

## UNIT NO. 3

## CHILDHOOD VACCINATION AND CHILDHOOD EXANTHEMS

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**ABSTRACT**

**The aim of vaccination is immunisation of the child against diseases to prevent mortality and morbidity from specific infections. Adequate immunization coverage is the prerequisite for creating herd immunity. The maintenance of these levels of population immunity requires continuous vigilance and changes to immunisation schedule in response to changing circumstances. Changes have been made over the years to optimise the immunisation of poliomyelitis, measles, mumps, rubella, and varicella. The introduction of hemophilus influenza type B vaccine and pneumococcal vaccine has reduced the incidence of these infections. Vaccination against human papillomavirus infection is being expanded to protect against cervical neoplasia in females and also anal intraepithelial neoplasia in both genders. Childhood exanthems due to viral and bacterial infections, as well as immunological causes continue to be important and the ability to recognise them is necessary.**

**Keywords:** Singapore National Immunisation Programme, childhood exanthems.

**SFP2014; 40(1): 18-26**

**INTRODUCTION**

The prevention of infectious diseases in children by vaccination has been one of the greatest achievements of research in the history of medicine (Lee et al, 2005)<sup>1</sup>. Vaccination originally referred to the inoculation of vaccinia virus to render individuals immune to smallpox. Today, the term “vaccination” means the administration by injection or by mouth of a vaccine. The aim of vaccination is immunisation of the child against diseases to prevent mortality and morbidity from specific infections. Six particular diseases across the world share two outstanding features in common: they kill young children; and young children can be protected against them by immunisation. The six killer diseases of children are diphtheria, tetanus (neonatal tetanus), pertussis, poliomyelitis, tuberculosis, and measles.

Over time, other diseases have been added to the basic list of six killer disease. These are immunisation against mumps, rubella, varicella, Hemophilus influenza type b, invasive pneumococcal disease, and human papillomavirus. See Figure 1.

**Vaccination and population immunity**

To control diseases that are transmissible from person to person such as those in the immunisation schedule, the concept of population immunity is important. If immunisation by vaccines is to be an effective means of controlling communicable diseases, then at least 80% of each age cohort in the case of diphtheria and poliomyelitis, and 92 to 95% in mumps, pertussis, and measles. This immunization coverage is the prerequisite for creating herd immunity. The maintenance of these levels of population immunity requires continuous vigilance and changes to immunisation schedule in response to changing circumstances that will be described in this update.

When a high proportion of people are immunised, even those few people who have not been vaccinated also get some protection because the disease has become so uncommon. There is a need to guard against public pressure that immunisation be stopped in such a situation because the susceptibles have been immunised and the incidence of a particular disease has fallen to a low level. Once immunisation has stopped there is a real danger of an epidemic occurring amongst all susceptibles who are unvaccinated. This is why it is so important to keep vaccination programmes going from year to year once they have been started, despite the low incidence. There is a need to explain this to the public as complacency sets in, and compliance may falter.

**Childhood viral exanthems**

Childhood viral exanthems are acute widespread eruptive rashes with fever. The classical four viral exanthems are measles, rubella, erythema infectiosum (slap cheek disease and roseola infantum). Their importance lies in the differential diagnosis of a child with a rash. These will be discussed in the second half of the paper.

**SINGAPORE NATIONAL IMMUNISATION SCHEDULE**

Figure 1 shows the current national immunisation schedule in Singapore. Medical practitioners are reminded to notify all immunisations to the National Immunisation Registry (NIR), Health Promotion Board. NIR can be accessed via [www.hpp.moh.gov.sg](http://www.hpp.moh.gov.sg). Notification forms 550A can be requested from NIR via email [hpb\\_nir@hpb.gov.sg](mailto:hpb_nir@hpb.gov.sg). There is also a need to keep abreast of the current developments in the national immunisation schedule.

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**FIGURE 1. Singapore National Immunization Schedule, June 2013**

Vaccination against	Birth	1 month	3 month	4 months	5 months	6 months	12 months	15 months	18 months	10-11 years <sup>^</sup>
TUBERCULOSIS	BCG									
HEPATITIS B	HepB (D1)	HepB (D2)			HepB (D3)#					
Diphtheria, Tetanus Pertussis			DTaP (D1)	DTaP (D2)	DTaP (D3)				DTaP (B1)	Tdap (B2)
Poliovirus			IPV (D1)	IPV (D2)	IPV (D3)				IPV (B1)	OPV (B2)
<i>Haemophilus influenzae</i> type b			Hib (D1)	Hib (D2)	Hib (D3)				Hib (B1)	
Measles, Mumps, Rubella							MMR (D1)	MMR (D2)##		
Pneumococcal Disease			PCV (D1)		PCV (D2)		PCV (B1)			
Human Papillomavirus	Recommended for females 9 to 26 years: three doses are required at intervals of 0, 2, 6 months									

