DOWNLOAD PDF FEVER AND ANTIPYRESIS

Chapter 1 : Antipyresis and Fever | JAMA Internal Medicine | JAMA Network

Fever or analogous behavioral thermal upregulation apparently has positive effects on defense against infection in some animal models. Retrospective studies in humans suggest that failure to mount a febrile response is associated with poor outcome in certain infections but do not establish a causal relationship.

The issue is clouded by a common misunderstanding that fever is the reason an individual with infection feels ill: From there, it is only a short step to conceive of the fever as the illness itself. Although this logical fallacy remains attractive to medical personnel and patients, what evidence exists that fever is harmful or beneficial to the course of an infectious illness? At first glance, studies to answer the question seem simple to perform. Unfortunately, however, to investigate the problem directly is virtually impossible, because every method available to reduce fever has secondary metabolic consequences: Perhaps the most powerful arguments to support a beneficial effect of fever on infection come from teleology and genetics. Fever is established as a phylogenetically ancient host response that is conserved highly in all mammals 1. That fever, despite high metabolic and nutritional costs, is conserved so highly argues forcefully for its evolutionary value, as does the endogenous nature of its mechanism, which requires a complex series of steps and interactions. Our inability to demonstrate directly the beneficial effects of fever in the intact vertebral host because of the diverse metabolic effects of antipyresis means that this evolutionary evidence is probably the best we have. Some support for fever comes from comparative biology. Cold-blooded animals such as lizards lack a mechanism to produce fever when they become infected. A "heat-seeking" instinct has been described in these creatures, however; this allows them to raise their body temperature by external means: The survival value of such behaviour has been shown clearly in the laboratory. A question often raised about the evolutionary argument is why fever would be beneficial in mild to moderately severe infections but demonstrably deleterious in fulminant disease 2. Such a difference can be explained by the fact that evolution has no interest in the preservation of the individual, only in preserving the species: As Russell et al. Obviously the duration of fever cannot be one endpoint, but what other sign or symptom can be objectively and quantitatively measured in a reproducible manner? Hundreds and probably thousands of patients would have to be enrolled in double-blind, placebo-controlled studies and followed in exquisite detail. This is why so little clinical data are available, and it seems unlikely that more will be obtained. The information summarized by Russell et al. On the other hand, good evidence supports the view that the high fevers encountered in septic states are deleterious to the host and that their suppression is helpful in assuring survival 2. As pointed out earlier, these instances are comparatively rare, and from an evolutionary perspective all of the affected individuals would have died. In addition to the probability that antipyretics may prolong the course of mild to moderate infectious illnesses, what other deleterious effects might they have? Even in developed countries, all available methods of antipyresis must be treated with respect. Warning labels became required for paracetamol recently and for aspirin in the more distant past. In addition to acute poisoning, the former has been implicated in the development of chronic renal disease, and perhaps liver failure, when repeatedly administered over prolonged periods of time 3. Perhaps more important is the fact that antipyretics mask symptoms or signs; children with pneumonia, for example, may not receive a proper diagnosis because their respiratory rate decreases 4 or because, when the body temperature starts to fall, the child may be considered to be on the way to recovery and thus needing no further observation. Finally, of course, the costs may consume a significant amount of resources that, in developing countries, could be better devoted to specific diagnosis and therapy. Other potential benefits of reducing fever are sometimes cited to justify the use of antipyresis. A common assumption is that these drugs make patients feel better, but no clear evidence shows that this is so. Parents and physicians consistently cannot distinguish between the effects of placebo and paracetamol in most circumstances 5. Perhaps the exceptions are conditions accompanied by pain, for which the analgesic effects of the medication provide the benefit. When fevers rise above Despite the firm belief in the effects of antipyretics, children do not feel any better, eat better, or become more active after their use than they do after they receive placebo. The argument that the use of antipyretics reduces the occurrence of febrile seizures also is not based on evidence: Even in children with previous febrile seizures, the use of antipyretics has not been helpful 7. Some physicians believe that the response to antipyretics can be used to differentiate between bacterial and viral infections, with the latter responding more completely and promptly. Numerous studies have shown this to be a fallacy 8, 9. In summary, what does the evidence seem to indicate? Fever represents a universal, ancient, and usually beneficial response to infection, and its suppression under most circumstances has few, if any, demonstrable benefits. On the other hand, some harmful effects have been shown to occur as a result of suppressing fever: It is clear, therefore, that widespread use of antipyretics should not be encouraged either in developing countries or in industrial societies. Unfortunately though, just as fever represents an ancient biological response, an emotional effect is embedded deeply. Thus, the fever has become synonymous with the illness. Annals of Internal Medicine ; American Journal of Medicine ; The effect of temperature reduction on respiratory rate in febrile illnesses. Archives of Diseases in Childhood ; Risks and benefits of paracetamol antipyresis in young children with fever of presumed viral origin. Correlating changes in body temperature with infectious outcome in febrile children who receive acetaminophen. Antipyretic effectiveness of acetaminophen in febrile seizures: European Journal of Pediatrics ; Fever response to acetaminophen in viral vs. Pediatric Infectious Diseases Journal ;6:

