INVITED ARTICLE

CHILDHOOD FEVER

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ABSTRACT

Childhood fever is a common symptom, reflective of multiple causes. As the child is often unable to express himself, the physician must rely on parents' observations and the physical examination. The majority of febrile children have non-bacterial upper respiratory tract infection and indiscriminate use of antibiotics is inappropriate, ineffective and leads to drug-resistance such as the emergence of Penicillin-resistant Streptococcus pneumoniae. In this article, we attempt to identify the possible causes of fever by a simple approach using the presence or absence of associated or localising symptoms. Infants less than 3 months constitute a unique group as the fever may be related to perinatal events and as serious bacterial infections can still occur despite unremarkable physical findings. Management of fever needs to take into account the toxicity, immune status and age of the patient as well as the source of the infection. Zealous overprescription of antipyretics needs to be avoided with attention directed to the cause of the fever, the child's capacity to cope with the illness and parental education.

Keywords: *childhood fever, pathophysiology, febrile fit, antipyretics*

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INTRODUCTION

Fever is a common symptom which prompts parents to bring their child to the clinic or hospital. As the child is often unable to express himself to give a detailed history, the doctor must decide the implications of the fever based on the parents' observations and the physical examination. The great majority of febrile children will have nonbacterial upper respiratory tract infection and indiscriminate use of antibiotics is inappropriate, ineffective and leads to drug-resistance. Clinicians should be aware of subtle historical facts, disease patterns and physical findings which would hint that further investigation may be required despite the child's relatively well appearance. Our goal is to establish what constitutes a fever, provide current thinking about its pathophysiology, review the common causes that will be seen in the clinic and provide an approach to the evaluation of fever in the neonate, infant and child.

DEFINITION

Fever is defined as a temperature (T°) above the normal range. A rectal T° > 38°C[1], an oral T° > 37.8°C and an axillary T° > 37.5°C are all fevers[2]. The normal T° range for babies is 36.7 – 37.9°C rectally and 35.6 – 37.2°C for axillary temperature[3,4]. The temperature fluctuates according to the time of day, from a low of 36.1°C between 2am to 8am to a high of 38°C rectally between 4pm to 9pm[3]. Mild elevations can be caused by exercise, warm clothing, hot weather or warm food and drink. If one of these causes is present, it should be eliminated and the temperature retaken in one half hour.

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METHODS OF TEMPERATURE TAKING

When a child is unable to cooperate with oral temperature taking, an axillary temperature is recommended.

1. Axillary – The axillary thermometer should be in place for 3 minutes.
2. Rectal – Rectal temperature taking is frightening and uncomfortable for small children. Axillary T° is 0.5°C < oral T° and rectal T° is 0.5°C > oral T°. There is a mean difference of 0.5°C between rectal and axillary temperature.
3. Forehead strips – Plastic forehead strips were found to be inaccurate substitutes for thermometers[5-7].
4. Tympanic membrane thermometers – In a comparison of infrared tympanic membrane thermometer readings with oral, rectal and axillary measurements, researchers disagreed about the usefulness of tympanic membrane temperature measurements[8-10]. Most felt tympanic membrane thermometer readings should be viewed with caution in children less than 3 months old[11,12], and possibly even up to 3 years old[13]. The tympanic membrane T° was less accurate if there was prior ear surgery excluding tympanostomy tubes or myringosclerosis; it was contraindicated in acute or chronic inflammation of the external ear canal or if there was bloody or purulent discharge from the external ear canal[14].

PATHOPHYSIOLOGY

Body temperature remains constant due to the thermoregulatory responses controlled by the hypothalamus eg heat production by shivering mechanisms, heat loss by increasing cutaneous blood flow and heat loss from the skin surface by conduction, convection and radiation.

The preoptic area, the anterior hypothalamus and septum[15] are involved in thermoregulation. Fever is due to a rise in the hypothalamic set-point. As such, the child will often shiver and be peripherally vasoconstricted to increase heat production during the rising phase of fever. When the fever "breaks", the thermoregulatory set-point has returned toward normal. The child feels warm and will sweat during deffervescence.

