Mumps and mumps vaccine: a global review

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Mumps is an acute infectious disease caused by a paramyxovirus. Although the disease is usually mild, up to 10% of patients can develop aseptic meningitis; a less common but more serious complication is encephalitis, which can result in death or disability. Permanent deafness, orchitis, and pancreatitis are other untoward effects of mumps. Based on data reported to WHO up to April 1998, mumps vaccine is routinely used by national immunization programmes in 82 countries/areas: 23 (92%) of 25 developed countries, 19 (86%) of 22 countries with economies in transition (mainly the Newly Independent States of the former Soviet Union), and 40 (24%) of 168 developing countries. Countries that have achieved high coverage have shown a rapid decline in mumps morbidity. Furthermore, in many of these countries, mumps-associated encephalitis and deafness have nearly vanished. This review considers the disease burden due to mumps; summarizes studies on the immunogenicity, efficacy, and safety of different strains of mumps vaccine; and highlights lessons learned about implementing mumps immunization in different countries. Countries already using mumps vaccine should monitor immunization coverage and establish routine mumps surveillance with investigation of outbreaks. Where mumps is targeted for elimination, countries need to add a second dose of mumps vaccine for children, keeping in mind that the disease may still occur in susceptible adults.

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Introduction

Mumps is an acute infectious disease caused by a paramyxovirus closely related to parainfluenza virus. Although the disease is usually mild, its burden should not be underestimated. Up to 10% of mumps patients developed aseptic meningitis; a less common but more serious complication is encephalitis, which can result in death or disability; and permanent deafness, orchitis and pancreatitis are other untoward effects that can be prevented by vaccination. As of mid-1998, mumps vaccine was routinely used by national childhood immunization programmes in 82 countries. Where high coverage has been achieved, countries have shown a rapid decline in mumps morbidity. Furthermore, in many countries encephalitis associated with mumps has almost totally vanished.

In this article we review the disease burden caused by mumps; summarize studies on the immunogenicity, efficacy, and safety of different strains of mumps vaccine; and highlight lessons learned about implementing mumps immunization from countries in different regions of the world. Guidance is provided for countries contemplating the introduction of mumps vaccine and for countries already using this vaccine.

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Disease burden due to mumps

Humans are the only natural hosts for mumps virus, which is usually spread by respiratory droplets. The incubation period of mumps averages 16–18 days, with a range of about 2–4 weeks (*1*). Infection with mumps virus is asymptomatic in one-third of cases. Nonspecific prodromal symptoms include low-grade fever, anorexia, malaise, and headache. The disease can vary from a mild upper respiratory illness to viraemia with widespread systemic involvement (Table 1). Classic mumps is characterized by enlargment of the parotid and other salivary glands; parotitis is bilateral in three-quarters of cases; and other salivary glands are involved in 10% of cases (*1*).

Epididymo-orchitis occurs in about 25% of postpubertal men who contract mumps. In one large cohort study the median age for mumps orchitis was 29 years (range, 11–64 years) (*2*). Testicular atrophy occurs in about one-third of patients with mumps orchitis, but sterility is rare. Mumps orchitis appears to be a risk factor for testicular cancer, though not a major one (*3*). In postpubertal women, mastitis and oophoritis can occur; one study found mastitis in 31% of women over 14 years of age (*4*). Among women who acquire mumps during the first 12 weeks of pregnancy, more than a quarter suffer spontaneous abortion; in a large cohort study, the rate of spontaneous abortion in the first trimester due to mumps infection was higher than that due to rubella infection (*5*). An increased incidence of con-

genital malformations following maternal mumps infection during pregnancy has not been found (*6*).

Pancreatitis is seen in about 4% of patients with mumps (*7*). There is evidence suggesting that mumps virus can infect human pancreatic beta cells, and may trigger the onset of insulin-dependent diabetes mellitus in some individuals (*8*).

In mumps cases the central nervous system is frequently infected and about 50% of asymptomatic patients exhibit pleocytosis in the cerebrospinal fluid (CSF) (*9*). Aseptic meningitis occurs in up to 10% of all mumps patients, more often in males. Meningitis is clinically manifest by severe headache aggravated by movement, photophobia, and neck stiffness due to spasm of the spinal muscles (*10*). Mumps meningitis is a benign condition that appears within a few days of parotid swelling, although some meningitis patients do not have any parotid swelling. Patients recover without complications, but many require hospitalization during the course of the illness. In the pre-vaccine era in Sweden, mumps was estimated to cause about 1000 cases of meningitis each year, leading to 20 000 days of hospitalization and 20 000–40 000 days of disability (*11*).

The incidence of mumps encephalitis is reported to range from 1 in 6000 mumps cases (0.02%) (*12*) to 1 in 300 mumps cases (0.3%) (*13*). The associated symptoms vary from mild alterations of consciousness to coma; emotional lability, irritability, and focal neurological signs are also common (*10*). The age distribution of encephalitis cases parallels that of mumps cases, with 75% of patients being below 15 years of age. For unknown reasons, mumps encephalitis affects three times as many males as females (*13*). In the USA, mumps was the main cause of viral encephalitis during the pre-vaccine era, and in 1967 was responsible for 36% of cases of viral encephalitis (*13*). In China, before mumps vaccine was routinely used, a retrospective study of children hospitalized for encephalitis found that mumps was the second most frequently identified viral pathogen after enteroviruses (*14*).

Deafness is a well-recognized complication of mumps. In Finland, among 298 military personnel with mumps who were assessed by audiometric tests, 13 (4%) had evidence of high frequency hearing loss (*8*); for 12 of these patients, hearing loss was reversible within a few weeks and one patient progressed to permanent deafness (*15*). In one Welsh community, 33 children acquired profound unilateral sensorineural hearing loss over 1 year, and in 12 (36%) of the children the onset of deafness was temporarily related to mumps (*16*). A study from the United Republic of Tanzania reported mumps as the etiology of permanent deafness in 53 (15%) of 354 students at a school for the deaf (*17*).

