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Practical approach to the febrile child in the emergency department

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Introduction

One of the most common daily problems faced by the emergency physician is the management of the febrile child. Among the heterogeneity of paediatric presentations of fever, it is important to identify which child is at risk of serious bacterial infection and what the key markers are.

Epidemiology of fever

Between 20 and 30% of all children's visits to emergency departments (ED) are for acute episodes of fever (Fig. 1).

In the first 2 years of life, children average four to six episodes of fever. In infants younger than 3 months of age, episodes of fever are less common and, at times, an infant may present with an acute infection without mounting a fever response.

Most frequently, the cause of the fever is a viral illness, usually in a seasonal pattern in Australia during the period from April through to September, when there is an increase in the community of acute infections caused mostly by respiratory and gastrointestinal pathogens, such as respiratory syncytial virus and rotovirus, respectively.

Other common viral pathogens frequently seen in the ED that cause fever include the following:

1. Varicella (chickenpox) is typified by generalized vesicles, more predominant on the trunk than limbs, with scalp lesions a diagnostic feature.
2. 'Slapped cheek disease' or erythema infectiosum caused by parvovirus B19, where a febrile illness with red cheeks is followed by a maculopapular rash that clears centrally, leaving a lacy pattern.
3. Roseola infantum is caused by Herpes virus type 6. Roseola infantum usually occurs in the first 2 years of life. Presentation is with fever and no focus (at times a febrile convulsion), then, as the fever resolves, a pink macular rash erupts.
4. Papulovesicular acro-located syndrome (PALS), in which papular lesions are located on acral parts of limbs and may take weeks to resolve (Fig. 2).
5. Enteroviral infections, which may present in a variety of ways, including malaise and fever often accompanied by a rash, Coxsackie B5 and echo 9, through to hand, foot and mouth disease, Coxsackie A16, where vesicles occur in a typical distribution over the hands, feet and occasionally on the buttocks. Lesions in the anterior mouth become painful ulcers.

Key words: *age, children, fever, guidelines outcome.*

See Commentary, page 405.

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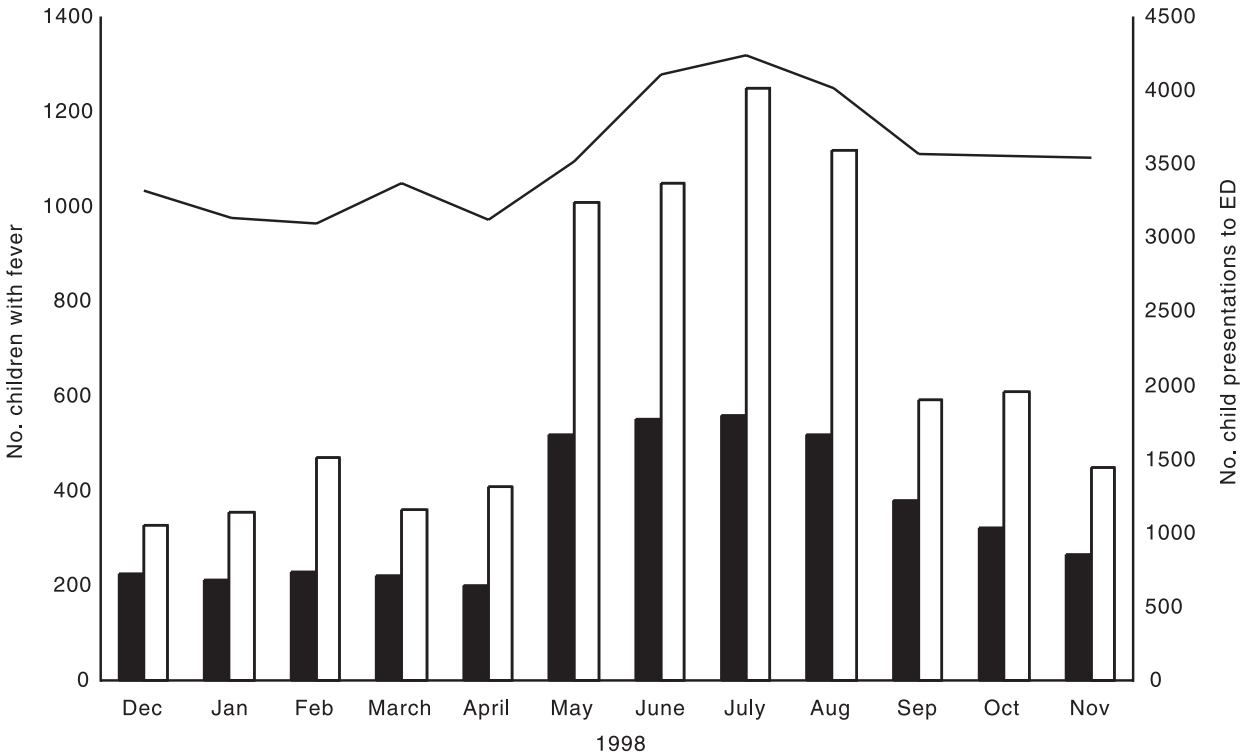

Figure 1. Epidemiology of fever at the New Children's Hospital Emergency Department (NCH-ED), showing children presenting with fever (≥ 38°C; □) and the proportion of children who were highly febrile (> 39°C; ■) in the 12 months of 1998. (—), total emergency department presentations.

