# **BMJ** Best Practice Acute varicella-zoster

Straight to the point of care



## **Table of Contents**

Overview	3
Summary	3
Definition	3
Theory	4
Epidemiology	4
Aetiology	5
Pathophysiology	5
Classification	5
Case history	5
Diagnosis	7
Approach	7
History and exam	9
Risk factors	11
Investigations	12
Differentials	14
Criteria	15
Screening	16
Management	17
Approach	17
Treatment algorithm overview	18
Treatment algorithm	19
Primary prevention	25
Secondary prevention	26
Patient discussions	27
Follow up	28
Monitoring	28
Complications	29
Prognosis	31
Guidelines	32
Treatment guidelines	32
Online resources	35
References	36
Images	49
Disclaimer	52

## Summary

Acute varicella-zoster (chickenpox) normally presents in childhood and is usually self-limiting.

Adults, pregnant women, immunosuppressed patients, and neonates are at high risk of complications from varicella, including pneumonia, neurological sequelae, hepatitis, secondary bacterial infection, and death.

Patients in high-risk categories should receive treatment with antiviral therapy.

While most countries in Europe do not currently vaccinate children against varicella, vaccination strategies differ widely within the EU, with a few countries incorporating the vaccine into routine childhood vaccination, and others recommending it to susceptible adolescents and adults. In the US, varicella vaccine is currently recommended for immunocompetent children and susceptible adults (e.g., healthcare workers, those occupationally exposed to children, people admitted to hospital, military recruits).

Patients with high risk for severe disease who have had significant exposure to the virus and in whom the vaccine is contraindicated (i.e., neonates, pregnant women, immunocompromised people, and those receiving high-dose systemic immunosuppressive therapy) may receive immunoprophylaxis or post-exposure antiviral prophylaxis.

## Definition

Varicella (chickenpox), one of the childhood exanthems, is caused by the human alpha herpes virus, varicella zoster. Varicella-zoster virus (VZV) is an exclusively human virus. The incubation period is about 14 days (range 9 to 21 days). Varicella is characterised by fever, malaise, and a generalised pruritic, vesicular rash. The disease normally presents in childhood and is usually self-limiting. Adverse outcomes are more common in immunocompromised people, adolescents, adults, and pregnant women.

## Epidemiology

Varicella-zoster virus (VZV) is found worldwide and is very contagious.[1] Over 90% of unimmunised people become infected, but infection occurs at different ages in different parts of the world; over 80% of people have been infected by the age of 10 years in the US, the UK, and Japan, and by the age of 20 to 30 years in India, Southeast Asia, and the Caribbean.[2][3] [4] The virus is more prevalent in temperate climates, and outbreaks are more common in late winter and spring.[5] Estimated hospital admission rates for varicella in developed countries range from 2 to 6 per 100,000 people and appear to be higher in African-American people and non-white Hispanic people.[6]



African patient with varicella Image provided by the CDC and the Public Health Image Library

Serosurveys in the US before immunisation was introduced have shown that more than 90% of individuals had VZV antibodies in adolescence and nearly 100% had them by adulthood.[7] The greatest incidence of varicella is in children 1 to 9 years of age, but in tropical climates, particularly in rural areas with smaller population densities, the disease is often acquired in adulthood.[1] [8][9] Immunocompromised patients are

## Aetiology

Varicella is caused by primary infection with the human alpha herpes virus, varicella zoster, in a non-immune host. Clinical disease is a manifestation of the second viraemic phase of the virus. Exposure to varicellazoster virus (VZV) initiates production of host antibodies and cell-mediated immune responses, which are important for early control and limiting dissemination of primary varicella infection. After initial presentation, the virus then establishes lifelong latency in cranial nerves and dorsal root ganglia. In up to one third of cases, VZV may re-activate later in life to produce shingles (herpes zoster).[11]

## Pathophysiology

Varicella occurs when a susceptible person is exposed to varicella-zoster virus (VZV) either by direct contact with lesions or through airborne spread from respiratory droplets.[12] After contact, the virus spreads to regional lymph nodes, resulting in a primary viraemic phase. On days 4 to 6, the infection spreads to the liver, the spleen, and other cells within the reticuloendothelial system.

A secondary viraemic phase occurs at about day 9, with mononuclear cells transporting the virus to the skin and mucous membranes, causing the classic vesicular rash.[13] VZV causes vasculitis of small blood vessels and degeneration of epithelial cells, leading to vesicles filled with fluid with high levels of virus.[13]

The virus is detectable in the nasopharynx 1 to 2 days before the onset of the rash, and patients are infectious at this time, before the rash develops.[14] Patients remain infectious for at least 5 days and until all lesions have crusted over. The incubation period is typically 14 days.

## Classification

## Clinical definitions of disease severity

Mild disease: in healthy children, the disease is generally mild and self-limiting, with malaise, pruritus (itching), and temperature up to 39°C (102°F) for 2 to 3 days.

Severe disease: associated with complications such as pneumonia, neurological sequelae, hepatitis, secondary bacterial infection, and even death.

## Case history

## Case history #1

A 6-year-old boy presents with fever, headache, and a diffuse, pruritic, vesicular rash, which is most prominent on the face and chest. He has had generalised malaise and low-grade fever for a few days prior to presentation. He developed high fever and a rash in the last 48 hours. Physical examination demonstrates a temperature of 39°C (102°F) and heart rate of 140 beats/minute. He has a few scattered

Theory

vesicular lesions in his oropharynx and his lung fields are clear. The lesions are prominent on the face and chest, but all extremities are also involved. In some areas the lesions are crusted, while in others they appear newly formed. He has no nuchal rigidity or other meningeal signs. The child has never been immunised for varicella, and a classmate at his school had chickenpox a few weeks ago.

## Case history #2

A 36-year-old man undergoing chemotherapy for non-Hodgkin's lymphoma presents with fever, shortness of breath, haemoptysis, and a diffuse rash. His family recalls that he had a fever the previous day, and that the rash started on his chest and progressed rapidly. In a review of recent exposures, his wife recounts that she was told that a child who visited their home later developed 'chickenpox'. His current medications are levofloxacin and an antidepressant. A review of his medical history indicates negative serological tests for varicella-zoster virus prior to starting chemotherapy, and his family does not recall him receiving the varicella vaccine. On examination he has a temperature of 40.1 °C (104.2 °F), a heart rate of 145 bpm, and an O2 saturation of 83%. Lung examination demonstrates bilateral crackles, and the patient has diffuse vesicular lesions, some of which appear to be haemorrhagic. Initial laboratory testing indicates a low haematocrit and platelets, a low absolute lymphocyte count (<100 cells/mL), and mild transaminitis. A chest x-ray demonstrates ground glass opacities or diffuse small nodular infiltrates.

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## Approach

## History

Varicella is normally acquired through contact with a patient with chickenpox (or, less frequently, direct contact with herpes zoster), so many patients have a history of such exposure. Exposure among children often takes place in the home, school, or day-care environments. Varicella is contagious with an attack rate of up to 90% in susceptible household members, but attack rates appear to be lower in classroom or day-care environments.[52] A prior history of chickenpox should be ascertained; 4.5% to 13.3% of people with varicella infection report previous varicella.[53] It is also important to review prior immunisation with varicella vaccine. Patients (or parents) may recall a prodrome consisting of fever, fatigue, headache, and/ or sore throat, prior to the onset of the rash.

