Mumps Virus Genotyping: Basis and Known Circulating Genotypes

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Abstract: Although mumps virus (MV) is considered antigenically monotypic, twelve different genotypes of MV based on genetic variation in the SH gene (A to L) are currently recognised by the WHO. Both dominance of a single genotype and co-circulation of different genotypes in the same geographical area, as well as temporal replacement of genotypes have been described in different countries. The different histories of genotype importation, variations in vaccine coverage and the use of different vaccine strains in each country results in a complex picture that could be the cause of the different geographical patterns of mumps virus genotype circulation observed in different countries. Lack of full cross-protection between different genotypes has been reported and has been suggested as a cause of vaccine failure, especially for vaccine strains belonging to genotype A, which is genetically distant to the remaining genotypes that include most of the currently circulating wild strains. Finally, a differential ability to invade the neural system has been suggested for some particular strains belonging to genotype D.

Keywords: Mumps, molecular epidemiology, genotypes.

INTRODUCTION

Mumps is a highly transmissible but usually benign disease characterized by fever and swelling of the salivary glands. It is distributed worldwide and in the absence of vaccination it is a childhood disease. However, in some cases, clinical complications can arise such as bilateral orchitis or self-limited meningitis. More serious complications such as encephalitis, deafness, sexual male sterility, and pancreatitis may occur but these are rare [1].

Mumps is caused by Mumps virus (MV), which belongs to the genus Rubulavirus of the subfamily Paramyxovirinae in the family Paramyxoviridae (Order Mononegavirales). Other important human pathogens belonging to the same genus are the human Parainfluenza virus 2 and the human Parainfluenza virus 4. MV is antigenically monotypic which in principle allows commercial vaccines to protect against all circulating strains. Thus, mumps vaccination has been incorporated into the regular immunization schedule of many countries, usually along with measles and rubella vaccines in a triple formulation. These vaccines have enabled the WHO to establish global strategies for the advanced control of measles and rubella leading to an elimination target in some regions. However, in contrast to rubella and measles, secondary vaccine failure occurs frequently in the case of mumps and circulation of MV within highly vaccinated populations has been frequently reported [2-7].

Twelve different genotypes of MV based on genetic variation in the SH gene are currently recognised by the WHO [8-10]. Although all of them are considered to be the same serotype, lack of full cross-protection between different genotypes has been reported [11] and has been suggested as a cause of vaccine failure. However, other reports did not find this lack of cross reaction among different genotypes [12]. Also, it has been suggested that different genotypes may differ in their ability to invade the neural system and cause disease [13, 14] although this is not universally accepted to be the case.

Previous experience with elimination programmes for other vaccine-preventable diseases as measles, rubella or polio suggests that genotyping is an important tool for epidemiological surveillance [15], since it makes it possible to trace the patterns of viral circulation. Recently, the WHO has recommended genotyping for monitoring circulating MV genotypes in the context of surveillance programmes and has provided the first standardization protocols.

This has led to a series of molecular epidemiology studies which providing data on MV genotype distribution [10, 16-29].

In the present manuscript we review these studies which demonstrate the usefulness of MV genotyping for the epidemiological surveillance of MV.
METHODS OF MUMPS VIRUS GENOTYPING

The WHO recommended a standardized scheme for MV genotyping established by an international group of experts in a Weekly Epidemiological Record published in 2005 [15]. It is based on sequence analysis of the so-called small hydrophobic (SH) gene. Standard nomenclature for strains (country code, year, strain and genotype) and criteria for establishing new mumps genotypes were also proposed. The following steps are required.

1. Sequencing of the 316 nucleotides of the SH gene to detect strains that diverge more than 5% from reference strains.
2. Identification of at least 2 identical strains (to avoid technical error).
3. Submission of sequence data to public databases such as GenBank, together with the strain name and data source.

A subsequent article published the same year by the same group [8] provided a table listing the reference strains for genotypes A to L, as well as for three possible new genotypes. Interestingly, one of these potential new genotypes includes the vaccine strains L-Zagreb and Leningrad-3, that remain unassigned. A new genotype (M) has been proposed for strains circulating in Brazil in 2006-2007 [30]. Although no specific procedures for sequence analysis were described, the authors use Neighbour-Joining analysis with Kimura 2p model and 1000 replications for bootstrapping. A similar tree containing the reference sequences is shown in Fig. (1).

Finally, different subgenotypes have been described for genotypes D (D1, D2), G (G1, G2) and H (H1, H2) [10] which are widely reported in the literature.

MUMPS VIRUS GENOTYPE DISTRIBUTION

Data about mumps genotypes are available in reports from different European countries such as Belarus [31],

![Diagram](image-url)
Mumps Virus Genotyping

Mumps Virus Genotyping and Neurotropism

Mumps Virus Genotyping and Vaccines

Mumps Virus Genotyping and Vaccine Failure

References
The mumps virus.


Mumps Virus Genotyping

