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Contents

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C. difficile Infection in Ireland

As of 4th May 2008, *Clostridium difficile* (toxin producing) has been included as a pathogen notifiable under the category of acute infectious gastro-enteritis (AIG). This specifically refers to a case of *Clostridium difficile*-associated disease (CDAD)/*Clostridium difficile* infection (CDI) in a patient two years or older in which one or more of the following criteria apply:

- Diarrhoeal* stools or toxic megacolon, with either a positive laboratory assay for *C. difficile* toxin A and / or toxin B in stools or a toxin-producing *C. difficile* organism detected in stool via culture or other means
- Pseudomembranous colitis (PMC) revealed by lower gastrointestinal endoscopy
- Colonic histopathology characteristic of *C. difficile* (with or without diarrhoea) on a specimen obtained during endoscopy, colectomy or autopsy

** Diarrhoea is defined as three or more loose/watery bowel movements (which are unusual or different for the patient) in a 24 hour period*

This definition excludes diarrhoea with other known aetiology (as diagnosed by the attending physician), and asymptomatic patients with a stool culture positive for toxin-producing *C. difficile* or an assay positive for *C. difficile* toxin A and / or toxin B. Notification under AIG is an interim measure until the disease and the related organism *C. difficile* (toxin producing) is specified under the Infectious Diseases Regulations schedule of notifiable diseases in the near future. Reports of CDAD/CDI will be produced and distributed each week by HPSC as for other infectious disease notifications and will be available at http://www.hpsc.ie/hpsc/NotifiableDiseases/WeeklyIDReports/.

National Guidelines

The *Clostridium difficile* Subcommittee has recently published national guidelines on CDAD/CDI in Ireland. These guidelines are aimed at healthcare professionals and outline recommendations for the surveillance, diagnosis, management, and prevention and control of CDAD/CDI in Ireland (available at http://www.hpsc.ie/hpsc/A-Z/Gastroenteric/Clostridiumdifficile/Publications/. The main recommendations of the guidelines include the following:

1. Implementation

Prioritisation (to include ring-fenced funding) should be given to the prevention of healthcare-associated infection (HCAI) in order to improve patient care and safety and to reduce all HCAI, including infections caused by *C. difficile*.

2. Surveillance

Healthcare facilities should perform surveillance of CDAD/CDI cases to enable baseline incidence to be calculated and a threshold incidence or prevalence of CDAD/CDI to be calculated locally that would trigger implementation of additional control interventions if necessary. This surveillance should, ideally, include awareness of changes in the rate and severity of complications from, or relapses of, CDAD/CDI and be performed in conjunction with surveillance of antibiotic use in that healthcare facility. CDAD/CDI figures should be collated nationally from laboratory based sources. The guidelines recommend that this should be mandatory at the laboratory level through the Computerised Infectious Disease Reporting System (CIDR). This will require that CDAD/CDI is made a notifiable disease in its own right through legislation. The guidelines also propose appropriate denominators for surveillance of CDAD/CDI in acute hospitals.

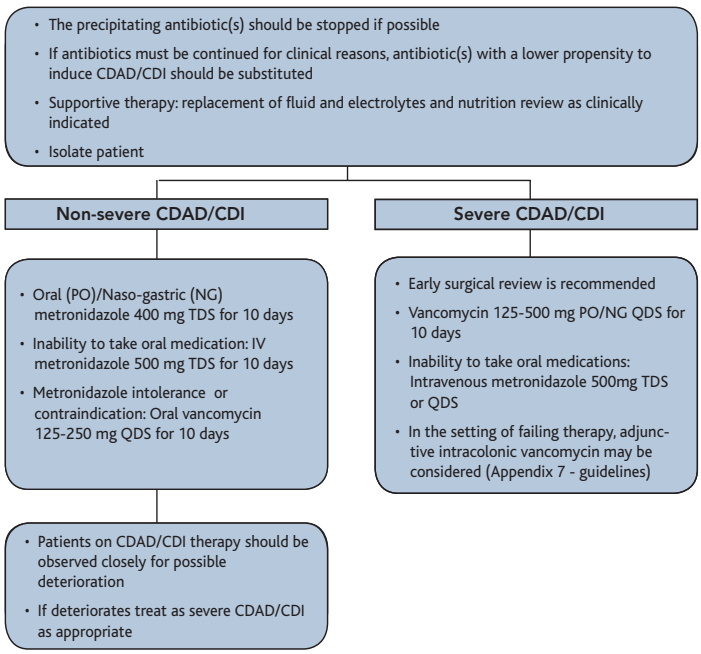

Fig 1. First-line-specific therapy of CDAD/CDI
(For paediatric doses refer to the British National Formulary for Children)

