Title:	**Varicella Zoster Virus Guideline: Neonatal risk, exposure and management** (Cheshire & Merseyside Guideline)
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VARICELLA ZOSTER VIRUS - NEONATAL RISK, EXPOSURE AND MANAGEMENT

Definition

This guideline details the management of babies and healthcare professionals, on the neonatal unit, in the event of a suspected exposure to Varicella Zoster virus (VZV).

Background

The varicella zoster virus (VZV) is responsible for both primary infection (chickenpox) and reactivation (shingles). This is a common childhood infection. 90-93% of adults are VZV antibody positive with acquired immunity post infection that is usually life-long. It is a mild and self-limiting infection but can have complications with pneumonia, secondary bacterial infections and encephalitis. Neonates, immunocompromised patients and pregnant women are at risk of severe disease.

Congenital varicella syndrome is caused by primary maternal infection during pregnancy (within the first 20 weeks gestation) leading to neonatal transfer and infection. This results in congenital abnormalities within the foetus (limb deformity, cataracts, chorioretinitis, scarring, microcephaly, tissue calcification, growth retardation and hydrocephalus). The incidence for congenital varicella syndrome is <1% within the first 12 weeks, and then 2% between 13-20 weeks gestation. Diagnosis can be made antenatally through imaging.

Neonatal chickenpox is caused by exposure to varicella infection within seven days prior to and following birth. If maternal infection occurs earlier (7-20 days prior to birth), although chickenpox can still occur, it tends to be less severe due to transplacental VZV antibody transfer, these antibodies partially protect the foetus. Elective delivery should be avoided if able to until 5-7 days after the onset of maternal rash to allow for the transfer of antibodies from mother to child. Neonatal ophthalmic examination will need to be arranged as a post-natal outpatient.

Transmission of VZV occurs through

- Personal contact with an infected individual
- Airborne spread of the virus through respiratory secretions
- Contact with inanimate objects contaminated with respiratory secretions or vesicular fluid

The incubation period is 10-21 days following exposure to an individual with chickenpox or shingles. Once viral transmission has occurred, individuals are deemed infectious from 24 hours prior to vesicle eruption until all the vesicles have scabbed over in the immunosuppressed.

The identification of risk for an individual exposed to shingles is different.

- If the individual exposed has previously had primary infection with chickenpox, the risk is minimal.
- If the individual exposed has not had primary infection with chickenpox, then they are susceptible to infection.
- If the area of skin is covered by clothing, the risk is deemed to be minimal.

- If the affected area is not covered by clothing and is exposed, the affected individual is deemed high risk and therefore exposure is deemed significant

Occupational Health keep records of healthcare professionals VZV status including previous primary infection or evidence of vaccination if VZV antibody-negative on testing.

ACTION

1. Liaise with Infection Prevention and Control team (IPCT) and Consultant Virologist or Microbiologist if there is an index case of chickenpox or shingles or exposure to chickenpox or shingles (Individuals are infectious up to 2 days before vesicle eruption until all the vesicles have scabbed over and dried up with no new vesicle development)

2. An incident meeting should include Consultant Neonatologist, Senior Neonatal Nursing Staff, Consultant Virologist or Microbiologist, representatives from the IPCT, Occupational Health, and Trust communication team.

3. Aim to confirm the diagnosis of VZV infection in the index case (either clinically or by requesting a virology swab of the vesicular fluid for VZV PCR).

4. Determine whether the exposure is significant (infection has potential to transmit), if in doubt contact virology consultant to discuss.

   Significant exposure is defined as: -

   - Face to face contact with a case of chickenpox (e.g. while having a conversation).
   - Contact in the same room or bay for 15 minutes or more.
   - Inadvertent administration of Zostavax shingles vaccine.
   - Immunosuppressed contacts on open large open wards, where airborne transmission at a distance has been reported or where the degree of contact may be difficult to define.

