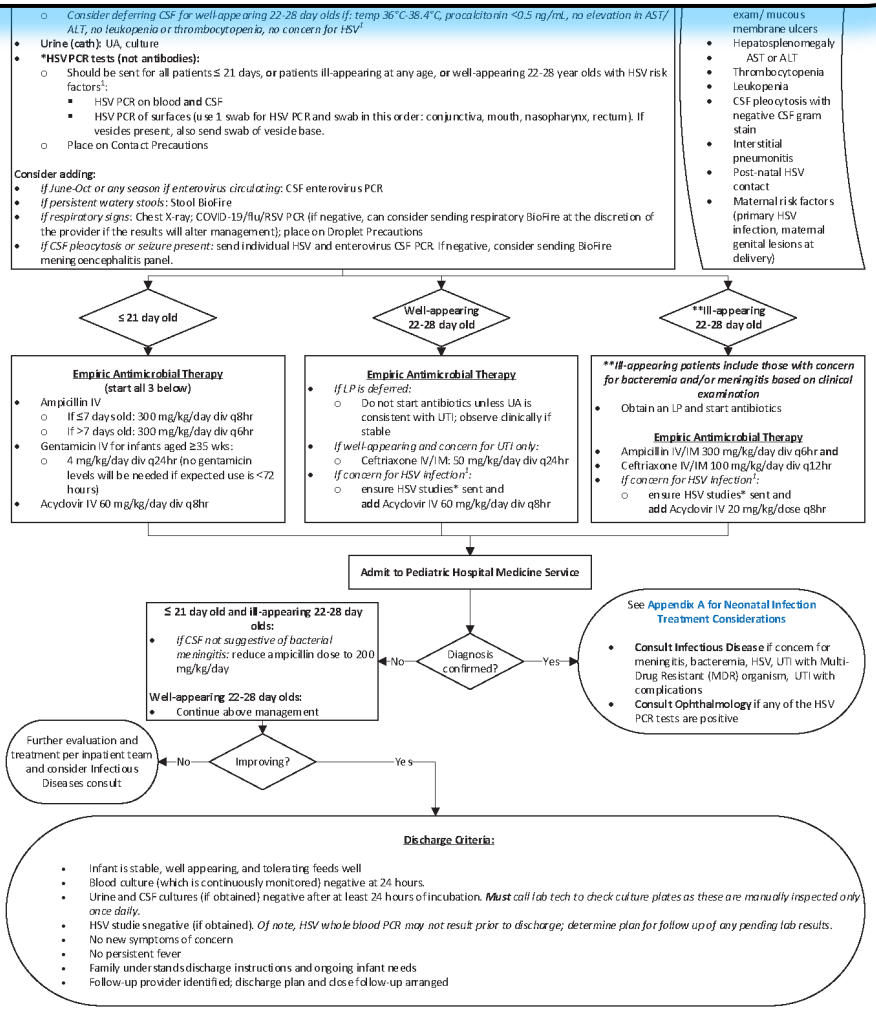
- This pathway is specifically for the neonate aged 0-28 days old who presents with fever, or presents with hypothermia that is persistent/recurrent or with any clinical concern
- "Risk factor for infection (e.g., GBS+ hx, late preterm, altered activity or feeding)" was removed to allow for the pathway to be utilized based on current clinical status

Exclusion Criteria:

- No new changes for 2023

Note:

- Prior versions included a notation on Multi-System Inflammatory Syndrome in Children (MIS-C). MIS-C in neonates is extremely rare and was removed from this algorithm in 2022



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The pathway's layout has been re-designed for ease of use.

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OR <36.0° C/96.8° F that is persistent/recurrent or with any clinical concern
Exclusion Criteria: Currently admitted to NICU (refer to the NICU Sepsis Evaluation and Antimicrobial Use Guideline), <35 weeks prematurity, immunodeficiency, prior antibiotics

Diagnostic Tests

- **Blood:** CBC w diff, culture, AST/ALT, procalcitonin, POCT glucose, (HSV PCR*)
- **CSF:** cell count, glucose, protein, gram stain, culture, (HSV PCR*)
  - Save extra for additional studies, if needed
  - *Consider deferring CSF for well-appearing 22-28 day olds if: temp 36°C-38.4°C, procalcitonin <0.5 ng/mL, no elevation in AST/ALT, no leukopenia or thrombocytopenia, no concern for HSV*[1]
- **Urine (cath):** UA, culture
- ***HSV PCR tests (not antibodies):**
  - Should be sent for all patients ≤ 21 days, **or** patients ill-appearing at any age, **or** well-appearing 22-28 year olds with HSV risk factors[1]:
    - HSV PCR on blood **and** CSF
    - HSV PCR of surfaces (use 1 swab for HSV PCR and swab in this order: conjunctiva, mouth, nasopharynx, rectum). If vesicles present, also send swab of vesicle base.
  - Place on Contact Precautions

Consider adding:

- *If June-Oct or any season if enterovirus circulating*: CSF enterovirus PCR
- *If persistent watery stools*: Stool BioFire
- *If respiratory signs*: Chest X-ray; COVID-19/flu/RSV PCR (if negative, can consider sending respiratory BioFire at the discretion of the provider if the results will alter management); place on Droplet Precautions
- *If CSF pleocytosis or seizure present:* send individual HSV and enterovirus CSF PCR. If negative, consider sending BioFire meningoencephalitis panel.

[1]**Risk factors for HSV**
(any of the following)
- Ill-appearing infant (including hypothermia, severe respiratory distress)
- Seizure history
- Conjunctivitis
- Vesicles on skin exam/ mucous membrane ulcers
- Hepatosplenomegaly
- AST or ALT
- Thrombocytopenia
- Leukopenia
- CSF pleocytosis with negative CSF gram stain
- Interstitial pneumonitis
- Post-natal HSV contact
- Maternal risk factors (primary HSV infection, maternal genital lesions at delivery)

≤ 21 day old

Well-appearing 22-28 day old

Discharge Criteria:

- HSV studies (if obtained). *Of note, HSV whole blood PCR may not result prior to discharge; determine plan for follow up of any pending results.*
- No new symptoms of concern
- No persistent fever
- Family understands discharge instructions and ongoing infant needs
- Follow-up provider identified; discharge plan and close follow-up arranged

****Ill-appearing 22-28 day old**

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Diagnostic Tests

No major changes have been made for 2023.

- All neonates should have blood and urine studies done.
- CSF studies should be sent, although can be deferred for the *well-appearing* 22-28 day old if they meet certain criteria. All of these criteria should be present to consider deferment.
- Save additional CSF in case extra studies are needed.