3. Laboratory diagnosis

All patients in whom a diagnosis of gastrointestinal infection is suspected should have a stool specimen sent promptly for microbiological analysis. Laboratories should perform *C. difficile* toxin testing on diarrhoeal stool specimens from patients 2 years and over.

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Varicella Vaccine: Policy Options for Ireland?

Introduction

Varicella zoster virus (VZV) is the cause of chickenpox, a common disease in childhood. While the illness is usually mild, it can be associated with more severe complications. Local reactivation of the virus leads to shingles which can result in pain, paresthesia and neurological sequelae. The risk of reactivation increases with age. A vaccine is available, and has recently been licensed for use in Ireland. This article describes the epidemiology of VZV-related disease in Ireland using available data sources; reviews the effectiveness, safety and cost-effectiveness of varicella vaccine; outlines VZV-related disease prevention and control internationally; and discusses the policy options for VZV-related disease prevention and control in Ireland.

Epidemiology of VZV-related disease

VZV infection is not currently notifiable on a case basis under the Infectious Diseases (Amendment) (No. 3) Regulations 2003 (S.I. No. 707 of 2003). Based on data from the GP sentinel surveillance system, operated by the Health Protection Surveillance Centre in collaboration with the Irish College of General Practitioners and the National Virus Reference Laboratory, there were approximately 13,854-16,187 and 9,187-11,739 primary care consultations per annum for chickenpox and shingles respectively, in Ireland in the 2005-2006 season. Data from the six sentinel surveillance system seasons to 2006 indicated that the annual crude rate of reporting of chickenpox and shingles ranged between 195.2-380.8/100,000 and 187.2-269.9/100,000 respectively (table 1 and figure 1). Most new cases of chickenpox presenting in primary care were in younger age groups, while most shingles cases were in older age groups (figure 2). The estimated age-specific incidence of chickenpox was greatest in the 0-4 year age group (3,183.4/100,000 (5% CI 2,829.2-3,537.5/100,000), 2005-2006 season) and declined steeply with increasing age, while the estimated age-specific incidence of shingles increased with age and was greatest in the over-65 year age group (651/100,000 (95% CI 523.12-779.3/100,000), 2005-2006 season).

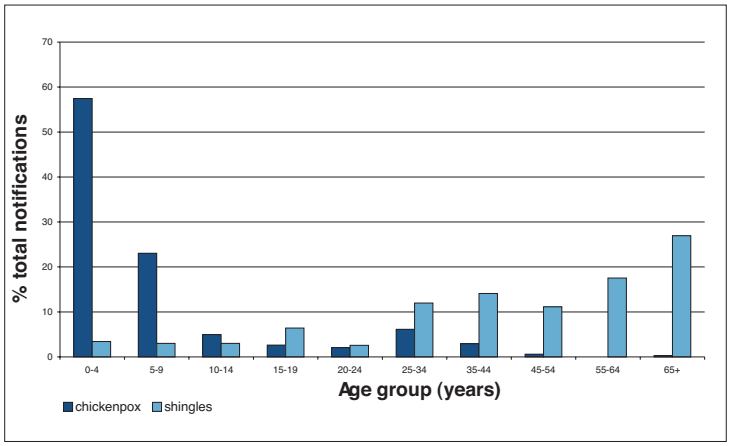

Figure 2. Age distribution of chickenpox and shingles cases in Ireland, 2005/2006
Source: HPSC

Table 1. Weekly and annual average crude rates of reporting of chickenpox and shingles in Ireland, 2000-2006

