

Problems in Family Practice

Fever in Childhood

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A clinical approach to the diagnosis of fever in childhood is presented. Fever can be caused by a viral or bacterial infection, drug reaction, collagen disease, neoplasm, central nervous disorder, blood diseases, or physiological changes.

Short-term fever is usually a viral infection but may be a bacterial infection. Careful history and physical examination play the major role in making the diagnosis, followed by appropriate studies: throat culture, urinalysis, blood counts, x-rays, blood cultures, and specific tests. The latter are indicated for the diagnosis of prolonged fevers, which also are usually caused by common disorders. A high sedimentation rate is more likely to be associated with a serious disorder and warrants immediate investigation. Treatment is symptomatic; one should reserve specific treatment and/or antibiotics for specific illness.

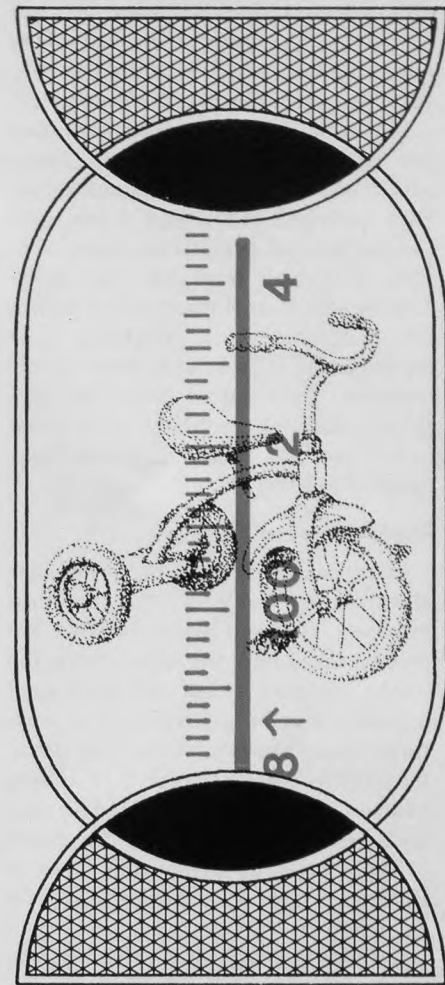
Fever in childhood is both common and challenging to the family physician and pediatrician in everyday practice. Although fever is most often caused by relatively minor, self-limiting illness, it may herald the onset of serious disease. This paper will outline some basic physiologic principles, describe the major causes for fever, and suggest some useful approaches to the diagnosis of its underlying cause in children that can facilitate rational and effective therapy.

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Basic Physiologic Principles

Humans, being homeothermic, with a delicate balance between heat loss and heat production, have an unrivalled adaptability to climatic conditions. If the body temperature rises, thermo-regulators in the hypothalamus induce peripheral vasodilatation and increase sweating with loss of heat. Inhibiting this loss by tight-fitting clothing, a high ambient temperature or humidity can increase the fever. Should the temperature fall, further loss of heat is prevented by peripheral vasoconstriction while extra heat is generated by increased metabolism and shivering. The newborn, more so if premature, exposed to cold cannot shiver and relies on brown adipose tissue for heat production.¹ The infant must be kept warm to prevent hypothermia.

The body temperature is not



constant. Soon after birth a circadian rhythm appears with a diurnal variation of over 2 F, being lowest in the early morning and highest in the late afternoon. Physicians may be persuaded by an overanxious parent to investigate a child for fever when both have misinterpreted the normal peak of the diurnal rhythm as abnormal. Eating and exercise raise the temperature. A teenager playing tennis on a hot afternoon can develop a fever.

The average oral temperature is 98.6 F (37.0 C) varying from 96.7 F to 99 F (36 C to 37.2 C). The rectal temperature is higher by 1 F and the axillary temperature correspondingly lower. The fever of infection is presumed due to the release of pyrogens, from granulocytes "injured" by microorganisms, which act on the thermo-regulators setting the thermostat at a higher level. No one is quite

sure whether fever is good or bad either for the host or the attacking microorganism and whether we do better to encourage or discourage it.²

Fever probably plays little if any part in resistance to infection.² Most adults with fever feel uncomfortable with malaise, aches and pains, and gastrointestinal symptoms. Many children with high fever will run about happily if left unclothed, while others are miserable with relatively low temperature. If insensible water loss is replaced, fever (apart from the rare febrile seizure) probably does little harm and has much diagnostic and prognostic value.

