## **RESEARCH NOTE**

# PREVALENCE OF ANTIBODIES TO PARVOVIRUS B 19 IN THAILAND

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**Abstract.** Infection with human parvovirus B 19, a single-stranded non-enveloped DNA virus of worldwide distribution, is rather common and displays a broad spectrum of clinical manifestations of varying severity, depending on the patient's immune response. As the target of infection are the erythroid precursor cells, patients can experience an aplastic crisis. Usually, at least in immunocompetent individuals, viremia ceases with the appearance of virus-specific antibodies in the patient's serum whereupon the patients retain lifelong immunity to reinfection. Since data as to the prevalence of this agent has not been established for Thailand, the purpose of the present study was to investigate its frequency among 3 distinct groups, comprising 30 healthy children, 64 children with acute unrelated illness, and 35 voluntary blood donors, respectively, by means of enzyme linked immunosorbent assay. Our results have shown that, as reported for other countries, anti-parvovirus IgG increases in an age-dependent manner and is established at an overall prevalence of 20.16%, inviting the conclusion that the local population is infected by this agent as frequently as those of other countries in the Far East. Further studies need to be undertaken in order to elucidate its prevalence among members of high-risk groups.

Parvovirus B 19 constitutes a non-enveloped human DNA virus of world-wide distribution whose single-stranded genome comprises 5.6 kb (Shade et al, 1986). It was first discovered in the sera of healthy blood donors and patients, one of whom had acute hepatitis (Cossart et al, 1975). Human parvovirus B 19 infection is rather common, with seroprevalence rates in adults amounting to approximately 50%. At the age of 70, seroprevalence reaches to more than 80% (van Elsacker-Niele and Kroes, 1999). It displays a broad spectrum of clinical manifestations such as erythema infectiosum in children, aplastic crisis in patients with hemolytic anemia, chronic bone marrow failure in immunocompromised hosts, and hydrops fetalis after intrauterine infection (Yoto et al, 1996). Infants surviving parvovirus B 19 induced hydrops fetalis can have congenital hepatic dysfunction (Metzman et al, 1989) and those who die have hepatitis (Naides, 1993).

Altogether, parvovirus B 19 is a ubiquitous virus so that by 15 years of age, approximately 50% of individuals display serologic evidence of past

infection (ven Elsacker-Niele and Kroes, 1999) which may have presented as the common childhood disease erythema infectiosum. Infection with this agent can induce several clinical manifestations of varying severity, depending on the respective patient's immune status. Along those lines, aplastic crisis in chronic hemolytic anemia, exanthematous disease and arthropathy, mainly in women, and chronic anemia in the immunocompromised host have been observed. After initial replication, probably in the respiratory tract, the virus enters its target cells in the bone marrow, erythroid precursor cells, through its receptor, the blood group P antigen (van Elsacker Niele and Kroes, 1999). Ensuing viral replication leads to an arrest in erythropoiesis which usually lasts approximately 1 week. At this stage, patients under 'erythropoietic stress' can experience an aplastic crisis. Viremia ceases as virus-specific antibodies appear in the patient's serum, which may trigger potentially immune-mediated symptoms such as a rash or arthralgia. Thereupon, at least in immunologically normal individuals, the infection is cleared within several weeks by humoral immune response, with detectable specific IgG conferring lifelong immunity to reinfection. In patients with dysfunctional or altogether absent humoral immunity, on the other hand, persistent infection resulting in chronic suppression of erythropoiesis with chronic anemia can occur (van Elsacker-Niele and Kroes, 1999).

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% ant-parvovirus B19 IgG

Fig 1–Prevalence of antibody against parvovirus B 19 among different age grougs.

In addition, in a pediatric patient group surprising similarities of presentation between human parvovirus B 19 infection and systemic lupus erythematosus (SLE) have been observed in that the patients not only displayed SLE-like symptomatology but also positive serology suggestive of SLE (Moore *et al*, 1999).

Since its discovery in 1975 (Cossart et al, 1975), the prevalence of parvovirus B 19 infection has been investigated in various geographic locations, such as the United Kingdom (Cohen and Buckley, 1989), Hong Kong (Lim et al, 1997), Taiwan (Lin et al, 1999) and Brazil (Nascimento et al, 1990), among patients positive for the human immunodeficiency virus in Spain (Negredo et al, 1998) and Sweden (Gyllensten et al, 1994), as well as among patient groups with defined hematologic diseases in the United States (Pardi et al, 1998; Ragni et al, 1996). In contrast, data for Thailand are altogether nonexistent. Hence, particularly in the context of transfusion- and transplant-related viral hepatitis which might affect pediatric patients receiving immunosuppressive therapy, our group initiated an investigation into the prevalence of parvovirus B 19 for epidemiological evaluation in Thailand.

The population investigated comprised three groups consisting of (a) 30 healthy children who attended the well-baby clinic, Chulalongkorn Hospital, for the purpose of hepatitis B immunization and/or follow-up, (b) 11 children with acute illness or elective surgery admitted to the Department of Pediatrics, Chulalongkorn Hospital, as well as 53 admitted to Hat Yai Hospital, Songkhla Province, and (c) 35 voluntary blood donors between 16 and 51 years at the National Blood Center, Thai Red Cross.

Blood samples were obtained in the course of two years, between 1998 and 1999, sera were separated by centrifugation and stored at -20°C until further analysis. The sera were subjected to enzyme linked immunosorbent assay (ELISA) using the commercially available Human Parvovirus B19 (recombinant) ELISA kit (Genzyme Virotech GmbH, Germany) according to the manufacturer's specifications.

