

**Pediatric Fever and Sepsis**

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FACEP, FACOEP**



2020 ROCKY MOUNTAIN  
Vail, CO, March 5 - 8, 2020



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***I have no conflicts and nothing to disclose***



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**Pediatric fever**



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## Learning Objectives

- ▶ What is pediatric fever.
- ▶ Fever vs hyperthermia.
- ▶ What is fever phobia.
- ▶ What is fever without a source vs fever of unknown origin.
- ▶ What is SBI and what is IBI.
- ▶ What are the "low risk criteria".
- ▶ Approach to fever in the pediatric population.
- ▶ What is the "step by step" approach.
- ▶ Adult vs pediatric sepsis.
- ▶ Approach to pediatric severe sepsis and septic shock.

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## What we know about fever

- ▶ Fever is among the most common presenting complaints in infants and children.
- ▶ Majority of febrile children will have mild self-resolving viral illness but a minority maybe at risk for a life threatening infection.
- ▶ Fever is a normal physiologic response with a role in fighting infection.
- ▶ Core temperature is subject to variations between and within individuals.

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## Fever in children

There is a large volume of literature with over 14,000 search yields in Pub Med on Pediatric fever but in spite of this there is no unified:

- practice guidelines
- clinical approach
- appropriate work up or
- disposition

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### Physiologic factors affecting body temperature

- Time of day nadir in am and peak late afternoon
- ▶ Level of activity
- ▶ Meals
- ▶ Age
- ▶ These variable prevents a single upper limit of normal
- ▶ For clinical purposes fever is defined as 38 °C or 100.4° F

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### How to measure body temp.

- ▶ Axilla , rectum , mouth , skin and ears all have differences among sites.
- ▶ Rectal temp most accurate for core temp and is recommended by the AAP for children less than four but contraindicated in neutropenic or immunocompromised.
- ▶ Oral temp for children over 5 year of age per AAP.
- ▶ In the United Kingdom the National Institute For Health and Care Excellence (NICE) recommends axilla for under 4 weeks and chemical dot or electronic thermometers others.

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### Fever

- ▶ Fever is present when there is a modification of the hypothalamic set point due to exogenous or endogenous pyrogens.
- ▶ Fever is the most common reason for increase in body temp in children.

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### Fever Pitfalls

- ▶ Bundling: leads to a rise in skin temperature but eventually rectal temp rises. T. Cheng, John Hopkins 1993.
- ▶ Rout of measurement: Tympanic/Axillary measurements do not correlate well with rectal temps. Craig 2000, Jean-Mary 2002.
- ▶ Antipyretics: No correlation between disease etiology/severity and response to antipyretics. Baker 1987 and many others.
- ▶ No Fever on presentation: 6 of 60 infants 0-3 month with bacteremia and meningitis were afebrile in clinic after being febrile at home. Pantell 2004.

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### Hyperthermia

- ▶ Hyperthermia occurs as a failure of thermoregulation due to increased heat absorption , heat production and /or reduced ability to dissipate heat.
- ▶ Hyperthermia does not represent a controlled physiologic response and in contrast to fever may have severe consequences.

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### Hyperthermia

- ▶ Most cases are caused by massive heat exposure.
- Other causes:
- ▶ Excessive fluid loss ( Gastroenteritis, Diabetes ,cystic fibrosis, diuretics ).
- ▶ Suboptimal sweating (spina bifida, dysautonomia, ectodermal dysplasia, Fabry's dx.).
- ▶ Neurogenic ( injury to the hypothalamus), status epilepticus.
- ▶ Thyrotoxicosis.

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### Hyperthermia Drug Induced

- ▶ Sympathomimetics (cocaine, Meth, MDMA)
- ▶ Anticholinergics (antihistamines, tricyclics)
- ▶ Serotoninergrics (Serotonin Syndrome)
- ▶ Salicylates
- ▶ Neuroleptic Malignant Syndrome ( antipsychotic meds and antiemetic agents)
- ▶ Malignant hyperthermia ( succinylcholine)

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### Fever phobia

- ▶ Parental misconceptions about fever.
- ▶ First looked at by Schmitt in 1980
- ▶ Again 20 years later by Crocetti
- ▶ Concern over harmful effects of the fever leading to brain damage ,seizures and death if untreated has persisted.
- ▶ More parents listed seizure as a potential harm of fever in the second study.