5. Determine if the exposure has taken place within the infectious period, Significant exposure is defined as:

   - 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 a case of chickenpox 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 for immunosuppressed individuals.
- 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).
- *Non-immune exposed individuals, should be considered as potentially incubating VZV (incubation period 10-21 days or 28 days if VZIG has been administered)) and as potentially infectious despite post exposure prophylaxis.*

6. Determine susceptibility (adults) of all individuals (parents, healthcare professionals, visitors) who have had contact with the index case within the infectious period.

   a. Previous chickenpox or shingles OR 2 doses of VZV vaccine– do not test, assume immune.

   b. Otherwise test for VZV IgG, evidence of IgG (>100 mIU/ml) to VZV – consider immune.

Ascertain if there is current or past history of immunosuppression in individuals considered to be immune as antibody levels may not be maintained (see appendix 1 for definitions of immunosuppression). Please be aware that a separate risk assessment needs to be undertaken for all exposed individuals (adults AND children) if these fall into risk groups such as, for example, the immunosuppressed or pregnant.

7. Determine susceptibility in NEONATES and BABIES: risk assess all, including babies that have been discharged. VZIG use should be discussed with the Neonatal Consultant, Consultant Virologist or Microbiologist and the Consultant Virologist at the VZIG issuing laboratory (see NOTES below).

   a, Neonates whose mothers develop chickenpox (but not shingles) within 7 days before birth to 7 days after birth.

      i. DO NOT TEST
      ii. Administer VZIG within 7 days of delivery OR within 7 days of onset of chickenpox vesicles in the mother, whichever is later.
      iii. Prophylactic intravenous aciclovir (10mg/kg IV 8 hourly for 10 days) should also be considered in addition to VZIG for infants whose mothers develop chickenpox four days before to two days after delivery as they are at the highest risk of fatal outcome despite VZIG prophylaxis.

   b, Neonates exposed to chickenpox or shingles (other than in the mother) in the first 7 days of life.

      i. If mother has a negative or uncertain history of chickenpox OR a history of VZV vaccine only – test the mother (preferred) or

neonate for VZV IgG. If negative (<150 mIU/ml) administer VZIG within 7 days.

c, Infants under 1 year who have remained in hospital since birth who were born before 28 weeks of gestation or had a birth weight of less than 1kg OR who have severe congenital or other underlying condition that requires prolonged intensive or special care during the first year of life.

i. test for VZV IgG antibody status in the infant only and if negative (<150 mIU/ml) provide PEP as follows:

1. If over the age of 4 weeks, administer aciclovir PEP (10mg/kg qds PO, day 7 to day 14 post exposure) unless contraindicated.
2. If under the age of 4 weeks administer VZIG within 7 days

8. **Treatment of neonates with varicella** - **If severe chickenpox develops despite VZIG**. A high dose intravenous aciclovir treatment of 20mg/kg every eight hours for at least seven days should be started as soon as possible.

9. NOTES:

- Varicella-zoster immunoglobulin (VZIG) is prepared by Bio Products Limited (BPL) from the pooled plasma from non-UK blood donors and is dispensed in vials of 250 mg (minimum 100 IU/ml). VZIG is issued by the:

  Rabies and Immunoglobulin Service UK Health Security Agency Colindale
  Telephone: 0330 128 1020

- VZIG is not required for infants with significant VZV exposure after seven days of life if they have already been discharged home.

- VZIG is not required for neonates exposed to VZV outside of the designated time period (seven days before and after birth) or born to mothers whose chickenpox started more than 7 days prior to birth or those born to mothers with shingles do not require VZIG.

- VZIG ameliorates chickenpox severity should it occur. It is postulated that VZIG may prevent infection in approximately 50% of neonates, and that close observation should continue for the next 4 weeks (VZIG extends the incubation period by one week). In the case that the neonate is discharged home within this time, clear instruction to seek urgent medical attention if concerned must be given to the parents and documented.

- There is a risk assessment table for neonates with a confirmed exposure to chickenpox or shingles in appendix 2.

10. Neonates that have been exposed on the neonatal unit
    a. nurse in incubators
    b. barrier nurse

c. ensure they are cared by healthcare workers who are VZV immune and care for as few infants in that room as possible

11. 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.

12. Breastfeeding - Mothers with chickenpox may breastfeed if the neonate is covered by VZIG or Aciclovir. If there are lesions near the nipple, it is advised that milk be expressed from that breast and given via syringe/bottle/tube.

