Clinical Guideline

VARICELLA EXPOSURE IN CHILDREN WITH INFLAMMATORY BOWEL DISEASE

SETTING Bristol Royal Hospital for Children

FOR STAFF Medical and Nursing Staff

PATIENTS Children with Inflammatory Bowel Disease

Introduction

Varicella (chickenpox) is an acute, highly infectious disease caused by the varicella zoster virus (VZV). The virus is plentiful in the nasopharynx in the first few days and in the vesicles before they dry up; the infectious period is from one to two days before the rash appears until the vesicles are dry. This may be prolonged in immunosuppressed patients. Varicella is transmitted directly by personal contact or droplet spread. The incubation period is between one and three weeks.

Chickenpox is more often severe or life threatening in immunocompromised patients, causing pneumonia, hepatitis, encephalitis or haemorrhagic disorders (thrombocytopenia or disseminated intravascular coagulopathy). They can have an atypical varicella rash with more lesions, and they can be sick longer than immunocompetent people who get varicella. New lesions may continue to develop for more than 7 days, may appear on the palms and soles, and may be haemorrhagic.

Herpes zoster (shingles) is caused by the reactivation of the patient's varicella virus, when they have previously had varicella infection. Virus from lesions can be transmitted to susceptible individuals to cause chickenpox. Although more common in the elderly, it can occur in children and is especially common in immunosuppressed individuals of any age. Shingles is more severe in immunocompromised patients, who also have an increased risk of post herpetic neuralgia.

The current guideline is focused on the clinical management of children and young people with inflammatory bowel disease (IBD) following exposure to VZV.

A. What happens after VZV exposure in patient with IBD (see also Appendix)

Patients with IBD who are exposed to varicella or shingles should be assessed for their susceptibility to severe infection, based on national guidelines (PHE 2017). IBD patients are considered susceptible when the fulfil <u>all</u> of the following three criteria:

1. They had significant exposure to chickenpox or shingles
2. They are immunosuppressed
3. They don't have protective antibodies to VZV

1. What is considered significant exposure to VZV

Three aspects of the exposure are relevant.

I. Closeness and duration of contact

- Household contacts
- Contact in the same small room (eg house or classroom or 2-4 bed bay in hospital) for 15 min or more
- Face to face contact, for example while having a conversation
- Immunosuppressed contacts on large open wards particularly in paediatric wards where the degree of contact may be difficult to define

II. Timing of exposure

- Contacts with a single exposure to chickenpox from 48 hours before onset of rash until the lesions have crusted over
- Contacts with a single exposure to shingles from onset of rash until the lesions have crusted over
- Continuous exposure to a case of chickenpox or shingles (e.g. household member, nursery, care worker)
- Where there has been more than one exposure to a case of chickenpox or shingles (eg family friend visiting on more than one occasion during the infectious period)

III. Type of VZV infection in the index case

Chickenpox, disseminated shingles, exposed shingles lesions in immunocompetent individuals (eg ophthalmic shingles) or localised shingles on any part of the body in immunosuppressed individuals in whom viral shedding may be greater.

2. What makes a patient with IBD immunocompromised

Patients with IBD should not be routinely considered to have altered immunocompetence unless they fall into either of the groups below:

Group A

1. All children receiving systemic high-dose steroids until at least 3 months after treatment has stopped. This would include children who receive prednisolone, orally or rectally, at a daily dose (or its equivalent) of 2mg/kg/day for at least one week, or 1mg/kg/day for one month. For adolescents/ young adults, immunosuppression should be considered in those who receive >40mg of prednisolone per day for more than one week or >20mg prednisolone per day for more than 14 days.

2. Children (<16 years) receiving non-biological oral immune modulating drugs (e.g. Methotrexate, Azathioprine, 6-Mercaptopurine, Cyclosporine) alone or in combination with steroids, until at least 3 months after terminating such treatment.

Group B

Patients receiving biological therapies alone or in combination with steroids, until at least six months after terminating treatment.

All immunosuppressed individuals will require an assessment at the time of exposure. Group A individuals should be able to develop and maintain adequate antibody from prior infection or vaccination. On the contrary, Group B individuals may have lost immunity from previous infection or vaccination (see section 3).

3. VZV immune status

Evidence of immunity to varicella includes any of the following:

• History of chickenpox or shingles

• Two recorded doses of varicella vaccine

• Previous VZV IgG positive (≥ 150 mIU/ml)

Group A individuals (see above) with previous evidence of immunity to varicella should be considered to be immune and do not require testing following significant exposure to VZV.

Group A individuals who do not have evidence of immunity to varicella should be tested at the time of exposure. Also, those who previously tested VZV IgG negative or equivocal more than 6 months should be retested.

Group B individuals are unlikely to have maintained adequate antibody levels from prior infection or vaccination and may have lost immunity since their previous antibody tests. Therefore, all

Group B individuals should be tested at the time of exposure irrespective of previous evidence of immunity.

