PARVOVIRUS B19 ANTIBODIES IN SERA OF PATIENTS WITH UNEXPLAINED EXANTHEMA FROM BELEM, PARA, BRAZIL

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Distinctive clinical syndromes have been associated with human parovirus B19 (B19) infection. Erythema infectiousum (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, Paroviruses 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). Parovirus B19 has also been implicated in the occurrence of chronic infection among immunocompromised 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, Paroviruses and Human Disease, Boca Raton, Florida, CRC Press).

In Brazil, the association between parovirus 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 dis-

ease.

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), in-
cluding children and adults of both sexes at-
tending 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 pro-
duced for the diagnosis of following infections: rub-
ella and measles (either fourfold rise in
haemagglutination inhibiting, HI, antibody or
presence of specific IgM); infectious mono-
nucleosis (as assessed by an elevated hetero-
philic antibody titer after absorption of the
serum with guinea-pig kidney); toxoplasmosis
(through the detection of specific, fluorescent
IgM antibody) and arboviral diseases (as dem-
onstrated 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
Birmingham Hospital”, Birmingham, U.K., to
be tested for the presence of anti-B19 antibo-
dies. 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-BAAV ri-
virus (EBV), arboviruses, enteroviruses and Toxo-
plasma 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 differ-
ence could be observed between male and
females.

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| Parvovirus B19 antibodies in sera of patients with
| unexplained exanthemata from Belem, 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 | 29 (40.0) | 19 (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 parvo-

virus 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 re-
cent 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 com-
pared. 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 essen-
tially the same, and age/sex distributions
were comparable, the above mentioned differ-
ence 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 di-
agosed, on clinical grounds, by local derma-
tologist (A. C. Linhares et al., 1991, An. B.
ras. Derm., 66: 281-287). In contrast, sera in-
cluded in the present study were mainly ob-
tained in 1990; serum samples from only 9
patients were collected in Nov./Dec. 1989. In
this latter period the number of cases clini-
cally diagnosed as EI were significantly lower
than in 1988/1989. In this respect it should be
pointed out that the prevalence of B19 infec-
tion, in addition to the seasonality, has a cy-
clical pattern characterized by several years of
high infection rates followed by several years

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.