

## LETTER TO EDITOR

### RESURGENCE OF MEASLES VIRUS IN SÃO PAULO, BRAZIL

São Paulo, December 30<sup>th</sup>, 2011

Dear Sir:

The resurgence of measles was reported in the state of São Paulo (SP) in 2011 after the endemic transmission of the virus had been interrupted for 10 years. Following the standards of the Pan American Health Organization (PAHO), with the use of several strategies of vaccination programs, Brazil managed to reduce its number of circulating chains of transmission of the virus<sup>5</sup>.

The epidemic that occurred in SP in 1997 showed the circulation of the D6 group. After this period there was a decrease in the individuals susceptible to it. Due to good strategies for the close observation of measles virus, the circulation of indigenous cases was not registered for the mentioned period. However, in 2001, 2002 and 2005, cases of an imported virus belonging to the group D5 was registered<sup>2,3,4</sup>.

The genetic characteristics of wild-type measles viruses were determined by sequencing the gene coding for the hemagglutinin (H) and the terminus of the nucleoprotein (N) genes that contain nucleotide variability from 7% to 12% among various wild-type viruses. Results assigned the viruses to various genetic groups. With the introduction of molecular analysis, it has become possible to evaluate if viruses have been introduced from external sources. As outbreaks of measles take place worldwide on a regular basis, the transmission of the newly introduced viral genotype is possible<sup>6</sup>.

In SP, the suspected cases of MV were reported by the Epidemiological Surveillance Center (CVE-SP). Measles infection was processed at the Adolfo Lutz Institute, and positive results were reconfirmed by Fundação Oswaldo Cruz (Rio de Janeiro, Brazil). The presence of MV infection was diagnosed using an IgM ELISA test commercial Kit (Enzygnost Anti-Measles-Virus/IgM/IgG, Siemens Healthcare Diagnostics, Marburg, Germany). The first and second serum samples by IgG conversion of title were also tested, according to the manufacturer's instructions. Peripheral blood lymphocyte cells (PBMCs) were separated from heparinized blood with Ficoll-hypaque gradients. MV was isolated from PBMC, nasopharyngeal swab and urine samples in a Vero/hSLAM cells line<sup>1</sup>. After seven days of culture, during the first and second passages, respectively, the isolated MV showed a cytopathic effect characteristic of MV. Samples of the virus isolated from growing and original samples were used for RNA extraction by QIAamp Viral RNA Mini Kit (Qiagen, CA, USA). Replicate serum samples were subsequently quantified by Real-Time Quantitative PCR (qRT-PCR) using the LightCycler technology, Invitrogen reagents (Carlsbad, CA, USA), which is the protocol recommended by the Centers for Disease Control and Prevention

(CDC). The COOH-terminal region of the nucleoprotein (N) was amplified<sup>6</sup>. The reaction products were analyzed by using the DyeDeoxy terminator v3.1 Cycle sequencing Kit (Applied Biosystems, Foster City, CA). Phylogenetic trees were constructed by maximum likelihood (ML) software and analysis was carried out using the PAUP 4.0 b10 software (Sinauer Associate, Inc., Sunderland, MA, USA).

In 2011, a total of 1,112 suspected cases of MV infection were analyzed. The patients were aged between six months and 40 years old, with and without vaccinations. Twenty-six of them (2.3%) were positive for measles-specific immunoglobulin (IgM) by ELISA or qRT-PCR, and the genetic characterization was carried out in 11 of the 26 confirmed cases. The amplified sequences were compared with the sequences of the GenBank reference strains. The results indicated that this virus had an identical N gene sequence and was a member of genotype D4.

Studies conducted by the World Health Organization (WHO) report that sequences registered at the database in 2010 belong to genotype D4, which shows that the recent outbreaks in different parts of the world have been caused by this genotype<sup>6</sup>.

In São Paulo, the virus was reintroduced as an imported case. The phylogenetic analysis showed only one genotype circulating group D4. This finding may contribute to establishing and maintaining international chains of transmission of the measles virus. This fact strengthens the importance to continue the close observation of measles in the state and as a means to investigate whether new policies are needed to eliminate measles worldwide.

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