In healthy children, the disease is generally mild and self-limiting, with malaise, pruritus (itching), and temperature up to 39 °C (102 °F) for 2 to 3 days. However, some patient groups are at risk of severe disease and complications such as pneumonia, neurological sequelae, hepatitis, secondary bacterial infection, and even death. Secondary bacterial infection should be considered in patients with persistent (i.e., >3 days) or recurrent fever.

Children and adults with known immunosuppression, such as caused by malignancy, immunodeficiency, organ transplantation, HIV infection, or corticosteroid use, are at greater risk for complications from varicella infection.[54] [55] [56] Immunosuppressed patients are more likely to have organ involvement, pneumonia, and haemorrhagic skin disease. While patients with underlying malignancy represent a small number of total varicella events, they account for a large proportion of deaths (up to 50%).[57] In children receiving cancer chemotherapy, 7% of patients died due to primary varicella. [58] Data on immunosuppressed adults is more difficult to ascertain due to the lower incidence of adult varicella, but case reports indicate that these patients are also at greater risk for major complications.[59] Pregnant women without evidence of immunity to varicella are at high risk for severe disease. [60] In addition, women who develop varicella from 5 days to 2 days prior to delivery have a high risk (17% to 30%) of transmitting the virus to their newborn. Because of the absence of maternal immunity to varicella-zoster virus (VZV), these children are at risk for severe infection.[21] [61] Premature babies exposed to varicella or herpes zoster may also be at high risk for severe disease, specifically hospitalised premature infants born at 28 or more weeks of gestation whose mothers do not have evidence of immunity and hospitalised premature infants born at less than 28 weeks of gestation or who weigh 1000 grams or less at birth regardless of their mothers' varicella immunity status.[60]

## **Physical examination**

Patients are often diagnosed by the classic rash associated with varicella. The rash is vesicular and usually first appears centrally (on the face, scalp, or torso), before spreading to the extremities.[62] Classically, lesions are described as 'dew drops on a rose petal', vesicular lesions filled with clear fluid and surrounded by erythema. Lesions appear in crops, so that lesions at different parts of the body are in different stages of development.[6] Lesions typically continue to appear over a few days and are often completely crusted over by 7 to 10 days. Vesicular lesions may also be noted in the oropharynx and other mucosal sites. Rarely, varicella can present with a haemorrhagic vesicle or a purpuric rash.[63]

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Varicella lesions in different stages of healing Image provided by the CDC



Varicella lesion on the hard palate of a young patient Image provided by the CDC and the Public Health Image Library

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#### Laboratory testing

Clinical findings are usually sufficient to make a diagnosis. In high-risk patients, adults, or other patients in whom the diagnosis is unclear, laboratory testing can confirm the diagnosis.

Polymerase chain reaction testing of skin lesions or cerebrospinal fluid is highly sensitive and will rapidly give an accurate diagnosis.[64]

Culture of vesicular fluid can be utilised to confirm the diagnosis, but may take up to 21 days to become positive. A Tzanck smear of vesicle fluid will show multi-nucleated giant cells; however, this test is less frequently used for diagnosis, particularly since it is not as accurate as direct fluorescent antibody (DFA) and it is not specific for VZV. Skin scrapings of the base of newer vesicles can be sent for DFA testing, which is rapid and fairly sensitive for the disease.[65]

Serology is not as useful for testing in acute disease, as early testing can be negative. However, serological testing may be useful in adult immunisation programmes, to identify people who do not need to be vaccinated. A variety of serological tests for varicella antibody are available. Tests include complement fixation, DFA, latex agglutination (LA), and enzyme-linked immunosorbent assay (ELISA). LA should not be used in acute disease, but can be useful in determining seroconversion after vaccination or documenting immune status.[66]

Serology is recommended in pregnant women who have possibly been exposed and have an unknown immune status.[61] If the results are negative or unavailable within 10 days from exposure, varicellazoster immunoglobulin (VZIG or VariZIG) should be administered. If immunoprophylaxis is unavailable, oral aciclovir should be given. Ultrasound is recommended for all women who develop varicella in pregnancy, to screen for fetal consequences of infection.[39] [50]

In some countries, including the US and Australia, varicella is a nationally notifiable disease.

## History and exam

#### Key diagnostic factors

#### presence of risk factors (common)

• Key risk factors include: exposure to varicella, young age, immunisation status, and occupation.

#### fever (common)

- Usually <38°C (101.5°F), but may be as high as 41°C (106°F).[6]
- Secondary bacterial infection should be considered in patients with persistent (i.e., >3 days) or recurrent fever.

#### vesicular rash (common)

- Classically described as a dew drop on a rose petal. The rash usually first appears centrally (on the face, scalp, or torso), before spreading to the extremities.[62]
- Lesions first appear as macules and quickly develop into fluid-filled vesicles.
- As the disease progresses, early lesions will begin to scab over as new peripheral lesions develop. This appearance of lesions in 'crops' (i.e., different stages of acuity/healing) is characteristic of varicella.



Typical vesicular rash of primary varicella; note that lesions are in different stages Image provided by the CDC and the Public Health Image Library



Varicella lesions in different stages of healing Image provided by the CDC

DIAGNOSIS

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#### vesicles on mucous membranes (common)

• Found most commonly in nasopharynx, but also on other mucous membranes such as conjunctiva, mouth, and vulva.



Varicella lesion on the hard palate of a young patient Image provided by the CDC and the Public Health Image Library

## Other diagnostic factors

#### pruritus (common)

• May be a feature in some patients prior to the onset of the rash.

#### headache (common)

• May be a feature in some patients prior to the onset of the rash.

#### fatigue/malaise (common)

• May be a feature in some patients prior to the onset of the rash.

#### sore throat (common)

• May be a feature in some patients prior to the onset of the rash.

#### tachycardia (common)

· May be present in infected patients.

## **Risk factors**

#### Strong

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#### exposure to varicella

• Occurs through family contacts or day care- or school-related exposure.

#### age 1 to 9 years

• Most common at-risk group is children aged 1 to 9.

#### unimmunised status

• While previous immunisation does not rule out varicella, it markedly decreases the risk of acquisition and appears to attenuate the disease presentation in those with breakthrough varicella.[15] [16]

#### occupational exposure

• Adults with occupational exposure to children, people admitted to hospital, military recruits, or other high-density at-risk populations are at higher risk for acquiring varicella.[17] [18]

## Investigations

#### 1st test to order

Test	Result
<ul> <li>clinical diagnosis</li> <li>Clinical findings are usually sufficient to make a diagnosis.</li> </ul>	typical vesicular rash at different stages, with pruritus, fever, malaise, frequently a history of exposure