Diagnostic Tests

- **Blood:** CBC w diff, culture, AST/ALT, procalcitonin, POCT glucose, (HSV PCR*)
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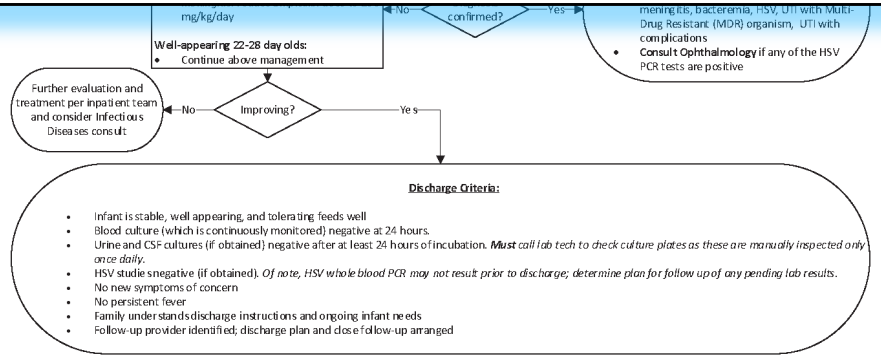

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CLINICAL PATHWAY:

THIS PATHWAY SERVES AS A GUIDE

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[1]Risk factors for HSV
(any of the following)

- Ill-appearing infant (including hypothermia, severe respiratory distress)
- Seizure history
- Conjunctivitis
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- CSF pleocytosis with negative CSF gram stain
- Interstitial pneumonitis
- Post-natal HSV contact
- Maternal risk factors (primary HSV infection, maternal genital lesions at delivery)

Herpes Simplex Virus (HSV)

- HSV studies should be sent if the patient is:
  - ≤21 days old, or
  - ill-appearing at any age, or
  - well-appearing but has HSV risk factors
- HSV antibodies and HSV cultures are not necessary (only send PCR tests)
- Maternal HSV risk factors were clarified to include only the highest risk scenarios

Additional Studies

Additional studies can be added on a case-by-case basis.

- Note: If respiratory signs are present and the provider wishes to send viral studies, send COVID-19, influenza and RSV studies **first**. Respiratory BioFire should generally not be sent unless the results will alter the management the neonate receives.

Diagnostic Tests

- **Blood:** CBC w diff, culture, AST/ALT, procalcitonin, POCT glucose, (HSV PCR*)
- **CSF:** cell count, glucose, protein, gram stain, culture, (HSV PCR*)
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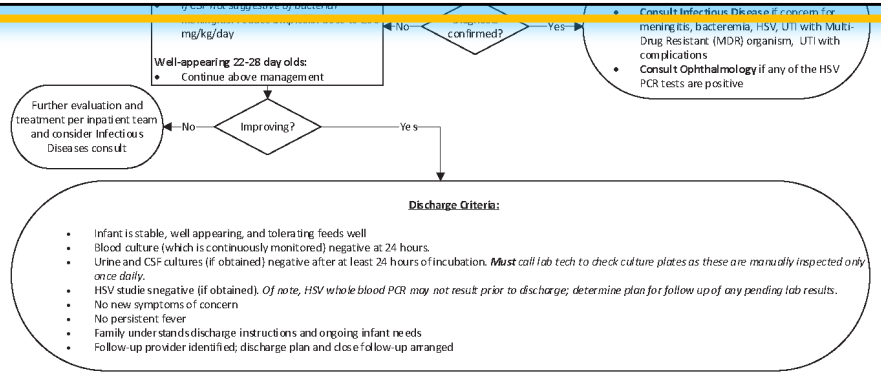

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Additional Studies

An additional note was made for patients with CSF pleocytosis or seizures.

- In these cases, individual HSV and enterovirus CSF PCRs should be sent first. If those tests are negative, consider sending the BioFire meningoencephalitis panel for additional studies.
- HSV and enterovirus are more common causes than other viruses and their individual PCR tests are more sensitive than the BioFire.

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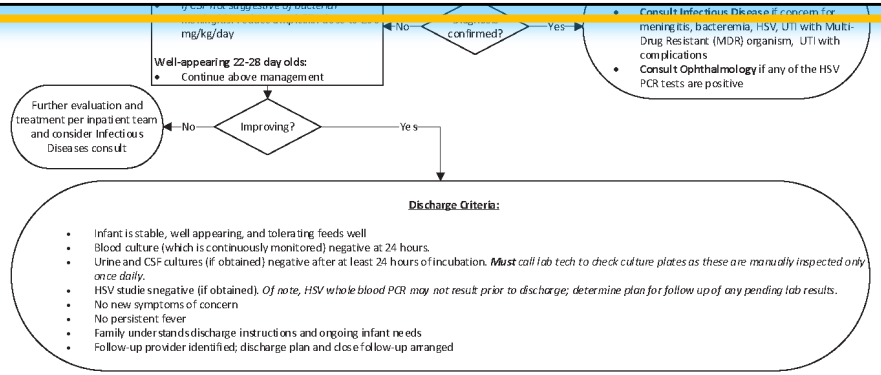

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The pathway then divides into empiric management based on age and appearance.

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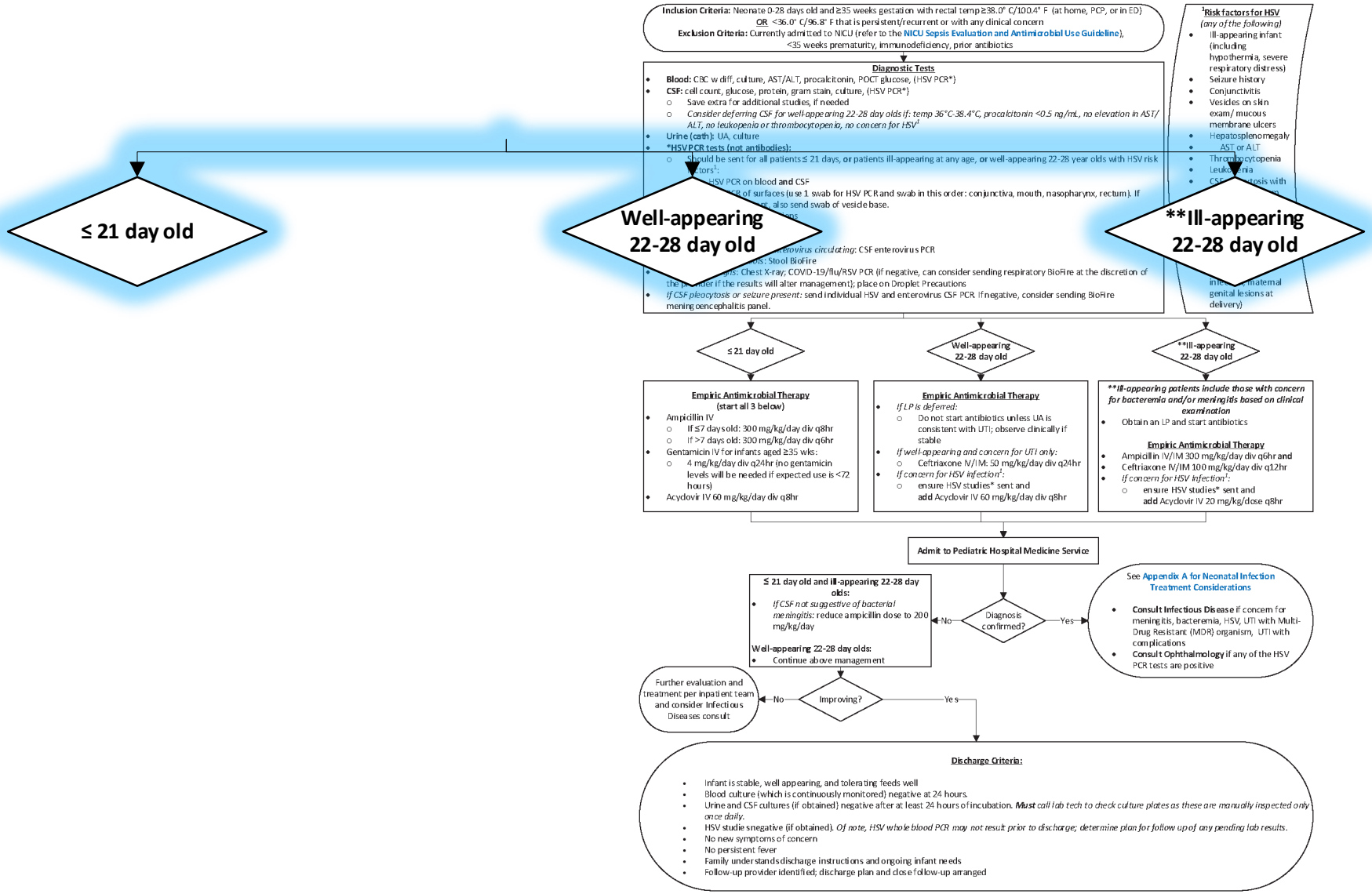

