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# IMMUNIZATION

## SURVEY OF RECENT RESEARCH

Volume 4



U.S. Department of Health and Human Services/Public Health Service/Centers for Disease Control

**CDC**  
CENTERS FOR DISEASE CONTROL

# **IMMUNIZATION**

## **Survey of Recent Research**

**Volume 4**

**Issued October 1990**

**U.S. Department of Health and Human Services  
Public Health Service  
Centers for Disease Control  
Center for Prevention Services  
Division of Immunization  
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# Search Parameters

Searches of the National Library of Medicine's databanks are restricted to those articles dealing with human subjects and having one of the following terms as a major or minor descriptor:

amantadine	mumps
antiviral agents	mumps vaccine
bacterial vaccines	pertussis vaccine
BCG vaccine	plague vaccine
brucella vaccine	poliomyelitis
bulbar poliomyelitis	poliovirus vaccine
chickenpox	poliovirus vaccine, oral
cholera vaccine	rabies vaccine
cytarabine	ribavirin
diphtheria	rickettsial vaccines
diphtheria-pertussis-tetanus vaccine	rubella
diphtheria toxoid	rubella vaccine
encephalitis, post-vaccinal	smallpox
fungal vaccines	smallpox vaccine
haemophilus infections	staphylococcal toxoid
herpes zoster	staphylococcal vaccines
herpes zoster, ocular	subacute sclerosing panencephalitis
immunization	tetanus
immunization, passive	tetanus toxoid
immunization schedule	toxoids
immunization, secondary	typhoid-paratyphoid vaccines
influenza	vaccines
influenza vaccine	vaccines, attenuated
measles	vaccination
measles vaccine	viral hepatitis vaccines
meningitis, haemophilus	viral vaccines
	whooping cough

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# MEASLES

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## General

### Protective Role of Human Antibody to the Fusion Protein of Measles Virus

*T.A. Sato, T. Kohama and A. Sugiura. Microbiol Immunol 1989;33(7):601-7.*

Authors' abstract: Absorption of a pooled human gamma globulin preparation with acetone-treated measles virus-infected cells removed all antibodies to measles virus antigens except a portion of the antibody to the fusion (F) protein. The residual anti-F antibody had hemolysis-inhibiting and virus-neutralizing activities, inhibited spread of infection through cell fusion, and was effective in protection of passively immunized mice from fatal measles encephalitis, providing evidence for the protective role of human antibody to the F protein of measles virus.

## Clinical and Laboratory

### A Study on Measles Immune Status by ELISA (Chinese)

*G.Q. Li. Chung Hua Liu Hsing Ping Hsueh Tsa Chih 1989 Apr;10(2):105-8.*

English summary: Both ELISA and HI tests have been used to test 85 paired sera collected shortly before and after a measles epidemic. Results showed that 22 children whose pre-exposure antibody titers were less than 1:2 by HI and less than 1:100 by ELISA contracted measles subsequently; 2 other children (one less than 1:2 by HI and 1:100 by ELISA and one 1:2 by HI and less than 1:100 by ELISA) contracted measles too. Three of 5 children whose pre-exposure antibody titers ranged from 1:2 to 1:8 by HI and 1:100 to 1:400 by ELISA contracted the disease, and 2 of them developed a subclinical infection. The 56 persons whose pre-exposure antibody titers were 1:16 by HI and greater than or equal to 1:400 by ELISA neither contracted measles nor displayed an antibody enhancement. The comparison between the two tests showed that when the ELISA antibody titer less than 1:200 was regarded as a

negative mark, the sensitivity of this test was 100% and specificity was 95.2%. The ELISA can be used in place of the HI test for immune status surveillance against measles.