A variety of other clinical symptoms are seen with mumps. Mild renal function abnormalities are common (*18, 19*), but these usually resolve spontaneously. Transient electrocardiogram abnormalities, mainly changes in T waves and ST segments, have been reported in up to 15% of cases *(20*), while rare case reports of fatal nephritis or myocarditis have been published (*21*).

Death due to mumps is exceedingly rare, and is mostly caused by mumps encephalitis. In the USA, over the period 1966–71 there were two deaths per 10 000 mumps cases, with 38% of such deaths involving persons aged ≥40 years (*13*). In the United Kingdom, 93 deaths were registered from mumps over the period 1962–81, with 53 (57%) of those who died being aged ≥45 years (*22*).

Table 1. **Major manifestations of mumps**[a]

Manifestation	Frequency (%)
Glandular	
Parotitis	60–70
Submandibular and/or sublingual adenitis	10
Epididymo-orchitis	25 (postpubertal men)
Oophoritis	5 (postpubertal women)
Pancreatitis	4
Neurological	
Asymptomatic pleocytosis of CSF	50
Aseptic meningitis	1–10
Encephalitis	0.02–0.3
Deafness (usually transient)	4
Other	
Mild renal function abnormalities	30–60
Electrocardiogram abnormalities	5–15

[a] Modified from ref. *1*.

Epidemiology of mumps in the pre-vaccine era

In countries where there is no vaccination against mumps, its incidence remains high, with epidemic peaks every 2–5 years and those aged 5–9 years consistently being the most affected. Historical records as far back as the eighteenth century document that mumps epidemics occurred worldwide, and were more frequent in crowded environments, including prisons, orphanages, boarding schools, ships, and military barracks (*23*). In the pre-vaccine era, mumps was a common infectious disease with a high annual incidence, usually >100 per 100 000 population based on routine passive surveillance (Table 2). One prospective community-based study in the USA found the annual incidence of mumps to be almost 2000 cases per 100 000 population – about 10 times greater than the number of passively reported cases (*24*). Incidences greater than 6000 cases per 100 000 have been reported in military populations (*25*). There are few data to assess the burden of mumps infection in developing countries. In Oman, where mumps vaccine was not used until 1997, the annual incidence of mumps over the period 1990–96 was 269–783 per 100 000 population (A.J. Mohammed, personal communication, 1997). In Israel, passive surveillance (with an unknown reporting fraction,

Table 2. **Average annual reported mumps incidence in several countries in the WHO European Region before and after introduction of mumps vaccine and in two countries with no mumps vaccination**[a]

Country	Pre-vaccine		Post-vaccine		
	Years	Average annnual incidence (per 100 000)	Years	Average annual incidence (per 100 000)	% reduction
Two-dose schedule					
Denmark	1977–79	726	1993–95	1	>99
Finland	1977–79	223	1993–95	<1	>99
Norway	1977–79	371	1993–95	11	97
Slovenia	1977–79	410	1993–95	4	>99
Sweden	1977–79	435	1993–95	<1	>99
One-dose schedule					
Armenia	1983–85	280	1993–95	16	94
Croatia	1983–85	101	1993–95	12	88
England and Wales	1983–85	40	1993–95	5	88
Israel	1983–85	102	1993–95	10	90
Latvia	1983–85	141	1993–95	3	98
No mumps vaccine					
Poland	1983–85	415	1993–95	361	—
Romania	1983–85	242	1993–95	217	—

[a] See ref. *82*

but possibly as low as 20%) found the annual incidence of mumps to be 80–162 per 100 000 population over the period 1977–88 prior to introduction of mumps vaccine (*26*).

Serosurveys to assess mumps immunity were conducted in a number of countries prior to the introduction of vaccine. Protective maternal antibody is passively transferred to the infant and its half-life is about 35–40 days (*27*). Data from England and Wales (*28*), Netherlands (*29*), Singapore (*30*), and St Lucia (*31*) document a steep increase in mumps antibody level from age 2–3 years; by 4–6 years of age, 50% of children had acquired natural antibodies; by 14–15 years of age, 90% of the population was seropositive (Fig. 1). The situation in other countries is different, with a large proportion of adults remaining susceptible, for example in Saudi Arabia (*32*) and Poland (*33*) (Fig. 1). Such findings may reflect real differences in transmission rates of mumps virus, time elapsed since the most recent outbreak, or differences in sampling or laboratory technique.

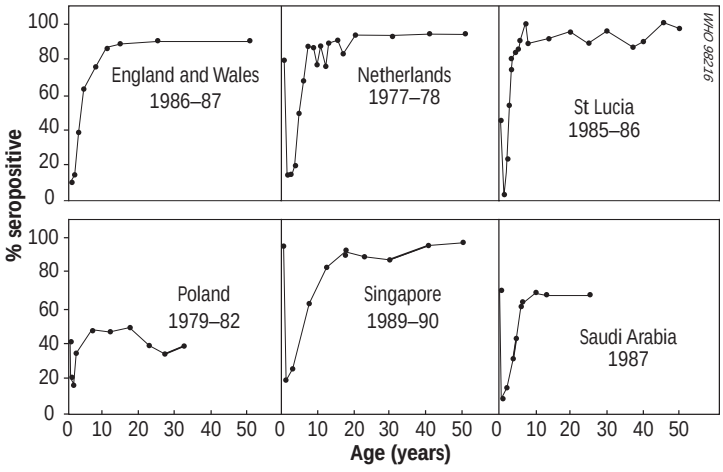
Mumps vaccines

General considerations

Live mumps vaccines are available as monovalent mumps vaccine, bivalent measles–mumps (MM) vaccine, and trivalent measles–mumps–rubella (MMR) vaccine. WHO requirements do not specify the minimum amount of vaccine virus that one human dose should contain; rather, this is determined by the national control authority of the country where the vaccine is produced (*34*). Most countries use at least 1000 $CCID_{50}$ of attenuated mumps virus per dose, but many vaccines contain higher amounts. Sorbitol and hydrolysed gelatin are used as stabilizers in mumps vaccine, and neomycin is added as a preservative. Once reconstituted, live attenuated mumps vaccines must be used immediately or stored at 0–8 ^{0}C, kept away from light, and discarded if not used within 8 hours (*34*).

