Prophylaxis of Varicella Zoster

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- Chickenpox (varicella) infection in **immunosuppressed** individuals, **susceptible pregnant** individuals and **neonates** can result in severe and even life-threatening varicella disease. Postexposure prophylaxis **(PEP)** is recommended to attenuate disease and **reduce the risk of complications** such as **pneumonitis**, rather than to prevent infection in these at-risk individual

Post-exposure risk assessment:

Does the person need PEP?

- Post-exposure prophylaxis is recommended for individuals **who fulfil all of the following 3 criteria**:
- **Significant exposure to chickenpox** (varicella) or shingles (zoster) during the infectious period
- **At increased risk of severe chickenpox such as immunosuppressed individuals, neonates and susceptible pregnant women**

- **No antibodies to varicella-zoster virus (VZV)** – urgent VZV antibody testing can be performed **within 24 hours**

- Chickenpox infection is transmitted from person to person primarily by **inhalation of aerosols** generated from vesicular fluid from varicella or herpes zoster lesions. Transmission may occur if infected respiratory tract secretions are aerosolised.

- Although historically, the infectious period for chickenpox was generally **considered as being from 48 hours before, to 4 to 7 days after, onset of rash**, a recent review suggested that transmission **rarely occurs before the onset of rash , and may continue until all the lesions have crusted over.**

- Marin M, Leung J, Lopez AS, Shepersky L, Schmid DS, Gershon AA. '**Communicability of varicella before rash onset**: a literature review' Epidemiology and Infection 7 May 2021: volume 149, article e131

- **In immunocompetent** individuals, as a general rule the infectious period should be taken as being **from 24 hours prior to rash onset to 5 days after rash first appears.**
- **For immunosuppressed** individuals, it is harder to generalize and therefore the infectious period should be taken **from 24 hours prior to rash onset until all lesions have crusted over.**

Definition of a significant exposure to Varicella Zoster virus (VZV)

- **A) Type of VZV infection in index case**
- **B) Timing of the exposure**
- **C) Closeness and duration of contact**

Type of VZV infection in index case

- Chickenpox
- Disseminated shingles
- Immunocompetent individuals with exposed shingles lesions (for example, ophthalmic shingles)
- Immunosuppressed individuals with localized shingles on any part of the body in whom viral shedding may be greater

- The risk of acquiring infection from contact with an immunocompetent individual with **nonexposed shingles lesions** (for example, **thoraco-lumbar**) is remote and therefore is not an indication for PEP.

Timing of the exposure

- Where there is **continuous exposure** to a case of chickenpox or shingles , for example **household member**, **nursery** or **care worker**
- Where there has been **more than one exposure to a case of chickenpox or shingles** (for example family friend who visited on more than one occasion during the infectious period)

- Where there has been a single exposure to an **immunocompetent case** of chickenpox during the **infectious period from 24 hours before onset of rash until 5 days after rash appearance or an immunosuppressed index case until all lesions have crusted over**

- Where there has been **a single exposure** to a case of shingles during the infectious period **from onset of rash until the lesions have crusted over (in immunocompetent individuals, this is usually 5 days after rash appearance)**

Closeness and duration of contact

- Those in the **same small room** (for example, in a house or classroom or a 2- to 4-bed hospital bay) for a significant period of time (**15 minutes** or more)
- **Face to face contact**, for example while having a conversation

- **Immunosuppressed** contacts on **large open wards**, where air-borne transmission at a distance has occasionally been reported, particularly in **pediatric wards** where the degree of contact may be difficult to define

Assessment of susceptibility

- VZ post- exposure prophylaxis is unlikely to confer any additional benefit for patients who already have varicella antibody (VZV IgG) and therefore **prophylaxis is not recommended for individuals with adequate levels of VZV IgG**

- For **immunocompetent** individuals including **pregnant** individuals, **a history of previous chickenpox**, **shingles or 2 doses of varicella vaccine** is sufficient evidence of immunity. In those **without such a history, antibody testing can help to identify** those individuals that would benefit from VZ PEP. This can be undertaken on a recent blood sample (booking blood samples are acceptable for pregnant women if available). Where testing is undertaken, **antiviral PEP is recommended if VZV IgG is less than 100 milli-international units per milliliter (mIU/ml)**