Major Causes of Fever

The major groups of fevers are classified in Table 1. For practical purposes, those of short duration are readily diagnosed and over within the week, whereas those of prolonged duration remain undiagnosed or continue more than two weeks. The latter, by tradition, are called F.U.O. (Fever of Unknown or Undetermined Origin) until resolved. Table 2 lists the causes of 206 cases of prolonged fever in children based on a recent study by Pizzo and co-workers.³

Over 80 percent of febrile illness in children is related to viral infection so that knowing the current epidemiology is useful. By far the most common site of infection is the upper respiratory tract, followed by the gastrointestinal and lower respiratory tracts.⁴

The common bacterial infections involve the middle ear, pharynx, skin, lungs, urinary tract and, in much smaller numbers although more serious, the brain meninges, bones, joints, and bloodstream. Localized abscess may be found in the brain, chest, or abdomen.

Many drugs (penicillin, ampicillin, atropine, sulfonamides, streptomycin, barbiturates, diphenylhydantoin, immunizations, etc) can induce fever in predisposed individuals. The fever starts about seven days after the drug is taken for the first time or soon after the first dose in a patient previously sensitized.⁵ The fever may be part of a generalized serum sickness syndrome or may be the only sign of hypersensitivity with no evidence of rash, urticaria, eosinophilia, or neutropenia and may precede more serious reactions.

Certain plants and berries found in fields and the home, if ingested, can poison. Those containing the alkaloid atropine (Deadly Nightshade, Jessamine, Thorn Apple) cause dilated pupils, flushed skin and high fever, and may be fatal.⁶ The newborn is very reliant on ambient temperature and if the nursery or incubator is too warm, the newborn becomes feverish. Dehydration and sepsis are the two major clinical problems associated with fever, although the latter, if overwhelming, causes hypothermic shock.

All severely burned children are in a state of hypermetabolism and have both elevated temperature and leucocytosis. Additional causes of fever in the burned child must be considered and ruled out, including wound sepsis, infected catheters in bladder or vein, atelectasis and pneumonia.

Diagnosis of Cause of Fever

Short-term Fever

1. Clinical Clues. A careful history and physical examination reviewing all systems for diagnostic clues (Table 3) will identify the cause of fever in the great majority of children seen in the office or at home.^{4,7} The height of the fever does not determine the severity of the illness. An infant with roseola infantum can have a temperature of 105 F (40.6 C) and look well, while a child with meningococcal septicemia may be hypothermic and moribund.

The nature of lymphadenopathy, enanths and exanths, often provides useful diagnostic clues in determining the cause of short-term fever in children. Table 4 presents those clinical problems which are characteristically associated with various locations of lymphadenopathy. Looking in the mouth and recognizing the enanthem can also be most rewarding to the physician pursuing the cause of fever, as shown in Table 5. The prodromal period of the classic exanths is likewise frequently of diagnostic value (Table 6).

Although measles and rubella are becoming uncommon, they still occur in the child not adequately immunized. The above rashes, being macular, blanch on pressure — purpura does not. Purpura in a feverish child is septicemia until disproved, usually by negative blood cultures and benign

Table 1.
Fever — Major Diagnostic Groups

Infectious
viral
bacterial — generalized and localized
Drug reactions
Collagen diseases
Neoplasms
Serum sickness
Central nervous system
hemorrhage
tumor
postoperative
Blood diseases
leukemia
hemolytic anemia
bleeding into viscera
Physiological
exercise
eating
circadian rhythm
ovulation
Miscellaneous
heat
burns
factitious

clinical course. This is one of the rare instances when immediate intensive antibiotic therapy is indicated pending the laboratory results. Purpura may be also found with viral infections, leukemia, and collagen disease. A feverish rash which does not conform with the above may be caused by an ever-increasing number of drugs⁵ or collagen disease.

Roseola infantum is a common cause of high fever in infancy which is often associated with febrile seizures. During the fourth-day prodrome the infant may have a temperature of 105 F (40.6 C) yet appear reasonably well. Pathognomonic enlargement of small clusters of suboccipital lymph nodes can be palpated on the second day. The white blood count shows a neutropenia with relative lymphocytosis. On the fifth day the fever falls and the "unexpected rash" (exanthem subitum) appears sparsely on the trunk. These infants when mistreated

with penicillin for the fever are often victimized as "penicillin sensitive" because of the roseola rash.

Bacterial pneumonias are nowadays less frequently seen in children outside of the hospital⁸ and should be suspected if the initial temperature is over 104 F (40 C), the white blood count is over 15,000/cu mm with polymorphonuclear leukocytosis, and the x-ray reveals a lobar involvement. The common organism is D. Pneumonia in children over six years of age, whereas H. Influenza must be considered in younger children.

