# VIRAL INFECTIONS

## Systemic viral infections with exanthema

Exanthems = fever + rash

Maternal antibody protects for the first 6–12 months.

Immunization → decrease in pediatric infections.

## Measles

The WHO has set the objective of eradicating measles globally using the live attenuated vaccine.

Natural illness produces life-long immunity.

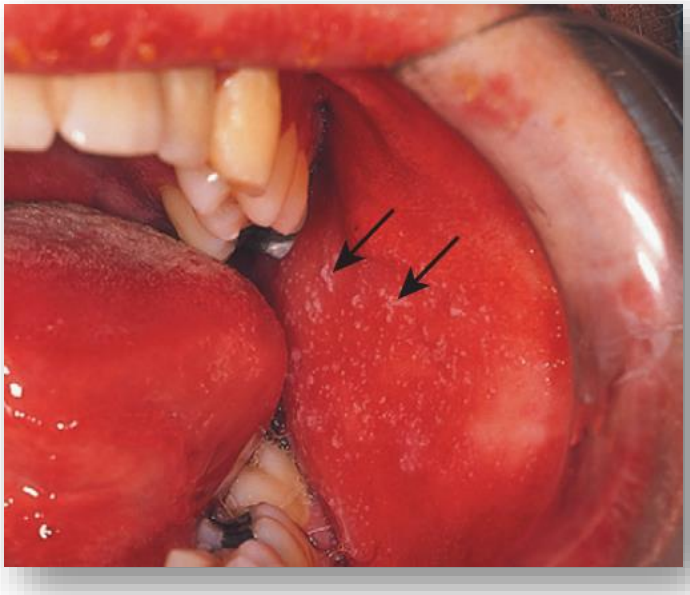
Route of transmission: respiratory droplets.

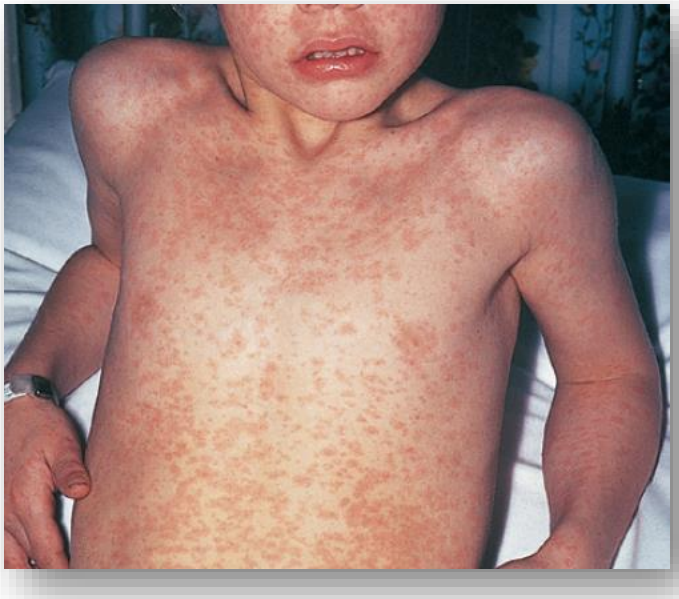
**Clinical features**

Incubation period: 6–19 days.

prodromal illness: 1–3 days before the rash,

- upper respiratory symptoms,
- conjunctivitis and
- the presence of the pathognomonic Koplik's spots, small white spots surrounded by erythema on the buccal mucosa.





- Maculopapular rash, spreading from the face to the extremities.
- Generalised lymphadenopathy
- Diarrhoea are common.

**Complications**: (are more common in older children and adults)

- otitis media,
- bacterialpneumonia,
- transient hepatitis and
- clinical encephalitis (approximately 0.1% of cases).
- A rare late complication is subacute sclerosing panencephalitis (SSPE), which occurs up to 7 years after infection.