THERMOREGULATORS

a. Exogenous Pyrogens – Exogenous pyrogens are derived

from bacterial, viral and fungal components. They cause release of endogenous pyrogens from host cells and, thus, fever. Examples are endotoxin from Gram– negative bacilli peptidoglycan of the bacterial cell wall and exotoxins.

b. Endogenous Pyrogens – Endogenous pyrogens are derived from the host's cells. They are produced in peripheral tissues and do not actually penetrate the blood-brain barrier but have their effect on the rich vascular network in the preoptic-anterior hypothalamus area. Cytokines thus far found to be endogenous pyrogens are IL-1 (interleukin-1), tumour-necrosis factor TNF, IL-6, IL-2, IL-8, alpha-beta-gamma-interferons and macrophage - inflammatory protein-1[16].

c. Prostaglandins – The effect of endogenous pyrogens on the hypothalamus is presumably due to an increase in prostaglandin E_1, the mechanism of which is currently unknown.

d. During fever, not only are pyrogens being produced but also antipyretic substances. Two of them are arginine vasopressin and melanocyte-stimulating hormone[16].

FEVER PATTERNS

Three main types of fever patterns are described:

1. **Continuous** – the T° is increased throughout the 24 hour. The total range of variation is < 0.3°C eg typhoid fever, *P. falciparum* infection, rickettsia infection and brucellosis.

2. **Intermittent** – the T° remains above normal but the daily range is > 1.4°C. If the swings are very wide the fever is referred to as hectic/spiking eg
   a) pyogenic abscesses, pyelonephritis
   b) double fever spike in one day (double quotidien): salmonellosis, double malaria, meningococcal endocarditis.

3. **Remittent** – the T° is normal for part of the day, or for several days eg *P. vivax/ovale P. malariae,* Hodgkin's lymphoma (Pel-Ebstein fever).

The height of the febrile response is not helpful in identifying a given disease or group of diseases. In general, if a disorder is capable of producing fever, it is capable of producing high fever.

BENEFITS OF FEVER

Animal studies have shown an enhanced resistance to infection and improved survival associated with temperature elevation[16,17]. Fever causes a general increase in immune system function eg increased proliferation of lymphocytes, increased Gamma-interferon production, increased chemotaxis of polymorphs, increased alternative complement pathway activation and increased antibody production[17]. Also, some antimicrobials are more active at febrile temperatures[18]. Some pathogens such as *Streptococcus pneumoniae* may be directly inhibited by elevated temperatures while others become more susceptible to the bactericidal effect of serum and/or antimicrobials[19,20].

COMPLICATIONS OF FEVER

Fever itself causes no harm unless it reaches at least 41.7°C. Seldom do children have fever > 40°C, especially if they are < 3 months old. Fortunately, the brain's thermostat keeps almost all untreated fevers due to infection below 41.7°C.

1. **Dehydration.** Children have a greater surface area per weight than adults, this leads to greater fluid losses through the skin. Thus when fluid intake is interrupted eg during gastroenteritis, dehydration is a more likely consequence in the child.

2. **Febrile fit.** Whereas all children will experience fevers, only 4% will have a febrile convulsion. For most normal children the seizure threshold is about 41.1°C. If the child is neurologically abnormal, seizures may occur at lower temperatures. Febrile seizures are caused by the height of the fever and not the rapidity of the rise. The seizure frequently is the first sign of the febrile episode. If the child has experienced fevers without a seizure and has not had a febrile seizure by 3 years of age, he will probably never have one[21]. The following factors would favour admission after a first convulsion:

   a. a complex febrile convulsion ie lasting more than 20 minutes, with focal features, repeated in the same episode of illness or with incomplete recovery after 1 hour;
   b. aged less than 18 months
   c. early review by a doctor at home not possible
   d. clinical signs of meningism
   e. child is unduly irritable or drowsy or systemically ill
   f. home circumstances inadequate or more than usual parental anxiety or parent's inability to cope.

   It should be remembered that a history of febrile fits does not exclude the possibility of meningitis[22]. Occasionally febrile status epilepticus can occur.

3. **Heat strokes.** Most heat strokes in children are due to inadvertent heat overload eg overwrapping, being left in a car in direct sunlight and are preventable[23].

   Fever can be detrimental to patients with congestive cardiac failure (due to increased metabolic requirements and increased cardiac output), respiratory failure, acute neurologic disease or endotoxic shock.

