Recurrent fever in children

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OBJECTIVES

1. Describe the differential diagnosis of a child with recurrent fever occurring at regular intervals.
2. Describe the differential diagnosis of a child with recurrent fever occurring at irregular intervals.
3. Identify important history and physical examination findings that must be ascertained in all children with recurrent fever.
4. Develop a rational approach to the initial laboratory testing of patients with recurrent fever.
5. Appreciate that most children with recurrent fever do not obtain a definitive diagnosis but nonetheless have an excellent prognosis.

Recurrent or periodic fever is a fairly common complaint in children, but the literature on this topic is sparse and largely confined to case reports or small case series. There are a number of misconceptions about recurrent fever in children, including a general idea that the differential diagnosis and workup of these children are similar to those for a child with prolonged fever of unknown origin. In this review we draw on clinical experience and the medical literature on this topic to generate a differential diagnosis specifically for the child with recurrent fever and to outline a rational approach to the workup of these children.

We arbitrarily define recurrent or periodic fever as three or more episodes of fever in a 6-month period, with no defined medical illness explaining the fevers and with an interval of at least 7 days between febrile episodes. Fever is defined as a temperature of \( \geq 38.0^\circ C \) rectally or \( 38.4^\circ C \) orally. This definition differentiates recurrent fevers from daily, persistent fevers, which after 4 weeks would meet the criteria for fever of unknown origin. The etiologies of fever of unknown origin are far more diverse than those of recurrent fever, so defining a fever as recurrent rather than persistent is an important differentiating factor.

Recurrent fever with a very regular interval between febrile episodes (“it comes every 4 weeks, like clockwork”) should be differentiated from recurrent fever without a regular, predictable interval. Very few diseases of children present with recurrent fever at regular, predictable intervals, and the most common diagnosis associated with this fever pattern, PFAPA syndrome (periodic fever, aphthous ulcers, pharyngitis and adenopathy), has classic historic and physical findings that allow for its identification. In contrast a number of diseases can present with recurrent fever at irregular intervals. This review will therefore divide the differential diagnosis for the child with recurrent fever into those with fever occurring at regular and irregular intervals.

RECURRENT FEVER WITH REGULAR FEVER INTERVALS

The differential diagnosis in the child with recurrent fever occurring at regular intervals is small (Table 1). In most cases a definitive diagnosis is not made and the fever is self-limited. PFAPA syndrome is by far the
TABLE 1. Differential diagnosis for the child with recurrent fever

<table>
<thead>
<tr>
<th>Fever occurring at regular intervals</th>
<th>Fever occurring at irregular intervals</th>
</tr>
</thead>
<tbody>
<tr>
<td>PFAPA syndrome (21–28 days)*</td>
<td>Undiagnosed cause*</td>
</tr>
<tr>
<td>Cyclic neutropenia (21–28 days)</td>
<td>Fever occasionally occurs at regular intervals</td>
</tr>
<tr>
<td>Relapsing fever (Borrelia spp. other than B. burgdorferi) (14–21 days)</td>
<td>Familial Mediterranean fever (7–28 days)</td>
</tr>
<tr>
<td>Unspecified cause*</td>
<td>Hyper-IgD syndrome (14–28 days)</td>
</tr>
<tr>
<td>Predominantly recurrent EBV infection</td>
<td>Epstein-Barr virus (6–8 weeks)</td>
</tr>
<tr>
<td>Undiagnosed cause*</td>
<td>Undiagnosed cause*</td>
</tr>
</tbody>
</table>

*Common cause of recurrent fever.

