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An analysis of infection control of varicella-zoster virus infections in Addenbrooke's Hospital Cambridge over a 5-year period, 1987–92

T. G. WREGHITT[1], J. WHIPP[2], C. REDPATH[2] AND W. HOLLINGWORTH[3]

[1] *Clinical Microbiology & Public Health Laboratory, Addenbrooke's Hospital, Cambridge CB2 2QW, UK*
[2] *Infection Control Nurse, Addenbrooke's Hospital, Cambridge CB2 2QW*
[3] *Department of Community Medicine, Institute of Public Health, University of Cambridge, Forvie Site, Robinson Way, Cambridge CB2 2SR*

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SUMMARY

This prospective study analyses infections with varicella-zoster virus (VZV) in Addenbrooke's Hospital, Cambridge during 1987–92 and examines the spread of infection. In total, 93 patients and staff experienced VZV infection. Twenty-one patients had varicella and 49 experienced zoster. None of 101 patients and 1 of 625 staff members in contact with varicella cases acquired infection. By contrast, 2 of 227 patients, and 5 of 1039 staff in contact with zoster cases acquired varicella. One out of 28 (3·6%) VZV antibody-negative patients and staff in contact with varicella acquired infection, compared with 5 out of 29 (17·2%) VZV antibody-negative patients and staff in contact with zoster. Thus, zoster was found to be a more frequent cause of nosocomial infection than varicella. Fourteen members of staff had VZV infection during the study period. One of 99 patients and none of 389 staff members in contact with these cases developed varicella. The cost of dealing with infection control for VZV infections in our hospital is estimated to be £714 per patient case and a total of £13204 per year.

INTRODUCTION

Varicella-zoster virus (VZV) is one of the most important organisms causing cross-infection between patients and staff in hospitals [1]. Primary infection, which results in varicella (chickenpox), most frequently occurs in childhood, when symptoms are usually fairly mild and mortality low [2]. However, there is an increasing trend for infection to be acquired by adults, in whom symptoms tend to be more severe [3]. Some adults experience life-threatening varicella encephalitis or pneumonia. Pneumonia is the most common cause of death in adults with chickenpox [4], especially in smokers [5], despite prompt treatment with acyclovir. Varicella is acquired principally by the respiratory route, the virus being transmitted by the inhalation of infected droplets or by direct contact with vesicular fluid [6]. After primary infection, VZV becomes latent in the dorsal root ganglia. Reactivation leads to zoster (shingles) which is usually confined to the determatome served by one sensory nerve [7].

VZV infection in immunocompromised patients may be more severe. Transplant recipients receiving immunosuppressive drugs may experience haemorrhagic varicella, which is frequently fatal, sometimes despite prompt acyclovir treatment [8]. Other patients, such as those receiving treatment for leukaemia, lymphoma or other malignancies are also at increased risk if they acquire varicella. HIV antibody-positive patients and transplant recipients have an increased prevalence of zoster compared to non-immunosuppressed age-matched patients [9]. Some patients have vesicles in more than one dermatome, and a few have widespread lesions which clinically resemble varicella.

Varicella in pregnancy is a problem not only

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because of the risk that the mother could develop encephalitis or pneumonia like other adults, but more particularly because infection can be transmitted transplacentally to the fetus. It is estimated that *c.* 1% babies infected *in utero* in the first 20 weeks of pregnancy will have the congenital varicella syndrome, which has a poor prognosis [2]. VZV infection of the fetus in the last week of pregnancy or in the first few weeks of life results in acute neonatal varicella which may be fatal [10].

Because varicella is frequently severe or life-threatening in immunocompromised patients and may damage the unborn child, it is important to minimize the risk of infection. In hospital, this is best achieved by isolating patients with varicella or zoster, particularly if they are being treated in wards, operating theatres or clinics in which immunocompromised or pregnant patients are also being cared for. The most effective means of preventing VZV cross-infection is to put VZV-infected patients into closed isolation units with negative pressure airflow. There have been reports of transmission in rooms without this provision [11]. Another important means of minimizing VZV cross-infection is the exclusion of VZV antibody-negative staff from patients who have had contact with persons with varicella or zoster. With increasing number of immunocompromised patients being treated in hospitals, minimizing VZV cross-infection is becoming more important.

