

Childhood infections

Diagnosis and management in general practice

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Key points

- Childhood infections often have characteristic features that enable diagnosis and management based on history and examination.
- Laboratory confirmation is important when there is potential for complications in the patient or susceptible contacts, or an unusual presentation.
- Close monitoring of clinical progress guides investigation and management, and may limit complications.
- Young infants may have atypical presentations and more severe disease.
- Rational antibiotic use is crucial to maximising patient benefit, avoiding side effects and minimising antibiotic resistance.

Infections are common in childhood, mostly self-limited and usually diagnosed clinically. A delayed antibiotic strategy or short-course empirical antibiotic therapy is often appropriate for the infections that are more frequently encountered. Possible complications and potential transmission should be considered.

Children are particularly susceptible to infection because of their immature and naïve immune systems. Australian epidemiological data suggest children experience at least five acute respiratory tract infections annually during the first four years of life, and infectious illnesses account for seven of the 10 most frequently managed childhood problems.^{1,2} Despite advances in diagnostics, clinical skill remains the key for general practitioners diagnosing an infectious disease, providing parents with sound advice, and using investigations and antibiotics wisely.

For any childhood infection, assessment of hydration, level of activity and parental and practitioner concern is important in deciding whether a child can be safely managed in the community or requires referral to hospital. General advice on paediatric care and infections is available from Australian state health departments and websites of some Australian

children's hospitals. Advice on antibiotic therapy is also available in the Australian antibiotic guidelines *Therapeutic Guidelines: Antibiotic. Version 15*.³

This review provides a brief overview of several childhood infections commonly encountered in primary care and some others that are now less common, with a focus on viral exanthems, group A streptococcal infections and infections of the urinary, respiratory and gastrointestinal tracts.

VIRAL EXANTHEMS

Measles

Measles (also known as rubeola) is characterised by a maculopapular, blanching rash that begins on the face and neck and spreads to the trunk and limbs over the ensuing days (Figure 1a). The rash is generally preceded by a three- to four-day history of fever, cough, coryza and conjunctivitis. Koplik spots (small white lesions

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on the buccal mucosa) are considered pathognomonic but not always apparent (Figure 1b). Clinical improvement occurs within days of the rash appearing, with complete resolution usually by seven days.

Complications include pneumonia, otitis media and croup. Encephalitis is an uncommon but serious complication (one in 1000 cases), with potential for permanent neurological sequelae.⁴

The measles virus is highly transmissible via airborne respiratory droplets from four days before onset of rash to four days afterwards. Patients should be excluded from childcare or school at first suspicion of measles to four days after the appearance of the rash. The incubation period is generally eight to 12 days. Public health notification is required on suspicion of measles to minimise spread to vulnerable contacts.

Laboratory diagnosis is typically made with identification of IgM antibody specific for measles virus (measles-specific IgM) in blood, or detection in urine or nasopharyngeal specimens of measles virus RNA (by polymerase chain reaction [PCR]) or antigen, usually the N protein (by monoclonal antibodies directed against the antigen). Treatment is mainly supportive

The current Australian two-dose measles vaccination schedule confers long-lasting immunity in 99% of recipients.⁵ Measles vaccination is provided using the combination vaccines measles, mumps and rubella (MMR) or measles, mumps, rubella and varicella (MMRV).

Rubella

Rubella (also known as German measles) acquired during childhood is generally a mild disease. Rubella has a prodrome of fever and malaise, which is followed by a maculopapular rash that begins on the face, becomes generalised within 24 to 48 hours, and lasts about three days (Figure 2). Postauricular and occipital lymphadenopathy is a common clue to diagnosis. This suggestive diagnosis can be supported by the detection of rubella-specific IgM, but cross-reactivity with rheumatoid factor and other viruses can occur. Discussion with a microbiologist may assist with interpretation of these results.

Patients should be excluded from school or



childcare for seven days after the onset of rash to minimise risk of transmission of the rubella virus. While infectious, children should not be in contact with pregnant women because of the risk of transmission and subsequent congenital rubella syndrome, which occurs in up to 85% of maternal infections during the first 12 weeks of gestation.⁶ Treatment is supportive.

The main preventive strategy for rubella is immunisation, with the Australian immunisation schedule recommending two doses of rubella vaccine.⁵ A single dose of rubella vaccine is immunogenic in 95% of recipients, with the second dose designed to confer immunity in those who did not respond.⁵ Rubella vaccination is provided using the combination vaccines MMR or MMRV.

