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درود

The Febrile Child And FWF / 2024

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Fever

- **One of the most common reason for office visit & hospitalization of children**
- Nearly 1/3 of pediatric outpatient visits are for fever
- 24.8% of office visits to E.S. 2022-23 - > 40% Febrile

  Lowest (17.5%) April – May (Ordibehesht) & Sept-Oct (Mehr)

  Highest (35%) Nov.-Dec. (Azar)

FWS, FWLS, FWF

- ✓ When the Hx & PE cannot identify a specific source of fever in an acutely ill, nontoxic-appearing child, <3 yrs of age, the illness is often called : Fever without a source (FWS) , Fever without localizing signs (FWLS) , or Fever without a focus (FWF)

Definition :

- ✓ Documented fever ≥ 38.4C ° [101 F°]
- ✓ Fever of ≤10 days duration
- ✓ Patient does not appear seriously ill (nontoxic)
- ✓ No abnormalities on PE (No specific source of fever)
- ✓ Normal urinalysis & -ve U/C

- ✓ Consider risk of OB in those < 2 yr old
- ✓ Infants < 3 mo old are excluded from these categories

Fever of concern

- In children 3-36 months of age, the Dx of fever is based upon core temperature, which is measured most accurately rectally, or tympanic thermometry.

- Fever 39°C (102.2 F) or higher is the threshold above which evaluation for a source of occult infection, including UTI, may be warranted
- specificinfections diseases:

  Occult bacteremia (OB), Pneumonia , & Meningitis.

Fever

- ✓The majority of children with fever have either self – limited febrile illness (SLFI) or Self-Limited Viral Infection (SLVI),
- ✓Or a recognizable source of bacterial infection.

Occult bacteremia, pneumonia & meningitis

Hib vaccine & pneumococcal vaccine has dramatically lowered the incidence of occult bacteremia and, as a result, changed the issues facing the clinician who is evaluating a young child with fever.

Clinical course

1. **Development of new signs**

   a. viral exanthem, such as Roseola infantum

   b. working Dx of FWNSS (Fever with nonspecific signs)

   hepatosplenomegaly, abd. Mass, are Present but not diagnostic .

2. **Persistence of fever**

   Fever persists for > 10 days;

   The working Dx of prolonged unexplained fever (PUF),

   Persistent perplexing pyrexia (PPP) or

   Fever of unknown origen (FUO)

3. **Complete, uneventful recovery (retrospective Dx)**

   Self limited febrile illness (SLFI) - SLVI (70%)

   Specific infectious disease (30%)

   UTI must reliably excluded

   No antibiotics should not have been used

Causes of fever I

Infectious or noninfectious processes

- The vast majority of young children with fever have an infectious etiology
- Non infectious etiologies include:

Drug fever, immunization reactions, CNS dysfunction, malignancy (eg. leukemia) & chronic inflammatory conditions (IBD & JIA)

causes of fever II

common viruses

a. (H HV) – 6 and (HHV) – 7

characteristic Rash – 20%

b. coxsachieviruses & echoviruses, para influenza, Adenovirus

and influenza.

causes of fever III

Bacteria

Earinfections, strep.

Pharyngitis,

Pneumococcal bacteremia

(can be self – limited)

Fever & Pneumonia

- ✓ Usually have some abnormalities on PE tachypnea, abnormal auscultation, or nasal flaring.
- ✓ 20- 30% of highly febrile young children (< 5yr) without clinical evidence of pneumonia, have WBC count of ≥ 20.000/ mm^3
- ✓ In one study 41% of children 3-36 mos of age with WBC > 25.000 had lobar or segmental pneumonia on chest xray.
- ✓ Strong association between leukocytosis & pneumonia even in the post-conjugate pneumococcal vaccine era .

Febrile infant & young children and UTI

- ✓ The prevalence of UTI is significantly influenced by sex, Age, race & circumcision status.
- ✓ Highest among grils & warrants U/A & U/C in all females age 3-24 mos with fever ≥ 39°c and no source.
- ✓ The risk of UTI is increased in uncircumcised compared with circumcised male infants with fever, with the greatest incidence in infants younger than 3 mos of age .
- ✓ in over 6 mos of age circumcised boys, the incidence of UTI is low.