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≤21 day old

- All patients ≤21 days old (ill or well-appearing) should start empiric therapy that includes **ampicillin** and **gentamicin** for bacterial coverage, and **acyclovir** for HSV coverage.
- Although either ceftazidime or gentamicin can be used, we have chosen gentamicin preferentially to avoid unnecessary cephalosporin use. Cephalosporins are more likely to induce resistance if used routinely.
- Gentamicin levels are not needed if it is expected to be used for less than 72 hours.

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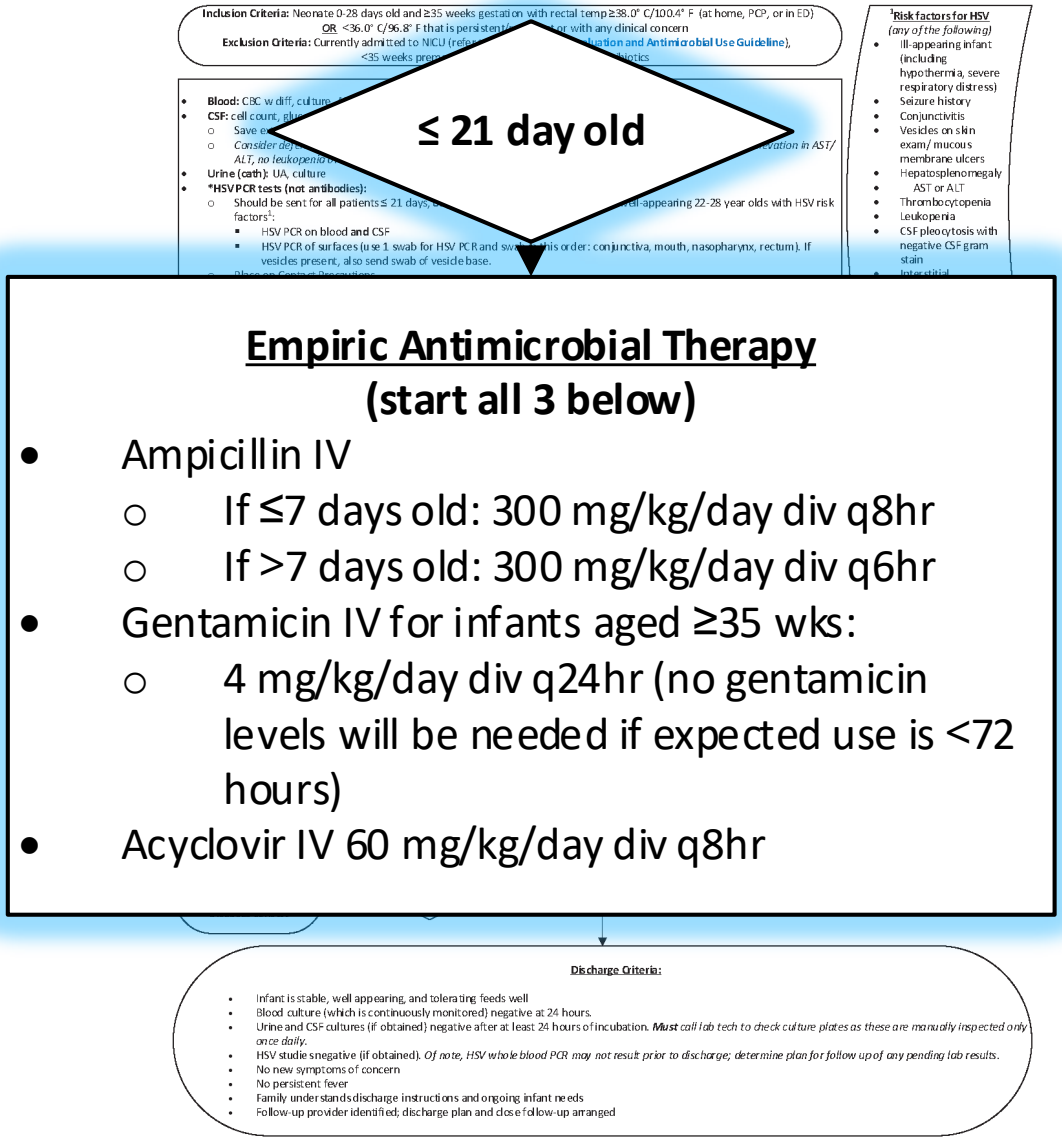

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Ill appearing 22-28 day old

- Ill-appearing 22-28 day olds include patients with a concern for bacteremia and/or meningitis on clinical examination.
- All ill-appearing patients should have an LP and be started on antibiotics.
- Empiric antimicrobial therapy in this group includes both **ampicillin** and **ceftriaxone**.
- If there is a concern for HSV infection, studies should be sent and **acyclovir** should be started.