**Diagnosis** is clinical (although this has become unreliable in areas where measles is no longer common) and by detection of antibody (serum IgM, seroconversion or salivary IgM).

Measles is a serious disease in the malnourished, vitamin-deficient or immunocompromised, in whom the typical rash may be missing and persistent infection with a pneumonitis or encephalitis may occur.

Measles does not cause congenital malformation but may be more severe in pregnant women.

Mortality clusters at the extremes of age, averaging 1 : 1000 in developed countries and up to 1 : 4 in developing countries.

Death usually results from a bacterial superinfection, occurring as a complication of measles, most often pneumonia, diarrhoeal disease or noma/ cancrum oris, a gangrenous stomatitis. Death may also result from complications of measles encephalitis.

Management and prevention:

Normal **immunoglobulin** attenuates the disease in the immunocompromised (regardless of vaccination status) and in non-immune pregnant women, but must be given within 6 days of exposure.

**Vaccination** can be used in outbreaks and **vitamin A** may improve the outcome in uncomplicated disease.

**Antibiotic therapy** is reserved for bacterial complications.

All children aged 12–15 months should receive measles vaccination (as combined measles, mumps and rubella (MMR), a live attenuated vaccine), and a further MMR dose at age 4 years.

# Rubella (German measles)

**Clinical features**

Mode of transmission: respiratory droplet

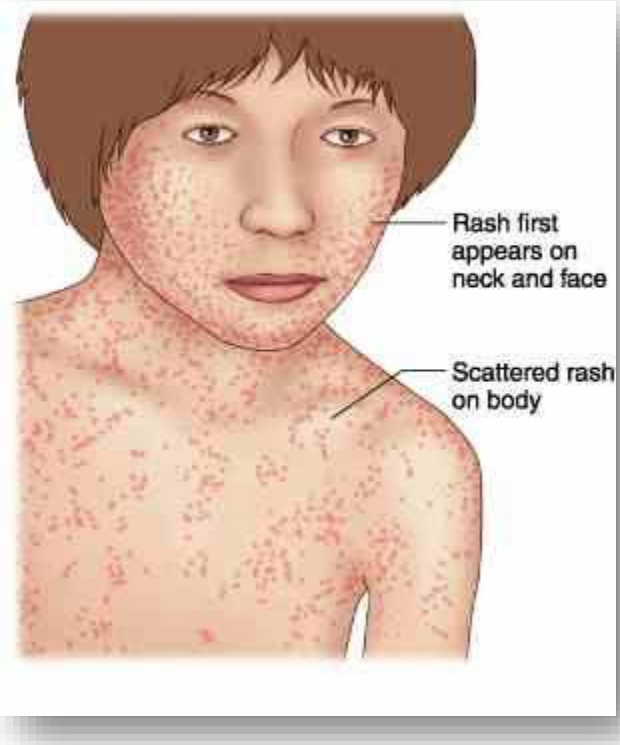
Infectivity: from up to 10 days before to 2 weeks after the onset of the rash.

The incubation period: 2-3 weeks.

- most cases are subclinical.
- fever,
- maculopapular rash spreading from the face, and
- lymphadenopathy.

**Complications**, are rare but include

- thrombocytopenia and
- hepatitis.
- Encephalitis and
- hemorrhage are occasionally reported.
- In adults, arthritis involving hands or knees is relatively common, especially in women.
- If transplacental infection takes place in the first trimester or later, persistence of the virus is likely and severe congenital disease may result. Even if normal at birth, the infant has an increased incidence of other diseases developing later, e.g. diabetes mellitus.



**Diagnosis**

Laboratory confirmation of rubella is required if there has been contact with a pregnant woman. This is achieved either by detection of rubella IgM in serum or by IgG seroconversion.

In the exposed pregnant woman, absence of rubella-specific IgG confirms the potential for congenital infection.