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## Diagnosis

## Other tests to consider

Test	Result
<ul> <li>polymerase chain reaction</li> <li>Most sensitive and specific test for varicella-zoster virus.</li> <li>Detects DNA in fluids and tissues.[67]</li> <li>May not be available at all laboratories.</li> </ul>	positive for virus DNA
<ul> <li>viral culture</li> <li>Positive in &lt;50% of samples, but can help distinguish from other viral pathogens.[65] May take up to 21 days for positive result.</li> </ul>	positive varicella-zoster virus in culture
<ul><li>direct fluorescent antibody testing (DFA)</li><li>More rapid results and more sensitive than viral culture.</li></ul>	positive for varicella- zoster virus antigen (indicating that virus is present)
<ul> <li>Tzanck smear</li> <li>Used less frequently for diagnosis, particularly since it is not as accurate as DFA and it is not specific for varicella-zoster virus.</li> </ul>	multi-nucleated giant cells under microscopic evaluation
<ul> <li>Iatex agglutination (LA)</li> <li>Should not be used in acute disease, but can be useful in determining seroconversion after vaccination or documenting immune status.[66]</li> <li>Recommended in pregnant women who have possibly been exposed and have an unknown immune status.[50]</li> </ul>	positive for IgG for varicella
<ul> <li>enzyme-linked immunosorbent assay (ELISA)</li> <li>Not useful in acute disease.</li> <li>Similar to LA in terms of sensitivity, and can be used to test for immunity after exposure to the varicella-zoster virus or vaccine.[68]</li> <li>Recommended in pregnant women who have possibly been exposed and have an unknown immune status.[50]</li> </ul>	positive for IgG for varicella
<ul> <li>complement fixation</li> <li>Insensitive and may not be specific at low titres.</li> <li>Recommended in pregnant women who have possibly been exposed and have an unknown immune status.[50]</li> </ul>	positive for IgG for varicella
<ul> <li>ultrasound (pregnant women)</li> <li>Ultrasound is recommended for all women who develop varicella in pregnancy, to screen for fetal consequences of infection.[50]</li> </ul>	screening for fetal abnormalities

## Differentials

Condition	Differentiating signs / symptoms	Differentiating tests
Smallpox	<ul> <li>Has more prominent fever and more noticeable constitutional symptoms than varicella.</li> <li>Greatest number of lesions are on face and extremities (centrifugal distribution), and lesions present at the same stage in development.[69]</li> <li>Review history of recent smallpox vaccine or other possible exposures. Since natural transmission has been eradicated, new cases would more probably occur through laboratory exposure or as an act of bioterrorism. If smallpox is considered a possible diagnosis, immediate consultation should be sought and the patient should be placed in immediate isolation (standard, contact, and airborne). The patient should not be permitted to leave isolation until smallpox has been excluded as a diagnostic possibility. Consultation with local health departments is also highly recommended.</li> </ul>	<ul> <li>Polymerase chain reaction (PCR) test for smallpox will be positive.</li> <li>PCR test for varicella-zoster virus will be negative.</li> </ul>
Herpes zoster infection (shingles)	<ul> <li>Commonly presents in adulthood, particularly after the age of 60.</li> <li>Rash typically follows a dermatomal distribution of a cranial nerve or dorsal root ganglion.</li> </ul>	<ul> <li>Varicella zoster is a clinical diagnosis based on examination of the rash and history of exposure. Differentiating tests are not usually indicated.</li> </ul>
Herpes simplex virus (HSV) infection	<ul> <li>Usually affects the mucous membranes of the oral or genital region, but skin infections, usually localised, can also be observed.</li> </ul>	<ul> <li>Laboratory tests positive for HSV 1 or HSV 2.</li> </ul>
Stevens-Johnson syndrome/toxic epidermal necrolysis	<ul> <li>Lesions can look like targets initially but eventually become flaccid blisters.</li> <li>A large proportion of patients also present with diffuse</li> </ul>	• Skin biopsy can be helpful; however, most often the diagnosis is made on clinical presentation.[71]

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Condition	Differentiating signs / symptoms	Differentiating tests
	<ul> <li>erythema (erythroderma), and a significant number of patients complain of pain in involved areas.</li> <li>Blisters can become confluent and are associated with a positive Nikolsky's sign (epidermal layer easily sloughs off when pressure is applied to the affected area).[70]</li> <li>Patients often have a history of exposure to an agent (medication) associated with the condition.</li> </ul>	
Mpox (Monkeypox)	<ul> <li>Recent travel to Africa or recent close contact (including sexual contact) with someone who has Mpox is likely to be present.[72]</li> <li>Lesions present in similar stages (monomorphic) but are found on the palms and the soles of the feet.</li> <li>Also associated with lymphadenopathy, which is rarely found in varicella.[73]</li> </ul>	PCR test for monkeypox will be positive.

## Criteria

## Centers for Disease Control and Prevention (CDC) 2024 case definition:[74]

Clinical criteria:

- · Acute illness featuring:
  - A generalised rash with vesicles (maculopapulovesicular rash) or
  - A generalised rash without vesicles (maculopapular rash), particularly in the absence of a more plausible diagnosis.

Laboratory criteria for confirmation:

- · Positive polymerase chain reaction (PCR) testing for varicella-zoster virus (VZV) DNA
- · Positive direct fluorescent antibody (DFA) for VZV
- Isolation of VZV in culture
- A significant rise (at least a fourfold increase or seroconversion) in serum VZV-specific immunoglobulin G (IgG) between acute and convalescent phases

Supportive laboratory evidence:

15

• Detection of VZV-specific immunoglobulin M (IgM) antibody in serum

Epidemiological linkage for confirmation:

- Exposure or contact with a confirmed varicella case, or
- · Linkage to a varicella outbreak with at least one laboratory-confirmed case
- · Contact with a person displaying herpes zoster symptoms, irrespective of lab confirmation

Criteria to distinguish new cases:

- New onset of symptoms that fulfil the criteria for a confirmed or probable case,
- A previously confirmed case showing a documented period of recovery followed by the reappearance of symptoms that meet case criteria,
- A prior report (not previously confirmed) supplemented by new information that supports a confirmed case

Case classification:

- Probable case: meets clinical criteria with generalised rash with vesicles; or meets clinical criteria with generalised rash and supportive epidemiological evidence or laboratory findings
- Confirmed case: meets both clinical criteria and confirmatory laboratory evidence or epidemiological linkage

## Screening

## Screening for varicella-zoster virus (VZV) immunity

Screening for VZV is important in specific populations. Those with a definite history of varicella or herpes zoster can be considered protected. Pregnant women, solid organ transplant candidates, bone marrow transplant candidates, and other highly immunosuppressed patients should be screened for evidence of VZV immunity.[49] [61] Healthcare workers with a negative or uncertain history of varicella or herpes zoster should be serologically tested and be vaccinated if they are found to be seronegative.[20]

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## Approach

Treatment type depends on the child's risk for severe disease.

## Otherwise healthy children at low risk of severe disease

In healthy children, varicella is a self-limiting disease and may just be treated symptomatically with paracetamol for pyrexia, emollient lotions, and antihistamines to assist with pruritus. Calamine lotion is often used to help relieve itching;[75] however, there is no published evidence to support its use in varicella infection.[76] Aspirin is not recommended for fever due to its association with Reye's syndrome.[77] There is also concern over the use of non-steroidal anti-inflammatory drugs (NSAIDs) in varicella and an increased risk of group A streptococcal (GAS) superinfection.[78] [79] Due to the potential increase in skin and soft tissue infections, NSAIDs should be avoided. Hydration is important, particularly in toddlers and children with fever.

While current recommendations do not advocate the routine use of antiviral therapy for this group of patients, aciclovir has been studied for primary therapy in immunocompetent children and has been shown to decrease the time to resolution of fever when given within 24 hours after onset of rash.[80] In addition, some experts recommend the use of oral aciclovir in secondary household cases in which the disease may be more severe than in primary cases.[41]

## Increased risk of moderate to severe disease

In addition to symptomatic treatment, oral antiviral therapy is recommended by the American Academy of Pediatrics for patients who are considered to be at increased risk for moderate to severe varicella, and this includes:[41]

- · Otherwise healthy patients aged 13 years or over
- Those with chronic skin disease (e.g., atopic dermatitis)
- Those with underlying pulmonary disease
- · Patients receiving long-term salicylate therapy
- Those receiving short-course or intermittent oral corticosteroids.