13. Any blood sampling which is required for testing should be fully discussed with parents and the Consultant Virologist or Microbiologist. This is to ensure that the appropriate tests are done, with consent, and that robust plans can be made for the timely transport and testing of these urgent samples.

14. High risk babies, if found to be immune to VZV (recent VZV IgG antibody test >150 on the quantitative assay), may move to a room in which the non-immune exposed babies are being nursed.

15. Non-immune exposed individuals should be considered as potentially incubating VZV (incubation period 10-21 days, or 28 days if VZIG has been administered) and as potentially infectious despite post exposure prophylaxis.

16. Step up of care for VZV exposed babies will be clinically indicated.

17. A decision should be made about restricting visiting on the neonatal unit during the incubation period following the exposure. Communication team should be involved in providing information and signage for parents and visitors.

18. In the event of a secondary case of chickenpox occurring on the neonatal unit due to an exposure, the on call neonatal consultant and virology or microbiology consultant should be notified and a new incident meeting should be arranged.

19. Healthcare professionals should refer to Occupational Health if they are unsure of their VZV status.

20. Women (healthcare professionals, visitors) should urgently contact their midwives if they are pregnant and have been exposed to VZV and are unsure about their VZV status.

21. Inform Public Health England (PHE) local representative of the VZV issue on the neonatal unit.

References

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7. NICE CKS Chickenpox guideline revised Oct 16.
8. Post exposure prophylaxis for chickenpox and shingles - GOV.UK (www.gov.uk)
9. Guidelines on post exposure prophylaxis for varicella or shingles (publishing.service.gov.uk)

ABBREVIATIONS

VZV – Varicella Zoster Virus
VZIG – Varicella Zoster Immunoglobulin
IPCT – Infection Prevention and Control Team

APPENDIX 1

DEFINITIONS OF IMMUNOSUPPRESSION

Individuals with primary or acquired immunodeficiency states due to conditions including:

- acute and chronic leukaemia's, and clinically aggressive lymphomas (including Hodgkin's lymphoma) who are less than 12 months since achieving cure
- individuals under follow up for a chronic lymphoproliferative disorders including haematological malignancies such as indolent lymphoma, chronic lymphoid leukaemia, myeloma, Waldenstrom's macroglobulinemia and other plasma cell dyscrasias (note: this list not exhaustive)
- immunosuppression due to HIV/AIDS with a current CD4 count of below 200 cells/µl (aged 5 years or less, with a CD4 count below 500 cells/µl)
- primary or acquired cellular and combined immune deficiencies – those with lymphopaenia (<1,000 lymphocytes/ul), including aplastic anaemia, or with a functional lymphocyte disorder
- those who have received an allogeneic (cells from a donor) or an autologous (using their own cells) stem cell transplant in the previous 24 months
- those who have received a stem cell transplant more than 24 months ago but have ongoing immunosuppression or graft versus host disease (GVHD)
- persistent agammaglobulinaemia (IgG < 3g/L) due to primary immunodeficiency (for example common variable immunodeficiency) or secondary to disease or therapy

Individuals on immunosuppressive or immunomodulating therapy including:

- those who are receiving or have received in the previous 6 months immunosuppressive therapy for a solid organ transplant
- those who are receiving or have received in the previous 3 months targeted therapy for autoimmune disease, such as JAK inhibitors or biologic immune modulators including B-cell targeted therapies (including rituximab but for which a 6 month period should be considered immunosuppressive), monoclonal tumour necrosis factor inhibitors (TNFi), T-cell co-stimulation modulators, soluble TNF receptors, interleukin (IL)-6 receptor inhibitors, IL-17 inhibitors, IL 12/23 inhibitors, IL 23 inhibitors (note: this list is not exhaustive)
- those who are receiving or have received in the past 6 months immunosuppressive chemotherapy or radiotherapy for any indication

Individuals with chronic immune mediated inflammatory disease who are receiving or have received immunosuppressive therapy:

- moderate to high dose corticosteroids (equivalent ≥20mg prednisolone per day; children 1 mg/kg/day) for more than 10 days in the previous month

- long term moderate dose corticosteroids (equivalent to ≥10mg prednisolone per day or children 0.5 mg/kg/day for more than 4 weeks) in the previous 3 months

- adults on non-biological oral immune modulating drugs for example methotrexate >20mg per week (oral and subcutaneous), azathioprine >3.0mg/kg/day; 6-mercaptopurine >1.5mg/kg/day, mycophenolate >1g/day, in the previous 3 months
- children on any dose of non-biological oral immune modulating drugs
- certain combination therapies at individual doses lower than stated above, including

  Those on ≥7.5mg prednisolone per day in combination with other immunosuppressants (other than hydroxychloroquine or sulfasalazine) and those receiving methotrexate (any dose) with leflunomide in the previous 3 months.