CAUSES OF FEVER

Fever is often accompanied by symptoms/signs that suggest a diagnosis or at least point to an organ system such as headache, cough, diarrhoea, dysuria, etc. However, this is not always the case. This distinction provides a convenient means of categorising causes of fever in children:

1) Localising symptoms or signs, (Table I)
2) Associated presentation eg rash. The approach to a child with fever and a rash requires consideration of the type of rash (Type II)
3) No localising signs (Table III)

Febrile infants < 3 months old

A serious bacterial illness can still occur in 5%-8%[24,25] of these patients despite unremarkable findings on clinical examination. 0.3%–5.4% of patients with serious bacterial infection were still not detected whether with screening tests or physical examination. As the height of fever increases, so also the likelihood of bacteremia[26].

A full history must be taken including perinatal history: prematurity, premature rupture of membranes, prolonged rupture of membranes, maternal fever, maternal urinary tract infection, invasive procedures in the neonate, birth asphyxia – these are associated with high risk of neonatal sepsis. In the postnatal history, the following 6 symptoms were found by Hewson[27] to be the most indicative of serious bacterial infection:

Table I – Causes of fever with localising symptoms or signs

Symptoms	Diseases		Comments
	Common	Uncommon	
Respiratory eg. Cough, rhinorrhoea	common cold, influenza, pharyngitis are by far the most common causes of fever	Otitis media, croup sinusitis	Normal children may experience up to 12 viral infections (mostly respiratory) a year. If all symptoms clear in between episodes, immunodeficiency is unlikely.
Urinary eg. dysuria frequency of micturition	urinary tract infection (UTI)	vulvitis balanoposthitis	All children (males any age, eg. females < 5 years or recurrent UTI if > 5 years old) with confirmed UTI need to be further evaluated.
Gastrointestinal			
Vomiting	Viral gastritis gastroenteritis food poisoning	Typhoid fever, acute (ac) appendicitis, acute hepatitis, acute meningitis	
Diarrhoea	Viral gastritis gastroenteritis food poisoning	Dysentery, cholera, acute appendicitis	Risk for bacterial diarrhoea are: a. a history of blood in the stools b. T° > 39°C c. > 10 stools in 24 hours.
Abdominal pain	Gastroenteritis – *Shigella,* – *Campylobacter jejuni* – *Yersinia Enterocolitica*	Acute appendicitis, acute hepatitis	
Central Nervous System			
Sensory changes	None	Acute meningoencephalitis acute encephalitis including mycoplasma, acute gastroenteritis with dehydration	
Headache	Acute sinusitis	Acute meningitis	
Neck stiffness	None	Meningitis	
Bulging fontanelle	None	Meningitis, benign intracranial hypertension	
Orthopaedic			
Joint pain/ swelling	Viral arthritis, mumps, rubella, enteroviral? infections	Septic arthritis, juvenile rheumatoid arthritis, systemic lupus erthyematosus	
Bone pain/ refusal to move the limb	Osteomyelitis septic arthritis		
Cardiac murmur	Functional due to tachycardia	Bacterial endocarditis, rheumatic fever acute myocarditis	

Table II – Causes of febrile rashes

Type of Rash	Causes	Comments
Erythematous eruptions	measles, rubella, roseola infantum/ exanthem subitum, erythema infectiosum/ Fifth disease, infectious mononucleosis, dengue fever, cellulitis, drug eruptions, erythema multiforme, connective tissue disease, Kawasaki's disease.	Exanthem subitum is a common exanthem caused by human herpes virus 6 and often mis-diagnosed as a drug allergy. Measles infection can still occur despite immunisation, especially in the school-going age due to primary vaccine failures (vaccine success is 95-97%).
Vesiculo-pustular eruptions	chicken-pox, hand-foot-mouth disease, Staphylococcus scalded skin syndrome, Herpes simplex, bullous impetigo	
Vasculitic/purpuric eruptions	Bacterial sepsis, subacute bacterial endocarditis, Henoch-Schonlein purpura	

Table III – Causes of fever with no localising symptoms or signs

Common	Uncommon	Comments
Urinary tract infection Viral fever	Sepsis syndrome, Typhoid fever, Malaria, Drug fever	Children < 3 months old or with immunodeficiency, asplenia, steroid therapy are at high risk for sepsis
	Immunisation reactions Hypothalamic lesion eg. intracranial haemorrhage encephalitis, brain tumour, Guillain-Barré syndrome Metabolic eg hyperthyroidism, dehydration from diabetes inspidus	
	Factitious	

1. Decreased feeding < 50% of normal in the past 24 hours,
2. Decreased activity,
3. Breathing difficulty/respiratory distress,
4. < 4 wet nappies in the past 24 hours,
5. Drowsiness,
6. Pale and hot.