As shown in Fig 1, immunity to parvovirus B 19 increases with age among healthy individuals in Thailand. Consequently, the percentage of antiparvovirus B 19 IgG rose steadily from 11.9% (5/ 42) within the lowest age group (0-6 years) over 19.05% (8/42) and 25% (3/12) within the intermediate age groups (7-12 and 13-19 years, respectively) to 30.3% (10/33) within the highest age group tested (20-51 years). The overall prevalence amounted to 20.16% (26/129).

From the age-specific prevalence of antiparvovirus B 19 IgG established for Thailand, we can conclude that the local population encounters this agent at frequencies comparable with those determined for some other countries in Asia. Along those lines, the overall prevalence of anti-parvovirus B 19 IgG and IgM was found to amount to 32.8% and 0.35%, respectively, in Taiwan (Lin et al, 1999). In Hong Kong, between 1983 and 1993, a low incidence of parvovirus infection leading to a shift in the prevalence rate among the general population was observed in that from 1991 to 1996, only 2.5% of patients presenting with illness potentially caused by parvovirus B 19 were positive for IgM and 19.6% for IgG (Lim et al, 1997). A seroepidemiological survey conducted in Singapore showed the prevalence of anti-parvovirus B 19 IgG at 0% among children below the age of 5 years, 3.5% among the 5-to-14-year olds, 7.7% among teenagers between 15 and 19 years, 10.3% among those between 20 and 24, 28% among those between 25 and 34, and 65% among those above the age of 35 years (Matsunaga et al, 1994). This study also very clearly mirrors the age dependent frequency of anti-parvovirus B 19 which we have observed in our study. Agedependent antibody prevalence has also been demonstrated, along with a drastically increased frequency, among the population of Rio de Janeiro (Nascimento et al, 1990) where anti-parvovirus B 19 IgG was demonstrated at 35% among children below the age of 5 years, at almost 80% in children between 11 and 15 years old, and above 90% among those older than 50 years.

Particularly with reference to the Brazilian study, it appears as though parvovirus B 19 infection were generally less prevalent in Southeast Asia than elsewhere. Elucidation of the reasons underlying this difference, as well as the clinical significance attributable to the virus infecting immunocompromised hosts in the same environment will require further investigations.

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#### REFERENCE

- Cossart YE, Cant B, Field AM, Widdows D. Parvoviruslike particles in human sera. *Lancet* 1975; 1: 72-3.
- Cohen BJ, Buckley MM. The prevalence of antibody to human parvovirus B 19 in England and Wales. J Med Microbiol 1988; 25: 151-8.
- Gyllensten K, Sonnerborg A, Jorup-Ronstrom C, Halvarsson M, Yun Z. Parvovirus B 19 infection in HIV-1 infected patients with anemia. *Infection* 1994; 22: 356-8.
- Lim WL, Wong KF, Lau CS. Parvovirus B 19 infection in Hong Kong. J Infect 1997; 35: 247-9.
- Lin KH, You SL, Chen CH, Wang CF, Yang CS, Yamazaki S. Seroepidemiology of human parvovirus B 19 in Taiwan. J Med Virol 1999; 57: 169-73.
- Matsunaga Y, Goh KT, Utagawa E, Muroi N. Low prevalence of antibody to human parvovirus B 19 in Singapore. *Epidemiol Infect* 1994; 113: 537-40.
- Metzman R, Anand A, deGiulio PA, et al. Hepatic disease

associated with intrauterine parvovirus B 19 infection in a newborn premature infant. J Pediatr Gastroenterol Nutr 1989; 9: 112-4.

- Moore TL, Bandlamundi R, Alam SM, Nesher G. Parvovirus infection mimicking systemic lupus erythematosus in a pediatric population. *Semin Arthritis Rheum* 1999; 28: 314-8.
- Naides SJ. Parvovirus B 19 infection. Rheum Dis Clin North Am 1993; 19: 457-75.
- Nascimento JP, Buckley MM, Brown KE, Cohen BJ. The prevalence of antibody to parvovirus B 19 in Rio de Janeiro, Brazil. *Rev Inst Med Trop Sao Paulo* 1990; 32: 41-5.
- Negredo E, Domingo P, Rabella N, Lopez-Contreras J, Fontanet A, Orellana I. Prevalence of parvovirus B 19 infection among patients with human immunodeficiency virus infection in Barcelona, Spain. Arch Intern Med 1998; 158: 680-1.
- Pardi DS, Romero Y, Mertz LE, Douglas DD. Hepatitisassociated aplastic anemia and acute parvovirus B 19 infection: a report of two cases and a review of the literature. Am J Gastroenterol 1998; 93:468-70.
- Ragni MV, Koch WC, Jordan JA. Parvovirus B 19 infection in patients with hemophilia. *Transfusion* 1996; 36: 238-241.
- Shade RO, Blundell MC, Cotmore SF, Tattersall P, Astell CR. Nucleotide sequence and genome organization of human parvovirus B 19 isolated from the serum of a child during aplastic crisis. J Virol 1986; 58: 921-36.
- van Elsacker-Niele AM, Kroes AC. Human parvovirus B 19: relevance in internal medicine. *Neth J Med* 1999; 54: 221-30.
- Yoto Y, Kudoh T, Haseyama K, Suzuki N, Chiba S. Human parvovirus B 19 infection associated with acute hepatitis. *Lancet* 1996; 347: 868-9.