TABLE 1. Differential diagnosis for the child with recurrent fever

<table>
<thead>
<tr>
<th>Fever occurring at irregular/unpredictable intervals</th>
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<tbody>
<tr>
<td>Infectious</td>
</tr>
<tr>
<td>Viral</td>
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<tr>
<td>Repeated viral infections*</td>
</tr>
<tr>
<td>Epstein-Barr virus</td>
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<tr>
<td>Parvovirus B19</td>
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<tr>
<td>?Herpes simplex viruses 1 and 2</td>
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<tr>
<td>Bacterial/mycobacterial</td>
</tr>
<tr>
<td>Repeated bacterial infections/occult bacterial infection*</td>
</tr>
<tr>
<td>Relapsing fever (Borrelia spp. other than B. burgdorferi)</td>
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<tr>
<td>Chronic meningoencephalitis</td>
</tr>
<tr>
<td>Occult dental abscess</td>
</tr>
<tr>
<td>Brucellosis</td>
</tr>
<tr>
<td>Versarailla enterocolitica</td>
</tr>
<tr>
<td>Mycobacteria, nontuberculous (e.g. Mycobacterium chelonae)</td>
</tr>
<tr>
<td>Parasitic</td>
</tr>
<tr>
<td>Relapsing malaria (Plasmodium vivax, Plasmodium ovale)</td>
</tr>
<tr>
<td>Reactivation of Plasmodium malaria</td>
</tr>
<tr>
<td>Inflammatory/immunologic</td>
</tr>
<tr>
<td>Inflammatory bowel disease, usually Crohn’s disease*</td>
</tr>
<tr>
<td>Still’s disease (systemic onset juvenile rheumatoid arthritis)*</td>
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<tr>
<td>Behet’s disease</td>
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<tr>
<td>Hereditary periodic fevers</td>
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<tr>
<td>FMF</td>
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<td>HIDS</td>
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<tr>
<td>TRAPS</td>
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<tr>
<td>Familial cold urticaria</td>
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<tr>
<td>Muckle-Wells syndrome</td>
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<tr>
<td>Neoplasia</td>
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<tr>
<td>Lymphoma</td>
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<tr>
<td>Other</td>
</tr>
<tr>
<td>Undiagnosed cause*</td>
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<tr>
<td>Drug fever</td>
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<tr>
<td>Factitious fevers</td>
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<tr>
<td>Central nervous system abnormalities (hypothalamic dysfunction, agenesis of corpus callosum)</td>
</tr>
</tbody>
</table>

PFAPA syndrome. PFAPA syndrome is characterized by periodic episodes of high fever (>39°C) lasting 3 to 6 days and recurring every 21 to 28 days, accompanied by aphthous stomatitis, pharyngitis and cervical adenopathy. Most cases occur in children <5 years of age. Fevers occur at such predictably regular intervals that the parents can often tell the physician when the next episode will occur. Not all children manifest all three of the nonfever signs; in the largest series reported to date, cervical adenopathy was the most frequent finding (88%), followed by pharyngitis (72%) and aphthous stomatitis (70%). Cervical nodes are rarely larger than 5 cm, and adenopathy of other body sites is not a feature of this syndrome. The pharyngitis is typically mild and nonexudative. Of the three physical findings seen in this syndrome, aphthous ulcers are the most likely to be missed. Often only one or two ulcers are seen, and they are typically small (<5 mm), either painless or only mildly painful and often transient. Other symptoms may include headache, mild abdominal pain and nausea; upper respiratory symptoms such as cough or rhinorrhea are unusual. Patients with PFAPA tend to appear relatively well even during episodes and are completely well between episodes. Laboratory testing in children with PFAPA usually reveals mild leukocytosis with a normal hemoglobin level and a moderately elevated erythrocyte sedimentation rate (ESR) (mean, 46; range, 5 to 190 in the series by Thomas et al). In between episodes the leukocyte count and ESR normalize. A definitive diagnosis of PFAPA requires exclusion of cyclic neutropenia, which can present with similar signs and symptoms (see below).

The intermittent fevers of PFAPA may continue for months or years, although there is often an increase in the interval between fevers as the child gets older. Children with PFAPA are otherwise healthy, with few complaints other than recurrent fever, and no long term sequelae from PFAPA have been noted to date. The cause of PFAPA is unknown, although viral and autoimmune mechanisms have been postulated. Treatment of children with PFAPA with a single dose of prednisone (2 mg/kg) at the initial onset of symptoms has resulted in a dramatic and immediate abatement of symptoms in many patients but has also been associated with a decrease in the interval between episodes. Prophylactic cimetidine has been used with moderate success in some centers. Tonsillectomy has resulted in the eradication of episodes in many but not all children. If treatment is undertaken for the child with PFAPA, prednisone therapy should probably be the first medication used; if episodes persist and remain bothersome or disruptive to the child and family, then prophylactic cimetidine or tonsillectomy should be considered.

