

DiPiro's Pharmacotherapy: A Pathophysiologic Approach, 12th Edition >

Chapter e9: Fever

Jamal Brown; Juan Mosley, II

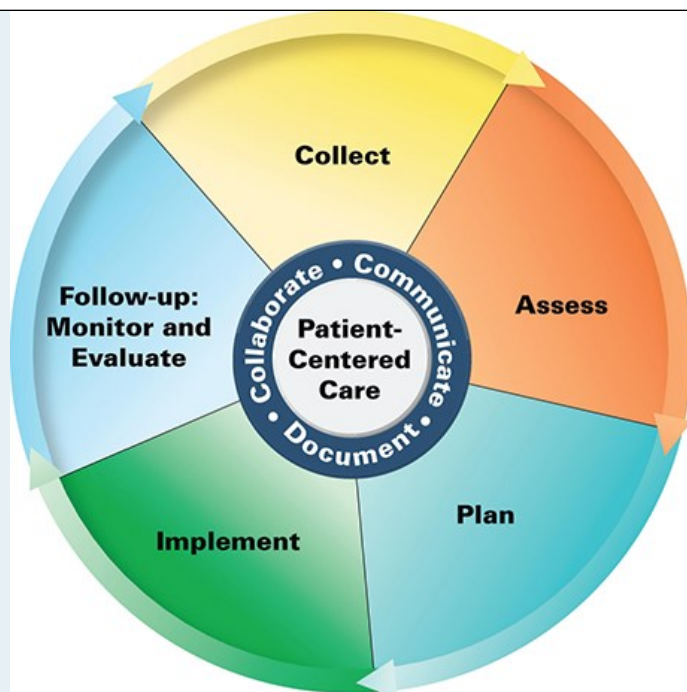
KEY CONCEPTS

KEY CONCEPTS

- 1 Fever can be a by-product of various infectious or pathologic processes, vaccinations, medications, and environmental exposure, or of vigorous activity.
- 2 Normal body temperature fluctuates and is regulated in the thermoregulatory center of the anterior hypothalamus. During a fever, prostaglandins cause an increase in the hypothalamic temperature set point and thereby increase production of heat in the periphery.
- 3 Healthcare professionals should COLLECT key information on medications, medical history, immunizations, recent travel, social history, barriers of care, and course of fever.
- 4 Using the gathered data, ASSESS information to differentiate symptoms from surrounding conditions, determine appropriateness for self-care, evaluate history for causes of fever, and consider the most appropriate medication for fever.
- 5 Goals of therapy include relieving discomfort, reducing body temperature, and when appropriate treating the underlying cause of fever.
- 6 Nondrug treatments include the use of cooling blankets, which should only be used along with antipyretics. Appropriate hydration and the use of fans also contribute to decreasing body temperature.
- 7 Nonsteroidal anti-inflammatory drugs (NSAIDs) reduce fever, but they can adversely affect the gastrointestinal tract and platelets. For this reason, acetaminophen is the preferred agent to reduce fever in most patients. Therapy with NSAIDs and acetaminophen combinations can be used in most but not all patients.
- 8 Medical evaluation should be sought if symptoms of fever do not resolve with over-the-counter treatment within 24 hours in children younger than 2 years, 48 hours in other children and 3 days in adults. Also, a medical evaluation should occur in patients with alarming symptoms regardless of their temperature.

PATIENT CARE PROCESS

Patient Care Process for Fever



Collect

- Patient demographics (eg, sex, age, pregnancy)
- Active medical problem list
- Medication history/list (prescription and over the counter) and adherence
- Inquire about immunizations
- Inquire about history of allergies and adverse effects
- Inquire about recent travel, climate, and social activities
- Gather log of temperatures and duration of current symptoms
- Collect information pertaining to the patient's medication experience (eg, beliefs, expectations, and cultural considerations related to medications)
- Inquire about the patient's ability to access medications, considering ability to pick up medications and ability to afford medications
- Inquire as to how the process of managing medications works at home (eg, pill boxes, calendars, reminders)

Assess

- Decipher appropriateness of self-care for the patient
- Complete differential diagnosis between fever, hyperthermia, and hyperpyrexia
- Evaluate activities and social factors that may predispose the patient to fever
- Assess recent travel and potential environmental causes of fever
- Analyze the patient's active and prior medical conditions for associations with fever

- Assess the indication, safety, adherence, and effectiveness of each medication the patient is taking
- Understand patient's willingness to take over-the-counter (OTC) therapy for fever and if religious/cultural barriers to therapy exist
- Consider interactions between current OTC, prescription, and herbal medications when assessing therapy options for fever

Plan

- Develop a care plan to reduce fever and underlying cause
- Identify the monitoring parameters such as temperature and discomfort to assess ongoing effectiveness, safety, and adherence, including frequency of follow-up monitoring
- Design personalized education on checking temperature consistently and nonpharmacological approaches to reduce temperature
- Review and reconcile all medication lists to arrive at an accurate and updated medication list
- Determine who will implement components of the care plan
- Determine the appropriate timeframe for patient follow-up
- Determine the appropriate mode for follow-up or referral

Implement*

- Discuss the care plan with the patient and direct selection of appropriate over-the-counter therapy
- Educate the patient on the most appropriate antipyretic medication and goals of therapy, adverse effects, interactions, and precautions
- Ensure patient understanding and agreement with the plan
- Communicate instructions for follow-up and discuss must appropriate follow-up if needed

Follow-up

- If therapy is not effective in 3 days in adults, within 48 hours in children age 2 years or older, or within 24 hours in children younger than 2 years, advise the patient or caregiver to seek medical care. Depending on the presence of alarming symptoms, urgent/emergent care may be needed.