There are very few contraindications to mumps vaccination. Mumps vaccine should not be administered to individuals with immune deficiency or immunosuppression; however, MMR vaccine can be given to asymptomatic and symptomatic individuals infected with human immunodeficiency virus (HIV) and who are not severely immunocompromised (*35*). Mumps vaccine should not be administered to pregnant women because of the theoretical

Fig. 1. **Age-stratified seroprevalence of mumps antibody during the pre-vaccine era in England and Wales** *(ref. 28),* **Netherlands** *(ref. 29),* **St Lucia** *(ref. 31),* **Poland** *(ref. 33),* **Singapore** *(ref. 30)* **and Saudi Arabia** *(ref. 32)***.**



risk of fetal damage, and pregnancy should be avoided for 3 months after vaccination (*35*). Individuals with common forms of allergy (atopic eczema, asthma, cow's milk allergy) can be vaccinated safely with MMR vaccine (*36*). In the past, egg allergy was considered a reason not to administer mumps vaccine; however, recent studies document that among 1227 known egg-allergic individuals who received a standard dose of mumps vaccine only two (0.16%) had any symptoms suggesting anaphylaxis (*37*). Other components of MMR vaccine, such as gelatin (*38*) and neomycin (*39*), can produce hypersensitivity to the vaccine in some individuals.

Immunogenicity, efficacy, and safety

We review data on immunogenicity, efficacy, and safety for the five most commonly used mumps vaccine strains below. The scope of this article does not permit comparisons of serological methods, case definitions, or methods of surveillance. Information on safety is limited to reported rates of vaccine-associated aseptic meningitis, which have been recalculated as rates per 100 000 vaccine doses.

Jeryl Lynn strain mumps vaccine. The Jeryl Lynn strain, named after the child from whom the virus was isolated, was developed in the USA by passaging the virus in embryonated hen's eggs, then in chick embryo cell cultures (*40*). The strain was licensed in the USA in 1967, and by 1992 it had been administered to approximately 135 million children and adults around the world (*34*).

Clinical studies in industrialized countries show that a single dose of Jeryl Lynn strain mumps vaccine leads to initial seroconversion rates of 80–100% (*41*). Further studies document persistence of antibody in a large proportion of vaccinees. In Sweden, 73% of 229 children who received MMR vaccine containing Jeryl Lynn strain mumps vaccine at 18 months of age remained seropositive 10.5 years later (*42*). In Finland, 4 years after the second MMR vaccine dose (with Jeryl Lynn mumps strain) and 9 years after the initial dose the seropositivity rate was 86% (*43*). The clinical protective efficacy of the Jeryl Lynn strain of mumps vaccine in outbreak-based studies in the USA has ranged from 75% to 91% (*44*). Two recent outbreak investigations in the USA found that the risk of mumps increased with time elapsed since vaccination, suggesting possible waning of vaccine-induced immunity (*45*, *46*). Few studies of Jeryl Lynn vaccine have been conducted in developing countries; however, in the Dominican Republic, a study of this vaccine reported 94% seroconversion among 72 seronegative children aged 1–6 years (*47*).

In the USA, a 10-year retrospective study of hospitalized cases of mumps found one case of aseptic meningitis per 100 000 doses of MMR vaccine (with Jeryl Lynn mumps strain) in a cohort of children aged 12–23 months (*48*). Although these findings are reassuring, further prospective studies are planned. In Germany, the Jeryl Lynn strain was associated with 0.1 aseptic meningitis cases per 100 000 vaccine doses (*49*).

Leningrad-3 strain mumps vaccine. The Leningrad-3 mumps attenuated strain was developed in the Soviet Union in guinea-pig kidney cell culture, with further passages in Japanese quail embryo cultures (*50*). Vaccines based on the Leningrad-3 strain have been used since 1974 in the former Soviet Union and other countries. Approximately 8–11 million doses of Leningrad-3 mumps vaccine are produced annually (*34*). Studies have shown 89–98% seroconversion among children aged 1–7 years following receipt of Leningrad-3 mumps vaccine, and a protective efficacy of 92–99% (*50*). A large-scale efficacy trial that enrolled more than 100 000 children found the vaccine to have 97% protective efficacy in the outbreak setting (*51*).

In Slovenia, passive surveillance over the period 1979–85 identified 20 cases of aseptic meningitis per 100 000 doses of MM vaccine with the Leningrad-3 mumps strain (*52*). Further retrospective review of the medical records of Slovenian patients hospitalized for aseptic meningitis during 1979–86 found an incidence of 100 cases of aseptic meningitis per 100 000 doses of MM vaccine containing Leningrad-3 mumps strain; however, at the time of discharge, all symptoms had resolved and no patient had any sequelae (*53*).

L-Zagreb strain mumps vaccine. In Croatia, the L-Zagreb strain was obtained by further attenuation of Leningrad-3 mumps virus by adaptation and passage on chick embryo fibroblast cell culture (*54*). Over the period 1976–87, more than 10 million doses of L-Zagreb mumps vaccine were distributed in the former Yugoslavia and elsewhere (*54*).