Cyclic neutropenia. Cyclic neutropenia is an uncommon, often inherited condition characterized by neutropenia that recurs every 21 days (range, 14 to 35 days). Associated stomatitis, gingivitis, cervical lymphadenopathy and fever are often seen. Although cyclic
neutropenia is far less common than PFAPA, the two may be clinically indistinguishable, because all the features of PFAPA can be seen in children with cyclic neutropenia, and both syndromes occur in children <5 years of age. Children with cyclic neutropenia may have repeated bacterial infections because of their recurrent neutropenia, but fever in children with cyclic neutropenia typically occurs in the absence of infection. Neutropenia may not be present at the time of fever. To test for cyclic neutropenia, leukocyte counts with differential must be done two to three times a week for a 6-week period during which the child has at least one febrile episode. The diagnosis is suggested if an absolute neutrophil count of <500 is documented and subsequent recovery of the neutrophil count to normal levels occurs in the absence of medical intervention. The diagnosis is confirmed by bone marrow examination at the time of neutropenia, which reveals maturation arrest in the myeloid lineage at the myelocyte stage. For symptomatic children with cyclic neutropenia, life-long therapy with granulocyte colony stimulating factor reduces the duration of neutropenia and markedly decreases the risk of infection.

**Other causes.** Familial Mediterranean fever, hyper-IgD syndrome and recurrent EBV infection may cause recurrent fevers at regular or irregular intervals, but they are much more likely to cause fevers at irregular intervals. All are rare in the United States. These diseases will be discussed in more depth in the section on recurrent fevers occurring at irregular intervals.

**RECURRENT FEVERS OCCURRING AT IRREGULAR INTERVALS**

The differential diagnosis of recurrent fevers occurring at irregular intervals is much larger than that for fevers occurring at regular intervals (Table 1). Infection is the most common cause of irregular recurrent fevers in children, followed by inflammatory or autoimmune disease.

**Infectious. Viral.** Repeated viral infections are almost certainly the most common cause of irregular recurrent fevers. Most children with repeated viral infections as the cause of recurrent fever are seen only by their primary physician; therefore they are rarely included in the case series of recurrent or periodic fevers in children, which are generally written by subspecialists seeing these patients in referral. Our definition of recurrent fevers as having “no defined medical illness” would exclude those children with clinically apparent viral illnesses such as lower or upper respiratory tract infections or diarrhea. However, many viral infections (most notably infections caused by the enteroviruses and some members of the herpesvirus family, but also infections with other viruses including adenovirus, influenza and parainfluenza viruses and parvovirus B19) can occasionally present with fever in the absence of any other defining signs or symptoms. Children with repeated viral infections are often in a day-care setting where they are exposed to other children with viral illnesses.

In our experience it is rare for children to have more than two viral infections in succession with no symptoms other than fever; three or more episodes of recurrent fever with no clinical signs of viral infection should suggest an alternative diagnosis. A provisional diagnosis of repeated viral infections can be made if child has signs and symptoms suggesting viral infection during febrile episodes, shows no evidence suggesting bacterial infection or other causes of recurrent fever by history or physical examination and is generally well between episodes. Laboratory values, including hemoglobin, leukocyte count and ESR, are typically normal in these children, although a mild lymphocytosis and a mild elevation of the ESR (generally <40) may be seen. Children with repeated viral infections are usually otherwise healthy.

EBV and parvovirus B19 have been reported to cause recurrent fevers at irregular intervals in single case reports. Accompanying signs and symptoms were noted in both cases. Recurrent oral ulcers caused by herpes simplex viruses 1 and 2 are occasionally accompanied by fever, but more often children with these ulcers are afebrile.