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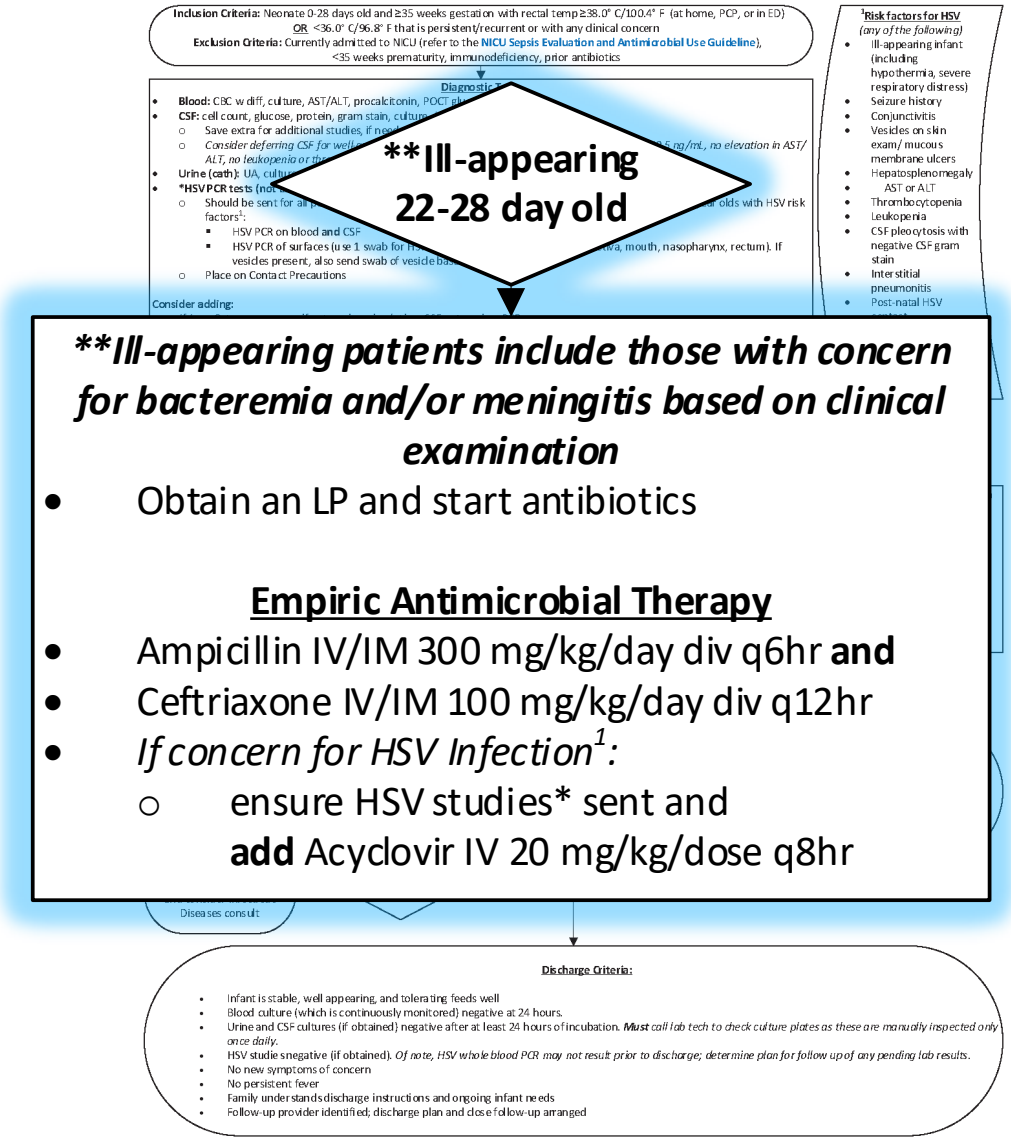

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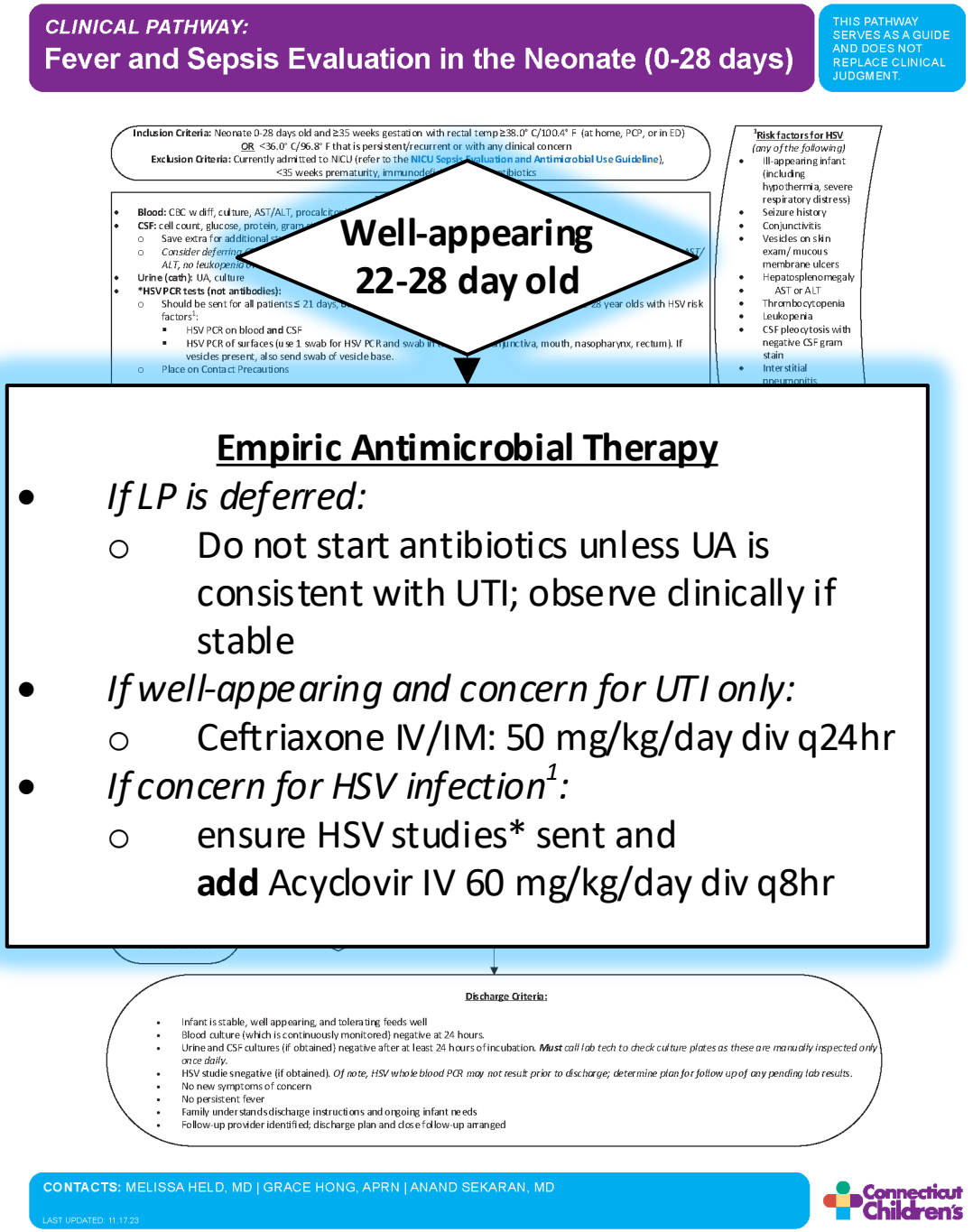
Well-appearing 22-28 day old:

- These recommendations are for WELL-APPEARING 22-28 days old only.
  - If the neonate is ill-appearing, they should follow appropriate recommendations.
- Remember that CSF studies can be sent, but can be deferred if certain criteria are met.
- If the LP is deferred, antibiotics should *not* be started unless the UA is consistent with a UTI. Continue to observe the neonate clinically.
- For those who are well appearing but have a concern for UTI only (e.g., no concern for other serious infection): start ceftriaxone

- If the well-appearing neonate had HSV risk factors present, and HSV studies were sent, start acyclovir.