**13.29 Rubella infection: risk of congenital malformation**

| Stage of gestation | Likelihood of malformations |
|---|---|
| 1–2 mths | 65–85% chance of illness, multiple defects/spontaneous abortion |
| 3 mths | 30–35% chance of illness, usually a single congenital defect (most frequently deafness, cataract, glaucoma, mental retardation or congenital heart disease, especially pulmonary stenosis or patent ductus arteriosus) |
| 4 mths | 10% risk of congenital defects, most commonly deafness |
| > 20 wks | Occasional deafness |

**Prevention**

All children should be immunised with MMR.

In view of the risks of congenital rubella syndrome, all women of child-bearing age should also be tested for rubella and vaccinated if seronegative.

# Parvovirus B19

Parvovirus B19 causes exanthem and other clinical syndromes. Some 50% of children and 60–90% of adults are seropositive.

Mode of transmission: respiratory route, although spread via contaminated blood is also possible.

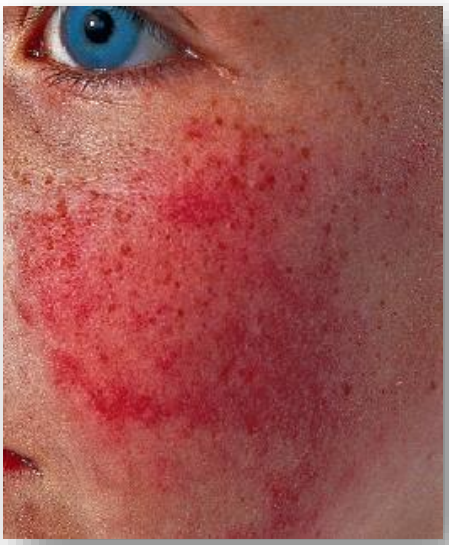
The virus has particular tropism for red cell precursors.

**Clinical features**

Many infections are **subclinical**.

Incubation period:2-3 weeks. The classic **exanthem** (erythema infectiosum) is preceded by a prodromal fever and **coryzal symptoms**.

A ‘slapped cheek’ **rash** is characteristic but the rash is very variable.



In adults, **polyarthropathy** is common. Infected individuals have a transient block in erythropoiesis for a few days, which is of no clinical consequence, except in individuals with increased red cell turnover due to haemoglobinopathy or haemolytic anaemia. These individuals develop an acute **anaemia** which may be severe. Erythropoiesis usually recovers spontaneously after 10–14 days.

Immunocompromised individuals, including those with congenital immunodeficiency or AIDS, can develop a more sustained block in erythropoiesis in response to the chronic viraemia that results from their inability to clear the infection.

Infection during the first two trimesters of pregnancy can result in intrauterine infection and impact on fetal bone marrow; it causes 10–15% of non-immune (non-Rhesus-related) hydrops fetalis, a rare complication of pregnancy.

**Diagnosis**

**IgM to parvovirus B19** suggests recent infection but may persist for months and false positives occur. Seroconversion to IgG positivity confirms infection but in isolation a positive IgG is of little diagnostic utility.

Detection of **parvovirus B19 DNA** in blood is particularly useful in immunocompromised patients.

**Management**

Infection is usually self-limiting. Symptomatic relief for arthritic symptoms may be required. Severe anaemia requires transfusion. Persistent viraemia in immunocompromised hosts may require immunoglobulin therapy to clear the virus.

Pregnant women should avoid contact with cases of parvovirus B19 infection; if they are exposed, serology should be performed to establish whether they are non-immune.

Passive prophylaxis with normal immunoglobulin has been suggested for non-immune pregnant women exposed to infection but there are limited data to support this recommendation. The pregnancy should be closely monitored by ultrasound scanning, so that hydrops fetalis can be treated by fetal transfusion.