**Source:** <http://www.nir.hpb.gov.sg> (under immunisation schedule)

Notes:

BCG = Bacillus Calmette-Guérin

HepB = Hepatitis B vaccine

DTaP = Paediatric diphtheria and tetanus toxoids and acellular pertussis vaccine

Hib = *Haemophilus influenzae* type b vaccine

Tdap = Tetanus toxoid, reduced diphtheria toxoid and acellular pertussis vaccine

MMR = Measles, mumps, and rubella vaccine

IPV = Inactivated polio vaccine

OPV = Oral polio vaccine

PCV = Pneumococcal conjugate vaccine

D1/D2/D3 = 1st dose, 2nd dose, 3rd dose

B1/B2 = 1st booster, 2nd booster

<sup>^</sup> = Primary 5

# = 3rd dose of HepB can be given with the 3rd dose of DTaP, IPV and Hib for the convenience of parents.

## = 2nd dose of MMR can be given between 15-18 months

## CURRENT DEVELOPMENTS IN THE SINGAPORE NATIONAL IMMUNISATION SCHEDULE

### Poliomyelitis

The current national immunisation schedule for poliomyelitis is 4 doses of IPV (inactivated polio vaccine) and 1 dose of OPV (oral polio vaccine).

### Why do we switch to IPV?

Intestinal immunity induced by oral poliovirus vaccine (OPV) is only partially protective against poliovirus replication and shedding. Children immunised with OPV may therefore be re-infected with poliomyelitis on subsequent exposure, while remaining immune to paralytic disease. Hence, older, OPV-vaccinated children may participate in transmission of wild-type poliovirus due to waning intestinal immunity.<sup>(Grassly, 2013)<sup>2</sup></sup>. Furthermore, since OPV is a live attenuated vaccine, it can

lose its attenuating mutations and become pathogenic. One added challenge today is therefore vaccine-derived poliovirus (VDPV) outbreaks. Inactivated poliovirus (IPV) will not have this problem but it is more costly to produce.

The world is now moving towards the final stages of global eradication of poliomyelitis. Apart from eradicating the wild-type poliovirus, there is a need to get rid of the attenuated poliovirus found in the Sabin OPV. Getting rid of OPV is not so difficult. Experience from Cuba and Mexico had shown that after mass immunisation with trivalent OPV, and in the absence of routine vaccination of OPV, Sabin polioviruses disappear from stool and environment samples within 4-5 months (Grassly, 2013)<sup>2</sup>. More recently, countries switching to routine immunisation with IPV have also documented disappearance of Sabin polioviruses several months after national immunization days or cessation of OPV (Grassly, 2013)<sup>2</sup>. The global accelerated endgame strategy of poliomyelitis eradication is to sequentially remove poliomyelitis serotypes from OPV.

### Why is OPV given as the second booster?

OPV is given as a second booster because of the greater immunogenicity of trivalent OPV.

For VDPV outbreaks, OPV provides a rapid response, equivalent to response to wild-type poliomyelitis. To prevent ongoing transmission, OPV should be given immediately to household contacts of those with suspected polio. Other people in the neighbourhood of the case may also require OPV. If OPV is contra-indicated (e.g. immunocompromised patients) and household members of immunocompromised patients give IPV.

### Comparison of IPV schedules in other countries as of 2013

This is shown in Table 1. The number of doses of IPV required depends on the policy evidence that four doses are needed to result in intestinal immunity to poliovirus infection.

### HEMOPHILUS INFLUENZA TYPE B VACCINE

This has successfully reduced the incidence of Hib Meningitis in Singapore. See Figure 2.

### MEASLES, MUMPS, RUBELLA AND VARICELLA MMR -- Why shortened schedule?

MMR is now given at 12 months. When measles immunisation was introduced in 1976 it was given between 12 to 24 months. It was made compulsory in 1985. The incidence of measles dropped sharply but resurgences occurred in 1992/1993 and again in 1997. As the vaccine is about 90% effective, the resurgences in measles were due to accumulation of susceptibles (non-immune persons or vaccine non-responders) and this highlighted the fact that one dose is inadequate. As

such a two dose regime was introduced in 1998. No outbreak has since occurred among those vaccinated with two doses of vaccine. However, in the last 2 years, cases of measles in infants in Singapore have been reported. Measles occurring in infancy is an indication of community spread. It is an indication for starting vaccination earlier than 15 months as it leaves a smaller proportion of children in each cohort still susceptible. Conversely, vaccinating infant below the age of 12 months would lower the efficacy of measles vaccination as the effectiveness of the vaccine is compromised by the presence of circulating maternal antibodies to measles.

