

## PARVOVIRUS OUTBREAK IN A KINDERGARTEN IN A MUNICIPALITY IN THE NORTH OF PORTUGAL, APRIL-JUNE 2008

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In response to an alert raised due to epidemic exanthematous rashes in children in a kindergarten, an outbreak investigation was carried out in a municipality in the north of Portugal in late spring 2008. The intention was to establish an aetiological diagnosis and take corrective measures if necessary. The warden at the kindergarten was interviewed, and a self-administered questionnaire was given to parents and staff. Blood samples from seven children with facial erythema were collected for serological investigation. Seventeen cases of erythema infectiosum, due to infection with parvovirus B19, were identified and classified as “confirmed”. No cases occurred among the eight adult staff members. An overall attack rate of 38% was observed among the 45 children (born in 2002 and 2003). All cases were mild and without fever. This parvovirus B19 outbreak made it possible to estimate the basic reproduction number ( $R_0$ ) at between 6 and 8 (or above). Staff members, parents and local clinicians were informed that the infection could pose a risk when caught by people with special clinical conditions. All children had received one dose of measles-mumps-rubella vaccine and 60% had received two doses. The seven children with serologically confirmed parvovirus B19 infection were immune to measles and rubella. All seven were negative for measles- or rubella-specific IgM.

### Introduction

The Portuguese vaccination programme includes two routine doses of the combined vaccine against measles, mumps and rubella (MMR), at the recommended ages of 15 months and five or six years [1]. Coverage with the first and second dose of MMR vaccine has reached high and sustained levels in the north of Portugal for years [2]; this also applies to the municipality where this outbreak occurred.

Epidemic exanthematous rashes can have different aetiological causes, and differential diagnosis may be needed in the context of measles elimination programmes in Europe [3]. Previous outbreaks caused by parvovirus B19 have been studied in Portugal [4]. Measles and rubella are statutory reportable diseases in Portugal, and guidelines to study cases of measles were issued in the context of a catch-up vaccination programme in 1998/9 [5]. The Health Ministry has recently issued warnings to all services and health professionals about the possibility of importation of measles due to the international epidemiological situation, and emphasised the need to sustain high vaccination coverage [6]. This is the setting for the alert and response described here.

### Alert

In the morning of 16 April 2008, the local health authority (LHA) was contacted by telephone by a nurse working in the school health programme team. She reported that several children in a kindergarten presented spots on the face. The kindergarten warden suspected that the nearby plane trees were causing an allergic reaction to several young children.

### Preliminary assessment

In the afternoon of 16 April, two members of the LHA visited the kindergarten premises and spoke with the warden. The team examined six children with the spots. The appearance was strikingly similar to pictures published in the literature describing cases of erythema infectiosum, with the typical “slapped face appearance”. All children were in a good physical condition, none had fever or other symptoms, and only one presented a rash in the abdominal region.

It was decided to conduct an outbreak investigation with the main objectives of:

- Testing the hypothesis that it was not a measles or rubella outbreak;
- Establishing an aetiological diagnosis;
- Providing information to the kindergarten community and clinicians on appropriate measures;
- Collecting data on MMR vaccination and taking corrective action if necessary.

### Methods

#### Collection of clinical information

The warden was asked to provide a list with names and birth dates of all members of the kindergarten community (staff and children). Staff members and parents were asked to fill a questionnaire which was collected in the last week of June, a few days before the kindergarten would close for the summer holidays. Just before the holidays, a phone call was made to confirm that no further cases had occurred.

A case was defined as “probable” if erythema on face, extremities or trunk, was observed in members of the kindergarten community between 5 April and 19 June 2008. A case was classified as “confirmed” if in addition to the “probable” case definition it was laboratory-confirmed or had an epidemiological link with a confirmed case.

Written vaccination data from all children and adults were checked by a nurse.

### Laboratory study

A nurse visited the kindergarten on 9 May 2008, to collect blood samples from seven of the children who had presented facial erythema and whose disease onset had been 11 to 34 days before. Enzyme immunoassays (EIA) for specific IgG and IgM antibodies levels against measles, parvovirus B19 and rubella were done by two local general practitioners (GPs), who had been treating the children and previously asked informed consent from the parents.

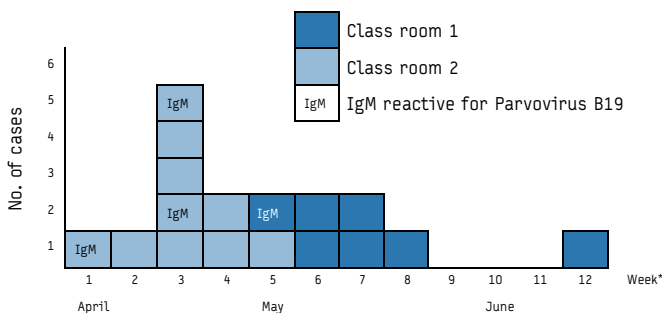
### Results

#### Kindergarten community

The 45 children attending the kindergarten (29 boys and 16 girls) were born between January 2002 and December 2003. There were two groups of children, 20 in class room 1 (13 boys and seven girls) and 25 in class room 2 (16 boys and nine girls). The eight adult staff members were all women, born between September 1954 and August 1972.