Childhood tuberculosis is now rare in the United States. If the tuberculin test is negative, infection with M. Tuberculosis is unlikely apart from the false negatives found after certain viral infections and immunizations.

A temperature of over 105 F(40.6 C) is uncommon in a child, but should it occur, the following causes should be considered: lesion within the brain, heat stroke, drug fever, fulminating infection, and cystic fibrosis (during a heat wave) and malignant hyperthermia after anesthesia.

2. Laboratory Studies. If the diagnosis is not obvious, the physician must decide whether to order laboratory tests, send the child home to be reviewed again later, or admit the child to the hospital. It is not the height of the fever that is important but the presence of other signs and symptoms and how ill the child appears. Laboratory tests play a small, albeit important, part in the diagnosis of the short-duration fever, the inexperienced clinician requesting far more tests than the experienced. The more useful tests are the throat swab confirming streptococcal infection, the x-ray detecting pneumonia, and the urinalysis. Children with urinary tract infection present with systemic rather than localizing signs and symptoms. Even though the yield is small, every child with undiagnosed fever must have the urine examined for pus cells and organisms.

The traditional white blood count can be helpful but confusing, since polymorphonuclear leukocytosis occurs not only with bacterial infection but also with collagen and viral disease. Routine blood cultures in the feverish child with no obvious signs and symptoms of septicemia will show positive bacteremia in only four percent, more so if the temperature is

Table 2. Prolonged Fever in Children*

Diagnosis	Under 6	Over 6	Total
Infections	34	18	52
Bacterial	20	12	32
Viral	13	4	17
Urinary tract	3	1	4
Bacterial meningitis	3	0	3
Pneumonia	3	1	4
Tonsillitis	3	1	4
Septicemia	2	0	2
Sinusitis	2	1	3
Malaria	1	0	1
Peritonsillar abscess	1	0	1
Osteomyelitis	1	1	2
Enteric fever	1	1	2
Endocarditis	0	3	3
Streptococcosis	0	2	2
Tuberculosis	0	1	1
Collagen — Inflammatory	4	16	20
Rheumatoid arthritis	3	7	10
Lupus erythematosus	0	3	3
Regional enteritis	0	4	4
Ulcerative colitis	0	1	1
Schönlein-Henoch	1	0	1
Malignancy	4	2	6
Leukemia	3	1	4
Lymphosarcoma	0	1	1
Reticulum cell sarcoma	1	0	1
Miscellaneous			
Central nervous system	2	0	2
Agranulocytosis	1	0	1
Lamellar ichthyosis	1	0	1
Milk allergy	1	0	1
Aspiration pneumonia	1	0	1
Agammaglobulinemia	1	0	1
Behçet's syndrome	0	1	1
Hepatitis	0	1	1
Ruptured appendix	0	1	1
Undiagnosed	3	9	12
Total	113	93	206

*Adapted from Pizzo et al³

Table 3. Diagnostic Clues to Cause of Fever

Sign or Symptom	Possible Diagnosis
Respiratory Tract	
coryza, sore throat, cough, enanthem	Viral URI
sore throat, temperature over 102 F, follicular exudate	Streptococcal
earache, crying infant with coryza	Otitis media, mumps
viral pneumonia with otitis media	Mycoplasma
sick bird in house	Psittacosis
grunting, tachypnea, alae nasi	Pneumonia
active cough	
conjunctivitis	Adeno-pharyngo conjunctival fever
Central Nervous System	
headache, vomiting	Meningitis
irritable, drowsiness, purpura	Meningitis
bulging fontanelle, neck rigidity, Brudzinski positive	
any infant with F.U.O.	Meningitis
previous meningitis	Subdural effusion
Gastrointestinal Tract	
abdominal pain, vomiting, diarrhea	Gastroenteritis
bloody diarrhea	Dysentery, regional enteritis
diarrhea with seizures	Shigella
tender right iliac fossa	Appendix abscess
with rigidity	
tender right iliac fossa	Mesenteric adenitis
dark urine, pale stools	Hepatitis
localized tenderness	Localized abscess
malabsorption, recurrent pneumonia	Cystic fibrosis
Genitourinary	
pyuria, bacilluria, frequency, bed-wetting	Urinary tract infection
Bones and Joints	
painful joints with swelling	Collagen disease, septic arthritis
migratory arthritis, carditis, erythema marginatum, subcutaneous nodules	Rheumatic fever
localized tenderness near epiphysis	Osteomyelitis
Black child with tender bones	Salmonella, osteomyelitis
Cardiovascular	
murmurs	Rheumatic fever, subacute bacterial endocarditis
Skin	
rash	Exanthem, collagen disease, drugs, septicemia
purpura	Septicemia, leukemia
palmar rash, tick bite	Spotted fever
cat scratch, tender lymph nodes	Cat scratch fever
septic lesion — red line, tender nodes	Lymphangitis
bluish cellulitis	Hemophilus influenza
Miscellaneous	
recurrent fever, abdominal pain, pleuritis	Periodic disease
recent immunization, insect bite	Serum sickness
pupils dilated, flushed	Poisoning with atropine or belladonna, plants
recent intramuscular injection	Sterile abscess
child from Vietnam	Malaria
contact with tuberculosis	Tuberculosis

