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Prolonged and recurrent fevers in children

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Summary Some children referred for prolonged fever are actually not having elevated temperatures; the approach here requires dissection of the history and correction of health misperceptions. Others have well-documented fevers associated with clinical, laboratory, or epidemiologic findings that should point to a specific diagnosis. "Fever-of-Unknown-Origin" (FUO) is the clinical scenario of daily fever for ≥14 days that defies explanation after a careful history, physical examination, and basic laboratory tests. The diagnostic approach requires a meticulous fever diary, serial clinical and laboratory evaluations, vigilance for the appearance of new signs and symptoms, and targeted investigations; the pace of the work-up is determined by the severity of the illness. Approximately half of children with FUO will have a self-limited illness and will never have a specific diagnosis made; the other half will ultimately be found to have, in order, infectious, inflammatory, or neoplastic conditions. Irregular, intermittent, recurrent fevers in the well-appearing child are likely to be sequential viral illnesses. Monogenic autoinflammatory diseases should be considered in those who do not fit the picture of recurrent infections and who do not have hallmarks of immune deficiency. Stereotypical febrile illnesses that recur with clockwork periodicity should raise the possibilities of cyclic neutropenia, if the cycle is approximately 21 days, or periodic fever, aphthous stomatitis, pharyngitis, and adenitis (PFAPA) syndrome, the most common periodic fever in childhood.

Introduction

In 1871, Wunderlich established 98.6 °F (range, 97.2—99.5) (37.0 °C, range 36.2—37.5), as the normal human body temperature, suggesting that temperatures above 100.4 °F (38.0 °C) were "suspicious".[1] Contemporary authors have argued that, given the wide variation between and within individuals, the concept of a "normal" body temperature should be abandoned.[2] Sites of measurement—rectum, mouth, axilla, tympanic membrane, temporal artery—vary in the degree (no pun intended) to which they approximate core body temperature.[3] Technique also matters; for example, oral temperatures are only accurate in those who can keep their mouths closed and the thermometer under their tongues.

Fever, or elevated core body temperature, is one of the most reliable indicators that something is wrong, yet all of the above make it difficult to define exactly what fever is. Most pediatricians would agree that inserting a glass or

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digital thermometer into the rectum is the most accurate way to measure core body temperature. This is feasible, however, only up to about 3 years of age. Oral temperatures, if properly done, are a close-enough approximation to core body temperature; this technique becomes feasible around 5 years of age. Between 3 and 5, one may have to settle for axillary temperatures (most physicians add 1 °F [0.6 °C] to approximate core body temperature). The Brighton Collaboration, a research network focused on vaccine safety, defines fever as "the endogenous elevation of at least one measured body temperature of ≥38 °C,"[4] irrespective of device used, anatomic site, age, or environmental conditions.

For purposes of this discussion, *undifferentiated fever* refers to the situation where a previously healthy child presents with fever as the chief complaint, without signs or symptoms of a specific clinical illness (e.g., upper respiratory tract infection, viral exanthem, etc.). A distinction is drawn between undifferentiated fever and *fever without source*, which refers to the special situation of an acute fever in an otherwise well-appearing child under 3 years of age, where there is well-documented risk for occult serious bacterial infection.[5]

Fig. 1 shows a conceptual framework for categorizing patients who present with undifferentiated fever.

Prolonged fever

In *prolonged fever*, the patient comes to medical attention because the illness has lasted beyond what might be expected for a self-limited viral illness, i.e., beyond a week or so.

Not-Fever-of-Unknown-Origin

Some such patients will actually not be having fever, at least not according to any medical definition, despite the complaint—this might be termed *Not-Fever-of-Unknown-Origin*, to distinguish it from (true) *Fever-of-Unknown-Origin*, as below. In evaluating patients with the complaint of prolonged fever, providers should be aware that elevated temperatures are seen with ovulation and after meals, exercise, and even chewing gum. Moreover, there is a normal diurnal variation in temperature, with lows in the morning and highs in the afternoon—in some healthy adults, temperatures during the day may fluctuate by as much as 2.4 °F (1.3 °C).[2] There are usually clues to the diagnosis of Not-Fever-of-Unknown-Origin[6]: the child appears healthy and has a normal physical exam; the weight is stable and growth and development are normal. The parents may have misconceptions about health and illness—in particular, what temperatures constitute true fever (parents may say, for example, that 99 °F [37.2 °C] is a fever because the child's temperatures "normally run low"). Complicated medical histories, behavioral problems, and multiple school absences for subjective complaints may point to a vulnerable child. Family stressors and fear of malignancy may be present. The approach should in carefully documenting the "fever" history, probing for underlying causes, correcting misconceptions, and reassuring parents.

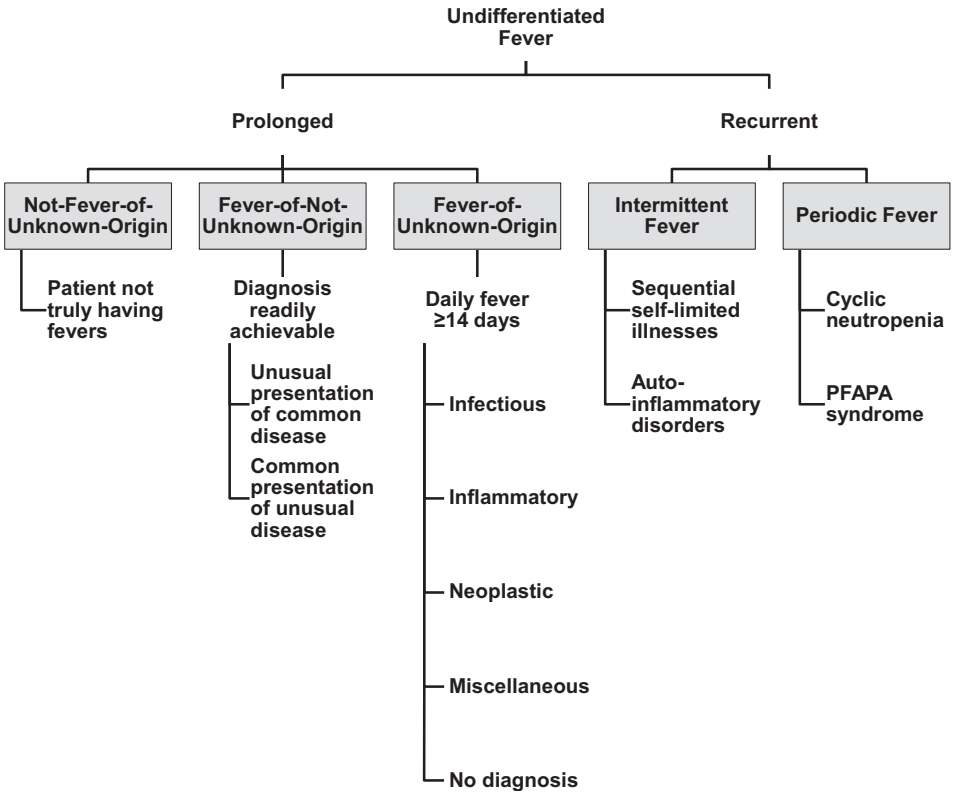

Figure 1 Algorithm for undifferentiated fevers in children (See text for explanation).