Measuring temperature

Temperature may be measured in a number of ways. The gold standard is rectal temperature, but parents and patients prefer axillary temperature assessments. The axillary temperature tends to be approximately 1° less than rectal or central core temperature and is the measurement of choice in most paediatric departments.

The use of devices such as tympanic thermometers and simple cutaneous temperature measuring devices are fraught with error and are not recommended.

A temperature of 38°C represents abnormal temperature elevation or fever. The traditional teaching that normal body temperature is 37°C is too restrictive because it has been found that the upper limit of normal body temperature is 37.7°C in adults and 37.9°C in children.[1,2] Temperature also shows a diurnal variation, with the lowest temperature occurring at 0600 h and the highest temperature occurring at 1800 h.

Pathophysiology of fever

Three pathophysiological mechanisms are important in managing febrile children.

First, the hypothalamic set-point in the central nervous system (CNS) is raised due to the action of cytokines released in response to various agents, most commonly viral or bacterial pathogens. Less commonly, such as in the setting of prolonged fever, the agent may be circulating immune complexes, as seen in autoimmune disease, or pyrogens released by tumour cells.

In such situations, fever may be lowered by antipyretics and removal of excessive clothing.

Once reset, the thermoregulatory centre maintains a high body temperature through mechanisms such as cutaneous vasoconstriction, heat conservation or shivering thermogenesis. Significantly, the infant's thermoregulatory response is less mature and hypothermia may occur with infection instead.

Second, fever can be due to heat production exceeding heat loss as, for example, in salicylate

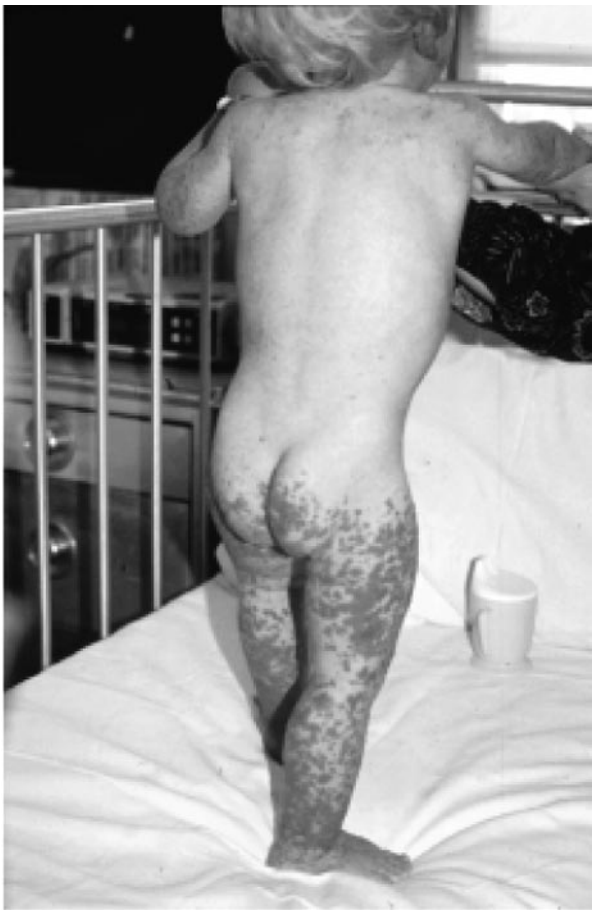

Figure 2. Papulovesicular acro-located syndrome (PALS) in a febrile infant. The lesions are limited to the acral parts of the limbs and, occasionally, the face, where occasional lesions may be vesicular. On the limbs, the lesions are commonly grouped in a linear distribution.

overdose, hyperthyroidism, excessive environmental temperature and malignant hyperthermia.

Third, fever can be caused by defective heat loss mechanisms, as seen in ectodermal dysplasia, heat stroke and poisoning with anticholinergic drugs.

In the latter two settings, antipyretics are not effective.

Vigilance is also required regarding the possibility of a focal cerebral lesion affecting the function of the thermoregulatory centre causing an elevated body temperature. Both CNS tumours and acute subdural haematomas may produce an elevated body temperature. Look for clinical features consistent with physical abuse in the irritable infant with unexplained fever, particularly where family circumstances may raise suspicion of possible physical abuse.

Fever: To treat or not to treat?

The routine use of antipyretics in the treatment of fever has been questioned. In particular, there has been concern that the use of antipyretics may prolong viral shedding and, hence, viral illness in children. In animal studies, the treatment of fever has also been shown to increase morbidity and mortality in a septic animal model.

