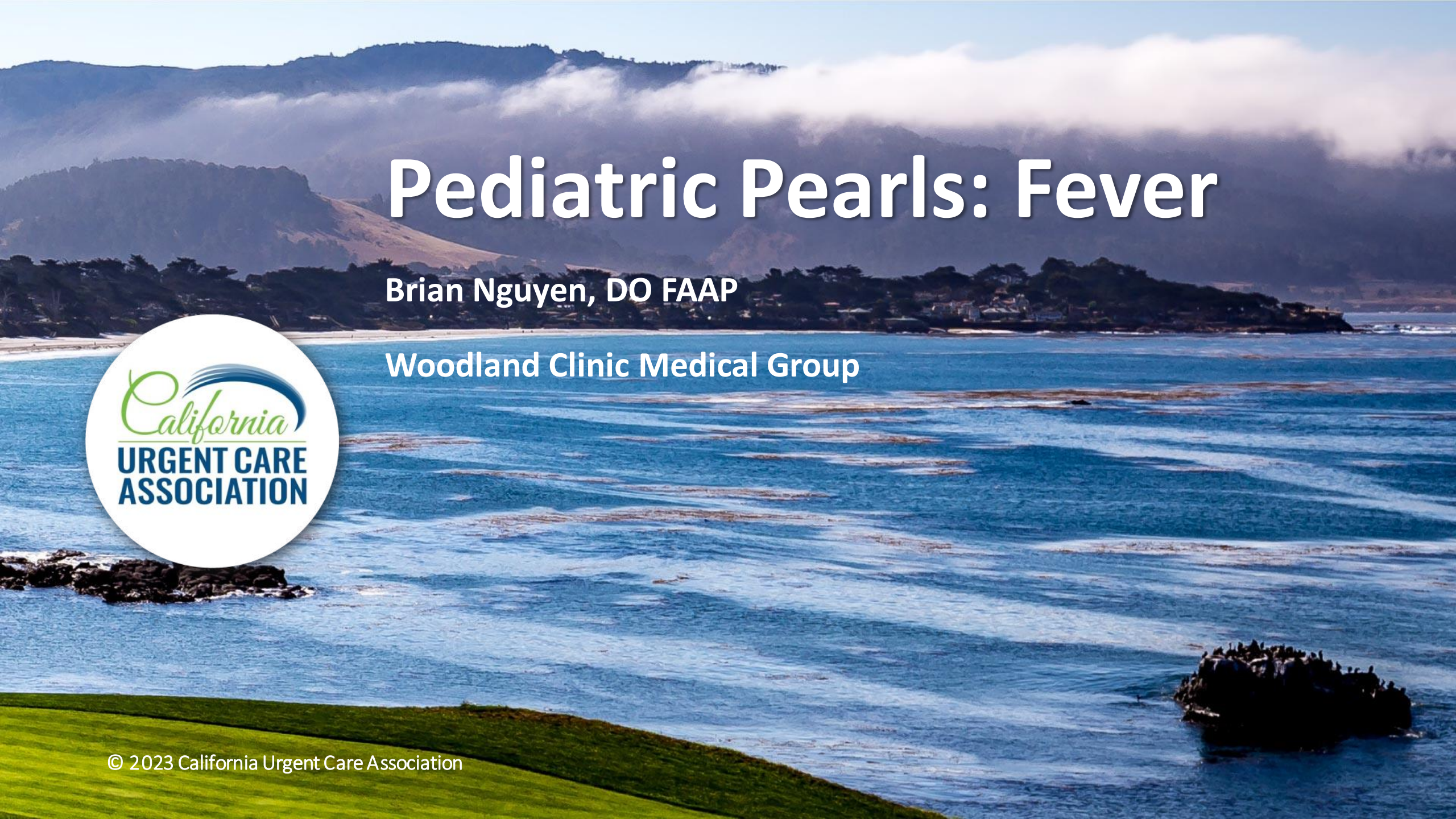
