

## Parvovirus B19 outbreak on an adult ward

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(Accepted 17 May 1994)

### SUMMARY

In November and December 1992, an outbreak of parvovirus B19 infection occurred among patients and staff on an adult mixed surgical ward at a large hospital in London. Three patients and 15 staff members were serologically confirmed as acute cases. The attack rate among susceptible members of staff was 47%. In those infected, arthralgia (80%) and rash (67%) were the most common symptoms. Of six susceptible in-patients on the ward, three became infected. One of the in-patients who had carcinoma of the mouth was viraemic for more than 10 days with marrow suppression resulting in the postponement of chemotherapy until intravenous immunoglobulin was given and he was no longer viraemic. Control measures taken included closure of the ward to new admissions, transfer of only immune staff to the ward, and restriction of the ward nursing staff to working only on that ward. Although no specific exposure was conclusively identified as a risk factor, there was a suggestion of an increased risk of acquiring parvovirus B19 infection among those staff who did not adopt strict hand washing procedures after each physical contact with a patient (RR = 2.33; P = 0.07). Knowledge of parvovirus B19 among interviewed health care workers was poor: only 42% reported knowing about parvovirus B19 and only 38% could name a patient category at risk of a severe outcome following infection. This is the first report of a nosocomial outbreak affecting an adult ward and of possible transmission of parvovirus B19 infection from staff to in-patients. Hospital control of infection teams should include parvovirus B19 in their outbreak containment plans.

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## INTRODUCTION

Parvovirus B19 is a small single stranded DNA virus discovered in asymptomatic blood donors in 1975 [1]. Infection with parvovirus B19, the causative agent of erythema infectiosum or fifth disease, is common [2–5]. In most healthy individuals it gives rise to a mild and self limiting illness [6, 7]. In some groups such as people with certain malignancies, chronic haematological disease or immunodeficiency, severe disease can occur [8–14]. Infection with B19 during pregnancy has been associated with hydrops fetalis and fetal death [15, 16]. Nosocomial outbreaks have occurred, but only two have been well documented and both affected children's wards [17, 18]. Respiratory secretions are considered to be the major vehicle of transmission [6, 10, 19].

At the end of 1992 and in the first half of 1993, there was a large increase in parvovirus B19 infections in England and Wales reported to the PHLS Communicable Disease Surveillance Centre [20]. In November 1992, an outbreak of parvovirus B19 infection occurred on an adult ward of a large London hospital, which led to an investigation that is described below.

## METHODS

*The outbreak and investigation*

On 1 December 1992, the infection control team of the hospital was informed that several in-patients and staff members, including nurses and doctors working on a surgical ward (Ward A) had been taken ill with symptoms suggestive of erythema infectiosum. Ward A was a busy 28 bed adult surgical ward with an average monthly admission of about 100 patients of varying specialties including ear, nose and throat (ENT) surgery, urology and orthopaedics. Adjacent to Ward A were one ward with renal dialysis and renal transplant patients and another with general surgical and oncology patients. Children's wards including one with AIDS patients were located two floors below the affected ward.

The epidemiological investigation consisted of a descriptive and analytical study both of recently infected and of non-infected in-patients and staff members. Parvovirus B19 antibody tests were carried out on all in-patients on Ward A between 1 December to 3 December and on members of staff who either had been working on the ward full time or who had come into contact with the ward over the preceding month. Staff and patients on other wards who had symptoms and signs suggestive of parvovirus B19 infection were also tested. The analytical study cohort consisted of members of staff who had been working on or who had visited Ward A during a period from 1 November to 14 December 1992 and who were categorized as either cases of recent infection or as susceptible to parvovirus B19 infection during the above period.

Cases of recent infection were defined as those persons with either a positive IgM (B19 IgM RIA > 3 units) and/or positive B19 DNA (dot blot hybridization test) between 1 November 1992 and 14 December 1992. Persons whose B19 IgG, IgM and DNA tests were negative were considered susceptible and were retested after 6 weeks to detect late seroconversion. Those whose B19 IgG test was positive

(including those with low levels of 1–3 units) with negative B19 IgM and DNA tests were considered immune.

The staff cohort was surveyed using a structured questionnaire which collected information on demographic characteristics, onset and duration of symptoms and exposure to possible risk factors. Detailed clinical information on in-patient cases was also collected. Data entry on computer was validated using a double entry technique and comparison of the infected and non-infected members of the study cohort was undertaken using  $\chi^2$  and *t*-probability tests.