**13.30 Clinical features of parvovirus B19 infection**

| Affected age group | Clinical manifestations |
|---|---|
| **Fifth disease (erythema infectiosum)** | |
| Small children | Three clinical stages: a 'slapped cheek' appearance, followed by a maculopapular rash progressing to a reticulate eruption on the body and limbs, then a final stage of resolution. Often the child is quite well throughout |
| **Gloves and socks syndrome** | |
| Young adults | Fever and an acral purpuric eruption with a clear margin at the wrists and ankles. Mucosal involvement also occurs |
| **Arthropathies** | |
| Adults and occasionally children | Symmetrical small-joint polyarthropathy. In children it tends to involve the larger joints in an asymmetrical distribution |
| **Impaired erythropoiesis** | |
| Adults, those with haematological disease, the immunosuppressed | Mild anaemia; in an individual with an underlying haematological abnormality can precipitate transient aplastic crisis, or in the immunocompromised a more sustained but often milder pure red cell aplasia |
| **Hydrops fetalis** | |
| Transplacental fetal infection | Asymptomatic or symptomatic maternal infection can cause fetal anaemia with an aplastic crisis, leading to non-immune hydrops fetalis and spontaneous abortion |

# Human herpesvirus 6 and 7

Human herpesvirus 6 (HHV-6) is a lymphotropic virus (tends to infect lymphocytes) that causes a childhood viral exanthem (exanthema subitum), rare cases of an infectious mononucleosis-like syndrome and infection in the immunocompromised host. Infection is almost universal, with approximately 95% of children acquiring this virus by 2 years of age.

Transmission: via saliva.

HHV-7 is very closely related to HHV-6, and is believed to be responsible for a proportion of cases of exanthem subitum. Like HHV-6, HHV-7 causes an almost universal infection in childhood, with subsequent latent infection and occasional infection in the immunocompromised host.

**Clinical features**

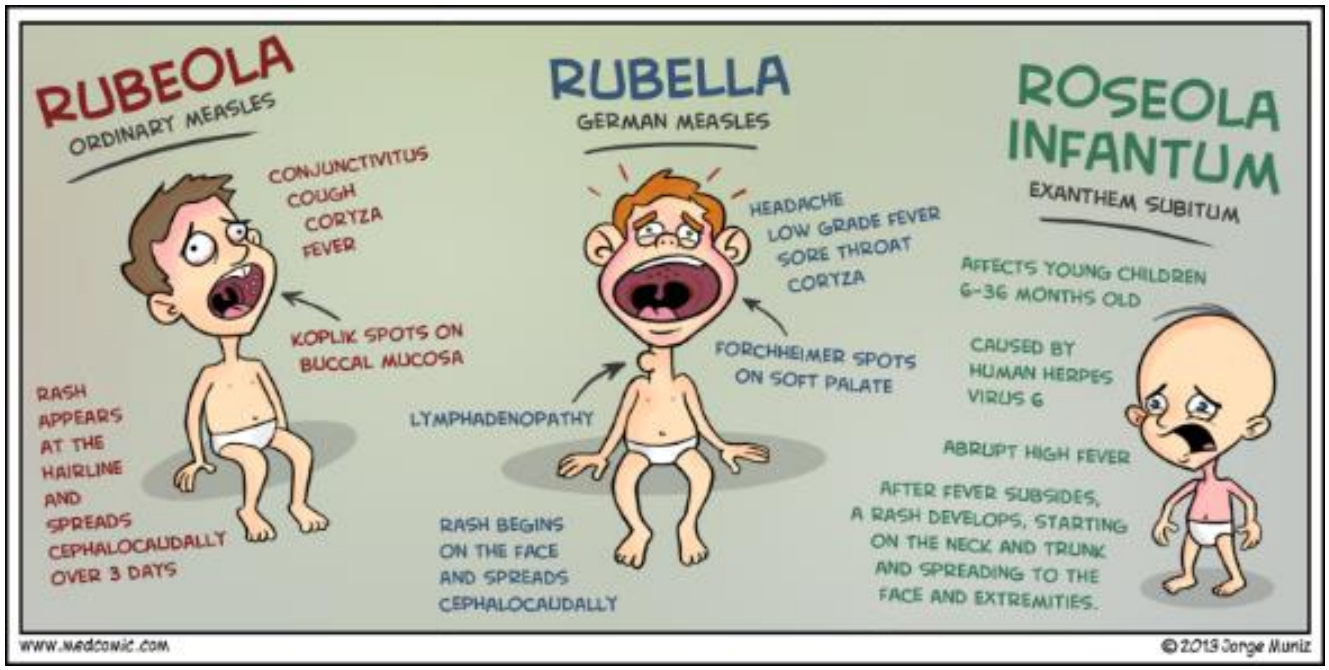
Exanthem subitum is also known as roseola infantum or sixth disease. A *high* **fever** is followed by a maculopapular **rash** as the fever resolves. Fever and/or febrile **convulsions** may also occur without a rash.

