MAJOR ARTICLE

Adverse Events Following Measles, Mumps, and Rubella Vaccine in Adults Reported to the Vaccine Adverse Event Reporting System (VAERS), 2003–2013

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Background. Limited data exist on the safety of the measles, mumps, and rubella (MMR) vaccine in adults. We reviewed reports of adverse events (AEs) to the Vaccine Adverse Event Reporting System (VAERS) to assess safety in this previously understudied group.

Methods. VAERS is the national spontaneous vaccine safety surveillance system coadministered by the Centers for Disease Control and Prevention and the US Food and Drug Administration. We searched the VAERS database for US reports of adults aged ≥19 years who received the MMR vaccine from 1 January 2003 to 31 July 2013. We clinically reviewed reports and available medical records for serious AEs, pregnancy reports, and reports for selected prespecified outcomes.

Results. During this period, VAERS received 3175 US reports after MMR vaccine in adults. Of these, 168 (5%) were classified as serious, including 7 reports of death. Females accounted for 77% of reports. The most common signs and symptoms for all reports were pyrexia (19%), rash (17%), pain (13%), and arthralgia (13%). We did not detect any new safety findings in empirical Bayesian data mining. We identified 131 reports of MMR vaccine administered to a pregnant woman; the majority of these vaccinations were in the first trimester and in 83 (62%), no AE was reported.

Conclusions. In our review of VAERS data, we did not detect any new or unexpected safety concerns for MMR vaccination in adults. We identified reports of pregnant women exposed to MMR, which is a group in whom the vaccine is contraindicated, suggesting the need for continued provider education on vaccine recommendations and screening.

Keywords. measles; mumps; rubella; MMR vaccine; Vaccine Adverse Event Reporting System (VAERS).

The Advisory Committee on Immunization Practices recommends 2 doses of measles, mumps, and rubella vaccine (MMR) for children [1]. One dose of MMR is recommended for unvaccinated adults born in 1957 or later or those without immunity to MMR [2]. Students in postsecondary educational institutions, healthcare workers, and adults traveling internationally should receive a second dose. More than 95% of individuals will develop immunity to measles after the first MMR dose and nearly all after a second dose [3]. MMR is well tolerated, and most adverse events (AEs) are mild and self-limited (eg, fever, rash, lymphadenopathy, parotitis, transient arthralgias/arthritis). MMR has been associated with febrile seizures [3–5] and, on rare occasions, idiopathic thrombocytopenic purpura in the 6 weeks

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following vaccination [6]. Information on safety of MMR in adults is limited, but data from large-scale vaccination programs are reassuring [7–9].

Although endemic measles transmission was eliminated in the United States in 2000, outbreaks related to imported cases continue [3]. In the first half of 2014, numbers of confirmed measles cases (288) exceeded each yearly total since elimination [10]. Recent large-scale measles outbreaks in European Union countries [11, 12], likely resulting from pockets of unvaccinated individuals, have prompted European Union countries to consider catch-up MMR vaccination programs targeting adults. To evaluate the safety of MMR in adults and inform potential catch-up vaccination programs, we reviewed reports to the Vaccine Adverse Event Reporting System (VAERS) following MMR for individuals aged ≥19 years.

METHODS

VAERS, coadministered by the Centers for Disease Control and Prevention (CDC) and US Food and Drug Administration is a passive surveillance system that accepts reports of AEs following vaccination from healthcare providers, vaccine manufacturers, patients, parents, and others [13]. VAERS data include demographic information about vaccine recipients, specific vaccine(s) received, details of AEs experienced, and patients' medical histories [14]. Trained personnel code signs and symptoms of AEs using Medical Dictionary for Regulatory Activities (MedDRA) terms [15]. Reports may be assigned 1 or more MedDRA preferred terms (PTs). Not all reports include adverse health events (eg, medication errors). Reports are classified as serious, defined by the Code of Federal Regulations, if any of the following are reported: death, life-threatening illness, hospitalization, prolongation of hospitalization, or permanent disability [14]. Medical records are requested and reviewed for serious reports, except reports submitted by vaccine manufacturers, which are subject to separate follow-up procedures.