Erythema infectiosum

Erythema infectiosum ('slapped cheek' or 'fifth disease') is caused by parvovirus B19. A non-specific prodrome of fever, coryza, malaise, myalgia and headache is followed by a characteristic erythematous and confluent facial rash,



Figures 1a and b. Measles. a (left). The typical maculopapular, blanching rash. b (right). Koplik's spots.

which gives a 'slapped-cheek' appearance (Figure 3). A lace-like (maculopapular with central clearing) rash can develop on the trunk and migrate to the buttocks and limbs. The illness generally lasts five to 10 days.

A clinical diagnosis is sufficient in most cases, but should diagnostic testing be considered then the preferred method is detection of parvovirus B19-specific IgM antibodies. Based on enzyme immunoassay, at least 90% of patients will have detectable antibodies by the time of rash onset.⁷ A PCR assay to detect parvovirus B19 DNA is also available and is useful in

immunocompromised patients with persistent infection as the presence of parvovirus B19 IgM antibodies can be variable in this setting. Diagnostic confirmation should be sought in immunocompromised patients and those with a suspected aplastic crisis.

Supportive treatment is generally sufficient for immunocompetent children. Intravenous immunoglobulin (IVIG) is effective and should be considered for immunocompromised patients with persistent infection.

In the community, transmission is primarily through contact with respiratory tract secretions of patients before the onset of the rash. Children with suspected parvovirus B19 infection should be kept away from pregnant women during this transmission period. Patients are not infectious once the rash has developed and therefore do not need to be excluded if the rash is apparent. Other possible routes of transmission include mother to child (vertical



Figure 2. Rubella, or German measles. The maculopapular rash of rubella is similar to that of measles but the lesions are less intensely red.



Figure 3. Erythema infectiosum, also known as slapped cheek and fifth disease.

transmission) and through exposure to blood or blood products.

Pregnant women exposed to an infectious contact have an up to 20% risk of acquiring infection, depending on the degree of exposure, with 10% of infections leading to loss of the fetus and 3% to hydrops.⁸ Counselling on fetal outcome and serological testing should be offered to at-risk pregnant women who have been exposed.⁸

Roseola

Roseola (exanthem subitum) is classically associated with human herpesvirus 6 (HHV-6) causing clinical disease in children aged 6 to 18 months. It begins with abrupt onset of high fever that lasts three to five days in association with nonspecific constitutional symptoms. The distinguishing feature of roseola is the development of a fine, blanching, macular or maculopapular rash at the time the fever subsides (Figure 4). The rash typically begins on the trunk and then spreads to the face and limbs, with a variable time course from hours to days.

Transmission generally occurs through contact with secretions (e.g. saliva) from asymptomatic shedders of HHV-6. Prior exposure is therefore often not established for patients with roseola. Laboratory confirmation is not usually necessary because of the characteristic clinical features of the disease and its benign and self-limited natural history. Treatment is supportive.

Hand, foot and mouth disease

Hand, foot and mouth disease (HFMD) is one of several illnesses throughout childhood caused by enteroviruses. Coxsackieviruses are most commonly implicated, followed by enterovirus 71 (EV71). HFMD is typically a mild febrile illness associated with maculopapular or vesicular lesions on the hands and feet and vesicles on the buccal mucosa (Figure 5). The incubation period is usually three to six days, with the illness lasting two to three days.

Laboratory confirmation of HFMD is not usually necessary. No specific therapy is

© FIGS 1A AND 1B: SPL/DR P. MARAZZI; FIG 2: PUBLIC HEALTH IMAGE LIBRARY/CDC; FIG 3: SPL



Figure 4. Roseola, or exanthem subitum. The fine, blanching macular or maculopapular rash develops as the three to five-day high fever subsides. It occurs in children aged 6 to 18 months.

available, and the illness generally resolves without complication.

Transmission occurs through direct contact with respiratory secretions, vesicular fluid or stools. The highest chance of transmission occurs within the first few days of clinically apparent disease. Children should be excluded from school or childcare while unwell and until any vesicles have crusted over.

Chickenpox (varicella)

Chickenpox is the common name for primary varicella-zoster virus (VZV) infection, or varicella. The disease is characterised by a spreading maculopapular rash that becomes vesicular, following a prodrome of fever, malaise and myalgia (Figure 6). Lesions arise in crops, leading to the appearance of lesions at different stages of development on examination of the patient. Individual spots crust over within two to four days. The varicella vaccine is protective in up to 80 to 85% of recipients.⁵ Vaccinated children who develop disease tend to have less widespread rash than unvaccinated children.



Figure 5. Hand foot and mouth disease. Typically there are maculopapular or vesicular lesions on the hands and feet and vesicles on the buccal mucosa.