The arguments for treating fever include the following:

1. Decreasing discomfort associated with fever often assists with settling an apprehensive home environment.
2. Preventing extreme temperature elevations from causing permanent damage to the CNS.
3. Decreasing, in theory, the likelihood of fever-related seizures in those who have a history of seizures. No study has actually demonstrated that treatment of fever decreases the incidence of febrile seizures.

Arguments against lowering fever incude:

1. The generally recognized view that most fever is short lasting and benign.
2. Situations where adverse drug side effects associated with the use of antipyretics outweigh the benefits of fever reduction.
3. Situations where reducing fever may obscure diagnostic or prognostic signs, as in neutropenic children who have recently received chemotherapy.
4. Recent information suggests that fever may protect the host.

Aspirin, paracetamol and non-steroidal anti-inflammatory medications exert their antipyretic effects by blocking the cyclo-oxygenase enzymes, thereby preventing the synthesis of prostaglandins from arachadonic acid. Because they do not suppress interleukin-2, these drugs do not diminish proliferation of T helper cells and, thus, do not adversely affect the body's ability to fight infection.

Because the rate of fluid loss may be increased as the temperature rises, it is important for the febrile child to receive adequate hydration. In addition, maintenance of adequate intravascular volume allows for better heat dissipation. Excessive clothing may be removed. Other non-pharmacological adjunctive measures, such as sponging with tepid water, are no longer recommended and may even result in an elevation of core body temperature.

Current recommendations for paracetamol include a dosage of 15 mg/kg per dose and an upper limit of 60 mg/kg per day. Serious toxicity has been reported

in children who are given high repeated doses over days, mostly occurring in children who have a febrile illness and are unwell with anorexia, vomiting and/or dehydration.[3]

The effect of antipyretics should not be used as a screening test in the assessment of possible pneumococcal bacteraemia. In one study, 40% of children who responded to a standard dose of paracetamol were ultimately found to be bacteraemic.[4]

What needs to be detected in the febrile child?

The vast majority of febrile illnesses in infants and young children are due to self-limiting viral infections only requiring supportive therapy and expectant observation. The febrile child with no focus of infection raises the question of the risk of occult bacteraemia and subsequent serious bacterial infections, such as meningitis or septic arthritis.

The risk of development of meningitis is related to the causative organism (Table 1).

Since the advent of *Haemophilus influenzae* vaccination, occult bacteraemia is essentially pneumococcal bacteraemia (Table 2). In children aged 3–36 months, pneumococcus accounts for 93% of bacteraemia and, although 70–85% of these cases may resolve without treatment, 2% will develop pneumococcal meningitis.[5] Yamamoto *et al.*, looking at an older population (4–10 year olds) and found that serious bacterial infection occurs in 3–8% of cases of *Streptococcus pneumoniae* infections.[6]

Table 1. Risk of meningitis in bacteraemic children aged 3–36 months

	Risk (%)
Pneumococcus	2
Haemophilus influenzae type B	13
Meningococcus	56

Table 2. Causes of occult bacteraemia in the post-*Haemophilus influenzae* type B era

	Frequency (%)
Pneumococcus	92
Salmonella	5
Meningococcus	1
Other	2

Data from The Children's Hospital Westmead.

The emergency physician may take one of two approaches to the febrile child with the potential for occult bacterial infection: (i) to minimize risk; or (ii) to minimize tests. Risk-minimizers aim to lower the risk of adverse sequelae from occult infections by using risk stratification to target higher-risk patient subsets for intervention in the ED. Risk-minimizers believe that a structured, methodical and laboratory intensive strategy minimizes adverse sequelae from occult bacterial infection. Test-minimizers take a greater chance of not detecting bacteriaemia in such infants and children. They perform a careful clinical examination and ensure close follow up, but do not treat with empirical antibiotics. Test-minimizers believe that the majority of children who develop serious bacterial illness will be identified through close follow up and repeat ED visits.

No one approach has been shown to be better than the other. In practice, emergency physicians often tailor their approach to suit the individual needs of the patient. Therefore, the approach chosen will depend on the patient population being treated in a particular ED and the reliability and availability of follow up for that patient population.

The approach used for the well-appearing febrile infant at The Children's Hospital Westmead has been described in this issue (p. 415).

Occult bacteraemia

Occult bacteraemia refers to a febrile illness where the infant or child does not have signs of serious illness or a focus for fever, but has bacteria growing on blood culture. The incidence of occult bacteraemia in febrile children younger than 24 months of age is between 1.8 and 9.8%. Occult bacteraemia is more prevalent in this group because of their difficulty in localizing specific infection.

