Mem. Inst. Oswaldo Cruz, Rio de Janeiro,
Vol. *88* (3): 497-499, jul./set. 1993

Research Note

PARVOVIRUS B19 ANTIBODIES IN SERA OF PATIENTS WITH UNEXPLAINED EXANTHEMATA FROM BELÉM, PARÁ, BRAZIL

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Distinctive clinical syndromes have been associated with human parvovirus B19 (B19) infection. Erythema Infectiosum (EI), or Fifth Disease, most commonly associated with B19 infection, occurs during childhood as a mild, exanthematous illness, characterized by a facial rash ("slapped cheek" appearance) and a reticulated rash on the extremities and the trunk (L. J. Anderson et al., 1987, *Pediatr. Infect. Dis. J., 6:* 711-718). In patients suffering from chronic haemolytic anemia (e.g. thalassaemia, hereditary spherocytosis, sickle cell disease and autoimmune haemolytic anaemia, as well as in all conditions that lead to severe acute or chronic blood loss) B19 causes transient aplastic crises (TAC) which may sometimes be life-threatening if not treated promptly. This mainly results from the replication of the virus in erythroid progenitor cells (G. R. Sergeant et al., 1988, p. 85-92, In J. R. Pattison, *Parvoviruses and Human Disease,* Boca Raton, Florida, CRC Press, 85-92). Joint involvement occurs as a complication of EI in 8% of cases in children, and up to 80% of adults cases, leading to acute arthritis which is very similar to that of patients with acute rubella infection (E. A. Ager et al., 1966, *N. Engl. J. Med., 275:* 1326-1331; M. J. Anderson et al., 1984, *J. Hyg, 92:* 85). Parvovirus B19 has also been implicated in the occurence of chronic infection among imunocompromised patients, followed by chronic anaemias (G. L. Kurtzman et al., 1988, *Lancet, ii:* 1159-1162). Although most of pregnancies complicated by B19 infection proceed without foetal damage, it is currently recognized that spontaneous abortion may occur; congenital malformation, however, has not been attributed to B19 infection (S. M. Hall et al., 1990, *Br. Med. J., 300:* 1166-1170).

The worldwide distribution of B19 has been assessed by several authors, affecting mainly children with ages comprised between 4 and 10 years. In addition, at least 60% of adults are seropositive (M. J. Anderson, 1988, p. 93-104, In: J. R. Pattison, *Parvoviruses and Human Disease,* Boca Raton, Florida, CRC Press.

In Brazil, the association between parvovirus B19 and Fifth Disease was first detected in Belém (M. F. R. de Miranda et al., 1989, *Rev. Inst. Med. Trop. São Paulo, 31:* 359-362). Seroprevalence studies conducted by J. P. Nascimento et al. (1990 *Rev. Inst. Med. Trop. São Paulo, 32:* 41-45) in Rio de Janeiro, Brazil, yielded rates which ranged from 35%, among children less than five years old, to over 90% in individuals older than 50 years. On the other hand, in Northern Brazil, R. B. de Freitas et al. (1990, *J. Med. Virol., 32:* 203-208) found a seroprevalence rate of 42.6% for an urban population, whereas rather lower frequencies (ranging from 4.7 to 10.7%) were recorded among Amerindians belonging to three relatively isolated communities.

During the past two decades, the aetiology of a significant proportion of "rubella-like illnesses" in our region (and probably in the whole country) could not be elucidated, in spite of the routine use of conventional laboratory techniques for diagnosis of rubella, measles, enteroviral and arboviral diseases, as well as other non-viral exanthemata. This leads us to postulate that B19, and possibly other viruses, such as human herpesvirus 6 (K. Yamanish et al., 1988, *Lancet i:* 1065-1067) might have caused some of those unexplained exanthemata, particularly in infancy and childhood. It would therefore be of practical importance setting up

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Received 4 March, 1993.
Accepted 8 June, 1993.

locally laboratory methodology that could broad the diagnostic scope for exanthematous disease.

The present report deals with the detection of parvovirus B19 antibodies in sera obtained from patients with unexplained exanthemata from Belém, Pará, Brazil, during 1989 and 1990. Serum samples were obtained from 42 (11.2%) out of 376 individuals (Table), including children and adults of both sexes attending the Virology Service of IEC, in whom exanthema, lymphnode swelling and fever were observed: acute – and convalescent – samples were obtained from 19 (45.2%) of them. All these "rubella-like illnesses" were routinely investigated by standard serological procedures for the diagnosis of following infections: rubella and measles (either fourfold rise in haemagglutination inhibiting, HI, antibody or presence of specific IgM); infectious mononucleosis (as assessed by an elevated heterophile antibody titer after absorption of the serum with guinea-pig kidney); toxoplasmosis (through the detection of specific, fluorescent IgM antibody) and arboviral diseases (as demonstrated either by high titers of HI antibody or seroconversion). This latter group included Oropouche, Mayaro and Dengue viruses. In addition both faecal specimens and throat swabs were inoculated onto monolayer cultures of Vero and HEp 2 cells and, intracerebrally, into suckling mice; both systems were observed daily, during two weeks, for signs of infection either by echo or coxsackie viruses. Because local facilities were not available, sera were sent to the "Regional Virus Laboratory, East Birminghan Hospital", Birmingham, U.K., to be tested for the presence of anti-B19 antibodies. Briefly, following inactivation of samples at 56 oC for 30 minutes, both anti-B19 IgM and IgG were determined by antibody capture radioimmunoassays, as essentially described by B. J. Cohen et al. (1983, J. Hyg. (Camb.), 91: 113-130).