Studies in Croatia showed 87–100% seroresponse to L-Zagreb mumps vaccine and a vaccine efficacy of 97–100% (*54*). In India, a single dose of locally produced MMR vaccine containing the L-Zagreb mumps strain increased mumps seropositivity from 12% to 92% among 15–24-month-olds (*55*).

In Slovenia, MMR vaccine containing the L-Zagreb mumps strain has been used since 1990, and passive surveillance over the period 1990–96 revealed two cases of aseptic meningitis per 100 000 doses (A. Kraigher, unpublished data, 1997). In Croatia, there were 90 cases of aseptic meningitis per 100 000 doses of MMR vaccine containing the L-Zagreb mumps strain over the period 1988–92 (*56*).

Rubini strain mumps vaccine. The Rubini mumps virus strain was passaged first in a human diploid cell line, serially passaged in embryonated hen's eggs, then adapted to the MRC-5 human diploid cell line (*57*). Mumps vaccine based on the Rubini strain was licensed in Switzerland in 1985, and by 1990 more than 4 million people around the world had been immunized with it (*34*).

A study in Germany of children aged 14–24 months who received a dose of MMR vaccine found that 95% seroconverted when the mumps strain was

Rubini, compared with 100% when the strain was Jeryl Lynn (*58*). Recent studies in Switzerland, Italy, and Portugal provide evidence that mumps vaccine based on the Rubini strain does not appear to offer long-term protection against the disease. In Switzerland, a study of secondary attack rates among the family contacts 16 y ears of age (median age, 6.9 years) of confirmed mumps cases (median age, 6.2 years) found a protective efficacy of 6% for the Rubini strain mumps vaccine compared with 73% for the Urabe strain vaccine and 62% for the Jeryl Lynn strain vaccine (*59*). Several other Swiss studies confirm the low efficacy of the Rubini strain vaccine (*60*, *61*). In Italy, a case–control study conducted during 1995–96 found that, compared with children vaccinated with Jeryl Lynn or Urabe strain mumps vaccine, children vaccinated with the Rubini strain vaccine had a higher risk of contracting mumps: 1.2 for children aged <4 years; 3.0 for 4–6-year-olds; and 12.8 for 7–12-year-olds (*62*). In Portugal, MMR coverage of children aged 12–23 months has been >90% since 1991; despite this, a large mumps epidemic occurred in 1995–96 with the highest incidence among children aged 1–4 years. A plot of the number of cases according to their probable month and year of vaccination showed that there was a large increase in mumps incidence among children vaccinated after October 1992, which corresponded to the date when Portugal began to use the Rubini strain of mumps vaccine exclusively (*63*).

Urabe strain mumps vaccine. The Urabe strain of live mumps vaccine was first licensed in Japan in 1979, and thereafter in Belgium, France, and Italy (*34*). It is produced either in the amnion of embryonated hen's eggs or in chick embryo cell cultures. By 1991, more than 60 million persons around the world had been immunized with the Urabe strain of mumps vaccine (*34*).

In a study in Finland, among children who received mumps vaccine at 14–20 months of age, 95% seroconverted with the Urabe strain, compared with 97% with the Jeryl Lynn strain (*64*). Several studies have assessed the immunogenicity of the Urabe strain mumps vaccine in developing countries. Among seronegative children who received Urabe strain mumps vaccine at 9 months of age, 99% seroconverted in Brazil (*65*), 98% in South Africa (*66*), and 75% in India (*67*). Among children aged 12 months, 100% responded in Brazil (*65*), 98% in China (Province of Taiwan) (*68*), and 92% in India (*67*). At 15 months of age, 100% of recipients responded in South Africa (*66*), and at 14–18 months, 98% responded in China (Province of Taiwan) (*68*).

In the United Kingdom, a study showed that 4 years after a single dose of MMR vaccine the seropositivity rates were 85% for the Urabe strain, compared with 81% for the Jeryl Lynn strain (*69*). In Canada, a study found that 5–6 years after one dose of MMR vaccine the seropositivity rate was 93% for the Urabe strain, compared with 85% for the Jeryl Lynn strain (*70*).

Following reports of aseptic meningitis cases temporally associated with the administration of MMR vaccine containing Urabe mumps virus strain, Canada initiated molecular studies, which showed that the Urabe vaccine is a mixture of viruses, with wild type A and variant G. Spinal fluid from Urabe strain vaccinees who developed aseptic meningitis or parotitis showed predominately wild type A (*71*). MMR vaccine containing the Urabe strain was therefore withdrawn from the market in Canada in 1990 (*72*).

Several studies in the United Kingdom have examined rates of aseptic meningitis following vaccination with Urabe strain vaccine. A study in Nottingham was followed by a multi-centre confirmatory study, which showed a rate of 9 aseptic meningitis cases per 100 000 vaccine doses (*73*). As a result, the Public Health Service in the United Kingdom stopped purchasing Urabe strain vaccine in 1992.

In Japan, nationwide surveillance conducted by the Ministry of Health and Welfare during 1989 demonstrated an overall rate of 49 cases of aseptic meningitis per 100 000 doses of domestically produced MMR vaccine containing Urabe mumps strain (*74*). Subsequent studies up to 1993 identified an incidence of approximately 100 aseptic meningitis cases per 100 000 doses of MMR containing Urabe mumps strain (although rates differed by manufacturer), and in April 1993 the Ministry of Health and Welfare of Japan withdrew all domestically produced MMR vaccines (*75*).