Table 1. Cumulative Data of febrile children 2015- 21

Total children reterred	**14240**
Follow up, check up	4525(31.8)
Illness **Febrile**	9715 (68.2) 3780(38.9)
FWF	210(5.5)

Seasonal distribution of childhood diseases 2015-16 NO (%)

Spring	Summer	Fall	Winter	Year around
Total disease 920	847	1179	1228	4174
URT 607(66)	356(42)	674(57)	758(62)	2395(573)
Non URT 313 (34)	491(58)	505(43)	470(38)	1779(42.6)
Total febrile Diseases 346	**229**	**416**	**436**	**1427(34.1)**
URI 291 (84)	161(70.3)	354(85)	406(93)	1212(85)
Non URI 55(16)	68(29.6)	62(15)	30(7)	215(15)

Children presented with febrile diseases

	Spring	Summer	fall	winter	Year total
total febrile	338	208	396	401	1344
Total febrile disease	346	229	416	436	1427
URI	291(86)	161(70.3)	354(85)	406(93.1)	1212(85)
Non- URI	55(16.2)	68(29.6)	62(15)	30(6.8)	215(15)
Febrile URI **Warm seasons**	**452 (37.2)**		**Cold seasons 760 (62.7)**		

Febrile URI in children 2015-16 NO (%)

PURULENT Rhinitis	650(53.6)
Rhinitis	313(25.8)
Otitis media	60(4.9)
Tonsillitis pharyngitis	46(3.8)
Purulent RCS	40(3.3)
Sinusitis	29(2.4)
Nasopharyngitis	12(0.9)
Vincent infec . 9 hand- food – mouth 9	
Gingivostomatitis 9 , Herpangina 5. ,	
Bronchitis complex 6 , croup 4	
Cervical LAP 10, Pneumonia 6 ,	
FLU- Like ill .2 conjunctivitis 2.	
Total URI	1212

Table 1. Cumulative Data of febrile and FWF children 2015- 2021No. (%)

Total children reterred	**23775**
Follow up, check up	7450
Illness	16325 (68.6)
Febrile	6245 (38.2)
FWF	384 (6.1)

Table 2. Sex & Age distribution of children with FWF 2015- 2021 No. (%)

M=133 (49.2) F= 137(50.7) M:F = 0.9 -1	
Age distribution	
≤ 6 mos.	43 (11.1)
6-12 mos.	54 (14)
12-24 mos	96 (25)
Infancy (0-2yr)	193 (50.2)
Preschool (2-5yr)	135 (35.1)
School (5-15 yr)	56 (14.5)
Total:	384 (100)

Table 3. Seasonal distribution of FWF Cumulative cases – 2015- 21 No (%)

Spring 100 (26) Summer 142 (36.9) Fall 86 (22.3) Winter 56 (14.5)	Spring + summer (warm season) Fall +Winter (Cold season)	242 (63) 142 (37)
	Spring + summer+ Fall	328 (85.4)
Total: 384 (100)		

Table 4. Final Dx of FWF No (%)

SLFI	269 (70.0)
Roseola	36 (9.3)
Pharyngitis (GABHS 9. BHS not A 3)	16 (4.1)
Viral Gastroenteritis	16 (4.1)
Rhinitis, Nasopharyngitis / Rhinitis conjunctivitis, Giongivo sttomatti vincent infection & hand – foot and mouth disease and purulent Rhinitis	16 (4.1)
UTI	8 (2.0)
Covid 19	6 (1.5)
Sinusitis	2 (0 .5)
Otitis media, leukemia, Treated sepsis, occult bacteremia (OB), Hyper lgE synd. Recument fever, drug rash each 1.7 (2.3), croup, dental abscess , teething fever, typhoid fever, septic arthritis, R/ O each 1-3 (3.3) purul. Rhinitis 4(1)	

Table 2. Cumulative data of children With FWF- 2015- 2021 No. (%)

M=103 (49) F= 107(51) M:F = 0.9 -1	
Age distribution	
≤ 6 mos.	20 (9.5)
6-12 mos.	36(17.1)
12-24 mos	49 (23.4)
Infancy (0-2yr)	105 (50)
Preschool (2-5yr)	73 (34.7)
School (5-15 yr)	32(15.2)
Total:	210

Table 3. Seasonal distribution of FWF Cumulative cases – 2015- 21 No (%)