Patients receiving other types of immunosuppressive therapy, such as monoclonal antibodies and tumour necrosis factor-alpha inhibitors, may also be at increased risk, but there is limited information on the use of antiviral agents in these patients. Clinical trials among adolescents and adults have indicated that aciclovir is well tolerated and effective in reducing the duration and severity of clinical illness if the drug is administered within 24 hours of rash onset.[21]

## High risk of severe disease

In addition to symptomatic treatment, prompt intravenous antiviral therapy is recommended for patients at high risk for severe disease and complications, and this includes:[41][60]

- People who are immunocompromised, such as those with leukaemia, lymphoma, or cellular immune deficiencies
- People who are on immunosuppressive medication, such as high-dose systemic corticosteroids or chemotherapeutic agents
- Neonates whose mothers have varicella from 5 days before to 2 days after delivery

- Premature babies, specifically hospitalised premature infants born at 28 or more weeks of gestation whose mothers do not have evidence of immunity and hospitalised premature infants born at less than 28 weeks of gestation or who weigh 1000 grams or less at birth regardless of their mothers' varicella immunity status
- Pregnant women.

On the basis of the limited experimental evidence that intravenous aciclovir may reduce the severity of illness compared with placebo in immunocompromised children, experts recommend the routine use of aciclovir for all patients at high risk for developing complicated disease.[21][49]

Pregnant women should be counselled about the risk of potential adverse maternal and fetal sequelae, options for antenatal diagnosis, and the risk of fetal transmission. Consultation with a neonatologist and an infectious disease specialist is recommended if there is peripartum varicella exposure, in order to optimise prevention or treatment strategies.[39] [50]

## Patients with severe disease who develop serious complications

Antiviral therapy is essential for all patients who develop serious complications from varicella infection (i.e., pneumonia, hepatitis, or encephalitis/central nervous system disease).

## Treatment algorithm overview

Please note that formulations/routes and doses may differ between drug names and brands, drug formularies, or locations. Treatment recommendations are specific to patient groups: <u>see disclaimer</u>

Acute		( summary )
otherwise healthy children at low risk of severe disease		
	1st	supportive care
increased risk of moderate to severe disease		
	1st	oral antiviral therapy
	plus	supportive care
high risk of severe disease		
	1st	intravenous antiviral therapy
	plus	supportive care
	adjunct	counselling and referral of pregnant women
severe disease		
	1st	intravenous antiviral therapy
	plus	supportive care

18

## Treatment algorithm

Please note that formulations/routes and doses may differ between drug names and brands, drug formularies, or locations. Treatment recommendations are specific to patient groups: <u>see disclaimer</u>

#### Acute

otherwise healthy children at low risk of severe disease

1st

#### supportive care

#### **Primary options**

» paracetamol: children <12 years of age: 15 mg/kg orally/rectally every 4-6 hours when required, maximum 75 mg/kg/day; children >12 years of age: 500-1000 mg orally/rectally every 4-6 hours when required, maximum 4000 mg/day

#### --AND--

» diphenhydramine: children 2-5 years of age: 6.25 mg orally every 4-6 hours when required, maximum 37.5 mg/day; children 6-12 years of age: 12.5 to 25 mg orally every 4-6 hours when required, maximum 150 mg/day; children >12 years of age: 25-50 mg orally every 4-6 hours when required, maximum 300 mg/day

Not recommended for children <2 years of age.

#### --AND--

» diphenhydramine topical: (1-2%) apply to the affected area(s) three to four times daily when required for up to 7 days -or-

» emollient topical: apply to the affected area(s) when required

» Symptomatic treatment with paracetamol, skin emollients, and antihistamines may be all that is required by children with low risk of developing severe disease. Hydration is important, particularly in toddlers and children with fever.

» Aspirin is contraindicated due to its association with Reye's syndrome.[77] There is also concern over the use of non-steroidal antiinflammatory drugs (NSAIDs) in varicella and an increased risk of group A streptococcal (GAS) superinfection.[78] [79] Due to the potential increase in skin and soft tissue infections, NSAIDs should be avoided.

» Calamine lotion is often used to help relieve itching;[75] however, there is no published

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evidence to support its use in varicella infection.[76]

» Antihistamine treatment for varicella in children has been associated with ataxia, urinary retention, and other adverse effects. In addition, a warning has been issued against the use of some cough and cold medicines (many of them antihistamines) in children under the age of 2 years.[81] Risks may outweigh benefits in young children.

## increased risk of moderate to severe disease

1st

#### t oral antiviral therapy

#### **Primary options**

» aciclovir: children >2 years of age: 20 mg/ kg orally four times daily for 5 days; children >40 kg body weight and adults: 800 mg orally five times daily for 5 days

» Oral antiviral therapy is recommended by the American Academy of Pediatrics for patients who are considered to be at increased risk for moderate to severe varicella, and this includes: otherwise healthy patients aged 13 years or over; those with chronic skin disease (e.g., atopic dermatitis); those with underlying pulmonary disease; patients receiving long-term salicylate therapy; those receiving short-course or intermittent oral corticosteroids.[41]

» Oral antiviral therapy within the first 72 hours improves the time to healing of cutaneous lesions and decreases duration of fever in adolescents and adults.[82] [83] [84] [85]

#### plus supportive care

Treatment recommended for ALL patients in selected patient group

#### **Primary options**

» paracetamol: children <12 years of age: 15 mg/kg orally/rectally every 4-6 hours when required, maximum 75 mg/kg/day; children >12 years of age and adults: 500-1000 mg orally/rectally every 4-6 hours when required, maximum 4000 mg/day

#### --AND--

» diphenhydramine: children 2-5 years of age: 6.25 mg orally every 4-6 hours when required, maximum 37.5 mg/day; children 6-12 years of age: 12.5 to 25 mg orally every 4-6 hours when required, maximum 150 mg/day; children >12 years of age and

MANAGEMENT

adults: 25-50 mg orally every 4-6 hours when required, maximum 300 mg/day Not recommended for children <2 years of age.

#### --AND--

» diphenhydramine topical: (1-2%) apply to the affected area(s) three to four times daily when required for up to 7 days -or-

» emollient topical: apply to the affected area(s) when required

» Symptomatic treatment with paracetamol, skin emollients, and antihistamines can be used in these populations.

» Patients admitted for varicella need to be placed in both airborne and contact isolation from potentially susceptible people for a minimum of 5 days after the onset of the rash and until all lesions are crusted.

» Hydration is important, particularly in toddlers and children with fever.

» Aspirin is contraindicated due to its association with Reye's syndrome.[77] There is also concern over the use of non-steroidal antiinflammatory drugs (NSAIDs) in varicella and an increased risk of group A streptococcal (GAS) superinfection.[78] [79] Due to the potential increase in skin and soft tissue infections, NSAIDs should be avoided.

» Calamine lotion is often used to help relieve itching;[75] however, there is no published evidence to support its use in varicella infection.[76]

» Antihistamine treatment for varicella in children has been associated with ataxia, urinary retention, and other adverse effects. In addition, a warning has been issued against the use of some cough and cold medicines (many of them antihistamines) in children under the age of 2 years.[81] Risks may outweigh benefits in young children.