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### Height of the fever

- ▶ Height of the fever does not define the severity of the illness.
- ▶ But there are some studies that suggest association with higher fever and increased risk of SBI.
- ▶ Study by De. et al 2015 , showed fever over 39°C ( 102.2°F) increases SBI especially in infants under 6 month of age .
- ▶ Study by Trautner et al, Pediatrics 2006, fever over 41°C associated with Significant risk for SBI

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### Height of the fever

- ▶ Fever of concern : Temp of 39°C ( 102.2°F) taken rectally (in a well appearing child) is the threshold for testing in children 3 mo. to 36 mo. of age if no identified source on exam.
- ▶ Fever over 40°C (104°F) called "Hyperpyrexia" rare in infants under 3 mo. but again associated with increase in SBI.
- ▶ Study by Bonadio et al. 1991 of 683 febrile infants 4–8 weeks of age , 4% had fever >40 degree but their rate of SBI was 26%, 51% had fever < 39 degree with rate of 3.2%
- ▶ 38.0°C ( 100.4°F) , 38.5°C (101.3°F), 39°C (102.2°F)

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### Duration of fever

- ▶ Viral infections usually cause fever for 3–4 days. Lasting longer in young infants and children with weak immunity.
- ▶ Association of duration of fever and severity of illness remains inconclusive.
- ▶ Fever for 5 days or longer think Kawasaki Disease .
- ▶ Fever in well appearing children with negative exam < then 7 days "FWS", Fever without a source.
- ▶ Fever > seven days "FUO" ,Fever unknown origin (based on negative initial investigation) .

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### SBI vs IBI

- ▶ SBI (Serious Bactrial Infection) included bacteremia, bacterial meningitis, bacterial pneumonia, soft tissue infection, osteomyelitis, septic arthritis, UTI.
- ▶ Post conjugate vaccine era a terminology shift.
- ▶ Now focus on specific type of infection.
- ▶ IBI ( Invasive Bacterial Infection) refers to bacteremia and meningitis.

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### To Work up or not Work up?

- ▶ Do all febrile children with no obvious site of infection need to be investigated?
- ▶ Specific Question:
  - Blood test
  - Lumbar puncture
  - UA/culture
  - CXR
  - Antibiotics
  - Observation

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### Approach To Fever In Pediatrics.

- ▶ Age
- ▶ Immunization status
- ▶ History
- ▶ Physical

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### Approach To Fever In Pediatrics

- ▶ Age: Immunization status: History: Physical:
  - Birth to 28 days( correct for gestational age).
    - Full septic work up , admit and antibiotics
  - 29 days to 60-90 days
    - Use a low risk prediction rule or national guidelines for risk assessment to guide work up and treatment and disposition
  - 60-90 days to 36month
    - Use immunization status with a structured observation score (i.e. YOS) or your gestalt .
  - Older pediatric patients use history and physical exam.

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## Approach To Pediatric Patients

- ▶ Age: Immunization Status : History: Physical:
  - Prior to the conjugate vaccine era 1990 (for Hib) and 2000( for Prevnar) all infants under 60-90 days had septic work up (+/-) LP.
  - The risk of SBI was 13% in neonates, 9% in 29-56 days, and 7% in infants < 90days.
  - The shifting epidemiology has led to a decline in bacteremia (0.004-2% according to various studies) and a change in the evaluation of fever with decrease in testing.
  - Herd Immunity typically between 85-95%, the herd will protect the other 10-15% but those underimmunized are still at greater risk for SBI.

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## Approach To Fever In Pediatrics.

- ▶ Age: Immunization: History: Physical:
  - Fever at home ( even tactile fever) , onset , duration,
  - History of exposure ( sick contacts),recent antibiotics , antipyretic use, recent travel
  - Previous illness, hospitalization, prematurity, immunocompromised diseases.
  - Mental status change , eating, behavioral pattern, irritability, lethargy, apnea, seizures, rash.
  - Immunization status.