Season	Chickenpox Crude rate/100,000			Shingles Crude rate/100,000		
	Weekly average (95% CI)	Min/ max	Annual average (95% CI)	Weekly average (95% CI)	Min/ max	Annual average (95% CI)
2000/2001	5.0 (1.6-11.7)	0-20.0	260.8 (229.1-276.9)	5.2 (1.6-11.7)	0-14.8	269.9 (237.7-302.1)
2001/2002	6.1 (2.2-13.1)	0-15.0	319.0 (284.0-336.9)	4.2 (1.1-10.2)	0-10.7	218.4 (189.4-247.4)
2002/2003	6.6 (2.8-14.4)	0-21.3	343.5 (307.2-362.0)	4.3 (1.1-10.2)	0-11.4	223.4 (194.1-252.7)
2003/2004	3.8 (1.1-10.2)	0-9.6	195.2 (167.8-209.1)	3.6 (1.1-10.2)	0-9.0	187.2 (160.4-214.0)
2004/2005	6.0 (2.2-13.1)	1-12.2	310.9 (276.4-328.6)	4.8 (1.6-11.7)	1-11.7	251.4 (220.4-282.5)
2005/2006	7.3 (2.8-44)	0-13.7	380.8 (342.6-400.3)	5.0 (1.6-11.7)	0-9.2	258.8 (227.2-290.3)

Source: HPSC

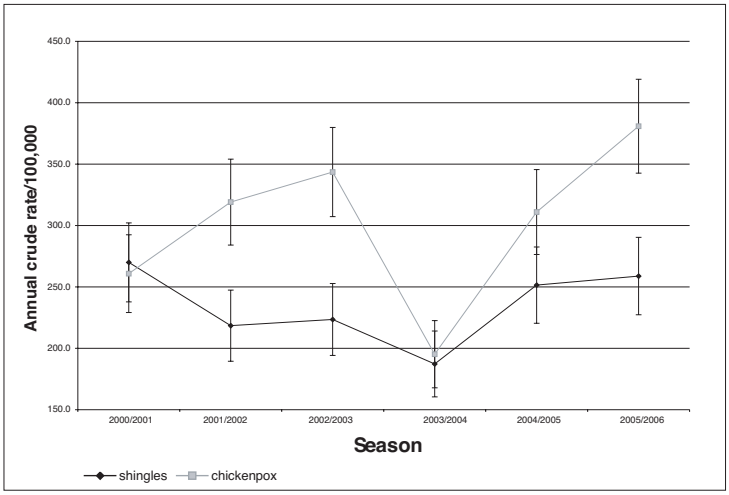

Figure 1. Time trends in annual average crude rates of reports of chickenpox and shingles in Ireland, 2000-2006
Source: HPSC

In recent years, Ireland has experienced an increase in the number of migrants arriving from other countries. While some arrive from countries with a similar epidemiology of VZV to Ireland, others arrive from countries, particularly those with tropical climates, where infection is less prevalent and therefore represent a susceptible cohort. Routine data are not available to examine VZV immunity or the occurrence of new infection in Ireland by country of birth. However, data from screening offered to asylum seekers in HSE South estimated that the prevalence of immunity in females aged over 12 years was 83.8%. A period prevalence study of immunity to VZV on pregnant women in a Dublin maternity hospital by Knowles *et al*, found that women from Sub-Saharan Africa had a higher prevalence of susceptibility to VZV compared with women from Ireland and Western Europe (21.7% versus 6.9% respectively, $p<0.001$).

Based on Hospital In Patient Enquiry System data (HIPE), in 2006, there were 346 and 527 episodes of hospitalisation in Ireland associated with chickenpox and shingles respectively, a crude rate for chickenpox- and shingles-associated hospitalisation of 8.1/100,000 (95% CI 7.3-9.0/100,000) and 12.4 (95% CI 11.4-13.5/100,000) respectively. The age-specific rate of hospitalisation for chickenpox was greatest in the 0-4 year age group, whereas the age-specific rate of hospitalisation for shingles was greatest in the oldest age group. Discharges associated with chickenpox showed a seasonal variation, rising over the winter months to a peak in late spring and early summer.