CLINICAL PATHWAY:

Fever and Sepsis Evaluation in the N[illegible]te (0-28 days)

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≤ 21 day old

Empiric Antimicrobial Therapy
(start all 3 below)

- Ampicillin IV
  - If ≤7 days old: 300 mg/kg/day div q8hr
  - If >7 days old: 300 mg/kg/day div q6hr
- Gentamicin IV for infants aged ≥35 wks:
  - 4 mg/kg/day div q24hr (no gentamicin levels will be needed if expected use is <72 hours)
- Acyclovir IV 60 mg/kg/day div q8hr

Well-appearing 22-28 day old

Empiric Antimicrobial Therapy

- *If LP is deferred:*
  - Do not start antibiotics unless UA is consistent with UTI; observe clinically if stable
- *If well-appearing and concern for UTI only:*
  - Ceftriaxone IV/IM: 50 mg/kg/day div q24hr
- *If concern for HSV infection[1]:*
  - ensure HSV studies* sent and **add** Acyclovir IV 60 mg/kg/day div q8hr

**Ill-appearing 22-28 day old

*****Ill-appearing patients include those with concern for bacteremia and/or meningitis based on clinical examination***

- Obtain an LP and start antibiotics

Empiric Antimicrobial Therapy

- Ampicillin IV/IM 300 mg/kg/day div q6hr **and**
- Ceftriaxone IV/IM 100 mg/kg/day div q12hr
- *If concern for HSV Infection[1]:*
  - ensure HSV studies* sent and **add** Acyclovir IV 20 mg/kg/dose q8hr

Admit to Pediatric Hospital Medicine Service

All patients should be admitted to the Pediatric Hospital Medicine Service.

CONTACTS: MELISSA HELD, MD | GRACE HONG, APRN | ANAND SEKARAN, MD

LAST UPDATED: 11.17.23

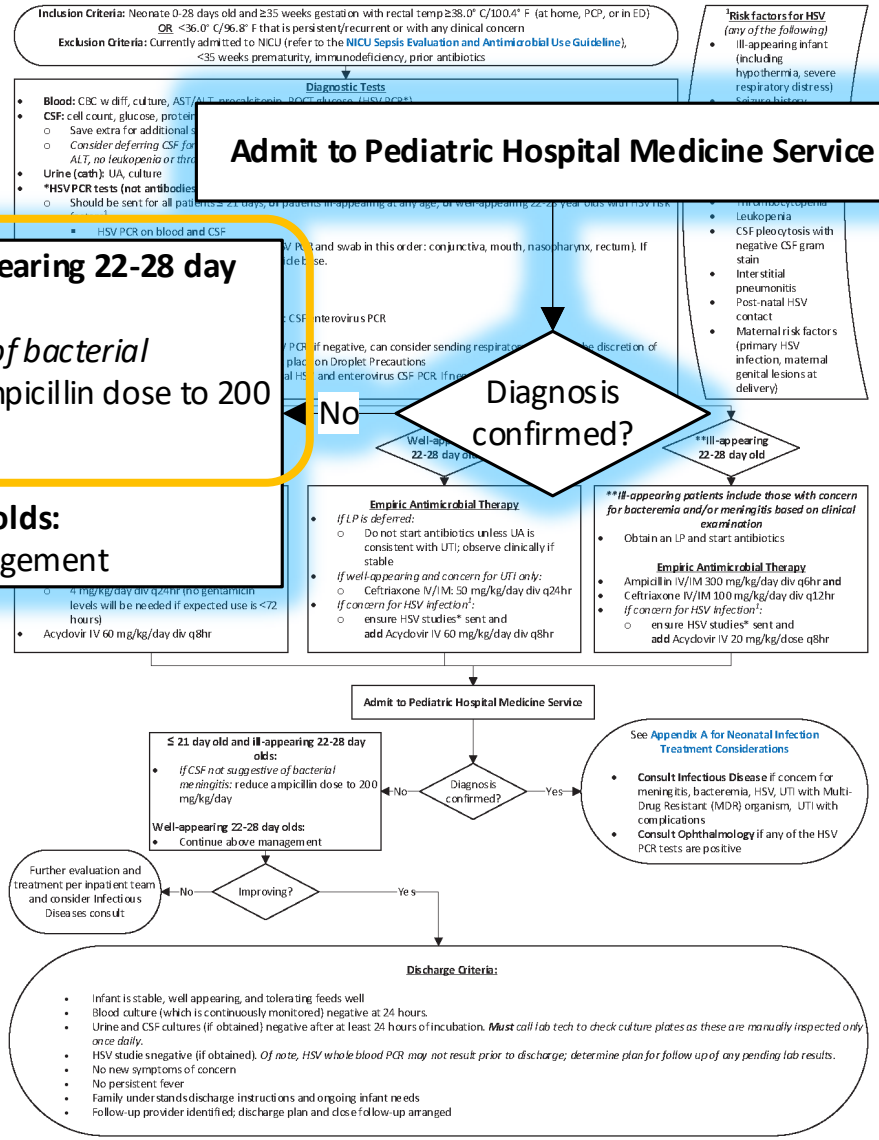
Diagnosis Not Confirmed

If the diagnosis is not confirmed…

- For those ≤21 day old or ill-appearing 22-28 day olds, if CSF is not suggestive of bacterial meningitis, then **ampicillin dosing can be reduced** as dosing for meningitis is not required.
- For those that are well-appearing 22-28 day olds, management should continue as previously outlined.

CLINICAL PATHWAY:
Fever and Sepsis Evaluation in the Neonate (0-28 days)

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



≤ 21 day old and ill-appearing 22-28 day olds:

- *If CSF not suggestive of bacterial meningitis:* reduce ampicillin dose to 200 mg/kg/day

Well-appearing 22-28 day olds:

- Continue above management

Admit to Pediatric Hospital Medicine Service

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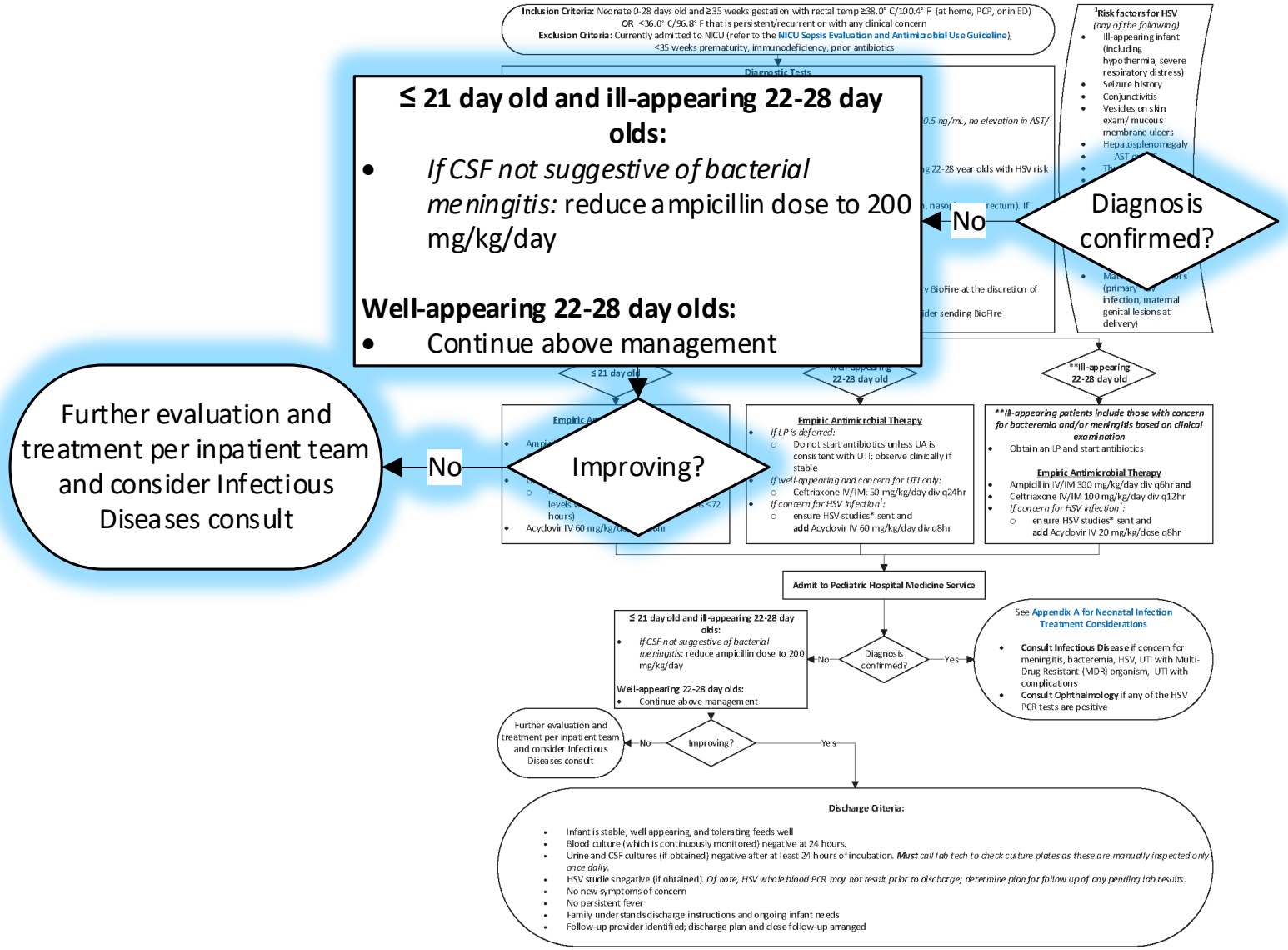
Diagnosis Not Confirmed and Patient Not Improving

- If the patient is **not** clinically improving, then further evaluation and management should be directed by the inpatient teams.
- Consider consulting Infectious Diseases.

CLINICAL PATHWAY:

Fever and Sepsis Evaluation in the Neonate (0-28 days)

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



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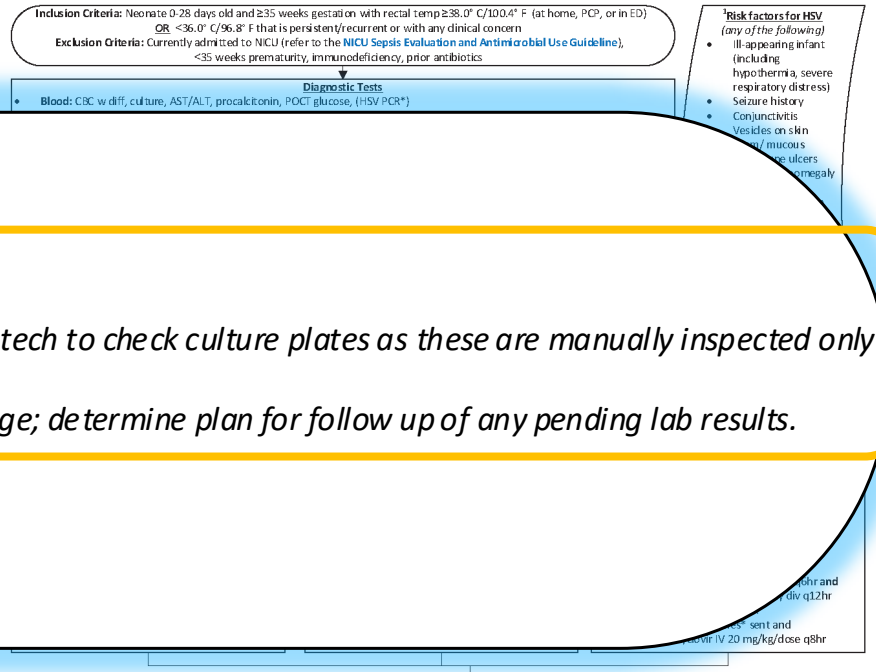
Improving? — Yes



Discharge Criteria:

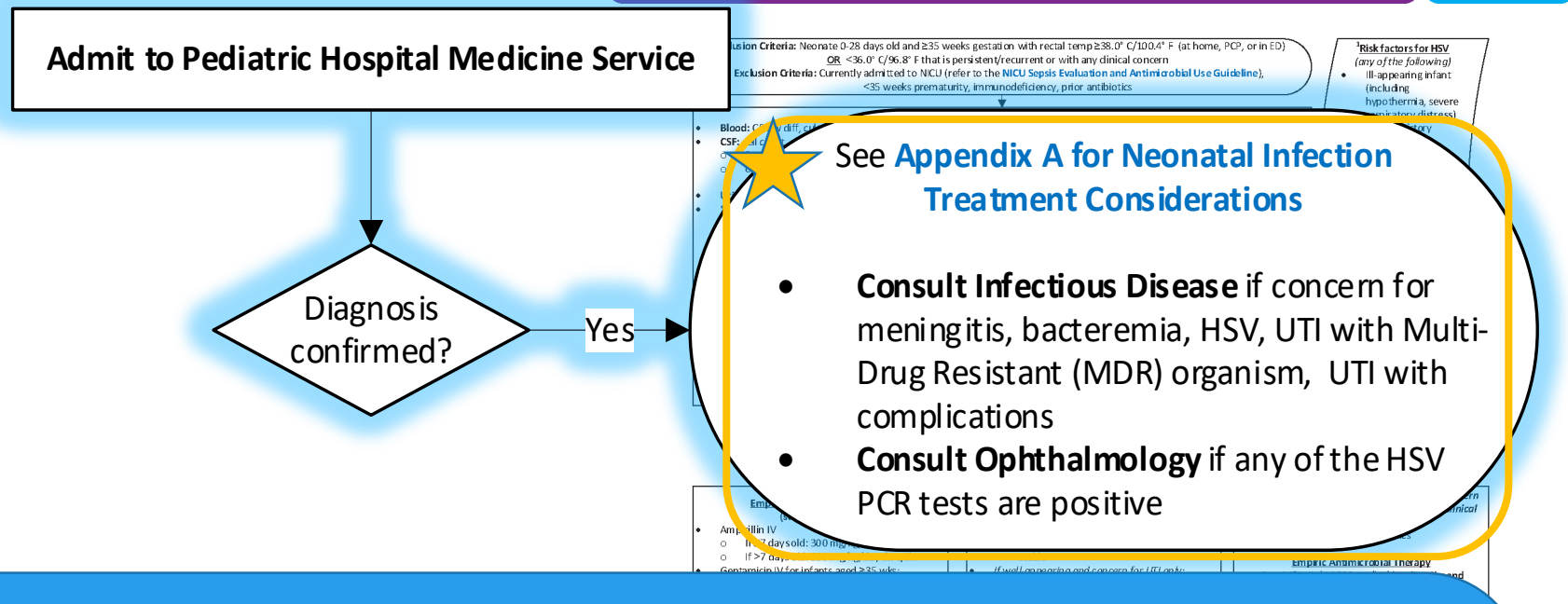
- Infant is stable, well appearing, and tolerating feeds well
- Blood culture (which is continuously monitored) negative at 24 hours.
- Urine and CSF cultures (if obtained) negative after at least 24 hours of incubation. ***Must*** *call lab tech to check culture plates as these are manually inspected only once daily.*
- HSV studies negative (if obtained). *Of note, HSV whole blood PCR may not result prior to discharge; determine plan for follow up of any pending lab results.*
- No new symptoms of concern
- No persistent fever
- Family understands discharge instructions and ongoing infant needs
- Follow-up provider identified; discharge plan and close follow-up arranged

