Fever in children is the most common presenting feature in pediatric emergencies. If the infant with fever appears well, a careful systematic approach is advised in order not to miss any serious bacterial etiology. Neonates with fever might have a serious bacterial infection, such as urinary tract infections or bacterial meningitis, despite appearing well. Therefore, a full diagnostic workup, including a lumbar puncture, is indicated. Older infants who present with a fever should be examined by an experienced emergency pediatrician but they usually do not need to undergo a lumbar puncture.

Definition of Fever in a Well-Appearing Infant

Fever is a common presenting feature that can be seen in infants who appear well or ill. The distinction between ill and well-appearing is usually based on the clinical evaluation of the infant to exclude severe bacterial infections like meningitis, bacteremia, and urinary tract infection.

Up to 20% of infants have no specific cause of fever. Fever is defined as a documented rectal temperature of 38.0°C (100.4°F) or more. In this discussion, we also define well-appearing infants presenting with fever as those that do not have a previous medical condition, were not recently admitted to the hospital, or who have taken antibiotics for
any other cause.

**Epidemiology of Serious Bacterial Infections and Fever in Infants**

Up to 70% of pediatric presentations to the clinic or emergency department are due to fever. Hence, fever can be considered the most common presentation in children who seek medical care.

A very important decision in the evaluation of the well-appearing infant with fever is to exclude the possibility of a serious bacterial infection. Approximately, 7–15% of well-appearing infants who have a fever are eventually diagnosed with a serious bacterial infection.

The most important factors in predicting whether a child has a serious bacterial infection or not, are the *age* and *toxic appearance* of the child. Any infant who appears ill should be considered as having a serious condition behind their fever and should not be managed in an outpatient setting.

In a recent study, neonates with fever were far more likely to have a serious bacterial infection. Therefore, the authors recommended that all neonates with fever, even if appearing well, should be considered sick and should be admitted to the hospital. For instance, the rate of serious bacterial infections in neonates was estimated to be around 20% in contrast to 12.6% in infants more than 28 days old.

**Organisms causing UTI, bacteremia, or meningitis**

- *Escherichia coli* (majority)
- *Group B streptococci* (in Group B streptococci-positive undertreated mothers)
- *Streptococcus pneumoniae*
- *Neisseria meningitidis*
- Enterococcus
- Klebsiella
- *Staphylococcus aureus* (osteomyelitis of the newborn)
- *Haemophilus influenzae type b*
- *Listeria monocytogenes*

**Most Common Diagnoses of Fever in a Well-Appearing Infant**
In the majority of the cases, no serious bacterial infection could be identified as the etiology of fever in a well-appearing infant. Approximately, 72% of infants presenting with fever who appear well are expected not to have a serious bacterial infection.

**Urinary tract infections** can present with fever in an otherwise well-appearing infant as they were the final diagnosis in up to 16% of the cases in one series. **Meningitis** was the final diagnosis in approximately 11.7% of infants who appear well despite having a fever. Further, **bacterial meningitis** was found to be the cause of fever in well-appearing neonates younger than 15 days. Infants of other ages who appeared well were unlikely to have bacterial meningitis as the etiology of their fever. Another diagnosis of fever in this group of infants was **pneumonia**, which was also noticed in neonates but not in older infants. Therefore, most infants above 28 days old and who have a fever but appear well are very unlikely to have any serious bacterial infection.

### Diagnostic Tests for Fever in a Well-Appearing Infant

It is a challenge to determine which laboratory or invasive tests to perform in a case of fever in a well-appearing infant. Invasive examinations such as a **lumbar puncture** can lead to significant discomfort to the infant, with a risk of localized skin infection.

However, withholding such investigations might put the infant at risk of significant **sequela**. Because of these hazards and benefits, one should follow a systematic approach in determining which investigations should be performed in a given patient.

As noted before, bacterial meningitis is very unlikely to present with fever alone in an otherwise well-appearing infant who is above 28 days old. Additionally, while lumbar puncture was performed in up to 20% of infants above 28 days of age, the diagnosis of bacterial meningitis in well-appearing infants was unnoted.