#### high risk of severe disease

#### 1st intravenous antiviral therapy

#### **Primary options**

 » aciclovir: neonates and children 1-3 months: 10-20 mg/kg intravenously every 8 hours for 7-10 days; children 3 months to 12 years of age: 250-500 mg/square metre

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21

of body surface area intravenously every 8 hours for 5-10 days; adults: 10 mg/kg intravenously every 8 hours for 5-10 days

» Prompt intravenous antiviral therapy is recommended for patients at high risk for severe disease and complications, and this includes: people who are immunocompromised, such as those with leukaemia, lymphoma, or cellular immune deficiencies; people who are on immunosuppressive medication, such as high-dose systemic corticosteroids or chemotherapeutic agents; neonates whose mothers have varicella from 5 days before to 2 days after delivery; premature babies (specifically hospitalised premature infants born at 28 or more weeks of gestation whose mothers do not have evidence of immunity and hospitalised premature infants born at less than 28 weeks of gestation or who weigh 1000 grams or less at birth regardless of their mothers' varicella immunity status); pregnant women.[41] [60]

» Delay in treatment can have serious consequences for these patients.

» Prospective studies that have evaluated aciclovir use in immunosuppressed children have demonstrated less risk of dissemination and a reduction in the duration of hospitalisation.[86] [87] [88] [89] [90]

» Alternate dosing may be required for preterm neonates.

#### plus

Treatment recommended for ALL patients in selected patient group

#### **Primary options**

supportive care

» paracetamol: neonates: 10-15 mg/kg orally/ rectally every 6-8 hours when required, maximum 60 mg/kg/day; children <12 years of age: 15 mg/kg orally/rectally every 4-6 hours when required, maximum 75 mg/kg/ day; children >12 years of age and adults: 500-1000 mg orally/rectally every 4-6 hours when required, maximum 4000 mg/day

#### --AND--

» diphenhydramine: children 2-5 years of age: 6.25 mg orally every 4-6 hours when required, maximum 37.5 mg/day; children 6-12 years of age: 12.5 to 25 mg orally every 4-6 hours when required, maximum 150 mg/day; children >12 years of age and

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adults: 25-50 mg orally every 4-6 hours when required, maximum 300 mg/day Not recommended for children <2 years of age.

#### --AND---

» diphenhydramine topical: (1-2%) apply to the affected area(s) three to four times daily when required for up to 7 days -or-

» emollient topical: apply to the affected area(s) when required

» Symptomatic treatment with paracetamol, skin emollients, and antihistamines can be used in these populations.

» Patients admitted for varicella need to be placed in both airborne and contact isolation from potentially susceptible people for a minimum of 5 days after the onset of the rash and until all lesions are crusted.

» Hydration is important, particularly in toddlers and children with fever.

» Aspirin is contraindicated due to its association with Reye's syndrome.[77] There is also concern over the use of non-steroidal antiinflammatory drugs (NSAIDs) in varicella and an increased risk of group A streptococcal (GAS) superinfection.[78] [79] Due to the potential increase in skin and soft tissue infections, NSAIDs should be avoided.

» Calamine lotion is often used to help relieve itching;[75] however, there is no published evidence to support its use in varicella infection.[76]

» Antihistamine treatment for varicella in children has been associated with ataxia, urinary retention, and other adverse effects. In addition, a warning has been issued against the use of some cough and cold medicines (many of them antihistamines) in children under the age of 2 years.[81] Risks may outweigh benefits in young children.

#### adjunct counselling and referral of pregnant women

Treatment recommended for SOME patients in selected patient group

» Pregnant women should be counselled about the risk of potential adverse maternal and fetal sequelae, options for antenatal diagnosis, and the risk of fetal transmission.

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23

#### severe disease

Consultation with a neonatologist and an infectious disease specialist is recommended if there is peripartum varicella exposure, in order to optimise prevention or treatment strategies.[50]

#### 1st intravenous antiviral therapy

#### **Primary options**

» aciclovir: children 1-3 months: 10-20 mg/ kg intravenously every 8 hours for 7-10 days; children 3 months to 12 years of age: 250-500 mg/square metre of body surface area intravenously every 8 hours for 5-10 days; adults: 10 mg/kg intravenously every 8 hours for 5-10 days

» Patients who develop serious complications from varicella should receive intravenous aciclovir. Treatment should begin empirically in patients with clinical symptoms suggestive of complications.[21][64] [91] [92] [93] [94] [95] Patients may need to be treated for longer than 7-10 days with aciclovir if they have severe disease or neurological complications.

#### plus supportive care

Treatment recommended for ALL patients in selected patient group

#### **Primary options**

» paracetamol: children <12 years of age: 15 mg/kg orally/rectally every 4-6 hours when required, maximum 75 mg/kg/day; children >12 years of age and adults: 500-1000 mg orally/rectally every 4-6 hours when required, maximum 4000 mg/day

#### --AND--

» diphenhydramine: children 2-5 years of age: 6.25 mg orally every 4-6 hours when required, maximum 37.5 mg/day; children 6-12 years of age: 12.5 to 25 mg orally every 4-6 hours when required, maximum 150 mg/day; children >12 years of age and adults: 25-50 mg orally every 4-6 hours when required, maximum 300 mg/day Not recommended for children <2 years of age.

#### --AND--

» diphenhydramine topical: (1-2%) apply to the affected area(s) three to four times daily when required for up to 7 days -or-

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» emollient topical: apply to the affected area(s) when required

» Patients admitted for varicella need to be placed in isolation for a minimum of 5 days after the onset of the rash and until all lesions are crusted.

» Symptomatic treatment with paracetamol, skin emollients, and antihistamines can be used in these populations.

» Hydration is important, particularly in toddlers and children with fever.

» Aspirin is contraindicated due to its association with Reye's syndrome.[77] There is also concern over the use of non-steroidal antiinflammatory drugs (NSAIDs) in varicella and an increased risk of group A streptococcal (GAS) superinfection.[78] [79] Due to the potential increase in skin and soft tissue infections, NSAIDs should be avoided.

» Calamine lotion is often used to help relieve itching;[75] however, there is no published evidence to support its use in varicella infection.[76]

» Antihistamine treatment for varicella in children has been associated with ataxia, urinary retention, and other adverse effects. In addition, a warning has been issued against the use of some cough and cold medicines (many of them antihistamines) in children under the age of 2 years.[81] Risks may outweigh benefits in young children.

## **Primary prevention**

While varicella immunisation is routine in the US, in Europe the use of varicella vaccine varies between countries.[19]

In the UK and in some other parts of Europe, the varicella vaccine is not currently recommended for routine use in children. However, it is recommended to protect those at risk of serious illness by immunising individuals who are in regular or close contact with these patients, such as non-immune healthcare workers and healthy susceptible close household contacts of immunocompromised patients.[20]

In the US, two preparations of live, attenuated varicella-zoster virus (VZV)-containing vaccines are available for prevention of varicella: a single-antigen varicella vaccine (VAR) for use in healthy children (aged 12 months and over), adolescents, and adults; and a combination measles, mumps, rubella, and varicella vaccine (MMRV) for use in healthy children aged 12 months to 12 years. Vaccination guidelines in the US recommend a routine 2-dose varicella vaccination program for children, with the first dose administered at 12 to 15 months of age and the second dose at 4 to 6 years.[21][22] For the first dose, the US guidelines recommend that the MMR and varicella vaccines are administered separately in children aged 12-47 months.[22] Routine vaccination (2 doses, 4 to 8 weeks apart) of all healthy adults without evidence of immunity is also recommended (or a second dose if they have received only 1 dose).[23] Vaccination is

contraindicated in pregnant women.[23] Vaccination may be considered in patients with HIV infection with CD4 percentages  $\geq$ 15% and CD4 count  $\geq$ 200 cells/mm<sup>3</sup> with no evidence of immunity (2 doses, 3 months apart); note that VAR is contraindicated in those with HIV infection with CD4 percentage <15% or CD4 count <200 cells/mm<sup>3</sup>.[23]