Many bacteraemic children will appear well, despite being febrile. Clinical scores, such as the Rochester criteria, have been devised to identify children at risk. However, in children younger than 3 months of age, the scores are unreliable, with sensitivity depending on the experience of the observer and ranging from 11 to 100%.[7] In children older than 3 months of age, the same scores only identified 30% of bacteraemic children.[8,9] Thus, the clinician cannot rely on clinical acumen alone.

In the febrile child without an identifiable focus of infection, two additional markers can be used to

Table 3. Height of fever and the risk of bacteraemia

Temperature (°C)	Risk (%)
< 39.5	1.2
> 40.5	4.4

Data taken from Lee and Harper (1995) and Kuppermann (1998).[5,9]

Table 4. Empiric antibiotics and the prevention of meningitis

	Odds ratio	95% Confidence interval
Antibiotics versus placebo	0.60	0.1–3.5
Intramuscular versus oral antibiotics	0.38	0.1–1.2
Bacteraemic		
Antibiotics versus placebo	0.34	0.05–2.3

identify the child at risk of bacteraemia: (i) the height of the fever; and (ii) the total white cell count.

A peripheral white cell count > 15000/mm^3 is highly indicative of bacteraemia in the highly febrile child with approximately one in four cases (31–52%) having positive blood cultures.[10]

The higher the fever, the more likely the child will be bacteraemic (Table 3);[5,9] however, the same studies indicate that bacteraemia is not excluded by the height of fever alone.[10]

In a child who is febrile without an identifiable cause, a full blood count and blood culture should be performed together with a screening urine examination. In infants, this requires culture of an appropriate specimen, ideally a sample obtained via catheter or suprapubic aspiration. A negative urinalysis does not exclude urinary tract infection and urinary tract infection may occur in the absence of pyuria. The chest X-ray in the absence of tachypnoea makes the diagnosis of pneumonia unlikely.

Having identified a child at risk of bacteraemia by this staged approach, the key decision is whether to treat empirically or not, as illustrated in case 1.[11,12] In the majority of children with pneumococcal bacteraemia, the illness will resolve without serious outcome. However, many of these bacteraemic children have persistently high fever with a long and protracted course, often taking a week for fever to resolve. In these cases, the selective use of antibiotics can be recommended (p. 415, this issue), with significant improvement in the morbidity caused by fever and, concomittantly, a decrease in the risk of serious bacterial infection. However, it remains to be proven whether treatment with antibiotics prevents meningitis in bacteraemic children because recent studies have shown no significant benefit (Table 4; Fig. 3).[13–16]

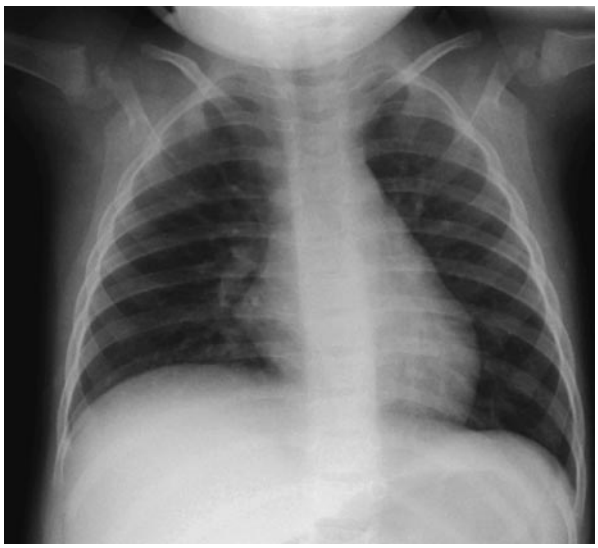

Figure 3. Chest radiograph demonstrating non-specific perihilar changes.

Case 1

A 12-month-old infant presented with a 4 day history of being miserable with fevers to 40°C at home and a runny nose and cough. Assessment on presenting to triage included temperature 39.5°C, respiratory rate (RR) 44/min, heart rate (HR) 168 b.p.m. and SaO_2 100%. The infant was miserable and rather irritable. He was not drinking and had last voided > 24 h previously.

Upon medical examination, temperature was found to be 38.8°C, HR 160 b.p.m. and RR 36 /min. The child remained miserable, although he was alert and responding to his parents appropriately. The infant was non-toxic in appearance, had noisy breathing with a runny nose and no obvious focus of infection.

Investigations performed included a full blood count (white blood cell count 21×10^6/L, range 5–17), film (negative) and urinalysis (+/– nitrites). Blood cultures were taken and a chest X-ray was performed (Fig. 3). No lumbar puncture was performed.

The infant was admitted for observation and rehydration to the observation unit. Intravenous penicillin was commenced at 30 mg/kg, q.i.d. The infant was discharged, afebrile and well, 12 h later

and continued on oral penicillin. Blood cultures were positive for penicillin-sensitive *S. pneumoniae*. The infant continued on oral penicillin as an outpatient.

