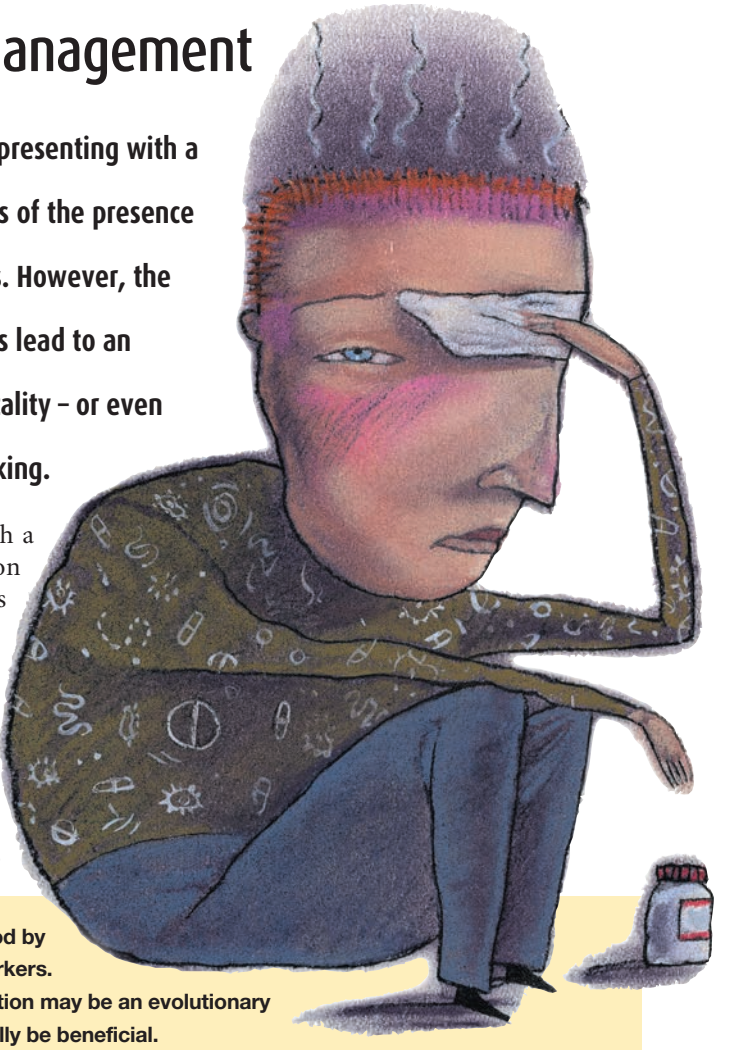
Fever in adults

Keys to rational management



It is often assumed that a patient presenting with a fever should be treated, regardless of the presence or absence of any other symptoms. However, the evidence that antifever treatments lead to an improvement in morbidity or mortality – or even patient comfort – is somewhat lacking.

PAUL PREISZ
MB BS, FACEM

DAVID WISE
MB ChB, FRCS(Ed)

Dr Preisz is Senior Staff Specialist in Emergency Medicine and Dr Wise is Registrar in Emergency Medicine at St Vincent's Hospital, Darlinghurst, NSW.

Patients will commonly present with a fever or be noted to have a fever on baseline observations. Often, a fever is assumed to be deleterious to health (rather than adaptive to the conditions), and measures to return the body temperature to normal are therefore thought to be necessary.

Patients are sometimes confused by advice on fever management from general practitioners[1] and other sources

IN SUMMARY

- **Fever is often misunderstood by patients and healthcare workers. The fever response to infection may be an evolutionary adaptation that could actually be beneficial.**
- **Normal core body temperature is 37±0.8°C, and varies with circadian rhythm, the menstrual cycle, and the method of measurement. This variation must be taken into account when interpreting a measured temperature.**
- **A fever greater than 40°C should prompt the clinician to exclude a specific hyperpyrexial syndrome.**
- **A fever associated with a specific underlying illness is managed by treating that illness.**
- **Treatment of a fever *per se* is indicated if the hypermetabolic demands imposed on the patient by the fever are excessive.**
- **Pharmacological antifever measures should be used before physical measures; the latter can then be added, if necessary.**
- **There is no evidence definitively supporting the use of paracetamol combined with an NSAID to reduce fever. Either paracetamol or an NSAID can be used alone.**

How is body temperature regulated?

The hypothalamus acts as the body's thermostat, initiating voluntary and involuntary responses in order to maintain a given temperature setpoint. Fever (pyrexia) occurs when the hypothalamic setpoint is raised.