Use of mumps vaccine around the world

Based on data reported to WHO up to April 1998, a total of 82 countries/areas (38%) are using mumps vaccine in their national immunization programme. This is similar to the situation for rubella vaccine, which is used on a national basis in 78 countries/areas (*76*). Based on the United Nations country classification scheme (*77*), mumps vaccine is used by 23 (92%) of 25 developed countries; 19 (86%) of 22 countries with economies in transition (mainly the Newly Independent States of the former Soviet Union); and 40 (24%) of 168 developing countries. Among the 82 countries/areas using mumps vaccine, 52 (63%) schedule one dose of mumps vaccine and 30 (37%) have a two-dose schedule. Mumps vaccine use varies widely by region (Table 3), as detailed below.

African Region

No countries in the WHO African Region include mumps vaccine in their national immunization schedule.

Region of the Americas

In the WHO Region of the Americas, 21 (45%) countries/areas use mumps vaccine: 15 give one dose of MMR vaccine and 6 give two doses of MMR vaccine (Table 3). Use of MMR vaccine is receiving

increasing attention in the Americas, and regional targets for mumps control and eventual elimination are under discussion.

Canada. In Quebec Province, one dose of MMR vaccine was introduced in 1976 for children at 12 months of age; coverage has been >95% since 1980. The annual number of reported mumps cases has fallen from 6858 in 1977 to fewer than 100 per year since 1981, with the exception of an outbreak in 1988–89 (*78*). Cases in the outbreak occurred largely among unvaccinated students aged 15–19 years, who were born prior to the introduction of vaccine. Because of the low incidence of mumps in Quebec, the province has elected not to add a second dose of mumps vaccine.

USA. Use of mumps vaccine began in the USA in 1967, when the incidence of the disease was almost 90 per 100 000 population (*79*). However, during the next decade mumps immunization was considered a low priority. In 1977, routine mumps immunization was recommended at 12 months of age or older, and this was facilitated by the availability of MMR vaccine. During 1985–86 large mumps outbreaks occurred among underimmunized cohorts born in the period 1967–77, resulting in a shift in peak incidence from 5–9-year-olds to 10–19-year-olds. In 1989, a second dose of MMR vaccine was recommended at 4–6 years of age. The incidence of mumps fell from 2 per 100 000 population in 1988 to 0.7 per 100 000 population in 1993 (*79*).

Eastern Mediterranean Region

In the WHO Eastern Mediterranean Region, 11 countries/areas (48%) include mumps vaccine in the national immunization schedule: six countries use one dose and five countries use two doses of MMR vaccine (Table 3).

European Region

Of the 51 countries/areas in the WHO European Region, 43 (84%) use mumps vaccine on a national basis (Table 3). In western Europe, most countries schedule one or two doses of MMR vaccine. Among the Newly Independent States of the former Soviet Union, 14 countries administer a single dose of monovalent mumps vaccine. In 1991, the European Region set a target of mumps elimination by the year 2000; and in 1993 this was defined as an annual mumps incidence of <1 case per 100 000 population in each country (*80*). The Health for All database of the European Regional Office includes the annual number of reported mumps cases and incidence by country (*81*). These data show that in the pre-vaccine era mumps incidence generally exceeded 100 per 100 000 population (Table 2). Following the introduction of mumps vaccine, the average annual incidence of the disease dropped significantly in countries using a one-dose immunization schedule, and reached levels <1 per 100 000 population in several countries using a two-dose schedule.

Croatia. In the Rijeka region (population, 340 000 in 1990), mumps immunization started in 1976. At 15 months of age children receive a dose of MMR vaccine containing the L-Zagreb strain; coverage has been ≥92% (*82*). In 1977 and 1981–82 mumps outbreaks occurred, and then there was an 8-year period with lower incidence (31–78 mumps cases per 100 000 population). Mumps vaccination led to a shift in the age distribution of cases, with the highest incidence being among 5–9-year-olds over the period 1976–82, and among 15–19-year-olds over the period 1983–90.

England and Wales. From 1962 to 1981 England and Wales had an annual mumps incidence of 160–1011 cases per 100 000 population (*22*). Mumps vaccine was introduced in October 1988, when MMR vaccine was scheduled for all children aged 12–15 months (*83*). In addition, all pre-school children were offered MMR vaccine in a 3-year catch-up programme. Since 1991, mumps vaccine coverage of children by their second birthday has exceeded 90%. The annual incidence of mumps fell to 5 per 100 000 population in the period 1993–95 (Table 2). The number of hospital admissions for mumps fell by 92% compared with the pre-vaccine era (*83*). Nevertheless, studies in vaccinated pre-school cohorts showed that 15% of children were seronegative for mumps. Therefore, in 1997 a second dose of MMR vaccine was added at age 4 years (*83*).

Finland. In the 1970s the mean annual incidence of mumps was 240 cases per 100 000 population, meningitis and orchitis were common complications, and occasional deaths were reported. In 1982 a national immunization programme was begun, with two doses of MMR vaccine (with Jeryl Lynn mumps strain) at age 14–18 months and 6 years (*84*). Over a period of 12 years, 1.5 million of the 5 million Finnish population were vaccinated. As a result, there was a 99% decrease in the incidence of mumps and the annual incidence dropped

Table 3. **National schedules for mumps immunization used by countries/areas in different WHO regions**[a]

WHO region	No. of countries/ areas[b]	One-dose mumps vaccine	Two-doses mumps vaccine	No. using any mumps vaccine
Africa	48	0	0	0
Americas	47	15	6	21 (45)[c]
Eastern Mediterranean	23	6	5	11 (48)
Europe	51	25	18	43 (84)
South-East Asia	10	0	0	0
Western Pacific	36	6	1	7 (19)
Total	**215**	**52**	**30**	**82 (38)**

[a] Based on data reported to the WHO Global Programme for Vaccines and Immunization.