Spring 61 (29) Summer 60(28.5) Fall 57 (27) Winter 32 (15.2)	Spring + summer (warm season)	121 (57.6)
	Fall +Winter	89 (42.3)
	(Cold season)	
	Spring + summer+ Fall	178(84.7)
Total: 210 (100)		

Table 4. Final Dx of FWF No (%)

SLFI	**154 (73.7)**
Roseola	18 (8.5)
GABHS Pharyngitis	7+1 = 8 (3.8)
(+1 BHS not A)	
Rhinitis, Nasopharyngitis / Rhinitis conjunctivitis	9 (4.3)
Virol GE	8 (3.8)
UTI	5 (2.3)
Sinusitis	2 (0.9)
Otitis media, Vincent, Hand- Foot & mouth disease, leukemia,Treated sepsis, occult bacteremia (OB) each 1.(7)	

Serious bacterial infectious synd.
(in children 3-36 mos)

- ✓Meningitis, Pneumonia, & Cellulitis
- ✓(Prior to the introduction of Hib & pneumococcal conjugate vaccine); of 996 febrile children < 36 mos of age
- <1% had meningitis
- 10% had focal soft tissue infections
- 30% had pneumonia

Occult sources of infection

The goal of the evaluation of a young child with fever is:

to identify sources of infection that require further evaluation & definitive Rx

Such infections are usually bacterial

- Although the majority of children who are well-appearing and have no identifiable source of infection have a nonspecific SLVI

Pneumonia

- Most children with fever & pneumonia have some abnormality on PE, usually

  Tachypnea, abnormal auscultation, or nasal flaring suggesting RT disease. A reliable PE can be a challenge

- **Radiographic pneumonia**
  - 20-30% of highly febrile young children (<5 yrs) without clinical evidence of pneumonia, but with WBC count of ≥ 20.000/mm^3
  - 41% of children 3-36 mos of age with WBC > 25000/mm^3 had lobar or segmental pneumonia on chest X-ray

  Strong association between leukocytosis & pneumonia even in the post-conjugate pneumococcal vaccine era

UTI

- The most common site of bacterial infection among febrile infants & young children
- The prevalence of UTI is significantly influenced by:

  sex, age, race, and circumcision status

- The prevalence of UTI is highest among girls & warrants U/A & U/C in all females age 3-24 mos with fever ≥ 39°C (10.2.2 F) and no source

UTI in febrile boys

- Increased in uncircumcised compared with circumcised male infants with fever, with the greatest incidence in infants younger than 3 mos of age
- Over 6 mos of age circumcised boys, the incidence of UTI is low.

  Do not routinely obtain a catheterized urine specimen for culture

Highly febrile boys

Temp ≥39°C or 102.2°F

- 3-24 months of age
- With no source of infection

The probability of UTI is 10-25% in uncircumcised and 2-4% in circumcised

The higher prevalence is found in younger boys

Bladder catheterization is a painful invasive procedure, that prefer to avoid if the probability of UTI is < 5%.

Evaluation for UTI

- Uncircumcised males ≤ 12 mos & circumcised males ≤ 6 mos
- High fever (≥ 39°C or 102.2°F) without a source is sufficient justification for urine studies on the 1st visit in all highly febrile boys between the age of 3 and 24 mos

Bacteremia

- Bacteremia that occurs in a seriously ill patient with a focal infection, such as meningitis, septic arthritis, or Cellulitis, is usually readily identified
- The risk of sepsis in a child who is ill-appearing, febrile, and without obvious source is also apparent

Occult Bacteremia (OB)

- Before routine immunization with Hib and either PCV7 or PCV13, The prevalence of OB was 5% in well-appearing febrile children
- The predominant pathogens were

S. Pneumonia	80%
Hib	20%
N. Meningitidis	Small No. of cases

Factors associated with an increased the risk of OB in unimmunized children to over 10% included:

- ✓Age 3-36 mos
- ✓Fever ≥ 39°C
- ✓WBC ≥15000/micro L

Neither response to antipyretics nor clinical appearance predicted bacteremia

Some children with bacteremia went on to have serious bacterial infection (SBI) including meningitis.

When children at risk for bacteremia were treated empirically with antibiotics until the results of B/C were known, they were less likely to develop these complications.