We searched VAERS for US reports of adults aged ≥19 years who received MMR. We included reports of patients vaccinated 1 January 2003 through 31 July 2013 that were received by 31 January 2014. We did not perform causality assessments.

Two CDC physicians (L. S. and M. M. M.) independently reviewed serious reports to determine the primary event prompting the report to VAERS and assigned reports to previously described diagnostic categories [16]; discrepancies were discussed as a group and consensus was reached. We prespecified conditions for clinical review: Guillain-Barré syndrome (GBS), anaphylaxis, arthritis/arthralgia, encephalitis/acute disseminated encephalomyelitis (ADEM)/transverse myelitis (TM), idiopathic thrombocytopenic purpura (ITP), myocarditis/pericarditis, myocardial infarction, vaccine virus infection in immunocompromised patients, and vaccination in pregnancy (Supplementary Data). We reviewed VAERS reports and medical records, if available, for prespecified conditions. For anaphylaxis, we included reports if symptoms began the day of vaccination or the day following vaccination (days 0–1). For other outcomes, no constraints were placed on onset interval. Although we limited analysis to vaccination dates prior to 1 August 2013, we extended the date for receiving MMR reports to 31 January 2014, to allow for reports of vaccine virus infection in immunocompromised patients, which can have a delayed onset. We applied Brighton Collaboration case definitions to prespecified conditions where available [17–20].

We identified reports of MMR vaccination in pregnancy using an automated search strategy previously described [21]. Gestational age at vaccination and at onset of AE symptoms was calculated based on date of last menstrual period or estimated delivery date in the VAERS report and/or medical records. If this information was not provided, we used other means (eg, ultrasound report). Trimester was defined as first (0–13 weeks), second (14–27 weeks), or third (≥28 weeks) [22]. Spontaneous abortion was defined as fetal demise prior to 20 weeks of gestation. Preterm delivery was defined as live birth before 37 weeks' gestation. If >1 AE was reported, we assigned the diagnosis that we determined was the primary event of concern. Additionally, if a single report contained AEs for the mother and infant, it was counted as 2 independent observations when describing AEs in pregnancy.

We used empirical Bayesian (EB) data mining [23] to identify AEs reported more frequently than expected following MMR in adults. We used published criteria [24] to identify MMR-AE pairs reported at least twice as frequently as would be expected (ie, lower bound of the 90% confidence interval surrounding the EB geometric mean [EB05 >2]). MMR reports were compared to all other vaccines in the VAERS database [25]. We clinically reviewed MMR reports with MedDRA PTs that exceeded the data mining threshold noted above. We excluded from review AEs described in the vaccine package insert as these are known and expected AEs.

RESULTS

During the study period, VAERS received a total of 3175 US reports following MMR in adults aged ≥19 years (Table 1). In 1599 (50.4%) reports, patients received MMR alone. For the remaining 1576 (49.6%), most commonly coadministered vaccines included varicella (429 [27.2%]), tetanus, diphtheria, and pertussis (395 [25.1%]), and hepatitis B (272 [17.3%]). Median interval from vaccination symptom onset was 2 days (range, 0–954 days). Median age of vaccine recipients was 37 years (range, 19–101 years). Females accounted for 2448 (77.1%) of the reports. In 1455 (45.8%) reports, no dose number was recorded; in the remaining reports dose number varied from 1 to 13, suggesting a lack of reliability in documented

Table 1. Reports to the Vaccine Adverse Event Reporting System Following Measles, Mumps, and Rubella Vaccine in Adults Aged ≥19 Years, 1 January 2003–31 July 2013

Characteristics	No. (%)
Total reports	3175
Serious reports	168 (5.3)
Female sex	2448 (77.1)
Median age (range), y	37 (19–101)
Median time to adverse event onset (range), d	2 (0–954)
US military reports	212 (6.7)
Type of reporter	
Vaccine provider	1599 (50.4)
Patient/parent	328 (10.3)
Manufacturer	360 (11.3)
Other	860 (27.1)

dose number. A total of 212 (6.7%) reports were in US military personnel. There were 168 (5.3%) serious reports, including 7 reports of death. The most common MedDRA PTs for all reports were pyrexia (614 [19.3%]), rash (524 [16.5%]), and pain (414 [13.0%]). Table 2 shows the most common MedDRA PTs reported for serious and nonserious reports.