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## Approach To Fever In Pediatrics

- Age: Immunization: History: Physical exam:
- ▶ The “Hands off phase is pivotal” it may give you that intuition that something is wrong.
  - ▶ The Pediatric Assessment Triangle
    - Circulation to skin
    - Work of breathing
    - General appearance

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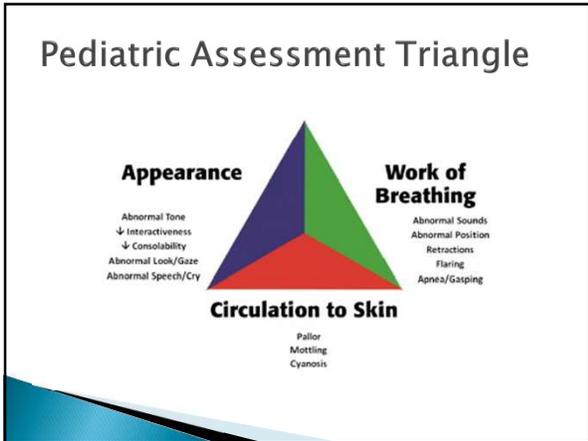
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### Yale Observation Scale 3 month –36month

- ▶ An acute illness observation scale, around for over 30 years.
- ▶ A 3 point scale with six ordinal variables.
- ▶ Total score of 6–30.
- ▶ A validated clinical index of quantifying the risk of serious illness in children 3–36 month with febrile illness.
- ▶ Cut off value of 10 to rule out critical illness.
- ▶ Has a NPV of 100% in children 3mo. To 36 month, Karuna et al, IJSR 2015.

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### Yale Observation Scale

Item	Normal (1)	Moderate (3)	Severe (5)
Cry	Strong/Content	Whimpering/Sobbing	Weak/High Pitched
Reaction to Parents	Brief Cry/Content	Cries on and off	Constant/poor response
State Variation	Awake/Awakens	eyes closed/strong stimulation	Falls asleep / unable to waken
Color	Pink	Pale Extremities/Achrocynosis	Pale, cyanotic, mottled, ashen
Hydration	Normal/moist mouth	Skin normal / dry mouth	Doughy, tented, sunken eyes
Response	Alert	Brief smile	no smile, no alerting

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### Yale Observation Score Limits

- ▶ Pediatrics 2019, Study by the PECARN infant febrile group showed that many febrile infants less  $\leq$  to 60 days of age with IBI( bacteremia and /or bacterial meningitis) had a normal YOS scores.
- ▶ The study reaffirmed what we have known that neither an unstructured clinical suspicion nor the YOS can reliably identify all febrile infants with SBI.

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### Low Risk Criteria Risk Assessment

- ▶ Why we developed them?
- ▶ Why do we still need them ?
- ▶ Traditional criteria.
  - Boston, Milwaukee, Philadelphia, Rochester
- ▶ What is new.
  - Step by step approach
  - Lab Score method
  - PECARN febrile infant and hospital( health system) system approach.

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### Low Risk Criteria:Risk assessment

- ▶ Historical perspective: Developed in an effort to decrease invasive testing ( LPs), avoid antibiotics, avoid hospital admissions, and lower cost. Initially applied to infants younger then 60–90 days.
  - Rochester criteria: Dagan et al. 1985 J.Peds
  - Boston criteria: Baskin et al. 1992 J.Peds.
  - Philadelphia criteria: Baker et al. 1993 NEJM
  - Milwaukee criteria: Bonadio et al. 1993 Clin. Peds

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### Rochester Criteria

- ▶ **Infants:** <60 days
- ▶ **History:**
  - Term Infant
  - not hospitalized longer than mother
  - no underlying dx
  - no prenatal or perinatal antibiotics
  - no unexplained jaundice
- ▶ **PE:** well appearing, no focal infection
- ▶ **Lab:** WBC >5K and <15K, absolute band count <=1.5K ,UA<10 wbc, stool( if diarrhea) < 5wbc
- ▶ **Management:** Home, no antibiotics, PCP in 1d