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Chapter 2 : Antipyretic - Wikipedia

One of the most common manifestations of disease is a regulated elevation in body temperature known as fever. A variety of experiments now indicate that fever is an integral part of the host defense response, which acts in synergy with other participants to combat disease.

About About fever reducers Various medications are available that offer relief to people who display symptoms of fever. In many cases, a single drug can both reduce fever and provide relief from pain. When used correctly, these drugs are safe for most people and usually cause few side effects. Fever is a natural body response to infection and other conditions. Chemicals of the immune system are sent to fight any invading agent such as bacteria or a virus. Some of these chemicals, called pyrogens also travel to the hypothalamus, the area of the brain that controls body temperature and cause the temperature to rise. Medications that are used to treat fevers are typically known as antipyretic agents. They work by blocking the mechanisms in the body that cause fever, but do not treat the underlying condition that triggers the fever. The most common antipyretics are acetaminophen, ibuprofen and aspirin. Aspirin should never be used to treat children, because it can cause Reye syndrome in children. Reye syndrome is a rare but extremely serious condition that affects all organs of the body and can be life-threatening. People who have mild fevers degrees Fahrenheit or less, or 39 degrees Celsius or less may not require treatment of any kind. Even patients with higher temperatures usually do not require treatment, because high temperatures generally are not dangerous in and of themselves. Many physicians argue that fevers should not typically be treated and cite evidence suggesting that fevers actually help to fight infection. The exception to this rule involves infants under 3 months of age. Children of this age often require medical treatment when they have a fever, even a mild fever, especially if they were born prematurely or if their fever is over Although fevers usually do not require treatment, patients may find that a fever reducer can relieve discomfort. In many cases, fever reducers are combined with medications used to block pain, commonly known as analgesics. In both cases, analgesics prevent the brain from processing pain signals, but do not rely on anesthesia or loss of consciousness to achieve the pain-relieving effect. Acetaminophen and ibuprofen are two of the most commonly recommended combination fever reducers and pain relievers. These medications have few side effects and are even considered safe for infants, who may take them in drop form. Liquids are also available for toddlers, whereas chewable tablets may be preferred by older children. Fever reducers should only be given as recommended by a physician. Taking too much of a medication, including over-the-counter medications, can have serious health consequences. The size of the patient and severity of the illness are usually the most important factors in determining dosage levels. These guidelines work well in most cases. When using a medicine dropper, it should be held at eye level. The dropper should be the one that was packaged with the medication. When measuring with a spoon, a specific measuring spoon or the spoon packaged with the medication should be used because kitchen table spoons vary in size. When using a medicine cup, patients are urged to fill the cup to the appropriate mark when the cup is at eye level. People should not deviate from the recommendations suggested by a physician or a drug manufacturer. In addition, individuals may respond differently to various medications. People are urged to consult their physician about which drugs might be most effective. Types Types and differences of fever reducers There are numerous types of medications that can be used to reduce fever, both prescription and over-the-counter. Both types of medications are strong drugs and should only be used as recommended. People are urged not to take any medications without first consulting a physician or other healthcare professional. There are two major categories of fever reducers â€” acetaminophen and nonsteroidal anti-inflammatory drugs NSAIDs. Acetaminophen and ibuprofen are available in formulations for both adults and children, but children should not take aspirin. Children should never take medications intended for adults, even in smaller doses. Acetaminophen Used to treat mild to moderate pain and fever. It is also used to treat headaches, minor pain, muscle aches and achy joints. It is less likely to cause stomach irritation than other fever reducers such as aspirin, but it is associated with other potential side effects such as skin rash or hives, breathing difficulties, and liver damage. Aspirin Derived from salicylate â€” a naturally occurring substance found in the bark of willow trees â€" aspirin has been used for more than years to reduce fever and relieve mild to moderate pain, redness, swelling and discomfort caused by various medical disorders. It also helps reduce clotting of blood. Although aspirin can be a powerful and effective drug, it also can be dangerous when used in children. Use of aspirin in children has been associated with Reye syndrome, a rare but extremely serious condition that affects all organs of the body and can be fatal. The danger is most likely in children who take aspirin when they have a viral infection, such as the flu or chickenpox. Symptoms include vomiting, lethargy and behavioral changes such as increased belligerence. Because of this danger, experts recommend that aspirin not be used by children and teenagers, especially if they have a viral illness. In addition, children may be more vulnerable to the side effects of aspirin than adults. Such side effects include stomach upset and intestinal bleeding. Because of these side effects, some experts recommend using antipyretics other than aspirin whenever possible. Ibuprofen A pain reliever that also reduces inflammation and fever. This NSAID is used to treat numerous types of pain, including headaches, muscle aches and many other causes of discomfort. Ibuprofen is typically considered to be particularly effective for treating high fevers. However, it should never be taken by patients who are dehydrated or who are vomiting continually. Ibuprofen also should not be used in children who are 6 months of age or younger. In April , the U. Food and Drug Administration FDA announced that it was asking all manufacturers of prescription NSAIDs â€" including ibuprofen â€" to include new warnings on labels about certain potential health dangers associated with these medications, such as an increased risk of cardiovascular events and gastrointestinal bleeding that could be potentially life-threatening. It also is used to reduce pain associated with arthritis and other musculoskeletal conditions. The safety and effectiveness of naproxen has not been established in children younger than This drug has been associated with stomach irritation and nausea. Ketoprofen is another NSAID used to reduce fever, as well as to relieve minor aches and pain from headaches, menstrual periods, toothaches, the common cold, muscle aches and other conditions.