[b] No. of countries/areas reporting is greater than the number of Member States.

[c] Figures in parentheses are percentages.

to <1 case per 100 000 population (Fig. 2); encephalitis with mumps (and rubella and measles) totally vanished (*85*).

Israel. Mumps vaccine was introduced in April 1984, but had to be discontinued 16 months later due to budgetary constraints. In December 1998, measles vaccine was replaced by MMR vaccine at age 15 months in the routine childhood vaccination schedule. In 1990 MMR coverage reached 91% nationwide (*26*). The incidence of mumps varied from 80 to 162 cases per 100 000 population over the period 1977–88. By 1993–95, the annual mumps incidence had fallen to 10 cases per 100 000 population (Table 2).

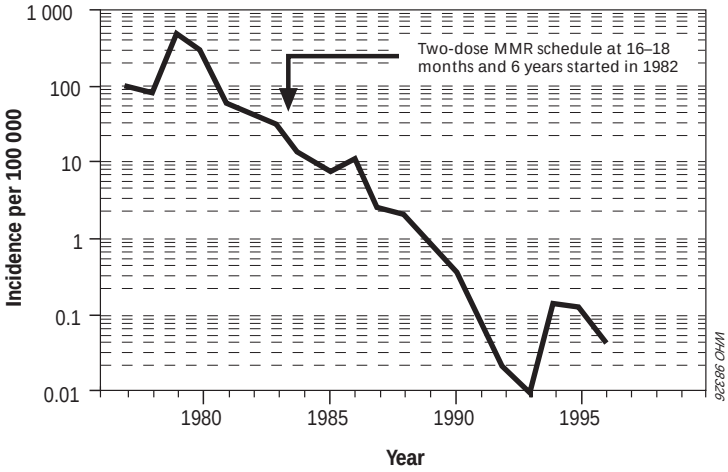
Portugal. In Portugal, a dose of MMR vaccine at age 15 months was introduced in 1987; in 1990 a second dose at age 11–13 years was added. The number of reported mumps cases decreased from 2197 in 1987 to 627 in 1993. Subsequently, the country experienced a large epidemic, with 1841 mumps cases in 1995 and 7620 cases in the first 8 months of 1996 (*63*). Epidemiological investigations suggest the outbreak may have been related to exclusive use of Rubini strain vaccine since October 1992.

Slovenia. Prior to 1979, over 400 cases of mumps were notified each year, and more than 50% of children contracted the disease before their second birthday (A. Kraigher, unpublished data, 1998). In 1979, the country scheduled two doses of MM vaccine (with Leningrad-3 mumps strain) at ages 12–16 months and 6–7 years. In 1990, MM vaccine was changed to MMR vaccine (with L-Zagreb mumps strain). Coverage for both doses has been >90% since 1990. Mumps has declined steadily to an annual incidence of <5 per 100 000.

Sweden. In May 1982, Sweden introduced a two-dose MMR immunization schedule (using the Jeryl Lynn strain of mumps vaccine), with the aim of eliminating measles, mumps, and rubella (*42*). MMR vaccine is given at 18 months and 12 years of age, with coverage being >95% in both groups. The rationale for the two-dose schedule is to boost declining antibody concentrations, reach those who did not receive the first dose or failed to respond to it, and avoid the build-up of susceptibles among young adults. Sweden experienced dramatic reductions in the incidence of mumps and its complications. One study in Gothenburg found no mumps- or rubella-associated hearing impairment among children after the introduction of MMR vaccine, whereas mumps and rubella had previously accounted for 12% of all hearing impairments among pre-school children in the country (*86*). In Sweden, the incidence of mumps has remained very low but stable, with 80% of cases occurring among persons born before the start of the programme (*42*).

Switzerland. In Switzerland, one dose of MMR vaccine at 15 months of age was introduced nationally in 1987, and coverage of children aged 27–36 months reached 80% in 1991. While the incidence of measles and rubella fell sharply, an initial drop in mumps incidence was followed by a steep increase in the 1990s, with an incidence above 400 per 100 000 population in 1994 (*59*). Several outbreak investigations found that the clinical protective efficacy of the Rubini strain used was very low (*59–61*); since October 1994, the Swiss Federal Office for Public Health has recommended using only MMR vaccine with the Jeryl Lynn mumps strain, except for children with allergies (*61*).

Fig. 2. **Annual incidence of mumps in Finland, 1977–96** *(ref. 81)*.



South-East Asia Region

In the WHO South-East Asia Region, no countries have a national policy for use of mumps vaccine.

Western Pacific Region

In the Western Pacific Region, seven countries/areas (19%) use mumps vaccine: six countries employ a one-dose MMR schedule and one country a two-dose MMR schedule (Table 3).

Singapore. Prior to the introduction of MMR vaccine, Singapore conducted a serosurvey of persons aged 6 months to 45 years (*30*). Overall 72% of the population possessed antibodies against mumps virus; in the 0–4-year age group only 22% were seropositive. In 1990, Singapore introduced a single dose of MMR vaccine at 12 months of age.

Lessons learned

By 1998, a total of 82 countries/areas had added mumps vaccine to their routine national immunization programmes. In addition, MMR vaccines are popular in the private sector, even in countries without a national mumps control programme (*87*). Vaccine has been introduced mainly in countries with the highest per capita income, which can afford the resources to sustain high coverage. Most countries did not introduce mumps vaccine into their national programmes until immunization coverage of infants with BCG, poliovirus, diphtheria–pertussis–tetanus, and measles vaccines exceeded 80%, often above 90%. Countries that introduced mumps vaccine into their immunization pro-

grammes exhibited a rapid decline in mumps morbidity. Countries implementing a one-dose schedule at high coverage levels reported reductions in mumps incidence of ≥88% (Table 2). Countries implementing a two-dose schedule at high levels of coverage for both doses show reductions in mumps incidence of ≥97%, and several countries reached the elimination target of <1 mumps case per 100 000 population (Table 2). Sustained high levels of vaccination against mumps can be expected to lengthen the inter-epidemic period, while susceptibles accumulate in the population; thus, mumps outbreaks can be expected 10–20 years after the introduction of routine mumps immunization. Such outbreaks are more likely to be seen among older age groups, especially those aged 15–30 years, who were too old to receive vaccine and whose exposure to wild mumps virus was reduced by the herd effect of the vaccination programme.

