An overview of the management of fever and its possible complications in infants and toddlers

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Abstract

Fever is a normal response to a variety of conditions, the most common of which is infection. Fever occurs when the body's temperature is elevated, because its thermostat is being reset to a higher-than-usual temperature. Nearly every child will develop a fever at some point in time. The challenge for health care workers is to know when to be concerned. This topic review will discuss the definition of fever, its pathophysiology and basic overview, how and when to treat fever, as well as the signs and symptoms that require further assessment and evaluation. A short overview of febrile seizures has also been included.

Keywords: fever, hyperthermia, paracetamol, febrile seizures, set point, pyrexia

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Introduction and definitions

Normal body temperature ranges in paediatrics are higher than in adults, and should be taken into consideration when diagnosing pyrexia (fever).[1,2] Normal paediatric temperature ranges are summarised in Table I.[1] A possible complication of pyrexia is febrile seizures. The threshold for convulsive temperature is independent of the intensity and duration of the heating stimulus and fever.[1-3] Individual differences, such as age and maturation, cause variations in the threshold for convulsive temperature in individual patients.[3,4] This is further modified by any changes in water and electrolyte balance, especially in the case of hyponatraemia.[3,4]

The following terminology is important to facilitate a thorough understanding of the significance of fever in paediatric practice settings:[1]

- Set point: The temperature at which the body temperature is regulated by the hypothalamus.
- Fever (pyrexia): An elevation in set point, to such an extent that the body temperature is regulated at a higher level – arbitrarily set and defined as a body temperature above 38 °C.
- Hyperthermia: A situation in which the body temperature exceeds the set point, which usually results from the body, or specific external conditions, creating even more heat. Examples include heat stroke, aspirin toxicity and hyperthyroidism.

The Health and Human Services guidelines of the Emergency Medical Services Authority in California describe the paediatric patient population as a diverse group of patients that includes preterm and newborn infants, and adolescents on the brink of adulthood.[5]

Table I: Normal body temperature ranges in paediatric practice[1]

Neonate	36.1-37.7 °C
Two-year-old child	37.2 °C
Twelve-year-old child	37 °C

The ages of paediatric patients were categorised according to the paediatric terminology defined by the National Institute of Child Health and Human Development (NICHD) (2015), developed by Eunice Kennedy Shriver in the USA (Table II).[5]

Febrile seizures constitute a fairly common seizure-disorder during childhood, and is associated with fever, but without any evidence of other intracranial infections

Table II: The classification of paediatric patients according to the National Institute of Child Health and Human Development[5]

Classification	Age
Neonates	0–27 days
Infants	Birth to 12 months
Toddlers	13 months to 2 years
Early childhood	2–5 years
Middle childhood	6–11 years
Early adolescence	12–18 years
Late adolescence	19–21 years

Simple	Complex	Symptomatic febrile
• *Fever in a child aged 6 to 60 months* • *Simple, generalised seizure lasting less than 15 minutes* • *Neurologically healthy by all assessments* • *Fever and seizure is not caused by infections (e.g. meningitis or encephalitis)*	• *Fever in a child aged 6 to 60 months* • *Neurologically healthy by all assessments* • *The seizure is either focal or prolonged (i.e. lasting > 15 minutes), or multiple seizures occur in close succession*	• *Fever in a child aged 6 to 60 months* • *Neurologically healthy by all assessments* • *The child has a pre-existing neurological abnormality or acute illness*

Figure 1: Epidemiologic division, or classification of febrile seizures[9]

or abnormalities.[6,7] It may be classified into three groups, namely simple, complex and symptomatic febrile seizures.[6,8] Children that have a genetic predisposition may be more prone to developing febrile seizures; viruses and bacteria have also been identified as possible causative agents.[2,3] Some vaccines have been associated with an increased risk for the development of seizures.[3]