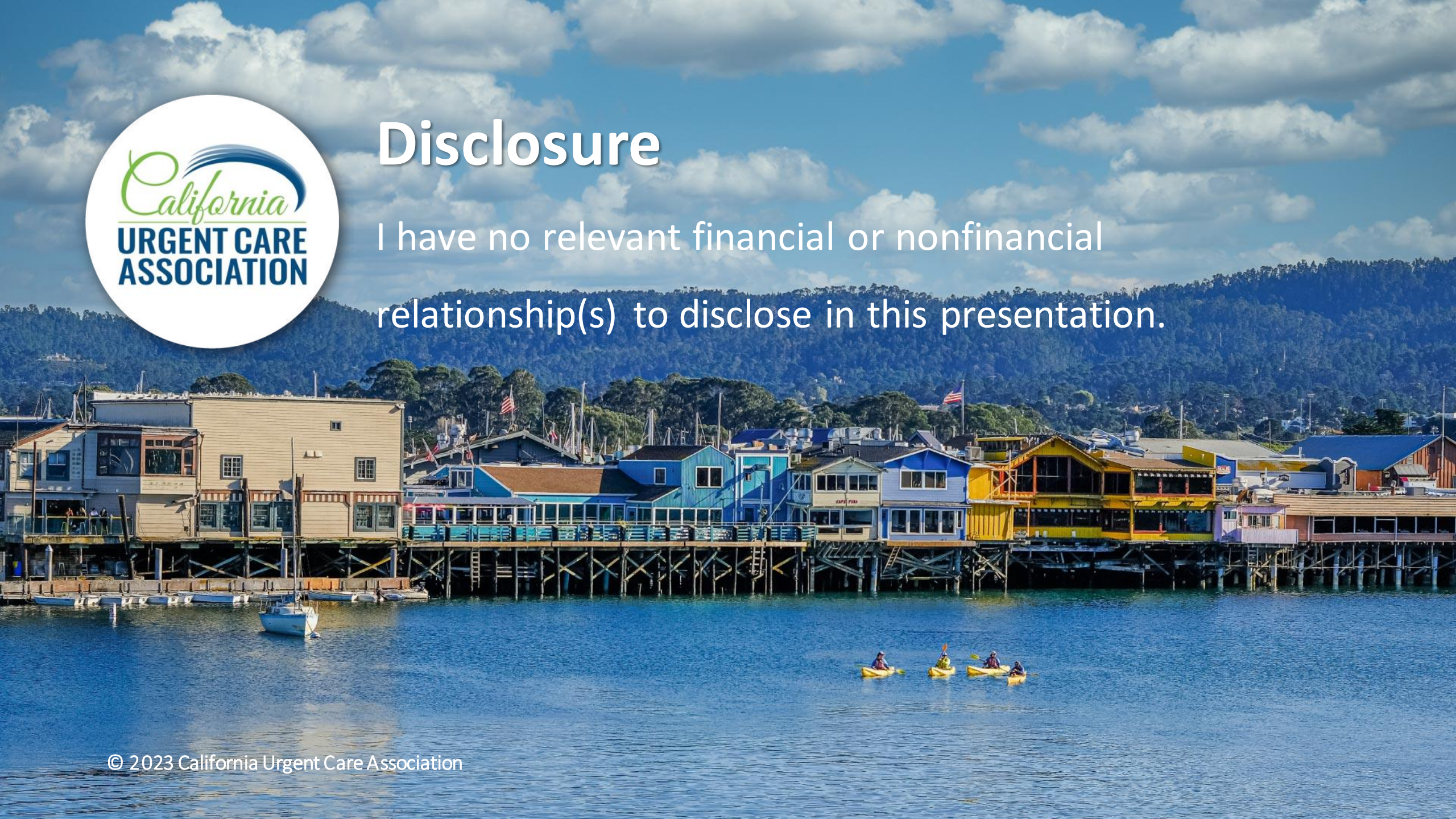


