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Importation of the Evolving Measles Virus Genotype D9 to Yamagata, Japan from Thailand in 2009

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The measles control project led by the World Health Organization (WHO) is ongoing with a current target of measles elimination in the WHO Western Pacific Region, including Japan, by 2012 (1). Laboratory-based surveillance plays an important role in the control of measles. Although IgM enzyme-linked immunosorbent assay (ELISA) is used as the standard method for confirming measles cases (2), virus isolation and genome detection by reverse-transcription PCR (RT-PCR) have also been carried out at most of the public health laboratories in Japan. WHO currently recognizes 23 genotypes of the measles virus (MV) (3). We reported an outbreak of measles caused by genotype D9 (D9) at a junior high school in Yamagata, Japan in 2004 (4).

We recently experienced an imported measles case caused by D9 in Yamagata Prefecture, Japan in 2009. The suspected case was an unvaccinated 7-month-old boy. He visited Bangkok, Thailand with his parents and returned to Japan at Narita International Airport on March 1st, and then moved to Yamagata City by airplane on March 2nd. He developed fever, cough, rhinorrhea, and rash on March 16th, 2009. He was clinically suspected of having measles. Throat swab and blood specimens were collected on March 19th for virus isolation, genome detection, and sequence analysis as described previously (4). There were no suspected cases of secondary infection.

MV (MVi/Yamagata/Jpn/12.09) was isolated using Vero/hSLAM and B95a cell lines from the blood specimen and the MV genome was detected in both throat swab and blood specimens. The blood specimen was positive for IgM antibody against MV by ELISA. The N gene sequences of the isolated MV and of the genomes detected in the specimens were identical. A BLAST search showed that this sequence (GenBank accession no. AB509376) was similar to D9 and identical to the three strains reported in Thailand (FJ356073, FJ356075, and FJ356077). The results along with the patient's history indicated that he was infected with MV D9 in Thailand. There was a 2.9% (13/456) divergence in the N gene and a 1.3% (24/1,854) divergence in the H gene (AB509377) between MVi/Yamagata/Jpn/12.09 and the D9 reference strain Victoria.AUS/12.99. The sequence divergence of greater than 2.5% in the N gene fulfilled the requirement for the classification

as a new genotype; however, the divergence of 2.0% in the H gene did not (5). There was a 1.3% (6/456) divergence in the N gene between MVi/Yamagata/Jpn/12.09 and D9 isolates in Yamagata in 2004. These results and a phylogenetic tree based on registered D9 sequences as shown in Fig. 1 suggest that the D9 strains have been evolving.

Virological surveillance has revealed that, in Japan, the predominant genotype was C1 before 1985, D3 in the 1987-1988 outbreak, D5 in 1991-1993, H1 in 2002-2003, and D5

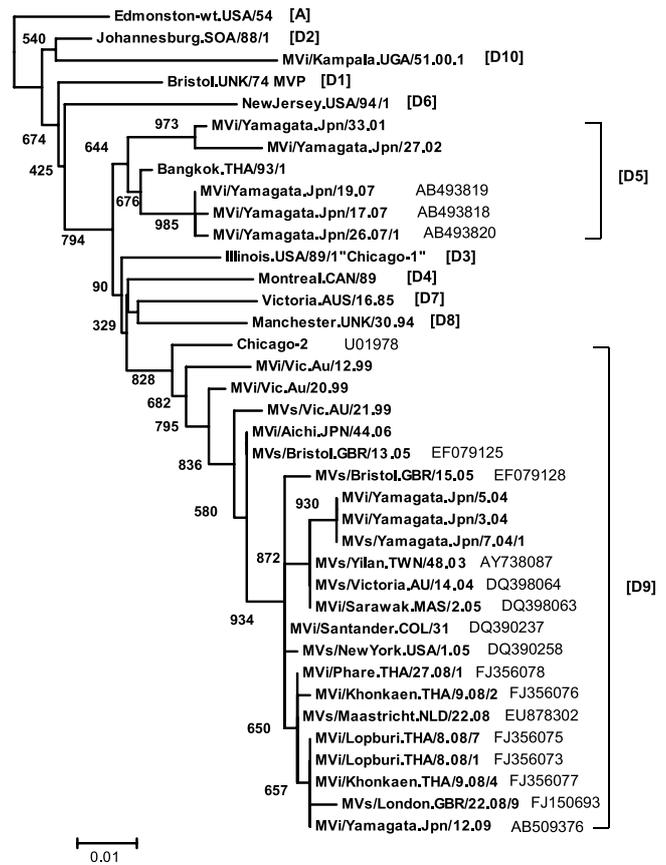


Fig. 1. Phylogenetic tree of genotype D measles viruses isolated in Yamagata, Japan in 2001-2009, genotype A and D reference strains (4-6,8), and genotype D9 strains registered in GenBank (accession numbers are shown after the strain name). The tree was based on the nucleotide sequences (456 bps) of the nucleoprotein and was generated by the CLUSTAL W program. The scale indicates 1% nucleotide differences. The numbers are the bootstrap probabilities (%).

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again since 2006 (1,6). The genotypes of MVs detected in Yamagata have been consistent with the changes in the national surveillance data (4). Minor genotypes have also been reported in Japan along with the predominant MV genotype. In 2004, we reported an MV outbreak caused by D9, which had not previously been reported in Japan (4). In May of 2008, a D4 strain was isolated from a patient returning from Israel, and possible imported cases due to H1 were reported in February and March of that year in Osaka, Japan (7). These findings suggest frequent importation of MVs into Japan from abroad.

Analysis of chronological and geographical changes in circulating genotypes reveals that MV D9 strains have evolved and circulated internationally. Although an increase in vaccination coverage is of primary importance for control of measles epidemics, careful surveillance of MV circulation and transmission pathways using laboratory-based surveillance techniques such as genotyping is also of importance.

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