**Bacterial.** Occult bacterial infection, particularly urinary tract infection, may cause recurrent fever in children, although most children with chronic bacterial infections demonstrate prolonged rather than recurrent fever. All children with recurrent fever and no obvious source should be tested for urinary tract infection. Repeated bacterial infections may also cause recurrent fever. Children with repeated invasive bacterial infections such as sinusitis, pneumonia, cellulitis or abscesses must be evaluated for immunodeficiency. Children with repeated pneumonia should also be evaluated for cystic fibrosis and for anatomic abnormalities such as vascular slings or bronchopulmonary sequestration. Unusual bacterial infections that cause recurrent fevers include occult dental abscesses, Yersinia enterocolitica, relapsing fever caused by Borrelia spp., chronic meningococcemia, nontuberculous mycobacterial infection and brucellosis. Almost all children with these bacterial infections have signs and symptoms specific to their disease process in addition to fever. Bacterial abscesses other than dental abscesses have not been noted as a cause of recurrent fever in children, though they are a common cause of prolonged fever or fever of unknown origin.

**Parasitic.** Plasmodium vivax and Plasmodium ovale may live dormantly in the liver as hypnozoites for months or years before causing clinical infections. Relapses may be seen if liver stage-specific therapy
with primaquine is not given. Although *Plasmodium malariae* does not have a hypnozoite stage, low level infection may be undetected and flare into clinical disease many years after exposure. *P. vivax*, *P. ovale* and *P. malariae* infections are seen in children who have traveled to or lived in areas endemic for these forms of malaria.

**Fungal.** Fungal infections have not been reported to cause recurrent fever in otherwise immunocompetent children.

**Inflammatory.** Inflammatory or autoimmune disease is the other major category of disease associated with recurrent fever.

**Inflammatory bowel disease:** Inflammatory bowel disease (usually Crohn’s disease in children) is a common cause of referral for recurrent fever, and fever may precede the other signs of inflammatory bowel disease by weeks or months. Typical symptoms of Crohn’s disease include weight loss, malaise, diarrhea and abdominal pain; signs include oral ulcers, erythema nodosum, perianal skin tags and uveitis. Children with Crohn’s disease typically have growth failure, hemopoietic stools, a chronically elevated ESR and mild to moderate anemia that is often microcytic at the time of initial presentation; however, they may have only one or none of these findings.

**Still’s disease:** Still’s disease, or systemic juvenile rheumatoid arthritis, may also present as recurrent fevers, although the interval between fevers is not typically >7 days. Fevers may be an isolated finding initially, but they are often accompanied by a transient rash. Eventually arthritis develops in one or more joints, but this may occur months after the first fever. Other common physical findings include hepatosplenomegaly and lymphadenopathy. Patients with Still’s disease typically have anemia, thrombocytosis and a very elevated ESR (often >100). Antinuclear antibodies and rheumatoid factor are less often positive in patients with systemic juvenile rheumatoid arthritis (JRA) than in patients with poly- or oligoarticular disease.

**Behçet’s disease:** Behçet’s disease is a less common inflammatory cause of recurrent fever in children. The hallmark features of Behçet’s disease are recurrent fever accompanied by oral and genital ulcers, although the genital ulcers may only appear years after the oral ulcers first appear. Behçet’s disease generally occurs in individuals between 20 and 30 years of age; the disease is rarely diagnosed in children, although the fevers and oral ulcers may first occur in childhood. The clinical features of Behçet’s disease mimic Crohn’s disease; recurrent fevers, oral and gastrointestinal ulcers, uveitis, arthralgias and erythema nodosum are all features seen in both diseases. ESR and C-reactive protein (CRP) are elevated during attacks but usually are only mildly elevated between attacks, and unlike patients with Crohn’s disease, patients with Behçet’s disease do not typically have anemia. Highly symptomatic Behçet’s disease may require oral steroids or other immunosuppressive therapy such as azathioprine or cyclosporin.

**Hereditary periodic fevers:** The hereditary periodic fevers, which include familial Mediterranean fever, hyper-IgD syndrome, tumor necrosis factor receptor-associated periodic syndrome and familial cold urticaria and Muckle-Wells syndrome, are another important group of inflammatory causes of recurrent fever in children.