### What dictates the Measles MMR 2 Schedule?

MMR 2 schedule is largely dictated by measles epidemiology. One dose is not enough to prevent the transmission of measles. A second dose at 15 to 18 months strengthens immunity.

### Mumps

Although vaccination alone does not prevent all mumps outbreaks, maintaining high measles, mumps, and rubella (MMR) vaccination coverage remains the most effective way to prevent outbreaks and limit their size when they occur.

### Varicella

Effectiveness of two doses of varicella vaccine was shown in a case controlled study (2006 to 2010) by Shapiro. (Shapiro et al, 2011)<sup>3</sup> with mean age of subjects of 10.7 years. The odds of developing breakthrough varicella was lowered by 95% with a second dose.

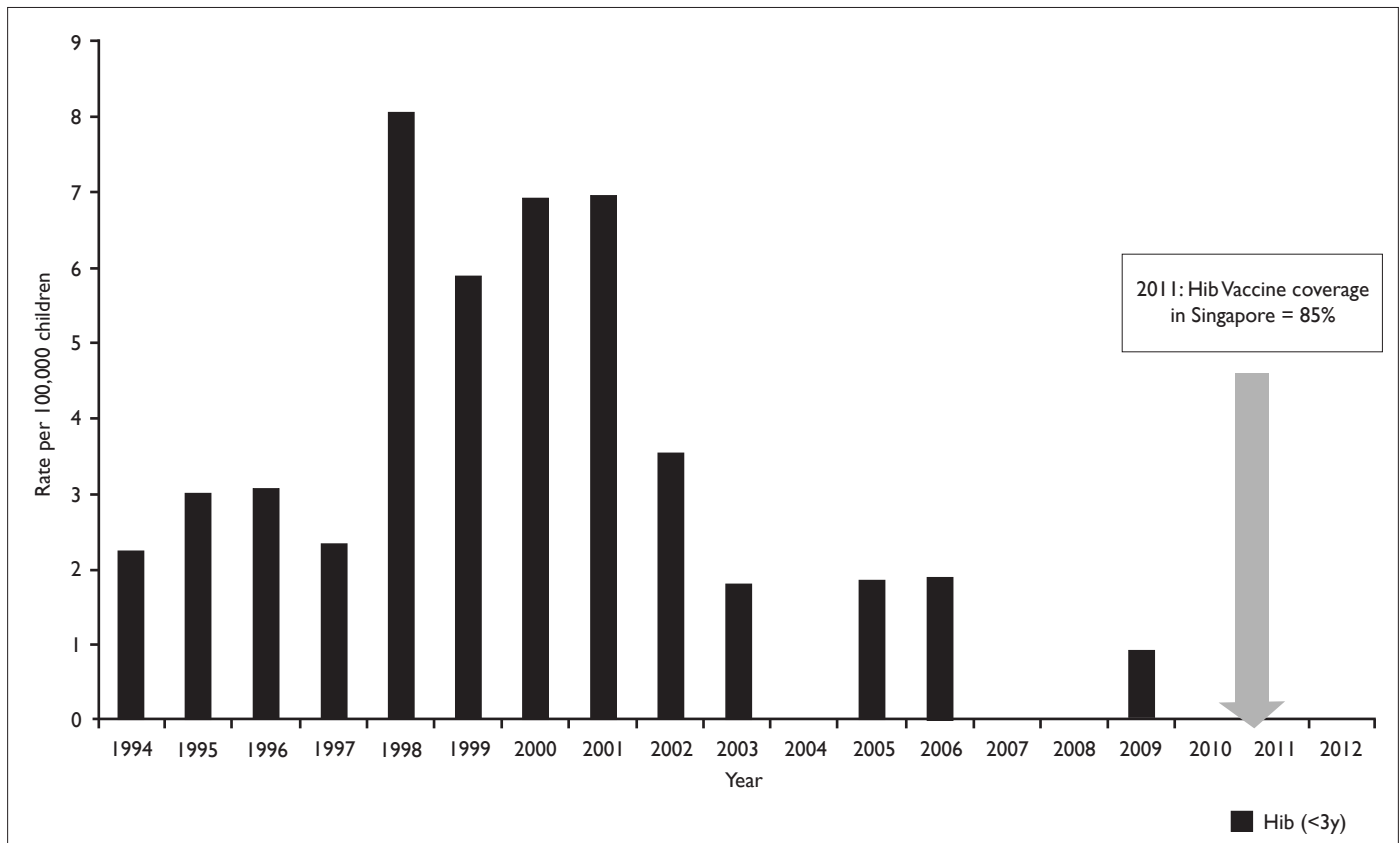
### What about MMRV or MMR-V?

