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Mumps Vaccine Effectiveness Against Orchitis

To the Editor: Yung et al. reported in the April 2011 issue of Emerging Infectious Diseases on the epidemiologic characteristics of the nationwide mumps outbreak in England and Wales in 2004−2005 (*1*). The associated effect of disease was considerable, with >43,000 reported cases and >2,600 hospitalizations. Compared with the prevaccine era, the average age of infection was higher, with infection occurring mostly in older teenagers and young adults (*2*). Older age at infection is associated with a higher risk of certain complications, particularly orchitis (*3*). Yung et al. reported that among cases of mumps, previous mumps measles rubella (MMR) vaccination offered considerable protection against orchitis, meningitis, and hospitalization (*1*).

In the Netherlands, mumps vaccination, using a 2-dose schedule with the MMR vaccine against measles, mumps, and rubella, was introduced in 1987, including catch-up vaccination of 3 birth cohorts (1983–1985). From birth cohort 1985 onwards, the coverage of the first and second dose of MMR has been consistently >92% (*4*). This coverage led to immediate control of mumps, with mumps related hospitalization dropping from 390 cases in 1987 to 11 in 1990 (*5*).

However, a major reemergence of mumps in the Netherlands occurred during August 2007–May 2009, when a large genotype D mumps outbreak affected mainly unvaccinated persons with a religious objection to vaccination (*6*). Subsequently, a genotype G outbreak of mumps started at the end of 2009, affecting mainly vaccinated adolescents. The outbreak started among university students in different cities, with a sudden increase in transmission after a large party for students in early 2009 (*7*).

The Dutch Centre for Infectious Disease Control advised Municipal Health Services in January 2011 to recommend MMR vaccination for university students who were unvaccinated or who had received only 1 dose of vaccine in the past. This policy was further implemented in the new academic year that began in August 2011. Information regarding the effectiveness of previous MMR vaccination against mumps complications is needed to support this policy and to predict the effect on mumps-related disease.

To study this policy, we analyzed mumps notifications in the Netherlands during December 1, 2009–June 14, 2011. Notifications include information about vaccination

Table. Mumps complications by MMR vaccination status, the Netherlands, December 1, 2009–June 14, 2011*

Complication	MMR doses received	No. mumps cases	No. (%) cases with complications	OR	aOR†	p value	Adjusted VE,‡ % (95% CI)
Orchitis§	0	86	20 (23)	Ref	Ref	Ref	Ref
	1	48	5 (10)	0.38	0.34	0.05	66 (1 to 88)
	2	338	31 (9)	0.32	0.26	<0.01	74 (49 to 87)
Other complications¶	0	117	1 (1)	Ref	Ref	Ref	Ref
	1	85	1 (1)	1.38	0.88	0.93	12 (–14 to 95)
	2	571	6 (1)	1.23	0.75	0.80	25 (–5 to 91)
Hospitalization	0	130	4 (3)	Ref	Ref	Ref	Ref
	1	83	2 (2)	0.80	0.70	0.69	30 (–312 to 88)
	2	535	6 (1)	0.40	0.43	0.25	57 (–84 to 90)

*Only those for whom complication and vaccination status were known are included; therefore, totals may differ. MMR, mumps, measles, rubella; OR, odds ratio; aOR, adjusted odds ratio; VE, vaccine effectiveness; ref, reference categories.
†OR and VE adjusted for age group (<18, 18−25, >25 y) and sex, except for orchitis, where the OR and VE were adjusted only for age group.
‡VE = 1 – OR where the OR is an approximation of the relative risk.
§Only male patients ≥12 years of age are included.
¶Includes the following reported complications: pancreatitis (n = 2), meningitis (3), thyroiditis (1), bronchitis (1), high fever and shortness of breath (1).

status and complications (e.g., orchitis, meningitis, encephalitis, pancreatitis). Vaccination status was confirmed by checking the national vaccination register, the general practitioner or patients' vaccination booklets. Vaccine effectiveness against complications and hospitalizations was estimated by using logistic regression, adjusting for age group and sex.

In the study period, 958 cases were reported, and 16 case-patients were hospitalized (1.9% of case-patients with a known hospitalization status; n = 842). The median age of case-patients was 22 years (range 1–86 years), and 58.7% were male. We had information on the vaccination status of 905 case-patients (94.5%). For this group, 68% of these vaccination statuses were confirmed. Of the 905 case-patients, 16% were unvaccinated, and 10% and 68% had received 1 and 2 doses, respectively; 6% were vaccinated at least once, but number of doses was unknown. Of case-patients with information on the occurrence of complications (95.7%, n = 917), 73 (8.0%) reported ≥1 complication. Orchitis was by far the most frequently reported complication (66 case-patients, 11.8% of men). Other complications included pancreatitis (2, 0.2%), meningitis (3, 0.3%), and thyroiditis (1, 0.1%).