Chapter 3 : Antipyresis and fever.

Abstract. Fever is an important mechanism of intrinsic resistance against infectious disease. A variety of studies point to a potential detrimental effect of temperature lowering in infectious disorders, but high-quality evidence from randomised controlled trials is lacking.

The hypothalamic thermosensitive neurons show a variety of firing patterns to local thermal stimulation. There are far fewer thermally sensitive neurons in the posterior hypothalamus, but there are some, and local heating there rather than initiating thermal responses can inhibit some previously generated thermal behaviours. There is also thermal sensitivity in the medial hypothalamus possibly related to behavioural thermoregulation. As yet there is no evidence that they play a role in body temperature control. It is of interest that there is recent evidence that the frontal neo-cortex can exert a modulating effect on thermogenic activity evoked by lateral hypothalamic lesions De Luca et aL, , and can cause thermogenic activity when stimulated electrically De Luca et aL, The brain stem and spinal cord There are both warm and cold sensitive neural units in the mid-brain reticular formation and in the medullary reticular formation. Many medullary thermosensitive units responded also to thermal stimulation of skin areas. The medulla responds to warming and cooling with physiological and behavioural thermoregulatory activities. The spinal cord responds to artificial heating and cooling by initiating thermoregulatory responses. Much of the work on spinal cord thermosensitivity and its importance in thermoregulation has been reported and discussed by Simon It appears that the spinal cord is an important source of thermal information as well as a region capable of modulating other thermal inputs. They were able to cause panting by intra-abdominal heating and to show that it was truly a response to heating structures within the abdominal cavity. It was suggested that the receptors lay in the walls of the intestine and rumen and possibly in the mesenteric veins. There may be some response to intragastric cooling in humans as a result of cooling of afferents from the stomach wall Nadel et al. There is evidence for temperature sensitivity in some blood vessels and muscles see Hensel, , and that neurons subserving other functions can also show thermosensitivity, e. Putative neurotransmitters The presence of high concentrations of noradrenaline and 5-HT in the hypothalamus was demonstrated by Amin et al. Using the formaldehyde condensation technique the presence of these amines in varicose terminals of neurons in the hypothalamus was established by Bertler and Carlsson et al. Mechanisms of temperature regulation 23 It was that the core temperature depended on the balance between the two amines secreted into the hypothalamus. He opted for the neurotransmitter concept. In , Cooper et al. Whereas in the cat 5-HT raised and noradrenaline lowered body temperature, the opposite was found in the rabbit. Others followed, with some species responding to the monoamines in one way and others in the opposite see Bligh, Bligh also proposed a neuronal model for sheep, goats and rabbits which used acetylcholine in synapses transmitting cold information and possibly heat production pathways and 5-HT in synapses transmitting warm information and possibly heat loss pathways with crossed inhibition possibly using noradrenaline. This model has been greatly expanded and is based on intraventricular or hypothalamic infusions of the amines. It has not yet been proved that the injected amines are acting on primary thermoregulatory circuits or whether they excite other non-thermoregulatory neurons which secondarily act on thermoregulatory neurons. In fact, we have little evidence with which to identify thermoregulatory neurons embedded in a mass of fibres subserving many functions in the hypothalamus. There are several other possible neurotransmitter substances which could be used in thermoregulatory synapses, and these include dopamine and a variety of pep tides. While some of these can, on local application within the brain, alter body temperature, the proof of their specificity as neurotransmitters in the thermoregulatory circuits needs further study. Effector mechanisms in thermoregulation and their efferent systems Two mechanisms are available to conserve or lose heat, namely behavioural and physiological. The former is of great importance in ectotherms and in many endotherms, and is a major component in human thermoregulation. In