  Individuals who have received a short course of high dose steroids (equivalent >40mg prednisolone per day or children 2 mg/kg/day for more than a week) for any reason in the previous month.

  Individuals who had received brief immunosuppression (≤40mg prednisolone per day) for an acute episode (for example, asthma, chronic obstructive pulmonary disease (COPD) or coronavirus (COVID-19)) and individuals on replacement corticosteroids for adrenal insufficiency are not considered severely immunosuppressed and can be treated with the standard post exposure treatment.

Appendix 2

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.	Administer VZIG within 7 days of delivery OR within 7 days of onset of disease in the mother, whichever is later. Consider intravenous aciclovir if mothers develop chickenpox between 4 days before to 2 days after delivery.
2	Infants (under 1 year) who have remained in hospital since birth with any one of the following: – born before 28 weeks gestational age or – weighed less than 1,000g at birth or – infants who 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.	Administer aciclovir if over the age of 4 weeks starting 7 days after exposure. If less than 4 weeks of age, administer VZIG within 7 days if found to be VZV antibody-negative by a qualitative assay or <150 mIU/ml by a quantitative assay.
3	Neonates exposed to chickenpox or shingles (other than in the mother) in the first 7 days of life.	Test either mother (preferred) or neonate for VZV antibody status for infants whose mothers have a negative or uncertain history of chickenpox or shingles or a history of previous varicella vaccine.	Administer VZIG within 7 days if found to be VZV antibody-negative by a qualitative assay or <150 mIU/ml by a quantitative assay.

Appendix 3

Has the neonate been born to a mother who has developed chickenpox between 7 days prior to and after delivery?
Need IV VZIG and potentially IV acyclovir, discuss with neonatal and microbiology consultant

Has the neonate been born to a mother who has developed shingles near the time of or after delivery?
No treatment is needed as the mother has had previous primary VZ infection and will have passed on immunity to baby.

Has the neonate been born to a mother who has not previously had chickenpox but in the time of delivery and postnatal care a sibling or family member at the family household has developed chickenpox?
If so, it would be advised that that neonate does not return to the family home in the first 7 days of life as they will be highly susceptible to infection.

Has a case of chickenpox developed in someone who has visited the SCBU in the 2-3 week incubation period?
Precautions and analysis of exposure must occur with the input of infection control. Significant exposure: face to face contact or over 15 minutes in the same room.

If no significant exposure has occurred - no further steps are needed.

If significant exposure has occurred -

- If the neonate was born less than 28 weeks' gestation or had a birthweight of <1kg or have had numerous blood transfusions - high risk. Such cases must be discussed with the on call neonatal and microbiology consultant to determine management.
- If the neonate has been exposed but mother states she has had chickenpox previously, neonatal and/or maternal VSV antibody status' can be tested. If positive, transmission is less likely and if negative, transmission is more likely and they would need IV VZIG +/- IV acyclovir.

Neonates exposed to VZV outside of the designated time period (seven days before and after birth), born to mothers who started with primary VZV infection over 7 days prior to birth and those born to mothers with shingles do not require VZIG.

Can mothers with active chickenpox breastfeed?
Guidance advises that mothers with chickenpox may breastfeed as long as the neonate is covered by VZIG and/or aciclovir. If there are lesions near the nipple, it is advised that milk be expressed and given via syringe/bottle/tube.

What if a staff member develops chickenpox or shingles?
If a staff member develops chickenpox, this is a significant event and a timeline of exposure needs to be developed. If they develop shingles, the risk is minimal if the affected area is covered by clothing. If not covered by clothing, they would be deemed high risk as with active chickenpox exposure.