Previous vaccination with 1 or 2 doses reduced the risk for mumps orchitis among male mumps case-patients ≥12 years of age by ≈70% (Table). This finding is consistent with that reported by Yung et al. (1). Because of a lower number of cases, we could not reliably estimate the effect of vaccination in preventing hospitalization and other complications. The estimated proportion of case-patients hospitalized derived from the enhanced mumps surveillance by Yung et al. is remarkably similar to our estimate (3% and 2%, respectively). It is likely that we underestimated the overall effect of disease associated with this outbreak. Notification is known to be incomplete and complications developing after the date of notification are not included. However, because the reporting of complications is unlikely to be associated with vaccination status, we believe our estimates of the vaccine's protective effects among cases of mumps are unbiased.

Whereas objection to vaccinate was the predominant cause for the 2007–2009 mumps outbreak in the Netherlands, the current outbreak seems to be caused by secondary vaccine failure. Potential causes of this failure include waning of vaccine induced immunity, a relative mismatch between vaccine and outbreak strain, and intense social contact in the affected group (8). Our observations that orchitis was the most frequently reported complication, and that previous MMR vaccination considerably reduced the risk of orchitis among cases of mumps, are important to justify recommending mumps vaccination to unvaccinated persons.

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Genetic Characterization of Peste des Petits Ruminants Virus, Sierra Leone

To the Editor: Peste des petits ruminants (PPR) is a highly infectious disease of small ruminants, characterized by high rates of illness and death and caused by a single-stranded RNA virus (peste des petits ruminants virus [PPRV]). PPRV can be divided into 4 genetically distinct lineages based on the nucleocapsid (N) gene (*1*). The lineages correlate well with geographic distribution of the virus, with lineages I and II mainly restricted to western and central Africa, lineage III to eastern Africa and the Arabian peninsula, and lineage IV to Southeast Asia, the Middle East, and more recently northern Africa (*2*).

PPRV is endemic to most of western Africa, and considered a major constraint on the livestock industry. In Sierra Leone, a country bordered by Guinea, Liberia, and the Atlantic Ocean, and having high goat and sheep populations, PPRV is believed to be the cause of outbreaks of respiratory disease with high death rates. Inadequate veterinary infrastructure and diagnostic capacity, exacerbated by the civil war in 1991–2002, however, has prevented confirmation. In this study, we confirmed presence of PPRV in Sierra Leone, which led to the official report of PPR to the World Organisation for Animal Health (Paris, France).

The study was conducted in April 2009 as part of a training mission organized at Teko Central Veterinary Laboratory, Makeni, Sierra Leone, by the World Organisation for Animal Health Collaborating Centre for Biotechnology–based Diagnosis of Infectious Diseases in Veterinary Medicine (www.sva.se/oie-cc) in collaboration with the Food and Agriculture Organization–Emergency Center for Transboundary Animal Diseases, Bamako, Mali. During the training, blood and serum samples were collected from goats (n = 9) and sheep (n = 1) from 2 smallholders with suspected outbreaks of PPR in the area around Makeni in central Sierra Leone. In addition, serum from 5 goats with respiratory disease was sampled at a livestock market in Kabala 100 km north of Makeni.

Serologic testing was performed at Teko. All serum samples (n = 15) were tested for PPRV antibodies by using a commercial ELISA (BDSL, Ayrshire, UK; *3*); 12 (80%) of the samples were positive for PPRV.

Blood samples were collected on Nobuto filter strips (Advantec MFS Inc., Tokyo, Japan) and transported to the BioSafety Level 3 laboratory at the National Veterinary Institute, Uppsala, Sweden, for nucleic acid detection (*4,5*). RNA was eluted from the blood impregnated filter strips and screened for PPRV by using real-time RT-PCR specific for the N gene (*6*). Viral RNA was detected in 13 (87%) of the samples, with most of the positive samples indicating high viral load (cycle threshold <20).

For determination of the genetic lineage of detected viruses, RNA from all samples was subjected to PCR amplification of a 351-bp segment of the N gene by using the NP3/NP4 primer pair (*7*), but with a modified protocol using the One-Step RT-PCR kit (QIAGEN, Hilden, Germany) (*5*). Amplified PCR products were separated by electrophoresis, gel extracted, purified, and processed for sequencing by using ABI PRISM BigDye Terminator v3.1 kit (Applied Biosystems, Foster City, CA, USA), according to the manufacturer's instructions.

N gene sequences were obtained from 10 (67%) of the samples, and showed 83%–100% nt identity level compared with sequences available in GenBank using the BLASTn tool (www.ncbi.nlm.nih.gov/blast) and 93%–100% identity between each other. Phylogenetic analysis was performed with 4 representative sequences (GenBank accession nos. JN602079–JN602082) from this study by using neighbor-joining and the Kimura 2-parameter model in MEGA5 (CEMI, Tempe, AZ, USA), including N gene sequences representing all 4 lineages.

The PPR viruses from Sierra Leone clustered in lineage II with viruses from Mali, Nigeria, and Ghana, and could further be distinguished into 2 clusters (Figure). One virus from Kabala clustered closely with viruses from Mali (Mali 99/1), whereas all others showed 100% identity with a virus from Nigeria (Nig/75/1), in many countries used as vaccine virus strain. In Sierra Leone at the time, however, PPR vaccination was not being performed, suggesting that obtained sequences originated from circulating field viruses related to Nig/75/1 rather than being vaccine derived. This suggestion was strongly supported by the clinical presentation typical of PPR. Surprisingly, no