Deaths from varicella are rare in Ireland. Over the period 1980-2004, the annual average crude mortality from VZV-related disease was 1.3/1,000,000 (95% CI 1.0-1.5/1,000,000) and varied between

0/1,000,000 (95% CI 0-0.9/1,000,000) to 2.8/1,000,000 (95% CI 1.3-5.2/1,000,000) per annum. The annual average age-specific mortality rate was greatest in the age group ≥65 years.

While routine data are unavailable given that VZV is not notifiable on a case basis, it is noted that new medical technologies such as TNF-alpha antagonists have been associated with severe VZV-related infection.

Effectiveness and safety of varicella vaccine

In published studies, a single dose of varicella vaccine was immunogenic in younger children, and had a vaccine efficacy of 95-100% at up to seven years follow up. The vaccine has been shown to be effective in reducing the incidence of clinical disease: the numbers needed to vaccinate to prevent one case of chickenpox were 6-12 children, and to prevent one complication were 550-1,180 children. Two doses of the vaccine were significantly more immunogenic than one dose in older children (>12 years). More extended follow up has recently shown a two-dose regimen to be more effective in younger children than a single-dose regimen.

No significant adverse events have been demonstrated in vaccine recipients. There are, however, concerns regarding potential undesirable effects for the general population. Firstly, universal vaccination in childhood may shift disease incidence to older age groups where the risk of complications is greatest. However, there is no clinical evidence to support this concern to date in countries that have implemented this policy. Models predict that while this is a potential adverse event, even if it occurs, the total burden of VZV-related disease will be less than in the pre-vaccine period since the absolute number of cases will fall dramatically. Secondly, there is also concern that, if exposure to wild-type virus in the community leads to immune boosting that reduces the risk of reactivation of VZV, then universal vaccination may lead to an increase in the incidence of shingles. There is no clinical evidence to date in countries that have implemented this policy to support this concern. Models predict that even if this consequence occurs, as vaccine recipients age, the total burden of shingles will dramatically reduce in the population compared with the pre-vaccine period.

VZV prevention and control – international practice

In the US, varicella vaccine is included in the recommended childhood immunisation schedule since 1995. Based on data from three US communities, the incidence of varicella declined by between 71-84% in the 5-year period 1995-2000. A benefit was observed across all age groups. In recent years, outbreaks of wild-type varicella have occurred with secondary cases of the disease reported in vaccinated and unvaccinated children, including incidents where the index case has been a vaccinated child. Breakthrough disease in vaccine recipients was, however, mild. A number of contributory factors have been proposed: one dose of varicella vaccine may not provide sufficient herd immunity levels to prevent cases where exposure is intense, for example in schools; effective transmission of VZV may still occur in vaccinated children who may not themselves develop symptoms. As a result, a second dose of varicella vaccine is now routinely recommended in the US to children aged 4-6 years who receive their first dose early in life (12-15 months).

Canada, Australia, and Germany have also implemented universal varicella vaccination in early childhood. Austria, Switzerland and Spain have implemented selective vaccination in early adolescence of varicella-susceptible individuals while other countries offer vaccination to individuals at high risk of severe disease (e.g. non-immune healthcare workers, pregnant women identified as susceptible (offered in the puerperium), individuals who undergo organ transplantation and require immunosupression).

VZV prevention and control – policy options for Ireland

Universal vaccination in early childhood offers the greatest potential for health gain through reduction in the incidence of chickenpox, and as vaccine recipients age, a reduction in shingles incidence. Potentially, this approach could eliminate the disease. However, the potential risks of age-shift in disease incidence and increasing shingles incidence would require close monitoring. A catch-up campaign in older age groups in addition to universal vaccination in early childhood could be considered to reduce the risk of an increase in disease incidence in these groups. Recent evidence from the US indicates an additional benefit from a second dose later in childhood.

Selective vaccination of susceptible children in early adolescence has more favourable risk-benefit and cost-benefit ratios than a universal policy. It is also relatively risk-free from a population perspective. However, it offers less potential for health gain since most children will be infected in childhood. The success of this approach is highly dependent on the validity of reported immunity to varicella infection. If there is false reporting of immunity then the potential for this programme to deliver health gain is reduced. If there is false reporting of susceptibility then the cost of the programme will be increased without any additional health gain.