## Epidemiology

### Measles Immunization Research: A Review

*P. Aaby and C.J. Clements. Bull WORLD Health Organ 1989;67(4):443-8.*

Authors' abstract: Most global estimates indicate that more than 1 million children a year die from acute measles. The actual number of deaths may, however, be considerably higher than this. In addition, the impact of delayed mortality as a result of measles infection is only now being realized. Many months after they contract measles, children continue to experience higher levels of mortality and morbidity than those who do not. Immunization of children against measles therefore prevents mortality and morbidity not only during the acute phase but also during subsequent months. The impact of measles immunization programs may therefore have generally been underestimated. The effects of measles infection on children during the early months of life are more damaging than those experienced by older children. Children should therefore be immunized against measles as early in life as possible, given the limitations of existing vaccines.

### Patterns of Transmission and Severity of Measles Infection: A Reanalysis of Data From the Machakos Area, Kenya

*P. Aaby and J. Leeuwenburg. J Infect Dis 1990 Feb; 161(2):171-4.*

Authors' abstract: Data on measles from the project in the Machakos District, Kenya, 1974-1981, were reanalyzed. In families with several cases, secondary cases (children infected in the home) had a relative mortality risk of 3.00 (95% confidence interval [CI]: 1.55-5.80) compared with index cases who caught the infection from someone outside the home. The case fatality rate (CFR) may be higher among secondary cases exposed to two or more index cases than among those exposed to only one index case (relative risk [RR] = 2.47; 95% CI: 0.93-6.56). The CFR was also higher among



secondary cases who had been exposed to a fatal index case than among those exposed to an index case who survived (RR = 4.69; 95% CI: 1.64-13.41). Children aged 12-23 months and those 5 years of age or older were more likely than other age groups to have been infected by someone outside the home. During the course of the project the CFR in families with several cases was reduced from 8.8% to 2.7%. Though there is no general explanation for this tendency, it was observed that the proportion of secondary cases per index case was reduced during the last part of the project (odds ratio = 0.73; 95% CI: 0.56-0.95).

### Medical Students as Sources of Rubella and Measles Outbreaks

*G.A. Poland and K.L. Nichol. Arch Intern Med 1990 Jan;150(1):44-6.*

Authors' abstract: Medical students demonstrate a high degree of susceptibility to rubella and measles, and hence are at risk for infection and transmission of these viruses. The purpose of our study was to examine the role medical students play as sources or vectors in rubella and measles outbreaks. We conducted a survey of all US and Canadian public health departments to determine how often students were implicated in outbreaks (response rate, 88.7%). We also performed a literature search to identify any cases not reported to health departments, as well as examined the medical, social, and economic consequences of such outbreaks in the medical setting. Since 1981, 9% of health departments have recorded at least one outbreak of rubella or measles in which medical students were specifically implicated as sources or vectors. Increased morbidity, mortality, and adverse economic consequences resulted from these outbreaks. Our data confirm that medical students are important sources/vectors in rubella and measles outbreaks. We recommend that all medical students be immune to these viruses.

## Prevention and Control

### Mumps Meningitis and MMR Vaccination

*Anonymous. Lancet 1989 Oct 28;2(8670):1015-6.*

The most common neurological reaction to mumps-containing live vaccines is meningitis, which carries the same favorable prognosis as mumps. A less common complication is vaccine-associated encephalitis. In the United States, according to the Immunization Practices Advisory Committee (ACIP), the frequency of encephalitis within 30 days of immunization is 0.4 per one million doses, a rate no higher than the incidence of central nervous system dysfunction in the general population. Even if the incidence of meningo-

encephalitis following immunization of children aged 1-14 years is as high as the Canadian estimate of one per 100,000 cases, this figure is close to the incidence of aseptic meningitis hospital admissions for the same age group, and is insignificant compared with the neurological complications of natural mumps. There is compelling evidence to support the present MMR vaccine strategy, despite occasional complications. Parents must be persuaded to protect their children with the MMR vaccine, while doctors must be aware of the rare complications, be prepared to allay the parents' fears, and to diagnose and treat complications as necessary.