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### Boston Criteria

- ▶ **Infants:** 28–89 days
- ▶ **History:**
  - No immunization in the past 48hrs
  - No antibiotics in the past 48hrs
  - Not dehydrated
- ▶ **PE:** well appearing , no focal infection.
- ▶ **Lab:** CSF <10wbc, WBC< 20K, UA< 10wbc , X-R (-).
- ▶ **Management:** Home, empiric antibiotics, PCP1d

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### Philadelphia Criteria

- ▶ **Infants:** 29–60 days
- ▶ **History:** not defined
- ▶ **PE:** Well appearing, unremarkable exam
- ▶ **Labs:**
  - CSF < 8wbc
  - WBC<15K
  - UA < 10 wbc, UA gram stain neg.
  - X-R neg.( if obtained)
  - Band to Neutrophil ratio < 0.2
  - Stool ( if indicated) no blood , few or no wbc.
- ▶ **Management:** home, no antibiotics, PCP in 1d.

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### Milwaukee Criteria

- ▶ Infants: 28 to 56 days
- ▶ History: not defined
- ▶ PE: well appearing ,not dehydrated, no focal infection.
- ▶ Labs:
  - CSF < 10wbc
  - WBC <15K
  - UA <5-10 wbc no bacteria, neg. leuk est., neg. nitrates
  - X-R neg.
- ▶ Management: IM ceftriaxone 50 mg/kg IM, PCP 1d

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### Low Risk Assessment Criteria

- ▶ The combined clinical and laboratory criteria (Rochester, Philadelphia, Boston, and Milwaukee) demonstrated similar overall accuracy
  - sensitivity 84.4-100%
  - NPV 93.7-100% for identifying SBI
  - PPV is low 12.3 to 14 %
- ▶ Designed to allow safe discharge at the expense of specificity and are still the basis of standard for care in many institutions.

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### Newer Criteria

- ▶ Lab-Score: Moldavan et al: 2015 JCCM
- ▶ Step-By-Step Approach: 2016 Pediatrics
- ▶ PECARN (Pediatric Emergency Care and Applied Research Network) Febrile Infant Rule: Kupperman et al JAMA 2019

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### Lab Score

- ▶ Infants with FWS
  - ▶ Using a score that combines CRP, PTC and urine dip stick.
- |            |                |                |
|------------|----------------|----------------|
|            | <u>2points</u> | <u>4points</u> |
| <u>PTC</u> | >0.5ng/ml      | >2.0 ng/ml     |
| <u>CRP</u> | >40mg/ml       | >100 mg/ml     |
| <u>UA</u>  | Positive 1 pt  |                |
- ▶ Sensitivity 59.8% and NPV 98.1. (= or >3 high risk)

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### Step by Step Approach

- ▶ Developed by a European group of Peds ER Physicians.
- ▶ Risk stratification of Infants between 21–90 days with FWS.
- ▶ PE:
  - Well appearing
  - Normal Pediatric Assessment Triangle
    - Work of breathing , Circulation, Appearance
- ▶ Lab: UA neg., PCT <0.5, CRP<20, ANC <10K
- ▶ Sensitivity 92%, NPV 99.3%.
- ▶ Caution in fever less then 2 hrs and infants 21–28 days.

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### PECARN Febrile Infant Rule

- ▶ Infants : 29–60 days ( JAMA 2019)
- ▶ History:
  - Full Term
  - No antibiotics in past 48hrs
  - no pre-existing medical condition
- ▶ PE : Well appearing , no indwelling devices, no soft tissue infection( otitis not excluded).
- ▶ Lab:
  - Negative UA( <5 wbc,neg leuk.est, neg Nitrite)
  - ANC <4,090/ml
  - PCT< 1.71 ng/ml
- ▶ Sensitivity 98.8%, Specificity 63.1% ,99.8% NPV.