Acute management of febrile seizures include basic emergency procedures and supportive measures, but also the use of appropriate anticonvulsants, depending on the severity and duration of the seizure.[7,9-11] Parents are often anxious and fear permanent brain damage, for which information regarding the condition and its management may decrease some of the anxiety.[7,10] These measures may also ensure proper management of the condition.[10,12] The likelihood of febrile convulsions causing neurological abnormalities, or developing mental disturbances, is low.[7,9,10,13] Some antiepileptic medication may be used to prevent recurrent febrile seizures (e.g. primidone and valproic acid). However, toxicities associated with these drugs outweigh the relatively minor risk associated with febrile seizures.[6,7] With education and proper medicine management, a simple febrile seizure is a benign condition that has an excellent prognosis.[6]

The rate at which the body temperature rises is not a factor in the mechanism of febrile seizures. The condition is defined as seizures occurring between the ages of 6 and 60 months, in children with fever.[6,8] These seizures are not accompanied by intracranial infections or other metabolic disturbances.[6,8] Febrile seizures may be the most common amongst all seizure disorders in children, affecting 2–5% of children between the ages of 6 and 60 months.[6] As already mentioned, febrile seizures may be classified into three groups, as outlined in Figure 1.[7,9]

Simple febrile seizures do not last longer than 15 minutes, are generalised, and occur once in a given 24-hour period, without a focal component.[7,9] Complex febrile seizures are prolonged (> 15 minutes), have a focal component, and occur more than once in 24 hours.[7,9]

Aetiology and pathophysiology

Fever occurs in response to the release of endogenous pyogenic mediators, namely cytokines. These cytokines

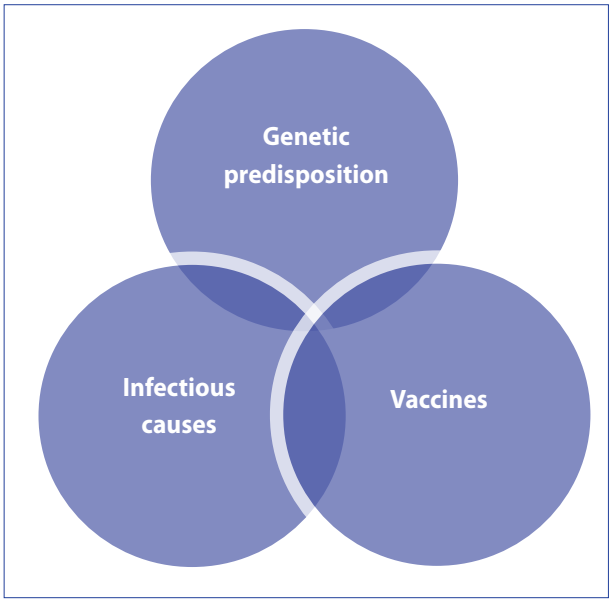

Figure 2: Possible causes involved in febrile seizures in paediatrics[7,9]

stimulate the production of prostaglandins by the hypothalamus; prostaglandins readjust and elevate the temperature set point.[1,14]

Fever plays an important and integral role in fighting infections and, in an otherwise healthy child, studies indicate that lowering the temperature can prolong some illnesses.[1,14] However, fever increases the metabolic rate and the demands on the cardiopulmonary system; thus, fever can be detrimental to children with pulmonary or cardiac compromise or neurologic impairment. It can also be the catalyst for febrile seizures, a typically benign childhood condition.[1,14]

Causes of fever differ based on whether the fever is acute (≤ 14 days), acute recurrent, or periodic (i.e. episodic fever separated by afebrile periods), or chronic (> 14 days), which is more commonly referred to as fever of unknown origin (FUO).[1,14] It is important to note that the response to antipyretics and the height of the temperature readings have no direct relationship to the aetiology or the degree of seriousness. A short description is provided in Table III.[1,14]

Possible causes involved that could increase the risk involved in developing febrile seizures are depicted in Figure 2.