### Mumps, Measles, and Rubella Vaccination and Encephalitis (Letter)

*N.T. Begg, N.D. Noah, S. Crowley, S.T. al-Jawad and I.Z. Kovar. BMJ 1989 Oct 14;299(6705):978.*

In the report of a case of encephalitis associated with measles, mumps, and rubella (MMR) immunization, the only evidence for a casual relationship was a fourfold rise in S antibody titer to mumps, and a temporal association. Publication of cases where a link has not been established may cause unnecessary harm by damaging confidence in a vaccine whose benefits clearly outweigh the risks. The authors state that the rate of encephalitis after MMR vaccination may be as high as 1 in 100,000. Compare this risk with the incidence of meningitis following natural mumps infection: meningeal signs are present in up to 15% of infections. It is important that all suspected vaccine reactions be reported, and serious reactions should be investigated to determine whether there is a casual link. We believe that the evidence of a casual link in the case reported was weak. Authors' reply: We thought that this case highlighted a complication of MMR vaccination that is not widely recognized, and should not be ignored. We would contend that in our case the temporal association of the clinical presentation, the fourfold rise in mumps antibody titer, and the absence of an alternative viral cause suggest that the encephalitis was a complication of the vaccination.

### Immunity to Measles in a Large Population of Varying Age. Significance With Respect to Vaccination

*H. Braunstein, S. Thomas and R. Ito. Am J Dis Child 1990 Mar;144(3):296-8.*

Authors' abstract: During a measles outbreak, 660 hospital employees of widely varying ages were screened for immunity to the disease using an automated indirect fluorescent antibody technique. Of these 660 employees, 623 indicated their year of birth. Of those born before 1957, 7 tested seronegative and 6 were borderline; 12 of those born between 1959 and 1964 were seronegative, and 3 were borderline. There are several

possible reasons for these findings. It is concluded that mass immunization of high-risk populations during outbreaks, while effective, is difficult to justify scientifically because only a small percentage of subjects are not immune. If facilities permit, mass screening during outbreaks may be feasible. Continuous screening and the vaccination of susceptible high-risk employees would be referable. Our study also does not validate excluding from immunization programs those born prior to 1957, since both seronegativity and disease occur in this age group with significant frequency.

### Measles Prevention

*CDC. MMWR 1989 Dec 29;(38 Suppl 9):1-18.*

Authors' abstract: These revised recommendations of the Immunization Practices Advisory Committee (ACIP) on Measles Prevention replace previous recommendations published in 1987 (1) and 1989 (2). The recommendations include a basic change in the routine childhood vaccination schedule from a one-dose to a two-dose schedule using combined measles-mumps-rubella (MMR) vaccine. Routine revaccination will generally be implemented one age group at a time starting with school enterers. New recommendations are also included for vaccination of preschool children at high risk of contracting measles, for students in colleges and other institutions of higher education, for health-care personnel and international travelers, and for outbreak control.

### An Evaluation of Measles, Mumps and Rubella Vaccine in a Population of Yorkshire Infants

*J.M. Dunlop, K. RaiChoudhury, J.S. Roberts and K.A. Bryett. Public Health 1989 Sep;103(5):331-5.*

Authors' abstract: In October 1988 combined measles, mumps and rubella (MMR) vaccination replaced monocomponent measles as part of the routine childhood vaccination program in the United Kingdom. Prior to this policy change a study was undertaken, in 335 children aged 15 months, to evaluate the clinical reactions and immunogenicity of the new combined MMR vaccine (Trimovax, Immravax, Merieux), in comparison with an established monocomponent measles vaccine (Rouvax, Merieux). Parents were asked to select whether their child should receive MMR vaccine or measles monocomponent; over 95% chose MMR. Children who were given the MMR vaccine had seroconversion rates of 96% for measles, 97% for mumps and 100% for rubella; those who received monocomponent measles vaccine had a seroconversion rate of 100%. The number of side effects reported was similar with both vaccines; all were mild and self-limiting. The results from this study confirm the efficacy and low reactogenicity of MMR vaccine and support its use as part of the routine childhood immunization program in the United Kingdom.