over 102.9 F (39.4 C) and the white blood count higher than 20,000/cu mm.⁹ The doctor in his office is unlikely to carry out this procedure. Reexamination of the child is far more useful since an enanthem, otitis media, pneumonia, rash, or lymphadenopathy then becomes obvious. Fluorescent antibody techniques have expedited bacteriological and virological confirmation but are not readily available.¹⁰ Bedside tests for infectious mononucleosis and the tine test have obvious value.

The need for a lumbar puncture will vary with the physician's confidence in recognizing the cause for the fever and his clinical exclusion of meningitis. The infant with meningitis may show no signs of meningeal irritation; and a lumbar puncture is essential to exclude this diagnosis.

Prolonged Fever

1. Clinical Clues. If the fever remains undiagnosed after one week, we aim our sights at the causes of prolonged fevers (Table 2). F.U.O. in adults is a problem lasting three weeks or more with the temperature exceeding 101 F (38.3 C) on several occasions and no established diagnosis after the first week.^{11,12} Prolonged fever in children continues at least two weeks with a rectal temperature over 101.3 F (38.5 C) on more than four occasions.³ These children do not have the exotic diseases found in the adult,^{3,11} but rather more common childhood illnesses either with an unusual presentation or confused by improper antibiotic or antipyretic therapy. Certain illnesses are more common at certain ages. Pizzo et al in their excellent review of prolonged fever in childhood found that most of the children had many nonspecific symptoms, presumably related to the fever. Children with malignancy, leukemia, and collagen disease had either a rash or pruritis, joint involvement, or significant cardiac murmurs.³ Lymphadenopathy with enlargement of spleen and liver was commonly found but was neither diagnostic nor related to outcome except in those children with malignancy. Children with pneumonia or various viral diseases often have a palpable spleen which disappears when the acute illness is over.

Chronic factitious fever is some-

Table 4. Lymphadenopathy and Cause of Fever

Site	Probable Diagnosis
Localized	
Axillary	Cat scratch fever, infection on hands
Supratrochlear	Rheumatoid arthritis, infectious mononucleosis
Cervical (posterior)	Viral URI, adenoiditis, infectious mononucleosis
Cervical (anterior)	Tonsillitis (viral, streptococcal) infectious mononucleosis
Submental	Herpes and coxsackie or circuncoral impetigo
Suboccipital	Roseola infantum, pediculosis capitis with staphylococcal infection
Retroauricular	Rubella
Inguinal	Infection on feet or perineum
Diffuse (with or without enlarged spleen, liver)	
	Generalized viral infection
	Infectious mononucleosis
	Leukemia
	Rheumatoid disease
	Malignancy, lymphosarcoma (a hard lymph node must be biopsied)

times seen in puberty. In spite of months of fever, these youths do not appear ill, have a normal pulse rate and sedimentation rate, and warrant psychological intervention.¹³

2. Laboratory Studies. Clinical acumen should dictate specific tests at appropriate times rather than a routine battery of investigations. For example, studies for immunologic deficiency may be indicated in the child with recurrent serious infections; bacteriological examination of swabs and various body fluids by gram stain, culture, or by fluorescent antibody technique is useful in specific infections;¹⁰ and ultrasound may be helpful in detecting a localized abscess in the abdomen.

In their study of prolonged fever in children, Pizzo and co-workers found that the white blood count was normal in 45 percent of cases, with a polymorphonuclear leukocytosis in 90 percent of the children with collagen disease, 75 percent with bacterial and 50 percent with viral infection. The erythrocyte sedimentation rate was raised in children with malignancy, leukemia, and bacterial infection, but

if under 10 mm (Wintrobe) a non-serious disease or viral infection was more likely. Examination of urinary sediment confirmed presence of urinary tract infection, endocarditis, and collagen disease, and urine culture revealed bacilluria. A reversed albumin/globulin ratio and various changes in electrophoretic pattern were more likely with collagen disease but could occur with viral infection. Radiological studies were useful in the identification of pneumonia and regional enteritis and in the later stages of osteomyelitis. Biopsy studies of bone marrow, lymph nodes, and liver were diagnostic in children with leukemia, lymphosarcoma and agranulocytosis.³