*Collaborate with patients, caregivers, and other healthcare professionals.

BEYOND THE BOOK

BEYOND THE BOOK

In a small group, create a drug treatment table of OTC products for fever. Consider appropriate age, mechanism of action, dosing schedule, disease interactions, drug interactions, and cost. Compare and contrast these agents based on these factors and create an "optimal" situation to use each medication. Also, create a list of conditions that mimic symptoms of fever. This will assist you during the Assess phase of the Patient Care Process.

INTRODUCTION

Healthcare professionals are often the first point of contact for patients who present with nonspecific symptoms that can be transient and self-limiting or that indicate the presence of serious disease. Collecting the information needed to assess these symptoms and make a recommendation to patients is a common and important activity of health professionals as they provide direct patient care.

1 Elevated body temperature is one of these cardinal manifestations of disease. Fever and elevated temperatures can be associated with many etiologies related to recent travel, illnesses, activity, and environmental factors. Healthcare professionals have an opportunity and responsibility to decipher information to help patients find an appropriate treatment to decrease temperatures and alleviate associated symptoms or to seek more extensive medical evaluations.

A systematic process for assessing elevated temperatures includes asking the patient or caregiver for specific facts about the condition, examining the patient and measuring the body temperature, assessing the collected information, developing and implementing a treatment plan (including referring the patient when red flags to self-treatment are present), and scheduling appropriate follow-up. This chapter reviews the causes of fever in a clinic or pharmacy setting and appropriate evidence-based treatment to alleviate symptoms.

EPIDEMIOLOGY AND ETIOLOGY

Fever and elevated temperatures are common reasons for visits to ambulatory care settings. According to the National Ambulatory Medical Care Survey, fever is the third leading cause of emergency department visits in all patients and the leading cause of these visits in patients younger than 15 years old.^{2,3} In emergency department settings, 5.5 million patients are treated annually for fever in the United States.

Fever and upper respiratory infections were the most common reasons for return visits to urgent care and emergency departments in a pediatric study.⁴ Fever is regarded as one of the most common reasons for office visits, emergency department encounters, and after-hours telephone calls.⁵

ANATOMY AND MECHANISM OF DISEASE

2 Body temperature is regulated by the thermoregulatory center in the anterior hypothalamus and fluctuates throughout the day.⁶ The circadian rhythm controls the internal thermostat, which is set between the morning low temperature and the afternoon peak temperature. When a patient has a fever, the hypothalamus has been “reset” to a higher temperature.

Fever is defined as a controlled elevation of body temperature above normal range, which is from 36.7°C to 37°C (98°F–98.6°F) orally. Rectal temperatures are 0.6°C (1°F) higher and axillary temperatures are 0.6°C (1°F) lower than oral temperatures.

Fever can originate from infections, malignancies, autoimmune disorders, and other causes.⁷ As causes of fever, inflammatory diseases and fever of unknown origin (often in complex patients with many potential causes) have increased over time, while infections and malignancies have decreased.¹ Many common infections can cause fever such as osteomyelitis, appendicitis, meningitis, and disorders of the skin, respiratory tract, urinary tract, sinuses, and ears.^{8,9} Common malignancies with a manifestation of fever include lymphoma, leukemia, renal cell carcinoma, and hepatocellular carcinoma.¹⁰

Various medications can also be the cause of fever and must be evaluated in patients presenting with symptoms (Table e9-1). A drug-induced fever is a persistent fever without an infection or another underlying condition. Drug regimens must be evaluated in patients presenting with signs and symptoms of fever to rule out potential causative agents. In this type of fever, symptoms coincide with the administration of the offending agent and subside on its withdrawal, after which the temperature remains normal. Numerous medications can produce fever, but β -lactam antibiotics, anticonvulsants, allopurinol, hydralazine, nitrofurantoin, sulfonamides, phenothiazines, and methyldopa are most often implicated.

TABLE e9-1

Medications that Can Cause Fever

- **Anticonvulsants**
 - Barbiturates
 - Carbamazepine (eg, Tegretol)
 - Phenytoin (eg, Dilantin)
- **Antimicrobials**
 - Carbapenems
 - Cephalosporins
 - Erythromycin
 - Isoniazid
 - Minocycline (eg, Minocin)
 - Nitrofurantoin (eg, Furadantin)
 - Penicillins
 - Rifampin
 - Sulfonamides
- **Cardiovascular drugs**
 - Captopril (eg, Capoten)
 - Hydralazine
 - Hydrochlorothiazide
 - Methyldopa
 - Nifedipine (eg, Procardia)
 - Procainamide
 - Quinidine
- **Histamine H₂ antagonists**
 - Cimetidine (eg, Tagamet)
 - Ranitidine (eg, Zantac)
- **Nonsteroidal anti-inflammatory drugs**
 - Ibuprofen
 - Salicylates
 - Sulindac (eg, Clinoril)
- **Others**
 - Allopurinol (eg, Zyloprim)
 - Heparin
 - Meperidine (eg, Demerol)
 - Phenothiazines

Data from References 11–14.

COLLECT

3 When patients present to a community or other ambulatory settings with symptoms of fever, the first step in the patient care is collecting information from the patient, medical chart, history, or family members. The complaint of fever should be based on a reading from a thermometer as compared to feeling a part of the forehead or other body part for an increase in warmth. During the course of the fever, patients should use the same thermometer and site of measurement, as temperatures can vary with different instruments and sites of measurement (Table e9-2).