Table III: Description of fever and its causes[1,14]

Acute	Chronic***
Infectious causes* include:	**Infectious causes include:**
• *Viral respiratory or GI infections (most common causes overall)* ◦ < 1 month: TORCH infections (toxoplasmosis, syphilis, varicella, coxsackievirus, HIV, parvovirus B19), rubella, cytomegalovirus (CMV), herpes simplex virus (HSV) ◦ ≥ 1 month: Enterovirus and respiratory viruses (e.g., respiratory syncytial virus, parainfluenza, adenovirus, influenza, rhinovirus, metapneumovirus), CMV, Epstein–Barr virus (EBV), HSV, human herpesvirus 6 • *Certain bacterial infections (otitis media, pneumonia, UTIs)* ◦ < 1 month: Group B streptococci, *Escherichia coli* and other enteric pathogens, *Listeria monocytogenes* (these organisms can cause bacteraemia, pneumonia, pyelonephritis, meningitis, and/or sepsis; also, *Salmonella* spp. and *Staphylococcus aureus* [e.g. in nursery outbreaks], which in addition to bacteraemia and sepsis, can cause soft-tissue, bone, and joint infections) ◦ 1–3 months: *Streptococcus pneumoniae*, group B streptococci, *Neisseria meningitidis*, *L. monocytogenes*; other common infections include otitis media (*S. pneumoniae*, *Haemophilus influenzae*, *Moraxella catarrhalis*), UTI (*E. coli* and other enteric pathogens), enteritis (*Salmonella* spp., *Shigella* and others), skin and soft-tissue infections (*S. aureus*, group A and B Streptococci), bone and joint infections ◦ 3–24 months: *S. pneumoniae*, *N. meningitidis* (these organisms can cause bacteraemia, meningitis, and/or sepsis; other common infections include otitis media and pneumonia (*S. pneumoniae*, *H. influenzae*, *M. catarrhalis*), UTI (*E. coli* and other enteric pathogens), enteritis (*Salmonella* spp., *Shigella* and others), skin and soft-tissue infections (*S. aureus*, group A streptococci), bone and joint infections (*S. aureus*, *Salmonella* spp., *Kingella kingae*) ◦ > 24 months: *S. pneumoniae*, *N. meningitides* (*S. pneumoniae*, *H. influenzae*, *M. catarrhalis*, mycoplasma), pharyngitis or scarlet fever (group A streptococci), UTI (*E. coli* and other enteric pathogens), enteritis (*Salmonella* spp., *Shigella* and others), skin and soft-tissue infections (*S. aureus*, group A streptococci), bone and joint infections (*S. aureus*, *Salmonella* spp., *K. kingae*) ◦ Mycobacterium tuberculosis in exposed or at-risk populations. Rickettsial infections in appropriate geographic locations.	• *Viral infections (e.g. EBV, CMV, hepatitis viruses, arboviruses)* • *Sinusitis* • *Pneumonia* • *Enteric infections (e.g. Salmonella)* • *Abscesses (intra-abdominal, hepatic, nephric)* • *Bone and joint infections (e.g. osteomyelitis, septic arthritis)* • *Endocarditis* • *HIV infection (uncommon)* • *TB (uncommon)* • *Parasitic infections (e.g. malaria – uncommon)*
Non-infectious causes include:**	**Non-infectious causes include:**
• *Kawasaki disease, heatstroke, and toxic ingestions (e.g. of drugs with anticholinergic effects).* • *Some vaccinations can cause fever, either in the first 24 to 48 h after the vaccine is given (e.g. with pertussis vaccination), or 1 to 2 weeks after the vaccine is given (e.g. with measles vaccination). These fevers typically last from a few hours to a day. If the child is otherwise well, no evaluation is necessary.*	• *Inflammatory bowel disease* • *Connective tissue disorders (e.g. juvenile idiopathic arthritis, SLE, acute rheumatic fever)* • *Cancer (most commonly lymphoreticular malignancies such as lymphoma or leukaemia but also neuroblastoma or sarcomas)* • *Drugs* • *Thermoregulatory disorders (e.g. dysautonomia, diabetes insipidus, anhidrosis)* • *Pseudo FUO* • *Factitious fever (e.g. factitious disorder imposed on another)*