Guidance for countries considering using mumps vaccine

So far, mumps vaccine has not been recommended as part of the global Expanded Programme on Immunization. Countries considering the use of mumps vaccine should review the WHO guidelines for introduction of new vaccines (*88*), paying careful attention to the aspects discussed below.

• Consider the disease burden

Information on the incidence of mumps and the age groups affected should be examined. Data on the proportion of encephalitis and meningitis due to mumps can help in determining the importance of the disease. In some countries, Japanese encephalitis, dengue, varicella, or tick-borne encephalitis may be the primary causes of encephalitis, but local data need to be examined to determine the relative disease burden due to mumps. Studies to assess hearing disabilities should consider mumps as a possible etiology.

• Decide on an appropriate routine schedule

Mumps vaccine can be most efficiently incorporated into the immunization schedule by using MMR vaccine. Separate delivery of single-antigen mumps vaccine is less practical, since this requires an extra injection and may also lead to an additional health care visit. Serological studies show that vaccine response rates are excellent from the age of 12 months. For the Urabe strain mumps vaccine, the seroresponse rates appear high from the age of 9 months. An initial target of mumps control would suggest use of a single dose of MMR vaccine at 9–15 months of age, and countries should aim for coverage of ≥80%. Using MMR instead of measles vaccine will require further considerations about what strategy is appropriate to prevent congenital rubella syndrome (*76*). If a large proportion of the adult population remains seronegative for mumps, care should be taken to provide mumps vaccine to adults who may be at special risk, including health workers, teachers, and military personnel.

• Select the mumps vaccine

Several mumps vaccines based on different attenuated strains are available. Recent studies indicate that the Rubini strain does not provide sufficient long-term clinical protection, although several other mumps vaccine strains do provide better long-term protection as demonstrated in outbreak investigations. Among the available strains, the rates of vaccine-associated aseptic meningitis vary; however, vaccine-associated meningitis resolves spontaneously in less than a week, and there are no sequelae. Natural mumps infection leads to aseptic meningitis in up to 10% of patients, and this also resolves spontaneously within a week without sequelae. It is of far greater concern that natural mumps infection can lead to encephalitis, with a risk of death or permanent disability. Thus, countries need to consider that the incidence and severity of meningitis and encephalitis following natural infection greatly exceed those associated with any protective mumps vaccine currently available in international commerce (*89*).

• Assess costs

Studies in several countries have found that the introduction of routine mumps vaccine is economically justifiable. In Austria, the benefit–cost ratio was 3.6 for routine immunization using Jeryl Lynn mumps vaccine (*90*). In Israel, the benefit–cost ratio was 5.9 for routine immunization with MMR vaccine at 15 months of age (*91*). The results of benefit–cost analyses may, however, differ from one country to another, and countries should consider local estimates of disease burden, costs of treatment, costs of vaccination, and the rates of adverse events for the vaccine strain of interest. Some countries which have attained high measles vaccine coverage and have concerns about the burden of mumps disease may find that they cannot afford to replace monovalent measles vaccine with MMR because of the cost of the vaccine. Benefit–cost analysis may help in approaching potential donors.

Recommendations for countries already using mumps vaccine

For countries already using mumps vaccine, mumps control programmes should include the activities discussed below.

• Monitor immunization coverage

Where mumps vaccine is delivered as MMR vaccine, immunization coverage monitoring is likely already to be in place. Countries that deliver single-antigen mumps vaccine need to be certain that the

coverage is monitored. When second doses are delivered to pre-school or school-aged populations, coverage should also be monitored.

• Conduct routine surveillance of mumps

Mumps should be a notifiable disease, recognizing that passive surveillance generally underreports disease incidence but it can monitor trends and signal outbreaks. It is important to remember that mumps affects adults; WHO surveillance guidelines, which include recommended case definitions, are being developed.

• Investigate outbreaks

Mumps outbreaks should be investigated to the extent that resources allow.

• Assess (and re-assess) control versus elimination strategies

Countries already using a single dose of mumps vaccine may eventually contemplate including a second dose. The potential benefit will depend on whether the objective of the programme is control or elimination of the disease. As countries use mass campaigns to deliver extra doses of measles vaccine to particular target groups, measles vaccine can be substituted by MMR vaccine; however, mass campaigns with MMR vaccine should be planned only where long-term routine immunization against rubella and mumps is being implemented.

• Conduct research

When new mumps vaccine strains are introduced, studies on their immunogenicity should be carried out in both industrialized and developing countries. The field effectiveness of vaccines, especially newer strains, needs to be monitored. A more difficult task is to establish and maintain sufficiently sensitive monitoring systems that can provide reliable data on rare adverse events. In countries where mumps vaccine has been in use for many years, there is a need for continued study of the duration of protection following vaccination in childhood, particularly if there is little natural boosting from exposure to wild mumps virus. ■

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Résumé

Les oreillons et le vaccin antiourlien : la situation dans le monde

Les oreillons sont une maladie infectieuse aiguë due à un paramyxovirus très proche des virus parainfluenza. En l'absence de vaccination, c'est une affection courante dont l'incidence annuelle est élevée : en général plus de 100 cas pour 100 000 habitants. La surveillance à base communautaire donne de son côté un taux d'incidence de 2000 pour 100 000 – soit environ 10 fois plus de cas que n'en dénombre la notification passive. Des épidémies d'oreillons se produisent tous les 2 à 5 ans.