TABLE e9-2

Normal Temperature Ranges when Measured at Different Body Sites

Body Sites (Type of Measurement)	Normal Ranges	Fever Point
Axillary (mercury in glass; electronic)	34.7°C-37.4°C (94.5°F-99.3°F)	37.4°C (99.4°F)
Sublingual (mercury in glass; electronic)	35.5°C-37.6°C (95.9°F-99.6°F)	37.6°C (99.6°F)
Rectal (mercury in glass; electronic)	36.6°C-37.9°C (97.9°F-100.2°F)	38°C (100.4°F)
Tympanic (infrared)	35.7°C-37.6°C (96.3°F-99.6°F)	37.6°C (99.6°F)
Temporal (infrared)	36.6°C (97.9°F) to temperature specific for patient age shown in next column	<ul style="list-style-type: none"> • 38.1°C (100.6°F) for (0-2 months old) • 37.9°C (100.2°F) for (3-47 months old) • 37.8°C (100.0°F) for (>4 years old)

Data from References 21,38.

Once a fever has been properly verified, the underlying cause should be determined. Relevant information includes the chronology of fever, existing conditions, current medications, vaccination history, exposure to infected individuals, and recent travel. Patients with conditions such as coronavirus disease 2019 (COVID-19) may have symptoms that appear as soon as 2 days after exposure.¹⁵ Moderate-to-severe illness with or without fever can occur with vaccinations.¹⁶ For recent travelers, a thorough geographical history, time of onset, and duration of fever symptoms is important.¹⁷ Patients returning from tropical areas with infections usually become symptomatic within 21 days of exposure to pathogens, and the majority of returning travelers who develop fever present within 1 month of exposure.^{15,18} Fever is more commonly associated with travel to sub-Saharan Africa, South and Central Asia, Southeast Asia, Latin America, and the Caribbean.¹⁷

Special Populations

Several types of patients with fever have red flags indicating that self-care is not appropriate. Fever, hyperthermia, and hyperpyrexia are similar conditions where patients will exhibit elevated temperatures. It is important to distinguish between fever and hyperthermia, as hyperthermia does not respond to antipyretics and can be rapidly fatal. Hyperthermia—an uncontrolled rise in body temperature—results from the body taking on or producing heat faster than peripheral mechanisms can lose it; the hypothalamic set point is not altered, and the elevated temperature will not respond to antipyretic agents. Hyperthermia can result from exposure to extremely high temperatures (such as in a closed car or other vehicles) or engaging in heavy labor or strenuous exercise.¹⁹ To appropriately distinguish this condition from fever, a careful examination of recent events with exposure to elevated temperatures or layering of clothing should be examined.¹⁹ Patterns of fluid intake should also be evaluated, as some patients with hyperthermia suffer from dehydration. In addition, providers should rule out medications that may have caused excess temperatures. If patients report taking antipyretics with no decrease in temperatures, this may also assist in differentiating hyperthermia from fever.

A fever of greater than 41.5°C (106.7°F) is defined as hyperpyrexia, which can be distinguished from fever and hyperthermia by the extreme elevation in temperature. An additional discriminating factor is that hyperpyrexia responds to antipyretics, unlike hyperthermia. Hyperpyrexia can result from bacterial or viral infections, and it occurs when the hypothalamic set point is increased, resulting in heat-producing responses in the periphery (such

as shivering). While hyperpyrexia will respond to antipyretic agents (unlike hyperthermia), the extremely high body temperature is a red-flag medical emergency that requires immediate attention.¹⁹ Those at risk for hyperthermia who have severe symptoms of infection that are not self-limiting, or who have impaired oxygen utilization, should see a medical professional immediately.²⁰ Also, patients who have an impaired immune function, or damage to the central nervous system (CNS) should see the physician immediately.

Children represent one of the largest groups of patients who may need evaluation by a physician immediately to avoid worsening of symptoms or further harm. Table e9-3 includes circumstances when children, adolescents, and adults presenting with fever should seek medical care.

TABLE e9-3
Red-Flag Symptoms in Patients with Fever

Patients presenting with a temperature greater than 38°C (100.4°F) and any of following symptoms should see a physician immediately^a:

- Unexplained dermatologic spots or rashes^{b,c,d}
- Loss of appetite, low energy, or is noticeably pale or flushed^{b,c,d}
- Inability to swallow and drooling excessively^{b,c}
- Difficulty breathing even after clearing nose with a bulb syringe^{b,c}
- Refusing oral fluids^b
- Very ill, drowsy or difficult to wake up^{b,c}
- Delirious, glassy-eyed, or extremely cranky or irritable^{b,c}
- Environmental exposure to high temperatures^{b,c,d}
- Vomiting without the ability to keep down fluids and/or sustained diarrhea^{b,c}
- History of seizures or febrile seizures^{b,c,d}
- Stiff neck, severe headache, severe ear pain, or sore throat^{b,c,d}
- Taking steroids or are immunocompromised with conditions such as cancer or sickle cell conditions^{b,c,d}
- Changes in mental status^{b,c,d}
- Dizzy or light-headed^d
- Recent chemotherapy^d
- Shortness of breath/chest pain^d
- Changes in the color of skin, lips, or nail beds^{b,c,d}

^aInfants younger than 3 months with a temperature above 38°C (100.4°F), children of any age with a temperature above 40°C (104°F), or adults with high fever (above 41°C [105.8°F]) should be seen by the physician irrespective of accompanying symptoms.

^bApplies to children.

^cApplies to adolescents.

^dApplies to adults.

Data from References 22-24.

ASSESS

4 After the information has been collected from the patient, the next step of the process is to make an assessment to draw conclusions of the condition and its origin. Assessing the patient should include differentiating fever from other conditions that produce elevated body temperatures,

including hyperthermia and hyperpyrexia. The pharmacist or other primary care practitioner must ensure that the symptoms are limited to a fever before treatment is given.