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Children’s Hospital of Colorado  
Clinical Pathway Fever Infants < 60 days

Initial evaluation OF FWS

- ▶ Maternal history : intra-partum fever, antibiotics use, group B-strep infection
- ▶ Infant history : Prior antibiotics, hospitalized longer then mother, unexplained jaundice, prematurity(<37 weeks), temp greater than 38.5° C, no underlying illness.
- ▶ PE: Well appearing and no suspicion of SBI, weight over weight over 2,000gms.

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Children’s Hospital of Colorado

Infants: 60 days or younger

- ▶ <=28 days: admit , full septic work up +/- ATB.
- ▶ Clinical Bronchiolitis: UA and urine culture, consider Flu PCR, CBC, Blood culture.
- ▶ PCT available Yes: PCT, UA and culture ,CBC, blood culture X 2 ( consider HSV if at risk).
- ▶ PTC No: UA and culture, CBC, Blood culture X 2.
- ▶ Consider LP( CSF), consider HSV if high risk).

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Children’s Hospital of Colorado

High Risk Criteria for SBI:

- ▶ <=28 days
- ▶ PCT >0.3ng/ml
- ▶ WBC <5Kor >15K
- ▶ ABC=> 1.5K
- ▶ CSF + Gram stain, >9 wbc
- ▶ High risk for HSV

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## Children's Hospital Of Colorado

### High Risk Criteria for HSV:

- ▶ CSF Pleocytosis with ( - )Gram stain.
  - 1-28 days old > 18 wbc
  - 29-60 days old > 9 wbc
- ▶ Seizures, Altered Mental Status, Exposure to HSV lesions, skin vesicles, elevated ALT.
- ▶ Leukopenia, Hypothermia , ill appearance
- ▶ Higher risk for infants < 21 days.

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## UpToDate

Last updated: Nov. 15<sup>th</sup> 2019

### Do a Full Sepsis Work Up, Admit and Empiric Antibiotics :

- ▶ For all Infants with Rectal temp of 38C who are :
  - ill appearing infants
  - <= 28 days
  - any infant suggestive of HSV
- ▶ Any Infant younger then 60 days (corrected for prematurity) with:
  - Rectal temp greater then 38.5C
  - Congenital or chromosomal defect
  - Technology dependent
  - Antibiotics in the past 3-7 days

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## UpToDate

- ▶ Infants 29 to 90 days with a focal infection with:
  - ill appearance
  - abnormal white count
  - abnormal ABC
  - elevate PCT or CRP
  - get a full work up with some experts recommending including an LP.
- ▶ Infants 29 to 90 days who are well appearing with no focal infection with rectal temp > 38.6°C obtain:
  - CBC with diff, PCT and CRP( if available w/in 1 hr.)
  - Blood culture, UA, urine culture via cath
  - chest x-ray if respiratory symptoms.
  - LP if any of the following : CBC <5K or >15K, ABC>1.5K  
PCT>0.5, CRP>20, abn chest x-ray

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### UpToDate

- ▶ Well appearing infants 29–90 days with recognizable viral infection :
  - Same evaluation without blood and LP
- ▶ Well appearing infants 61–90 days :
  - with temp  $\leq$  to 38.6°C: UA and culture only.
- ▶ Some experts advise CBC and Blood culture if they have not received their first conjugated vaccine.

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### UpToDate

- ▶ Well appearing 3–36 month of age with fever  $\geq 39^{\circ}\text{C}$  with no underlying medical condition. Approach is based on Immunization.
- ▶ Fully immunized with fever: no blood work, consider urine testing if at risk.
- ▶ Unimmunized or incomplete Immunization:
  - PCT( if available <1 hr), CBC with diff, ABC, Urine testing. Send Blood culture if testing positive. Re-evaluate at 24 and 48hrs.

