Commentary: Ongoing debate over the safety of the different mumps vaccine strains impacts mumps disease control

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The worldwide use of vaccines has resulted not only in significant achievements in controlling disease but also in disease eradication; smallpox was eradicated in 1977 and there is a global goal for polio eradication by 2005. Additionally, global efforts are already underway towards accelerated measles control. In 1992, mumps disease was recognized as one of six potentially eradicable diseases by the International Task Force for Disease Eradication (ITFDE).\(^1\) The ITFDE is a group of scientists convened through the Carter Center of Emory University in Atlanta, GA, that met from 1989 to 1992 to evaluate the potential for eradication of more than 90 diseases. The ITFDE also recognized the potential for the eradication of rubella and suggested that the effort to eradicate measles, mumps and rubella be combined through the use of the trivalent MMR (measles-mumps-rubella) vaccine.

Today, as many countries embark on accelerated measles control or elimination activities, there is a unique opportunity to control mumps and rubella diseases and to work towards the ITFDE goal of eradication through use of the MMR vaccine. However, this opportunity is being missed while debate continues concerning the safety profiles of the different mumps vaccine strains to be incorporated in MMR formulations. Opportunities for control are also affected by differences in the cost of vaccines prepared with the different strains. The present paper\(^2\) adds to the debate by contributing additional data on the safety profile of the Leningrad Zagreb strain of the mumps vaccine and discussing the issues of cost as they relate to national immunization programmes.

Both safety and cost have implications for the global use of mumps-containing vaccines and the control of mumps disease worldwide. The most frequent serious complication following wild mumps infection is aseptic meningitis.\(^3\) Wild virus mumps infection leads to aseptic meningitis in up to 10% of patients. The attenuated vaccine-strain virus poses a much lower risk of aseptic meningitis following vaccination, however the risk varies from strain to strain. Estimates ranging from 1 case in 150,000 doses of vaccine administered for the Jeryl Lynn strain, developed in the US,\(^4\) to 1 case in 1000 for the Leningrad-3 strain, developed in Russia, have been found.\(^5\) In the early 1990s, use of the Urabe strain of mumps vaccine virus, developed in Japan, was discontinued in many countries (Japan, Canada and the UK) due to the occurrence of aseptic meningitis following vaccination.\(^6\) It is important to note that cases of aseptic meningitis following vaccination resolve completely and without sequelae. The Rubini strain of mumps vaccine virus, developed in Switzerland, is a strain about which there is no debate concerning its use; the use of vaccines made with this strain are not recommended by WHO for use in national programmes due to their low effectiveness.

This risk of aseptic meningitis following vaccination has caused some countries to elect not to use the MMR vaccine made with either the Urabe strain or one of the two Leningrad series of strains (the Leningrad-3 vaccine virus was further attenuated to the Leningrad-Zagreb strain, which was developed in Croatia) for mass vaccination campaigns. These countries have elected to use either the bivalent measles-rubella vaccine or the monovalent measles vaccine rather than use the more expensive Jeryl Lynn MMR vaccine. An opportunity to control mumps disease is thus lost.

The issue of cost differences between strains of mumps vaccine viruses used in preparation of the MMR vaccine is not a trivial one. The most recent information from UNICEF indicates that the cost per dose of MMR made with the Urabe mumps strain is USD\$1.00 while the cost per dose of MMR made with the Jeryl Lynn strain is USD\$2.50.\(^7\) A similar price difference between these two vaccine preparations is reflected in the pricing offered by the Pan American Health Organization (PAHO) to countries in Latin America and the Caribbean.\(^8\) Such cost differences are important factors for consideration in many countries that are working to finance basic immunization programmes. A limited number of cost/benefit studies have been reported; the majority of these studies have been performed with the Jeryl Lynn strain.\(^9\)\(^-\)\(^13\) Despite their focus on the more expensive Jeryl Lynn strain, these studies found vaccination to be cost effective and beneficial. In developing countries, where few cost/benefit analyses have been performed, the cost of the vaccine-related adverse events and the underlying health burden associated with wild mumps also needs to be clarified and included in considerations for immunization programmes.

The most recent World Health Organization (WHO) position paper on mumps vaccine concluded that while ‘the available data suggest that vaccines using certain strains may have higher rates of aseptic meningitis … all available mumps vaccine preparations are acceptable for use in immunization programs’.\(^14\) However, it is imperative that there be continued compilation and analysis of available data on the risk of aseptic meningitis associated with the administration of mumps and mumps-containing vaccines.

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vaccines. The present paper thus makes an important contribution towards further understanding the differences in safety profiles of the different mumps vaccine virus strains. As noted by the authors, there are limited published data on the occurrence of aseptic meningitis following vaccination with the Leningrad-Zagreb strain; however, it is important to note that a recent article by da Cunha et al. reports on a similar outbreak of aseptic meningitis following a mass campaign using the Leningrad-Zagreb strain in two states in Brazil.

Both studies highlight the specific challenges encountered in the setting of mass campaigns. The setting of a mass campaign, where doses are administered over a short period of time, enhances visibility of even rare adverse events associated with vaccination. The occurrence of serious adverse events can undermine efforts to maintain the public's trust in national immunization programmes. This trust is a key component to the continuing success of these programmes. Public concern generated by the occurrence of adverse events can present opportunities for the improvement of surveillance for adverse events and for initiating dialogue about vaccine safety issues.

The Urabe and Leningrad series of mumps vaccine virus strains continue to be used around the world, particularly in developing countries where cost is an issue. The WHO has recognized that countries need to balance the risks and benefits of vaccination with the cost of each vaccine preparation. In an effort to more clearly define the risks of aseptic meningitis following vaccination WHO has called for 'better data ... to establish more precise estimates ...'. These data must come from studies with similar methods so that valid comparisons can be made. As more data are forthcoming regarding safety profiles of the different mumps vaccine strains, such as is provided by this study, a clearer recommendation may yet emerge.

References

1 CDC. Recommendations of the International Task Force for Disease Eradication. MMWR 1993;42(RR-16).