There are few reports of studies on hospital acquired VZV infections [12, 13]. Weber and colleagues [12], in a 1-year prospective study, documented 37 VZV exposures in their 580 bed hospital. Forty-three percent of the VZV cases in patients were chickenpox and 57% were zoster. Krasinski and colleagues [13], in a retrospective study of 95 VZV infections in their hospital reported 65% VZV cases were zoster and 35% were chickenpox. In neither studies were nosocomial VZV infections resulting from exposure to chickenpox or zoster examined separately.

In this study, we report VZV infections in patients and staff in Addenbrooke's NHS Trust, Cambridge, between 1987–92 and review the efficacy of infection control procedures for minimizing VZV cross infection.

METHODS

Notification and diagnosis

Throughout the period of this study, it has been the policy at Addenbrooke's Hospital to notify all inpatients, immunocompromised and pregnant outpatients, or staff members with varicella or zoster to the infection Control Nurses or the Duty Virologist. Whenever possible, the Duty Virologist or a member of the relevant Clinical Team have taken samples to confirm VZV infection. Vesicle fluid was collected with a capillary tube or syringe needle and processed for negative stain electron microscopy. A lesion swab was taken, transported in virus transport medium and inoculated into fibroblast cell culture. VZV infection of cell cultures was established by the detection of characteristic cytopathic effect (CPE) and slow growth, typically taking 3–15 days [7]. Paired serum samples were also sought for VZV serology. VZV infection was confirmed by a significant rise in VZV antibody titre and/or the detection of VZV-specific IgM [7]. In those few instances where clinical samples were not available, a clinical diagnosis of varicella or zoster was made.

Infection control measures

When a diagnosis of varicella or zoster was made, an Infection Control Nurse or the Duty Virologist evaluated the implications for infection control. In wards where immunocompromised or pregnant patients were being treated, priority was given for moving the VZV infected patient to an isolation unit with negative pressure ventilation (achieved for all but one patient). We have one ward for this purpose and three cubicles in our adult intensive care unit. We lack this facility for paediatric patients who require intensive care.

All patients in contact with cases of varicella or zoster were questioned about any history of previous varicella or zoster. Contact was defined as being in the same room or bay of a ward as the patient with VZV infection. If they had no previous history they were tested for evidence of VZV immunity. In immunocompromised patients, the patients' previous history was disregarded, because we have found this to be unreliable, and all patients were tested for evidence of VZV immunity. Whenever possible, VZV antibody-negative patients were placed in isolation from 10–21 days after the first contact.

We do not test all staff prospectively for VZV antibody. All staff in contact with the patient were asked about their previous varicella or zoster history. Only staff who had no previous history of varicella or zoster were followed up as it has been our experience that staff with a previous history of varicella or zoster

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Table 1. *Patients with varicella*

	Number of patients with varicella	Number of patients			Number of staff		
		In contact	Not immune	Who developed varicella	In contact	Not immune (excluded from work after contact)	Who developed varicella
In ward with immunocompromised or pregnant patients	17	99	13	0	521	12 (11)	1
In ward with no immunocompromised or pregnant patients	4*	2	0	0	104	3 (3)	0

* One patient probably acquired infection from a nursing auxilliary who developed varicella 5 days after working on a ward and 19 days before this patient developed varicella.
One patient acquired varicella from another patient with whom she shared a room and who had zoster 2 weeks previously.

are VZV antibody-positive [14], a finding endorsed by other studies [15]. A 10 ml clotted blood sample was requested from all these staff members, which was tested for VZV antibody. In the early part of this study, an indirect immunofluorescence test was used [14], but we now employ a more sensitive ELISA (Promed, Diamedix).

When possible, staff members who had no detectable VZV antibody were excluded from patient contact from 10–21 days inclusive after their first contact with the infected patient. Staff members in continuous clinical contact were assumed to be in contact with VZV 2 days before the onset of symptoms in the patient.