Varicella can be given as MMRV or MMR-V. A Policy statement from the American Academy of Paediatrics provides guidance.

**TABLE 1: Comparison of IPV schedules in other countries (as of 2013)**

	United States	Canada	United Kingdom	Australia
<b>Number of doses</b>	4 doses	4 doses	5 doses	4 doses
<b>Schedule</b>				
• <b>Primary series</b>	2, 4, 6-18 months	2, 4, 6 months	2, 3, 4 months	2, 4, 6 months
• <b>1st booster</b>	4-6 years	18 months	3 years 4 mths	4 years
• <b>2nd booster</b>	Nil	Nil	13-18 years	Nil
<b>Vaccine Type</b>	Combination: DTaP-IPV (Kinrix) DTaP-HepB-IPV (Pediatrix) DTaP-IPV/Hib (Pentacel)  Monovalent: IPV (Ipol)	Combination: DTaP-IPV-Hib (Pediatrix) DTaP-HepB-IPV-Hib (Infanrix Hexa)	DTaP-IPV-Hib  DTaP-IPV (1st booster)  Td-IPV (2nd booster)	Combination: DTaP-IPV (Infanrix-IPV) DTaP-HepB-Hib (Infanrix Penta) DTaP-HepB-IPV-Hib (Infanrix Hexa)  Monovalent: IPV (Ipol)

**Hongkong: 6 doses IPV**

**FIGURE 2: INCIDENCE OF Hib MENINGITIS IN SINGAPORE**

Source: MOH Singapore 2013

#### Facts

- Data after vaccination at 12 to 23 months of age show that 7 to 9 febrile seizures occur per 10,000 children who receive the MMRV, compared to 3 to 4 febrile seizures occur per 10,000 children who receive the measles-mumps-rubella and varicella (MMR-V) vaccines administered concurrently but at separate sites.
- The period of risk for febrile seizures is from 5 through 12 days after receipt of the vaccine(s). Febrile seizures do not predispose to epilepsy or neurodevelopmental delays later in life and are not associated with long-term health impairment.
- No increased risk of febrile seizures is seen among patients 4 to 6 years of age receiving MMRV. (AAP, 2011)<sup>4</sup>

#### Recommendations of the American Academy of Pediatrics

- Either MMR and varicella vaccines separately (MMR-V) or the MMRV be used for the first dose of measles, mumps, rubella, and varicella vaccines administered at 12 through 47 months of age.
- For the first dose of measles, mumps, rubella, and varicella vaccines administered at ages 48 months and older, and for dose 2 at any age (15 months to 12 years), use of MMRV generally is preferred over separate injections of MMR and varicella vaccines. (AAP, 2011)<sup>4</sup>

#### INVASIVE PNEUMOCOCCAL DISEASE

The 7-valent pneumococcal conjugate vaccine (PCV7) which contains conjugate polysaccharides directed at 7 of the 91 pneumococcal serotypes causing disease namely serotypes 4, 6B, 9V, 14, 18C, and 23F was successful in reducing invasive pneumococcal disease (IPD) in the United States and worldwide – there was a 94% reduction of IPD. Although effective there were IPD caused by serotypes not covered. Consequently, PCV13 was created which contained the polysaccharides of the 7 serotypes plus an additional 6 serotypes (1, 3, 5, 6A, 7E, and 19A). The 19A serotype in particular was increasing in the post PCV7 era. PCV13 is given as a 3-dose primary series in the first year of life (3, 5, 12 months) in the Singapore national immunisation programme. Children who have initiated their vaccination program with PCV7 can transition to PCV13 at any point in the schedule. Children aged more than 15 months who have completely vaccinated with PCV7 can receive a single dose of PCV13 to induce immunity to the 6 additional serotypes. (Paradiso, 2011)<sup>5</sup>.

#### HUMAN PAPILLOMA VIRUS (HPV) INFECTION

Human papillomavirus vaccine is recommended for females 9 to 26 years and 3 doses are required at intervals of 0, 2, 6 months. (Singapore National Immunisation Programme, 2014).

