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Appropriateness of Immunoglobulin M Testing for Measles, Mumps, and Rubella

Thomas D. Filardo, MD^{1, #}, Nina B. Masters, PhD^{1, #}, Jessica Leung, MPH¹, Sarah Baca, BS^{2, 3}, Heartley Egwuogu, PhD^{2, 3}, Oscar Rincon Guevara, PhD², Julia Raykin, PhD², David E. Sugerman, MD¹

¹Viral Vaccine Preventable Disease Branch; Division of Viral Diseases; National Center for Immunization and Respiratory Diseases; Centers for Disease Control and Prevention, Atlanta, Georgia;

²Office of Public Health Data, Surveillance, and Technology; Centers for Disease Control and Prevention, Atlanta, Georgia;

³GAP Solutions Inc, Herndon, Virginia

Abstract

Introduction: Testing for immunity to measles, mumps, and rubella should include only immunoglobulin G (IgG); immunoglobulin M (IgM) testing is appropriate only if acute illness is suspected. The appropriateness of measles, mumps, and rubella IgM testing was evaluated in a national administrative dataset.

Methods: Laboratory testing for measles, mumps, and rubella during 2019–2022 was analyzed in 2024 using HealthVerity administrative claims and laboratory data. IgG, IgM, and reverse-transcriptase polymerase chain reaction (RT-PCR) testing are described by year, demographics, and region. IgM testing was examined for appropriateness, defined as an IgM test combined with diagnostic codes indicative of acute illness.

Results: During 2019–2022, IgM testing represented a small proportion of serologic testing (measles: 3.3%, mumps: 2.4%, rubella: 2.1%) but appeared to be appropriately performed in only 15.4% of cases for measles, 32.8% of cases for mumps, and 10.2% of cases for rubella. IgM testing was more commonly performed for female patients, with the largest discrepancy seen for

Address reprint requests to: Thomas D. Filardo, MD, Centers for Disease Control and Prevention, Mailstop 24-8, 1600 Clifton Rd NE, Atlanta, GA, 30329. rhx1@cdc.gov.

[#]These authors contributed equally to this report.

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The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention (CDC).

CREDIT AUTHOR STATEMENT

Thomas D. Filardo: Conceptualization, Investigation, Methodology, Project administration, Supervision, Writing – original draft. Nina B. Masters: Conceptualization, Investigation, Methodology, Project administration, Supervision, Writing – original draft. Jessica Leung: Data curation, Investigation, Methodology, Supervision, Validation, Writing – review & editing. Sarah Baca: Data curation, Formal analysis, Writing – review & editing. Heartley Egwuogu: Data curation, Formal analysis, Writing – review & editing. Oscar Rincon Guevara: Data curation, Formal analysis, Writing – review & editing. Julia Raykin: Data curation, Formal analysis, Supervision, Writing – review & editing. David E. Sugerman: Conceptualization, Supervision, Writing – review & editing.

rubella (90.5% female vs 9.5% male). IgM for measles and mumps was more often performed appropriately for persons aged 0–19 years (37.6% and 60.1%) compared with persons aged 20–49 years (11.8% and 22.0%) and 50+ years (16.5% and 33.8%).

Conclusions: The majority of IgM testing for measles, mumps, and rubella during this period appeared inappropriate. Clinicians and health systems could ensure that IgG testing alone is performed when evaluating for immunity through modifications to electronic medical records and commercial laboratories could ensure that providers are able to test for IgG alone when evaluating immunity.

INTRODUCTION

Measles, mumps, and rubella are vaccine-preventable illnesses which continue to cause substantial global morbidity, mortality, and long-term sequelae despite a highly effective, widely available combination vaccine. Although general serologic screening for immunity for measles, mumps, and rubella is not recommended, some populations do receive routine immunity screening, including women of reproductive age and people with occupational risk for exposure (e.g., healthcare workers). While not routinely recommended, some providers may also opt to use serologic testing for immunity to determine the need for vaccination in the event of unknown or undocumented vaccination history.¹

Screening for immunity to infectious pathogens requires testing for pathogen-specific immunoglobulin G (IgG). Testing for immunoglobulin M (IgM), by contrast, evaluates recent infection and is an indicator of acute disease. Importantly, IgM is not appropriate for measuring immunity. Inappropriate use of IgM when acute infection is not clinically suspected would be expected to yield only false positive results, which can occur due to antibody cross-reactivity with other infections, test interference (e.g., by rheumatoid factor), or by prolonged IgM positivity after vaccination.^{2,3}