*However, potential infectious causes of acute fever vary with the child's age. Neonates (infants < 28 days) are considered functionally immunocompromised, because they often fail to contain infection locally and, as a result, are at higher risk of serious invasive bacterial infections most commonly caused by organisms acquired during the perinatal period. The most common perinatal pathogens in neonates are group B Streptococci, *Escherichia coli* (and other gram-negative enteric organisms), *Listeria monocytogenes*, and herpes simplex virus. These organisms can cause bacteraemia, pneumonia, pyelonephritis, meningitis, and/or sepsis.
Most febrile children between 1 month to 2 years of age, without an obvious focus of infection on examination (fever without source [FWS]), have self-limiting viral disease. However, a small number (perhaps < 1% in the post-conjugate vaccine era) of such patients are early in the course of a serious infection (e.g. bacterial meningitis). Thus, the main concern in a patient with FWS is whether occult bacteraemia (pathogenic bacteria in the bloodstream without focal symptoms or signs on examination) is present. The most common causative organisms of occult bacteraemia are *Streptococcus pneumoniae* and *Haemophilus influenzae*. The widespread use of vaccinations against both of these organisms has made occult bacteraemia much less common.
**Teething does not cause significant or prolonged episodes of fever.
***Potential categories of causes include localised or generalised infection, connective tissue disease, and cancer. Miscellaneous specific causes include inflammatory bowel disease, diabetes insipidus with dehydration, and disordered thermoregulation. Pseudo-FUO is likely much more common than true FUO, because frequent, minor viral illness may be over-interpreted. In children, despite the numerous possible causes, true FUO is more likely to be an uncommon manifestation of a common disease, rather than an uncommon disease; respiratory infections account for almost one-half of cases of infection-associated FUO.

Febrile seizures occur at a time in childhood when the seizure threshold is low.[7] This type of epilepsy is unique in that it is always associated with a fever.[9] Causes that have been identified include a genetic predisposition, with possible polygenic inheritance.[7,9] A small number of families have been identified with an autosomal dominant inheritance pattern, where possible mutations have been found in genes that encode for the sodium-channel and the gamma amino-butyric acid-A (GABA-A) receptor.[8]

Febrile seizures can also be classified into three heterogeneous subgroups, based on the aetiology and the clinical features:[2]

- The largest subgroups consist of children having seizures in response to fever and an individual susceptibility which is genetically determined. The children in this subgroup have been convulsive only in response to the fever and, thus, their seizures are normally referred to as "true" or "pure" febrile convulsions.
- A smaller subgroup includes children that become convulsive with fever resulting from an unrecognised brain insult due to a febrile condition.
- The third group are children where the fever acts as a trigger to elicit true epilepsy and the convulsions continue to occur even in an afebrile state.

Children with simple febrile seizures may have the same risk of developing epilepsy by the age of seven years as others in the general population (1%).[6] The risk increases in children who have had multiple simple febrile seizures at the age of 12 months and younger, with a positive family history. The risk involved in these children increases to 2.4% for the development of generalised afebrile seizures by the age of 25 years.[6] There may be a possibility that genetic susceptibility to febrile seizures may eventually lead to epilepsy later in life. The increased risk has not been related to structural brain damage, but rather to the genetic predisposition.[2,6]

An infectious origin may also be a predominant cause of febrile seizures.[6] Viral illnesses have been identified in 2.6% of cases as the cause of fever leading to a febrile seizure.[3] Human herpesvirus (HHV)-6 is one of the viruses mostly associated with first-time cases of febrile seizures in children up to two years of age.[3] Other causes include influenza A virus and respiratory syncytial (RS) virus (usually during early spring and winter in annual epidemics).[3] Viral infections may be complicated by secondary bacterial infections. However, they are found to be lower in febrile children suffering from influenza A or RS virus infections.[2,3] To reduce the use of unnecessary antibiotics, children presenting with pyrexia should preferably be tested for virus infections.[2,3]

Mechanisms through which viruses have been postulated to cause febrile seizures include:[3]

- fever,
- a degree of fever to such an extent that exceeds the individual's threshold for convulsions, and
- an abnormal immune response to an infection and the presence of elevated cytokine levels.