The gathered information must be examined in detail to ascertain whether recent travel, drugs, illnesses, or other identifiable factors have led to fever. For medications, this includes an assessment of indication, effectiveness, safety, and adherence. A problem list of active medical problems and medication therapy problems is then created to prioritize medication therapy recommendations and achieve goals of therapy.

After evaluating the possibility of these and other potential red-flag symptoms, the health professional must decide whether to recommend use of self-care agents for fever. If patients have red flag symptoms such as those shown in [Table e9-3](#), the pharmacist should assist the patient in seeking immediate medical care. Religious and cultural preferences should be considered so that patients are able to make a joint decision that aligns with their values. Economic barriers must be assessed as they may alter decisions of care based on cost. Guiding patients to generic equivalents may allow them to be more adherent to regimens because of the affordability of the needed treatment.

Concurrent prescription medications, dietary supplements, and OTC therapies should also be considered. Drug interactions can affect therapy options. If available, a comprehensive medical chart may also provide information on key laboratory values including complete blood count, kidney function, liver function, and basic metabolic panel. When laboratory data are not available, the medical history can provide insight on whether conditions such as liver dysfunction or renal dysfunction are present.

DEVELOP A CARE PLAN

5 Upon completion of the assessment of the patient with fever, an individualized patient-centered care plan that is evidence-based and as affordable as possible is created for the patient. This plan includes recommendations of nonpharmacologic and pharmacologic strategies to reduce fever and prevent further complications.

6 Nonpharmacologic methods of managing fever include the patient wearing light clothing, keeping a low room temperature to stay comfortable, and taking a sponge bath with warm water.²⁴ Patients should not receive alcohol or ice baths due to the potential for shock. If patients begin shivering when sponging with tepid water, that intervention should be terminated.²⁴ Because sponging does not reduce the hypothalamic set point, sponging should follow oral antipyretic therapy by 1 hour to permit the appropriate reduction of the hypothalamic set point and a more sustained temperature-lowering response.²⁰ Since fever will cause a more rapid loss of fluids, patients should make sure to increase fluid intake to avoid dehydration.

7 All antipyretics are dosed on an as-needed basis for fever. When considering pharmacologic therapy, over-the-counter antipyretics include acetaminophen, ibuprofen, and aspirin. Acetaminophen reduces fever by inhibiting the production and release of prostaglandins in the CNS and by inhibiting endogenous pyrogens at the hypothalamic thermoregulatory center.²⁵

In adults, acetaminophen is dosed at 650 mg every 4 to 6 hours (maximum dose of 3,250 mg/24 hr) or 1,000 mg every 6 hours (maximum dose of 3000 mg/24 hr). Patients with liver disease should consult a medical professional before using acetaminophen. In the United States, product labeling warns against use of more than 4,000 mg/day, with other drug products containing acetaminophen (eg, combination products such as those containing opioids plus acetaminophen, or in those who consume three or more alcoholic drinks every day during use of the product).²⁵ Because this medication is marketed in 325 mg, 500 mg, and 650 mg tablets, the pharmacist should help the patient to identify the proper dosage and dosing schedule to avoid confusion.

In children, the dose is 10 to 15 mg/kg every 4 to 6 hours as needed with a maximum of 75 mg/kg/day for infants and lesser of 100 mg/kg/day or 1,625 mg/day in children.²⁵ Dosing amounts are provided by weight and age on product labeling; weight should be used rather than age to guide dosing amounts whenever possible.²⁵

Oral acetaminophen is safe to use in pregnancy and lactation and is classified as Food and Drug Administration pregnancy category B.²⁵ As dose adjustments are required for renal impairment, patients should consult their physician if renal complications exist. This medication is contraindicated in active and severe hepatic impairment. Patients with a history of alcohol abuse should use acetaminophen with caution.

Ibuprofen reduces fever by inhibiting the production and release of prostaglandins in the CNS and periphery. Ibuprofen is dosed at 200 to 400 mg

orally every 4 to 6 hours with a maximum of 1,200 mg/day in children greater than 12 years old and in adults.²⁶ In children 6 months to 12 years of age, the dose is 5 to 10 mg/kg orally every 6 to 8 hours as needed, with a maximum of 4 doses/day.²⁷ Patients younger than 2 years of age should use the 50 mg/1.25 mL suspension and children 2 years or older should use the 100 mg/5 mL formulation. Parents with children in mixed-age ranges should be advised to pay close attention to formulations to avoid overdose.

Patients with a history of renal complications should only take ibuprofen with the approval of their physician, as dose adjustments may be required. Ibuprofen should be avoided in older adults with heart failure because of possible fluid retention and heart failure exacerbation. Ibuprofen should also be avoided in older adults with stage 4 or 5 chronic kidney disease stage as renal injury may occur.²⁸ Patients with cardiovascular disease should discuss treatment with a physician, as nonsteroidal anti-inflammatory drugs (NSAIDs) may increase the risk of serious cardiovascular thrombotic events, myocardial infarction, and stroke.²⁹ Also, ibuprofen cannot be used in patients undergoing coronary artery bypass graft surgery and can cause serious gastrointestinal adverse events, including bleeding, ulceration, and perforation of the stomach or intestines.²⁹ This medication should not be used in pregnancy or during breastfeeding, as risks to the fetus or infant cannot be ruled out.³⁰