Evaluation

The young well-appearing, febrile child without an apparent source of infection

1. To identify a subtle bacterial infection and /or
2. The risk of a more serious occult bacterial infection,

Both of which require further investigation & antibiotic Rx

Historical feature

- May be subtle & not immediately obvious
- Although Hx must include information about the child's functional status including
  - Oral intake
  - Presence of irritability or lethargy
  - And associated symptoms

<u>The duration of fever appears to be a poor predictor of unsuspected bacteremia</u>

Specific question regarding cough, vomiting, or change in activity

Cough & tachypnea: Pneumonia

- Signs or symptoms of UTI:
  - Dysuria, frequency, abd. Pain, back pain & new onset incontinence, should be specifically sought
  - Vomiting with or without diarrhea, can occur in young children with UTI
  - Foul-smelling urine

A young child with a deep soft tissue or bone infection may protect the affected area

- A careful hx must identify any known underlying medical conditions that increases the child's risk for serious infection, such as
  - Sickle cell disease
  - Urinary tract reflux
- The immunization history-incomplete or complete

Physical examination

The child who is being evaluated for a subtle infection or fever without a source should be: **well appearing**

- Acutely ill with symptoms such as:

  Lethargy, poor perfusion, hypoventilation or hyperventilation & cyanosis:

  Appear **toxic** or **septic**

Such an ill child is considered to have a significant bacterial infection unless proven otherwise:

B/C, U/C, CSF culture when meningitis is suspected.

IV fluid, antibiotic Rx & admission to the hospital

Clues to identification of a source of infection

- Abnormal vital signs
- Tachycardia, tachypnea, or pulse oxymetry ≤95%
- Lesions in oropharynx

  Herpetic gingivostomatitis

  Coxsackie virus (pharyngeal vesicles)
- Increased work of breathing indicated by:

  Nasal flaring, retractions or use of accessory muscle, or focal lung findings (Rales or ↓BS)
- Pain with bone palpation or passive joint ROM, skin finding (petechiae, Cellulitis or viral exanthem)

Lab testing

- Screen for the risk of bacterial infection

  To Dx specific infection

- Age, immunization status & obvious findings of infection (OM, bronchiolitis, croup)
- WBC & ANC counts

✓Increased risk of occult pneumococcal bacteremia among unimmunized children with WBC ≥ 15.000/μL & ANC ≥ 10.000/μL

1911 children, 3-36 mos of age with fever ≥ 39°C WBC ≥ 15.000, sensitivity 86% & specificity 77% for occult bacteremia (after the introduction of Hib vaccine)

The frequency of bacteremia in these patients was 1.5%

- Multicenter study 6579 children

  WBC ≥ 15.000, sensitivity 80% specificity 69% For occult bacteremia

  ANC ≥ 10.000, sensitivity 76% specificity 78%

  The frequency of bacteremia 2.5%

A WBC > 15.000/microL

- While not ideal in screening for OB,

  it is helpful in determining which incompletely Immunized children deserve B/C & Rx in the post-conjugate vaccine era.
- An elevated WBC, by itself, has both limited sensitivity and specificity as an indicator of SBI, particularly as other pathogens, such as S. aureus become more prominent isolate in children with bacteremia

Cultures

Blood culture

Continuously monitored blood culture systems have decreased the length of time for a blood culture to turn +ve

The mean time to +ve B/C for pathogens is approximately 15 hrs, compared with 31 hrs for contaminants

Urine culture

- For the diapered child,

  Urine for culture should be collected by catheterization,

  Or in exceptional cases (Tight phimosis), suprapubic aspiration

  Bag specimens should not be sent for culture because they are frequently contaminated

  A clean catch is the preferred method of urine collection for culture in the child who is toilet-trained

CSF

- Children who are being evaluated for FWS should be well-appearing and therefore, not require LP.
- CSF should be obtained from any patient with suspected meningitis

Chest X-ray

Should be obtained in pts with

- Tachypnea, RD or oxygen saturation ≤95%
- WBC> 20.000/μL even in the absence of these findings

Inflammatory mediators

- Elevations in levels of inflammatory mediators (CRP & procalcitonin) may be better markers of SBI than WBC & ANC in children of significant risk for SBI, although usefulness in practice is uncertain