The natural incubation period of chickenpox ranges from 10 to 21 days, and those infected can transmit the virus from 48 hours prior to the onset of rash until all lesions have crusted over. Patients should be excluded from childcare or school on first suspicion of chickenpox until all lesions have crusted over.

Complications include secondary bacterial skin infection, pneumonia, hepatitis, encephalitis and acute cerebellar ataxia. Children with impaired cellular immunity and neonates whose mothers develop varicella five days before to two days after delivery are at increased risk for disseminated varicella and severe disease.

If laboratory confirmation of the clinical diagnosis is required, the preferred test is detection by PCR of VZV DNA in vesicular fluid. For pregnant women exposed to varicella, urgent confirmation of immunity to VZV through prior completion of the varicella-zoster vaccination schedule, known previous infection or demonstration of varicella-specific IgG is important for management.

Antiviral therapy is not required for most children with chickenpox. In those who are immunocompromised, prophylaxis with varicella-zoster immune globulin or treatment with antiviral therapy (aciclovir or valaciclovir) may be required; specialist advice should be sought.

GROUP A STREPTOCOCCUS INFECTION

Infection with the group A streptococcus (GAS; a single species, *Streptococcus*

pyogenes) causes a wide range of clinical disease, with acute pharyngitis the most common manifestation (Box 1; Figure 7a). Immune-mediated complications of GAS throat infections include glomerulonephritis and rheumatic fever. GAS skin infections (impetigo, cellulitis and erysipelas) are also common and are generally due to colonising GAS penetrating areas of skin breakdown (Figure 7b); they are also associated with immune-mediated glomerulonephritis.

Toxin-producing GAS strains may cause the less common diseases scarlet fever and streptococcal toxic shock syndrome, an acute febrile illness with generalised exfoliative dermatitis, hypotension and rapidly progressive multiorgan failure. Invasive disease is uncommon but serious.

Isolation of *S. pyogenes* on culture (of throat or skin swabs) is the gold standard for diagnosis of current GAS infection.



Figure 6. Chickenpox, or varicella. The rash involves successive crops of vesicular lesions that develop from a spreading maculopapular rash.

© FIG 4. SCOTT CAMAZINE/PHOTOTAKE/DIOMEDIA.COM; FIG 5. SPL/DR P. MAPAZZI; FIG 6. PUBLIC HEALTH IMAGE LIBRARY/ODC/JOE MILLER



Figure 7a and b. Group A streptococcus infection. a (left). Pharyngitis, or strep throat. b (right). Impetigo (*Staphylococcus* is often also involved).

Antistreptolysin (ASO) antibodies are produced one week to one month after infection but may remain detectable for several months. The ASO antibody test is used to help determine whether a recent throat infection is the cause of glomerulonephritis or rheumatic fever.

Penicillin is the antibiotic of choice in the treatment of GAS infection, with the aims of therapy being to decrease the risk of noninfectious complications and reduce transmission. Chemoprophylaxis, with

either cephalexin or clindamycin, should be considered for close contacts of people with invasive disease.⁹

URINARY TRACT INFECTIONS

The cumulative incidence of urinary tract infections (UTIs) is 3% in prepubertal girls and 1% in prepubertal boys.¹⁰ It is important to thoroughly evaluate any young child in whom a UTI is suspected, as it may be associated with an underlying urological abnormality and lead to long-term complications if not adequately addressed.

Isolation of bacteria in sufficient amounts from a noncontaminated urine specimen is required to confirm the diagnosis of a UTI. Urinalysis that shows presence of leucocytes and/or nitrites may help in deciding whether to commence empirical antibiotic therapy. Collection of urine specimens in children not toilet-trained may require suprapubic aspiration or urethral catheterisation to avoid contamination. *Escherichia coli* is the most common urinary pathogen, accounting for close to 80% of urinary isolates, followed by *Enterococcus* spp., *Proteus* spp., *Klebsiella* spp. and *Enterobacter* spp.¹¹ Most children with UTIs can be treated with oral antibiotics, which may be commenced empirically (Box 2), but should be tailored once antimicrobial sensitivities of the isolated bacteria are known.³ For infants younger than 12 months and those appearing toxic, initial intravenous therapy in hospital is recommended.

In younger children (less than 6 months

of age) or children with complicated (e.g. pyelonephritis or urosepsis) or recurrent UTI, a renal tract ultrasound examination is required to assess for any underlying urological abnormalities, such as obstruction or vesicoureteric reflux, that might predispose to recurrent UTIs and renal scarring. The need for further investigations and the role of prophylactic antibiotics should be considered in consultation with a general paediatrician.