High-risk vaccination is a policy adopted by many countries internationally who have not implemented universal childhood varicella vaccination and targets those at greatest risk of severe disease including the immunocompromised and their contacts, susceptible healthcare workers, and susceptible women of childbearing age. The risk-benefit and cost-benefit ratios are most favourable with this approach. However, there is little impact on the burden of disease since most cases, and most severe and fatal cases of the infection occur in individuals without pre-morbid risk.

Universal varicella vaccination in early childhood is an attractive policy option, however, the costs and benefits of this addition to the schedule of childhood immunisation need to be carefully weighted against the benefit to the population of implementing other options for programme expansion in Ireland. The National Immunisation Advisory Committee has identified other priorities for strengthening and developing the schedule of childhood immunisation at the moment, and a high-risk approach to varicella vaccination is recommended. In the meantime, consideration can be given to the development of a robust framework for policy monitoring and evaluation through the strengthening of sentinel surveillance and/or mandatory notification of VZV-related disease in Ireland.

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References on request

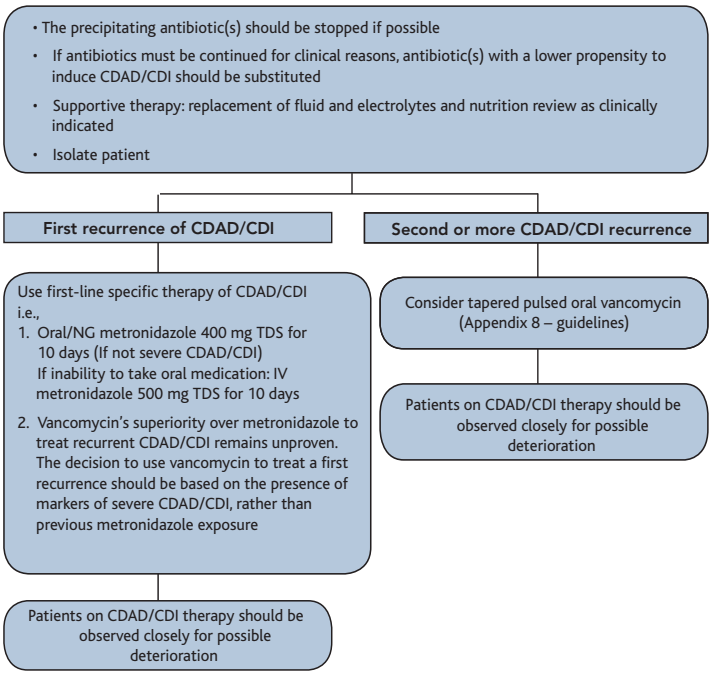

Fig 2. Treatment of recurrent CDAD/CDI
(For paediatric doses refer to the British National Formulary for Children)

Testing stool of children < 2years for *C. difficile* toxin is not recommended. In the case of ileus and suspicion of CDAD/CDI, testing of formed stool is acceptable and other diagnostic procedures may be required (e.g., abdominal CT, colonoscopy). It is recommended that all diarrhoeal specimens are tested for *C. difficile*, rather than relying on appropriate clinical information on the specimen request form. However, this will have service implications for laboratories in terms of workload and staffing that will need to be addressed. The guidelines provide advice on specimen selection, transportation, storage, testing and culture of specimens. It is recommended that laboratories should use a method that can detect both toxin A and toxin B. In cases of severe CDAD/CDI, or in an outbreak setting, specimens should be referred to a reference laboratory for epidemiological typing or stored at 4^{O}C for culture at a later stage. It is recommended that an Irish reference laboratory is established with appropriate funding. Pending establishment, specimens should be sent to an international reference laboratory for typing.

4. Management

Asymptomatic carriers of *C. difficile* should not be treated. Antiperistaltic agents should be avoided because of lack of evidence that they improve diarrhoea in this situation and the theoretical risk of precipitating toxic megacolon by slowing clearance of *C. difficile* toxin from the intestine. First-line specific therapy of CDAD/CDI is outlined in Figure 1 and treatment of recurrences in Figure 2.