**Familial Mediterranean fever (FMF):** FMF is an autosomal recessive disease resulting from mutations in the Mediterranean fever gene that occurs in people of Mediterranean ancestry (typically of Jewish, Turkish, Armenian or Arabic descent). Onset is generally before 20 years of age, and 50% of individuals have onset before 10 years of age. FMF classically presents as recurrent fever with peritonitis: fever occurs in virtually all cases, and peritonitis occurs in 89 to 96% of cases. Other signs and symptoms may include serositis of other organs (pleuritis, pericarditis, arthritis), as well as an erysipelas-like rash and splenomegaly. ESR, CRP and white blood cell count are elevated during attacks but normal between attacks. Diagnosis can now be confirmed by genetic testing for mutations of the Mediterranean fever gene; 75 to 85% of patients have one of the three major mutations. Daily colchicine is highly effective, reducing the frequency of attacks or completely preventing them and substantially decreasing the frequency of amyloidosis, the most worrisome long term complication of FMF.

**Hyper-IgD syndrome (HIDS):** HIDS is an autosomal recessive disease, first described in six Dutch patients, that is caused by a mutation in the mevalonate kinase gene. The classic triad of HIDS clinical features is fever, lymphadenopathy (typically cervical) and diarrhea; virtually all patients with HIDS have fever, 94% have lymphadenopathy and >80% have diarrhea. Other signs include abdominal pain, polyarthritis, a macular skin rash and splenomegaly. In >70% of individuals with HIDS, the first attack occurs at <1 year of age. Attacks typically last 3 to 7 days and often occur after immunizations. The frequency of attacks is highly variable, ranging from once a week to twice a year. ESR is usually highly elevated during attacks (in one series the mean ESR was 90 during an attack), and leukocytosis and neutrophilia are also common. As with FMF these tests normalize between attacks. An IgD level of >100 is required to make the diagnosis of HIDS, but clinical signs may precede the elevated IgD level, and repeated measurements may be required for confirmation. IgD levels are sometimes normal in very young patients younger than 3 years of age. IgA levels are also elevated in ~80% of patients.
with HIDS. Diagnosis is confirmed by identification of the V377I mutation in the mevalonate kinase gene, which is present in >80% of patients with HIDS. Colchicine and steroids have been effective in ameliorating symptoms in some patients but not others. The overall prognosis, even without treatment, is excellent, and attacks tend to diminish with age.

Tumor necrosis factor (TNF) receptor-associated periodic syndrome (TRAPS): TRAPS is an autosomal dominant disease that is caused by a mutation in the gene for the type 1 TNF receptor. First described as Hibernian fever in a large Irish and Scottish family, it is characterized by recurrent fever with localized pain and tightness of a muscle group and a migratory pattern of symptoms; this complex occurs in >80% of individuals with TRAPS. Other common symptoms include abdominal pain, painful conjunctivitis, periorbital edema, chest pain (from pleuritis), arthralgias and skin lesions (painless erythematous macules or edematous plaques). Attacks last at least 1 or 2 days and often more than 1 week. Laboratory findings include neutrophilia and an elevated CRP. As with FMF the most serious complication of TRAPS is amyloidosis, which occurs in 25% of untreated individuals. The diagnosis is made by measuring serum levels of soluble type 1 TNF receptor, which are typically extremely low in these patients, or by DNA sequencing the exon 2, 3 and 4 regions of the type 1 TNF receptor to detect mutations. Prednisone therapy is highly effective initially, but a waning response with time necessitates increased dosing. Etanercept, a drug that binds soluble and cell-bound TNF-α and decreases its biologic effects, has been effective in a small series of patients.

Familial cold urticaria and Muckle-Wells syndrome: Familial cold urticaria (FCU), also known as familial cold autoinflammatory syndrome, is characterized by intermittent episodes of rash, arthralgia, fever and conjunctivitis after cold exposure. Muckle-Wells syndrome has a similar phenotype except that symptoms are not typically triggered by cold and sensorineural deafness develops later in life. An autosomal dominant inheritance pattern is seen in both diseases, and amyloidosis with renal involvement may occur in either disease. Mutations of the CIAS1 gene underlie both diseases, and the presence of modifier genes may determine whether disease is expressed as FCU or Muckle-Wells syndrome. Uncomplicated Muckle-Wells syndrome or FCU may respond to low dose steroid treatment, but patients with renal amyloidosis often require colchicine or more aggressive immunosuppressive therapy.