this way control of the micro-environment has been regulated in the presence of severe conditions of temperature in the general environment. But, adopting particular patterns of behaviour is not confined to humankind. Many species of lizard can in the daytime shuttle between the shade and the sunlight, and by adjusting the time spent in each, can achieve a body core temperature well above the shady ambient temperature and so keep at maximum activity for catching prey. Another behaviour is that of body orientation. An example of this is to be seen in the jack rabbit Lepus alleni , sitting in the shade, with the position of its large ears set so that they radiate heat to the sunless part of the sky. Other animals may, in the heat, orientate their bodies so as to present minimal surface area to the solar radiation. A further mode is that of huddling together to share the heat of the whole group and insulating those in the middle of the huddle. In some newborn animals this behaviour not only contributes to keeping warm but reduces their energy expenditure Mount, These are but few of the types of behavioural thermoregulation which, as we will see later, can be of great significance in fever. In endotherms there is co-ordination between behavioural and physiological thermoregulation with both usually being used at the same time. Control of behavioural thermoregulation starts with detection of the environmental thermal conditions and the thermal topography of the body. Both hypothalamic and surface temperatures are used in causing behavioural thermoregulatory responses. Earlier, Cabanac et al. There are many reports of behavioural thermoregulatory corrective responses induced by altering the hypothalamic temperature see Hensel, , p. Similarly, Mechanisms of temperature regulation 25 operant behavioural responses, e. The confirmations of this result have been obtained in many species including primates. Physiological or autonomic mechanisms Heat production Sources of heat production include the basal energy release resulting from the necessary cellular metabolism of the body tissues, the level of voluntary muscular activity, shivering thermogenesis and non-shivering thermogenesis. To these sources of heat must be added heat gained from solar radiation, from contact with warm objects such as electric blankets and heat gained by ingestion of warm food or drinks. The basal metabolic rate cellular metabolism is itself temperature dependent. This change is termed the Q 10 value. Measurements in one human in whom there were, as a result of hypothalamic disease, no active thermoregulatory responses gave a Q 10 of 2. The so-called basal metabolism, that is the energy release by metabolism at complete rest, both mentally and physically, in a neutral thermal environment and in a post-absorptive condition can be assessed by measuring the O 2 consumption. This was measured in patients under maximal sedating doses of thiopentone, and gave more consistent data the meaning of which was sometimes questioned. Some have standardized the conditions under which 26 Thermoregulation - an outline the resting metabolism can be measured as including being awake but fully relaxed and fasted for 12 hours in a thermoneutral environment, and this gives the minimum metabolic rate. Further modifications of the measurement of standard metabolic rate in infants have been described Bruck, Active processes altering metabolism Voluntary muscular activity A well-used mechanism is raising or lowering the level of voluntary muscular activity. Relaxing, where possible in the heat, decreases metabolic rate, and muscular exercise in the cold produces increased heat. These responses really fall into the category of behavioural thermoregulation. Shivering The involuntary twitching of groups of muscles, which perform no useful work, in the cold is known as shivering. Shivering can be induced by cooling the spinal cord and the hypothalamus Simon, Heat production of the order of kcal. The ability to shiver may take some days to develop after birth in the human baby Bruck, , and is absent in many people over the age of 69 years Collins et al. Dogs with their spinal cords severed can, when the limbs are immersed in cold water, shiver in the muscles innervated from above the lesion Sherrington, These observations imply the existence of thermoreceptors within the central nervous system which can initiate shivering without cold receptor input from the periphery. The central nervous pathways involved in shivering are complex and include the septal region, the