Acute viral exanthems

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Abstract

Exanthems/rashes are common in childhood and account for a large number of consultations in primary care and attendances to the emergency department. They are typically caused by allergic reactions, by viruses and occasionally by severe life-threatening bacterial infections. A careful history (including prodrome, associated symptoms, exposure to infectious contact, foreign travel, animals and immunization status), examination of the rash (including distribution, morphology, nature and site) and generalized examination (including presence of conjunctivitis, genital lesions, enanthems, hepatosplenomegaly and lymphadenopathy) can inform diagnosis. Molecular testing has led to a cause being identified in approximately 50% of cases. Early diagnosis is particularly important in the context of severe systemic infection, in immunocompromised hosts and in pregnancy. This review outlines the most common infectious exanthems, including measles, rubella, varicella, erythema infectiosum, roseola infantum and enterovirus infection.

Keywords Childhood; erythema infectiosum; exanthem; measles; MRCP; rash; rubella; varicella

Key points

- Viral exanthems in children are common. A careful history and examination are essential to elucidate the cause
- Molecular testing, such as polymerase chain reaction, has improved the sensitivity of laboratory diagnosis
- Maintaining high MMR vaccine coverage is crucial to reduce the incidence of measles and rubella
- Varicella can cause significant complications that should be identified early to prevent fulminant disease

Introduction

Viral exanthems are classically maculopapular in appearance. It is essential that other causes of rash are considered, i.e. infectious (e.g. bacterial including meningococcal, streptococcal, staphylococcal skin syndrome and toxic shock syndromes, tick-borne, e.g. *Borrelia* and rickettsial disease, tubercular, fungal) and non-infectious (e.g. drug-induced, allergic, Henoch–Schönlein purpura, juvenile idiopathic arthritis, malignancy) so appropriate treatment can be tailored accordingly.

Recognizing patterns of rash and having a knowledge of epidemiology is important to understand the likely pathogen and predict prognosis (Table 1). In the absence of a specific pattern, it is important to ascertain whether there has been any recent travel or arthropod exposure, and determine the complete vaccination history and whether the child is immunocompromised.

Laboratory confirmation of viral exanthems is often made using serology. Pathogen-specific immunoglobulin M (IgM) is suggestive of acute infection, but false-positive results commonly occur because of cross-reactivity with other viruses. IgG seroconversion (or a 4-fold or greater rise in antibody titres between acute and convalescent sera) is regarded as definitive evidence of infection, but confirmation of infection may be delayed.

Molecular testing (polymerase chain reaction (PCR) assays) of blood, respiratory and cerebrospinal fluid (CSF) specimens has higher sensitivity and specificity than serological testing and are often more rapid.

The management of viral exanthems remains largely supportive except in immunocompromised individuals. Infection control measures must be considered carefully in order to prevent further spread and exposure in vulnerable individuals.

Measles

Measles (rubeola) is caused by a paramyxovirus. It is spread by respiratory contact through air droplets. Measles is a highly infectious virus and has a transmission rate of 90% in close household contacts. Worldwide, measles is still a major cause of death, especially among children in resource-poor countries. In 2015, 134,200 people died worldwide of measles.[1]

The combined measles, mumps and rubella (MMR) vaccine was introduced into the UK immunization schedule in 1988. In that year, approximately 86,000 cases and 16 deaths were reported in England and Wales. In 1996, a second dose of MMR was added to the routine vaccination schedule at around 4 years of age. After a second dose of measles-containing vaccine, around 99% of children are protected.

In 1998, a small study published data suggesting an association between the MMR vaccine and autism. This study has been widely discredited and withdrawn. A plethora of studies have since been published demonstrating no link between MMR and autism or gastrointestinal conditions. However, safety concerns among parents persisted, and in 2003–2004 MMR coverage in 2-year-old children fell to just below 80% in England, with lowest levels in London, which led to outbreaks across all age groups from a loss of individual and herd immunity. A national catch-up campaign introduced in 2008 improved MMR coverage across the UK, especially in preschool children.

