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Emergency Tips

Fever Without Focus

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Fever is one of the commonest symptom in a sick child. It accounts for more than 50% of visits to our Pediatric emergency service. Many febrile children have a variety of characteristic signs and symptoms indicative of a specific infectious or noninfectious disease. Others especially those under 36 months of age and with underlying malnutrition may have more subtle and nonspecific signs of disease. Such patients account for 4-5% of the total visits to our Emergency service. The major concern in such febrile children with no evident focus is rapid and early detection, and treatment of serious bacterial infections (SBI) and bacteremia which can otherwise lead to serious and life threatening

consequences. Life-threatening non-infectious illnesses especially heat-stroke, and certain poisonings which may also present predominantly as fever and nonspecific signs and symptoms are uncommon compared to bacterial infections.

What are the specific variables that may help in selecting those febrile children below 3 years of age who are 'at high risk' of 'low risk' of serious bacterial infection?

Is the Temperature Grade Helpful?

Pantell *et al.*(1) found that in infants <3 months of age fever >38.3°C was associated with a 21.5 times the risk of serious underlying infection than infants >3 months with a similar temperature. Temperatures $\geq 39^\circ\text{C}$ appear to be linked with a higher risk of bacteremia and bacterial infections. In an analysis of the published data McLellan and Giebank found that the probability of a temperature >39°C in children with proved bacteremia was as high as >90% and low grade fever was an excellent discriminator of absence of bacteremia(2). The evidence that temperature >41°C (hyperpyrexia) is associated with a higher risk of serious bacterial infection than a temperature between 39-41°C is poor. Alpert *et al.*(3) in a retrospective case-control study compared three groups of 76 children each, with temperatures between 39.1-40°C, 40.1-41°C and >41.1°C. Bacteremia was detected in seven children; only one of them was hyperpyrexia, while four had temperature 40.1-41°C. The only child in the study who had meningitis had a temperature of 39.1-40°C. The data suggest that in previously healthy children, 2-36 months of age, a temperature between 39-41°C is associated with as much risk of SBI as any hyperpyrexia and should receive as much attention. Temperature <39°C of

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short duration are more likely to be due to non-serious infections.

Response to Antipyretic and Severity of Infection

There is a common myth that if a child's fever does not come down in response to antipyretic therapy the child is more likely to have a serious infection. Recently, several authors had tried to answer this question(4-8). They conclude that temperature response to acetaminophen (paracetamol) is a poor discriminator between bacteremic and nonbacteremic illness(4,5), bacterial and viral infections(6,7) and within different diagnostic categories(8).

Clinical Assessment of 'Toxicity' or Sickness

Experienced physicians often find an overall 'subjective' assessment of the severity of underlying illness useful in final decision making. Most of this assessment is based on evaluation of behavioral and functional response of the child to the illness. In the last decade several studies have aimed at enlisting these signs for an objective assessment of febrile sick children(9-11). These are shown in *Table I*.

To quantify the general assessment, Nelson(10) and McCarthy *et al.*(11) evolved observation scales which could be predictive of serious illness. Severity index scoring system of Nelson had a positive predictive value of 98.7% for non-severe illness with a false negative value of 1.3%. The false positive prediction for the serious illness was only 15.8%. The acute illness observation scale (AIOS), also called Yale Observation Scale (YOS), developed by McCarthy *et al.*(11) is more detailed and has found a wider acceptance. However,

TABLE I—*Historical Data and Signs Useful in General Assessment of a 'Toxicity' in a Febrile Child*

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1. History: Not feeding/eating well.
 2. Sleepy, decreased level of activity/playfulness.
 3. Cry-sobbing, whimpering, weak, moaning, high pitched, continuous.
 4. Level of consciousness: altered.
 5. Responsiveness: no smile, face-anxious dull or expressionless.
 6. Color: pale, cyanotic, mottled or ashen grey.
 7. Respiratory efforts: obvious distress.
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the scales formally quantifying this assessment may not be completely predictive of severe illness, especially in very young febrile infants(12). More studies in our own setting are needed to validate the scales and increase their objectivity.

Laboratory Tests and 'Sepsis Screen'

A vast array of laboratory and radiological tests may be helpful and requisitioned in a febrile child. Some of these, such as examination of blood film for malaria parasite, X-ray chest, bacterioscopy of freshly voided urine and CSF examination may give immediate answer to the diagnosis and guide the therapeutic decision. Other tests such as blood counts, ESR, qualitative C-reactive protein (CRP) as shown in *Table II* in the specified ranges have been suggested as useful in screening for presence of sepsis(2,13). We found that WBC >15000 had a sensitivity of 26% and specificity of 100% and mESR ≥ 25 mm, one hour, had a specificity of 97% and a sensitivity of 63% for bacteremia (unpublished observation).

TABLE II—Investigations Useful in Rapid Assessment of a Febrile Child

1. Blood Counts
(i) Malaria parasite on smear exam
(ii) TLC >15,000/mm ³ , <5000/mm ³
(iii) Absolute neutrophil count <10,000/mm ³
(iv) Unsegmented polymorphs >500/mm ³
Unsegmented: segmented ratio 0.15-0.3
(v) Platelet: 100,000/mm ³
2. CRP: Qualitative: +ve, suggestive
3. Urine: Bacterioscopy: >2 bacteria/16 small squares of Neubaur's chamber 90% chance of UTI
4. X-ray chest

However, none of these tests individually or in different combination has been found to be fully reliable. Children with proven viremia may also have counts >15000/mm³(14). McLellan and Giebank(2) have commented that absence of leukocytosis is an excellent discriminator of the absence of bacteremia in the febrile child but its presence is a poor indicator of bacteremia while leukopenia (total WBC <5000/mm³) strongly suggest bacteremia. Bonadio *et al.*(15) suggested a WBC differential ratio (% lympho + % mono)/(% PMN + % band forms). If the ratio is <1.5 it has 100% sensitivity in discriminating bacterial meningitis. This needs further evaluation.

Should blood cultures be obtained routinely in evaluation of febrile children, aged 3-24 months, temperature >39°C, duration <4 days, without evident focus? Kramer *et al.* say no(16) on the basis of statistical probabilities and utilities of performing blood culture compared to intravenous

antibiotic treatment of children whose bacteremia would have resolved spontaneously. They found 'no culture' strategy had the highest expected utility. Stephen *et al.*(17) on the other hand from a cost-benefit analysis found that identification of high risk groups by means of blood counts and blood culture and expectant treatment at first visit to be the most cost effective and procedure effective method of clinical evaluation of febrile children at risk of bacteremia.

Combination of Clinical Observation and 'Sepsis-Screen'

Noting the limited usefulness of clinical observation and sepsis screen individually in predicting SBI, efforts have been made toward evolving a combination of clinical and laboratory criteria which may discriminate children at 'high risk' or 'low risk' of SBI.

Crain *et al.*(9,18,19) have shown that, in infants <8 weeks, a combination of clinical impression of sepsis, total WBC count ≥15000 and ESR ≥30 mm identifies 80-100% of all the ill bacteremic infants, while excluding 82-99% of those who did not have bacteremia or meningitis.

Studies of Dagan *et al.*(20,21) in infants <3 months have demonstrated that previously healthy infants are unlikely to have serious bacterial infection ('at low risk') if they had no finding consistent with ear, soft tissue or skeletal infections and have normal white blood cell (5000-15000) and band cell counts (<1500), and normal urine findings. The negative predictive value of the criteria in different studies has ranged between 95.6-99.7%(19-22).

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