5. Prevention and control

Interventions for the prevention and control of CDAD/CDI include prudent antibiotic stewardship and compliance with infection prevention and control measures. The prevention and control of *C. difficile* may be best achieved by the use of Standard and Transmission-based (Contact) Precautions (Appendix 9 of the guidelines). Standard Precautions should be used when exposure to blood, body fluids, non-intact skin or mucous membranes is anticipated. Contact Precautions are designed to reduce the risk of transmitting *C. difficile* by direct or indirect contact. The principles of caring for the patient with CDAD/CDI are similar irrespective of whether the patient is located in a healthcare facility or at home:

a. Patient placement

Prompt isolation of all patients with confirmed or suspected CDAD/CDI, using Standard and Contact Precautions, in a single room with clinical hand washing sink and ensuite facilities is recommended. If ensuite facilities are not available, patients with CDAD/CDI should be allocated a designated toilet or commode and not permitted to use the general toilet facilities on the ward. Isolation with Contact Precautions may be discontinued when the patient has had at least 48 hours without diarrhoea and has had a formed or normal stool for that patient. The movement and transport of the CDAD/CDI patient should be limited to essential purposes only and the guidelines outline advice for this.

b. Hand hygiene and protective clothing

Hand washing with soap (non-antimicrobial or antimicrobial) and water must be performed before and after all patient and equipment contact and after glove removal. The physical action of rubbing and rinsing is the only way to remove spores from the hands. Alcohol-based hand rubs do not have reliable sporicidal activity and are not recommended as the only hand hygiene measure when caring for confirmed or suspected CDAD/CDI patients. In addition to Standard Precautions, gloves and aprons should be worn for contact with the patient and the patient environment.

c. Environmental and equipment decontamination

It is recommended that the environment of patients with CDAD/CDI and all patient care equipment should be thoroughly cleaned with a neutral detergent and disinfected daily with a sporicidal disinfectant (e.g., hypochlorite solution – 1000 ppm available chlorine), paying special attention to frequently touched sites e.g., bedrails, over bed table, toilets, commodes etc. Particular attention should be given to immediately cleaning and disinfecting items likely to be faecally contaminated e.g., the under surfaces and hand contact surfaces of commodes. These items should be cleaned and disinfected after each use. All equipment used for patients should be in a state of good repair in order to facilitate effective cleaning. Bedpan/commode utensils should be placed directly into a bedpan washer-disinfector. Bedpan washers must reach a temperature of 80°C for a minimum of one minute. Scheduled maintenance and validation records according to appropriate standards should be maintained to ensure appropriate cleaning and disinfection.

d. Laundry and healthcare risk waste management

All laundry should be placed into an alginate stitched or water-soluble bag at the bedside. The sealed bag should be placed immediately into a laundry bag clearly identified with labels, colour-coding or other methods so that healthcare workers handle these items safely according to organisational and national guidelines. Linen should be heat disinfected during the wash process by raising the temperature to either 65°C for not less then 10 minutes or preferably 71°C for not less then 3 minutes. Disinfection of heat labile materials (according to manufacturer instructions) can be achieved at low temperatures, by introducing 150 ppm of chlorine into the penultimate rinse.

Patient information leaflet

A patient information leaflet is included in the guidelines (Appendix 10) and can also be downloaded at http://www.hpsc.ie/hpsc/A-Z/Gastroenteric/Clostridiumdifficile/Publications/.

Conclusion

CDAD/CDI is a relatively common disease and can be associated with significant morbidity and mortality. While CDAD/CDI is mainly healthcare-associated, there is increasing recognition of the existence of community-associated cases. In one study, a high percentage of patients with CDAD/CDI (9.3%) was found among 703 patients with diarrhoea visiting their general practitioner over a three month period, in comparison to *Salmonella enterica* (4.8%) and Campylobacter (3%). Developing high quality health intelligence around CDAD/CDI in Ireland is essential for the development, implementation and evaluation of policy and practice to prevent and control the disease at local and national levels.

Fidelma Fitzpatrick, Chair, *C. difficile* Subcommittee, HPSC

References on request