Pediatric Pearls: Fever

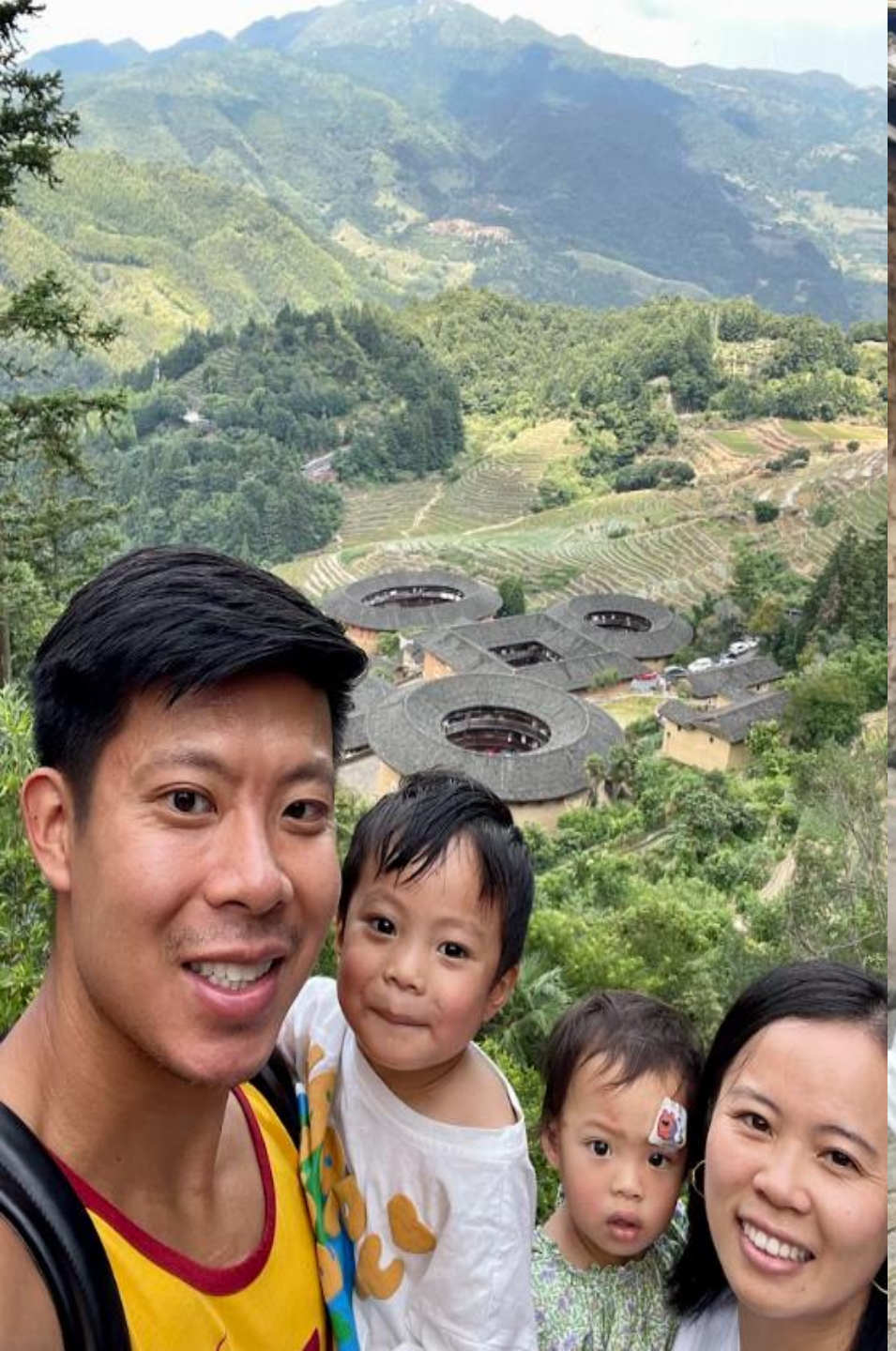
Brian Nguyen, DO FAAP

Woodland Clinic Medical Group



Disclosure

I have no relevant financial or nonfinancial relationship(s) to disclose in this presentation.



LECOM

LAKE ERIE COLLEGE OF OSTEOPATHIC MEDICINE

Learning Objectives

- Identify the differential diagnosis of fever without localizing signs in young children
- Plan the workup and management of fever without localizing signs in young children
- Identify special groups of children who present with fever
- Identify and workup fever of unknown origin (FUO)
- Identify SIRS vs sepsis in children

Case #1

- **A 29-day-old infant presents with tactile fever and mildly decreased PO. No other symptoms, sick contacts, or recent travels.**
- **Birth hx: born at 39 wks to a 28 y/o G2P2 via vaginal delivery. GBS negative. Hospital course was uncomplicated and was discharged at DOL#2.**
- **Vitals: 38.0, HR 165, RR 50, Pulse ox 97%. Physical Exam: Non-toxic, breastfeeding well**

- **What should be the *initial* steps in management?**

A. Admission, Full Septic Workup

B. Tylenol, Reassurance, PCP F/U

C. Hydrate, Admit for Observation

D. UA/Urine Cx, Blood Cx, Inflammatory marker(s)

E. Viral Studies

Case #2

- **You are evaluating an 11-month-old girl who has had a temperature up to 102.0°F (38.9°C) for 2 days. She has been slightly fussy without any other symptoms. Her immunizations are up to date. Her home rapid COVID-19 antigen test was negative. She is well-appearing on exam. Which of the following tests is *most* helpful in establishing a diagnosis in this child?**

A. Blood culture
B. Chest radiograph
C. Complete blood count
D. Inflammatory marker(s)
E. Urine analysis and urine culture

Fever (Pyrexia)

- Rectal temperature **≥ 38˚C (100.4˚C)**
- ***Regulated*** elevation of body temperature mediated by hypothalamus
- Response to a disease, NOT a diagnosis
- 30% acute care visits and 5 million ED visits annually
- Beneficial: ⬆ leukocyte mobility/activity, T-cell function, Interferon
- Harmful: ⬆ metabolism/fluid loss, harmful in traumatic brain injury

Height and Duration of Fever

- Hyperpyrexia: 40°C (104°F)-41.5°C (106.7°F) or greater
  - In < 3 months if temp > 40°C : 38% have serious bacterial infection (SBI)
- ⬆ chance of pneumococcal bacteremia w/ ⬆ temperature
- Height of fever does not differentiate viral from bacterial illness
- Duration of fever does not predict bacteremia

Vital Changes

- Increase in HR 10-15 bpm/C
- Increase in respiratory rate 3-5 bpm/C rise
- Added stress on children with chronic illness, cardiovascular or pulmonary disease
- Relative bradycardia:
  - 1. Typhoid
  - 2. Mycoplasma
  - 3. Tularemia
  - 4. Factitious fever
  - 6. Drug fever

Causes of Fever

- Infection
- Vasculitis
- Autoimmune
- Neoplastic
- Endocrine
- Chronic inflammatory
- Hematologic
- Immunization reaction
- Poisoning
- CNS abnormality
- Heat illness
- Factitious fever
- Drug fever

Serious Bacterial Infections (SBI)

- Invasive bacterial infections (IBI)
  - ***Bacterial Meningitis***
  - Bacteremia
- Pneumonia
- Urinary tract infection (most frequent)