Compared to viral infections, bacteraemia is a less frequent cause of febrile seizures.[2,3] However, *Streptococcus pneumoniae* has been implicated as a basis of simple febrile seizures by causing bacterial meningitis.[2,3,15] Meningitis should be ruled out in a child presenting with pyrexia. However, it is very unusual for a child with meningitis to present with only one seizure.[2,3,15] Other discriminate factors should also be taken into consideration, e.g. the presence of one or more of the major signs of meningitis, such as petechia, nuchal rigidity, etc.[2,3,15] Febrile seizures associated with shigellosis has not been related to the toxin of *Shigella dysenteriae*, but rather with the degree of fever and the level of dehydration associated with the accompanying loss of water and electrolytes.[3]

The use of alcohol and cigarette smoking during the prenatal period have been associated with an increased risk of developing febrile seizures in some studies.[16-18] In a Cohort study conducted,[19] prenatal exposure to low-to-moderate levels of alcohol and coffee had no impact on the risk for developing febrile seizures. However, modest smoking as a risk factor could not be ruled out completely.[19]

Evaluation and management of fever

In managing children with fever, the origin should be carefully investigated.[7,9,20] The following should be considered in the evaluation and management of fever:[1,14]

History of present illness

Note the degree and duration of the fever, method of measurement, and the dose and frequency of antipyretics used (if any).[1,14] Important associated symptoms that suggest serious illness, include poor appetite, irritability, lethargy, and changes in crying patterns (e.g. duration, character).[1,14] Conversely, associated symptoms that may suggest a possible cause, include vomiting, diarrhoea (including the presence of blood or mucus in the stools), coughing, difficulty breathing, favouring of an extremity or joint, and strong or foul-smelling urine. The patient's drug or medication use history should be reviewed for indications of drug-induced fever. Agents most commonly associated with causing fever, include the penicillins, cephalosporins, antitubercular agents, quinidine, procainamide, methyldopa, and phenytoin.[1,14]

If an infection is suspected, factors that predispose infants and children to infection should be identified:[1,14]

- In neonates, these factors include prematurity, prolonged rupture of membranes, maternal fever, and positive prenatal tests (usually for group B streptococcal infections, cytomegalovirus infections, or sexually transmitted diseases).
- For all children, predisposing factors include a recent exposure to infection (including family and caregiver infections), indwelling medical devices (e.g. catheters, ventriculoperitoneal shunts), recent surgery, travel and environmental exposures (e.g. to endemic areas, ticks, mosquitoes, cats, farm animals, or reptiles), and known or suspected immune deficiencies.

Review of systems

A thorough evaluation of symptoms suggesting possible causes, including runny nose and congestion (viral URI), headache (sinusitis, meningitis), ear pain or waking in the night with signs of discomfort (otitis media), cough or wheezing (pneumonia, bronchiolitis), abdominal pain (pneumonia, strep pharyngitis, gastroenteritis, UTI, abdominal abscess), back pain (pyelonephritis), and any history of joint swelling or redness (e.g. osteomyelitis).[1,14] A history of repeated infections (immunodeficiency) or symptoms that suggest a chronic illness, such as poor weight gain or weight loss (TB, cancer), should be identified.[1,14] Identify certain symptoms that can help direct the evaluation toward non-infectious causes; they include heart palpitations, sweating, heat intolerance (hyperthyroidism), and recurrent or cyclic symptoms (e.g. a rheumatoid, inflammatory, or hereditary disorder).[1,14]

Past medical history

Include and note previous fevers or infections and known conditions predisposing to infection (e.g. congenital heart disease, sickle cell anaemia, cancer, and immunodeficiency).[1,14] A family history of an autoimmune disorder or other hereditary conditions (e.g. familial dysautonomia) should be investigated. The vaccination history should be reviewed to identify patients at risk of infections that are vaccine preventable.[1,14]

Physical examination

As part of a physical examination, vital signs should be taken, noting abnormalities in temperature, heart and respiratory rate.[1,14] In ill-appearing children, the blood pressure (BP) should also be measured.[1,14] Temperature should be measured and any child with cough, tachypnoea, or laboured breathing requires pulse oximetry.[1,14]

The child's overall appearance and response to the examination are important.[1,14] A febrile child who is overly compliant or listless is of more concern than one who is uncooperative. However, an irritable infant or child who is inconsolable is also of concern.[1,14] The febrile child who looks quite ill, especially when the temperature has come down, is of great concern and requires in-depth evaluation and continued observation.[1,14] However, children who appear more comfortable after antipyretic therapy do not always have a benign disorder.