Very recently, a reduced 2 dose HPV vaccination schedule (0, 6 months) has been approved by Health Services Authority of Singapore for children 9 to 14 years of age. There are two vaccines against HPV. Cervirix is designed to prevent infection from HPV types 16 and 18; and the quadrivalent Gardasil HPV vaccine is active against HPV types 6, 11, 16, and 18. (Marsh et al, 2014)<sup>6</sup>

Gardasil was originally licenced for protection against premalignant genital lesions (cervical, vulvar and vaginal), cervical cancer causally related to certain oncogenic HPV types, and external genital warts (EGW). Since its original licensing Gardasil is also demonstrated to be effective in preventing anal HPV infection and anal intraepithelial neoplasia in both genders. Universal HPV vaccination (vaccinating males and females) is therefore promoted. (Marsh et al, 2014)<sup>6</sup>.

The Vaccine Uptake Rate (VUR) and Vaccine Adherence has been studied in 21 HPV vaccination programs and found to be successful in school and health clinic based models. (Ladner et al, 2014)<sup>7</sup>.

**CHILDHOOD EXANTHEMS** (Promerance 2005; Murtagh 2011; Primary Care Dermatological Society)<sup>8,9,10</sup>

A sudden onset of rash in a child (or adult) is often termed as an exanthema (usually implying a viral cause). Usually, diagnosis is based on history and morphology of the rash. The diagnostic consideration for children is different from adults due to prior exposure in adults conferring immunity to some of the viruses.

In adults, a drug reaction is more common than in children. However, this does not mean that drug reaction cannot occur in children. Hence, a good history is vital for differentiating viral from non-viral rashes, which includes bacterial and drug causes.

**Exanthem.** The word “exanthem” is derived from the Greek “exanthema” which means “a breaking out.” “Anthos” in Greek is “a flower,” particularly a flower blossom, so a child breaking out with a rash is likened to a flower bursting into bloom.

**Enanthem.** Enanthem or enanthema, on the other hand, is a rash inside the body namely, the mucous membranes. The spots in measles (Koplik’s spots) inside the mouth that look like a tiny grains of white sand surrounded by a red ring is an example. Note that many enanthems have rashes on the skin (exanthems) too.

### Aetiology

This can be

- Viral. Most (not all) are benign and self-limiting.
- Other possible diagnoses:
  - Bacterial – e.g. Scarlet fever, Meningococemia.
  - Kawasaki disease.
  - Drug eruption.

### Approach

The approach in diagnosing the childhood exanthems (and enanthems) is pattern recognition:

- Purpura/petechie – seen in Meningococemia, Dengue, Parovirus, Scarlet fever.
- Edema – seen in Kawasaki, Drug eruption.
- Enanthem – seen in Kawasaki, Measles, HFMD, Parvovirus, Scarlet fever.
- Conjunctivitis – Kawasaki, Drug eruption, Measles, Adenovirus infection.

### CLASSIC EXANTHEMS

The classic childhood exanthems are commonly called “first” to “sixth diseases” based on their historical appearance and description.

- Measles (syn. Rubeola, morbilli) – caused by measles virus which is a Paramyxovirus.
- Scarlet Fever – caused by Group A streptococcus.
- Rubella (syn German measles) – caused by rubella virus.
- Filatow-Dukes Disease – no longer in use – See below.
- Erythema Infectiosum (syn slapped cheek disease) – caused by Parvovirus B19.
- Roseola Infantum (syn exanthema subitum) – caused by Herpes virus-6, Herpes virus-7.

Dukes’ disease, named after Clement Dukes, also known as fourth disease or Filatov’s disease (after Nil Filatov) This is an obsolete term. It was never associated with a specific pathogen, and the terminology is no longer in use.

### (I) First disease – Measles

Measles which is also known as morbilli or rubeola and not to be confused with rubella or roseola infantum is an infection of the respiratory system, immune system and skin caused by a virus, specifically a paramyxovirus of the genus *Morbillivirus*. The rash is described as “morbilliform exanthemata”. This rash consists of flat, red eruptions usually 2–10 mm in diameter but may be confluent in places.

### Incubation period

Incubation period is about 8–12 days. There is a prodrome of about 7–11 days after exposure followed by fever, cough, coryza, conjunctivitis. An enanthem Koplik’s spots on the oral mucosa appear 2 days before the rash, lasting till about 2 days into the rash. The infectious period is about 1–2 days before prodrome to 4 days after onset of rash.

### Clinical features

Symptoms usually develop 7–14 days (average 10–12) after exposure to an infected person and the initial symptoms usually include a high fever (often > 40 °C [104 °F]), Koplik’s spots (spots in the mouth, these usually appear 1–2 days prior to the rash and



last 3–5 days), malaise, loss of appetite, hacking cough (although this may be the last symptom to appear), runny nose and red eyes. After this comes a spot-like rash that covers much of the body. The course of measles, provided there are no complications, such as bacterial infections, usually lasts about 7–10 days. Those at risk includes preschool-age children who escaped vaccination; school-age children/adolescents in whom vaccination failed.