Diagnosis Not Confirmed but Patient Improving

- If the patient is improving, consider discharge if the neonate is stable, well-appearing, tolerating feeds well, and cultures are negative at **24 hours.**
- Note: blood cultures are continuously monitored, and should be negative at **24 hours.**
- Urine and CSF cultures (if they were obtained), should be negative after ***at least* 24 hours** of incubation. These are manually inspected only once a day, so providers **must** call the lab tech to check on these culture plates!
- HSV whole blood PCR may not result prior to discharge, so plans to follow up the pending results should be made.

CLINICAL PATHWAY:
Fever and Sepsis Evaluation in the Neonate (0-28 days)

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



Diagnosis Confirmed

- If the patient has a diagnosis that is confirmed, a new appendix has been added for additional antimicrobial treatment considerations.

- Consult Infectious Diseases if there is a concern for meningitis, bacteremia, HSV, UTI with MDR organism, or UTI with complications as they can help with additional work up and guide specific therapy. In addition, ID will be available for follow up at the time of discharge.
- Consult Ophthalmology if any of the HSV PCR tests become positive to assess for ocular involvement.

Appendix A

Consulting Infectious Diseases

- Remember to consult Infectious Diseases if needed.
- ID can assist with further management and tailoring antimicrobial therapy.

Neonatal Infection Treatment Considerations (0-28 days)

Consult Infectious Diseases if concern for meningitis, bacteremia, HSV, UTI with Multi-Drug Resistant (MDR) organism, or UTI with complications

≤21 day old:

Appendix A: Neonatal infection Treatment Considerations

REPLACE C
JUDGMENT.

Neonatal Infection Treatment Considerations (0-28 days)

Consult Infectious Diseases if concern for meningitis, bacteremia, HSV, UTI with Multi-Drug Resistant (MDR) organism, or UTI with complications

- If well-appearing and concern for UTI only:
  - Ceftriaxone IV/IM 50 mg/kg/day div q24hr
  - If urine culture grows *Enterococcus*: **change** to ampicillin 100 mg/kg/day div q6hr
  - Adjust antibiotics according to sensitivities of organism
  - Treatment duration considerations:
    - Mild pyelonephritis with rapid response to antibiotics: 7 days
    - Severe pyelonephritis with delayed response to antibiotics: 10 days
    - Pyelonephritis complicated by intrarenal or perinephric abscess: at least 14 days, to be followed by Infectious Diseases
- If LP is obtained and suggestive of bacterial meningitis:
  - Start **all 3 antimicrobials** below:
    - Ampicillin IV/IM 300 mg/kg/day div q6hr **and**
    - Gentamicin 4 mg/kg/day div q24hr **and**
    - Ceftriaxone IV/IM 100 mg/kg/day div q12hr

Ill-appearing 22-28 day old:

- If gram negative bacterial meningitis is proven:
  - In addition to ampicillin, ceftriaxone and acyclovir, **add** gentamicin 4 mg/kg/day div q24hr

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LAST UPDATED: 11.17.23

Appendix A

≤21 day old with CSF suggestive of bacterial meningitis

- If CSF is suggestive of bacterial meningitis, **ceftazidime** should be **added** to ampicillin, gentamicin and acyclovir, to broaden gram negative coverage.
- Remember to consult Infectious Diseases to help assist with tailoring management.

Note: For patients who weigh less than 2000 g, smaller doses and/or longer intervals of ceftazidime may be needed. Infectious Diseases can assist with dosing.

Neonatal Infection Treatment Considerations (0-28 days)

Consult Infectious Diseases if concern for meningitis, bacteremia, HSV, UTI with Multi-Drug

≤21 day old:

- If CSF is suggestive of bacterial meningitis:
  - In addition to ampicillin, gentamicin and acyclovir, **add** ceftazidime IV:
    - 150 mg/kg/day div q8hr
    - *Note: if patient is less than 2000 g in weight, Infectious Diseases to help direct dosing*
  - If gentamicin is expected to be used for >72 hours, follow pharmacist protocol for monitoring

  - Adjust antibiotics according to sensitivities of organism
  - Treatment duration considerations:
    - Mild pyelonephritis with rapid response to antibiotics: 7 days
    - Severe pyelonephritis with delayed response to antibiotics: 10 days
    - Pyelonephritis complicated by intrarenal or perinephric abscess: at least 14 days, to be followed by Infectious Diseases
- If LP is obtained and suggestive of bacterial meningitis:
  - Start **all 3 antimicrobials** below:
    - Ampicillin IV/IM 300 mg/kg/day div q6hr **and**
    - Gentamicin 4 mg/kg/day div q24hr **and**
    - Ceftriaxone IV/IM 100 mg/kg/day div q12hr

Ill-appearing 22-28 day old:

- If gram negative bacterial meningitis is proven:
  - In addition to ampicillin, ceftriaxone and acyclovir, **add** gentamicin 4 mg/kg/day div q24hr

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LAST UPDATED: 11.17.23

Appendix A

≤21 day old with CSF suggestive of bacterial meningitis

- If gentamicin is expected to be used for >72 hours, then the pharmacist protocol for monitoring should be followed.

Neonatal Infection Treatment Considerations (0-28 days)

Consult Infectious Diseases if concern for meningitis, bacteremia, HSV, UTI with Multi-Drug

≤21 day old:

- If CSF is suggestive of bacterial meningitis:
  - In addition to ampicillin, gentamicin and acyclovir, **add** ceftazidime IV:
    - 150 mg/kg/day div q8hr
    - *Note: if patient is less than 2000 g in weight, Infectious Diseases to help direct dosing*
  - If gentamicin is expected to be used for >72 hours, follow pharmacist protocol for monitoring

  - Adjust antibiotics according to sensitivities of organism
  - Treatment duration considerations:
    - Mild pyelonephritis with rapid response to antibiotics: 7 days
    - Severe pyelonephritis with delayed response to antibiotics: 10 days
    - Pyelonephritis complicated by intrarenal or perinephric abscess: at least 14 days, to be followed by Infectious Diseases
- If LP is obtained and suggestive of bacterial meningitis:
  - Start **all 3 antimicrobials** below:
    - Ampicillin IV/IM 300 mg/kg/day div q6hr **and**
    - Gentamicin 4 mg/kg/day div q24hr **and**
    - Ceftriaxone IV/IM 100 mg/kg/day div q12hr

Ill-appearing 22-28 day old:

- If gram negative bacterial meningitis is proven:
  - In addition to ampicillin, ceftriaxone and acyclovir, **add** gentamicin 4 mg/kg/day div q24hr

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Appendix A

Well-appearing 22-28 day olds with concern for UTI only

- If there is only a concern for UTI, well-appearing 22-28 day olds can be started on ceftriaxone.
- In the rare case that the urine culture grows *Enterococcus,* antibiotics should be changed to ampicillin while awaiting sensitivities.
- Antibiotics should then be adjusted according to the sensitivities of the organism.
- Consult ID if there is a concern for MDR organism or there is a UTI with complications.
- Treatment duration depends on the severity of disease and clinical response.