Clinical Review

Death Reports

We identified 7 reports of death following MMR (Table 3). In 6 (86%) reports, patients received other vaccines, and in 5 (71%) reports, preexisting illness was documented. Interval from vaccination to time of death ranged from 2 hours to 102 days (median, 5 days). In 4 reports, the listed cause of death was cardiac or cardiovascular in origin. One death occurred in a patient receiving MMR vaccine alone. This was a 48-year-old man with a history of cardiovascular disease who died 2 days after vaccination from cardiovascular disease.

Nondeath Serious Reports

Table 4 shows characteristics of 161 nondeath serious reports, 66 (41.0%) of which were in patients receiving MMR vaccine alone. The most common presenting symptom or diagnosis was neurologic (31 [19.3%]). The most common diagnoses among neurologic reports were encephalitis (8) and seizures (5). In addition to general neurologic events, there were 17 (10.6%) GBS reports. The next most common diagnostic category was "other noninfectious" (27 [16.8%]), followed by "other infectious" (24 [14.9%]). "Other noninfectious" is a nonspecific category incorporating a variety of diagnoses (eg, syncope, thrombocytopenia).

Anaphylaxis

We identified 13 anaphylaxis reports following MMR; 11 (84.6%) were serious. Seven reports met Brighton level 1 case definition of anaphylaxis. The other 6 were Brighton level 2. All had symptom onset within 24 hours of vaccination; most (10) within 1 hour. Eight patients received only MMR. Nine patients with anaphylaxis had a history of other allergies, including medications and environmental allergens. One patient had documented neomycin allergy (MMR vaccine contains approximately 25 μg neomycin) prior to receiving MMR.

Table 2. Serious and Nonserious Reports to the Vaccine Adverse Event Reporting System Following Measles, Mumps, and Rubella Vaccine and Common Medical Dictionary for Regulatory Activities Preferred Terms[a] in Adults Aged ≥19 Years, 1 January 2003–31 July 2013

Reports and MedDRA Preferred Terms	No. (%)
Serious reports	168
Pyrexia	40 (23.8)
Headache	36 (21.4)
Asthenia	32 (19.0)
Hypoesthesia	32 (19.0)
Arthralgia	30 (17.9)
Pain	27 (16.1)
Dyspnea	26 (15.5)
Muscular weakness	24 (14.3)
Rash	22 (13.1)
Fatigue	21 (12.5)
Nonserious reports	3007
Pyrexia	574 (19.1)
Rash	502 (16.7)
Pain	387 (12.9)
Arthralgia	373 (12.4)
Injection site erythema	344 (11.4)
Pruritus	313 (10.4)
Erythema	310 (10.3)
Headache	296 (9.8)
Lymphadenopathy	246 (8.2)
Injection site pain	223 (7.4)

Abbreviation: MedDRA, Medical Dictionary for Regulatory Activities.

[a] A report may contain >1 MedDRA preferred term.

Myocarditis

We identified 4 myocarditis reports following MMR. Three were serious, including 1 report of death. Interval from time of vaccination symptom onset ranged from 7 to 13 days. Three patients had concomitant administration of other live vaccines, all of whom received smallpox vaccine and one of whom also received varicella vaccine. One patient who received concomitant Dryvax smallpox vaccine had a history of myocarditis after receiving the same vaccine 6 years earlier. Two patients continued to have chest pain at 2 and 5 months post-vaccination; information was unavailable on the third patient.