### Complications

Complications of measles include the following:

- Otitis media.
- Bronchopneumonia.
- Encephalitis.
- Myocarditis.
- Pericarditis.
- Subacute sclerosing panencephalitis which is a late sequelae due to persistent infection of the CNS.

### (2) Second disease – Scarlet fever

Scarlet fever (syn scarlatina) most commonly affects children. This is a bacterial and not a viral exanthema. Most of the clinical features are caused by an erythrogenic exotoxin-producing group A beta-hemolytic streptococci. Symptoms include sore throat, fever and a characteristic red rash. There is no vaccine, but the disease is effectively treated with antibiotics.

### Incubation period

Scarlet fever is usually spread by inhalation. The incubation period is about 2–4 days. The infectious period include the acute infection, gradually diminishes over weeks. Those at risk belong to the age group <10 years, peaking at the range of 4–8 years of age.

### Clinical features

- Abrupt onset fever, headache, vomiting, malaise, sore throat.
- Exanthem – a raised rash that feels like sand paper.
- Enanthem present – bright red oral mucosa, palatal petechiae, strawberry tongue.

### Complications

- Purulent complications.
- Otitis media.
- Sinusitis.
- Peritonsillar/retro-pharyngeal abscesses.
- Cervical adenitis.
- Nonsuppurative sequelae – Rheumatic fever, Acute glomerulonephritis.

### (3) Third disease – Rubella

Rubella, also known as German measles or three-day measles, is a disease caused by the rubella virus. The name “rubella” was derived from Latin, meaning *little red*. Rubella is also known as German measles because the disease was first described by

German physicians in the mid-eighteenth century. The name rubella is sometimes confused with *rubeola*, an alternative name for measles in English-speaking countries; the diseases are unrelated.

### Incubation period and importance

Those at risk are usually the unvaccinated adolescents and adults. Incubation period is about 14–21 days. The infectious period is about 5–7 days before rash to 3–5 days after rash.

This disease is often mild and attacks often pass unnoticed. The disease can last one to three days. Children recover more quickly than adults. Infection of the mother by rubella virus during pregnancy can be serious; if the mother is infected within the first 20 weeks of pregnancy, the child may be born with congenital rubella syndrome (CRS), which entails a range of serious incurable illnesses.

The virus is transmitted by the respiratory route and replicates in the nasopharynx and lymph nodes. The virus is found in the blood 5 to 7 days after infection and spreads throughout the body. The virus has teratogenic properties and is capable of crossing the placenta and infecting the fetus where it stops cells from developing or destroys them.

### Clinical features

- Asymptomatic infection in up to 50%.
- Prodrome – Children: Absent to mild; Adolescents and Adult: Fever, malaise, sore throat, nausea, anorexia.
- Exanthem – Unlike measles, the rash appears almost immediately (on day 1), starting on the face and rapidly spreading to the entire body. It is maculopapular and not confluent. The rash is generally completely resolved by day 3 (thus the name “3-day measles”).
- Lymph nodes – enlargement of the postauricular and occipital lymph glands.

### Complications

- Arthralgias/arthritis in older patients.
- Peripheral neuritis, encephalitis, thrombocytopenic purpura—rare.
- Congenital rubella syndrome.
- Infection during first trimester.
- IUGR, eye findings, deafness, cardiac defects, anemia, thrombocytopenia, skin nodules.

### (4) Fifth disease – Erythema Infectiosum

Erythema infectiosum or fifth disease is one of several possible manifestations of infection by erythrovirus, previously called parvovirus B19. The disease is also referred to as slapped cheek syndrome, slapcheek, slap face or slapped face.

### Incubation period

At risk: school-age children; Incubation period: 4–14 days; Infectious period: up until onset of the rash.

**Clinical features**

- Over 50% of infections are asymptomatic.
- Prodrome of mild fever (15–30%), sore throat, malaise.
- In adults, there are flu-like symptoms, arthralgias/arthritis (potentially chronic), rash in up to 40%.
- Hematological changes: proerythrocyte-tropic virus can cause a drop in red cell count.

**Complications**

- Immunocompromised—chronic infection with severe, persistent, relapsing and remitting anemia, prolonged viral shedding.
- Patients with decreased RBC survival time (hemoglobinopathies, hemolytic disease)—aplastic crises, prolonged viral shedding.
- Fetal infection—hydrops fetalis (overall risk of fetal death 1–9%).