Rarely, older children or adults may develop an infectious mononucleosis-like illness, hepatitis or rash. In the immunocompromised, infection is rare but can cause fever, rash, hepatitis, pneumonitis, cytopenia or encephalitis.

**Diagnosis and management**

Exanthem subitum is usually a clinical diagnosis but can be confirmed by **antibody** and/or **DNA detection**.

The disease is self-limiting. Treatment with ganciclovir or foscarnet is used in immunocompromised hosts infected with HHV-6.



# Chickenpox (varicella)

أبو خريان، الجدري المائي

Varicella zoster virus (VZV) is a dermotropic and neurotropic virus that produces primary infection, usually in childhood, which may reactivate in later life.

Mode of transmission: aerosol and direct contact. It is highly infectious to non-immune individuals.

Disease in children is usually well tolerated. Manifestations are more severe in adults, pregnant women and the immunocompromised.

**Clinical features**

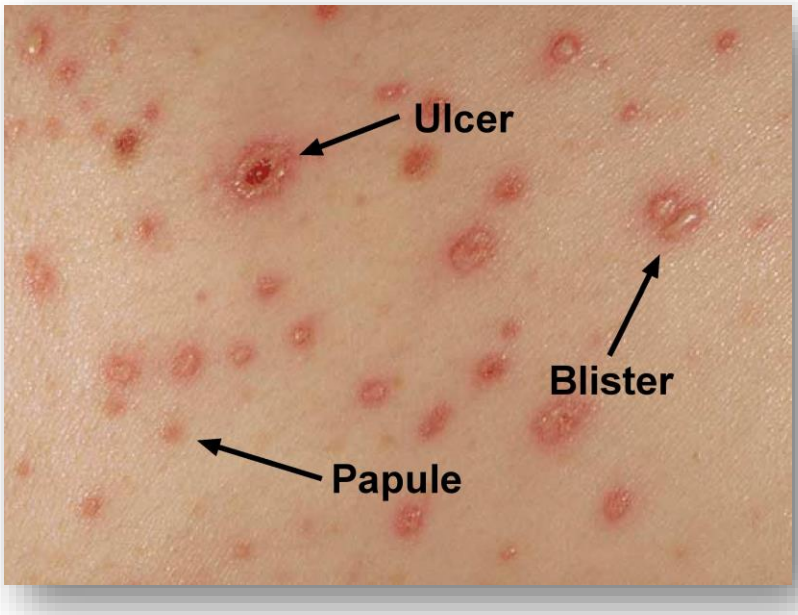
The incubation period is 11–20 days, after which a vesicular eruption begins, often on mucosal surfaces first, followed by rapid dissemination in a centripetal distribution (most dense on trunk and sparse on limbs). New lesions occur every 2–4 days and each crop is associated with fever. The rash progresses from small pink macules to vesicles and pustules within 24 hours. Infectivity lasts from up to 4 days (but usually 48 hours) before the lesions appear until the last vesicles crust over.