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### Risk Assessment For UTI

- ▶ Based on a large study by Gorlich et al. Archives of Pediatrics and Adolescent Medicine:
  - Absence of other infection
  - Temp  $> 39^{\circ}\text{C}$
  - Fever => then 2 days
  - White Race
  - Younger than age 1
- ▶ Presence of 2 or more in girls 95% sensitivity for UTI

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### Risk Assessment for UTI

- ▶ For boys:
  - Age under 6 month
  - Uncircumcised
  - Absence of another potential source
- ▶ All boys with a UTI had at least one of the above

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### UTI

- ▶ An estimated 75% of children under age 5 with UTI have upper tract infection (pyelonephritis) .
- ▶ Resulting in renal scarring in 27% to 64% which can lead to HTN and ESRDx.

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### Older children

History and Physical exam:

- ▶ Routine use of CBC and blood culture to screen for bacteremia in immunocompetent child not recommended .CBC low PPV for bacteremia
  - Bacteremia rates are <1% in post vaccine era
  - Bacteremia spont. Resolution >90% (-ATB)
  - High false positive blood culture
  - Costly and invasive.

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## Leukocytosis

- ▶ Bacterial Infections are more likely than viral infections to have leukocyte count over 15,000.
- ▶ Viral infections are much more common than bacterial infections.
- ▶ The majority of febrile children with elevated white counts will have viral infections.

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## Chest X-ray

- ▶ An unexplained and persistent fever can be the only manifestation of pneumonia. When faced with a persistent high fever and a WBC count of  $>20,000$  think Pneumonia.
- ▶ Up to 26% of children under 5yrs of age with unexplained fever of  $39^{\circ}\text{C}$  and WBC count  $\geq 20,000$  with no respiratory symptoms may have pneumonia.
- ▶ In the absence of respiratory symptoms chest X-rays are usually negative.

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## UTI

- ▶ Children with repeat bouts of fever suspect urinary tract infection.
- ▶ The diagnosis of a UTI must be confirmed by a culture.
- ▶ Febrile infants under 3 month should be catheterized or have a bladder tap.
- ▶ Older children who have a positive urine analysis by bag specimen should be catheterized for culture.

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### Empiric Antibiotics

- ▶ May reduce the number of serious bacterial complication.
- ▶ It does not prevent meningitis.
- ▶ Oral antibiotics may delay the diagnosis of meningitis.

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### What is new on the Horizon

- ▶ New advances in biomarkers: IL-27, Neutrophil CD-64, Prepepsin, cf DNA, miRNA, suPAR ect.
- ▶ Genomic approach: Bacteria and viral infections induce specific host response which can be analyzed and differentiate viral from bacterial infections. Some 66 + classifier genes classified.
- ▶ New syndromic molecular testing: cable of rapid diagnosis of systemic infections utilizing multiplex real-time polymerase chain reaction test ,mPCR.

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### Common Pitfalls

- ▶ Failure to recognize hypothermia ( SBI )
- ▶ Failure to perform LP if indicated
- ▶ Failure to get a vaccination history
- ▶ Failure to consider a fever at home
- ▶ Failure to get work up because fever resolved with antipyretics
- ▶ Failure to consider a second site of infection
- ▶ Failure to get a blood culture when getting a CBC

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## Pediatric Sepsis

- ▶ Sepsis is about 10 times less common in pediatric patients than adults but is not rare.
- ▶ Estimated 72-89 cases per 100,000 pediatric population in the US.
- ▶ Estimated 50,000 -75,000 hospitalizations for pediatric sepsis annually.
- ▶ Mortality is 4-11% for pediatric sepsis, median age is 3.

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## Making The News

Image of BBC news coverage on 2 July 2014  
"Death of Sam Morrish 'absolutely shocking'"

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## Time



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### Defining Pediatric Sepsis

- ▶ 2005 The International Pediatric Consensus conference published definition for pediatric sepsis, severe sepsis and septic shock.
- ▶ The framework was based on the prevailing view of adult sepsis at the time and modified using age based physiology.
- ▶ Definition of sepsis is systemic inflammatory response syndrome due to infection (pSIRS).