- Toxic appearance in young children:
  - ***Bulging fontanelle***
  - ***Fever with petechiae below the nipples***
  - Lethargy or extreme irritability
  - Poor feeding
  - Grunting respirations
  - Impaired perfusion
  - Pallor

Risk Factors for IBI in Febrile Infants < 90 days of age

- Age <28 days
- Ill appearance
- Rectal temperature ≥38.6°C (101.5°F; infants 22 to 60 days old only)
- Prematurity (gestational age <37 weeks)
- Focal infection: cellulitis, abscess, pneumonia, osteomyelitis, bacterial arthritis, and omphalitis.
- Maternal risk for early-onset sepsis (neonates <14 days only, any one of the following):
  - Peripartum fever
  - Prolonged rupture of membranes
  - Vaginal culture positive for group B *Streptococcus*
- Comorbidities or chronic illness
  - Perinatal course complicated by surgery or infection
  - Medically fragile (technology dependent or require specific therapies to sustain life)[Δ]
  - Documented or suspected immune compromise
  - Congenital or chromosomal abnormality
- Recent ABX
  - Neonates: within 7 days of presentation
  - Infants 29-60 days old: within 3 days of presentation

California URGENT CARE ASSOCIATION

Fever Without Localizing Signs in Young Children

- 20% of fevers are without apparent source after history and physical
- Divide by age
  - 0-8 days
  - 8-21 days
  - 22-28 days old
  - 29-60 days old
  - 2 months-36 months old

Fever: 0-8 Days

- Nearly mandatory admission
- Invasive bacterial illness (IBI) in 7-8 %, meningitis in 2%
- Pathogens:
  1. GBS
  2. *E. coli*
  3. *Klebsiella*
  4. *Enterobacter*
  5. *Listeria*

FULL SEPSIS WORK-UP-Neonates

- CBC with diff
- Blood c/s: A single culture with 1-2 ml is sufficient for detection of bacteremia (even as low as 0.5ml)
- Urinalysis: catheter or suprapubic urine c/s (gold standard)
- LP in all (do not delay antibiotics)
- Herpes PCR
- CXR and stool if indicated

Treatment-Neonate

- HOSPITALIZE
- Preferred: Ampicillin + Gentamicin
- Alternative (> 3 days old from community): Cefotaxime or Ceftazidime + Ampicillin
- NOT Ceftriaxone
- PLUS Acyclovir if risk factors for HSV:
  - Maternal genital lesions or fever from 48 hours before to 48 hours after delivery
  - + vesicles, seizures, hypothermia, mucous membrane ulcers, CSF pleocytosis in the absence of a positive Gram stain result, leukopenia, thrombocytopenia, or elevated alanine aminotransferase levels

CLINICAL PRACTICE GUIDELINE

American Academy of Pediatrics

DEDICATED TO THE HEALTH OF ALL CHILDREN™

Clinical Practice Guideline: Evaluation and Management of Well-Appearing Febrile Infants 8 to 60 Days Old

Robert H. Pantell, MD, FAAP,[a] Kenneth B. Roberts, MD, FAAP,[b] William G. Adams, MD, FAAP,[c] Benard P. Dreyer, MD, FAAP,[d] Nathan Kuppermann, MD, MPH, FAAP, FACEP,[e] Sean T. O'Leary, MD, MPH, FAAP,[f] Kymika Okechukwu, MPA,[g] Charles R. Woods Jr, MD, MS, FAAP[h] SUBCOMMITTEE ON FEBRILE INFANTS

8 to21 days old,
well-appearing,
no evident source of infection,
and temperature ≥ 38.0 °C

Obtain urinalysis (1),[a] blood culture (2), and perform LP(4).[c]
May obtain inflammatory markers (IMs) (3).[b]

Increased HSV risk?[d]

Yes

Send HSV studies.[d]