**complications**

Due to intense itching, **secondary bacterial infection** from scratching is the most common complication of primary chickenpox. Self-limiting **cerebellar ataxia** and **encephalitis** are rare complications.

Adults, pregnant women and the immunocompromised are at increased risk of visceral involvement, which presents as **pneumonitis**, **hepatitis** or **encephalitis**.

Pneumonitis can be fatal and is more likely to occur in smokers. Maternal infection in early pregnancy carries a 3% risk of neonatal damage with developmental abnormalities of eyes, CNS and limbs. Chickenpox within 5 days of delivery leads to severe neonatal varicella with visceral involvement and haemorrhage.



**Diagnosis**

Diagnosis is primarily **clinical**, by recognition of the rash. If necessary, this can be confirmed by detection of antigen (**direct immunofluorescence**) or DNA (**PCR**) of aspirated vesicular fluid. **Serology** is used to identify seronegative individuals at risk of infection.

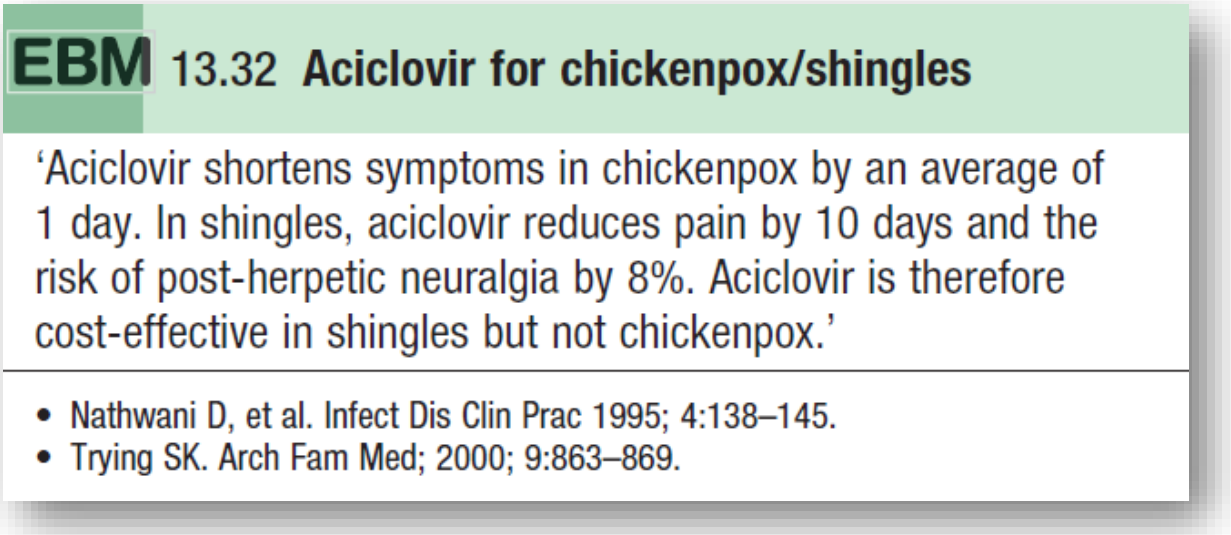
**Management and prevention**

The benefits of antivirals for uncomplicated primary VZV infection in children are marginal and treatment is not required.

**Antivirals** are, however, used for uncomplicated chickenpox when

- the patient presents within 24–48 hours of onset of vesicles,
- in all patients with complications, and in those who are
- immunocompromised, including pregnant women, regardless of duration of vesicles.

More severe disease, particularly in immunocompromised hosts, requires initial parenteral therapy. Immunocompromised patients may have prolonged viral shedding and may require prolonged treatment until all lesions crust over.




