

Seropositivity Rates for Measles, Mumps, and Rubella IgG and Costs Associated with Testing and Revaccination

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Retrospective analysis of IgG test results and patterns for measles, mumps, and rubella revealed generally high seropositivity rates, with that of mumps being the lowest. A simplified cost analysis shows that when there is a suspicion of nonimmunity, serological testing may be cheaper than vaccination.

Since the introduction of the measles, mumps, and rubella single injectable vaccine (MMR) in 1971, the incidence of each infection has declined and is now very low in the United States (1). Nevertheless, maintaining population immunity is important to prevent outbreaks. Currently, the Centers for Disease Control and Prevention Advisory Committee on Immunization Practices (ACIP) considers receipt of one documented dose of the MMR vaccine as evidence of immunity to rubella and two documented doses of the MMR vaccine as evidence of immunity for mumps and measles (2). In the absence of vaccination documentation, serological testing is accepted as laboratory evidence of immunity (2).

We investigated immunization screening practices using retrospective analysis of measles, mumps, and rubella IgG testing performed at ARUP Laboratories (Salt Lake City, UT). Our goals were to illustrate seroprevalence rates as a surrogate for laboratory evidence of immunity among individuals screened, to evaluate observed ordering practices, and to estimate potential cost-effectiveness of vaccination versus serological screening.

This study was approved by the University of Utah Institutional Review Board (IRB no. 7275). A deidentified data set was created of all 159,257 tests for measles, mumps, and rubella IgG antibodies ordered at ARUP Laboratories between 1 February 2011 and 31 January 2012. We linked measles, mumps, and/or rubella testing for each sample, yielding results for 98,023 individuals from 646 institutions in 44 states. Antibody titers were measured for more than one virus in 51,026 individuals and for all three viruses in 10,210 individuals. Testing for IgG antibodies was performed at ARUP Laboratories according to the manufacturer's guidelines. Briefly, measles and mumps testing were performed using enzyme immunoassays (EIA) manufactured by SeraQuest (Miami, FL) by following standard EIA protocols with sample index value cutoffs determined by the manufacturer of <0.90 (negative), 0.90 to 1.09 (equivocal), and >1.09 (positive). Rubella testing was performed using the Siemens rubella quantitative IgG chemiluminescent EIA on the Siemens IMMULITE 2000, with cutoffs of <5 IU/ml (negative), 5 to 9 IU/ml (equivocal), and >10 IU/ml (positive).

IgG seropositivity rates were high for all three viruses, regardless of test order combination (Table 1). Seropositivity rates were highest for rubella and lowest for mumps, which correlates with previous studies that show mumps titers decrease most rapidly (3–8). It was assumed that the 10,210 individuals tested for all three viruses were tested for immunization status screening rather than for acute infection, since natural infection with three viruses would be extremely uncommon in the United States, and recom-

TABLE 1 Serostatus in individuals tested for measles IgG, mumps IgG, and rubella IgG ($n = 10,210$)

Rubella status	Mumps status	% (n) who are measles IgG:	
		Positive	Equivocal/negative
Positive ($n = 9,539$)	Positive	72.0 (7,351)	5.2 (528)
	Equivocal/negative	13.2 (1,351)	3.0 (309)
Equivocal/negative ($n = 671$)	Positive	2.6 (263)	0.8 (82)
	Equivocal/negative	1.6 (163)	1.6 (163)

mendations from ACIP would drive this testing (9). Additionally, the proportion of individuals positive for any single viral titer was significantly lower ($P < 0.001$) than when all three titers were tested, indicating that single orders may be testing for natural infection rather than immunity (Table 2).

Of individuals tested in our laboratory for more than one virus, 77.1% were tested for both measles and mumps IgG and 20.0% were tested for measles, mumps, and rubella IgG. The high proportion of testing that is ordered for measles and mumps IgG in combination is likely a result of the ACIP guidelines, which consider persons with a single dose of a rubella vaccine as immune; this, combined with the disparate signs and symptoms of measles and mumps, suggests that this test order combination is being used as a marker for vaccine-induced immunity and not acute infection (2). By looking at seropositivity rates when all three tests are ordered, it can be calculated that if only measles and mumps IgG titers are measured, 2.6% of individuals requiring vaccination would be missed (individuals that would test positive for both measles and mumps IgG but should be revaccinated as a result of having a negative or equivocal rubella IgG titer; Table 1). Because of the low positivity rate of mumps IgG relative to other viral titers, it may be hypothesized that this alone could be used as a determination of whether revaccination is needed. However, if mumps IgG was ordered alone, 8.6% of individuals requiring re-