- For **immunosuppressed patients**, a **history of previous infection or vaccination is not a reliable history of immunity and VZV antibody levels should be checked urgently.** Individuals with VZV antibody levels of 150 mIU/ml or greater are unlikely to benefit from PEP, and therefore individuals with **VZV IgG less than 150 mIU/ml in a quantitative assay, or negative or equivocal in a qualitative assay should be offered treatment.**

- **Quantitative antibody testing is recommended for all patients** where IVIG is being considered, except for **Group 1 neonates whose mothers develop chickenpox (but not shingles) in the period 7 days before to 7 days after delivery**

Types of post-exposure prophylaxis

- **Antivirals** (aciclovir or valaciclovir)
- **Varicella immunoglobulin** for i.v. administration (Varitect CP)
- Normal intravenous immunoglobulin **(IVIG)**

Antivirals (aciclovir or valaciclovir)

- **Oral aciclovir (or valaciclovir**) is now the first choice of PEP for **susceptible immunosuppressed** individuals, all **susceptible pregnant** women at any stage of pregnancy and **infants at high risk**.
- **Oral antivirals** may also be considered for other groups who have **increased risk of severe disease including those with neurodisabilities.**

- **Antivirals** (oral aciclovir or valaciclovir) should be given **from day 7 to day 14 after the first day of exposure**. The day of exposure is defined as the **date of onset of rash if the index is a household contact** and date of first or only contact if the exposure is on multiple or single occasions respectively

- **The only exception in starting treatment on day 7 is in Group 1 neonates whose mothers develop chickenpox (but not shingles) in the period 7 days before to 7 days after delivery.** To mitigate against potential in utero exposure in this group, **antivirals should be initiated as soon as possible after the baby is born and recognition of the onset in the mother**. If the patient presents after day 7 of first exposure, a 7-day course of antivirals can be started up to day 14 after first exposure.

- In a study evaluating **the comparative effectiveness of a 7-day course of aciclovir given either immediately after exposure or starting at day 7 after exposure** to healthy children, the **incidence and severity of varicella infection was significantly higher in those given aciclovir immediately after exposure (77%) who received aciclovir immediately developed clinical varicella compared with (21%) who started aciclovir at day 7** . A 7-day post-exposure prophylaxic course of aciclovir or valaciclovir is therefore recommended to start from day 7 after exposure.

- **If there is a second or subsequent exposure to chickenpox or shingles within the first 7 days of treatment, the course of antivirals may need to be extended until 14 days after the first day of exposure.** If the exposure occurs **8 or more days are the first exposure, then a new course of antivirals should be started**

Varicella immunoglobulin for i.v. administration (Varitect CP)

- Varicella-zoster immunoglobulin for i.v. administration (Varitect CP) is produced by Biotest as a solution for i.v. infusion and is dispensed as **25 IU/ml**. It is recommended that a treatment dose of **25 IU/kg to 50 IU/kg (1to 2ml/kg) (up to a maximum of 5mls (one vial**)) is administered as a **single dose as post-exposure prophylaxis for neonates, exposed to intrauterine VZ infection within the last 7 days of pregnancy, with rash onset in the mother presenting within 1 week of delivery**

- The product should be given by slow i.v. infusion **(0.1 ml/ kg/ hr for the first 10 minutes and then slowly increased to a maximum for 1ml/kg/ hr for the rest of the infusion)**. Treatment should be started as soon as possible after exposure, preferably **within 96 hours, and no longer than 10 days after exposure**

Normal intravenous immunoglobulin (IVIG)

- Contacts who cannot receive antivirals should be given **IVIG at a dose of 0.2g per kg body weight (4 ml/kg for a 5% solution) instead**. This will produce serum VZV antibody levels equivalent to those that were achieved with VZIG. IVIG can also be offered as an alternative for **Group 1 neonates if there are likely to be delays in sourcing varicella-specific immunoglobulin preparations**

- **IVIG should ideally be administered within 10 days (preferably 7 days for neonates and immunosuppressed contacts), of the first contact,** but can be given later if necessary.

Thank You