**Human VZ immunoglobulin** (VZIG) is used to attenuate infection in people who have had significant contact with VZV, are susceptible to infection (i.e. have no history of chickenpox or shingles and are seronegative for VZV IgG) and are at risk of severe disease (e.g. immunocompromised, steroid-treated or pregnant)

Ideally, VZIG should be given within 7 days of exposure, but it may attenuate disease even if given up to 10 days afterwards. Susceptible contacts who develop severe chickenpox after receiving VZIG should be treated with aciclovir.

Children receive one dose after 1 year of age and a second dose at 4–6 years of age; seronegative adults receive two doses at least 1 month apart. The vaccine may also be used prior to planned iatrogenic immunosuppression, e.g. before transplant.

## 13.31 Herpesvirus infections

| Virus | Infection |
|---|---|
| ***Herpesvirus hominis* (herpes simplex, HSV)** | |
| HSV-1 (p. 325) | Herpes labialis ('cold sores')<br>Stomatitis, pharyngitis<br>Corneal ulceration<br>Finger infections ('whitlows')<br>Eczema herpeticum<br>Encephalitis |
| HSV-2 (p. 325) | Genital ulceration and neonatal infection (acquired during vaginal delivery)<br>Acute meningitis or transverse myelitis.<br>Rarely, encephalitis |
| **Varicella zoster virus (VZV)** (p. 316) | Chickenpox (varicella)<br>Shingles (herpes zoster) |
| **Cytomegalovirus (CMV)** (p. 321) | Congenital infection<br>Infectious mononucleosis (heterophile antibody-negative)<br>Hepatitis<br>Disease in immunocompromised patients: retinitis, encephalitis, pneumonitis, hepatitis, enteritis<br>Fever with abnormalities in haematological parameters |
| **Epstein–Barr virus (EBV)** (p. 320) | Infectious mononucleosis<br>Burkitt's and other lymphomas<br>Nasopharyngeal carcinoma<br>Oral hairy leucoplakia (AIDS patients)<br>Other lymphomas |
| **Human herpesvirus 6 and 7 (HHV-6, HHV-7)** | Exanthem subitum<br>Disease in immunocompromised patients |
| **Human herpesvirus 8 (HHV-8)** (p. 326) | Kaposi's sarcoma, primary effusion lymphoma, multicentric Castleman's disease |

## 13.33 Therapy for herpes simplex and varicella zoster virus infection

| Disease state | Treatment options |
|---|---|
| **Primary genital HSV** | Famciclovir 250 mg 3 times daily for 7–10 days<br>Valaciclovir 1 g twice daily for 7–10 days<br>Oral aciclovir 200 mg 5 times daily or 400 mg 3 times daily for 7–10 days |
| Severe and preventing oral intake | Aciclovir 5 mg/kg 3 times daily IV until patient can tolerate oral therapy |
| **Recurrent genital HSV-1 or 2** | Oral aciclovir 200 mg 5 times daily or 400 mg 3 times daily for 5 days<br>Famciclovir 125 mg twice daily for 5 days<br>Valaciclovir 500 mg twice daily for 3–5 days or 2 g twice daily for 1 day. Shorter durations increasingly favoured |
| **Primary or recurrent oral HSV** | Usually no treatment<br>If required, usually short duration, e.g. valaciclovir 2 g twice daily for 1 day |
| **Mucocutaneous HSV infection in immunocompromised host** | Aciclovir 5 mg/kg 3 times daily IV for 7–10 days<br>Oral aciclovir 400 mg 4 times daily for 7–10 days<br>Famciclovir 500 mg 3 times daily for 7–10 days<br>Valaciclovir 1 g twice daily for 7–10 days |
| **Chickenpox in adult or child** | Oral aciclovir 800 mg 5 times daily for 5 days<br>Famciclovir 500 mg 3 times daily for 5 days<br>Valaciclovir 1 g 3 times daily for 5 days |
| Immunocompromised host/pregnant woman | Aciclovir 5 mg/kg 3 times daily IV until patient is improving, then complete therapy with oral therapy until all lesions crusting over |
| **Shingles** | Treatment and doses as for chickenpox but duration typically 7–10 days |
| **Visceral involvement (non-CNS) in HSV** | Aciclovir IV 5 mg/kg 3 times daily for 14 days |
| **Visceral involvement (non-CNS) in VZV** | Aciclovir IV 5 mg/kg 3 times daily for 7 days |
| **Severe complications** (encephalitis, disseminated infection) | Aciclovir IV 10 mg/kg 3 times daily (up to 20 mg/kg in neonates) for 14–21 days |
| **HSV disease suppression** | Aciclovir 400 mg twice daily<br>Famciclovir 250 mg twice daily<br>Valaciclovir 500 mg daily |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# Shingles (herpes zoster)