RESPIRATORY TRACT INFECTIONS

Acute otitis media

Acute otitis media (AOM) is the most common reason for children presenting to medical services, and is the leading reason for antibiotic prescription in children.^{12,13} Peak incidence is in children under the age of 2 years, with 80% of children experiencing at least one episode by the age of 3 years.¹² Contributing factors in children may include Eustachian tube dysfunction, viral infection and bacterial colonisation. Bacteria implicated include *Streptococcus pneumoniae*, *Haemophilus influenzae* and *Moraxella catarrhalis*. AOM is diagnosed clinically by the acute onset of fever and ear pain with evidence of an inflammatory exudate in the middle ear.

AOM is a self-limited disease in

1. DISEASE ENTITIES ASSOCIATED WITH GROUP A STREPTOCOCCUS INFECTION

Localised disease

- Cellulitis
- Erysipelas
- Impetigo
- Pharyngitis

Invasive disease

- Bacteraemia
- Gangrenous myositis
- Necrotising fasciitis
- Osteomyelitis
- Pneumonia
- Septic arthritis

Immune-mediated disease

- Glomerulonephritis
- Rheumatic fever

Toxin-mediated disease

- Scarlet fever
- Toxic shock syndrome

2. UTIS IN CHILDREN: COMMON BACTERIAL CAUSES AND EMPIRICAL ORAL ANTIBIOTIC OPTIONS^{3,11}

Causative organisms

- *Escherichia coli* (most common)
- *Enterococcus* spp.
- *Proteus* spp.
- *Klebsiella* spp.
- *Enterobacter* spp.

First-line empirical oral antibiotics

- Amoxicillin–clavulanate
- Cephalexin
- Trimethoprim, with or without sulfamethoxazole

ABBREVIATION: UTI = urinary tract infection.

two-thirds of cases, and simple analgesia is sufficient to relieve symptoms.¹³ Antibiotics are warranted in young infants (less than 6 months of age) and children whose symptoms have not resolved over 24 to 48 hours.³ Amoxicillin is recommended and provides cover for the most common pathogens.³ Follow up is important to monitor clinical improvement and avoid complications, such as mastoiditis and conductive hearing loss.

Bronchiolitis

Bronchiolitis is a viral lower respiratory tract infection affecting children under the age of 2 years. The typical natural history consists of progressive respiratory distress that peaks between days three and five of the illness and then gradually resolves over two to three days. Respiratory syncytial virus accounts for most cases of bronchiolitis overall, although epidemiology varies with season and climate.

Diagnosis is clinical and treatment is supportive, and thus virological or radiological diagnosis is not routinely required. Corticosteroids are not recommended, except in children for whom asthma is considered likely. Referral to hospital is warranted for children with moderate respiratory distress, poor feeding or oxygen saturation below 95% in room air (if testing is available), and for those who are at increased risk of complications (e.g. premature infants, infants with underlying lung or cardiac disease). Complications include dehydration, apnoea, secondary bacterial infection and respiratory failure.

Croup

Croup (viral laryngotracheobronchitis) is a syndrome with an abrupt onset of inspiratory stridor and barking cough, often preceded by fevers and coryza. It most commonly affects pre-school-aged children. Parainfluenza viruses are the most common aetiological agents, but almost any virus affecting the respiratory tree may be implicated.

Inflammation in the larynx and larger airways results in cough and respiratory distress. Diagnosis is based on the characteristic stridor and barking cough; however, in the absence of associated viral symptoms (e.g. fever, cough), other important diagnoses require consideration (e.g. foreign body, allergic reaction, congenital anomalies).

Mild croup, with cough only and no stridor, does not require treatment. Oral corticosteroids (prednisone or dexamethasone) are therapy for moderately severe croup, and nebulised adrenaline is given in addition to corticosteroids for severe croup with respiratory distress, which is a medical emergency.

Pertussis

Pertussis (whooping cough) is a bacterial upper respiratory tract infection caused by *Bordetella pertussis*. It has a characteristic natural history commencing with a coryzal illness (catarrhal phase), which progresses to paroxysms of cough (paroxysmal

3. COMMON BACTERIAL AND VIRAL CAUSES OF COMMUNITY-ACQUIRED PNEUMONIA

Bacteria causing 'typical' pneumonia

- *Streptococcus pneumoniae* (most common)
- *Haemophilus influenzae*
- *Staphylococcus aureus*

Bacteria causing 'atypical' pneumonia

- *Chlamydia* spp.
- *Mycoplasma pneumoniae*

Viruses

- Adenovirus
- Human metapneumovirus
- Influenza virus
- Parainfluenza virus
- Respiratory syncytial virus
- Rhinovirus