METHODS

The CDC-licensed HealthVerity dataset was used for analysis, which includes administrative claims data from multiple payer sources linked to laboratory testing data for patients who had any healthcare encounter possibly related to COVID-19 during the study timeframe. HealthVerity includes data from all 50 U.S. states and Puerto Rico. The analysis was restricted to closed payer medical claims data (September 2023 data release) during 2019–2022 and to persons enrolled at least 14 days before and after a laboratory test for measles, mumps, and/or rubella. Analyses were performed in 2024. Pregnant persons were identified using diagnostic and diagnosis related group (DRG) codes (Appendix). Testing was identified using logical observation identifiers names and codes (LOINC) and text string searches in the variables “test ordered” and “result name.”

Type of tests included in this analysis included IgG alone, IgM alone, both IgG and IGM, and reverse transcriptase polymerase chain reaction (RT-PCR). Testing was described by year, by demographic and geographic characteristics, and type of test. Additionally, IgM testing was assessed for appropriateness, defined as an IgM test combined with diagnostic codes most likely indicative of acute illness within 7 days of the IgM test, which were codes

associated with RT-PCR testing and indicative of acute illness evaluation (Appendix). This activity was reviewed by the CDC, deemed not research, and was conducted consistent with applicable federal law and CDC policy (45 C.F.R. part 46.102(l)(2), 21 C.F.R. part 56; 42 U.S.C. Sect. 241(d); 5 U.S.C. Sect. 552a; 44 U.S.C. Sect. 3501 et seq.).

RESULTS

Between 2019–2022, IgM testing represented a small proportion of the serologic testing being performed (Table 1: 3.3% for measles, 2.4% for mumps, and 2.1% for rubella). Most IgM tests were performed among adults aged 20–49 years; rubella showed the largest proportion of testing in this age group (Table 2: 85.4% of IgM testing).

During 2019–2022, most IgM tests appeared to be performed inappropriately for all three pathogens (Table 1). Overall, IgM testing was appropriately performed in only 15.4% of cases for measles, 32.8% of cases for mumps, and 10.2% of cases for rubella. IgM testing for measles and mumps was more often performed appropriately for younger persons, aged 0–19 years, (37.6% and 60.1%) compared with adults aged 20–49 years (11.8% and 22.0%) and 50+ years (16.5% and 33.8%) (Table 2).

DISCUSSION

An analysis of administrative data from the Health Verity Full COVID dataset suggests that a large proportion of IgM testing for measles, mumps, and rubella is performed inappropriately – when there is no clinical suspicion for acute disease. The high proportion of IgM testing occurring among adults, despite all pathogens being primarily pediatric diseases; paired with the sex discrepancy in testing, provide evidence of inappropriate IgM testing. Anecdotally, CDC has been informed by jurisdictional partners of reports of positive IgM tests for measles, mumps, or rubella, where subsequent investigation often reveals that the testing was performed without clinical suspicion for any acute viral illness. A prior report from New York City showed that almost 80% of rubella IgM testing reported during 2012–2013 was performed inappropriately.⁴ The scale of inappropriate IgM testing has not been well defined nationally, given that most serologic testing for vaccine preventable diseases in the United States is performed in commercial laboratories. Additionally, given overall test specificity of $\geq 80\%$, false positive IgM results reported to public health which stem from inappropriate testing likely represent a small fraction of all IgM testing.^{5,6}

Inappropriate diagnostic testing has the potential to lead to unnecessary public health investigations, inappropriate diagnosis of disease, and inappropriate implementation of disease-specific mitigation strategies (e.g., quarantine or isolation). In the context of rubella, false positive tests may impact decision-making surrounding pregnancies given the devastating potential impact of congenital rubella syndrome.⁷ Additionally, unnecessary diagnostic testing contributes to overall healthcare waste, which has been estimated to be as high as 25% of all healthcare spending in the US.⁸ Ensuring that the right test is performed for the right question (i.e., IgG alone is performed when evaluating for immunity) can help reduce both wasteful laboratory testing and unnecessary public health investigation.