B. Post-exposure prophylaxis in susceptible IBD patients

In response to a significant shortage of VZIG in 2018 and a review by a Public Health England (PHE) convened expert working group, updated interim guidelines on PEP for high risk contacts have been published in June 2019. Antiviral agents are recommended for post-exposure prophylaxis for immunosuppressed individuals, except for those where there are significant concerns of renal toxicity or malabsorption.

Immunosuppressed individuals who are exposed to chickenpox or shingles should still be assessed for susceptibility as described in the national guidelines. For those identified as susceptible, and who would otherwise be offered VZIG, antivirals (oral aciclovir or valaciclovir) should be given from day 7 to day 14 after exposure. The day of exposure is defined as the date of the rash if the index is a household contact and date of first or only contact if the exposure is on multiple or single occasion(s) respectively. If the patient presents after day 7 of exposure, a 7-day course of antivirals can be started up to day 14 after exposure, if necessary.

There is limited evidence for dosing for valaciclovir prophylaxis but given the improved bioavailabilty, fewer daily doses and better side effect profile, valaciclovir may be preferred. The dosage of valaciclovir is based on the therapeutic dose for chickenpox (table 1).

	Oral Aciclovir	Oral Valaciclovir
Children under 2 years of age	10mg/kg 4 times daily, Days 7-14 after exposure	Not recommended
Children 2-17 years of age	10mg/kg (up to a maximum of 800mg), 4 times daily Days 7 to 14 after exposure	20mg/kg (up to a maximum 1000mg) 3 times daily, Days 7 to 14 after exposure
Adults	800mg 4 times daily, from days 7 to 14 after exposure	1000mg 3 times daily, from Days 7-14 after exposure

C. Treatment of VZV infection in immunosuppressed patients with IBD

If, despite having taken prophylactic aciclovir/valaciclovir, an immunosuppressed patient with IBD presents with a chickenpox rash, they should be changed onto a therapeutic dose starting from the day of onset of the rash. It may be advisable to stop immunomodulator therapy until clinical resolution, after careful assessment of each individual patient and with specialist advice. Immunomodulator therapy should be discontinued in severe cases, if possible. If discontinued, immunomodulator therapy can be reintroduced after all vesicles have crusted over and fever has resolved, If severe chickenpox develops, the patient may need to be hospitalised and given IV aciclovir.

Aciclovir by intravenous infusion

3 months- 11 years: 500mg/m2 every 8 hours usually for 5 days

12- 17 years: 10mg/kg every 8 hours usually for 5 days

Aciclovir by mouth

1-23 months: 200mg 4 times a day for 5 days

2-5 years: 400 mg 4 times a day for 5 days

6-11 years: 800 mg 4 times a day for 5 days

12-17 years: 800mg 5 times a day for 7 days

D. Prevention

The role of VZV serology at IBD diagnosis

European Crohn's and Colitis Organisation (ECCO) recommends screening patients at IBD diagnosis by history for susceptibility to primary VZV infection and recommend testing for VZV IgG only those without a clear history of chickenpox, shingles or receipt of two doses of varicella vaccine.

Currently, there is no formal recommendation for VZV IgG screening in all patients with IBD. Nevertheless, negative history of VZV exposure is a poor predictor of seronegativity, but history-positive patients may still be seronegative and exposed to VZV infection (Kopylov et al, 2012; Aggarwal et al, 2014). There is some evidence that early VZV screening and immunisation may be of increasing importance with the paediatric IBD population, especially with the emergence of novel therapeutic strategies, such as JAK inhibitors (Harris et al, 2020).

Our current practice in Bristol Children's Hospital is to screen all patients with inflammatory bowel disease at diagnosis.

VZV vaccination

Where possible, seronegative patients should complete the two-dose course of varicella vaccine a month or more apart, completing the course at least 3 weeks prior to commencement of immunomodulatory therapy. Subsequent immunisation can only be administered after a 3–6 month cessation of all immunosuppressive therapy.

D. Frequently asked questions

1. Can a family member of a patient with inflammatory bowel disease be vaccinated?

Yes, but vaccine recipients who develop a vaccine-related rash should avoid contact with the immunosuppressed patient.

2. Should varicella vaccination be given in immunosuppressed patients?

Current guidelines recommend avoiding varicella vaccination in the immunosuppressed. However, this is not based on strong evidence and further research is needed to determine the safety and efficacy of live VZV vaccines in immunosuppressed IBD patients. in this area. On one hand, some studies have shown a reduced response to the vaccine in patients receiving immunosuppression (Wasan et al, 2016). However, Tthe potentially disastrous consequences of varicella infection in an immunosuppressed patient may potentially be a greater risk to the patient than the theoretical risk of infection from a live vaccine (Cullen et al, 2012). On the other hand, some studies have shown a reduced response to the vaccine in patients receiving immunosuppression (Wasan et al, 2016). Further studies are required to determine the safety and efficacy of live VZV vaccines in immunosuppressed IBD patients.