In wards where immunocompromised or pregnant patients were not being treated and were not likely to be treated in the next 2 weeks, staff who had no previous history of varicella or zoster were followed up but VZV antibody-negative staff were not always excluded from patient contact. However, they were told to stay away from work if they felt unwell between 10–21 days after VZV contact, particularly if they had a varicella-like illness. It has not been our routine practice to screen patients in these wards for evidence of VZV immunity unless they had close contact with a case of varicella or zoster.

Antiviral prophylaxis

Immunocompromised patients in contact with cases of VZV infection and at risk of severe chickenpox were given varicella-zoster immune globulin (VZIG) and prophylactic acyclovir (400 mg qds for 14 days). Susceptible pregnant patients and staff in contact with VZV cases received VZIG.

Resource use

Resource use data were collected throughout the 5 years of the study. Costs of controlling VZV infection were incurred in the following areas: (a) antibody tests, (b) isolation of infected and high risk patients, (c) exclusion of staff from work, (d) prophylactic VZIG treatment, (e) acyclovir treatment, (f) infection control staff time.

The total costs were calculated using data of the 1994–5 costing information of the Cambridge Clinical Microbiology and Public Health Laboratory (a), the hospital finance department (b, c, f), and the hospital pharmacy (d, e).

RESULTS

Varicella

In the 5-year study period, 21 patients were identified with varicella, 17 were in wards with immunocompromised or pregnant patients, and 4 were not (Table 1). Despite the fact that 101 patients had been in contact with these varicella cases and 13 had no evidence of VZV immunity, none developed varicella. Of the 625 staff in contact with cases of varicella, 15 had no evidence of VZV immunity and 14 were excluded from working with patients (Table 1). The

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Table 2. *Patients with zoster*

	Number of patients with zoster	Number of other patients			Number of staff		
		In contact	Not immune	Who developed varicella	In contact	Not immune (excluded from work after contact)	Who developed varicella
In ward with immunocompromised or pregnant patients	16	194	6	1	501	10 (10)	2
In ward with no immunocompromised or pregnant patients	33	33*	0*	1	538*	13 (8)	3

* Patients and staff members were not checked for VZV immunity in all incidents if infection arose in a ward where immunosuppressed or pregnant patients were unlikely to be treated.

Table 3. *Staff with varicella or zoster*

	Number of staff members	Number of patients			Number of staff		
		In contact	Not immune	Who developed varicella	In contact	Not immune (excluded from work after contact)	Who developed varicella
Chickenpox	13	89	10	1	385	9 (3)	0
Zoster	1	10	2	0	4	0 (0)	0

one staff member who was allowed to work because of severe shortage of staff in the intensive care unit did not acquire varicella, but one of the excluded staff did.

Zoster

Forty-nine patients with zoster were identified during the 5-year study period, 16 were in wards with immunocompromised or pregnant patients and 33 were not (Table 2). Of the 227 patients in contact, 6 did not have antibody to VZV and 2, who had been in close contact, developed varicella. However, not all patients in contact with VZV in wards with no immunocompromised or pregnant patients were tested for VZV antibody. One of the non-tested contact patients acquired varicella. Of the 1039 staff in contact with zoster patients, 23 were not immune to VZV, 18 were excluded from work and 5 developed varicella. In one incident, two intensive care unit nurses, one of whom had already been excluded from work because of contact with VZV twice previously, were in contact with a liver transplant recipient with

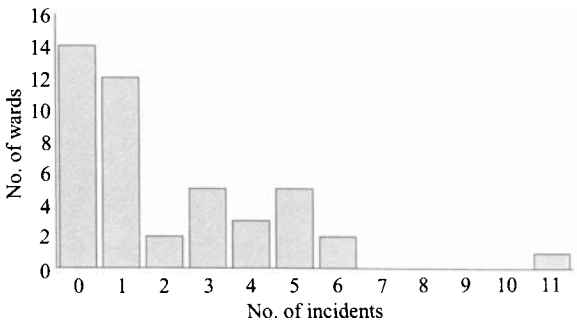

Fig. 1. Number of VZV incidents per ward at Addenbrookes's Hospital, 1987–92.

two zoster vesicles on her chest. They both nursed this patient for only one shift, they were both excluded from work and both acquired varicella, one of them severely, 2 weeks later [16]. This incident highlights the high infectivity of immunocompromised patients with zoster.