Similar to ibuprofen, aspirin reduces fever by inhibiting the production and release of prostaglandins in the CNS and periphery. In children aged 12 years or older and adults, aspirin is taken at the dose of 325 to 650 mg orally every 4 to 6 hours as needed with a maximum of 4 g in 24 hours. Children and teenagers who have or are recovering from chickenpox or flu-like symptoms should not use aspirin, as Reye's syndrome may occur.³¹ Patients with renal or hepatic disease should discuss the use of this medication with a physician; use in severe hepatic and renal impairment is contraindicated. At doses used for treatment of fever, aspirin should be avoided in pregnancy and lactation.³¹

IMPLEMENT

After the therapy options have been identified, the step of implementation includes starting the treatment plan along with the patient and in consultation with other healthcare practitioners when appropriate. Based on patient-specific parameters, therapy options are discussed with the patient and education is provided on the goal of reducing temperature and discomfort associated with fever. The patient should be advised to check body temperatures using the same instrument in a specific-body location and to take antipyretic agents on the recommended schedule. Contraindications, cautions, adverse effects, and pertinent interactions of the selected medication should be discussed with the patient and/or caregivers.

An open-ended dialogue should occur to verify that the patient is comfortable with the medication choice, affordability of the agent, and schedule/duration of therapy.

FOLLOW-UP

8 Monitoring and evaluation of fever treatment is focused on symptom management. Worsening or improvement of symptoms aids in the evaluation of the treatment that is administered. Patients should be instructed to keep a fever diary with recorded temperatures every 8 hours and symptoms they experience.³² A fever diary can assist in evaluation if further treatment becomes necessary by the healthcare team. If fever or associated symptoms have not changed within 3 days of the start of antipyretic therapy, the patient should seek further evaluation.²⁰

During treatment for fever, development of other symptoms is concerning. Headache or neck stiffness may be indicative of meningitis; a lumbar puncture may be needed for diagnosis.^{6,33} Fever presenting with diarrhea and abdominal pain can indicate a bacterial infection that requires evaluation using laboratory tests.³² Documented recent travel history and new symptom presentation further increase the possible causes of fever. For example, prolonged fever with symptoms such as rash, myalgias, gastrointestinal upset, or headaches can indicate dengue fever in those with recent travel history to tropical and subtropical climates.³⁴

The symptoms of fever, cough, or shortness of breath were reported by 70% of patients with COVID-19. Common signs and symptoms of COVID-19 tend to overlap with other infections and fever causing ailments. Differentiation by further evaluation and testing is needed to adequately identify and treat the underlying cause.³⁵ Although some patients infected with COVID-19 are asymptomatic, recommending antipyretic therapy in those of need should be indistinguishable from the red-flag symptoms, recommendations, and treatments previously outlined.³⁵ If COVID-19 infection or exposure is

suspected, patients should be advised to follow guidance protocols set forth by the Centers for Disease Control and Prevention.

In patients with hyperthermia, antipyretic therapy is not effective. In addition to fever, the patient may experience confusion, hypotension, dehydration, dry and hot skin, and delirium.^{6,36,37} Cooling techniques such as cool blankets, fans, and sponging can be used in patients with hyperthermia, but further and immediate evaluation is needed to determine and treat the true underlying cause.³⁷

Fever in children may present with other symptoms such as loss of appetite, sleep, and decreased activity.³⁶ When these symptoms occur, alleviating other symptoms of discomfort is vital.³⁶ If the child's condition worsens or there is no improvement within 24 hours for children younger than 2 years or 48 hours for children older than 2 years, the child should be further evaluated by a physician.²¹

CONCLUSION

Patients in the community and ambulatory settings frequently seek care for fever. These practitioners have the opportunity to implement the patient care process in a systematic way to understand the causes of fever and assist patients in meeting therapy goals. Assessments can be made as to whether present medication regimens may be optimal and if patients have red-flag symptoms that make self-care inadvisable.

Patient-specific factors, values, beliefs, and comfort are considered in developing, implementing, and following-up on a treatment plan. At-home measures are used to assist with decreasing temperature safely, and in those self-treating fever, counseling should be provided on how to most effectively and safely use antipyretics to resolve symptoms. Patients whose fever does not resolve and those who develop other symptoms that are indicators of red-flag conditions should be referred for immediate medical evaluation.

This patient-centered care model ensures that the symptoms of fever are adequately resolved and that the encounters patients have with healthcare professionals are trustworthy, meaningful, and comprehensive.

ABBREVIATIONS

CNS	Central nervous system
COVID-19	Coronavirus disease 2019
NSAIDs	Nonsteroidal anti-inflammatory drugs

REFERENCES

1. Horowitz HW. Fever of Unknown Origin or Fever of Too Many Origins? *N Engl J Med*. 2013;368(3):197–199. [PubMed: 23323894]
2. National Center For Health Statistics. National Hospital Ambulatory Medical Care Survey: 2018 Emergency Department Summary Tables. 2018. Available at https://www.cdc.gov/nchs/data/nhamcs/web_tables/2018-ed-web-tables-508.pdf. Accessed July 1, 2021.
3. National Center for Health Statistics. Emergency Department Fact Sheet: Medications Provided or Prescribed at Visits. 2017. <https://www.cdc.gov/nchs/data/nhamcs/factsheets/2017-NHAMCS-ED-Fact-Sheet-508.pdf>. Accessed July 1, 2021.
4. Montalbano A, Rodean J, Kangas J, Lee B, Hall M. Urgent care and emergency department visits in the pediatric medicaid population. *Pediatrics*. 2016;137(4):e20153100–e20153100. doi: 10.1542/peds.2015-3100.
5. In: Hay WW, Levin MJ, Deterding RR, Abzug MJ, eds. *Current Diagnosis & Treatment: Pediatrics*. New York, NY: McGraw-Hill; 2018. <https://accessmedicine.mhmedical.com/content.aspx?bookid=2390§ionid=189071532>. Accessed August 23, 2018.