Serious bacterial infection

Early consideration of which febrile infant is at risk of developing serious bacterial illness is important. The greatest risk of serious bacterial infection (SBI) is in an infant younger than 3 months of age, where one in every 10 febrile episodes will be due to a localized infection, either meningitis, bacteraemia, pneumonia, urinary tract infection, enteric pathogen or soft tissue infection. An example is outlined in case 2.

Sites of possible infection in febrile infants are periorbital cellulitis, osteomyelitis, septic arthritis, meningitis, urinary tract infection and pneumonia.

These infants will most likely require investigation, empirical antibiotic treatment and hospital admission (p. 415, this issue).

Because young children are less able to localize disease processes, they require special consideration. Factors that indicate high risk for underlying serious disease include low birthweight or prematurity, previous frequent hospitalization, developmental disability, poor nutrition, age < 4 weeks, rapid onset of symptoms, social disadvantage, parental reliability problems, current antibiotic use, prolonged febrile illness or chronic illness.

A parental history of fever mandates careful observation, even if the infant on presentation is afebrile; parental assessment of the well-being of the infant or child also deserves consideration.

As in any presentation with fever, ask about a history of infectious contact and overseas travel. Immunization status is particularly important.

The introduction of *H. influenzae* type B conjugate vaccine has been one of the greatest advances in the last decade in almost eradicating *H. influenzae* as a cause of serious bacterial infections, such as meningitis, epiglottitis, pneumonia, periorbital cellulitis and mastoiditis. Emergency physicians may promote immunization by using every consultation as an opportunity to check the infant or child's status and perform 'on-the-spot' immunization where needed.

The 'toxic'-appearing infant is at significant risk of serious bacterial illness until otherwise proven. One simple system devised by Oberklaid *et al.* that has proven to be useful in the ED is the ABC, fluids in, fluids out system.[17] Infants with one or more of these symptoms or signs should be considered toxic until otherwise proven.

- A: Poor arousal alertness and activity
- B: Breathing difficulty
- C: Poor perfusion
- Fluids in: The frequency of feeding over the 24 h prior to presentation, a fluid intake of < 50% of normal over 24 h suggests dehydration
- Fluids out: Significantly abnormal urine output of < 50% (< four wet nappies) of usual output

Features on examination that strongly suggest this include purpuric rash, a high-pitched scream, bulging fontanelle, biphasic stridor, linear burn or bruising, pallor, lethargy, decreased responsiveness, cool extremities, tachycardia, tachypnoea or irregular breathing, mottled skin and prolonged capillary return.

Careful clinical examination may confirm an initial impression that the infant appears relatively well. It may also identify a focus of likely infection requiring investigation and management. Clinical review is essential.

Case 2

A 4-month-old boy, from an Asian background and with a normal perinatal history, presented with being unsettled for the past 12 days, pallor, refusal to feed, 4 days intermittent fever (Fig. 4) and three episodes of screaming and drawing his legs up.

Examination revealed a thriving infant, 6.3 kg, non-dysmorphic with a pulse rate (PR) of 162/min, RR 24/min and SaO_2 99%. He was unsettled with a temperature of 38.5°C. There was marked pallor, soft anterior fontanelle, the ear, nose and throat were normal, the chest was clear and heart sounds normal. There was no organomegaly in the abdomen and no rashes.

Investigations performed included catheter urine (white cells > 100, red cells 10–100, epithelial cells $< 10 \times 10^6$/L), blood culture, a full blood count (haemoglobin, Hb, 57 g/L; white cell count 41.9×10^9/L; platelets 802×10^9/L; reticulocytes 4.9×10^9/L). Liver function tests and EUC were normal. No lumbar puncture was performed and chest X-ray was normal.

Initial treatment included cefotaxime (50 mg/kg, q.i.d.).

Urine culture revealed > 10^8 organisms/L *Escherichia coli*, sensitive to ampicillin, gentamicin and