Thirteen members of staff with varicella and 1 with zoster were in contact with 99 patients in the 5-year

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Table 4. *Measures to control VZV in 84 primary cases in 1987–92*

No. and source of cases	No. of patients isolated*	No. of contacts VZV antibody tested	No. of staff excluded from work†	No. of doses VZIG (250 mg)	No. of patients requiring acyclovir	Infection control staff time‡
70 Patients	34	182	35	48	8	140 h
14 Staff	1	104	3	63	8	28 h

* Including three patients who developed varicella.
† Including six staff members who developed varicella.
‡ An average time of 2 h per case was estimated by infection control staff.

Table 5. *The cost of VZV control 1987–92*

Method of control	Units	Cost per unit (£)	Cost (at 1994/5 prices) (£)
Serological testing of contacts for VZV antibodies	286 tests	9	2574
Patient isolation	245 days	40·50*	9923
Exclusion of staff from work	445 days	68·07†	30301
Prophylactic VZIG treatment	111 doses	180	19980
Acyclovir treatment	16 doses	107·30	1717
Infection control staff time	168 h	9·08†	1525
Total cost of control 1987–92			66020
Cost per year			13204
Number of source cases			84
Cost per case			786

* Extra cost per day of isolation ward.
† Based on mid-grade nursing salary.

study period (Table 3). of the 12 patients who had no evidence of VZV immunity, 1 developed varicella. Of the 389 staff members in contact with these infected staff, 9 were not immune to VZV and 3 were excluded from work with patients (Table 3). None developed varicella.

Thirty (68%) of the 44 wards at Addenbrooke's Hospital reported VZV incidents during the study period. The distribution of the number of incidents is shown in Figure 1. Most incidents were reported from a ward in which kidney and liver transplant patients are treated. A total of 17 incidents were recorded in the 6 wards which predominantly care for elderly patients. Nine notifications were received from the Maternity Hospital, 18 from the 4 wards caring for paediatric patients and 4 from the adult intensive care unit. Ten incidents were reported from 4 wards in which patients with neurological conditions were being treated.

The differences in transmission rates from patients and staff with varicella and zoster to other patients and staff were not statistically significant.

Table 4 details the measures taken to control the spread of VZV infected in 84 primary cases. Thirty-five patients were moved to an isolation ward as a result of acquiring or being in contact with VZV infection. Three contact patients developed varicella. Patients who were moved into isolation cubicles, whilst remaining in the intensive care unit are not included in this figure as the hospital does not provide independent cost data for these cubicles. In total 286 tests for VZV antibody were performed on patients and staff with no VZV history and immunocompromised patients. Thirty-eight staff were excluded from work from days 10–21 after contact and 6 developed varicella. Sixteen patients received prophylactic acyclovir and 111 vials of VZIG were used. Each of the 84 primary cases was estimated to require 2 h of the infection control staff's time.

The total cost of controlling nosocomial infections of VZV in Addenbrooke's over the 5-year period was estimated to be £66020 (Table 5). The largest components of this total cost were the exclusion of staff from work (46%), prophylactic VZIG treatment (30%) and patient isolation (15%). Attempts to control the spread of VZV infections cost on average £786 per case (£714 per primary patient case and £1147 per primary staff case).