1. Initiate parenteral antimicrobial(s), including acyclovir(5).
2. Observe in hospital(6).

No

1. Initiate parenteral antimicrobial(s)(5).
2. Observe in hospital(6).

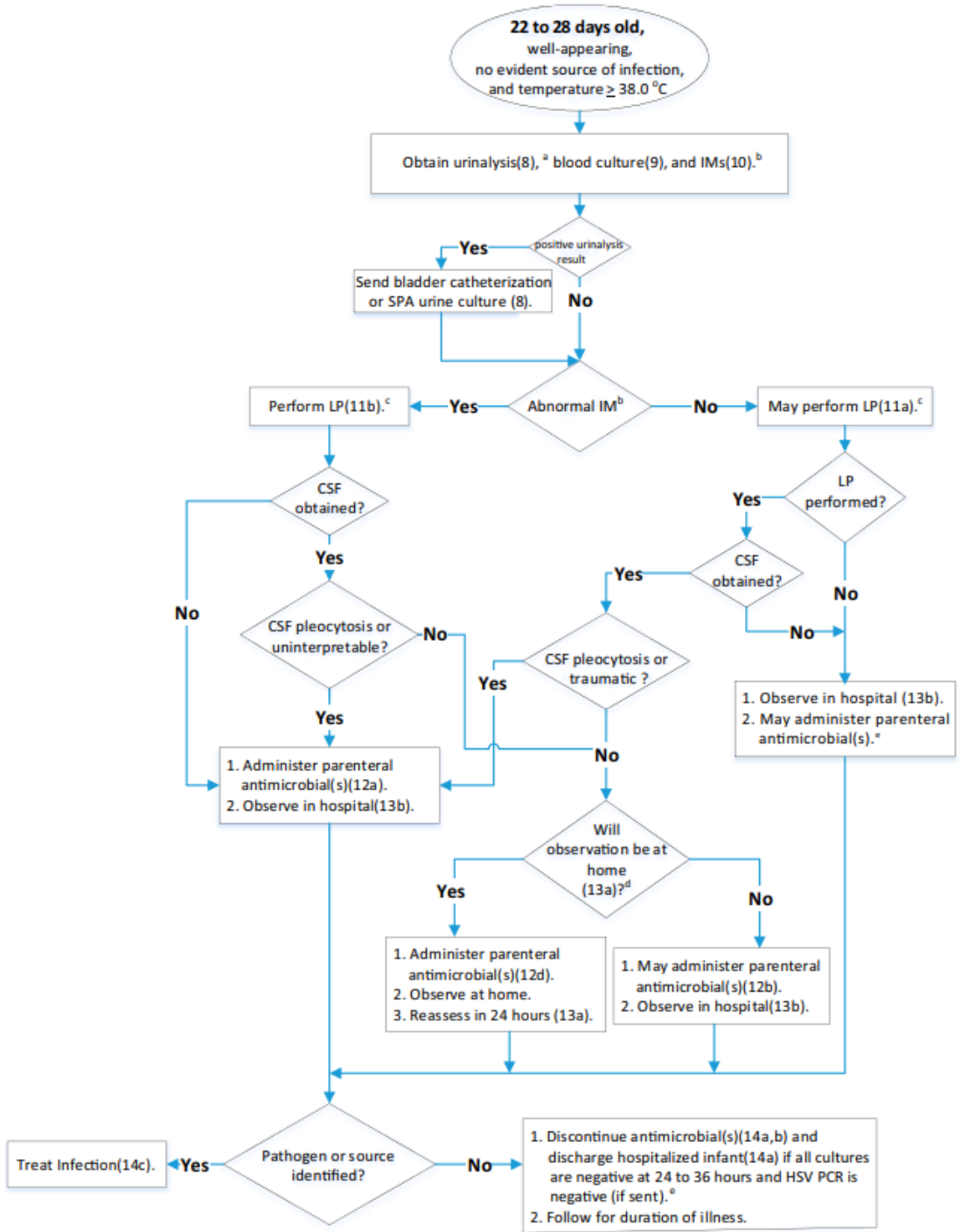
Pathogen or source identified?