The fever mechanism is thought to involve inflammatory chemical mediators which stimulate the release of endogenous pyrogens that act on the anterior hypothalamus. Secondary mediators stimulate the posterior hypothalamus and the vasomotor centre. Subsequent responses (such as shivering) increase heat production while other responses (such as peripheral vasoconstriction and some behavioural changes) reduce heat loss.[4] At the extremes of age, hypothalamic temperature regulation is impaired and less effective.

Hyperpyrexial syndromes

By convention, the term 'hyperpyrexia' is used in association with a group of specific clinical entities that involve loss of hypothalamic regulation (see below). In a hyperpyrexial syndrome, temperature is allowed to rise unchecked by the body's usual adaptive mechanisms. Temperatures greater than 40°C may be achieved.

Treatment is usually undertaken in an intensive care environment and may include early elective muscle paralysis and ventilation, active cooling, dantrolene (Dantrium Powder for Injection), and aggressive treatment of complications. Without treatment, a patient is at risk of rhabdomyolysis, cerebral oedema, disseminated intravascular coagulation, adult respiratory distress syndrome and, ultimately, multisystem failure and death.

Syndrome	Features
Malignant neuroleptic syndrome	Altered consciousness, autonomic dysfunction, muscle rigidity and fever associated with neuroleptic medication[5]
Malignant hyperthermia anaesthetic drugs[6]	Muscle rigidity and fever associated with some
Heat stroke	Association with hot weather, dehydration and exertion, particularly amongst endurance athletes and soldiers; may occur in older people with minimal exertion[7]
Sympathomimetic poisoning	Hyperpyrexia as a complication of the use of cocaine, amphetamine or ecstasy[8]
Serotonin syndrome	Progressive muscle rigidity and fever associated with a combination of monoamine oxidase inhibitors and serotonin reuptake inhibitors, including SSRIs[9]

(such as the internet)[2]. The management of fever in children is the subject of much published debate,[3] but this is not the situation in adults. This article takes an evidence based, rational approach to assist practitioners in deciding whether adult patients require treatment of their fever, and explains which methods of fever reduction are effective.

Normal body temperature and fever

Normal adult core body temperature is 37±0.8°C. Measured temperature is a dynamic balance between heat production and heat loss; a wide range of factors may affect each side of the equation. The regulation of body temperature is discussed in the top box on this page.

A fever may reflect a wide variety of pathological processes including infection, inflammation, trauma, malignancy and connective tissue diseases. On occasion, no significant underlying disease process is found. Temperatures greater than 40°C are uncommon – the specific hyperpyrexial syndromes should be considered in such cases (see the bottom box on this page).

Measuring body temperature: pitfalls in interpretation

A 'normal' temperature reading depends on when, in whom and how the measurement is taken. The commonly agreed normal of 37°C is a simplification but a useful guide, provided that its important shortcomings are understood. Saying that an individual does or does not have a fever – particularly a low grade fever – may be misleading if variables in the time, patient and method of measurement are not considered.

The time

Assuming a night–day, sleeping–waking pattern, normal core body temperature shows a circadian rhythm. Temperature is lowest between 4 a.m. and 8 a.m., and highest between 4 p.m. and 8 p.m.

The patient

Women are slightly warmer than men. In women of reproductive age, temperature is affected by the menstrual cycle – a temperature rise of up to 0.4°C may be found in the second half of the cycle (after ovulation). This cyclical change in temperature is the basis for one method of contraception, and may assist when planning a pregnancy.

The method of measurement

Rectal temperature measurements approximate to core body temperature. Tympanic and oral measurements underestimate temperature by about 0.5°C and are prone to inaccuracies. Axillary measurements may underestimate temperature by as much as 1.0°C.

Some tools used to measure body temperature are shown in Figures 1 and 2.

To treat or not to treat?

Fever may be beneficial. Most people feel good after a hot bath or exercise, even though either activity can increase core body temperature by 1 to 2°C. It has long been established that an elevated temperature can be harmful to pathogenic micro-organisms,[10] and may enhance several parameters of immune function, including antibody production,[11] T cell activation,[12] and neutrophil function.[13]

Several warm and cold blooded species select a warmer environment when they have a bacterial or viral infection.[14] It is possible that, in some circumstances, the fever response is an evolutionary adaptation to infection.

Low grade fever in a previously well patient

A previously well patient with a low grade fever that is exerting minor physiological stress and thought to be due to a minor self-limiting illness (such as a viral illness) may require no fever-reducing treatment. In this case, a watch and wait policy may be adopted, remembering that the fever may actually be beneficial.