hypothalamus and the spinal cord. Andersson stimulated the septal region electrically in goats and found that this produced shivering, peripheral vasoconstriction and inhibited panting in heat exposed animals, and sometimes caused piloerection. Studies in which electrical stimulation of hypothalamic areas Stuart et al. It is also of interest that the baroreceptors and the chemoreceptors have been shown to influence shivering in the rabbit Mott, Baroreceptor stimulation enhanced shivering and chemoreceptor stimulation suppressed it. It is therefore important in studies of the initiation and levels of shivering to ensure that such factors as blood pressure and blood chemistry do not confound the observations. The other major source of heat production during cold exposure in newborns and many adult animals, such as the rat and some hibernating species, is BAT. This specialized fatty tissue is found in the interscapular region, near the kidneys, in the thoracic cavity close to the heart and the aorta and sometimes in the inguinal region. It has an abundant vascularization with veins which drain the blood from it towards the central vital organs such as the heart. The fat globules are small and numerous. BAT has a rich sympathetic nervous innervation and has a high density of mitochondria. The nerve terminals contain neuropeptide Y in addition to noradrenaline. The following sequence of events between the activation of the sympathetic nerves to BAT and heat production is quoted verbatim from Himms-Hagen BAT occurs in the newborn in many species, and in some, such as the rat, it persists as an important heat source into adult life. It is of great importance to hibernating animals as a source of heat during awakening from hibernation. The control of heat production by BAT involves the ventromedial hypothalamus, and there is some argument concerning the possible role of the dorsomedial hypothalamus and the paraventricular nucleus. Since many parts of the hypothalamus are involved in endocrine functions which play adjunct roles to thermoregulation one would expect that their interconnexions with the ventromedial hypothalamus would influence BAT metabolism. In fever the nucleus of the tractus solitarius is an important part of the sympathetic outflow which controls BAT activation. As with other aspects of thermoregulation the complexity of the hypothalamic and brainstem circuitry involved, and its close integration with other autonomic functions has made our understanding of the neuronal cytoarchitecture difficult to unravel, and for the most part we are grossly ignorant of the essential connectivities. Heat elimination The physical factors involved in heat loss or elimination are conduction, convection, radiation and evaporation. Heat conduction occurs between the body and any object with which it is in contact. Thus sitting on cold ground will drain heat from the body as will being immersed in cold water, and the heat flow will be proportional to the temperature difference between the body surface and the medium to which heat is lost. Convection involves the heating of the air, or other medium, at the body surface which becomes more buoyant, moves upward over the body surface and is replaced by cooler denser air. This process requires gravity and thus cannot take place in gravity-free conditions in space. Mechanisms of temperature regulation 29 Wind blowing over a surface extracts heat by a process known as forced convection. Radiation is a major route of heat loss or gain. Evaporation requires heat for the change in state, e. The full mathematical treatment of these physical routes of heat exchange are given in Kerslake The heat balance equation is: Cd is small except under special circumstances such as lying on the snow! Heat loss from the skin is determined by the superficial skin temperature and this in turn is set by a combination of the environmental temperature and the skin blood flow. The neural control of the latter is of paramount importance and is mediated via the sympathetic nervous system. There are two main skin regions where the sympathetic nervous control differs. The skin of the hands and feet and to a lesser extent the distal parts of the forearms and the calves have a high density of arterio-venous anastomoses near the surface, and the vascular innervation is that of tonic vasoconstrictor impulses. Vasodilatation in these areas is achieved by release of vasoconstrictor tone, and the huge blood flows which can occur in the fingers, for example, happen by the opening up of the arterio-venous shunts.