Table 3. Death Reports to the Vaccine Adverse Event Reporting System Following Measles, Mumps, and Rubella Vaccine in Adults Aged ≥19 Years, 1 January 2003–31 July 2013

Age, y, Sex	Vaccine(s)	MMR Dose	Comorbidities, Medical History	Onset to Symptoms	Onset to Death	Cause of Death
48, M	MMR	2	Hypertension, arteriosclerotic cardiovascular disease, pulmonary emphysema	2 d	2 d	Cardiovascular disease
22, M	Smallpox, anthrax, hepatitis A, hepatitis B, tetanus diphtheria, MMR, polio	1[a]	None	5 d	5 d	Drug overdose leading to cardiopulmonary arrest
21, M	Hepatitis A, hepatitis B, influenza, meningococcal, MMR, inactivated polio, tetanus diphtheria	1[a]	None	7 d	86 d	Chronic myocarditis
43, F	MMR, hepatitis B	1	Diabetes mellitus, hypothyroidism	9 h	9 h	Arrhythmia and cardiac arrest
50, F	MMR, Tdap	Unknown	Lung cancer, polyneuropathy, seizures, developed transverse myelitis after vaccination	7 d	102 d	Pulmonary embolism
49, M	MMR, Tdap	Unknown	Atherosclerosis	Day prior to vaccination	2–3 h	Coronary artery disease
45, F	MMR, varicella[b]	Unknown	Lupus, kidney disease, s/p renal transplant on immunosuppression	31 d	34 d	Disseminated vaccine strain varicella

Abbreviations: F, female; M, male; MMR, measles, mumps, and rubella; s/p, status post; Tdap, tetanus, diphtheria, and pertussis.

[a] Vaccinations given in US military personnel.

[b] Tdap, hepatitis A, and pneumococcal polysaccharide vaccines given 1 week after MMR and varicella.

Idiopathic Thrombocytopenic Purpura

We identified 5 ITP reports following MMR. Onset ranged from 3 days to 2 months following vaccination. Three were serious and required hospitalization; all met Brighton level 1 case definition of ITP. One patient had a prior history of ITP. Of the 2 nonserious reports, 1 met Brighton level 2 case definition of ITP and the other had insufficient information for evaluation.

Guillain-Barré Syndrome

We identified 18 GBS reports following MMR; 17 (94.4%) were serious. Four met Brighton level 1 case definition of GBS, 8 met level 2 case definition, 3 met level 3 case definition, and 3 had insufficient information for evaluation. Four patients received MMR alone, whereas 14 patients received concomitant vaccines. The most commonly coadministered vaccines were hepatitis B (12), influenza (11), and hepatitis A (11). Interval from vaccination to symptom onset ranged from 1 to 127 days; in 17 reports, symptom onset fell within the expected 1- to 42-day GBS risk interval [26]. Nine patients had evidence of preceding illnesses, of whom 1 had positive EBV titers on hospital admission.

Encephalitis/Acute Disseminated Encephalomyelitis/ Transverse Myelitis

We identified 9 reports of encephalitis, ADEM and TM, all of which were serious and required hospitalization. Median interval from vaccination to symptom onset was 9 days (range, 1–227 days). There were 5 reports of encephalitis (2 met Brighton level 2 case definition, 2 were level 3, and 1 was level 3A). Two of these patients received MMR alone. There were 3 cases of ADEM (1 each Brighton level 2, level 3, and level 3A). One patient with ADEM received MMR alone. This patient was diagnosed with demyelinating encephalitis while overseas, and no further information was available. One patient with Brighton level 2 TM received concomitant MMR, hepatitis A, and live attenuated influenza vaccines. None of the reports included documentation of known infectious etiologies for encephalitis. In a patient with symptom onset the day following vaccination with MMR, hepatitis B, and tetanus-diphtheria vaccines, a neurologist determined the event was not related to vaccination.

