

# Cooling Fever Phobia

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## Pediatrics

Classic emergency medicine textbooks don't dwell too much on the treatment of benign fever — for adults or kids. As ER docs our job is to seek out the dangerous, to nab bacterial infections, arrest sepsis, and prevent status epilepticus. However, when we find ourselves left with a non-toxic kid tolerating her viral syndrome just fine, we must address the parents' final concern. "But, she still has a fever. What do we do?"

Most disciplines define fever as 38°C or 100.4°F. This is a good starting point for the conversation with parents. Now they can stop worrying about all those bland readings of 99.9°F. When it comes to "real" fever, it's our job to educate and advise there too — and act by example.

Fever is not a disease in itself but a physiologic response of the immune system with beneficial effects in fighting infection. Recent guidelines by the American Academy of Pediatrics (AAP) seek to calm "fever-phobia" in parents and practitioners, reinforce its beneficial qualities, and encourage antipyretics for comfort rather than absolute temperature control. Even in the case of febrile seizures, fever control does little to prevent recurrence.<sup>1</sup>

Fever is a natural increase in the hypothalamic "set point" in response to internal and external pyrogens. Specifically, "fever retards the growth and reproduction of bacteria and viruses, enhances neutrophil production and T-lymphocyte proliferation, and aids in the body's acute-phase reaction. The degree of fever does not always correlate with the severity of illness ... Risks of lowering fever include delayed identification of the underlying diagnosis and initiation of appropriate treatment and drug toxicity."<sup>1</sup>

The AAP guidelines urge clinicians to spread the message that fever is not known to harm children and may even be of benefit. The goal of antipyretics is comfort, rather than to normalize temperature.

There is precedence in the adult literature that fever is a strong protective mechanism for the body against infection. One study was stopped early due to overwhelming evidence on preliminary review that tight fever control actually increased infection rates and mortality in Trauma ICU patients.<sup>2</sup>

After screening 572 patients over nine months, 82 ICU patients were enrolled in a University of Miami study and randomized into either an aggressive fever-control group (acetaminophen 650mg q6h for T>38.5°C, and cooling blanket added for T>39.5°C) or a permissive group (acetaminophen 650mg q6h and cooling blanket both for T>40°C). Patients required an ICU stay over three days, and were excluded for other hyperthermic conditions (heat stroke, malignant hyperthermia, neuroleptic malignant syndrome), previous history of traumatic brain injury, or any other potentially compromising neurocognitive condition (seizures, strokes, hepatic cirrhosis). Because acute brain injury is the only condition in which literature shows that fever worsens neurologic outcomes and antipyretics improve them, the authors hypothesized that aggressive fever control would actually compromise the immune competence of critically ill patients and make them more susceptible to infection.

Physician judgment determined the need for prophylactic and empiric antibiotics, and further treatment was culture-directed. The study was stopped on preliminary review, well before it reached the sample size of 672 subjects needed for statistical significance (for 95% CI, 90% power, to determine 25% increase rate of infection). The review showed rates of 4 ± 6 infections per patient in the aggressive-control group (131 amongst 44 patients) and only 3 ± 2 infections per patient in the permissive group (85 amongst 38 patients), p=0.26. There were seven deaths in the aggressive group (16%) and only one in the permissive group (3%), p=0.06.

While we should not act in a reactionary fashion to fever, neither should we disregard its significance as a marker of immune system response. It is our job to determine the disease etiology, benign or not. For most emergency physicians, this work up comes naturally. The appropriate exam and laboratory tests should help identify the source of infection, the presence of sepsis syndrome or immunocompromise; and any need for antibiotics, resuscitation, or admission. Because fever is so non-specific, workups can be simple or complex — as that proposed by a recent Chilean study that sought to validate a prediction model for severe sepsis in pediatric cancer patients within the first 24 hours of admission. All 447 subjects were ≥12 years old and had high risk neutropenic fever, prompting atypical decision points such as serum C-reactive protein (CRP) ≥90mg/L and interleukin-8 (IL-8) ≥300pg/ml.<sup>3</sup>

That said, once we determine and address the disease process causing the fever, guidelines tell us that fever management need only revolve around comfort. Importantly, we can maintain this same standard for children with a history of simple febrile seizures. The AAP guidelines note that "no long-term effects of simple febrile seizures have been identified," including degradation of patient IQ, risk of epilepsy, or death. The only increased risk is that of recurrent febrile seizure itself, an incidence that ranges from 30-50%.<sup>4</sup>

Studies have compared both antipyretics vs. placebo, and anti-epileptics combined with either antipyretics or placebo, and in neither case did strict fever control significantly decrease the incidence of febrile seizures. Ibuprofen was compared to placebo in a randomized, double-blinded study of 230 children with febrile seizures who were treated for any temperature over 38.5°C or 101.3°F. The outcome was insignificant, with 28% and 30% recurrent seizures, respectively.<sup>5</sup>

Despite our efforts to follow best practices, however, underlying personal discomforts play out in our daily patient encounters. In a survey of 118 Italian pediatricians, there remained deviations in practice compared to their national guidelines — which essentially mimic ours. While most pediatric hospitalists, community practitioners, and residents chose acetaminophen over ibuprofen as their first antipyretic, and chose 38.5-38.9°C as a typical starting point for treatment, many did not reconsider antipyretic use based on the patient's physical comfort (59%, 60%, and 45%, respectively), and the majority "often" lowered the treatment threshold for patients with a history of febrile seizures despite the lack of evidence for benefit (54%, 77%, and 100%, respectively). A number

in each group continued to recommend physical methods for cooling, also a non-evidence-based practice.<sup>6</sup>

Italian Pediatric Society guidelines, like American guidelines, recommend treating with antipyretics solely for comfort rather than absolute temperature. They promote oral acetaminophen or ibuprofen but note no value in using dual or alternating therapy, or in changing the threshold for treatment in patients with history of febrile seizures, or in adding physical or homeopathic methods for cooling.<sup>7</sup>

Across the border in Switzerland, another study of practicing pediatricians collected 322 replies from 922 original surveys. It too showed a gap between evidence-based guidelines and clinical practice, apparently more pronounced in the French and Italian speaking regions than in the German speaking regions. The former practitioners favored treatment based on absolute temperature and treated fever more aggressively.<sup>8</sup>

Should we ignore fever? No. But next time a mother asks you what to do about baby Betsy's fever, we should be coaching her on the natural value of fever and the use of antipyretics for comfort alone. We can start by trying our best to lead by example.

*Dr. Ross is a former AAEM/RSA president and currently works in private practice in Virginia — a job she loves! As a young doc, she's learning to balance the thrill of attending life with the responsibilities of staying well-read, thoughtful, and efficient in the ED. She welcomes your feedback at [tmrossmd@gmail.com](mailto:tmrossmd@gmail.com).*

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