6. Fletcher TE, Bleeker-Rovers CP, Beeching NJ. Fever. *Medicine (Baltimore)*. 2017;45(3):177–183. doi: 10.1016/j.mpmed.2016.12.013.
7. Hersch EC, OH RC. Prolonged febrile illness and fever of unknown origin in adults. *Am Fam Physician*. 2014;90(2):91–96. [PubMed: 25077578]
8. Leggett J. 288. Approach to fever or suspected infection in the normal host. In: Goldman L, Schafer AI, eds. *Goldman's Cecil Medicine*. 2011. doi: 10.1016/B978-1-4377-1604-7.00288-8.
9. Nield LS, Kamat D. Chapter 176 – Fever. In: Kliegman, R, et al. eds. *Nelson Textbook of Pediatrics*. 20th ed. Philadelphia, PA: Elsevier, 2016.
10. Foggo V, Cavenagh J. Malignant causes of fever of unknown origin. *Clin Med*. 2015;15(3):292–294. doi: 10.7861/clinmedicine.15-3-292.
11. Roth A, Basello G. Approach to the adult patient with fever of unknown origin. *Am Fam Physician*. 2003;68(11):2223–2228. [PubMed: 14677667]
12. Cunha BA. Fever of unknown origin: Clinical overview of classic and current concepts. *Infect Dis Clin North Am*. 2017;21(4):867–915.
13. Tolia J, Smith LG. Fever of unknown origin: Historical and physical clues to making the diagnosis. *Infect Dis Clin North Am*. 2007;21(4):917–936. [PubMed: 18061082]
14. Johnson DH, Cunha BA. Drug fever. *Infect Dis Clin North Am*. 1996;10(1):85–91. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/8698996>. Accessed August 18, 2018. [PubMed: 8698996]
15. National Center for Immunization and Respiratory Diseases (NCIRD), Division of Viral Diseases. Centers for Disease Control and Prevention. Symptoms of COVID-19. <https://www.cdc.gov/coronavirus/2019-ncov/symptoms-testing/symptoms.html>. Accessed July 1, 2021.
16. Kroger A, Bahta L, Hunter P. Centers for Disease Control and Prevention General Best Practice Guidelines for Immunization. <https://www.cdc.gov/vaccines/hcp/acip-recs/general-recs/index.html>. Accessed July 1, 2021.
17. Johnston V, Stockley JM, Dockrell D, et al. Fever in returned travellers presenting in the United Kingdom: Recommendations for investigation and initial management. *J Infect*. 2009;59(1):1–18. [PubMed: 19595360]
18. Wilson ME, Weld LH, Boggild A, et al. Fever in Returned Travelers: Results from the GeoSentinel Surveillance Network. *Clin Infect Dis*. 2007;12(12):1560–1568.
19. Dinarello CA, Porat R. Fever. In: Kasper D, Fauci A, Hauser S, Longo D, Jameson JL, Loscalzo J, eds. *Harrison's Internal Medicine* 19th ed. McGraw-Hill; 2015. <https://accessmedicine.mhmedical.com/content.aspx?bookid=1130§ionid=79720773>.
20. Feret BM. Fever. In: Young L, ed. *Handbook of Nonprescription Drugs: An Interactive Approach to Self-Care*. 17th ed. Washington DC: American Pharmacists Association; 2012:87–100.
21. When to Call the Pediatrician: Fever—HealthyChildren.org. Available at <https://www.healthychildren.org/English/health-issues/conditions/fever/Pages/When-to-Call-the-Pediatrician.aspx>. Accessed August 18, 2018.
22. Tess AV. Chapter 8. Fever. *The Patient History: An Evidence-Based Approach to Differential Diagnosis*. New York, NY: McGraw-Hill; 2012. Available at: <http://accessmedicine.mhmedical.com/content.aspx?bookid=500§ionid=41026551>.
23. Johnson & Johnson Consumer Inc. Fever Warning Signs. [Tylenol.com](https://www.tylenol.com/children-infants/fever/symptoms). Available at <https://www.tylenol.com/children-infants/fever/symptoms>. Published 2016. Accessed October 8, 2018.
24. Education on Call: Treating Fever. Available at https://www.tylenolprofessional.com/sites/tylenol_hcp_us/files/parent-education-treating-fever_0.pdf. Accessed August 22, 2018.