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### DEFINITIONS

#### SIRS

- Requires 2 of the following 4 features to be present:
  - Temperature → >38.5° or <36.0° C
  - Tachypnea → >2SD ABOVE NORMAL FOR AGE
  - Tachycardia → >2SD ABOVE NORMAL FOR AGE
  - WBC → ELEVATED OR DEPRESSED FOR AGE/>10% IMMATURE NEUTROPHILS

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### Defining Pediatric Sepsis

- ▶ At the 2016 the Third International Consensus Definition for Sepsis and Septic Shock Taskforce (Sepsis -3).
- ▶ Sepsis was re-defined as a concept of "life threatening organ dysfunction caused by a dysregulated host response to infection."
- ▶ The concept of septic shock incorporates profound circulatory, cellular and metabolic abnormalities with an increase in mortality.
- ▶ The Definition was derived and validated in adult cohort only.

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## SOFA SCORE

### THE SEQUENTIAL ORGAN FAILURE ASSESSMENT (SOFA) SCORE

SYSTEM	0	1	2	3	4
<b>Respiration</b> PaO <sub>2</sub> /FiO <sub>2</sub> mm Hg (kPa)	≥400 (53.3)	<400 (53.3)	<300 (40)	<200 (26.7) with respiratory support	<100 (13.3) with respiratory support
<b>Coagulation</b> Platelets ×10 <sup>9</sup> /L	≥150	<150	<100	<50	<20
<b>Liver</b> Bilirubin mg/dL (μmol/L)	<1.2 (20)	1.2-1.9 (20-32)	2.0-5.9 (33-101)	6.0-11.9 (102-204)	>12.0 (204)
<b>Cardiovascular</b>	MAP ≥70mmHg	MAP <70mmHg	Dopamine <5 or Dobutamine (any dose)	Dopamine 5.1 - 15 or Epinephrine ≤ 0.1 or Norepinephrine ≤ 0.1	Dopamine >15 or Epinephrine >0.1 or Norepinephrine >0.1
<b>CNS</b> GCS Score	15	13-14	10-12	6-9	≤5
<b>Renal</b> Creatinine, mg/dL (μmol/L)	<1.2 (110)	1.2-1.9 (110-170)	2.0-3.4 (171-299)	3.5-4.9 (300-440)	>5.0 (440)
<b>Urine Output, mL/d</b>				<500	<200

Catecholamine Doses = μg/kg/min for at least 1hr

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## Quick SOFA

qSOFA	
RR > 22bpm	0 = Mortality < 1%
sBP < 100mmHg	1 = Mortality 2-3%
Altered GCS	≥2 = Mortality ≥10%
Screening for outcome rather than diagnosis	

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## Defining Pediatric Sepsis

- ▶ Currently there is no definition of pediatric sepsis that is harmonized with Sepsis-3 which is based on the patient's Sequential Organ Failure Assessment (SOFA) Score .
- ▶ This shortcoming was recognized by the 2016 Taskforce .
- ▶ In 2017 update the American College of Critical Care Medicine defined pediatric septic shock as hypothermia or hyperthermia plus clinical signs of inadequate tissue perfusion.

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## Understanding Pediatric Sepsis

- ▶ Dr L.Schlapbach ( an Australian leading researcher):
  - "We should abandon the old view of sepsis disease progression which proposes progression from infection to SIRS to severe sepsis to septic shock because most children with Infection do manifest signs of SIRS."
  - "The tachycardia , tachypnea and the fever should be considered more adaptive then maladaptive response."
  - "The goal of the pediatric sepsis redefinition project is to come up with something more useful then the Sepsis -3 definition."
- ▶ SIRS lacks the specificity for recognizing early sepsis in children.

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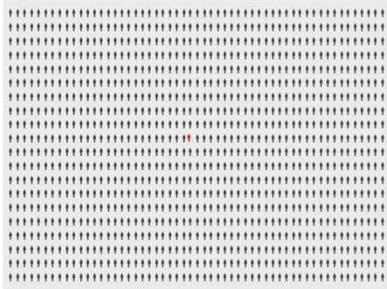
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## Recognizing Sepsis



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## Recognizing Sepsis



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### ACCM Recommendation

- ▶ The American College of Critical Care Medicine recommendation for treatment of severe sepsis and septic shock:
  - Sampling of blood cultures , appropriate antibiotics, fluid boluses of up to 60cc/kg followed by inotropic support if not fluid responsive . All within 1 hr ( ideally in 15 minutes) in children with septic shock.
  - A corner stone of treatment for septic shock is fluid resuscitation , but IS there a potential for harm related to large volume resuscitation?