All investigations for infections with rubellavirus, measlesvirus, Epstein-BAAR virus (EBV), arboviruses, enteroviruses and *Toxoplasma gondii* had ruled out recent infection by these agents. Two out of the 42 patients (4.8%) had serological evidence of recent B19 infection and eleven (26.2%) had evidence of past parvovirus infection. No antibody response could be detected among infants aged less than one year. On the other hand, the highest seroprevalence rate was noted in the 6-15 year-old group, 67.0%. As to the frequencies of antibody among sexes, no consistent difference could be observed between male and females.

TABLE

Parvovirus B19 antibodies in sera of patients with unexplained exanthemata from Belém, Pará, Brazil

	Sex			B19 IgG antibody (%)		
Age	F	M	F+M	F	M	F+M
< 1	6	5	11	0 (0.0)	0 (0.0)	0 (0.0)
1 – 5	5	8	13	2[a] (40.0)	1[a] (13.0)	3 (23.0)
6 – 15	6	3	9	3 (50.0)	3 (100.0)	6 (67.0)
> 15	8	1	9	3 (38.0)	1 (100.0)	4 (44.0)
All ages	25	17	42	8 (32.0)	5 (29.0)	13 (31.0)

a: numbers indicate *numbers* of sera; 1 serum parvovirus B19 IgM positive.

A remarkable difference ($p < 0.001$) is noted if a comparison is made between the frequency of B19 IgM positive patients with rash in the present investigation, 5%, with the rate of recent parvovirus infection in cases of exanthem, 28.2%, previously reported by R. B. de Freitas et al. (loc. cit.). Results from both studies also do not parallel if seroprevalence rates, as measured by B19 IgG antibody only, are compared. In the previously conducted study, 11.5% of patients were B19 IgG seropositive, whereas 26.2% of individuals included in the presently described serosurvey had evidence of past parvovirus infection. Since the laboratorial methodology used in the two studies were essentially the same, and age/sex distributions were comparable, the above mentioned difference could not, in principle, be attributable to these factors. However, it should be pointed out that serum samples from the first study were collected during 1988/1989, when an unusual high number of cases of EI were diagnosed, on clinical grounds, by local dermatologist (A. C. Linhares et al., 1991, *An. B. ras. Derm., 66:* 281-287). In contrast, sera included in the present study were mainly obtained in 1990; serum samples from only 9 patients were collected in Nov./Dec. 1989. In this latter period the number of cases clinically diagnosed as EI were significantly lower than in 1988/1989. In this respect it should be pointed out that the prevalence of B19 infection, in addition to the seasonality, has a cyclical pattern characterized by several years of high infection rates followed by several years

of low infection rate (L. J. Anderson, 1990, *J. Infect. Dis., 161:* 603-608).

Although the current knowledge on B19 epidemiology indicates that infection is most commonly acquired between 4 and 10 years of age (M. J. Anderson, 1982, *J. Hyg., 89:* 1-8; J. M. B. Edwards et al., 1981, *J. Infect. Dis., 3:* 316-326), only two cases of recent B19 infection in the present investigation occurred among children aged 1-5 years.

With respect to the aetiology of the studied 42 exanthematous cases, the possible role of cytomegalovirus in "mononucleosis-like" syndromes cannot yet be ruled out, as specific diagnostic tests could not be performed. In addition, both the clinical examination of patients (performed by experient dermatologists) and absence of leucocytosis in many cases make the bacterial aetiology very unlike.

A satisfactory awareness of local physicians on the importance of B19 as a human pathogen, as well as the local availability of both rapid and sensitive techniques for diagnosis of infection by this agent can be currently regarded as goals to be yet fully achieved in our region and probably in the rest of Brazil. In addition, in the Amazonia the potential of arboviruses for causing exanthematous illnesses should be routinely considered, particularly in rural areas. The currently emerging importance of human herpesvirus 6 (W. L. Irving, 1992, *J. Med. Microbiol., 36:* 221-222), the causative agent of exanthema subitum, anticipates the need to further broaden our diagnostic scope of viral agents of exanthemata.

Acknowledgements: to Dr Elisabete Santos for performing rubella diagnosis and to Mr Antonio de Moura for technical assistance.