25. TYLENOL® Dosing Guidelines TYLENOL® Professional. Available at <https://www.tylenolprofessional.com/dosage>. Accessed August 21, 2018.
26. Ibuprofen Adult Dosing Chart MOTRIN® Products. Available at <https://www.motrin.com/safety-dosing/adult-dosing-chart#motrin-ib-dosing-chart>. Accessed August 22, 2018.
27. Children & Infants Dosage by Age & Weight MOTRIN®. Available at <https://www.motrin.com/children-infants/dosing-charts?icid=home%7Ctout%7C1#infants-motrin-suspension-drops-50-mg-1-25ml>. Accessed August 22, 2018.
28. American Geriatrics Society 2015 Beers Criteria Update Expert Panel. American Geriatrics Society 2015 Updated Beers Criteria for Potentially Inappropriate Medication Use in Older Adults. *J Am Geriatr Soc*. 2015;63(11):2227–2246. doi: 10.1111/jgs.13702.
29. Pain & Fever Relief with Ibuprofen MOTRIN® IB. Available at <https://www.motrin.com/products/motrin-ib>. Accessed August 22, 2018.
30. U.S. Food and Drug Administration. FDA Warns that Using a Type of Pain and Fever Medication in Second Half of Pregnancy Could Lead to Complications. <https://www.fda.gov/news-events/press-announcements/fda-warns-using-type-pain-and-fever-medication-second-half-pregnancy-could-lead-complications>. Accessed July 1, 2021
31. Bayer Extra Strength Aspirin - 500 mg Tablets Bayer Aspirin. Available at <https://www.bayeraspirin.com/products/bayer-extra-strength-aspirin/>. Accessed August 22, 2018.
32. Chusid MJ. Fever of unknown origin in childhood. *Pediatr Clin North Am*. 2017;64(1):205–230. doi: 10.1016/j.pcl.2016.08.014.
33. Rossoff J, Mithal LB. Initial management of fever and neutropenia: A practical approach. *Clin Pediatr Emerg Med*. 2018;19(2):145–152. doi: 10.1016/j.cpem.2018.05.002.
34. Ellis J, Hearn P, Johnston V. Assessment of returning travellers with fever. *Med (United Kingdom)*. 2018;46(1):2–9. doi: 10.1016/j.mpmed.2017.10.006.
35. Stokes EK, Zambrano LD, Anderson KN, et al. Centers for Disease Control and Prevention. MMWR - Coronavirus Disease 2019 Case Surveillance — United States, January 22–May 30, 2020. <https://www.cdc.gov/coronavirus/2019-ncov/php/reporting-pui.html>. Accessed July 1, 2021.
36. Sullivan JE, Farrar HC; Section on Clinical Pharmacology and Therapeutics; Committee on Drugs. Fever and antipyretic use in children. *Pediatrics*. 2011. doi: 10.1542/peds.2010-3852.
37. Zomorodi A, Attia MW. Fever: Parental concerns. *Clin Pediatr Emerg Med*. 2008;9(4):238–243. doi: 10.1016/j.cpem.2008.09.007.
38. El-Radhi A, Barry W. Thermometry in paediatric practice. *Arch Dis Child*. 2006;91(4):351–356. doi: 10.1136/adc.2005.08883.

SELF-ASSESSMENT QUESTIONS

1. Which of the following medications is generally preferred in treating fever?

- A. Ibuprofen
- B. Naproxen
- C. Aspirin
- D. Acetaminophen
- E. Magnesium Salicylate

2. Which of the following nonpharmacologic methods of reducing fever is preferred?
 - A. Use of an alcohol bath
 - B. Using cooling fans
 - C. Wearing tight clothing
 - D. Using a cold water sponge bath
 - E. Using an ice bath
3. Cindy is a 27-year-old woman who has had an elevated temperature for the last 2 days. She reports having a slightly elevated temperature and calls your pharmacy for dosing advice. At home, she has acetaminophen 500-mg tablets to treat her fever. What is the daily maximum recommended dose of this medication for her to use?
 - A. 2,000 mg
 - B. 2,400 mg
 - C. 3,000 mg
 - D. 3,250 mg
 - E. 4,000 mg
4. How long should adults use over-the-counter treatment with no changes in temperature before seeking care of the physician?
 - A. 2 days
 - B. 3 days
 - C. 5 days
 - D. 7 days
 - E. 10 days
5. Matthew is an 11-month-old child who is being brought to your pharmacy by his father. He has no history of medical conditions and weighs 10 kg. The father reports that Matthew's temperature at home has been 101°F (38.3°C) and has developed a slight rash behind his left ear. He does not appear to be irritable and has been properly hydrating at home. Which of the following is your recommendation for Matthew?
 - A. Take a bath in tepid water.
 - B. Take Ibuprofen 100 mg q 4 hours.
 - C. Dress Matthew in loose clothing.
 - D. Take Naproxen 110 mg q 4 hours.
 - E. See the pediatrician.
6. If symptoms do not improve or worsen with over-the-counter therapy in children less than 2 years old, when should the pediatrician be seen?
 - A. 12 hours
 - B. 24 hours

-
- C. 36 hours
- D. 48 hours
- E. 72 hours
7. Which of the following medications is likely to produce symptoms of the fever?
- A. Bactrim
- B. Lisinopril
- C. Lovenox
- D. Doxycycline
- E. Hydroxychloroquine
8. On a Tuesday morning, a 37-year-old man presents to your pharmacy with a 2-day history of fever symptoms. Ted has been taking ibuprofen 400 mg every 6 hours over the last 2 days but has noticed that his fever has not decreased. He reports that he competed in a track meet over the weekend where the temperatures were above 95°F (35°C). Upon checking his temperature this morning, his last reading was 102.3°F (39.1°C). What do you recommend?
- A. Switch to acetaminophen 1,000 mg every 6 hours.
- B. Switch to aspirin 650 mg every 4 hours.
- C. Continue therapy for another 24 hours.
- D. See a physician immediately for possible hyperpyrexia.
- E. See a physician immediately for possible hyperthermia.
9. Christina is a 24-year-old pregnant woman who presents to your pharmacy. She explains to you that she is in her 2nd trimester of pregnancy. She has had a fever for the last 24 hours and has a temperature of 103°F (39.4°C). She has no history of renal or hepatic complications. Which of the following medications is the most appropriate for her to use?
- A. Ibuprofen
- B. Acetaminophen
- C. Naproxen
- D. Aspirin
- E. Magnesium Salicylate
10. Children of any age should be referred to the physician if they have a temperature that exceeds what temperature?
- A. 101°F (38.3°C)
- B. 102°F (38.9°C)
- C. 103°F (39.4°C)
- D. 104°F (40°C)
- E. 105°F (40.6°C)
-