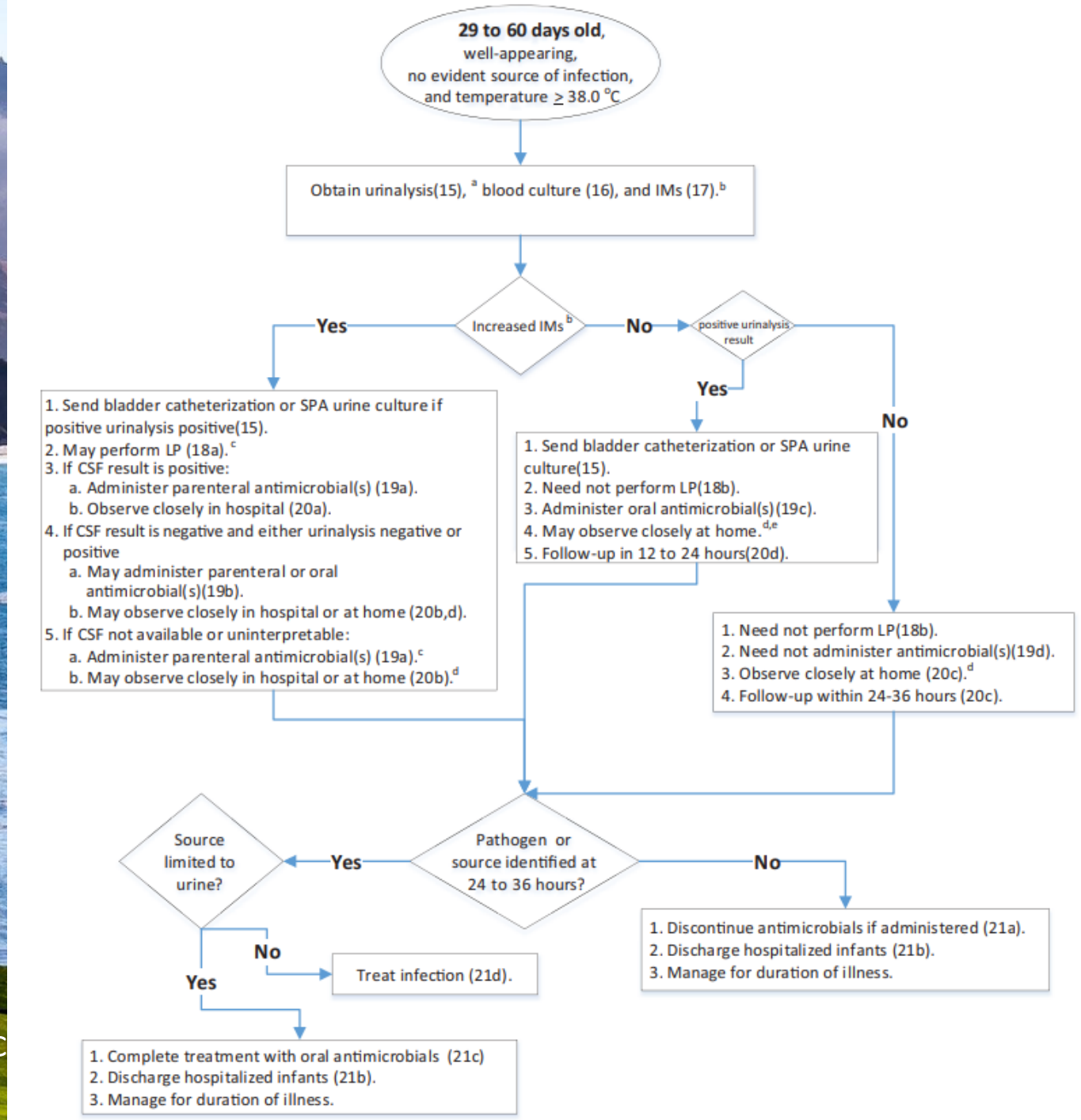
Yes

Treat Infection(7b).

No

1. Discontinue antimicrobial(s)(7a) and discharge hospitalized infant(7a) if all culture results are negative at 24 to 36 hours and HSV PCR result is negative (if sent).
2. Manage for duration of illness.





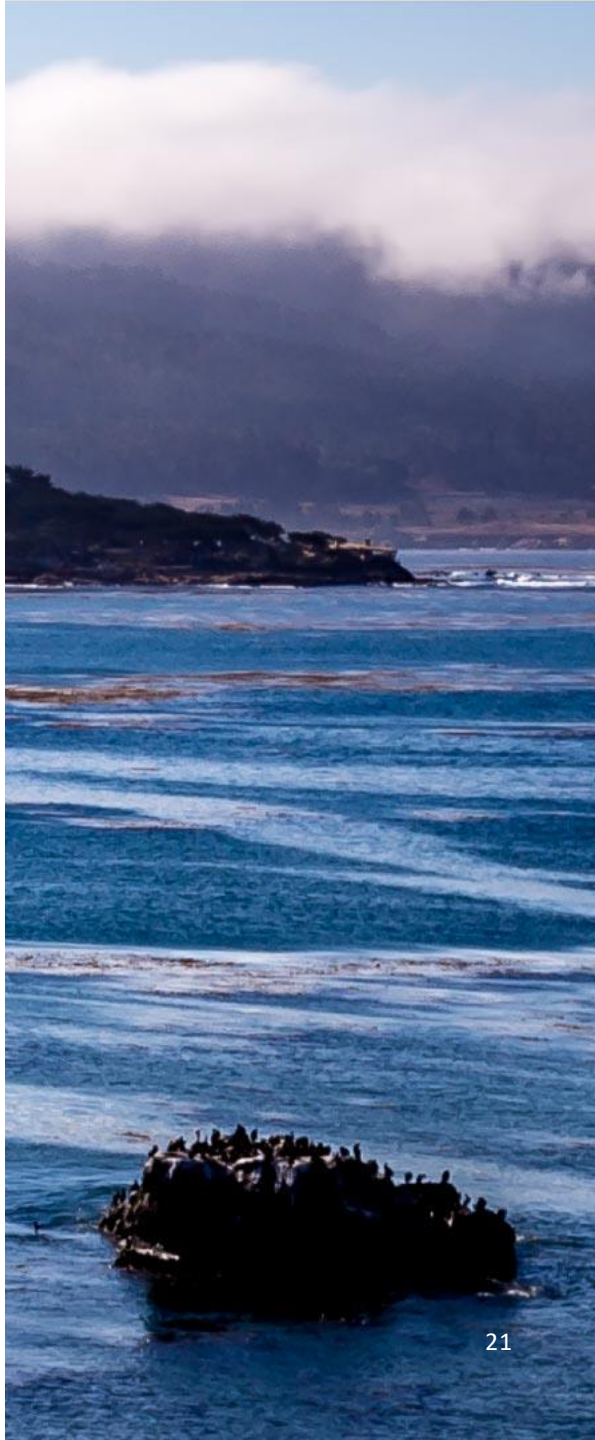


TABLE 3 Initial Empirical Antibacterial Therapy for Well-Appearing Febrile Infants 7 to 60 Days Old