4. AETIOLOGICAL AGENTS OF GASTROINTESTINAL INFECTIONS

Viruses

- Adenoviruses
- Astroviruses
- Norovirus
- Rotaviruses

Bacteria

- *Campylobacter jejuni*
- *Clostridium difficile*
- *Escherichia coli*
- *Salmonella* spp.
- *Shigella* spp.
- *Vibrio* spp.
- *Yersinia enterocolitica*

Protozoa

- *Cryptosporidium* spp.
- *Entamoeba histolytica*
- *Giardia lamblia*

phase), followed by gradual resolution of symptoms (convalescent phase). Each phase typically lasts one week, but coughing may persist for up to three months. In young infants symptoms vary, including apnoeas, poor feeding and post-tussive vomiting. A high index of suspicion is required in such cases. Diagnosis can be assisted by the detection of *B. pertussis* through PCR on a nasopharyngeal specimen.

Antibiotic therapy can improve symptoms if commenced in the catarrhal phase, and reduce infectivity if given within 21 days of symptom onset. First-line treatment is with macrolide antibiotics (azithromycin, clarithromycin or erythromycin), and trimethoprim plus sulfamethoxazole is suitable for those unable to take macrolides.³ Antibiotic prophylaxis is recommended for close contacts at risk of severe disease (e.g. young infants, women in late third trimester of pregnancy). Patients are considered infectious (via respiratory droplets) for the first three weeks after onset of cough or until five days of appropriate antibiotic therapy are completed.

The acellular pertussis vaccine schedule is more than 70% effective in preventing disease, but studies suggest that waning of immunity occurs five to six years after the last immunisation.⁵

Pneumonia

Pneumonia remains one of the leading causes of mortality worldwide in children under the age of 5 years, with the major burden experienced in under-resourced settings.¹⁴ Viruses are the most common cause of lower respiratory tract infections in preschool-aged children, but differentiating between viral and bacterial pneumonia is often not possible, and thus children are often treated for bacterial pneumonia. Common bacterial and viral causes of pneumonia are shown in Box 3, with *S. pneumoniae* being the main bacterial pathogen.

The clinical features of 'typical' pneumonia include a classic constellation of fever and tachypnoea (with or without cough), often with unilateral chest signs and nonspecific symptoms such as lethargy, poor feeding and abdominal pain. Amoxicillin is first-line therapy in older

infants (3 months and over) and children with 'typical' pneumonia to cover *S. pneumoniae*. Assessment of the severity of illness is important in determining whether hospitalisation is warranted. This includes respiratory rate and effort, hydration status and oxygen saturations (if testing is available).

Macrolide antibiotics are used to treat 'atypical' pneumonia, which may follow a more indolent course than 'typical' pneumonia and typically presents with bilateral chest signs.³ Chest x-ray changes do not always correlate with clinical severity or aetiology.

Laboratory investigations are generally not necessary for patients in the community, who may be treated empirically. Newborns or young infants (less than 3 months of age) may deteriorate quickly and require urgent assessment and treatment. Additional pathogens that cause congenital infections should be considered and paediatric advice obtained.

GASTROINTESTINAL INFECTIONS

Acute diarrhoea is one of the most common clinical presentations throughout infancy and childhood. In the developed world, 70 to 80% of episodes are caused by viruses, and 10 to 20% by bacteria (Box 4).¹³ Clinical features suggestive of bacterial enterocolitis include sudden-onset high-grade fevers, cramping abdominal pain and mucousy or bloody loose stools. Viral gastroenteritis is more common, may or may not have systemic features in addition to diarrhoea, and has an absence of blood in the stool. Infections with *Giardia* or *Cryptosporidium* species cause enteritis with abdominal pain and loose watery stools.

Most gastrointestinal infections are self-limited, and laboratory confirmation of a causative agent is not required. Microbiological or infectious diseases advice should be obtained if the course of infection is atypical or severe, or if bacterial or protozoal pathogens are found, as antibiotic therapy or further investigations may be recommended.

CONCLUSION

Infections are common in childhood and mostly self-limited. A clinical diagnosis is possible in many cases and a delayed antibiotic strategy or short-course empirical antibiotic therapy is often appropriate. Laboratory confirmation is warranted when there is potential for complications (e.g. urinary tract and GAS infections), transmission to vulnerable contacts (e.g. pertussis) or an undifferentiated presentation (e.g. prolonged fever without focus). Clinical review and assessment of disease severity and progress is important to decide whether to manage patients in the community or in hospital. **MT**

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