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Chapter 4 : Fever Reducers (Fever Medications) | Antipyretics

While understanding of the mechanisms of fever has progressed in recent years, much uncertainty remains as to whether fever in itself (as distinct from its cause) is beneficial or harmful, and what circumstances warrant antipyretic therapy.

Abstract Fever is an important mechanism of intrinsic resistance against infectious disease. A variety of studies point to a potential detrimental effect of temperature lowering in infectious disorders, but high-quality evidence from randomised controlled trials is lacking. In ambulatory care settings, we need to know whether antipyretics influence the severity and duration of illnesses and, in critically ill patients, whether antipyretics affect mortality. This observation led Julius Wagner-Jauregg to propose, in , that inoculation of malaria might be a justifiable therapy for progressive paralysis. His rationale was that one could replace an untreatable condition with a treatable one â€” malaria being treatable with quinine. In , he tested his hypothesis in nine patients who had paralysis due to syphilis by injecting them with blood from patients who had malaria. Remission of paralysis occurred in three patients. Even among the sickest patients in our intensive care units, the use of antipyretics to treat fever is ubiquitous. The reasons for the use of antipyretics having become so common are complex. These medicines have dual effects of analgesia and antipyresis. The availability of many antipyretic medicines over the counter has led to a widely held view that they are without risk. Evidence in support of paracetamol administration in a general practice setting comes from a randomised placebo-controlled trial in children with viral illnesses. In intensive care patients, administration of ibuprofen has been shown to reduce heart rate and minute ventilation; 2 proponents of antipyretic administration argue that this may be important in critically ill patients with limited cardiac or respiratory reserve. These considerations need to be balanced against the numerous studies which suggest that administration of antipyretics has the potential to adversely affect the course of infectious disorders. In adults, administration of antipyretics increases rhinovirus shedding and worsens nasal symptoms in patients with the common cold. It is interesting to consider whether, if the history of development of paracetamol as a medicine had been different, and its mechanism of action had been known from the outset, this calming effect in children would have been viewed in such a positive light. However, we lack high-quality evidence on which to base clinical practice. Randomised controlled clinical trials evaluating the effects of antipyretics are needed. In ambulatory care settings, we need to know whether antipyretics influence the severity and duration of illnesses and, in the most critically ill, we need to know whether antipyretics affect mortality. Julius Wagner-Jauregg in black jacket watching the transfusion of blood from a patient with malaria to a patient with neurosyphilis, to trigger fever.

Chapter 5 : Fever and Antipyresis: the Role of the Nervous System - PDF Free Download

This book provides a detailed overview of the function of the nervous system in fever and its role in antipyresis. The volume opens with an introductory account of fever, its physiology and adaptive role, and explains the mechanisms of thermoregulation.

Chapter 6 : Fever and antipyresis in infection | The Medical Journal of Australia

Fever is established as a phylogenetically ancient host response that is conserved highly in all mammals (1). That fever, despite high metabolic and nutritional costs, is conserved so highly argues forcefully for its evolutionary value, as does the endogenous nature of its mechanism, which requires a complex series of steps and interactions.

Chapter 7 : SaÃºde PÃºblica - Fever and antipyresis Fever and antipyresis

Abstract. To determine whether the prevention of fever affects the survival of an animal infected with pathogenic bacteria, lizards (Dipsosaurus dorsalis) were infected with live Aeromonas hydrophila and received varying doses of *sodium salicylate, an antipyretic drug.*

Chapter 8 : Antipyresis and fever | Read by QxMD

The developed questionnaire included 10 multiple-choice, knowledge-evaluating items about fever and antipyresis, 10 Likert-type attitude-evaluating items towards fever and 10 towards antipyresis. Multiple linear regression analysis was used to identify the predictors of attitudes towards fever and antipyresis.

Chapter 9 : Fever, Friend or Foe? | LITFL

Antipyretics (/ ËŒ Ã¦ n t i p aÉª Ëˆ r É› t Éª k s /, from anti-'against' and pyretic 'feverish') are substances that reduce fever. Antipyretics cause the hypothalamus to override a prostaglandin-induced increase in temperature.