Suspected Source of Infection	8–21 d Old	22–28 d Old	29–60 d Old
UTI[a]	Ampicillin IV or IM (150 mg/kg per d divided every 8 h) and either ceftazidime IV or IM (150 mg/kg per d divided every 8 h) or gentamicin IV or IM (4 mg/kg per dose every 24 h)	Ceftriaxone IV or IM (50 mg/kg per dose every 24 h)	Ceftriaxone IV or IM (50 mg/kg/dose every 24 h). Oral medications for infants older than 28 d.[b] Cephalexin 50–100 mg/kg per d in 4 doses or cefixime 8 mg/kg per d in 1 dose
No focus identified[c]	Ampicillin IV or IM (150 mg/kg per d divided every 8 h) and either ceftazidime IV or IM (150 mg/kg per d divided every 8 h) or gentamicin IV or IM (4 mg/kg per dose every 24 h)[d]	Ceftriaxone IV or IM (50 mg/kg per dose every 24 h)	Ceftriaxone IV or IM (50 mg/kg/dose every 24 h)
Bacterial meningitis[e]	Ampicillin IV or IM (300 mg/kg per d divided every 6 h) and ceftazidime IV or IM (150 mg/kg per d divided every 8 h)	Ampicillin IV or IM (300 mg/kg per d divided every 6 h) and ceftazidime IV or IM (150 mg/kg per d divided every 8 h)	Ceftriaxone IV (100 mg/kg per d once daily or divided every 12 h) or Ceftazidime IV (150 mg/kg per d divided every 8 h) and vancomycin[f] IV (60 mg/kg per d divided every 8 h)

Viral-Positive Infants with Fever

- Infants younger than 28 days old:
  - IBI of 13% regardless of RSV status
  - Prospective PECARN study: bacteremia 1.1%, meningitis 0.8% in + viral infections
  - **Admission, full septic workup (role of inflammatory markers for 22-28 days old)**
- Infants 29-60 days old:
  - IBI of 5.5%. All were UTIs. No bacteremia or meningitis.
  - **Obtain blood cx, urine cx, admission VS discharge with close follow-up**
  - CSF may be deferred if well-appearing

2 Month-36 Month Old

- Immunized (Hib, S. pneumoniae) VS Incompletely Immunized
- Occult bacteremia: *S. pneumoniae, N. meningitides, Salmonella*
  - Risk of progression to PNA, meningitis, osteomyelitis, cellulitis, etc.
- Overall risk of meningitis or death with occult bacteremia is 1.8%
- Temp threshold for workup is >39°C (>102.2°F)
  - *What about Roseola?*
  - *Role of viral studies?*

2 Month-36 Month Old

- Completely immunized:
  - UA and Urine C/S:
    - Girls up to 36 months
    - Uncircumcised boys up to 24 months
    - Circumcised boys < 6 months
- Incompletely immunized up to 36 months:
  - CBC, UA, Blood and Urine C/S
  - CXR if WBC > 20,000 (20% have PNA even in the absence of clinical signs)
  - Antibiotic therapy if WBC > 15,000
- Test urine in ALL infants with prior history of UTI

2 Month-36 Month Old

- UTI Prevalence: 2.1% to 8.7%
  - Highest in girls < 1 year old
  - Lowest in circumcised boys older than 6 months

- Pneumonia
  - Tachypnea and low oxygen saturations have a high positive predictive value (75%)
  - Rales, cough > 10 days and fever > 5 days also predict PNA
  - If fever is >39° C and WBC >20,000, there is a 19% incidence of occult PNA

Immunocompromised Patients

- Sickle cell disease
- Asplenia
- Complement or properdin deficiency
- Agammaglobulinemia
- AIDS
- Congenital heart disease
- Malignancy
- Long term steroid use
- Indwelling medical devices-VP shunt, Central venous line
- Neurologically impaired

Sickle Cell Disease (SCD)

- Infection is the leading cause of death: 6mo- 3yrs at greatest risk
- If febrile:
  - admission in most cases
  - empiric IV ABX (Ceftriaxone ± Vanc), CBC w/diff, blood c/s, CXR, UA and urine c/s, throat c/s
- SCD complications: stroke, pain, aplastic crisis, splenic sequestration, acute chest syndrome, bacteremia, meningitis
  - Parvovirus may cause acute aplastic crisis

VP Shunts and Central Venous Lines

- **VP Shunt:**
  - Fever usually occurs within 4-6 months of a revision or placement
  - If it occurs later, consider obstruction or an ascending infection from abdominal cavity
- **Central Venous Line:**
  - Fever may be the only sign of a line infection
  - Obtain c/s from both periphery and central line
  - Antibiotics should include Staphylococcus and gram negative coverage

Other Considerations

Long Term Steroid Use

- Steroids mask signs and symptoms of infection
- Low threshold for work up and antibiotics therapy
- Steroids > immunosuppresion
- Cell mediated immunity is affected more than humoral

Neurologically Impaired

- Assess clinically and depend on family to tell deviation from baseline
- Higher risk for aspiration pneumonia

Fever of Unknown Origin (FUO)

- Temp >38.3°C (101°F) at least once per day for ≥8 days with no apparent diagnosis after initial outpatient or hospital evaluation that includes a detailed history, thorough physical examination, and initial laboratory assessment
- (Decreased from 3 weeks)
- Fever without a source (FWS): fever for ≤1 week without adequate explanation after a thorough history and physical examination
- Daily w/ ongoing evaluations
- Differentiate two short febrile illness at a short interval
- Focused approach