While a single dose has about 80% to 85% effectiveness, the currently recommended second dose increases effectiveness to over 95%.[24] [25] [26] [27] [28] Clinical trials to assess the effectiveness of the vaccine typically follow patients in the short term (1- to 2-year follow-up). Protective concentrations of antibody among immunised people in Japan have been shown to persist for more than 20 years after immunisation, and in one long-term study the estimated proportion of vaccine recipients who remained varicella-free at the end of 7 years was 95%.[24][29] Another study of 10-year follow-up by the same group demonstrated an estimated vaccine efficacy for the 10-year observation period of 94.4% for 1 injection and 98.3% for 2 injections.[25] A Cochrane review found the MMRV (measles, mumps, rubella, varicella) vaccine to be 95% effective at preventing varicella after two doses in children aged 11 to 22 months in a 10-year follow-up.[30] Implementation of universal immunisation strategies has also been shown to significantly decrease varicella-associated deaths.[31]

Some countries have not recommended routine childhood varicella vaccination, in part due to concerns that decreases in exogenous boosting from natural infection (i.e., children with varicella) will lead to increased risk for herpes zoster in adults.[32][33] In Europe, varicella vaccination recommendations remain heterogeneous, with only 7 European Union countries recommending universal vaccination.[34] Retrospective studies have shown conflicting results, and have been limited by notable increases in herpes zoster prior to the implementation of such childhood vaccination programmes.[35][36] [37] [38]

The live vaccine is contraindicated in neonates, pregnant women, and immunocompromised individuals or those receiving high-dose systemic immunosuppressive therapy; however, in some countries, vaccination is recommended for all non-immune women as part of pre-pregnancy and postpartum care.[39] Varicella immunity status and history of vaccination should be documented in all pregnant women, and all seronegative patients should be counselled about the increased risk of primary varicella in pregnancy and the need to seek immediate medical help in the case of possible exposure.[40] The vaccines are also contraindicated in patients with a history of hypersensitivity to any component of the vaccines, including gelatin, or a history of anaphylactoid reaction to neomycin. Additional contraindications should be noted and additional precautions taken for children receiving a combination vaccine (measles, mumps, rubella, and varicella vaccine).[41]

In non-randomised studies, varicella vaccine appears to be safe in some patients with organ dysfunction and low levels of immunosuppression.[42] [43] [44] [45] [46] [47] Reviews of recommendations for the use of varicella vaccines in high-risk transplant populations are also available.[48][49] Patients with leukaemia, lymphoma, or other malignancies whose disease is in remission and whose chemotherapy has been terminated for at least 3 months can receive live-virus vaccines. When immunising patients in whom some degree of immunodeficiency might be present, only single-antigen varicella vaccine should be used. Immunisation of leukaemic children who are in remission or of other immunocompromised hosts who do not have evidence of immunity to varicella should be undertaken only with expert guidance and with the availability of antiviral therapy should complications ensue.[21]

In some countries, it is recommended that varicella-zoster immunoglobulin should be administered to all neonates born to mothers who developed the disease between 5 days before and 2 days after delivery, as these infants are at risk for severe disseminated varicella.[50] [51]

## Secondary prevention

Post-exposure prophylaxis through use of varicella vaccine, immunoglobulin, or antivirals is recommended for some patients following exposure to a person with acute varicella zoster or herpes zoster.

Varicella immunisation:

• US guidelines recommend administering varicella vaccine to healthy people without evidence of immunity who are aged 12 months or older (including adults), as soon as possible after exposure,

preferably within 3 days and up to 5 days.[41] Effectiveness has been demonstrated to be more than 90% when given within 3 days of exposure, and about 70% at 5 days.[21]

Passive immunoprophylaxis:

- UK guidelines recommend use of varicella-zoster immunoglobulin (VZIG) for susceptible individuals who are unable to take oral antivirals, and for susceptible neonates exposed within one week of delivery (in utero or post-delivery).[129]
- US guidelines recommend use of varicella-zoster immunoglobulin (VariZIG) for high-risk patients who do not have evidence of varicella immunity and in whom varicella immunisation is contraindicated.[41]
   [49] [51] [130] [131] [132] Specific groups where VariZIG is recommended include:[41][130]
  - Immunocompromised patients
  - Neonates whose mothers have signs and symptoms of varicella around the time of delivery (i.e., 5 days before to 2 days after)
  - Premature infants born at ≥28 weeks of gestation who are exposed during the neonatal period and whose mothers have no evidence of immunity to varicella
  - Premature infants born at <28 weeks of gestation or who weigh ≤1 kg at birth and were exposed during the neonatal period, regardless of their mothers' evidence of immunity to varicella
  - Pregnant women without evidence of immunity.
- VariZIG should be given as soon as possible and within at least 10 days of exposure.[41] [51] Patients eligible for the varicella vaccine should have the immunisation delayed by 5 months after administration of VariZIG.[21]
- Intravenous immunoglobulin (IVIG) is an alternative option when varicella-zoster immunoglobulin can not be used.[41][129]

Antiviral prophylaxis

- In the UK, antivirals are now recommended for post-exposure prophylaxis for all at-risk groups (apart from susceptible neonates).[129] Antivirals are given from day 7 to day 14 after exposure.
- US guidelines note that pre-emptive antiviral therapy may be used in select patients if VariZIG and IVIG are not available.[41]

## Patient discussions

Patients are infectious for two days prior to developing the rash.[14] The incubation period is typically 14 days, but because the incubation range varies, susceptible exposed healthcare workers and family members of high-risk patients are recommended to be isolated for 10 to 21 days (28 days if the patient received varicella immunoglobulin). Patients remain infectious for at least 5 days and until all lesions have crusted over. [Centers for Disease Control and Prevention: chickenpox (varicella): questions and answers] (http://www.immunize.org/catg.d/p4202.pdf) [Centers for Disease Control and Prevention Pink Book: varicella] (http://www.cdc.gov/vaccines/pubs/pinkbook/downloads/varicella.pdf)

In addition to treatments, the use of soothing baths to reduce the skin itch and discomfort from the rash may be helpful for some patients. It is preferable to keep the skin cool. Wearing light clothing can do this as well as avoiding hot baths or showers.

Secondary infection of the sores can be avoided by keeping the open skin sores clean and avoiding scratching. For younger children, who have difficulty controlling their urge to scratch, it is useful to cut their fingernails short. Another option is for them to wear gloves or mitts.

27

## Monitoring

## Monitoring

No long-term monitoring is recommended for varicella.