### Mumps Meningitis Following Measles, Mumps, and Rubella Immunization (Letter)

*J. A. Gray and S. M. Burns. Lancet 1989 Jul 8;2(8654):98.*

We report mumps meningitis in a girl aged two years three months, following measles, mumps, and rubella (MMR) immunization. The child was admitted following a day of lethargy, vomiting, headache, dry cough, and fever. Twenty-one days before, she had received MMR vaccine. Her mother and 5-year-old sibling were well, and she had no other known contact with mumps. Florescent antibody studies with rabbit polyclonal antiserum confirmed the virus to be mumps. Her response to the measles and rubella content of the MMR was normal, but her antibody response to mumps was transient. General practitioners, pediatricians, and healthcare workers should be aware of the rare but possible occurrence of mumps meningitis after MMR immunization.

### Measles-mumps-rubella (MMR) Vaccine in Japan

*H. Kuno-Sakai and M. Kimura. Acta Paediatr Jpn Overseas Ed 1988 Apr;30(2):167-74.*

The purpose of this paper is to report the past and current situations of the Japanese MMR vaccine and to report the results of the field trial of the national MMR vaccine. The 1986 trial revealed that three manufacturers are able to make equally effective and safe vaccines from common bulk materials. This enables the large-scale production and distribution of national MMR when it is approved for use in Japan. We compared the 1980 and 1981 national MMR with the 1986 national MMR, and concluded that the 1986 vaccine gives the highest seroconversion rate for mumps, while no difference was observed in measles and rubella.

### Two Doses of Measles Mumps Rubella (MMR) Vaccine

*H. Kuno-Sakai, K. Ozaki and M. Kimura. Acta Paediatr Jpn Overseas Ed 1989 Dec;31(6):690-7.*

Authors' abstract: A schedule of two doses of measles mumps rubella vaccine (MMR) at an interval of six weeks was tried in children aged between 12 and 48 months. One hundred percent seroconversion was attained in the measles HI (hemagglutinin inhibition) test, rubella HI test, and mumps ELISA in both groups of children who received NIH (National Institute of Health, Japan) MMR lot B-30 and Kitasato MMR lot TV-1. The possibility of vaccine failure with one dose of measles vaccine is not negligible, and the frequency of vaccine failure increases if three vaccines are combined in the form of MMR. Our observations revealed that a few of the children who had received one dose of MMR remained seronegative with regard to measles HI antibody and rubella HI antibody, and that some of the children remained seronegative with

regard to mumps ELISA antibody. A schedule of two doses of MMR was shown to be helpful in reinforcing immunity in children who did not respond satisfactorily to one dose of MMR. We concluded that two doses of MMR are preferable to control measles, mumps and rubella infections.

### **Antibodies to Measles Virus Surface Polypeptides in an Immunized Student Population Before and After Booster Vaccination**

*M.J. Makela, R.G. Marusyk, E. Norrby, D.L. Tyrrell and A.A. Salmi. Vaccine 1989 Dec;7(6):541-5.*

Authors' abstract: Serum specimens collected from 82 students before and after booster immunization with live measles virus (MV) vaccine were tested for MV surface protein-specific antibodies using a previously developed competitive enzyme immunoassay (EIA). The specificity of the assay in measuring antibodies against three sites on the hemagglutinin (H) and two on the fusion (F) protein was demonstrated. All subjects in this study were vaccinated at one to two years of age—three times with inactivated killed vaccine and later once or more with live vaccine. Fifty-three students were administered only live measles virus vaccine (M), whereas 29 were vaccinated with the MV combined with mumps and rubella (MMR). There was a clear tendency to a lower increase in antibody titers when MMR vaccine was used. This difference between the groups was most pronounced in antibodies against the site defined by a monoclonal antibody (mAb) I29. Antibodies to the site defined by the mAb 16AG5 on the F protein had no correlation with any of the other tests which suggests that subjects originally vaccinated with killed vaccine may have developed a distinct response to this site.