#### *Parvovirus B19 tests*

Parvovirus B19 specific IgM and IgG were measured by solid phase antibody capture radioimmunoassays [21]. Parvovirus B19 DNA was detected by dot blot hybridization as described previously [22] except that a digoxigenin-labelled probe was used followed by chemiluminescent detection. The quantity of viral DNA in clinical specimens was estimated by comparison with a known concentration of B19 DNA cloned in plasmid pGEM-1 [22].

## RESULTS

Out of 262 health care workers and in-patients tested, 98 (37%) were identified to have been susceptible to parvovirus B19 infection. The mean age was higher ( $P < 0.05$ ) and rates of susceptibility lower ( $P = 0.06$ ), among in-patients compared to those of members of staff (Table 1).

Eighteen subjects were serologically confirmed by specific IgM assay as having had recent parvovirus B19 infections. In addition, four subjects were B19 DNA positive at presentation with concentrations of viral DNA ranging from 10 ng to equal to or greater than 1  $\mu\text{g}/\text{ml}$  of serum. This is equivalent to  $10^9$  to equal to or greater than  $10^{11}$  genomes per ml. Of 18 B19-infected subjects, 3 were in-patients of ward A and 15 were members of staff. Fourteen of the infected members of staff worked on or had regular contact with ward A. No further cases were identified on retesting of susceptible individuals.

#### *Staff cases*

Three subjects had asymptomatic infections. The epidemic curve for the 12 symptomatic cases is shown in Figure 1. Dates on onset of illness were defined as onset of rash (10 cases) or joint pain if rash was not present (2 cases) and ranged from 16 November to 11 December. The first known and possible co-index cases in the ward A outbreak were two staff nurses on the admission ward on the first floor of the hospital. They worked together and regularly accompanied patients to Ward A. It was not possible to assess the degree of contact between the co-index cases and the other staff and patients infected. One of the B19-infected members of staff on Ward A, a doctor, was a close friend of one of the co-index cases. The latter also had frequent social meetings with staff members of Ward A.

The commonest symptoms were joint pain ( $n = 12$ ), rash ( $n = 10$ ) and fever ( $n = 9$ ) with median durations of 3–4.5 days. Nine of the 10 cases with rash reported it to be itchy.

Table 1. Results of B19 antibody tests on staff and patients

Subjects	Tested	Mean age in years	Susceptible (% of those tested)	Recent infection (% of those susceptible)
Ward A patients	22	(59)	6 (27)	3 (50)
Other patients	36	(44)	10 (28)	0 (0)
Ward A staff*	76	(32)	30 (39)	14 (47)
Other hospital staff	128	(30)	52 (40)	1 (2)
Total	262	(35)	98 (37)	18 (18)

\* Includes staff from other departments or wards, who visit ward A regularly.

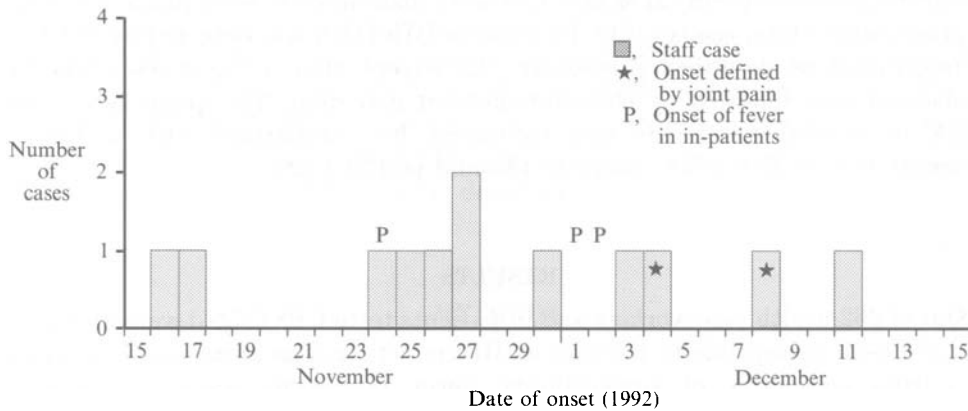


Fig. 1. Onset of illness in staff and in-patients infected with parvovirus B19.

#### *In-patient cases*

Six (27%) of 22 patients on the ward between 1 December and 3 December were susceptible to parvovirus B19 infection. Of these, three acquired the infection. They all had fever but none had any rash or joint pain. All recovered from the infection.