~~Neonatal Infection Treatment Considerations (0-28 days)~~

Consult Infectious Diseases if concern for meningitis, bacteremia, HSV, UTI with Multi-Drug

Well-appearing 22-28 day old:

- If well-appearing and concern for UTI only:
  - Ceftriaxone IV/IM 50 mg/kg/day div q24hr
  - If urine culture grows *Enterococcus*: **change** to ampicillin 100 mg/kg/day div q6hr
  - Adjust antibiotics according to sensitivities of organism
  - Treatment duration considerations:
    - Mild pyelonephritis with rapid response to antibiotics: 7 days
    - Severe pyelonephritis with delayed response to antibiotics: 10 days
    - Pyelonephritis complicated by intrarenal or perinephric abscess: at least 14 days, to be followed by Infectious Diseases
- If LP is obtained and suggestive of bacterial meningitis:
  - Start **all 3 antimicrobials** below:
    - Ampicillin IV/IM 300 mg/kg/day div q6hr **and**
    - Gentamicin 4 mg/kg/day div q24hr **and**
    - Ceftriaxone IV/IM 100 mg/kg/day div q12hr

Ill-appearing 22-28 day old:

- If gram negative bacterial meningitis is proven:
  - In addition to ampicillin, ceftriaxone and acyclovir, **add** gentamicin 4 mg/kg/day div q24hr

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LAST UPDATED: 11.17.23

Appendix A

Well-appearing 22-28 day olds with CSF suggestive of bacterial meningitis

- If CSF was obtained and is initially suggestive of bacterial meningitis, then **ampicillin**, **gentamicin**, and **ceftriaxone** should be started.
- Gentamicin is added to ampicillin and ceftriaxone to broaden gram negative coverage.
- Infectious Diseases should be consulted to help tailor therapy.

Neonatal Infection Treatment Considerations (0-28 days)

Consult Infectious Diseases if concern for meningitis, bacteremia, HSV, UTI with Multi-Drug

Well-appearing 22-28 day old:

- If well-appearing and concern for UTI only:
  - Ceftriaxone IV/IM 50 mg/kg/day div q24hr
  - If urine culture grows *Enterococcus*: **change** to ampicillin 100 mg/kg/day div q6hr
  - Adjust antibiotics according to sensitivities of organism
  - Treatment duration considerations:
    - Mild pyelonephritis with rapid response to antibiotics: 7 days
    - Severe pyelonephritis with delayed response to antibiotics: 10 days
    - Pyelonephritis complicated by intrarenal or perinephric abscess: at least 14 days, to be followed by Infectious Diseases
- If LP is obtained and suggestive of bacterial meningitis:
  - Start **all 3 antimicrobials** below:
    - Ampicillin IV/IM 300 mg/kg/day div q6hr **and**
    - Gentamicin 4 mg/kg/day div q24hr **and**
    - Ceftriaxone IV/IM 100 mg/kg/day div q12hr

Ill-appearing 22-28 day old:

- If gram negative bacterial meningitis is proven:
  - In addition to ampicillin, ceftriaxone and acyclovir, **add** gentamicin 4 mg/kg/day div q24hr

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LAST UPDATED: 11.17.23

Appendix A

Ill-appearing 22-28 day old with proven gram negative bacterial meningitis

- Ill-appearing 22-28 day olds are already empirically started on ampicillin and ceftriaxone.
- If gram negative bacterial meningitis is confirmed, **gentamicin** should be added to ampicillin and ceftriaxone (and acyclovir if there is a concern for HSV infection).

Note: If gentamicin is expected to be used for >72 hours, then the pharmacist protocol for monitoring should be followed.

Neonatal Infection Treatment Considerations (0-28 days)

Consult Infectious Diseases if concern for meningitis, bacteremia, HSV, UTI with Multi-Drug Resistant (MDR) organism, or UTI with complications

≤21 day old:

- If CSF is suggestive of bacterial meningitis:
  - In addition to ampicillin, gentamicin and acyclovir, **add** ceftazidime IV:
    - 150 mg/kg/day div q8hr
    - *Note: if patient is less than 2000 g in weight, Infectious Diseases to help direct dosing*
  - If gentamicin is expected to be used for >72 hours, follow pharmacist protocol for monitoring

Ill-appearing 22-28 day old:

- If gram negative bacterial meningitis is proven:
  - In addition to ampicillin, ceftriaxone and acyclovir, **add** gentamicin 4 mg/kg/day div q24hr

14 days, to be followed by Infectious Diseases

- If LP is obtained and suggestive of bacterial meningitis:
  - Start **all 3 antimicrobials** below:
    - Ampicillin IV/IM 300 mg/kg/day div q6hr **and**
    - Gentamicin 4 mg/kg/day div q24hr **and**
    - Ceftriaxone IV/IM 100 mg/kg/day div q12hr

Ill-appearing 22-28 day old:

- If gram negative bacterial meningitis is proven:
  - In addition to ampicillin, ceftriaxone and acyclovir, **add** gentamicin 4 mg/kg/day div q24hr

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Review of Key Points

- Standardized work up/management depends on neonatal age, presence of HSV risk factors, and well or ill-appearing clinical status
- Well-appearing 22-28 day olds may be able to defer an LP if certain clinical criteria are met
- A new appendix was added to help guide management for certain neonatal infections
- Infectious Diseases should be consulted if there are concerns for meningitis, bacteremia, UTI with Multi-Drug Resistant (MDR) organism, or UTI with complications

Quality Metrics

- % Patients with pathway order set
- % HSV testing performed as indicated by pathway
- % of patients with appropriate first line antibiotics received, per pathway
- % of patients with normal testing that have antibiotics discontinued within 48-50 hours
- % of patients with CSF studies completed, or not completed, per pathway
- # of ED returns within 72 hours of discharge
- ALOS (inpatient, days)
- Pathway bundle: % patients with antibiotics received, as indicated by pathway (correct med and correct dosage), % of patients with antibiotic administration within 2 hours of CSF collection time

Pathway Contacts

- Melissa Held, MD
  - Connecticut Children's Infectious Diseases and Immunology
- Grace Hong, APRN
  - Connecticut Children's Infectious Diseases and Immunology
- Anand Sekaran, MD
  - Connecticut Children's Pediatric Hospital Medicine

References

- [1]Jain, et al. *Management of Febrile Neonates in the US Pediatric Emergency Departments*. 2014. Pediatrics. Volume 133, Issue 2.
- [2]American Academy of Pediatrics. Herpes Simplex. In: eds. *Red Book: 2021-2024 Report of the Committee on Infectious Diseases.* American Academy of Pediatrics; 2021; 407-417.
- [3]Pantell, R., et al. *Evaluation and Management of Well-Appearing Febrile Infants 8 to 60 Days Old.* Pediatrics. August 2021, 148 (2) e2021052228; DOI: https://doi.org/10.1542/peds.2021-052228.

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.