### **Immunization of Six-month-old Infants With Different Doses of Edmonston-Zagreb and Schwarz Measles Vaccines**

*L.E. Markowitz, J. Sepulveda, J.L. Diaz-Ortega, J.L. Valdespino, P. Albrecht, E.R. Zell, J. Stewart, M.L. Zarate and R.H. Bernier. N Engl J Med 1990 Mar 1;322(9):580-7.*

Authors' abstract: Because measles causes an estimated 2 million deaths per year among children in developing countries, including a substantial proportion of infants less than nine months old—the age at which vaccination is recommended—there has been interest in using different strains of vaccine and higher doses to achieve immunization of younger infants. We conducted a randomized trial of three different doses of Edmonston-Zagreb and of Schwarz measles vaccines in infants to evaluate the effect of the strain and dose of vaccine on the serologic response and acute adverse reactions to vaccination. Six-month-old infants received a standard, medium, or high dose of one of the vaccines, and nine-month-old infants received a standard dose. Antibody

levels were measured before and after vaccination, by means of a plaque-reduction neutralization assay, in 1061 six-month-olds and 299 nine-month-olds. Edmonston-Zagreb vaccine produced higher rates of seroconversion and seropositivity than comparable doses of Schwarz vaccine. Among the six-month-old infants, the seroconversion rate 18 weeks after vaccination with the standard dose of Edmonston-Zagreb vaccine was 92 percent, that with the medium dose was 96 to 97 percent, and that with the high dose was 98 percent; the rates for the corresponding doses of Schwarz vaccine were 66 percent, 76 percent, and 91 percent, respectively. Higher seroconversion rates were observed with an increase in the dose of either Edmonston-Zagreb ( $P$  less than 0.01) or Schwarz ( $P$  less than 0.001) vaccine. The seroconversion rates produced by high and medium doses of Edmonston-Zagreb vaccine in six-month-olds were equal to or significantly higher than the rate produced by a standard dose of Schwarz vaccine in nine-month-olds (87 percent). Clinical adverse reactions were not associated with the strain or dose of a vaccine. We conclude that Edmonston-Zagreb vaccine is more immunogenic than Schwarz vaccine in infants and can induce effective immunization against measles at six months of age.

### **Surveillance of Symptoms Following MMR Vaccine in Children**

*C. Miller, E. Miller, K. Rowe, C. Bowie, M. Judd and D. Walker. Practitioner 1989 Jan;233(1461):69-73.*

Preceding the introduction of MMR vaccine in Britain, post-vaccination symptoms were assessed in more than 10,000 children for whom parents completed daily diaries. The vaccine was accepted by over 90% of parents. Parotitis occurred in about 1% of children; other symptoms were similar to those commonly reported after measles vaccine.

### **Incidence of Subacute Sclerosing Panencephalitis Following Measles and Measles Vaccination in Japan**

*Y. Okuno, T. Nakao, N. Ishida, T. Konno, H. Mizutani, Y. Fukuyama, T. Sato, S. Isomura, S. Ueda and I. Kitamura et al. Int J Epidemiol 1989 Sep;18(3):684-9.*

