East of England Neonatal ODN
(Hosted by Cambridge University Hospitals)

Clinical Guideline: Management of babies exposed to varicella zoster/ herpes zoster virus

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For use in: EoE Neonatal Units
Guidance specific to the care of neonatal patients.

Used by: Medical Staff, Neonatal Nurse Practitioners, pharmacists, microbiologists and infection prevention and control teams.

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Aetiology

Varicella-zoster virus (VZV) is a DNA virus of the herpes family responsible for varicella (chickenpox) and herpes zoster ("shingles"). VZV is a member of the herpesvirus family.

Transmission

Transmission can occur in utero, perinatally, or postnatally. Intrauterine or perinatal infection of the foetus is facilitated through transplacental transmission while postnatal varicella is transmitted primarily through inhalation of aerosols from vesicular fluid from varicella zoster lesions but also from direct contact with said lesions.
Transmission from shingles infection is generally through direct contact but is rare.

Risks

Risks to the foetus and neonate from maternal chickenpox are related to the time of infection in the mother

- First 20 weeks of pregnancy – congenital (foetal) varicella syndrome. The mortality rate is high
- Second and third trimesters of pregnancy – herpes zoster in an otherwise healthy infant. Occasional cases of foetal damage comprising chorioretinal damage, microcephaly and skin scarring have been reported
- 7 days before, to 7 days after delivery – severe and even fatal disease in the neonate.

Signs and Symptoms

Congenital varicella syndrome

- Intrauterine growth restriction (IUGR)
- Cicatricial skin lesions, which may be depressed and pigmented in a dermatomal distribution.
- Ocular defects, such as cataracts, chorioretinitis, Horner syndrome, microphthalmos, and nystagmus.
- Limb abnormalities, which often include hypoplasia of bone and muscle.
- Central nervous system abnormalities, such as cortical atrophy, seizures, and intellectual disability

Neonatal varicella

- Vesicular eruption. In mild cases, the lesions heal within 7 to 10 days.
- Disseminated disease may ensue, with varicella pneumonia, hepatitis, and meningoencephalitis being the most common visceral manifestations.

Definition of a significant exposure to VZV

Three aspects of the exposure are relevant when considering post exposure prophylaxis(PEP):

- **Type of VZ infection in the index case**. The issue of PEP should be restricted to those in content with:
  - Disseminated shingles
  - Immunocompetent individuals with exposed shingle lesions (e.g. ophthalmic zoster)
  - Immunosuppressed patients with localised shingles on any part of the body (in whom viral shedding may be greater).

- The **timing of the exposure** in relation to onset of rash in the index case:
  - Continuous exposure to a case of chickenpox/ shingles e.g. household member, care worker
  - More than one exposure to a case of chicken pox/ shingles e.g. a visitor / friend who visited on more than one occasion during an infectious period.
  - Single exposure to a case of chicken pox during the infectious period from 24 hours before onset of rash until 5 days after rash appearance in immunocompetent individuals and until all lesions have crusted over
  - Single exposure to shingles during the infectious period from onset of rash until lesions have crusted over. This is usually 5 days after rash appearance in the immunocompromised.

- **Closeness** and **duration** of contact:
  - Contact in the same room (e.g. in a house /classroom /2 to 4 bed hospital bay) for 15 minutes or more
  - Face-to-face contact, e.g. while having a conversation
  - Immunosuppressed contacts on large open ward, where airborne transmission at a distance has occasionally been reported, particularly in paediatric wards where degree and duration of contact can be difficult to define.

In the case of large open wards, giving VZIG to all susceptible high-risk contacts should be considered (particularly on the neonatal unit where the degree of contact may be difficult to define – see below).

Investigations (where indicated – see below)

- Antibody testing- Serum bottle -1 ml minimum
- Viral PCR- EDTA bottle - 1 ml minimum

Risk Assessment for infants and neonates

Although infants (under one years old) may be at increased risk of severe chickenpox infection, the risks of life threatening complications are particularly important in neonates in

the **first week of life**. The risk assessment needs to take a number of factors into account including the presence of maternal antibodies, prematurity, timing of exposure, and whether the infant is still hospitalised.