Fever of Unknown Origin (FUO)

- Causes:
  - Infection: 50%
  - Rheumatic: 10-20%
  - Malignancy: 8%
  - Undiagnosed: 10-20%

Fever of Unknown Origin (FUO): Infections

- 1.EBV
- 2.Osteomyelitis
- 3.Bartonella
- Others: TB, Chronic UTI, pneumonia, HIV, chronic meningococcemia
- Recent travel: Malaria, dengue, typhoid

Diagnostic Criteria for Kawasaki Disease

- The diagnosis of KD requires the **presence of fever lasting at least 5 days* without any other explanation combined with at least 4 of the 5 following criteria.** A significant proportion of children with KD have a concurrent infection; therefore, ascribing the fever to such an infection or to KD requires clinical judgment.
  - Bilateral bulbar conjunctival injection
  - Oral mucous membrane changes, including injected or fissured lips, injected pharynx, or strawberry tongue
  - Peripheral extremity changes, including erythema of palms or soles, edema of hands or feet (acute phase), and periungual desquamation (convalescent phase)
  - Polymorphous rash
  - Cervical lymphadenopathy (at least 1 lymph node >1.5 cm in diameter)
  - *** If ≥4 of the above criteria are present, a diagnosis of KD can be made on day 4 of illness.**

IN-PATIENT UNIT

Center for Quality & Innovation

Early Identification and Timely Management of Pediatric Sepsis

Electronic alert/Automatic Page to Charge /or Clinical Coordinator

SIRS definition: Temperature >38.5°C or < 36°C and/or abnormal WBC *AND* abnormal HR and/or abnormal RR for age (see table below).

Or > 10% Immature Neutrophils

Age Group	Heart rate (beats/min)		Respiratory rate (breaths/min)	Systolic Blood Pressure mm/Hg	WBC x 1000/mm³		
	Tachycardia	Bradycardia					
0 to 1 wk	> 180	< 100	> 50	< 65	> 34	or	< 5
1 wk to 1 mo	> 180	< 100	> 40	< 75	> 19.5	or	< 5
1 mo to 1 yr	> 180	< 90	> 34	< 100	> 17.5	or	< 5
1 - 5 yrs	> 140	N/A	> 22	< 94	> 15.5	or	< 6
6 - 12 yrs	> 130	N/A	> 18	< 105	> 13.5	or	< 4.5
13 - 18 yrs	> 110	N/A	> 14	< 117	> 11.5	or	< 4.5

Score PEWS - Add 1 to PEWS if: Nursing concern OR Parental concern OR Pre-disposing conditions (immune-compromised)

Sepsis > Severe Sepsis > Septic Shock > Multiple Organ Failure

- **Sepsis** — The systemic inflammatory response syndrome in the presence of suspected or proven infection constitutes sepsis
- **Severe sepsis** – Sepsis is considered severe when it is associated with cardiovascular dysfunction*, acute respiratory distress syndrome (ARDS), or dysfunction in two or more other organ systems.
- **Septic shock** – Septic shock refers to sepsis with cardiovascular dysfunction* that persists despite the administration of ≥40 mL/kg of isotonic fluid in one hour.

**Hypotension, or reliance on a vasoactive drug to maintain blood pressure, or two of the following: metabolic acidosis, elevated arterial lactate, oliguria, or prolonged capillary refill.*

Back to Learning Objectives

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- Identify SIRS vs sepsis in children

Case #1

- **A 29 day old infant presents with tactile fever and mildly decreased PO. No other symptoms, sick contacts, or recent travels.**
- **Birth hx: born at 39 wks to a 28 y/o G2P2 via vaginal delivery. GBS negative. Hospital course was uncomplicated and was discharged at DOL#2.**
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- **What should be the *initial* steps in management?**

A. Admission, Full Septic Workup

B. Tylenol, Reassurance, PCP F/U

C. Hydrate, Admit for Observation

D. UA/Urine Cx, Blood Cx, Inflammatory marker(s)

E. Viral Studies

What should be the *initial* steps in management?

- **D. UA/Urine Cx, Blood Cx, Inflammatory marker(s)**

Large majority of children with fever w/o localizing signs in the 1-3 month age group likely have a viral syndrome (i.e. RSV/Flu in winter, enterovirus in summer/fall, COVID)

Case #2

- **You are evaluating an 11-month-old girl who has had a temperature up to 102.0°F (38.9°C) for 2 days. She has been slightly fussy without any other symptoms. Her immunizations are up to date. Her home rapid COVID-19 antigen test was negative. She is well-appearing on exam. Which of the following tests is *most* helpful in establishing a diagnosis in this child?**

A. Blood culture
B. Chest radiograph
C. Complete blood count
D. Inflammatory marker(s)
E. Urine analysis and urine culture

Which of the following tests is *most* helpful in establishing a diagnosis in this child?

- **E. Urine analysis and urine culture**

UTI Prevalence: 2.1% to 8.7%

- *Highest in girls < 1 year old*

Citations

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Thank You!

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