**(5) Sixth disease – Roseola infantum**

Roseola infantum (or rose rash of infants) and also called Exanthema subitum (meaning *sudden rash*) is a disease of children, generally under two years old. It is caused by two human herpesviruses, HHV-6 (*Human herpesvirus 6*) and HHV-7, which are sometimes referred to collectively as *Roseolovirus*.

**Incubation period**

Those at risk include the age of 6–36 months, with peaks at age 6–7 months of age. There is no specific season as it occurs sporadically.

**Clinical features**

- High fever for 3–4 days.
- Abrupt defervescence with appearance of rash.

**COMMON PRESENT DAY VIRAL EXANTHEMS****(1) Hand-foot-mouth disease**

Hand, foot and mouth disease (HFMD) is a human syndrome caused by enteroviruses of the picornaviridae family. Coxsackievirus A16 and Enterovirus 71 (EV-71) are the most common strains known to cause HFMD, but many other strains of coxsackievirus or enterovirus are known to cause this viral syndrome. Consequently, the child may suffer from more than one episode of HFMD.

**Incubation period**

It is highly contagious and the incubation period is about 4–6 days. The prodrome lasts about 1–2 days before rash.

HFMD is a common and highly contagious viral infection that typically causes a mild febrile illness followed by a maculopapular rash that may involve the skin of the hands, feet,

and oral cavity. HFMD is fairly common and typically affects infants and children, but may affect immunocompetent adults on occasions.

**Clinical features**

A child with HFMD typically has some of the following:

- fever.
- sore throat.
- ulcers in the throat, mouth and tongue.
- headache.
- rash with vesicles (small blisters 3–7 mm) on hands, feet and diaper area. The vesicles are typically on the palm side of the hands the sole side of the feet and very characteristic in appearance. The rash may also be present on the buttocks, arms and legs.
- loss of appetite.
- vomiting and/or diarrhoea.

**(2) Varicella (Chicken Pox)**

Chicken Pox is a common and highly infectious disease. The characteristic crops of small vesicles have a central distribution affecting mainly the face, scalp and trunk, and subsequently generalised to the extremities.

**Incubation period**

The incubation period is 10 to 21 days. The period of infectivity is 1–2 days before rash appears until all lesions have crusted over (commonly about 5–6 days after onset of illness).

**Clinical features**

- It affects people mainly during childhood especially between the ages of two and eight.
- In children, the onset usually has no prodrome but in adults, an influenza-like prodrome of myalgia, fever and headaches may be experienced for two to three days.
- In children, the maculopapular rash appears almost at the same time as the fever, starting at the scalp and descending to the body and the extremities. The oral mucosa is not spared.
- Within 24 hours, the typical recognisable vesicles form. In the next few days, successive crops may repeat this cycle. This “cropping” phenomenon results in vesicles, papules, crusting lesions being present together. Scalp lesions can become infected. The rash is pruritic.
- The number of vesicles can vary from fewer than ten to thousands. In mild cases, the vesicles can be missed. The extent of rash is usually more severe in adults, especially in the immunocompromised.

**Diagnosis**

Varicella is readily diagnosed on clinical grounds. The diagnosis can also be established serologically and the virus may be detected

by immunofluorescence or isolated from fluid within the vesicles. Varicella has to be differentiated from impetigo, insect bites and papular urticaria.

### Complications

- Bacterial infection of the cutaneous lesions (usually staphylococcal or streptococcal) and can take the form of cellulitis or bullous impetigo and may leave pitted scars.
- Uncommon complications include viral pneumonia, thrombocytopenia and acute cerebellitis presenting with ataxia with a normal mental state.
- Other rare complications include meningoencephalitis and purpura fulminans. Death is rare except in the immunocompromised and neonates with congenital varicella.
- The varicella virus remains latent after infection. Clinical reactivation later in life results in herpes zoster.
- Varicella encephalitis is a complication occurring in approximately one case per 1000. The encephalitis complicating varicella tends to present between the fifth and eighth day of the illness and may complicate either mild or severe disease. Undoubtedly, cerebellar signs are the most characteristic feature of varicella encephalitis. Most cases resolve completely (Robinson & Gilbert, 1994).

### (3) Pityriasis Rosea

Pityriasis rosea is a self-limiting rash that can occur in both adults and children. Pityriasis rosea is more common in children and young adults. It is most common in people aged between 10 and 35 years. The cause is unknown though usually thought to be viral in origin as suggested by its seasonality, mild prodromal symptoms, associated upper respiratory symptoms and clustering of cases.