Post-exposure prophylaxis is not usually required for

- neonates born more than seven days after the onset of maternal chickenpox
- neonates whose mothers develop shingles before or after delivery (neonates will have maternal antibody)

Post-exposure prophylaxis is not indicated for

- neonates less than 7 days old whose mothers have been exposed during pregnancy **and** have been found to be VZV IgG negative **unless the mother develops chickenpox**

Post-exposure prophylaxis is recommended for

- **Group 1**

  Neonates whose mothers develop chickenpox (but not shingles) in the period 7 days before to 7 days after delivery –VZIG (Varitect CP) can be given without VZV IgG antibody testing of the neonate or mother and should be given as soon as possible and preferably within 7 days of exposure. Where VZIG cannot be obtained within 96 hours of the onset then IVIG should be offered immediately rather than waiting to offer Varitect CP.

  Treatment should be initiated as soon as possible, initially with prophylactic IV Aciclovir (20mg/kg 8 hourly for a minimum of 48hours), with conversion to oral antivirals (aciclovir 20mg/kg 4 times a day) if preferred, until day 21 post delivery.

- **Group 2a**

  VZV antibody-negative infants under one year who have remained in hospital since birth who are born before 28 weeks gestation OR weighed less than 1,000g at birth or :

  VZV antibody-negative infants who have a severe congenital or other underlying condition that requires prolonged intensive or special care during the first year of life

- **Group 2b**

  VZV susceptible neonates exposed to chickenpox/ shingles (other than in the mother) in the first 7 days of life

  For group 2a and 2b oral antiviral dosing should be started from day 7 POST exposure and continued for 14 days (neonatal oral aciclovir PEP dose is 20mg/kg 4 times a day.

In infants over the age of 4 weeks (regardless of gestation at birth) oral aciclovir (10mg/kg 4 times a day) is the recommended PEP, unless contraindicated (renal toxicity or malabsorption). If contraindicated, VZIG should be given.

Risk assessment for neonates with a confirmed significant exposure to chicken pox or shingles

Group	Criteria	Testing	Action
1	Neonates whose mothers develop chickenpox (but not shingles) in the period 7 days before to 7 days after delivery.	Not required for mother or infant.	Treatment with IV varicella immunoglobulin (Varitect CP) or IVIG should be administered as soon as possible following exposure, ideally within 96 hours. In addition, commence IV. aciclovir as soon as possible following exposure and for a minimum of 48 hours; thereafter an oral switch can be considered. Treatment should be continued until day 21.
2a	Neonates who have remained in hospital since birth (but are less than 1 year of age) with any one of the following: Born < 28 weeks OR birthweight < 1000g OR Have severe congenital or other underlying condition that require prolonged intensive or special care during the first year of life	Test for VZV antibody status in the infant only.	If found to be VZV antibody-negative by a qualitative assay or <150 mIU/ml by a quantitative assay, oral aciclovir or valaciclovir should be started from day 7 post-exposure and continued for 14 days.

2b	Neonates exposed to chicken pox or shingles (other than in the mother), in the first 7 days of life.	Test either the mother (preferred) or neonate for VZV antibody status for infants whose mothers have a negative or uncertain history of chickenpox/ shingles or history of previous varicella vaccine.	If found to be VZV antibody negative by a qualitative assay or <150 mIU/ml by a quantitative assay, oral aciclovir or valaciclovir (or equivalent) should be started from day 7 post-exposure and continued for 14 days.

Treatment for post exposure prophylaxis

VZIG (Varitect CP: Dose 250mg slow im injection

- Refer to local SOP for VZIG ordering process which must be made by the clinician to UKHSA Rabies and Immunoglobulin service (RIgS).
- The RIgS team will arrange immunoglobulin issue and delivery directly to a specified hospital location in agreement with the initiating clinician and pharmacistfollowing a risk assessment of the exposed individual.
- Contact the RIgS Service for advice and supply (tel: 0330 128 1020) (between 9am and 5pm 7 days a week).
- Prescribe VZIG for the baby and contact NICU pharmacist via bleep.
- A treatment dose of VZIG (Vatitect CP) 50 units/kg (2mL/kg up to a maximum of 5mL is administered as a single dose a PEP for neonates.
- VZIG (Varitect CP) is administered as a slow IV infusion (0.1mL/kg/hr for the first 10 minutes and then increased slowly to a maximum of 1mL/kg/hr for the rest of the infusion)
- NB Varitect CP is not licensed in the UK and is supplied and prescribed as an ‘off-label’ medication.
- When VZIG is being used for prevention of varicella, it must be remembered that it may interfere with the subsequent development of active immunity from live virus vaccines for a period of at least 6 weeks and up to 3 months. After administration of Varitect CP, an interval of 3 months should elapse before vaccination with live attenuated live vaccines.
    - However, deferral of BCG vaccine is not required because immunoglobulins are unlikely to interfere with the cellular response to this vaccine. The rotavirus vaccine can also be administered before, at the same time as, or after

administration of any blood product, including those containing antibody/ immunoglobulin.