11. Children with a temperature exceeding 100.4°F (38°C) and the following symptoms should see the physician immediately EXCEPT:
 - A. Children who refuse intake of fluids
 - B. Children who appear irritable or very ill
 - C. Children with a history of asthma
 - D. Children that report with a stiff neck
 - E. Children who have been in a very hot place like a car
12. As sponging does not reduce the hypothalamic set point, it should be used after what time period has elapsed after administration of oral antipyretic therapy?
 - A. 1 hour
 - B. 2 hours
 - C. 3 hours
 - D. 4 hours
13. Jennifer brings her 13-year-old daughter, Suzie, to the pharmacy with a temperature of 101°F (38.3°C). Jennifer only has aspirin at home but is on a limited income and would prefer not to spend her money on additional drugs if possible. What is your recommendation for treatment of Suzie?
 - A. Yes, aspirin can be taken without complication.
 - B. Yes, aspirin can be taken, but with the physician's approval.
 - C. No, aspirin cannot be taken due to Reye's syndrome risk.
 - D. No, aspirin cannot be taken because it is not indicated for fever.
 - E. No, aspirin cannot be taken because exclusions for self-care are present.
14. Which of the following categories requires a referral to the physician?
 - A. Infants younger than 3 months with a temperature above 98.6°F (37°C)
 - B. Children with a temperature above 100.4°F (38°C) refusing oral fluids
 - C. Children of any age with a temperature above 100.4°F (38°C)
 - D. Children with a temperature above 100.4°F (38°C) who appear hungry
 - E. Adults with a temperature above 104°F (40°C)
15. Which of the following are proper at-home measures to take when treating fever?
 - A. Using the same thermometer during the course of fever
 - B. Using cool water baths to bring down the temperature
 - C. Using the hand to check the temperature on the forehead
 - D. Using versatile measurement sites to ensure accuracy

E. Using alcohol baths to cool the skin

SELF-ASSESSMENT QUESTION-ANSWERS

1. **D.** Acetaminophen is generally the drug of choice for fever, as it does not cause unwanted side effects on platelets and the gastrointestinal tract such as Aspirin and NSAIDs. See section “[Develop a Care Plan](#)” for more details.
2. **B.** The usage of alcohol baths is dangerous and can induce shivering. Ice baths are also dangerous and can lead a patient to shock. Patients should use tepid water instead. Clothing should be light and loose. See the nonpharmacological recommendations under section “[Develop a Care Plan](#).”
3. **C.** The maximum dosage of Tylenol to be used for adults if taking the 500-mg tablets is 3,000 mg. If taking the 650-mg tablets, 3,250 mg is the daily maximum. See more dosage maximum information under section “[Develop a Care Plan](#).”
4. **B.** Adults should use self-care in 3 days if symptoms have not improved with the fever. Seeing the physician at this point allows for a more in-depth assessment of an underlying cause that is not improving. See section “[Follow-Up](#)” for more details.
5. **E.** Matthew has developed a small rash behind his ear. Children with temperatures exceeding 100.4°F (38°C) and who have developed a rash should see the pediatrician.
6. **B.** If symptoms do not improve or get worse with over-the-counter therapy in children less than 2 years old, a pediatrician should be seen in 24 hours. In children who are greater than 2 years old, this is extended to 48 hours. See section “[Follow-Up](#)” for more details.
7. **D.** Bactrim contains a sulfonamide drug, which can cause fever. Please see [Table e9-1](#) for a more comprehensive list of medications.
8. **E.** Ted has hyperthermia and should seek medical care immediately. He was at a very hot event outside and has a temperature that has not decreased with the proper use of ibuprofen. His temperature has not exceeded 106.7°F (41.5°C), so we know that he does not have hyperpyrexia. See section “[Assess](#)” for more details.
9. **B.** The most appropriate drug to be used in pregnancy is acetaminophen. NSAIDs can cause adverse effects if used in pregnancy. See section “[Develop a Care Plan](#)” for more details.
10. **D.** Children of any age should be referred to the physician if they have a temperature that exceeds 104°F (40°C). Children with temperatures this high do not need to have accompanying symptoms to see the physician. See [Table e9-3](#) for more details.
11. **C.** Asthma is not a part of the conditions that cause a child to seek treatment from a pediatrician with elevated temperatures. Although “impaired oxygen utilization” is mentioned in the chapter, patients are able to have a well-controlled asthma without this severe status. See [Table e9-3](#) and section “[Assess](#)” for more details.
12. **A.** Sponging should occur 1 hour after the use of antipyretics to adequately decrease temperature. Sponging outside of the use of antipyretics is inappropriate, as this method does not decrease the hypothalamic set point. See section “[Develop a Care Plan](#)” for more details.
13. **A.** Children greater than 12 years old can safely take aspirin. Reye’s syndrome becomes an issue in patients that are recovering from flu-like symptoms and the chickenpox. See section “[Develop a Care Plan](#)” for more details.
14. **B.** Hunger is not a part of the classic symptoms that patients experience in fever. The appropriate temperatures for medical referral (without considering symptoms) are greater than 100.4°F (38°C) in infants, greater than 104°F (40°C) in children, and greater than 105.8°F (41°C) in adults. See [Table e9-3](#) for more details.
15. **A.** Water baths should be with tepid water, instead of cold water or alcohol baths that can induce shivering. While checking the temperature with a hand to the forehead may be a classic method of assessing fever, the recommended method is to use an appropriate thermometer. In addition, sites and measuring devices should remain the same during the course of therapy. See section “[Develop a Care Plan](#)” for more details.