### Clinical features

A 'herald patch' usually appears on the skin first. This is usually an oval- or round-shaped patch which can vary from 2–5 cms in diameter. This is usually pink/red in colour. It most commonly appears on your chest or upper back although it can sometimes appear on your tummy (abdomen), neck, back, thigh or upper arms. However, many cases do not have a herald patch or it goes unnoticed.

Around 5–15 days later a more widespread rash gradually appears over about 10 days. This rash can spread over most of your body. However, it does not usually affect your face.

The rash usually consists of oval-shaped spots 1–3 cm in diameter which are pinky in colour. These spots are smaller than the herald patch. Often the spots seem to form lines in parallel with your skin creases.

This rash may be very itchy. The rash fades in time but this may take several weeks. It leaves no marks or scarring. Second attacks are very rare, but have been reported.

This description is the typical case which most people seem to have. Occasionally, the rash may just affect the arms and legs. Rarely, it can cause scaling or flaking of the skin, which can be troublesome.

## RASH DUE TO IMMUNOLOGICAL CAUSES

There are many immunologic causes of skin exanthems. In fact, most viral and bacterial causes of skin exanthems do so via immunologic means. All the conditions usually ascribed to vasculitides may produce skin rashes. However, only the 2 more common ones will be discussed here.

### (I) Kawasaki Disease (mucocutaneous lymph node syndrome) (Golshevsky, 2013)<sup>11</sup>

Kawasaki disease was first described by Kawasaki in Japan in 1967. Its cause is unknown but it is most likely to be an immunologic vasculitis to a large number of suspected triggers as disparate as propionibacterium acnes, spirochaetes, rickettsia, retroviruses, and house dust mite.

### Clinical features

Kawasaki's disease affects children at all ages and has also been described in adults but is chiefly seen in children up to three years of age, with the most severe cases occurring below the age of one year. It is an uncommon, acute multi-system disorder in children, characterised by onset of fever of five days or more and accompanied by the following features:

- bilateral non-exudative conjunctivitis.
- often inconsolably irritable.
- maculopapular polymorphous rash.
- with or without cervical lymphadenopathy more than 1.5 cm.
- dryness, redness and cracking of the lips.
- erythema of the oral cavity.
- erythema of palms and soles with induration and oedema.
- peeling of the skin of the finger and pulps some time during the illness (a characteristic feature).

The major complication is vasculitis that causes coronary aneurysms in 17 – 31 percent of cases, with an overall case fatality of 0.5 – 2.8 percent. The aneurysms usually develop between the second week and the second month of the illness. Echocardiography is indicated to detect these aneurysms and to determine prognosis.

### Diagnosis

The diagnosis of Kawasaki's disease can be made when the clinical features are clear-cut. It can be elusive as variations with incomplete manifestations occur. There is no specific test but the ESR and CRP are usually elevated. Think of it in a miserable child with a high fever more than 5 days with poor response to paracetamol (Murtagh & Rosenblatt, 2011).



## Treatment

The disease is self-limiting in some but it is important to make an early diagnosis because treatment can prevent complications. Early treatment with i/v IgG immunoglobulin and aspirin has been shown to be effective in reducing the prevalence of coronary artery arteritis. (Golshevsky, 2013)<sup>11</sup>

## (2) Henoch-Schonlein purpura

There are many other immunologic vasculitides which produce exanthems. In children, Henoch Schonlein purpura is one of the commonest. The purpuric rash starts off as an urticaria in the region of the buttocks and spreads to the lower extremities.

The appearance and distribution of the rash is often typical and the diagnosis usually confirmed by associated abdominal pain due to vasculitis of the abdominal vessels especially of those supplying the ileum. This often mimics acute appendicitis. Arthritis or arthralgia may also be seen.

## CONCLUSIONS

The rationale to the changes to the Singapore National Immunisation programme in recent years are presented. The classical childhood exanthems and common present day exanthems are revisited.

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## LEARNING POINTS

- Adequate immunization coverage is the prerequisite for creating herd immunity.
- The maintenance of these levels of population immunity requires continuous vigilance and changes to immunisation schedule in response to changing circumstances.
- Changes have been made over the years to optimise the immunisation of poliomyelitis, measles, mumps, rubella, and varicella.
- The introduction of hemophilus influenza type B vaccine and pneumococcal vaccine have reduced the incidence of these infections.
- Vaccination against human papillomavirus infection is being expanded to protect against cervical neoplasia in females and also anal intraepithelial neoplasia in both genders.
- Childhood exanthems due to viral and bacterial infections, as well as immunological causes continue to be important and the ability to recognise them is necessary.