It is reasonable to institute therapy for comfort in some patients with subjective symptoms related to pyrexia; however, this therapy should be monitored and withdrawn if no benefit is apparent.

Fever as part of a serious illness

In some patients, fever is part of the manifestation of a serious illness, such as an infection, malignancy or active connective tissue disease. If a significant fever-associated illness is present and specific therapy has been commenced for that illness, the temperature can be expected to return to normal (without any additional therapy to treat the fever *per se*) as the patient improves. Successfully treated pneumonia is a classic example. Artificially lowering the temperature of a febrile patient may mask the signs of infection and make diagnosis or monitoring more difficult.

Fever causing excessive physiological disturbance

In some patients, the hypermetabolic effect of fever imposes an unacceptable physiological strain. This is particularly true of elderly patients, patients with pre-existing disease of the cardiorespiratory systems, and patients taking medications that may limit ability to respond to a heat stress (such as beta blockers, diuretics and sedatives). Some people, such as those with dementia, may be unable to take appropriate action in response to fever.

In some patients, a prolonged high fever may cause adverse effects, such as cerebral oedema, rhabdomyolysis, disseminating intravascular coagulation and, ultimately, multisystem failure. This situation occurs particularly with very high temperatures (that is, temperatures above 40°C) associated with hyperpyrexial syndromes.

Antifever measures

If the decision is made to adopt antifever measures (in addition to specific therapy, if appropriate), two allied approaches – pharmacological and physical – are available.

Figure 1 (above). A disposable rectal probe used to measure body temperature.

Figure 2 (right). A machine used to measure body temperature and concurrent blood pressure, oxygen and pulse. The probe shown on the right hand side is used for measuring oral temperature.

In order to treat fever rationally, it is relevant to refer to physiological principles (see the top box on page 70). In a patient with fever, the hypothalamic setpoint has been raised and the body is already responding as if in a cold environment. Therefore, trying to make the patient colder using physical measures alone may exacerbate this response and the subsequent hypermetabolism may prolong the fever. This phenomenon has been demonstrated in animal studies.[15] It is appropriate, therefore, to first reset the hypothalamus setpoint towards normal, which is currently achieved pharmacologically. If necessary, the cooling can then be supplemented with physical measures.

Pharmacotherapy

Paracetamol and the nonsteroidal anti-inflammatory drugs (NSAIDs) have been shown to be useful in fever management.

Paracetamol works by an incompletely understood mechanism involving central inhibition of prostaglandin synthesis. In children, paracetamol has been implicated in toxicity when prescribed at just above normal doses.[16,17] However, there are few data for paracetamol toxicity in adults when prescribed at just above normal doses.

NSAIDs diminish peripheral and central inflammatory mediators by interfering with cyclo-oxygenase in the prostaglandin pathways. The gastrointestinal side effects of NSAIDs are well described,[18] but their safety in previously healthy younger patients is established. COX-2 specific inhibitors also lower fever, and may be safer than less selective NSAIDs in some patients. Of the NSAIDs, ibuprofen (ACT-3, Actiprofen, Brufen, Nurofen, Nurofen for Children, Rafen, Tri-Profen) has been the most extensively studied.

We could find no published data supporting fever reduction by combining paracetamol with an NSAID.[19] Paracetamol and an NSAID are equally effective – there is no evidence showing either to be superior.[20] Note that aspirin should not be used in children because of the possible risk of Reye's syndrome.

Physical measures

There is no definitive evidence base for the use of physical measures alone to reduce fever in adults,. These methods should be used only after administration of antipyretic drugs. In children, sponging with tepid water after antipyretic therapy has not been shown to be better at reducing fever than antipyretic therapy alone.[21] With this in mind, the main physical therapies available for adults with fever are:

- removing excessive bedding or clothing
- staying in a cool room
- eating and drinking only cool fluids or solids
- fanning or using a fan
- resting.

Note that ice baths or ice packs should not generally be used to reduce fever in adults. These methods are unpleasant and may cause cold injury, and should be reserved for the management of hyperpyrexial syndromes.

Conclusion

It is important to remember that fever may be an evolutionary adaptation which could be of benefit in some situations. By referring to physiological principles involved in the regulation of body temperature, it is possible to identify patients who require treatment of their fever and to institute rational management. MT

A list of references is available on request to the editorial office.

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PAUL PREISZ MB BS, FACEM **DAVID WISE** MB ChB, FRCS(Ed)

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