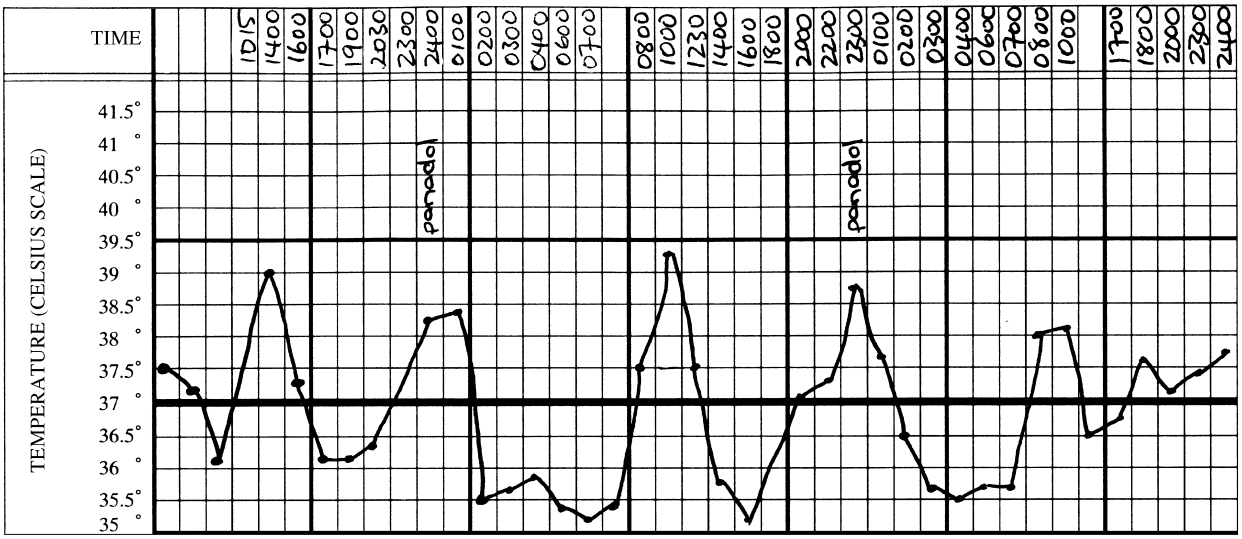

Figure 4. A persistent fever in a pattern that suggests a search for focal bacterial infection should be made.

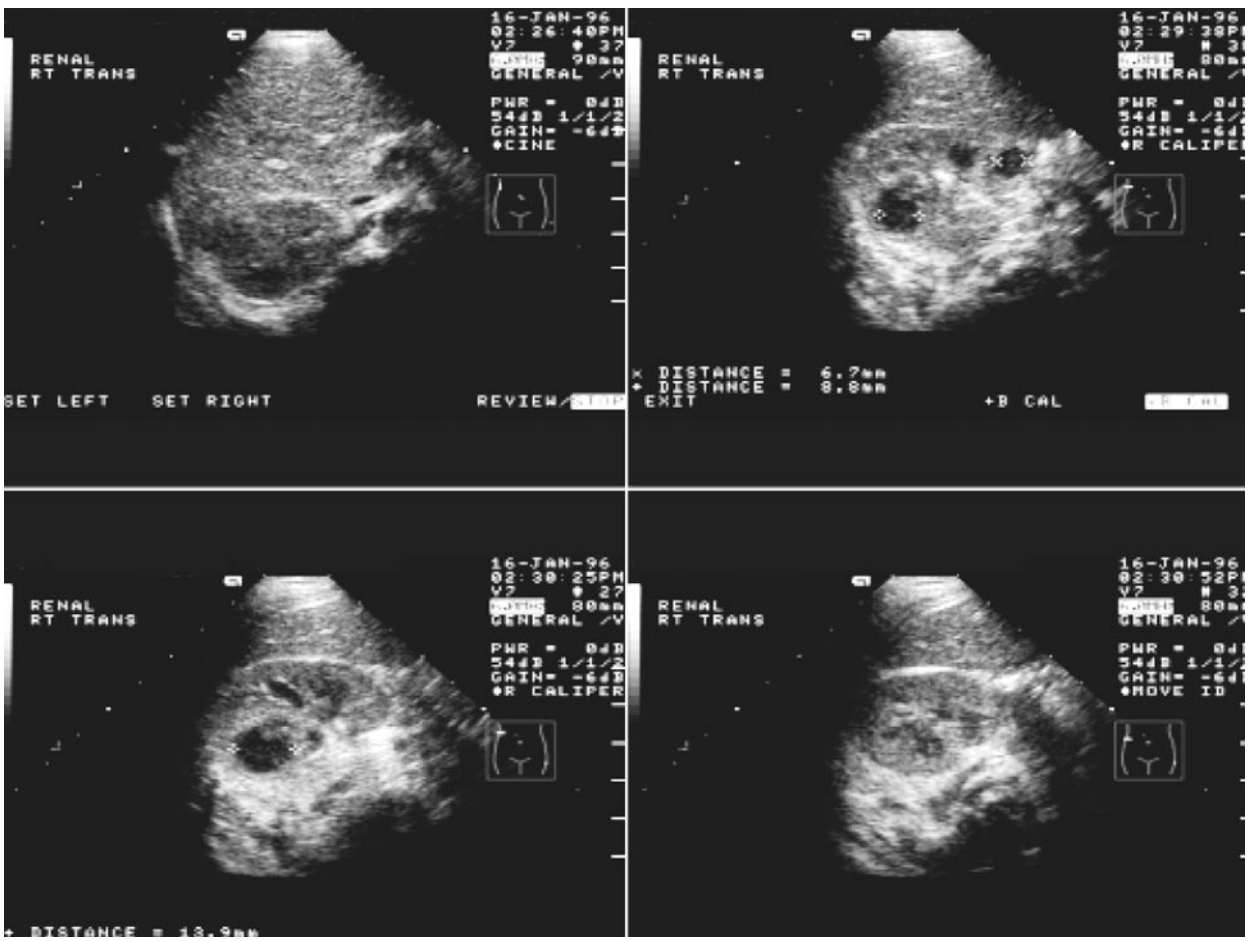

Figure 5. On ultrasound, the infant has markedly dilated kidneys due to renal collections. A diagnosis of pyelonephritis with renal abscess formation was made. Surgical intervention was required in this case.

cotrimoxazole (antibiotics changed to ampicillin and cefotaxime for 14 days i.v.). Renal ultrasound showed right renal abscesses seen in two areas.