Inappropriate diagnostic testing for other pathogens has been observed. For example, one analysis found that a majority of serologic testing for viral hepatitis appeared to be inappropriate; implementation of interventions through the electronic medical record improved appropriate test usage.⁹

LIMITATIONS

This analysis has several limitations. First, use of administrative claims data is limited to diagnostic codes, which may not fully capture a patient's clinical evaluation. Second, given the small number of RT-PCR tests performed in this dataset, diagnostic codes associated with RT-PCR may not fully capture codes used to represent evaluation for acute measles, mumps, or rubella. As a result, our estimation of appropriate IgM testing may be lower than the actual proportion. Additionally, use of a 1-week window around lab testing to identify codes suggestive of appropriate IgM testing may over- or underestimate appropriateness of IgM testing. Finally, the data are a convenience sample of persons with COVID-19 related encounters and may not be representative of all persons in the US.

CONCLUSIONS

When there is an identified epidemiologic risk for acute measles, mumps, or rubella, pursuing appropriate diagnostic testing for acute disease is important. For mumps, the preferred test is RT-PCR of a buccal swab, with an additional serology specimen for IgM recommended if the patient is tested ≥ 3 days after parotitis onset.¹⁰ For measles and rubella, evaluation for acute disease is recommended to include both a respiratory specimen for RT-PCR (i.e., nasopharyngeal or throat swab) and a serum specimen for IgM.^{11,12}

Interventions to improve appropriate use of IgM would likely be multi-faceted and could include: (1) Healthcare providers and healthcare systems can ensure that providers have access to isolated testing for IgG for common pathogens for which immunity is assessed, including measles, mumps, and rubella; (2) Specific order sets or order prompts could assist providers in choosing the right test (i. e., IgG alone) when testing for immunity; and (3) Commercial laboratories could include information within their ordering directories to appropriately point providers to the right test when assessing for immunity.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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REFERENCES

1. McLean HQ, Fiebelkorn AP, Temte JL, Wallace GS. Prevention of measles, rubella, congenital rubella syndrome, and mumps, 2013: summary recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep*. 2013;62(RR-04):1–34.
2. Wandinger KP, Saschenbrecker S, Steinhagen K, et al. Diagnosis of recent primary rubella virus infections: significance of glycoprotein-based IgM serology, IgG avidity and immunoblot analysis. *J Virol Methods*. 2011;174(1–2):85–93. 10.1016/j.jviromet.2011.04.001. [PubMed: 21513745]
3. Woods CR. False-positive results for immunoglobulin M serologic results: explanations and examples. *J Pediatric Infect Dis Soc*. 2013;2(1):87–90. 10.1093/jpids/pis133. [PubMed: 26619450]
4. Isaac BM, Zucker JR, Giancotti FR, et al. Rubella surveillance and diagnostic testing among a low-prevalence population, New York City, 2012–2013. *Clin Vaccine Immunol*. 2017;24(9):e00102–17. 10.1128/cvi.00102-17. [PubMed: 28701468]
5. Zubach V, Beirnes J, Hayes S, Severini A, Hiebert J. Diagnostic accuracy of commercially available serological tests for the detection of measles and rubella viruses: a systematic review and meta-analysis. *J Clin Microbiol*. 2024;62(2):e01339–23. 10.1128/jcm.01339-23. [PubMed: 38275299]
6. Sowers SB, Anthony K, Mercader S, et al. Performance characteristics of six immunoglobulin m enzyme-linked immunosorbent assays used for laboratory confirmation of measles. *J Clin Microbiol*. 2022;60(12): e0122722. 10.1128/jcm.01227-22. [PubMed: 36409098]
7. Best JM, O'Shea S, Tipples G, et al. Interpretation of rubella serology in pregnancy—pitfalls and problems. *Bmj*. 2002;325(7356):147–148 Jul 20. 10.1136/bmj.325.7356.147. [PubMed: 12130613]
8. Shrank WH, Rogstad TL, Parekh N. Waste in the US Health Care System: estimated costs and potential for savings. *JAMA*. 2019;322(15):1501–1509. 10.1001/jama.2019.13978. [PubMed: 31589283]
9. Hammami MB, Hussaini K, Chhaparia A, Khalid H, Chamberland R, Neuschwander-Tetri B. Inappropriate testing for acute viral hepatitis is common-impact of an intervention using the electronic health record in a tertiary teaching hospital in the United States. *Ochsner J*. Fall 2020;20(3):293–298. 10.31486/toj.19.0062.
10. Centers for Disease Prevention and Control. Mumps testing job-aid for providers. Accessed May 1, 2024. <https://www.cdc.gov/mumps/health-departments/mumps-testing-job-aid.html>
11. Centers for Disease Prevention and Control. Manual for the surveillance of vaccine-preventable diseases. Chapter 7: Measles. Updated April 1, 2014. Accessed May 1, 2024. <http://www.cdc.gov/vaccines/pubs/surv-manual/chpt07-measles.pdf>
12. Centers for Disease Control and Prevention. Test types typically available to clinicians and descriptions for measles, mumps, rubella, and varicella. Accessed April 12, 2024. Available at: <https://www.cdc.gov/chickenpox/downloads/MMRV-Testing-for-Clinicians.pdf>.