CRP

- An AFR released by the liver following inflammation or tissue damage
- Screening tool for OB infection

  wide range of sensitivity & specificity
- Generally do not increase until 12 hrs after the onset of fever & can rise in both viral & bacterial infections

Procalcitonin (PCT)

- Levels rise in response to bacterial infections more rapidly than those of CRP
- PCT levels may be more sensitive & specific markers for severe invasive bacterial infection in infants and children than WBC, ANC & CRP
- In most clinical settings, PCT has limited availability

A meta-analysis of 5 studies (1379 febrile children up to 36 mos of age, including infants younger than 3 mos):

Found that the diagnostic accuracy of CRP & procalcitonin were comparable for SBI

✓**The optimal values for identifying a high-risk of serious infection were;**

- ≥ 80 mg/dl for CRP
- 2 ηg/ml for procalcitonin
- Sensitivity 40-50%, specificity 90% fore each

CRP & PCT

The best values suggesting a low risk for serious infection;

- < 20 mg/dl for CRP
- < 0.5 mg/dl for procalcitonin

Sensitivity >80%, specificity 70% for both

Approach to evaluation

1. CBC with diff.
2. B/C should be obtained if the WBC is ≥15.000/μL – B/C drawn with CBC & sent if the WBC is ≥ 15.000

   (May prefer to always send a B/C in these pts)
3. U/A. & U/C by bladder catheterization or in exertional cases (eg. tight phimosis), suprapubic aspiration
4. Chest X-ray in children with WBC ≥ 20.000/μL

- ✓Abnormal U/A, should be Rx ed for a UTI in ? cases awaiting results of U/C represent a reasonable alternative

Rx recommendations

In FWS who are incompletely immunized who have a WBC ≥ 15.000/μL

Receive parenteral antibiotic therapy

Pending B/C & U/C

❖Ceftriaxone (50 mg/kg, IM) is preferred because of its antimicrobial spectrum & prolonged duration of action

Allergic to cephalosporins

- ❖ Clindamycin (10 mg/kg, IV followed by oral Clinda 8 hrs later)
- ✓ Outpatient follow-up within 24 hrs
- ✓ outpatient follow-up is uncertain: admit

(AAP & ACEP)

Empiric parenteral antibiotic therapy IM ceftriaxone

(4 randomized controlled trials of 7899 children)

- ✓ Reduces the chance of SBI by approx. 75%
- ✓ P.O. antibiotic is not effective
- ✓ The mean probability of subsequent meningitis was 8.2% (all Hib) Rx ed with oral antibiotics & 0.3% in Pts Rx ed with parenteral antibiotics VS 9.8% in untreated children

  No child treated with ceftriaxone developed culture +ve meningitis

Amoxicillin P.O.

- ✓A randomized, double-blind, placebo controlled trial of 955 children (3-36 mos, temp ≥ 39°C)

  No difference in major infectious morbidity between bacteremic children receiving P.O. amoxicillin or placebo

- ✓The incidence of diarrhea

  15% VS 11% in placebo group

  The overall rate of bacteremia was 2.8% in this study

  (an unblind, randomized controlled) trial of 6733 children overall rate of bacteremia was 2.8%

5 definitive focal infections

(3 meningitis, 1 pneumonia, & 1 sepsis)

In 3344 children receiving Amox P.O. VS None in those Rx ed with IM ceftriaxone

An unblind, randomized trial of 96 children, between 6-24 mos of age with a temp. > 40°C 4.3% of untreated (2 of 46) developed pneumococcal meningitis VS none of the 50 children treated with IM PCN G at the initial visit followed by P.O. PCN × 10 days (bacteremia in 10.4% of all children)

Conclusion

- ✓Unimmunized children with FWS avoid progression of bacteremia to focal infections esp. meningitis, when treated with parenteral antibiotics
- ✓Given the increasing prevalence of PCN resistant S. Pneumoniae, IM ceftriaxone remains a preferred parenteral agent

Follow up I

- ✓Should be arranged within 24hrs for those children with FWS who have received parenteral antibiotics.
- ✓Not treated with antibiotics,

  Should be instructed to seek medical attention within 48 hrs if they have persistent fever.

Follow up II

- ✓**Return immediately**

  if fever become higher,

  The patient look sicker

  or local symptoms or signs develop

  (eg, cough, diarrhea, Cellulitis)


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LANDSCAPE ARTWORK