The following paediatric patients will require immediate attention and referral:

- Age < 1 month
- Lethargy, listlessness, or toxic appearance
- Respiratory distress
- Petechiae or purpura
- Inconsolable crying
- Seizures
- Difficult to awake
- Stiff neck

Treatment depends on whether the cause of the increased body temperature is due to fever or hyperthermia. Because the set point is normal in hyperthermia, but increased in fever, different approaches should be considered.[1,14]

The following principles apply to the management of fever:[1,14]

- Relief of the discomfort using pharmacological or environmental interventions to reduce the temperature set point back to normal.
- Antipyretics considered safe in paediatrics include paracetamol and selected nonsteroidal anti-inflammatory drugs (NSAIDs).
- Environmental measures to reduce fever include cooling measures, such as minimum clothing, exposing the skin to moving air, reducing room temperature, increasing air circulation, and cool moist compresses to the skin will be effective if used one hour AFTER the antipyretic has been administered.

Hyperthermia management principles include:[1,14]

- Antipyretics are of no value in hyperthermia as the set point of the temperature is already normal – thus, other cooling measures, as described in the aforementioned text, are more effective.

Temperature elevation in a critically ill child, whether caused by fever or hyperthermia, should be dealt with more aggressively, especially in cases of cardiovascular or neurological involvement.[1,14]

In all children with hyperthermia or fever, special attention should be given to the hydration status of the patient.[1,14]

Pharmacotherapeutic interventions

The following non-opioid related medicines are available for managing fever in children: paracetamol and NSAIDs, for example, naproxen, ibuprofen and mefenamic acid.[21]

Paracetamol

Paracetamol is one of the drugs of choice in fever and pain management due to its excellent safety profile and lack of any significant side effects.[22] It acts as a prodrug, with an

active cannabinoid metabolite. In the brain and spinal cord, paracetamol follows deacetylation to its primary amine (p-aminophenol) which is conjugated with arachidonic acid to form *N*- arachidonolylphenolamide, a compound known as an endogenous cannabinoid. The enzyme involved is called fatty acid amide hydrolase.[23] *N*-arachidonolylphenolamide is an agonist at the transient receptor potential cation channel, subfamily V member 1 (TRPV1) receptors and an inhibitor of cellular anandamide uptake, which leads to increased levels of endogenous cannabinoids, inhibiting cyclooxygenases in the brain at concentration that are probably not attainable with analgesic dosages of paracetamol.[23] It is of interest to note that a cannabinoid-1 receptor antagonist, given at a dosage level that completely prevents the analgesic activity of a selective cannabinoid receptor agonist, completely inhibits the analgesic activity of paracetamol as well. This fact allows us to explain the mechanism of action of paracetamol in more detail.[23] Despite this finding, however, the definite proof that the analgesic and antipyretic effects of paracetamol are dependent on COX-inhibition is still unclear. Hence, it works effectively when is combined with codeine for more effective control of moderate-to-severe pain and discomfort.[23]

Paracetamol-induced hepatotoxicity has been reported with a high dose, above the recommended dosage for paediatrics, which is 20 mg/kg/dose, given 8-hourly, and a maximum of 60 mg/kg/24 hours (or per Table IV), pointing to the fact that paracetamol may have a narrow therapeutic index.[8] Paracetamol is available orally, in several tablet and liquid formulations; however, the dosage should be guided by the age and general condition of the patient.[24]

Rectal administration of paracetamol in the postoperative setting has gained a lot of interest over the past few years, for children who are unable or unwilling to take this medication orally.[23] Recommended rectal dosages of paracetamol, for children over four weeks of age, are 20–30 mg/kg three times daily, with a maximum daily dosage of one gram.[23] Even though this is a useful route of administration, absorption of analgesics may vary in children, because of its unreliable bioavailability when using suppositories, thus limiting its applicability.[23] Most importantly, the slow onset of action caused by a limited rate of rectal absorption is a disadvantage in postoperative analgesia, hence the use of liquid formulation is highly recommended in children that are able to swallow the oral formulation.[23]

An intravenous formulation for children is also available; however, the current label indication is for the management of postoperative pain, during the first 24 hours only.