Anaemia resolved 1 month later (due to bone marrow suppression related to acute systemic infection (Fig. 5). A micturating cystourethrogram (MCUG) was performed and demonstrated grade 1 vesicoureterec refux.

Treatment

The following are the empirical antibiotic recommendations for children with fever with no focus (normal cerebrospinal fluide, urine microscopy) at The Children's Hospital Westmead.

At 0–3 months of age, ampicillin at 200 mg/kg per day in four divided doses and gentamicin are 7 mg/kg per day in one to three doses is recommended. For infants aged 4 months to 4 years, benzylpenicillin at 120 mg/kg per day in four divided doses is used. In children over 4 years of age (rare), benzylpenicillin at 120 mg/kg per day in four divided doses and flucloxacillin at 200 mg/kg per day in four divided doses are recommended.

Rapidly rising antibiotic resistance

Resistance of *S. pneumoniae* to penicillin has been reported since the 1960s.[18] In almost all cases, these were low (minimum inhibitor concentration, MIC, < –0.1 mg/mL) to moderate (MIC 0.12–1.0 mg/mL) levels of resistance of isolates from non-sterile sites, mainly ear swabs. Current data from The Children's Hospital at Westmead are consistent with other representative adult data from Australasia showing high levels of pneumococcal resistance from sterile isolates, such as cerebrospinal fluid.

Of concern recently has been the rapidly rising rate of high (MIC > 1 mg/mL)-level penicillin resistance, both of non-sterile and sterile isolates. Resistance is now being reported to cephalosporins, resulting in the addition of vancomycin in the treatment of suspected cases of bacterial meningitis (p. 415, this issue).

A meta-analysis has shown that the use of corticosteroids in meningitis has the potential to decrease long-term sequelae.[19] At The Children's Hospital Westmead, the recommended dose of dexamethasone is 0.4 mg/kg given b.d. for 48 h.

Prolonged fever

Infants and children who have a fever persisting > 7–10 days, or a fever that appears to be occurring in a repetitive pattern, should be considered at risk of potential serious disease. Despite this risk, viral illness remains the most common cause of fever.[7,20,21] Prolonged fever is an important marker of potential underlying disease requiring further investigation, such as erythrocyte sedimentation rate, C-reactive protein, repeat full blood count and film, blood cultures, specific viral and atypical mycobacterial cultures, and imaging, such as ultrasound, bone scan and, possibly, CT scan and echocardiography. Hospital admission may also be required.

Kawasaki disease is an important consideration in an infant or child presenting with prolonged fever. It is often underdiagnosed. There is a degree of urgency in diagnosis because early treatment aids in prevention of the development of coronary artery aneurysms.

Case 3

A 7-month-old female infant presented to the ED with a 1 month history of fever (38.5°C) and cough and

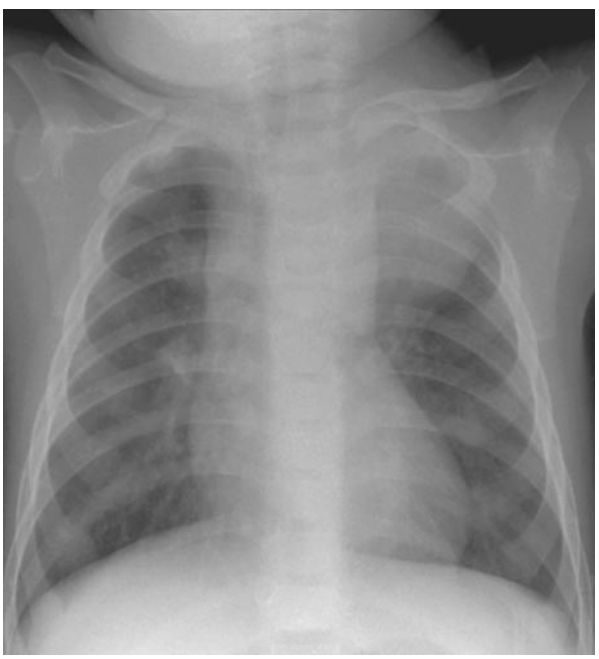

Figure 6. A 6-month-old infant treated for left apical pneumonia for 4 weeks without resolution of fever or the round lesion.