Other causes: Neoplasm must be included in the differential diagnosis of any child with an unexplained, prolonged fever, but only lymphoma has been reported in the medical literature to cause truly recurrent fever. Factitious fever should be excluded by clear documentation of fever in the office setting. Other causes of recurrent fever include drug fever and central nervous system abnormalities such as agenesis of the corpus callosum and hypothalamic dysfunction. Most children with recurrent fever who are otherwise well never receive a definitive diagnosis, despite the numerous conditions that have been described as causing recurrent fever in children.

### TABLE 2. Frequency of specific physical signs in conditions that may present as recurrent fever

<table>
<thead>
<tr>
<th></th>
<th>Oral Ulcers</th>
<th>Arthralgia/Arthritis</th>
<th>Cervical Adenopathy</th>
<th>Abdominal Pain</th>
<th>Skin Lesions/Rash</th>
</tr>
</thead>
<tbody>
<tr>
<td>PFAFA</td>
<td>+++</td>
<td></td>
<td>++</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cyclic neutropenia</td>
<td>+++</td>
<td></td>
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<td></td>
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<tr>
<td>IBD</td>
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<tr>
<td>Systemic JRA</td>
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<tr>
<td>FMF</td>
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<td>Hyper-IgD</td>
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<tr>
<td>TRAPS</td>
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<tr>
<td>Muckle-Wells/FCU</td>
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<tr>
<td>Behçet’s disease</td>
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<td>Recurrent viral</td>
<td>+++</td>
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<tr>
<td>Recurrent HSV</td>
<td>+++</td>
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<tr>
<td>Recurrent bacterial</td>
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<tr>
<td>Drug fever</td>
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IBD, inflammatory bowel disease; HSV, herpes simplex virus.
reactions with other spirochete antigens or with anti-
zyme-linked immunosorbent assay testing for antibod-
have blood smears performed for malaria. Those who have been out-
area within the past year should have thick and thin
抽血。那些在过去一年内去过疟疾高发地区的人应做厚、薄
a petechial rash is present, blood cultures should be
neutropenia before making a final diagnosis of PFAPA.
physical examination and the results of initial labora-
tory testing. As noted previously if a diagnosis of
specific intervention and have no long term sequelae from
occult bacterial infection, Crohn's disease, systemic
JRA), whereas they decrease in conditions that either
do not require intervention (e.g. most cases of PFAPA
and HIDS) or require it primarily for prevention (e.g.
FMF). Specific testing for conditions like Crohn’s dis-
ese, FMF or HIDS should be based on the history and
physical examination and the results of initial labora-
tory testing. As noted previously if a diagnosis of
PFAPA is considered, it is prudent to perform twice
weekly CBC and differential testing to rule out cyclic
neutropenia before making a final diagnosis of PFAPA.
If the child with recurrent fever is ill appearing or if
a petechial rash is present, blood cultures should be
drawn. Those who have traveled to a malaria-endemic
area within the past year should have thick and thin
blood smears for malaria. Those who have been out-
doors in areas with the appropriate tick vectors should
have blood smears performed for Borrelia spp. En-
zyme-linked immunosorbent assay testing for antibod-
ies to the Borrelia species that cause relapsing fever
may yield false positive results because of cross-
reactions with other spirochete antigens or with anti-
gen of Borrelia burgdorferi, the cause of Lyme disease.
As noted previously the child with recurrent fever who
has repeated bacterial infections should be evaluated
for immunodeficiency.

FOLLOW-UP AND PROGNOSIS
After the initial evaluation described above, the child
with recurrent fever needs no further evaluation other
than continued clinical follow-up if he or she meets the
following criteria: (1) no signs and symptoms sugges-
tive of a specific disease in the differential diagnosis for
recurrent fever; (2) no anemia or neutropenia; (3) no
growth on bacterial urine culture; and (4) a normal
ESR and CRP with fever or normalization of ESR and
CRP between episodes of fever. No further laboratory
testing is necessary in this child unless new signs or
symptoms develop; extensive laboratory testing in such
children in the absence of specific signs or symptoms to
guide the testing is invasive, expensive and yields no
additional useful information. The prognosis for chil-
dren who have recurrent fevers with no defined under-
lying diagnosis is excellent. Fevers resolve over time,
and the child’s growth and development are typically
unaffected. A subset of children with recurrent fevers
in one study were subsequently diagnosed with neuro-
logic diseases (primarily attention deficit hyperactivity
disorder and developmental delay), but it is unclear
whether these diseases had any true relation to the
recurrent fevers.