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### Fluid Therapy In Sepsis

- ▶ In 2008 Santhanam et al. found no difference in mortality or resolution of shock comparing:
  - 147 children with septic shock using 40cc/kg over 15 minutes followed by dopamine vs.
  - 20cc/kg over 20 minutes up to 60cc/kg /hr followed by dopamine.

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### Fluid Expansion As Support Therapy FEAST

- ▶ The landmark (FEAST) clinical trial demonstrated that fluid boluses significantly increased 48hr mortality in acutely ill children with impaired perfusion in the resource limited setting in South Saharan Africa.
- ▶ A re-analysis of the study found that cardiovascular collapse from cardiotoxicity or ischemia-reperfusion injury accounted for the increase in motality.
- ▶ 2018 Pilot study (RIFTS) Restrictive Intravenous Fluid Trial in Sepsis showed no increase in mortality limiting fluids to 60ml/kg in the 1<sup>st</sup> 72 hrs.
- ▶ (Clovers) Crystalloid Liberal or Vasopressors Early Resuscitation in Sepsis is currently on going.

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## UpToDate

- ▶ The ideal goal of initial Resuscitation of severe sepsis and septic shock:
  - Early recognition
  - IV or IO access within 5 minutes( 2 lines)
  - Fluid resuscitation within 30 minutes
  - Antibiotics within 60 minutes
  - For fluid-refractory shock start inotropic support ideally in 60 minutes
- ▶ Not always achievable depending on resources.

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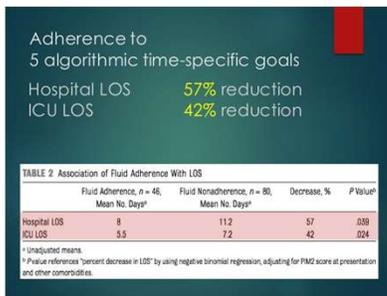
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## Mortality Reduction




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## UpToDate

- ▶ All patients in septic shock should receive 100% supplemental Oxygen initially, then titrate to avoid >97%.
- ▶ RSI intubation if needed using Ketamine if not contraindicated. Avoid Etomidate if possible. Use pressure support and use atropine in infants to avoid bradycardia.
- ▶ Fluid resuscitation using balanced crystalloids initially 20cc/kg over 5minutes ( push), alter if signs of CHF or volume overload . Repeat as needed.

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### UpToDate

- ▶ Fluid-refractory patients ( within 1<sup>st</sup> hr) should receive vasoactive therapy tailored to blood pressure and manifestations of septic shock.
- ▶ Initial agent is low dose epinephrine 0.05-0.1mcg/kg/minute up to 1.5mcg/kg/minute rather than dopamine.
- ▶ Pt with persistent shock should receive stress dose hydrocortisone 2-4mg/kg/day.
- ▶ Pt with persistent shock look for unrecognized causes .

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### UpToDate

- ▶ Treat hypoglycemia and or hypocalcemia since children in septic shock are at risk.
  - Hypoglycemia : treat with rapid infusion of dextrose and maintain level at 70-150.
  - Ionized calcium < 1.1mmol/l ( 4.8mg/dl) should receive calcium gluconate 10% solution 50-100mg/kg up to 2 grams.

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### Pitfalls

- ▶ Failure to recognize sepsis: the physical exam of the septic child may be as subtle as isolated tachycardia or as flagrant as hypotension or poor perfusion with altered mental status .
- ▶ Failure to follow the 1 hr sepsis bundle with rapid fluid resuscitation, timely antibiotics and use of vasoactive drugs in refractory shock.
- ▶ Failure to recognize hypoglycemia or hypocalcemia.
- ▶ Failure to look for alternate etiology for the hypotension .
- ▶ Failure to undergo timely transfer to PICU using a pediatric specialized transport team .

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## Questions?

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