FIGURE 1

Epidemic curve of the outbreak of erythema infectiosum in a kindergarten; disease onset by week and class room, Portugal, April-June 2008 (n=17)



\* First day of first week = 31 March 2008

TABLE

Laboratory results of the serological study of kindergarten children with clinical manifestations typical of erythema infectiosum, Portugal, April-June 2008 (n=7)

Case	Age / Sex MMR doses	Ig Class	Measles		Rubella		Parvovirus B19	
			Concentration	Interpretation	Concentration	Interpretation	Assay index	Interpretation
4y / F 1		IgG IgM	3,974 mIU/ml -	Immune Negative	160 IU/ml -	Immune Negative	6.22 <1.00	Reactive Not reactive
4y / F 1		IgG IgM	4,012 mIU/ml -	Immune Negative	68 IU/ml -	Immune Negative	5.18 <1.00	Reactive Not reactive
5y / F 2		IgG IgM	4,093 mIU/ml -	Immune Negative	164 IU/ml -	Immune Negative	6.32 1.32	Reactive Reactive
5y / M 2		IgG IgM	5,090 mIU/ml -	Immune Negative	125 IU/ml -	Immune Negative	6.27 <1.00	Reactive Not reactive
6y / M 2		IgG IgM	5,227 mIU/ml -	Immune Negative	75 IU/ml -	Immune Negative	6.67 2.06	Reactive Reactive
6y / F 2		IgG IgM	6,361 mIU/ml -	Immune Negative	340 IU/ml -	Immune Negative	5.66 1.22	Reactive Reactive
6y / F 2		IgG IgM	538 mIU/ml -	Immune Negative	42 IU/ml -	Immune Negative	6.16 1.47	Reactive Reactive

Note: concentration and interpretation of the results as proposed by the assay manufacturer.

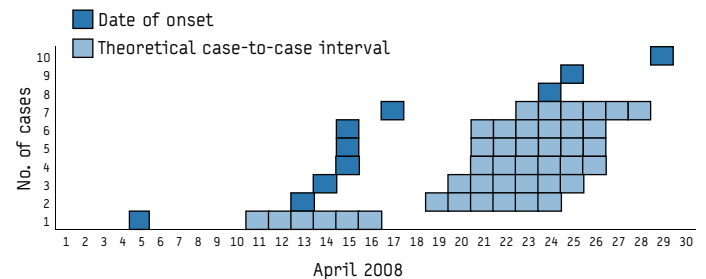
None of the staff members had ever been vaccinated against measles but, following the Portuguese guidelines for their age group, only one was young enough (born in 1972) to have received one dose of that vaccine. All children had received one dose of MMR vaccine at between 15 and 20 complete months of age (mean age at vaccination = 15.9 months). Twenty-seven children (60%) had received a second dose between 60 and 73 complete months of age (mean age at vaccination = 63.9 months). Among the children that had received only one dose, nine had not yet completed six years of age, and the remaining nine had not yet completed the age of seven years.

### Epidemiology

In total, 17 cases were observed among the 45 children and none among the eight staff members. The date of onset of the first known case was on 5 April 2008 and the date of onset of the last case on 19 June 2008. The peak of the outbreak was in the third week, when five cases occurred (Figure 1). The attack rate (AR) among the children was 38% (17/45), 35% among the group in class room 1 and 40% among the group in class room 2 (Figure 1; difference not statistically significant:  $p=0.73$ ). The AR

FIGURE 2

Erythema infectiosum outbreak in class room 2 by date of disease onset, Portugal, April-June 2008 (n=10), with the theoretical case-to-case interval of 6-11 days as proposed by Heegaard and Brown, 2002 [7]



was higher among females (41.7%) than among males (24.1%) but the difference was not statistically significant ( $p=0.29$ ). Five additional cases were reported among the household contacts of the 17 kindergarten cases: four siblings and one parent. None of the staff members became ill.

The days of onset of the 10 cases from class room 2 are graphically represented in Figure 2. If the case-to-case interval is six to 11 days [7], then it is very likely that the first case on 5 April was the primary case, infected outside the kindergarten, while the following six cases were secondary cases, probably infected by the first case. Cases 8 to 10 were a third generation, infected by one or more of the secondary cases (Figure 2). Thus, provided that all children were susceptible before this outbreak and taking into account the definition of the basic reproduction number ( $R_0$ ) [8], the estimated value of  $R_0$  in this outbreak was 6. However, if 25% or more of infections were asymptomatic [9], the  $R_0$  for this outbreak is likely to have had a value of up to 8 or more.

#### **Laboratory study**

Blood samples had been collected from seven of the 17 cases that had occurred before the nurse visited the kindergarten on 9 May. The specific IgM antibody tests for measles and rubella were negative for all seven children tested. Measles IgG concentrations varied from 538 to 6,361 mIU/ml, and all children were classified as "immune". Rubella IgG concentrations varied from 42 to 340 IU/ml and all children were classified as "immune". Regarding parvovirus B19-specific antibodies, all seven children were "reactive" for IgG, but only four were also "reactive" for IgM (Table).