Nonsteroidal anti-inflammatory drugs

NSAIDs, such as ibuprofen, diclofenac, ketorolac and mefenamic acid, have antipyretic, analgesic and anti-inflammatory properties[23] NSAIDs works by inhibiting the enzyme cyclooxygenase (COX), which catalyses the conversion of arachidonic acid to prostaglandin E_2. Aspirin, however, should rather be avoided in paediatric practice (due to its potential for causing Reye's syndrome, especially in children between the ages of 4–12 years).[22,23]

Ibuprofen is one of the most frequently used NSAIDs for mild and moderate pain, because of its availability in a liquid form, allowing for easy administration to younger children.[25] The medicine has gained advantage in the market as it is available as an over-the-counter medication for fever reduction, as well as pain relief in infants and children. Studies have shown ibuprofen to be superior in terms of its safety profile, compared to ketorolac.[25] However, ketorolac has been used as a single agent for the treatment of postoperative pain, especially when used as an adjuvant to opioid analgesia, in children and adolescents, following painful interventional procedures.[26]

Mefenamic acid is a potent inhibitor of cyclooxygenase, with both central and peripheral analgesic action. It has efficacy and tolerability in paediatric patients with fever and is helpful in treating febrile illness in the paediatric populations.[27] It is recommended as a suitable alternative, second-line treatment for pyrexia in selected children; however, more clinical evidence is still required for wider routine use.[27]

The following should be taken into account when prescribing antipyretics to children:[28]

- Accurate dosing calculation based on an up-to-date measurement of weight.
- Prescribed strengths of liquid formulations should be double-checked.
- Ensure that the total volume of medicine does not exceed what is required.
- Ensure the child is not on any over-the-counter medicines, to avoid medicine duplication.

The use of paracetamol and ibuprofen should be individualised according to the child's age and weight, to ensure the most effective therapeutic effect. Certain conditions such as malnutrition, a poor nutritional state and the administration of other medicines should be taken into consideration, because they might have an influence on the rate of metabolism of paracetamol and ibuprofen, for example.[28] Table IV provides an overview of the dosage ranges for pain relief with paracetamol and ibuprofen.[28]

Febrile seizures should be distinguished from "seizures with fever".[23] The latter include seizures in any child with a fever of any cause.[23] Conditions such as meningitis, encephalitis, or cerebral malaria do not have febrile seizures, but rather seizures with fever.[23] Routine diagnosis using lumbar puncture in children presenting with simple febrile seizures

is not recommended.[23,25] However, the risk of meningitis is higher in younger children, and children that seem unwell, or where altered consciousness presents, further investigation is recommended.[23] Prophylactic treatment, such as the use of antiepileptic agents, is not recommended and has not proven to reduce the likelihood of future febrile seizures.[8,9,20]

Acute management of febrile seizures

Acute management of febrile seizures include the measures outlined in Table V.[7,9-11]

Children should be observed for several hours before they are to be discharged.[7,10] Discharge should only be considered if the origin of the fever has been established and treated, and if the child is clinically stable according to the treating physician.[7,10]

Parents

Parents are often anxious and fear that the child will die or suffer permanent brain damage.[7,10] These concerns have to be addressed and the parents should be reassured.[4,15] Upon discharge, the following information and health education should be given to the parents:[10,12,13]

- Most febrile seizures have an excellent prognosis.
- Educating the parents on first-aid when a seizure has occurred, e.g. correct body positioning (i.e. supine position turning the head so as to face sideways while tilted upward), do not attempt to insert anything into the mouth and do not give any drugs or fluids orally.
- Simple techniques, e.g. how to measure temperature, how and how much of the antipyretic to administer, etc., should be reinforced.
- Should the child have another seizure, the parents should note the following:
  - an accurate description of the seizure, including its duration,
  - information about the nature of the seizure,
  - the child's body temperature at the time of the seizure, and
  - any other signs and symptoms that may have accompanied the seizure.