Table 1.
Testing for Measles, Mumps, or Rubella, Stratified by Pathogen, 2019–2022

Any Testing	Measles N (%)	Mumps N (%)	Rubella N (%)
Type of testing ^a	525,143	451,571	1,226,511
IgG alone	507,109 (96.6)	438,440 (97.1)	679,366 (55.4)
IgM alone	15,592 (3.0)	10,781 (2.4)	24,004 (2.0)
IgG AND IgM	1,689 (0.3)	158 (0.0)	1,140 (0.1)
IgM any	17,281 (3.3)	10,939 (2.4)	25,144 (2.1)
IgM appropriate ^b	2,667 (15.4)	3,588 (32.8)	2,562 (10.2)
RT-PCR	21 (0.0)	1,023 (0.2)	59 (0.0)

Note: Data presented are from the CDC-licensed HealthVerity dataset.

Abbreviations: Immunoglobulin G, IgG; Immunoglobulin M, IgM; Reverse-transcriptase polymerase chain reaction, RT-PCR

^aTests coded as “antibody (unspecified)”, IFA, or culture are excluded from this portion of the table broken out by test type, but included in ‘Any Testing’.

^bAppropriate indications for IgM testing for measles, mumps, and rubella are defined in Supplementary Table S1, and calculated as the % of appropriate IgM tests / all IgM tests for that pathogen

Table 2. Characteristics of Persons Tested for Measles, Mumps, or Rubella, Stratified by Condition, 2019–2022