Management of Fever

Treatment of Underlying Cause

Fever is clearly but a symptom of an underlying process which requires careful diagnosis of its specific cause before rational and effective therapy can be instituted. Antibiotic treatment of viral infection, for example, neither shortens the illness nor prevents secon-

dary infection. Such treatment may confuse the issue and should be resisted.¹⁴ Antibiotic therapy, as with other forms of therapy, should be based upon a specific diagnosis. Organisms are constantly becoming resistant, and recent reviews of antimicrobial therapy should be consulted.¹⁵

Symptomatic Treatment

In instances where the cause of fever is viral or diagnostic procedures are in process, it may be appropriate to provide symptomatic treatment. Although reducing fever may be irrational, it is more difficult to persuade a parent or nurse to allow the fever to continue. Some feverish children seem restless and miserable and are made more comfortable by the following simple procedures. These measures are particularly important if there is a previous history of febrile convulsion.

1. Undress the child with fever. This permits exposure of the skin and facilitates loss of heat. The undressed child with fever seems much more comfortable, whereas the overclothed child is miserable as the fever rises higher. An electric fan will increase heat loss.
2. Lukewarm sponging or bathing is the best way to reduce the fever and is even more effective when combined with antipyretics. Alcohol rubs are no longer used and ice packs are reserved for children with heat stroke.
3. Antipyretics. These must be used with caution as more children die from antipyretics than from pyrexia.

A. *Salicylates.* Aspirin (10 mgm/kg dose every six hours). Once the antipyretic of choice, aspirin has certain disadvantages. It causes gastrointestinal irritation with bleeding, it may induce hypersensitivity, and it is still the leading cause of death by poisoning.¹⁶

B. *Acetaminophen* has become popular because it causes no gastrointestinal bleeding, will not mask the arthritis of rheumatic fever, and has no effect on coagulation in therapeutic doses. However, the drug is toxic and must be treated with respect. Adverse reactions include hepatic necrosis (often fatal), agranulocytosis and hypoglycemia.^{17,18}

The feverish child, by tradition, is put to bed, yet no one has proven the value of bed rest. Studies have shown

Table 5. Correlation of Enanthem with Cause of Fever

Diagnosis	Enanthem	Exanthem
Coxsackie (Herpangina)	Painful vesicles and ulcers, posterior oropharynx	Maculae — "bug bites" vesicles Hand, foot, mouth
Herpes	Painful vesicles and ulcers, anterior oropharynx	Papules, vesicles, ulcers Face, hands, diaper area
Echo 16	Ulcers, palate	Maculae, papules
Echo 9	Vesicles — buccal mucosa	Maculae, papules, sometimes associated with aseptic meningitis
Measles	Koplik's spots	Blotchy maculae
Varicella	Vesicles and ulcers	Dew drop vesicles
Adeno virus	Vesicles, pharynx, and buccal mucosa	May be conjunctivitis (Adeno-pharyngo-conjunctival fever)
Streptococcal	Scarlet oropharynx Follicular exudate Palatal petichiae Strawberry tongue	Punctate erythema Circumoral pallor
Infectious mononucleosis	Tonsillo-pharyngeal exudate Palate petichiae	Maculae (especially after ampicillin)

Table 6. Common Exanthems

Prodromal Period*	Diagnosis	Rash	Confirmatory Signs
(Days)			
1	Varicella	Fragile vesicles "Dew drops"	Also in mouth and on scalp
	Rubella	Discrete maculae	Retroauricular nodes
	Erythema infectiosum	Lattice work erythema	Comes and goes
2	Scarlet fever	Punctate erythema	Streptococcal pharyngitis
3	Spotted fever	Palmar maculae Centripetal spread	Tick bite
4	Measles	Blotchy erythema	Koplik's spots
5	Roseola infantum	Sparse maculae	Suboccipital nodes Temperature falls before rash appears

*From onset of fever and eruption of rash.

that feverish children allowed to remain up and about do no worse than children confined to bed, and they are much happier.^{16,19,20} Bundling a feverish child can only inhibit heat loss and lead to a higher temperature. If a child has a fever parents are fearful of drafts, but leaving the windows open or closed makes no difference.²¹

If the child and parent are well known to the physician, and if a recognizable viral illness is epidemic, telephone advice for the symptomatic management of fever may at times be permissible. The parents must report if the child gets worse. Telephone prescription for antibiotics when the child has not been seen should generally be avoided.

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