## Complications

Complications	Timeframe	Likelihood
secondary bacterial infection	short term	low
Most commonly reported complication.[57] Associated with <i>Stap</i> streptococcus (GAS) infection.[96] Key feature is fever that persiprimary rash.	<i>phylococcus aureus</i> a sts (or recurs) beyond	nd group A 3 days of the
Patients with localised or diffuse spreading skin erythema and/o infection and considered for empirical antibiotics.	r persistent fever shou	ld be evaluated for
Invasive GAS may lead to complications such as streptococcal to myositis, and glomerulonephritis.[97]	oxic shock syndrome,	necrotising fasciitis,
Surgical consultation to evaluate for necrotising fasciitis should be than 2 or 3 days after the onset of rash with symptoms that inclu- band count in association with erythematous, indurated, painful	be requested in patien de fever, tachycardia, lesion(s).[98]	ts who present more and an elevated
Data suggest an increased risk of bacterial skin infections in vari steroidal anti-inflammatory drugs, so these should be avoided du	cella following treatme uring treatment.[78]	ent with non-
varicella pneumonitis or pneumonia	short term	low
Uncommon in children; rates are higher in adolescents, adults, people, and smokers.[99] [100] [101] It is the most common life- affecting 1 in every 400 adults with varicella.[99] [102] Adults are pulmonary disease.[5]	pregnant women, imm threatening complicati also more likely to de	unosuppressed on in adults, evelop haemorrhagic
Pregnant women may be more likely to develop varicella pneum and/or are known smokers.[103] Pregnant women who do devel death.[104]	onia if they have 100 o op pneumonia are at o	or more skin lesions greater risk for
Presents 1 to 6 days after the onset of the rash with cough, dysp and sometimes with pleuritic chest pain or haemoptysis.[91] [108	onoea, tachypnoea, fev 5]	ver, and hypoxia,
Chest x-ray shows nodular or interstitial changes, often with a pe	eribronchial distribution	n.[105] [106]
varicella encephalitis	short term	low
Presents with headache and fever, but is most classically associ occurs anywhere from 2 to 6 days after the onset of rash.[107] In varicella encephalitis without rash.[108]	ated with an altered so nmunocompromised p	ensorium, and often patients may have
May develop into generalised seizures, nuchal rigidity, and other	signs of meningeal in	volvement.
Cerebrospinal fluid typically demonstrates elevated total protein	and lymphocytic pleoc	cytosis.[64]
varicella-associated cerebellar ataxia	short term	low
Most common neurological complication in children below 15 ye children.[99] Presents with broad-based gait disturbance that oc Associated symptoms can include irritability, vomiting, tremor, he speech, hypotonia, and nuchal rigidity.[64]	ars of age, occurring i curs over the course c adache, and, rarely, r	n 1 in 4000 of a few days. nystagmus, slurred

	Timeframe	Likelihood
Cerebrospinal fluid (CSF) examination is usually normal, but m protein concentration.	ay be associated with i	ncreased CSF
Complete recovery occurs by 2 to 4 weeks, and long-term com-	olications are rare.[109	0]
varicella-associated meningitis	short term	low
Patients with varicella can also present with central nervous symeningitis.[6] Rarely, bacterial meningitis can occur after varice neningitis.[110]	stem complications sud Ila, especially group A	ch as aseptic streptococcal
varicella-associated intracranial vasculitis	short term	low
Patients with varicella can also present with central nervous system vasculitis due to post-varicella arteriopathy. This is an important	stem complications suc t risk factor for paediat	ch as intracranial ric stroke.[6] [111]
/aricella hepatitis	short term	low
Aild sub-clinical hepatitis is common in immunocompetent child iver enzymes, and recovers uneventfully.[112] [113] Symptomatic hepatitis is a rare complication, found mainly in in with marked elevation in liver enzymes and coagulopathy.[114]	dren, is associated with	n mild increases in ents; it is associated
severe infection in the newborn	short term	low
Nomen who develop varicella from 5 days to 2 days prior to de ransmitting the virus to their newborn. Because of the absence virus, these children are at risk for severe infection.[21]	livery have a high risk of maternal immunity	(17% to 30%) of to varicella-zoster
Nomen who develop varicella from 5 days to 2 days prior to de ransmitting the virus to their newborn. Because of the absence virus, these children are at risk for severe infection.[21]	livery have a high risk of maternal immunity long term	(17% to 30%) of to varicella-zoster <b>Iow</b>
Nomen who develop varicella from 5 days to 2 days prior to de ransmitting the virus to their newborn. Because of the absence virus, these children are at risk for severe infection.[21] <b>cutaneous scarring</b> Scarring, which can also be associated with keloid formation, o post-varicella and is most commonly found on the face.[115]	livery have a high risk of maternal immunity long term ccurs in about 19% of	(17% to 30%) of to varicella-zoster <b>Iow</b> children at 1 year
Nomen who develop varicella from 5 days to 2 days prior to de ransmitting the virus to their newborn. Because of the absence virus, these children are at risk for severe infection.[21] cutaneous scarring Scarring, which can also be associated with keloid formation, o post-varicella and is most commonly found on the face.[115] congenital varicella syndrome	livery have a high risk of maternal immunity Iong term ccurs in about 19% of Iong term	(17% to 30%) of to varicella-zoster <b>Iow</b> children at 1 year <b>Iow</b>
Nomen who develop varicella from 5 days to 2 days prior to de ransmitting the virus to their newborn. Because of the absence virus, these children are at risk for severe infection.[21] <b>cutaneous scarring</b> Scarring, which can also be associated with keloid formation, o bost-varicella and is most commonly found on the face.[115] <b>congenital varicella syndrome</b> Fransmission of varicella across the placenta can occur during second trimester of pregnancy, although it is rare.[61] [116] [11 Fetal damage can occur during gestation. May present as cicat paresis microcephaly, and ophthalmic lesions [61] [119][120]	livery have a high risk of maternal immunity long term ccurs in about 19% of long term maternal varicella infer 7][118]	(17% to 30%) of to varicella-zoster Iow children at 1 year Iow ction in the first or
Nomen who develop varicella from 5 days to 2 days prior to de ransmitting the virus to their newborn. Because of the absence virus, these children are at risk for severe infection.[21] <b>cutaneous scarring</b> Scarring, which can also be associated with keloid formation, o bost-varicella and is most commonly found on the face.[115] <b>congenital varicella syndrome</b> Fransmission of varicella across the placenta can occur during second trimester of pregnancy, although it is rare.[61] [116] [11 Fetal damage can occur during gestation. May present as cicat baresis, microcephaly, and ophthalmic lesions.[61] [119][120] Reve's syndrome	livery have a high risk of maternal immunity Iong term ccurs in about 19% of Iong term maternal varicella infer 7][118] ricial skin lesions, limb	(17% to 30%) of to varicella-zoster Iow children at 1 year Iow ction in the first or hypoplasia or
Nomen who develop varicella from 5 days to 2 days prior to de ransmitting the virus to their newborn. Because of the absence virus, these children are at risk for severe infection.[21] cutaneous scarring Scarring, which can also be associated with keloid formation, o post-varicella and is most commonly found on the face.[115] congenital varicella syndrome Fransmission of varicella across the placenta can occur during second trimester of pregnancy, although it is rare.[61] [116] [11 = etal damage can occur during gestation. May present as cicat paresis, microcephaly, and ophthalmic lesions.[61] [119][120] Reye's syndrome Associated with the use of aspirin or other salicylates. Presents netabolic disturbances such as hyperammonaemia and elevator	livery have a high risk of maternal immunity Iong term ccurs in about 19% of Iong term maternal varicella infer 7][118] ricial skin lesions, limb variable s with vomiting, enceph ed liver enzymes.[77]	(17% to 30%) of to varicella-zoster Iow children at 1 year Iow ction in the first or hypoplasia or Iow
Women who develop varicella from 5 days to 2 days prior to de ransmitting the virus to their newborn. Because of the absence virus, these children are at risk for severe infection.[21] cutaneous scarring Scarring, which can also be associated with keloid formation, o bost-varicella and is most commonly found on the face.[115] congenital varicella syndrome Fransmission of varicella across the placenta can occur during second trimester of pregnancy, although it is rare.[61] [116] [11 Fetal damage can occur during gestation. May present as cicat baresis, microcephaly, and ophthalmic lesions.[61] [119][120] Reye's syndrome Associated with the use of aspirin or other salicylates. Presents netabolic disturbances such as hyperammonaemia and elevate Since the fatality rate of children with this rare syndrome reached are not recommended for use during varicella.	livery have a high risk of maternal immunity Iong term ccurs in about 19% of Iong term maternal varicella infer 7][118] ricial skin lesions, limb variable with vomiting, enceph ed liver enzymes.[77] es up to 30%, aspirin a	(17% to 30%) of to varicella-zoster Iow children at 1 year Iow ction in the first or hypoplasia or Iow alopathy, and and other salicylates

