

Wishing You a Happy Holiday and a New Year Filled with Peace and Prosperity.
The Saskatchewan Drug Information Service

Our Holiday Hours

HEALTHCARE PROFESSIONAL LINE: closed Friday, December 25th and Friday, January 1st.
CONSUMER LINE: closed during regular office hours Friday December 25th and Friday, January 1st.
On call service available 5 PM to midnight every day including weekends and holidays.

FEVER Q&A

'Tis the season for colds, flu's and other illnesses that cause fever. Some current questions regarding the treatment and prevention of fever are addressed below.

Fever is an increase in body core temperature. The average normal core temperature is 37° C. (range 35.6 to 37.7° C). Core temperature has a daily circadian rhythm with the lowest value occurring in the early morning and the highest in the late afternoon. Temperature is maintained within the normal range by the thermoregulatory centre in the hypothalamus. Body temperature measured rectally is about 0.5° C higher than the corresponding oral measurement while auxiliary (armpit) temperature measurements are about 0.5° C lower than oral temperatures.^{1,2}

The most common cause of fever is infection. Organisms or the toxins they produce stimulate the release of endogenous pyrogens which "turn up" the hypothalamic thermostat. Typical symptoms of fever such as chills, sweating and increased heart rate occur as the body adjusts to the new temperature set point. Fever may also be accompanied by muscle and joint pain, headache, malaise, anorexia and irritability.^{1,2}

1. How dangerous is fever?

- Fever is a symptom of illness not a medical condition in itself.^{1,2}
- Usually self-limiting and non-threatening to patients.^{1,2}
- Temperature does not continue to rise indefinitely; it plateaus once it reaches the new set point.³
- Fever temperatures rarely exceeds 41 – 42° C ; there is no evidence that temperatures of less than 42° C cause harm.³
- In fact, there is accumulating evidence that fever plays an important role in the body's host-defence system.
 - Fever inhibits the growth of bacteria and viral replication.⁴
 - Fever-inducing pyrogens heighten antigen recognitions, increase T-cell activity and enhance immune response.³
 - Fever has been associated with decreased duration of viral shedding and more rapid recovery from certain illnesses.³
- Two to five percent of children may experience febrile seizures.¹
 - Although frightening, are usually benign and do not cause brain damage.^{1,2,5}
 - Recur in about one-third of children but are associated with a low risk of epilepsy.⁵

2. When should fever be treated?

- Current evidence does not support the routine use of antipyretics to treat fever in asymptomatic or mildly symptomatic patients.^{3,6}
- Primary indication for treatment is the relief of associated symptoms if causing significant patient discomfort.^{1,2,3,6}
- Exceptions are bronchiolitis in young children, severe asthma, COPD and heart failure. Fever-induced increases in metabolic rate and oxygen demand could exacerbate these conditions.^{1,2,3,6}
- Inappropriate treatment with antipyretics may counteract the beneficial effects of fever and expose patients unnecessarily to the risk of antipyretic adverse effects (accidental overdose, gastrointestinal bleeding, liver toxicity, renal failure).³

3. How should fever be treated?

- The Canadian Paediatric Society recommends acetaminophen as first choice for fever therapy for children because it has the most safety data. If acetaminophen is not effective (or only partially effective), therapy can be switched to ibuprofen or naproxen.⁷ ASA is another option for adults.⁵
- Although Ibuprofen is reported to be slightly more effective than acetaminophen after a single dose (faster onset, extent of fever reduction and longer duration of effect), the difference disappears with multiple dosing.⁸
- Antipyretic practices that are NOT supported by evidence and NOT recommended include:
 - Alternating doses of acetaminophen and ibuprofen.^{1,2,3,5,7,9}
 - Concurrent dosing of acetaminophen and ibuprofen.^{3,7,9}
 - Decreasing the dosing interval from four to two hours for resistant fevers.⁷
 - Loading doses of antipyretics.⁷
- Studies to date have not reported a clinically significant difference in the benefit of combinations of antipyretics^{3,8,9}: combining antipyretics exposes patients unnecessarily to the increased risk of side effects associated with taking two drugs versus one drug as well as increasing the potential for dose mix-ups and overdose^{3,6,7,9}.

4. Can antipyretics be used to prevent febrile reactions and / or febrile seizures?

- Antipyretic treatment has not been proven to prevent febrile seizures.⁹
- In a recent study, administration of antipyretics at the time of vaccination (with various vaccines) reduced the desired immune response. More study is needed to confirm this effect.¹¹
- In the meantime, the authors recommend against the routine use of antipyretics as prophylaxis for vaccine-induced fever. Antipyretics can be used if needed to treat fever or related adverse effects after the vaccine has been administered.¹¹

5. What is drug fever?

- Drug-induced hyperthermia - not technically “fever” because this syndrome does not involve resetting of the body core temperature.¹
- Responsible for 3 – 5 percent of all adverse drug effects; occurs in up to 10 percent of hospitalized patients¹
- Often unrecognized especially if the condition being treated is associated with fever.¹
- Temperature usually ranges from 38.8 – 40° C but has been reported as high as 42.2° C.¹
- Drug-induced hyperthermia should be suspected if :
 - Temperature becomes elevated after the administration of a new drug,
 - Other symptoms of condition being treated improve,
 - Hives, rash or other symptoms of a hypersensitivity reaction emerge at the same time.¹
- The suspected medication should be stopped if possible. Temperature will decrease in 24 – 72 hours if the fever was drug-induced.^{1,2}
- Many drugs have been implicated in cases of hyperthermia: antibiotics (e.g. cephalosporins, macrolides, sulphonamides, tetracyclines), anticancer agents, cardiovascular agents (e.g. hydralazine, nifedipine, quinidine), CNS agents (e.g. benzotropine, carbamazepine, lithium, phenytoin, SSRIs, TCAs), allopurinol, azathioprine, corticosteroids, and metoclopramide.^{1,2}

Key Points

- **Mild fever is not harmful and treatment may be counterproductive.**
- **Advise a wait-and-see strategy. Temperature can be used to monitor the severity of the illness.**
- **Base recommendations for antipyretic treatment on symptoms. Reserve antipyretics for fever-associated symptoms causing excessive discomfort.**
- **Discourage sequential or concurrent use of acetaminophen and ibuprofen**
- **Maintain a high index of suspicion for drug fever when fever occurs after initiation of a medication.**

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Posted with references on the SDIS website www.druginfo.usask.ca.

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