Authors' abstract: The Japanese Committee for the National Registry of Subacute Sclerosing Panencephalitis (SSPE) confirmed that 215 cases of SSPE occurred in the 20 years from 1966 to 1985, as discovered in the 10-year surveillance from April 1976 through March 1986. The annual incidence in recent years has been between 10 and 23 cases. Among cases with a certain history of measles illness or measles vaccination, 184 (90.2%) had a history of measles illness without receiving measles vaccine. There were 11 probable measles vaccine-associated cases (5.4%), three (1.5%) being vaccinated with a

combined use of killed and live vaccine and eight (3.9%) with further attenuated live vaccine. There were nine cases (4.4%) without a history of either measles illness or measles vaccination. Intervals between measles illness and the onset of SSPE varied from 1 to 16 years (mean, 7.0 years). The periods following measles vaccination with further attenuated live vaccine were 2 to 11 years (mean, 4.6 years). Annual incidence rates of SSPE per million cases of measles ranged between 6.1 and 40.9 (mean, 16.1) in the 10 measles epidemic years 1968-1977; those following vaccination with further attenuated live vaccine were zero in most years and at the highest were 3.08 (mean, 0.9) per million doses of distributed vaccine.

### **Immunization of Asymptomatic HIV-infected Children With Measles Vaccine: Assessment of Risks and Benefits**

*I.M. Onorato, W.A. Orenstein, A.R. Hinman, M.F. Rogers and J.P. Koplan. Med Decis Making 1989 Apr-Jun;9(2): 76-83.*

Authors' abstract: Because HIV infection is associated with immunologic abnormalities, concerns have been expressed about the safety and efficacy of vaccination of infected children with live virus vaccines. The authors used decision analysis to assess the likely impacts of four alternative policies for immunization of asymptomatic HIV-infected children with measles vaccine. Probabilities for vaccine efficacy, vaccine-related adverse events, and measles complications in HIV-infected children and the prevalence of HIV infection in the birth cohort were obtained from a modified Delphi survey. Using median estimates from the Delphi survey, there were no major differences in outcomes under any proposed policy. Using the most extreme estimates, serologic testing and exclusion of seropositive children from vaccination or exclusion of all high-risk children decreased vaccine-associated adverse events without greatly increasing measles complications, primarily because of the current low incidence of measles. Under conditions assumed to exist in the United States today, alternate immunization policies have only minor differences in societal impact although costs would certainly differ.

### **Measles, Mumps, and Rubella Vaccines**

*M. Wharton, S.L. Cochi and W.W. Williams. Infect Dis Clin North Am 1990 Mar;4(1):47-73.*

Authors' abstract: With widespread use of the live virus vaccines for measles, mumps, and rubella, there has been a dramatic decrease in the incidence of all three diseases. At the same time, an increasing proportion of the remaining cases are occurring in adolescents and adults. Thus, vaccinations for these three diseases of childhood must be included in a comprehensive program for adult immunization. The vaccines have a proven history of safety and efficacy and are usually administered together as combined measles-mumps-rubella (MMR) vaccine. Vaccination for measles, mumps, and rubella is particularly important for susceptible adults likely to come in contact with infected children. Adults at particularly high risk for exposure may include daycare center workers, teachers and other school employees, college students, medical personnel, and those planning to travel outside the United States.

### **Study on the Immunity to Measles in Pre-school Children**

*M.S. Yang, E.R. Chen, H.J. Hou and Y.C. Ko. Kao Hsiung I Hsueh Ko Hsueh Tsa Chih 1989 Sep;5(9):476-81.*

English summary: One hundred and ninety-seven pre-school children, composed of 109 boys and 88 girls, who resided in a rural community in southern Taiwan were studied. The age range was from 6 months to 5 years old and vaccination coverage was determined by home visits and the vaccination records of the health station. Immunological status was tested by an enzyme-linked immunosorbent assay (ELISA) to determine the positive rate of measles-specific IgG. The results were as follows: (1) vaccination coverage in the studied sample was 87.9%; (2) the educational level of fathers had a significant influence on vaccination; (3) the positive rate of measles antibody in the vaccinated children was 73.9%; (4) the measles immunity level in the studied sample was 67.8%; and (5) the positive rate of measles antibody, as analyzed by a stratified test, indicated that vaccination age, the current age, and the number of siblings were the significant influence factors. When adjusted to the above variables, it was found that the number of siblings was the significant influencing factor.



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## Epidemiology

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