#### **Clinical manifestations**

The seventeen erythema episodes were classified as "confirmed cases" of erythema infectiosum. All other members of the kindergarten were classified as "non-cases", while there were no situations compatible with the definition of "probable case".

The 17 cases presented facial erythema, lasting between two and five days (in 16 children) and 10 days in one child. Eight patients had only facial erythema while the remaining nine also had the rash on the trunk and/or extremities. Itching was reported by two children and none of the cases were febrile. All cases were very mild and no clinical complications were observed.

#### **Control and prevention measures**

The premises were inspected and the procedures were verified; they complied with the Portuguese legal requirements.

The kindergarten staff was informed about the benign nature of erythema infectiosum and the possible risk for pregnant women and those with anaemia and immunodeficiencies. It was recommended to exclude children from the kindergarten if they developed fever. Strict handwashing procedures after contact with patients were recommended. The same information was issued by letter to all parents.

The medical coordinator of the local National Health Service (NHS) unit was informed about the outbreak, the data to be collected and the measures to be taken. An email explaining the situation and the clinical conditions under which parvovirus B19 infection poses a particular risk was sent to all GPs working at the local NHS unit.

#### **Discussion and conclusion**

It was confirmed that the described outbreak was due to infection by parvovirus B19. All seventeen cases unequivocally

met the case definition criteria. The three cases that were not reactive for parvovirus-specific IgM (see Table) had very typical clinical symptoms, and the blood samples had been collected 15, 25 and 26 days, respectively, after the onset of symptoms. We are not sure about the reasons for these negative laboratory results, but we think that low sensitivity of the laboratory method cannot be excluded because the levels of parvovirus B19-specific IgM were generally very low, even in the reactive samples. Although it is arguable whether effective preventive measures can be taken [4,8], the usual recommendations were issued.

Several parvovirus outbreaks had been detected and studied in a neighbouring municipality in 2004 [4]. Should there be a connection between these outbreaks and the one described in this paper, it would be consistent with the reported periodicity of between three and seven years for parvovirus B 19 epidemics in a given community [9]. In 2004, the children described here had not been exposed to the infection because they were attending any kindergarten and didn't have much contact with other children. Moreover, seroprevalence data in 2001-02 showed that the infection was rare in young age groups [10]. We therefore believe that our estimated range for  $R_0$  is likely to be valid. Should there be immune children, then the reported  $R_0$  values would be an underestimate.

No cases were observed among staff members, probably because they were all immune. Recent Portuguese seroprevalence data [10] have shown a high proportion of immune individuals in the age groups of the staff members of the described kindergarten. Furthermore, we believe that their professional activity is associated with increased exposure to parvovirus, compared with the general population.

The virus seems to have entered the kindergarten with the first case and spread first into class room 2 and then into class room 1 (Figure 1). For class room 2, we can identify a likely transmission chain (Figure 2). However, this is more difficult for class room 1, where one or more cases seem to be missing in the period from 20 May to 18 June 2008. This may have been the result of a recall bias by parents and staff or of an unidentified transmission chain outside the kindergarten.

We did not recommend vaccination against measles for adult staff members because previous studies have shown that Portuguese women in those age groups are not only immune to measles but have measles-specific IgG levels well above protective levels [11].

We were able to prove that the outbreak was not measles or rubella. Furthermore, all children had received one dose of MMR vaccine and the levels of measles- and rubella-specific IgG among the seven studied children were well above the protection thresholds. Those children who had not received the second MMR dose were still within the age range recommended for that vaccination. Such high coverage values are consistent with what has been observed in the north of Portugal [2] and in the annual internal evaluations in our municipality (unpublished data).

After the described outbreak investigation, a report on imported cases of measles in Portugal was published [12]. Two importation episodes (in 2005 and in 2008) were identified and reported. The measles cases imported in 2005, affecting migrant Romanian communities, were studied by community physicians (see

Acknowledgements) in two neighbouring municipalities, including the one where the present parvovirus outbreak was observed. These experiences have been helpful in the current parvovirus investigations. Once again, our local public health unit was able to quickly respond to an alert due to an eruptive epidemic disease, and would have detected a measles (or rubella) outbreak, if that had been the aetiology of the cases.

#### **Acknowledgements:**

We acknowledge the parents and staff members of the kindergarten, namely the warden Alexandrina Pereira who was very helpful in this investigation. We are grateful to the nurse Paula Borges who collected the seven blood samples and checked the vaccination records from all kindergarten children. We are also grateful for the valuable cooperation of Graça Cardoso and Deolinda Carneiro, GPs from the local NHS unit, and Eduardo Gouveia and Fátima Basto, community physicians from our public health unit. The community physicians Ana Correia, Alice Pinto and Elisabete Machado, kindly informed us on the investigation of imported measles cases in 2005.

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This article was published on 27 November 2008.

Citation style for this article: Gonçalves G, Dias M. Parvovirus outbreak in a kindergarten in a municipality in the north of Portugal, April-June 2008. *Euro Surveill.* 2008;13(48):pii=19053. Available online: <http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=19053> =