In the UK, the number of cases fell in 2014 and 2015, but increased again in 2016 to 531. Most cases are recorded in unvaccinated individuals. A significant number of these have been linked to large public gatherings such as music festivals. In the

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Clinical features of common viral exanthems

Virus	Incubation period and infectivity	Clinical features	Comment
Measles	*Incubation period:* 7–14 days *Infectivity:* 2 days before prodrome to 5 days after rash appears	*Rash:* cephalocaudal progression, morbilliform with confluent maculopapular lesions. Koplik spots *Associated features:* prodrome of fever, malaise and upper respiratory symptoms. Child generally unwell	*Lab diagnosis:* oral fluid toolkits that detects salivary specific IgM or viral RNA *Treatment:* supportive. Antibiotics should only be started if there is secondary bacterial infection
Rubella	*Incubation period:* 14–23 days *Infectivity:* 7 days before to 5 days after rash appears	*Rash:* cephalocaudal progression of maculopapular rash *Associated features:* petechial macules can be present on the soft palate (Forschheimer's spots), and tender lymphadenopathy in head and neck	*Lab diagnosis:* >4-fold increase in antibody titre between acute and convalescent periods, or seroconversion between acute and convalescent IgG serum *Treatment:* supportive
Varicella	*Incubation period:* 10–21 days *Infectivity:* 2 days before onset of rash until crusting of lesions	*Rash:* generalized but mainly on head and trunk. Pruritic rash of macules that develop into papules and finally crust over. Appear in crops *Associated features:* prodrome of cough, coryza and fever	*Lab diagnosis:* PCR of vesicular fluid *Treatment:* supportive. Aciclovir in severe cases/immunocompromised patients, within 48 hours of rash. Varicella-zoster Ig in immunocompromised patients
Erythema infectiosum	*Incubation period:* 4–14 days	Rash: slapped cheek appearance over face. Symmetrical lacy macular rash over trunk and limbs Associated features: fever, coryza and malaise	*Lab diagnosis:* high titre of viral DNA on PCR *Treatment:* supportive in most cases. Blood transfusion if aplastic crisis. Intravenous Ig if severe in immunocompromised patients
Roseola infantum	*Incubation period* HHV-6 9–10 days (incubation period for HHV-7 unknown)	*Rash:* pink maculopapular rash *Associated features:* fever for 3–7 days that defervesces, followed by abrupt onset of rash	*Lab diagnosis:* seroconversion from negative to positive in paired sera is evidence of recent primary infection *Treatment:* supportive. Cidofovir or ganciclovir in immunocompromised patients with recurrent severe infection
Hand, foot and mouth disease	*Incubation period:* 3–10 days	*Rash:* vesicles in mouth and on digits, palms and soles *Associated features:* prodrome of low-grade fever and reduced appetite	*Lab diagnosis:* PCR of vesicular fluid *Treatment:* supportive IVIG if severe disease in immunocompromised patients

Table 1

UK in 2015, MMR coverage at 5 years was 94.9%, which was the highest level since its introduction in 1998 but still fell short of the World Health Organization (WHO) target of 95%.[2]

Measles has a prodromal period of typically 7–14 days. Symptoms include fever, cough, coryza and conjunctivitis before a rash develops. The rash usually starts behinds the ears and spreads to the forehead, around the mouth and over the trunk and limbs. Koplik spots are pathognomic and appear as white spots on the buccal mucosa 1–2 days before the rash.

The rash is classically morbilliform and can be confluent (Figure 1). It progresses from the face downwards. Generally, the more severe the rash appears, the more unwell the child is. The rash lasts for approximately 5 days and can leave a brown discoloration. Children usually improve within 3 days of onset of the rash and 7–10 days after onset of the illness. Measles can progress to serious complications. These include central nervous system (CNS) sequelae (encephalitis, subacute sclerosing panencephalitis (SSPE), acute disseminated encephalomyelitis (ADEM), pneumonia, pericarditis, myocarditis, scleral ulceration and otitis media, particularly in younger infants and those who are immunocompromised or have poor nutritional status.

Laboratory diagnosis can be made using direct PCR testing on throat swabs, usually using specific kits. This has the advantage

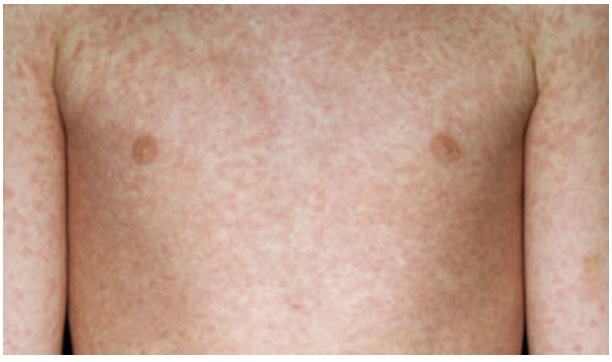

Figure 1 Measles.

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