Characteristic	Measles					Mumps					Rubella				
	IgG alone N (%)	IgM any N (%)	IgM appropriate ^a N (Row %)	RT-PCR N (%)	IgG alone N (%)	IgM any N (%)	IgM appropriate N (Row %)	RT-PCR N (%)	IgG alone N (%)	IgM any N (%)	IgM appropriate N (Row %)	RT-PCR N (%)	IgG alone N (%)	IgM any N (%)	RT-PCR N (%)
Year															
2019	176,724 (34.8)	8,105 (46.9)	1,498 (18.5)	0 (0.0)	144,799 (33.0)	4,314 (39.4)	1,537 (35.6)	454 (44.4)	59,975 (8.8)	7,241 (28.8)	782 (10.8)	25 (42.4)			
2020	110,992 (21.9)	3,713 (21.5)	356 (9.6)	0 (0.0)	95,443 (21.8)	2,559 (23.4)	825 (32.2)	201 (19.6)	54,844 (8.1)	6,523 (25.9)	657 (10.1)	10 (16.9)			
2021	118,380 (23.3)	3,100 (17.9)	397 (12.8)	4 (19.0)	106,039 (24.2)	2,231 (20.4)	658 (29.5)	157 (15.3)	309,962 (45.6)	6,522 (25.9)	654 (10.0)	12 (20.3)			
2022	101,013 (19.9)	2,363 (13.7)	416 (17.6)	17 (81.0)	92,159 (21.0)	1,835 (16.8)	568 (31.0)	211 (20.6)	254,585 (37.5)	4,858 (19.3)	469 (9.7)	12 (20.3)			
Total ^b	507,109	17,281	2,667 (15.4)	21	438,440	10,939	3,588 (32.8)	1,023	679,366	25,144	2,562 (10.2)	59			
Age Group															
0–19 years	37,174 (7.3)	1,729 (10.0)	650 (37.6)	14 (66.7)	35,664 (8.1)	2,427 (22.2)	1,459 (60.1)	472 (46.1)	42,519 (6.3)	1,961 (7.8)	261 (13.3)	13 (22.0)			
20–49 years	357,999 (70.6)	11,557 (66.9)	1,359 (11.8)	6 (28.6)	308,230 (70.3)	6,320 (57.8)	1,389 (22.0)	413 (40.4)	591,516 (87.1)	21,477 (85.4)	2,147 (10.0)	41 (69.5)			
50+ years	111,938 (22.1)	3,995 (23.1)	658 (16.5)	1 (4.8)	94,548 (21.6)	2,192 (20.0)	740 (33.8)	138 (13.5)	45,337 (6.7)	1,706 (6.8)	154 (9.0)	5 (8.5)			
Total	507,111	17,281	2,667	21	438,442	10,939	3,588	1,023	679,372	25,144	2,562	59			
Sex															
Male	135,049 (26.7)	4,305 (24.9)	1,033 (24.0)	7 (33.3)	122,698 (28.0)	3,801 (34.8)	1,646 (43.3)	506 (49.5)	64,361 (9.5)	2,367 (9.4)	267 (11.3)	15 (25.4)			
Female	371,642 (73.3)	12,967 (75.1)	1,633 (12.6)	14 (66.7)	315,378 (72.0)	7,131 (65.2)	1,940 (27.2)	517 (50.5)	614,674 (90.5)	22,771 (90.6)	2,295 (10.1)	44 (74.6)			
Pregnant (%)	72,350 (14.3)	3,907 (22.6)	285 (7.3)	0 (0.0)	46,253 (10.6)	773 (7.1)	115 (14.9)	22 (2.2)	385,311 (56.7)	13,886 (55.2)	1,833 (13.2)	26 (44.1)			
Total	506,691	17,272	2,666	21	438,076	10,932	3,586	1,023	679,035	25,138	2,562	59			
Region															
Midwest	46,002 (9.1)	1,151 (6.7)	212 (18.4)	4 (20.0)	42,466 (9.7)	1,430 (13.1)	547 (38.3)	231 (22.6)	71,495 (10.5)	2,416 (9.6)	203 (8.4)	2 (3.4)			
Northeast	255,918 (50.7)	5,939 (34.4)	824 (13.9)	5 (25.0)	224,017 (51.3)	3,006 (27.5)	951 (31.6)	321 (31.4)	194,115 (28.6)	6,492 (25.9)	470 (7.2)	9 (15.5)			

Characteristic	Measles				Mumps				Rubella			
	IgG alone N (%)	IgM any N (%)	IgM appropriate ^a N (Row %)	RT-PCR N (%)	IgG alone N (%)	IgM any N (%)	IgM appropriate N (Row %)	RT-PCR N (%)	IgG alone N (%)	IgM any N (%)	IgM appropriate N (Row %)	RT-PCR N (%)
South	72,754 (14.4)	3,896 (22.6)	612 (15.7)	9 (45.0)	65,696 (15.1)	3,046 (27.9)	1,148 (37.7)	308 (30.2)	195,693 (28.9)	8,695 (34.7)	1,139 (13.1)	21 (36.2)
West	130,136 (25.8)	6,269 (36.3)	1,013 (16.2)	2 (10.0)	104,136 (23.9)	3,432 (31.4)	936 (27.3)	161 (15.8)	216,590 (32.0)	7,473 (29.8)	747 (10.0)	26 (44.8)
Total	504,810	17,255	2,661	20	436,315	10,914	3,582	1,021	677,893	25,076	2,559	58

Note: Data presented are derived from the CDC-licensed HealthVerity dataset.

Abbreviations: Immunoglobulin G, IgG; Immunoglobulin M, IgM; Reverse-transcriptase polymerase chain reaction, RT-PCR

^a Appropriate indications for IgM testing for Measles, Mumps, and Rubella are defined in Supplementary Table S1, and calculated as the % of appropriate IgM tests / all IgM tests for that pathogen

^b The table represents test-level data, and individual persons may be repeated in the data if they received multiple tests during the study period. As a result, the total number of persons tested may reflect a smaller number than the total number of laboratory tests individually indexed in the table above. For Measles, there were 455,240 persons tested by IgG alone, 15,088 persons tested by IgM alone, and 1,656 persons tested by IgG and IgM. For Mumps, there were 396,798 persons tested by IgG alone, 10,370 persons tested by IgM alone, and 158 tested by IgG and IgM. For Rubella, there were 609,800 persons tested by IgG alone, 22,234 tested by IgM alone, and 1,117 tested by IgG and IgM over the study period.