Sous sa forme habituelle, la maladie se caractérise par une tuméfaction parotidienne avec atteinte associée des autres glandes salivaires. Elle est le plus souvent bénigne mais peut se compliquer d'une méningite aseptique dans 10% des cas. L'encéphalite est une complication moins fréquente mais plus grave et peut entraîner la mort ou du moins une invalidité permanente. Après la puberté, il peut se produire une épididymo-orchite dans 25% des cas. Chez la femme enceinte, la maladie provoque dans un quart des cas un avortement spontané lorsqu'elle est contractée au cours du premier trimestre. Chez 4% des malades, on observe une surdité passagère qui, chez un petit nombre d'entre eux, peut évoluer vers une perte auditive importante et définitive. Les pays qui ont inscrit la vaccination contre les oreillons à leur programme national de vaccinations courantes et sont parvenus à assurer une bonne couverture, ont vu la morbidité ourlienne décliner rapidement. En outre, dans nombre d'entre eux, les encéphalites et les surdités consécutives aux oreillons ont presque totalement disparu.

Selon les données communiquées à l'OMS jusqu'en avril 1998, la vaccination antiourlienne fait partie des vaccinations de l'enfance dans 82 pays (38%). Selon le système de classification des pays adopté par les Nations Unies, la vaccination antiourlienne est pratiquée dans 23 pays développés sur 25 (92%), dans 19 pays en transition économique sur 22 (86%) (principalement les nouveaux Etats indépendants de l'ancienne Union soviétique) et dans 40 pays en développement sur 168 (24%).

Dans 52 pays, la vaccination comporte l'administration d'une seule dose de vaccin alors que dans 30 autres elle en comporte deux.

Les pays qui envisagent d'introduire la vaccination antiourlienne pour lutter contre la maladie, doivent évaluer la charge que cette maladie représente, définir l'âge de vaccination systématique et choisir la souche vaccinale de virus vivant atténué à acquérir. Une analyse coût-avantages ne serait pas inutile à cet égard. Les pays qui pratiquent déjà la vaccination contre les oreillons doivent contrôler la couverture vaccinale, mettre en place une surveillance systématique des oreillons et faire une enquête chaque fois qu'une flambée se produit. Là où l'on s'est fixé pour but d'éliminer la maladie, il faut ajouter une seconde dose de vaccin chez l'enfant, sans perdre de vue que les oreillons peuvent aussi frapper les adultes sensibles.

Resumen

La parotiditis y la vacuna antiparotidítica: situación mundial

La parotiditis, o paperas, es una enfermedad infecciosa aguda causada por un paramixovirus estrechamente relacionado con el virus parainfluenza. Si no se vacuna contra ella, la parotiditis es una enfermedad común, con una alta incidencia anual, generalmente superior a 100 casos por 100 000 habitantes. La vigilancia comunitaria ha revelado cifras de incidencia del orden de 2000 casos por 100 000 habitantes, esto es, unas diez veces más que el número de casos notificados pasivamente. Cada 2-5 años se declaran epidemias de parotiditis.

La parotiditis clásica se caracteriza por una inflamación de la glándula parótida y de otras glándulas salivales. Aunque suele ser benigna, hasta un 10% de los pacientes desarrollan meningitis aséptica. Una complicación menos frecuente, pero más grave, es la encefalitis, que puede ser causa de muerte o de discapacidad permanente. Además, un 25% de los hombres que contraen la enfermedad tras la pubertad sufren epididimorquitis. Entre las mujeres afectadas durante el primer trimestre de embarazo, una cuarta parte sufren aborto espontáneo. Aparece sordera transitoria en un 4% de los pacientes, una pequeña proporción de los cuales queda aquejado permanentemente de pérdida de oído profunda. Los países que han incluido la vacuna contra la parotiditis en sus programas nacionales de inmunización sistemática y han logrado una alta cobertura han mostrado un rápido descenso de la morbilidad por la enfermedad. Por añadidura, en muchos de esos países los casos de encefalitis y sordera asociados a la parotiditis han desaparecido casi por completo.

Según los datos notificados a la OMS hasta abril de 1998, la vacuna contra la parotiditis se utiliza sistemáticamente en los programas nacionales de inmunización de 82 países (38%). Según el sistema empleado por las Naciones Unidas para clasificar los países, utilizan la vacuna antiparotidítica 23 (92%) de 25 países desarrollados, 19 (86%) de 22 países con economías en transición (principalmente los nuevos Estados independientes de la antigua Unión Soviética) y 40 (24%) de 168 países en desarrollo.

En 52 países se administra una sola dosis de la vacuna, mientras que en los otros 30 se emplean dos dosis.

Los países interesados en implantar la vacunación contra la parotiditis para combatir esa enfermedad tendrán que evaluar la carga de morbilidad que representa, determinar la edad idónea para la vacunación sistemática, y seleccionar la cepa de vacuna viva atenuada que deba comprarse. Los análisis costo-beneficio pueden ser de utilidad a ese efecto. Los países que ya utilizan la vacuna contra la parotiditis deberían seguir de cerca la cobertura de inmunización y establecer mecanismos de vigilancia sistemática de la enfermedad, incluida la investigación de los posibles brotes. Allí donde se haya fijado la meta de eliminar la parotiditis, los países habrán de añadir una segunda dosis de vacuna para los niños, sin olvidar que la enfermedad puede afectar con todo a adultos susceptibles.

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