The first, aged 44 years, was admitted on 11 November 1992 and remained in a single room while being treated for carcinoma of the floor of the mouth. He needed extensive oral care as part of his jaw and mouth had been removed. On 24 November, he had fever, was generally very unwell and was suspected of having septicaemia. Blood cultures taken at the time were negative and he was not on any chemotherapy at that stage. A full blood count when compared to another sample taken 10 days earlier showed a substantial drop in haemoglobin level (11.8 g/dl to 9.9 g/dl), in platelet count ( $449 \times 10^9/l$  to  $289 \times 10^9/l$ ) and in granulocyte count ( $9.5 \times 10^9/l$  to  $4.6 \times 10^9/l$ ). His serum was positive for B19 DNA on 1 December and 10 December, suggesting his viraemia had lasted at least 10 days. A planned course of anti-cancer chemotherapy was postponed when his parvovirus B19 infection was confirmed. He was transfused four units of packed red cells on 3 December. On 17 December, he was given an intravenous infusion of normal immunoglobulin (HNIG). He was started on a course of chemotherapy for his cancer on 21 December. His B19 specific IgG response, first recorded on 16 December, remained low at 10 RIA units on 28 January 1993.

The second B19 infected in-patient had been admitted to the ward on 15 November. She was aged 89 years and had been treated for a fractured neck of the femur. The third, aged 59 years, was admitted on 6 November and had been treated for a fractured neck of the femur and osteomyelitis. They had fever on the 1 December and 2 December, respectively. Their infections were uneventful and they were not given HNIG. These two in-patients were in different, non-adjacent open-bays and did not have direct contact with each other or with the first patient.

#### *Risk factor study results*

A total of 76 staff subjects with a mean age of 32 years were identified as having had contact with Ward A during the period of the outbreak (Table 1). Thirty (39%) were initially susceptible to parvovirus B19 infection, of whom 14 (47%) became infected. Twenty-nine of the 30 susceptible and recently infected staff were interviewed.

The attack rates among female subjects and nurses were 59% and 62% compared to attack rates of 33% among male subjects and 38% among non-nursing staff ( $P = 0.2$ ). There was little difference in the mean ages of these groups.

The evaluation of possible risk factors for acquiring parvovirus B19 infection suggested that those who reported washing their hands rarely or only occasionally after patient contact may have been at increased risk compared to those who reported always washing their hands after patient contact (RR = 2.33,  $P = 0.07$ ) (Table 2). It was not however possible to assess the effect of extent of contact with the known infected in-patients. Increased number of hours worked on ward A itself and various locations and rooms, the degree of patient contact, exposure to blood or body fluids, and sharing accommodation with other staff were also not shown to be significant risk factors in acquiring parvovirus B19 infection.

#### *Knowledge of parvovirus B19*

The staff subjects were asked whether they had heard of parvovirus B19 infection, fifth disease, slapped cheek syndrome or erythema infectiosum before the present outbreak. Twelve (42%) of those interviewed including 9 (75%) doctors, 4 (23%) nurses and 1 (25%) other health care worker, reported previous knowledge of parvovirus B19 and parvovirus B19 associated diseases. Eleven (38%) knew of at least one category of patient at risk but only two (7%) of the subjects, both doctors, could list three categories of patients at risk.

#### *Control measures*

Control measures which were implemented from 3 December 1992 by the Hospital Control of Infection committee included (a) the closure of the ward to new admissions until 21 days after the onset of illness of the last case, (b) the screening for B19 immunity of all staff or patients who might be transferred to the ward over the Christmas period before transfer and (c) the restriction of nursing staff on ward A at the time of the outbreak to working only on that ward. As a further measure, to prevent B19 associated fetal morbidity, pregnant women were not allowed access to the ward.

Table 2. *Evaluation of other exposures as risk factors for parvovirus B19 infection*

Exposure	Levels	Infected	Non-infected	RR	95% CI*	Probability†
Wash hands after patient contact	Sometimes	6	1	2.33	1.20-4.51	0.07
	Always	7	12			
Wash before eating	Sometimes	4	6	0.76	0.32-1.82	0.70
	Always	10	9			
Children at home	Yes	2	2	1.04	0.36-3.01	1.00
	No	12	13			
Share accommodation with staff	Yes	6	4	1.42	0.69-2.96	0.45
	No	8	11			
Contact with patients	Many	13	12	2.08	0.37-11.9	0.60
	Few	1	3			
Contact with infected patients	Yes	1	3	0.50	0.09-2.86	0.60
	No	12	12			
Contact with blood	Multiple	12	11	1.57	0.47-5.18	0.65
	Few	2	4			
Contact with infected staff	Yes	10	8	1.48	0.55-3.97	0.67
	No	3	5			

\* Obtained using formulae by Greenland and Robins and are not exact limits.

† Fishers exact probability used due to low cell counts.