- Avoid concomitant use of loop diuretics (e.g. furosemide) whilst Varitect CP is administered.
- If VZIG cannot be administered within 96 hours of exposure due to lack of supply, intravenous immunoglobulin (IVIG) should be considered. The recommended dose is 0.2g per kg body weight (4ml/kg for a 5% solution). Contact pharmacy for supply of IVIG. If IVIG is unavailable prophylaxis with aciclovir may be considered and should be discussed with microbiology and the attending neonatal Consultant.

Recommended doses of oral aciclovir	
	Oral aciclovir
Neonates	20mg/kg 4 times daily
Infants and children under 2 years age	10mg/kg 4 times daily, days 7 to 14 after exposure

Treatment for neonates who develop chicken pox

For those where VZIG has been administered chicken pox may develop up to 28 days post exposure.

If chicken pox develops despite VZIG, high dose **intravenous** acyclovir of 20mg/kg every 8 hours for at least 7 days should be started as soon as possible.

Breastfeeding

Breastfeeding is encouraged in newborns exposed to or infected with varicella because antibody in breast milk may be protective.

Discharging babies home from the postnatal ward in whom a household member has chicken pox

There is no reason to prevent a new baby going home if other members of the household have chickenpox, and the mother has had chickenpox or is shown to have VZV antibody. If the mother is susceptible, contact with household members with chickenpox should ideally be delayed until the new baby has reached 7 days of age.

Management of Chicken Pox exposure on the neonatal unit

Exposure to any infant who is an inpatient on the neonatal unit can cause severe infection and complex capacity management problems.

Communication: Ensuring that parents understand the implications of chicken pox exposure to their baby but also others on the neonatal unit (NNU) is important. On admission, parents should be given standard advice about seeking medical support from the GP or by calling the NNU prior to visiting if they are unwell or have had contact with others who are unwell, this should include advice on chicken pox exposure.

Steps in Management

- Confirm diagnosis of person with chicken pox
- Ascertain current immunity status of all nursing and medical staff
- Notify microbiologist and infection control team
- Identify which areas of NNU have been exposed
- Trace babies who may have had contact
- **Restrict** movement of babies until decisions about cohort /isolation have been made

Capacity Management strategy

A management strategy must be discussed with the following staff present:

- Lead nurse NNU
- Clinical director NNU
- Consultant in charge
- Microbiologist
- Infection control team
- Midwifery/ obstetric representative
- General manager
- Escalate to trust board if closure is necessary

Keep neonatal network informed of progress especially around capacity and closure.
Obtain a clear history of when exposure occurred and the progress of the symptoms. Identify movements of exposed person/ baby (cot space) and identify possible contacts.

- If contact is a parent / visitor try to identify movements.
- If contact is a staff member assume all patients have been exposed.

Isolation

Any infant who has been exposed should be isolated from the unexposed infants on the NICU.

- If one or two infants have been exposed isolate those infants in the isolation cubicles
- If the whole nursery has been exposed all infants should be checked for immunity but no movement from that nursery should occur
- If an infant has been transferred to another unit during the incubation period the unit must be contacted
- If isolation of all exposed infants can be managed in one nursery, babies can continue to be admitted to the other nursery if appropriate
- If babies in both nurseries have been exposed a decision to close the unit to admission may be taken. A contingency area must then be identified to support unexpected sick babies until transfer

Immunity status

Any exposed infants must have their immunity status checked (refer to risk assessment and management Page 5-6).

Isolation and incubation time

Any infant who has been exposed and been identified as non- immune should be isolated from up to 8 days post exposure to 21days following the last exposure. If VZIG is given this is extended until 28 days post last exposure.

Where possible all infants who have been exposed should be nursed in closed incubators

On-going management

- Admit all babies to non-exposed area or contingency area
- All infants entering the unit should be checked for immunity
- Cohort immune and non -immune/ exposed and non- exposed infants together
- Discharges of immune infants can take place

- Non immune babies can be discharged home
- Daily assessment of cohort areas, capacity and patient flow, decisions around acceptance of activity

Audit and Training

Audit of case notes during morbidity and mortality meeting as directed by the audit lead.

New guidance to be highlighted in audit newsletter distributed to the neonatal team.

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Exceptional Circumstances Form

Form to be completed in the **exceptional** circumstances that the Trust is not able to follow ODN approved guidelines.

Details of person completing the form:	
Title:	Organisation:
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Surname:	Telephone contact number:
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