#### Complications

## Timeframe Likelihood

**Follow up** 

Patients receiving varicella immunisation may have lower rates than those who naturally acquire varicellazoster virus.[121] [122] [123] In immunocompetent children, rates of herpes zoster have been shown to be reduced in those receiving immunisation when compared with those who acquire wild-type varicella infection.[124] [125] [126] Similarly, the risk of herpes zoster in immunocompromised children may also be less in those who have had varicella vaccine than in those who previously acquired wild-type varicella infection.[125] [126] [127] [128] However, due to short-term follow-up in most of these studies, further epidemiological data are still needed to determine the long-term risk of herpes zoster in children and adults receiving vaccination.[122]

## Prognosis

Typically, varicella is a self-limiting disease. After initial infection and clinical syndrome, no follow-up is necessary. In up to one third of infected people, varicella-zoster virus reactivates later in life as shingles or herpes zoster.

## **Treatment guidelines**

## **United Kingdom**

Guidelines on post exposure prophylaxis (PEP) for varicella or shingles (https://www.gov.uk/government/publications/post-exposure-prophylaxis-forchickenpox-and-shingles)

Published by: UK Health Security Agency

Last published: 2023

Immunisation against infectious disease 'The Green Book': varicella (https:// www.gov.uk/government/publications/varicella-the-green-book-chapter-34)

Published by: Department of Health (UK)

Last published: 2019

Chickenpox in pregnancy (Green-top guideline no. 13) (https:// www.rcog.org.uk/en/guidelines-research-services/guidelines/gtg13)

Published by: Royal College of Obstetricians and Gynaecologists Last published: 2015

#### Europe

Guidance: varicella vaccination in the European Union (https:// ecdc.europa.eu/en/publications-data/public-health-guidance-varicellavaccination-european-union)

Published by: European Centre for Disease Prevention and Control Last published: 2015

## International

Varicella and herpes zoster vaccines: position paper, June (https://www.who.int/publications/i/item/who-wer-8925-265-288)

Published by: World Health Organization

Last published: 2014

#### **North America**

Cytomegalovirus, parvovirus B19, varicella zoster, and toxoplasmosis in pregnancy (https://www.gov.uk/government/publications/post-exposure-prophylaxis-for-chickenpox-and-shingles)

**Published by:** The American College of Obstetricians and Gynecologists

Last published: 2016 (reaffirmed 2024)

Last published: 2023

Last published: 2023

Recommended adult immunization schedule for ages 19 years or older, United States, 2024 (http://www.cdc.gov/vaccines/schedules/hcp/adult.html)

Published by: Centers for Disease Control and Prevention

Recommended child and adolescent immunization schedules for ages 18 years or younger, United States, 2024 (https://www.cdc.gov/vaccines/ schedules/hcp/child-adolescent.html)

Published by: Centers for Disease Control and Prevention

Guidelines for the prevention and treatment of opportunistic infections in adults and adolescents with HIV: varicella-zoster virus disease (https:// clinicalinfo.hiv.gov/en/guidelines)

Published by: Centers for Disease Control and Prevention; NationalLast published: 2022Institutes for Health; HIV Medicine Association of the Infectious DiseasesSociety of America

Varicella zoster virus in solid organ transplantation: guidelines from the Infectious Diseases Community of Practice (https://onlinelibrary.wiley.com/ toc/13990012/2019/33/9)

Published by: American Society of Transplantation

Last published: 2019

Guidelines for the prevention and treatment of opportunistic infections in HIV-exposed and HIV-infected children: varicella-zoster virus (https:// clinicalinfo.hiv.gov/en/guidelines)

Published by: Centers for Disease Control and Prevention; NationalLast published: 2019Institutes for Health; HIV Medicine Association of the Infectious DiseasesSociety of America

Updated recommendations for use of VariZIG: United States, 2013 (http://www.cdc.gov/vaccines/hcp/acip-recs/vacc-specific/varicella.html)

Published by: Centers for Disease Control and Prevention

Last published: 2013

FDA approval of an extended period for administering VariZIG for postexposure prophylaxis of varicella (http://www.cdc.gov/vaccines/hcp/acip-recs/vacc-specific/varicella.html)

Published by: Centers for Disease Control and Prevention

Last published: 2012

Prevention of varicella (http://www.cdc.gov/vaccines/hcp/acip-recs/vacc-specific/varicella.html)

Published by: Centers for Disease Control and Prevention

Last published: 2007

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33

#### Asia

## IAP guidebook on immunization (https://iapindia.org/iap-guidebook-on-immunization/)

Published by: Indian Academy of Pediatrics

Last published: 2020

#### Oceania

Varicella (chickenpox) (https://immunisationhandbook.health.gov.au/ contents/vaccine-preventable-diseases/varicella-chickenpox)

Published by: Australian Government Department of Health and Aged Last published: 2023 Care

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## **Online resources**

- 1. Centers for Disease Control and Prevention: chickenpox (varicella): questions and answers (http:// www.immunize.org/catg.d/p4202.pdf) *(external link)*
- 2. Centers for Disease Control and Prevention Pink Book: varicella (http://www.cdc.gov/vaccines/pubs/ pinkbook/downloads/varicella.pdf) (external link)

## **Key articles**

- UK Health Security Agency. The Green Book: Varicella. Jun 2019 [internet publication]. Full text (https://www.gov.uk/government/publications/varicella-the-green-book-chapter-34)
- Marin M, Güris D, Chaves SS, et al; Centers for Disease Control and Prevention. Prevention of varicella: recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR Recomm Rep. 2007 Jun 22;56(RR-4):1-40. Full text (httphttp://www.cdc.gov/mmwr/ preview/mmwrhtml/rr5604a1.htms:/) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/17585291? tool=bestpractice.bmj.com)
- Royal College of Obstetricians and Gynaecologists. Chickenpox in pregnancy (Green-top guideline no. 13). January 2015 [internet publication]. Full text (https://www.rcog.org.uk/globalassets/documents/ guidelines/gtg13.pdf)
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42

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## Images



#### Figure 1: African patient with varicella

Image provided by the CDC and the Public Health Image Library



#### Figure 2: Varicella lesions in different stages of healing

Image provided by the CDC

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Figure 3: Varicella lesion on the hard palate of a young patient Image provided by the CDC and the Public Health Image Library



#### Figure 4: Typical vesicular rash of primary varicella; note that lesions are in different stages

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