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DISCUSSION

In Addenbrooke's Hospital, patients with zoster were a more significant cross-infection problem than those with varicella. In the two 1-year studies of nosocomial VZV infections in hospitals [12, 13], zoster infections in patients were more numerous than cases of chickenpox, but neither study documented separately the rate of secondary infections resulting from chickenpox and zoster cases in patients. Addenbrooke's Hospital is a University Teaching Hospital and tertiary referral centre, and our experience of VZV infection control is probably different to that experienced by a District General Hospital. Of the 23 identified VZV antibody-negative staff members at Addenbrooke's Hospital in contact with patients with zoster, 5 (22%) developed varicella. Two patients also acquired varicella but this route. In contrast, of the 15 identified VZV antibody-negative staff members in contract with patients with varicella, only 1 (7%) developed varicella and no patient was infected. Therefore 1 out of 28 (3·6%) VZV antibody-negative patients and staff in contact with varicella acquired infection, compared with 5 out of 29 (17·2%) VZV antibody-negative patients and staff in contact with zoster. This may be because patients with varicella are usually admitted when symptomatic and are unlikely to be cared for by staff who have no known history of varicella. In contrast, many patients with zoster develop symptoms while in hospital and therefore staff with no known history of varicella will not be excluded from caring for them until the patient's symptoms are recognized as zoster.

Routine VZV antibody testing of staff would not alleviate this problem.

None of the 13 VZV antibody-negative patients in contact with varicella in hospital acquired infection. This may be in part due to the fact that most of them received VZIG and/or prophylactic acyclovir shortly after contact, and also because they had less contact with the patients with varicella than did non-immune staff. During the study period, we have had no known tertiary cases of VZV in our hospital.

Our policy to encourage notification and investigation of patients and staff with VZV infections, and to identify VZV antibody-negative staff and patients in contact, particularly in wards where pregnant or immunocompromised patients are cared for has been time consuming. Our Occupational Health Department does not screen staff for evidence of VZV immunity. With a turnover of nursing staff of up to 25% in recent years, this would also have been very time-consuming and costly to implement, because all staff with no or doubtful history of previous varicella would have to be identified and tested. Testing all staff would be even more expensive. Since many staff such as casual cleaners and agency nurses are employed in our hospital, it is unlikely that the Occupational Health Department could ever have a complete knowledge of staff VZV immunity. Of the 6 staff members who acquired varicella from patients, 5 were nurses, and 1 was a temporary cleaner, who would not have been known to the Occupational Health Department. This also emphasizes the fact that any category of staff who has contact with patients is liable to be infected if in close enough contact. Knowledge of VZV immune status of agency and temporary staff would be beneficial for infection control purposes.

In practice, cases of varicella are usually initially admitted to paediatric or isolation wards, and cases of zoster to general medicine, oncology, transplant, intensive care, or isolation wards and wards caring for the elderly. In our experience, when a new patient with VZV infection is identified, the VZV history or immune status of the majority of the staff is already known because of investigations from previous incidents. Some workers have recommended the investigation of the VZV immune status of all hospital staff, especially those working in maternity units or with immunosuppressed patients [15, 17]. We believe this would be expensive, incomplete and more time consuming. It would not eliminate the need to produce lists of staff and patients in contact and to check the VZV antibody status of those staff members who have no history of varicella. In the 5-year period of this study, 32% of wards had no reported VZV incident (Fig. 1).

VZV vaccine, although not currently licensed in the UK could be considered for VZV antibody-negative healthcare workers with patient contact. However, only 80% of adults seroconvert after one dose and 94% after two doses [18]. Breakthrough infections occur in some adults who have seroconverted to VZV vaccine and long-term clinical protection is only 70%. Therefore, if this policy were to be instituted, it is probable that transmission of VZV would still occur in some hospital staff.

The cost of controlling VZV infection over the 5 years is not insignificant. The largest part of that cost relates to the opportunity cost of removing from patient contact antibody-negative staff who have had

contact with cases of varicella or zoster. However, had we not done so, five members of staff could have transmitted VZV infection to other staff and patients and tertiary cases would have been likely to occur. The cost of VZIG prophylaxis was also a major factor in overall costs, and there is doubt about its efficacy [19].

This 5-year study, the longest prospective study to be done, highlights the cross-infection problems caused by VZV infection and re-emphasizes the significance of zoster as a cause of nosocomial infection in hospitals.

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