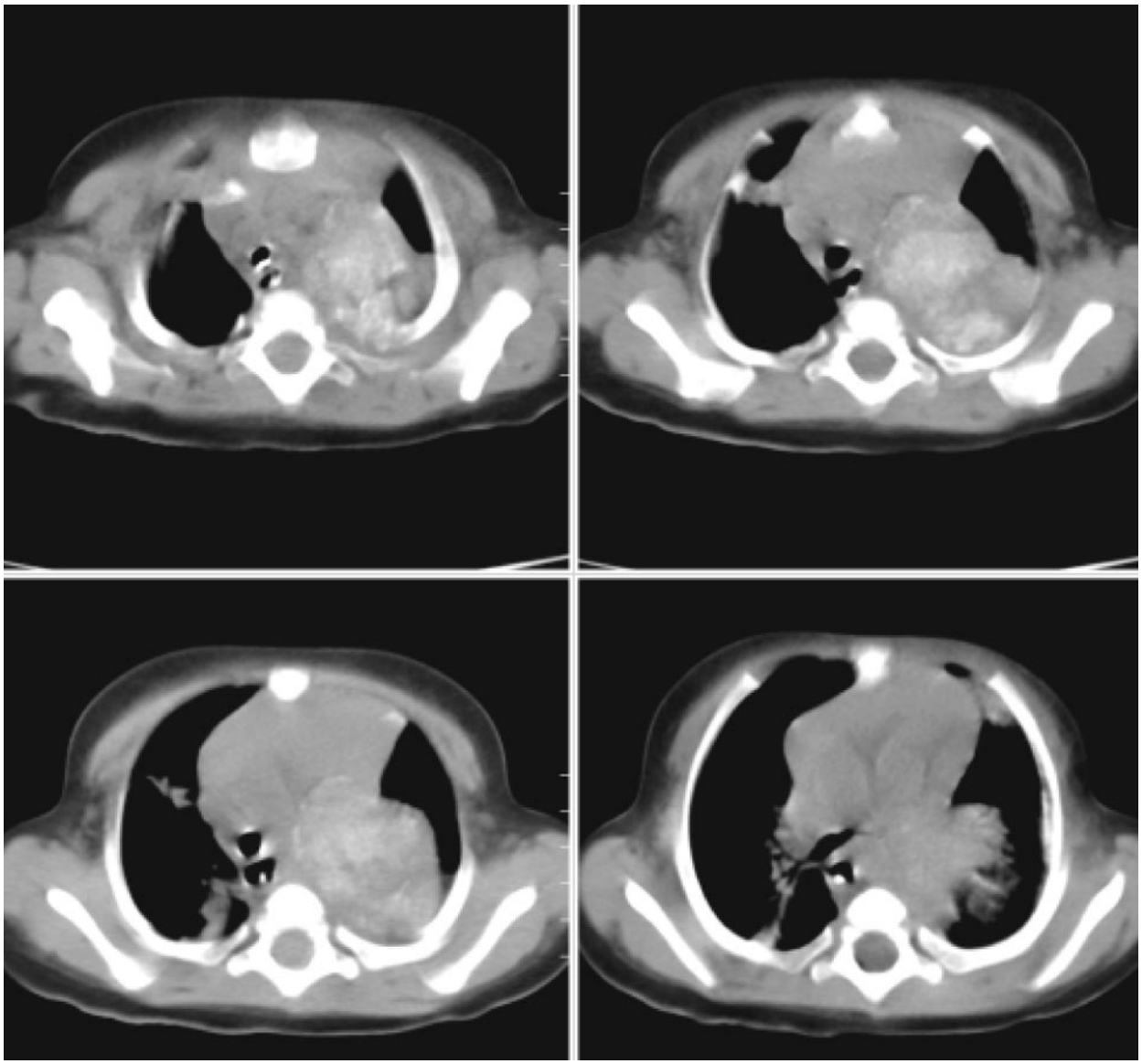

Figure 7. Computed tomography scan of the thorax shows a large neuroblastoma at the apex of the left thorax.

wheeze. Otherwise, she seemed well and non-toxic. The infant was observed for 6 h, was found to be well and was sent home.

The infant returned 1 week later with fever and cough, but was otherwise well. Her white cell count was 10×10^9/L and a blood culture was taken. Chest X-ray demonstrated right upper lobe consolidation (Fig. 6). The infant was treated with oral amoxycillin at 20 mg/kg.

The clinical progression was that the infant remained highly febrile, alert, non-toxic and was sitting comfortably. Her temperature was 39.5°C, RR 40/min and HR 130 b.p.m. There were scattered upper zone crackles/wheezes and chest X-ray was repeated, demonstrating a left upper zone consolidation/mass; CT revealed a neuroblastoma (Fig. 7).

Conclusion

The febrile infant continues to be a challenging problem to the emergency physician. Sound clinical

acumen supported by a staged approach, such as that used at The Children's Hospital Westmead, and knowledge of changing trends will ensure the best outcome for our patients.

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