Prognosis

Most authors agree that the likelihood of febrile convulsions causing neurological abnormalities, or developing lasting mental disturbances is low.[7,9,10,13] The risk of developing an intellectual deficit is higher in those that already suffer from a pre-existing neurological or developmental abnormality, or in those patients that subsequently develop afebrile seizures.[10] About one-third of children that develop a single febrile seizure will develop another; this ratio may increase to half of patients if the initial onset was below one year of age.[10,13]

Children suffering from febrile seizures have a slightly higher risk of developing epilepsy compared to other children (2% vs 1%). The risk factors for developing epilepsy are also dependent on:[10]

- pre-existing neurological defects/abnormalities,
- family history of afebrile convulsions, and/or
- complex first febrile convulsion.

Prophylaxis for recurrent febrile seizures

There may be some evidence that both continuous antiepileptic therapy with phenobarbital, primidone, or valproic acid, as well as intermittent therapy with oral diazepam, are effective in reducing the risk of recurrence of febrile seizures. The toxicities associated with these drugs outweigh the relatively minor risks associated with febrile seizures.[6,7] Phenobarbital depresses cognitive performance

Table IV: Recommended dosages of paracetamol and ibuprofen for the relief of pain and fever in neonates, infants and children (oral route)[28]

Medicine	Neonates from 0 to 29 days	Infants from 30 days to 3 months	Infants from 3 to 12 months, or children from 1 to 12 years	Maximum daily dosage
Paracetamol	5–10 mg/kg every 6–8 hours	10 mg/kg every 4–6 hours	10–15 mg/kg every 4–6 hours	Neonates, infants and children: 4 dosages per day
Ibuprofen	-	-	5–10 mg/kg every 6–8 hours	Children: 40 mg/kg/day

Table V: Acute management measures for the treatment of febrile seizures[7,9-11]

Measure		✓
1	Airway – Maintain a patent airway	✓
2	Breathing – Ensure effective breathing; oxygen may be administered if available	✓
3	Protect the child from injury – Place in a semi-prone position and remove any excess or loose clothing	✓
4	Fever – Treat the fever by sponging down with lukewarm water and administer antipyretics, e.g. paracetamol or ibuprofen	✓
5	Depending on the duration of the seizure the following may be administered according to the physician's prescription: • *Rectal diazepam if the seizure lasts for more than 5 minutes* • *A suitable intravenous anticonvulsant (i.e. diazepam, lorazepam or phenobarbital) if the patient is still convulsing for longer than 15 minutes*	✓

in children treated for febrile seizures and this side-effect outlasts the administration of the drug by several months; is not offset by the benefit of seizure prevention.[29]

The use of diazepam may decrease the number of febrile seizures when administered at the onset of fever.[7,10] Intravenous diazepam controls seizures more quickly compared to intranasal midazolam. However, intranasal midazolam may be just as safe and effective as diazepam, and could be used not only in hospitals and medical centres but with appropriate instructions by families of children suffering from febrile seizures at home.[30]

Carbamazepine and phenytoin has not proven to be effective in preventing simple febrile seizures. This may be the case even when the agents are within their respective therapeutic ranges.[6]

Evidence that antipyretic treatment prevents the recurrence of febrile seizures remains scarce. The use of an antipyretic agent should be given to provide comfort to the patient and to prevent dehydration. Adequate fluid intake should be maintained.[31] The two widely-preferred antipyretics used in the management of fever in children remains paracetamol and ibuprofen, in their relevant paediatric dosage ranges, given to relieve discomfort secondary to fever.[7]

Conclusion

Most acute fevers in children are caused by viral infections. The other possible causes and evaluation of acute fever differ depending on the age of a child. A rare but real number of children below the age of 24 months, with fever without localising signs (primarily those who are incompletely immunised), can have pathogenic bacteria in their bloodstream (occult bacteraemia) and be early in the course of a potentially life-threatening infection. Teething in itself does not cause significant fever. The use of antipyretic agents does not alter the outcome but may make children feel better.

Febrile seizures are a more common seizure disorder in childhood. Children suffering from febrile seizures should be evaluated to ensure that there are no underlying disorders; however, should one be discovered, this should be treated. Prompt diagnosis, reassurance and education of the parents should decrease anxiety. Medicine management should be individualised to the type of seizure and the patient's specific health care needs.

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