CONCLUSION
The child with recurrent fever presents a unique
clinical challenge. Recurrent fever can be the present-
ing symptom of several serious illnesses that require
medical intervention, but most often recurrent fever
has no defined etiology despite exhaustive evaluation.
Knowledge of the differential diagnosis for recurrent
fever in children and a carefully obtained history and
focused physical examination in light of this differen-
tial allow the physician to tailor the potentially enor-
mous laboratory evaluation to a few tests focusing on
specific, likely diagnoses. Careful follow-up is critical in
the child with recurrent fever, because fever may
precede other symptoms of serious disease by weeks to
months. Most children require minimal laboratory
evaluation, have resolution of fevers without any spe-
cific intervention and have no long term sequelae from
their fevers.
REFERENCES


The Pediatric Infectious Disease Journal®
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November, 2002
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Multiple Choice Questions
1. Recurrent fevers with a regular interval are typically seen in:
a. Crohn’s disease
b. Lymphoma
c. PFAPA syndrome
d. Recurrent bacterial infections
2. A child presents with intermittent fevers for the past 6 months that occur at irregular intervals and are occasionally associated with a runny nose. The child appears otherwise healthy and has no abnormalities on physical examination. The most likely cause of this child’s fevers is:
a. Muckle-Wells syndrome
b. Relapsing fever
c. Recurrent bacterial infection
d. Recurrent viral infection
3. The initial laboratory testing of a child with recurrent fever during a 6-month period, sometimes associated with a rash and malaise, and no abnormalities on physical examination should include which of the following:
a. Electrolytes and creatinine
b. Complete blood count with differential
c. Liver function tests
d. Lyme disease titers
4. Common causes of recurrent fever in children include:
a. Hereditary periodic fevers
b. Malaria
c. PFAPA syndrome
d. Cyclic neutropenia
5. Initial laboratory workup of a child with recurrent fever at irregular intervals for the past 8 months reveals an erythrocyte sedimentation rate (ESR) of 36 but no other abnormalities. The child has a history of occasional cold symptoms and sometimes complains of headaches with the fevers but is generally well in between fevers. His examination is normal except for mild anterior cervical adenopathy. Further workup should include:
a. Computed tomography (CT) scan of the head
b. Repeat ESR when not febrile
c. Toxoplasma titers
d. Bartonella titers
The Pediatric Infectious Disease Journal®

CME Exam

EXAM ANSWER SHEET

November 2002

Name: _______________________________ M.D./D.O./Other: ____________

Address: ______________________________

1. a  b  c  d
2. a  b  c  d
3. a  b  c  d
4. a  b  c  d
5. a  b  c  d
EVALUATION FORM

The Pediatric Infectious Disease Journal® CME Exam

November 2002

Your evaluation of this CME activity will help guide future planning. Please respond to the following questions:

1. Did the content of this activity meet the stated learning objectives?
   [ ] Yes [ ] No

2. On a scale of 1 to 5, with 5 being the highest, how do you rank the overall quality of this educational activity?
   [ ] 5 [ ] 4 [ ] 3 [ ] 2 [ ] 1

3. On a scale of 1 to 5, with 5 being the highest, how do you rank the effectiveness of this educational activity as it pertains to your practice?
   [ ] 5 [ ] 4 [ ] 3 [ ] 2 [ ] 1

4. Did you perceive any evidence of bias for or against any commercial products? If yes, please explain.
   [ ] Yes [ ] No

5. How long did it take you to complete this CME activity?
   ________ hour(s) ________ minutes

6. Please state one or two topics that you would like to see addressed in future issues.

____________________________________________________________________

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