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TABLE 2 Seropositivity rates of measles IgG, mumps IgG, and rubella IgG stratified by test ordering patterns

Ordered test ^a	Median age (% 18+ yrs old)	Seropositivity rate (%)		
		Measles IgG	Mumps IgG	Rubella IgG
Measles IgG (<i>n</i> = 11,359)	34 (95.4)	86.0		
Mumps IgG (<i>n</i> = 22,049)	38 (97.6)		78.9	
Rubella IgG (<i>n</i> = 13,587)	28 (96.8)			90.5
Measles IgG, mumps IgG, rubella IgG ^b (<i>n</i> = 10,210)	34 (96.5)	89.4	80.5	93.4

^a Tests listed are exclusive.

^b Seropositivity of individual test orders was significantly less than when all tests were ordered when adjusted for age and sex ($P < 0.001$).

vaccination would be missed (summation of all patients that had all three tests ordered that had a positive mumps IgG titer but a negative measles IgG and/or rubella IgG; Table 1).

A simplified cost analysis was done to determine whether it is appropriate to test for all three viral titers and follow up with vaccination if necessary or simply vaccinate without performing any serological testing. Because ACIP guidelines require two doses of the MMR vaccine as evidence of immunity for measles and mumps and a single dose for rubella, individuals lacking immunity were partitioned appropriately. To determine the cost of testing, the Medicare reimbursement cost of \$57.99 for all three tests was used (10). The cost of the vaccine is \$52.07 based on the CDC vaccine fee schedule (11). For this analysis, only the 10,210 patients with all three tests ordered were used. A weighted cost per patient was determined to be \$85.81 per patient if testing was performed followed by appropriate vaccination based on the negative viral titers (Table 3). This cost is greater than the cost of a single vaccine; however, it is less than the cost of two vaccines, indicating there may be cost savings if a single vaccine is administered without serological testing in cases where immunity to rubella is of greatest concern but not measles or mumps (as the case may be in women of childbearing age) (12). The recommendation for vaccination in certain cases without serological testing can also be made due to the low incidence of vaccine-related complications, especially in individuals who may have been previously vaccinated (2, 13). It is important to note that this scenario is calculated at the Medicare reimbursement rate, which may not be an accurate price for all institutions. Each facility must determine its cost of testing and whether it outweighs the cost of vaccination alone using this simple model.

TABLE 3 Weighted cost of serological testing for all three virus antibody titers plus vaccination or vaccination alone

Status	No. (%) of individuals	Associated cost (\$)		
		Serological testing	Vaccine	Total
Require single-dose vaccination ^a	263 (2.6)	57.99	52.07	110.06
Require double-dose vaccination ^b	2,596 (25.4)	57.99	104.14	162.13
Immune ^c	7,351 (72.0)	57.99	N/A	57.99
Total	10,210			85.81 ^d

^a Individuals with negative or equivocal viral titers to rubella.

^b Individuals with negative or equivocal viral titers to measles.

^c Individuals positive for all three viral titers.

^d Weighted average cost = (cost of vaccination and testing × percentage of individuals requiring vaccination) + (cost of testing × percent of individuals not requiring vaccination).

According to the data presented, which is likely representative of individuals without other evidence of immunity and represents a large geographic sampling that can effectively account for regional differences in vaccination rates, laboratory evidence of immunity to measles, mumps, and rubella appears to be high in this U.S. population. It is important to note that while serology can be used as evidence of immunity in regard to vaccination guidelines, it cannot necessarily be correlated with protective immunity (14). These data also outline the potential feasibility of different approaches to ensure measles, mumps, and rubella immunity in targeted populations. For instance, the common practice of screening measles and mumps antibodies as a surrogate for vaccine-induced immunity will identify a majority of nonimmune individuals, whereas screening for only mumps antibodies would be ill advised for identifying nonimmune individuals. Institutions using the latter approach should strongly reconsider this policy based on this analysis. While it is important to balance financial expenses in determining institutional policy, screening for immunity cannot be subjected to insensitivity of the algorithm adopted. The framework of this data set allows institutions to apply their own costs of testing for both serology and vaccination in order to formulate appropriate decisions regarding institutional policies on immunity screening.

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