## DISCUSSION

In contrast to the two previous well documented reports of nosocomial parvovirus B19 outbreaks [17–18], this one was confined to an adult ward and to our knowledge none of the patients or staff working on nearby children's wards in the hospital were infected. As reported by others [17–18, 23], the proportion of susceptible in-patients (27%) was lower than that of susceptible staff (40%). This was expected as the mean age of the staff was less than that of the patients and the prevalence of immunity increases with age. The attack rate among susceptible staff in contact with ward A was 47%. This was higher than previous reports [17–18] and underlines the infectivity of parvovirus B19 in a hospital setting. A B19-infected patient does not, however, invariably pose a risk of nosocomial transmission. The level of viraemia appears to be an important factor as illustrated by one report documenting the lack of transmission from a chronically infected patient with a low level ( $10^6$  genomes/ml) 19 viraemia [24]. Only 1 of the 18 cases in the present study was immunocompromised and viraemia in him and 3 others was detected at a level of  $10^9$  to equal or greater than  $10^{11}$  genomes/ml. This high level of viraemia may have contributed to the high rate of transmission observed in this outbreak. The high degree of social interaction among members of staff may also have played a part.

The greater proportion of susceptible women becoming infected was a reflection of the higher attack rate among nurses working on that ward than that among other health care workers. The symptoms described by infected individuals were similar to those in other reports although a higher proportion (90%) with a rash described it to be itchy [6, 7, 17, 18].

The first infected in-patient had fever after or at the same time that some of the infected members of staff reported rash illness. The other two in-patients infected were among the last cases to be identified in this outbreak and had no contact with each other or the first in-patient case. It is likely that transmission occurred from staff to these patients and not the other way round. This is the first report of an outbreak where patients may have acquired parvovirus B19 infection from health care workers. This raises the issue of whether serological screening of health care workers caring for patients at higher risk of severe disease following B19 infection (the pregnant, immunocompromised, and those with chronic haemolytic anaemias) and the subsequent monitoring of their susceptibility to parvovirus B19 should be considered.

No particular risk factor for acquiring parvovirus B19 infection could be conclusively identified during this study. This could be due to the number of cases being too small for statistical significance to be obtained. Washing hands rarely or only occasionally after patient contact approached statistical significance as a risk factor (RR = 2.33,  $P = 0.07$ ). The Centers for Disease Control in the United States have suggested that hand washing before and after contact with an infected patient or a contaminated article, although not evaluated, could be a simple and effective measure in the control of parvovirus B19 infections [23]. The importance of hand washing in the control of respiratory spread nosocomial infections, especially on intensive care units (ICU) has been documented [25, 26]. For example in a hospital in Oxford, the incidence of nosocomial infections due to

respiratory syncytial virus (RSV) on a paediatric ward was significantly reduced by a combination of cohorting babies on the ward and encouraging parents and staff to wash their hands before and after patient contact [25]. The possible mechanism for transmission, like RSV [27–28] could be via fomites or respiratory and nasal secretions carried on the hands of infected individuals. Since the period of highest infectivity of parvovirus B19 infection normally occurs before the onset of symptoms or signs of disease, it would now seem prudent that rigorous hand washing practice should be extended to staff touching any patient on an affected ward.

Prophylaxis of susceptible in-patients with intramuscular normal immunoglobulin [17] and respiratory isolation of infected in-patients [18] had been previously reported in other nosocomial outbreaks. These were considered unnecessary here as none of the non-infected patients were regarded to be at high risk of severe sequelae from parvovirus B19 infection. The only high risk in-patient was infected and received intravenous immunoglobulin therapy.

The degree of knowledge of parvovirus B19 virus and related illness was relatively low among non-medical health workers and those with medical backgrounds had trouble naming three categories of persons at risk of more severe sequelae. The outbreak provided an opportunity to increase awareness among hospital staff of a common infection which may have serious consequences for certain categories of patients.

This outbreak also highlighted the need of guidelines in the management of parvovirus B19 infection in hospitals. The measures we instituted were not derived from any existing protocol but devised on the basis of published information about parvovirus B19. It is not known how much they contributed to the containment of the outbreak. The 1993 epidemic of parvovirus B19 in the UK is likely to continue into 1994 and we recommend that hospital control of infection teams plan in advance for nosocomial outbreaks of this infection.

#### ACKNOWLEDGEMENT

We thank Sisters R. Cashman and J. Hunt for contribution to the infection control team; Ms C. Bates and Mr S. Beard for technical assistance with parvovirus B19 assays, and Dr Christine McCartney for help in co-ordinating this study.

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