3. Should immunosuppression be discontinued in the context of VZV infection in IBD?
There is no consensus. Such decisions will need to be made on an individual basis in conjunction with an ID specialist, taking into account the severity of the infection and the need for immunosuppression to treat the IBD. We recommend involving ID in any immunocompromised patient with suspected varicella or zoster (Cullen et al, IBD 2012).

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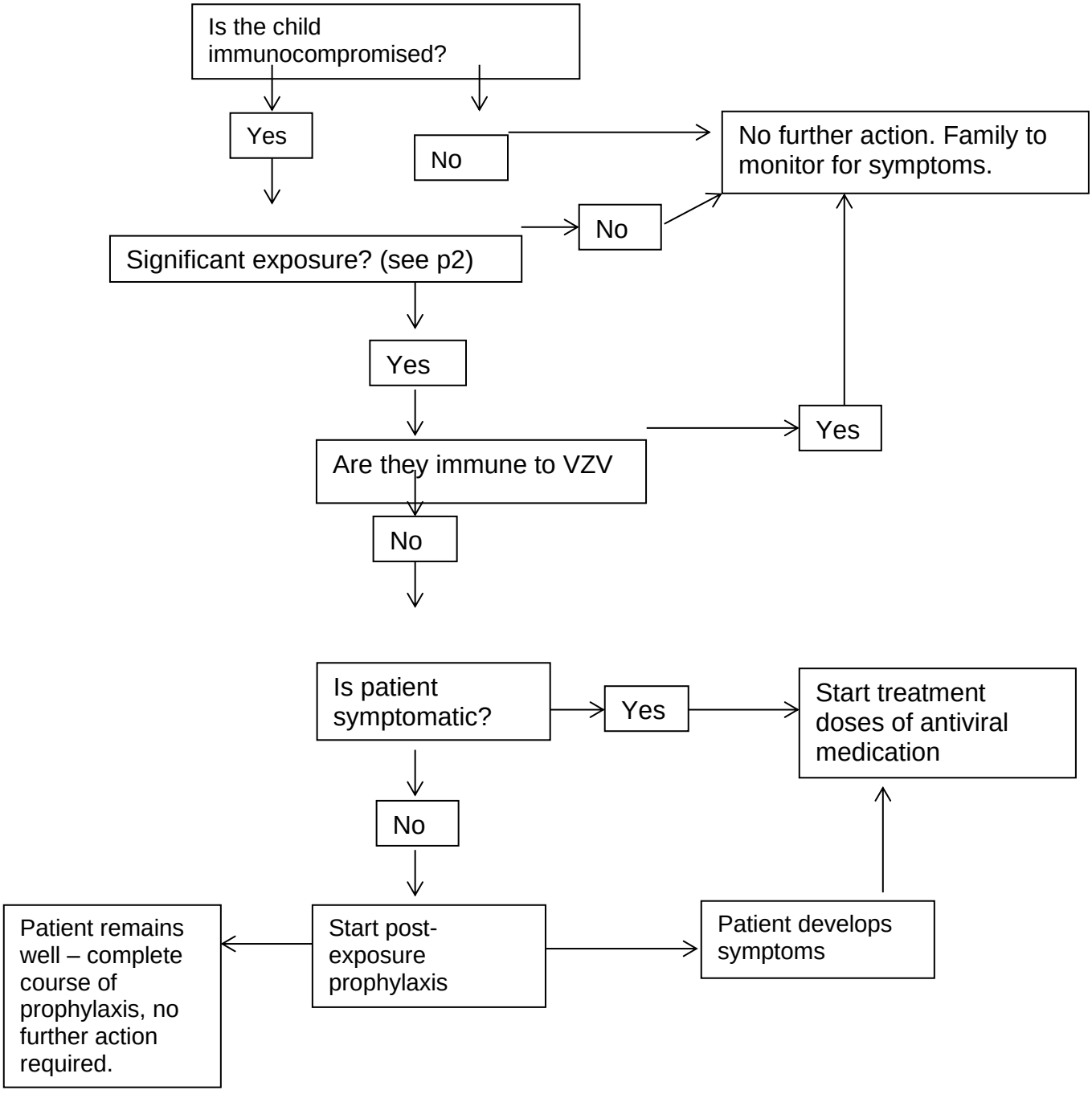
RELATED DOCUMENTS AND PAGES	none
AUTHORISING BODY	Paeds Gastroenterology Governance Group
SAFETY	No
QUERIES AND CONTACT	Gastroenterology secretaries 01173429451

Appendix

Quick Reference Guide- VZV Exposure in Children with IBD



Post exposure prophylaxis

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Adults	800mg 4 times daily, from days 7 to 14 after exposure	1000mg 3 times daily, from Days 7-14 after exposure