However, a diagnosis of bacterial meningitis was made in 2 of 81 cerebrospinal fluid examinations in well-appearing neonates with fever. Therefore, despite the low risk, this condition is very significant and a lumbar puncture should be performed in neonates who...
present with fever, even if they appear well.

While a complete blood count can show leukocytosis or leukopenia, these findings rarely point towards a single etiology in well-appearing infants presenting with fever. Regardless, a complete blood count with differentials should be performed in all infants presenting with fever because it can reliably differentiate between infants who are likely to have a serious bacterial infection and those who are not. A white blood cell count above 15,000 cells/mL or less than 5,000 cell/mL is highly suggestive of a severe bacterial infection, even if the infant looks well.

**Urinalysis**

Perhaps, the most important investigation in a well-appearing infant with fever is a urinalysis. Up to 15% of infants who appear well despite having a fever were eventually diagnosed with a urinary tract infection.

**Interpreting the UA**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>WBC count</td>
<td>0.74</td>
<td>0.86</td>
</tr>
<tr>
<td>Bacteria present</td>
<td>0.88</td>
<td>0.92</td>
</tr>
<tr>
<td>Leukocyte esterase</td>
<td>0.79</td>
<td>0.87</td>
</tr>
<tr>
<td>Nitrite</td>
<td>0.46</td>
<td>0.98</td>
</tr>
<tr>
<td>Entire urinalysis</td>
<td>0.97</td>
<td>0.70</td>
</tr>
</tbody>
</table>

If the urinalysis is inconclusive, a urine culture might be a reasonable diagnostic test to reliably exclude the diagnosis of urinary tract infections. Again, the decision to go for a urine culture might be skewed towards neonates who are more likely to have atypical presentations of febrile illnesses.

Special imaging studies, such as chest X-rays, are most likely not indicated in well-appearing infants with fever, unless they are younger than 28 days. Even though only 1% of well-appearing neonates with fever might have pneumonia, the condition can still be considered severe enough to warrant a chest X-ray in this group. A chest X-ray should be reserved for infants who present with fever associated with cough or tachypnea, but appear well.

Finally, the most important diagnostic method to determine whether invasive investigations such as a lumbar puncture are needed in a febrile infant is perhaps the consultation of an emergency pediatrician. If an experienced emergency pediatrician is not available and the patient is less than 1 month of age, a complete blood count, urinalysis, and lumbar puncture should be routinely included in your evaluation of the feverish child, even if appearing relatively well.

**Herpes Simplex Virus (HSV) Infection in the Neonate**

Tests to order (in addition to febrile infant testing):

- HSV PCR of blood (best test)
- HSV culture: eyes, nose, mouth, rectum
- HSV PCR of CSF (only 90% sensitive!)
- Liver function tests

**Critical:** Do not start acyclovir until you get the culture results!
When to worry about HSV in a newborn?

Management of Well-Appearing Infants With Fever

Less than 28 days old

Admitted infants should be watched for 24–36 hours. Discharge if cultures are negative.

- Urinalysis
- Urine culture
- Complete blood count/CRP/Procalcitonin
- Blood culture
- Lumbar puncture (almost all)

If the lab results are abnormal, the patient should be admitted and started on Ampicillin/Gentamicin or Ampicillin/Cefotaxime. If the lab results are normal, admit the patient with or without antibiotics.

29–60 days old

If the only complete blood count is abnormal, consider discharge (on oral antibiotics?), and watch closely at home. Admitted infants should be watched for 24–36 hours, and discharged if cultures are negative.

- Urinalysis
- Urine culture
- Complete blood count/CRP/Procalcitonin
- Blood culture

If the lab results are abnormal, the patient requires admission and a lumbar puncture. If only the urinalysis is abnormal, consider discharging the patient on oral antibiotics. If the lab results are normal, discharge the patient with close follow-up.

61–90 days old

- Urinalysis
- Urine culture

If the lab results are abnormal, the patient requires oral antibiotics and close follow-up closely. If the lab results are normal, discharge the patient with close follow-up.
Morbidity and Mortality

A physical examination and patient history do not always identify patients with serious bacterial infections. Serious infections that are not recognized promptly, and are misdiagnosed and inappropriately managed, can cause significant morbidity or mortality.

References

Well appearing young infants with fever without known source in the emergency department: are lumbar punctures always necessary? via nih.gov

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