The most predictive signs of serious bacterial infection were:

1. Chest wall retraction,
2. Tender abdomen,
3. Respiratory grunting,
4. Cold calves.

A variety of test algorithms have been devised to predict risks of serious bacterial infection in well-looking infants eg total white cell count < 5000 /mL, or > 20,000/mL, immature/mature neutrophil ratio > 0.2, absolute neutrophil count < 1000 /*u*L, C-reactive protein, positive haptoglobin, positive micro-ESR > 15 mm/hr. Even with a combination of 5 tests by Philip[28], not all septic patients were identified.

Pyrexia of unknown origin

Definition: Fever > 2 weeks without a known cause.
Causes: Urinary tract infection, typhoid fever, malaria, subacute bacterial endocarditis, cyclical neutropenia, inflammatory bowel disease, postransfusion Cytomegalovirus infection. Antibiotic fever.

Investigations for fever

1. Full blood count.– The total Wbc count or band count is elevated in 30% – 55% of well-looking young infants with bacteremia or UTI[24].

2. Urinanalysis – Up to 50% of children with UTI have normal urinanalysis, with Gram stain slightly more sensitive than dipstick or leukocyte esterase. Screening for UTI using Microstix which depends on bacteria to reduce nitrate to nitrite has a false-negative rate of 4%–20%. Proper urine cultures must be taken either by midstream, suprapubic aspiration (if < 6 months old) or catheter.

3. Chest radiograph – Only 1% of asymptomatic febrile infants had abnormal CXR[29], thus in the absence of respiratory signs or symptoms, febrile young infants are unlikely to require a CXR.

4. Other specialised investigations. These may need to be done in the hospital, eg blood cultures.

Managing fever

With regard to managing fever, the factors to consider include: toxicity of patient, immune status, age (an older child is better equipped to contain infections), and source of infection.

1) **Antipyretic drugs**
Zealous overprescription of antipyretics in children needs to be avoided with attention being redirected to the cause of the fever and the child's capacity to cope with the illness. Overuse of antipyretics can lead to delayed prescription of antimicrobial drugs. Antipyretics should only be used if the temperature is >38.5°C[21] or if associated with discomfort or the child has had febrile seizures before or has cardiac disease. Caution should be exercised regarding the use of antipyretics – the correct dose for the child's age or weight (paracetamol: 10-15mg/kg every 4-6 hourly and <90mg/kg/24 hours; ibuprofen: 5-10mg/kg every 6 hourly). These drugs will reduce the fever but will not normalise it. Do not use antipyretics if the child is <3 months old. Aspirin should not be given to children with influenza, chickenpox or any febrile infection because of the risk of Reye's Syndrome.

2) **Sponging**
Sponging should be used for T° > 38.5°C and after administration of antipyretic drugs. If the fever is >38.5°C half an hour after drugs have been given, sponge the child for 30 minutes in lukewarm water (temperature of the water: 29.5°C – 32°C). Sponge immediately if the child is delirious or fitting from fever. Sponging works much faster than immersion. Sit the child in 2 inches of water and keep wetting the skin surface. If the child shivers, raise the water temperature. Do not expect to lower the child's temperature below 38.3°C. One study found that sponging febrile children with tepid water after antipyretic therapy had no more effect on defervescene than the antipyretic drugs alone[30].

3) **Other measures** include light clothing, hydration and antibiotics. Blind treatment with antibiotics can mask physical signs, resulting in delay in making a correct diagnosis, increase bacterial resistance, cause drug fever, induce potentially toxic side-effects, and vitiate subsequent bacterial investigations. Judicious use of antibiotics is therefore recommended.

CONCLUSION

Fever in a child is a common problem encountered in the clinic or hospital. It is important to define the cause of the fever instead of just treating the fever empirically. Persistent fever reported by parents may be a series of self-limited viral illnesses rather

than a persistent pyrexia. In other instances the parent has a misunderstanding of what constitutes fever, the normal diurnal variation of fever or the effect of activity on core temperature. Parental education regarding fever is important. It is worth emphasising that strict attention to clinical detail and an understanding of symptoms and signs in the young infant still play a role in illness detection.

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