After initial infection, VZV persists in latent form in the dorsal root ganglion of sensory nerves and can reactivate in later life.

**Clinical features**

**Burning discomfort** occurs in the affected dermatome, where discrete **vesicles** appear 3–4 days later. This is associated with a brief viraemia, which can produce distant satellite 'chickenpox' lesions. Occasionally, **paraesthesia** occurs without rash ('zoster sine herpete').

❶Severe disease, ❷a prolonged duration of rash, ❸multiple dermatomal involvement or ❹recurrence suggests underlying immune deficiency, including HIV. Chickenpox may be contracted from a case of shingles but not vice versa.

Although thoracic dermatomes are most commonly involved, the ophthalmic division of the trigeminal nerve is also frequently affected; vesicles may appear on the cornea and lead to ulceration. This condition can lead to blindness and urgent ophthalmology review is required. Geniculate ganglion involvement causes *the Ramsay Hunt syndrome of facial palsy, ipsilateral loss of taste and buccal ulceration, plus a rash in the external auditory canal*. This may be mistaken for Bell's palsy (p. 1163). Bowel and bladder dysfunction occur with sacral nerve root involvement. The virus occasionally causes cranial nerve palsy, myelitis or encephalitis. Granulomatous cerebral angiitis is a cerebrovascular complication that leads to a stroke-like syndrome in association with shingles, especially in an ophthalmic distribution.

Post-herpetic neuralgia causes troublesome persistence of pain for 1–6 months or longer, following healing of the rash. It is more common with advanced age.

# Mumps

Mumps is a systemic viral infection characterised by swelling of the parotid glands. Infection is endemic worldwide and peaks at 5–9 years of age. Vaccination has reduced the incidence in children but incomplete coverage and waning immunity with time have led to outbreaks in young adults. Infection is spread by respiratory droplets.

Many outbreaks reported in Iraq in the last few years.

**Clinical features**

incubation period: 19 days, (range of 15–24 days).

Classical tender **parotid enlargement**, which is bilateral in 75%, follows a prodrome of **pyrexia** and **headache**. **Meningitis** complicates up to 10% of cases. The CSF reveals a lymphocytic pleocytosis or, less commonly, neutrophils. Rare complications include **encephalitis**, transient **hearing loss**, **labyrinthitis**, **electrocardiographic abnormalities**, **pancreatitis** and **arthritis**.

Approximately 25% of post-pubertal males with mumps develop **epididymo-orchitis** but, although testicular atrophy occurs, sterility is unlikely. Oophoritis is less common. Abortion may occur if infection takes place in the first trimester of pregnancy. Complications may occur in the absence of parotitis.

**Diagnosis**

The diagnosis is usually clinical. In atypical presentations without parotitis, serology for mumps-specific IgM or IgG seroconversion (four-fold rise in IgG convalescent titre) confirms the diagnosis. Virus can also be cultured from urine in the first week of infection or detected by PCR in urine, saliva or CSF.

**Management and prevention**

Treatment is with **analgesia**. There is no evidence that corticosteroids are of value for orchitis. Mumps **vaccine** is one of the components of the combined MMR vaccine, which is a live attenuated vaccine.