Arthritis/Arthralgia

We identified 15 reports of arthritis or arthralgia following MMR. All were in females, and onset ranged from 0 to 19 days postvaccination. One report was serious and involved a patient subsequently diagnosed with rheumatoid arthritis. Four patients had reported arthralgia (joint pain or physician reported arthralgia), and 11 had evidence of arthritis (swelling, limited range of motion, or physician reported arthritis). Seven patients had reported an associated rash. One patient, who also received

Table 4. Diagnostic Categories[a] and Selected Conditions for 161 Nondeath Serious Reports to the Vaccine Adverse Event Reporting System After Measles, Mumps, and Rubella Vaccine in Adults Aged ≥19 Years, 1 January 2003–31 July 2013

Body System Category	MMR Vaccine Alone, No. (%)	MMR and Other, Vaccines No. (%)	All MMR Vaccines, No. (%)
Total No. of nondeath serious reports	66	95	161
Neurological	15 (22.7)	16 (16.8)	31 (19.3)
Encephalitis	3	6	9
Seizure	1	4	5
Multiple sclerosis	3	2	5
Other noninfectious	9 (13.6)	18 (18.9)	27 (16.8)
Multiple symptoms	1	5	6
Thrombocytopenia	1	2	3
Syncope	0	2	2
Other infectious	11 (16.7)	13 (13.7)	24 (14.9)
Febrile illness	6	1	7
Meningitis	2	3	5
Varicella rash	0	4	4
Guillain-Barré syndrome	3 (4.5)	14 (14.7)	17 (10.6)
Allergy	4 (6.0)	8 (8.4)	12 (7.5)
Anaphylaxis	7 (10.6)	4 (4.2)	11 (6.8)
Musculoskeletal	2 (3.0)	8 (8.4)	10 (6.2)
Respiratory	3 (4.5)	3 (3.2)	6 (3.7)
Psychiatric	2 (3.0)	3 (3.2)	5 (3.1)
Cardiac	2 (3.0)	3 (3.2)	5 (3.1)
Local reaction	2 (3.0)	3 (3.2)	5 (3.1)
Ear, nose, and throat	4 (6.0)	0 (0.0)	4 (2.5)
Gastrointestinal	2 (3.0)	1 (1.1)	3 (1.9)
Pregnancy complication	0 (0.0)	1 (1.1)	1 (0.6)

Abbreviation: MMR, measles, mumps, and rubella.

[a] Diagnostic categories as described in Velozzi, C et al. Adverse events following influenza A (H1N1) 2009 monovalent vaccines reported to the Vaccine Adverse Event Reporting System, United States, 1 October 2009–31 January 2010. Vaccine 2010; 28:7248–55.

varicella vaccine, was diagnosed with a varicella infection. Another patient was diagnosed with a "case of measles" following vaccination.

Myocardial Infarction

We identified 1 report of myocardial infarction following MMR in a 56-year-old man with a history of peripheral vascular disease. The event occurred 6 days postvaccination while the patient was undergoing cardiac rehabilitation.

Vaccine Virus Shedding

There were no reports of vaccine virus infection in immunocompromised patients following MMR.

Table 5. Characteristics of 131 Pregnancy Reports to the Vaccine Adverse Event Reporting System Following Measles, Mumps, and Rubella Vaccine in Adults Aged ≥19 Years, 1 January 2003–31 July 2013

Characteristics	MMR Vaccine Alone	MMR With Other Vaccines	All MMR Vaccines
Total No. of pregnancy reports	42	89	131
Median maternal age (range), y	28 (19–44)	28 (19–40)	28 (19–44)
Trimester at time of vaccination			
First (0–13 wk)	28 (66.7)	54 (60.7)	82 (62.6)
Second (14–27 wk)	2 (4.8)	4 (4.5)	6 (4.6)
Third (>28 wk)	1 (2.4)	0 (0.0)	1 (0.8)
Unknown	11 (26.2)	31 (34.8)	42 (32.1)

Abbreviation: MMR, measles, mumps, and rubella.

Pregnancy

We identified 131 total pregnancy reports (Table 5). In 42 (32.1%) reports, the patient received MMR alone. Median maternal age at vaccination was 28 years (range, 19–44 years). The majority of vaccinations (82 [62.6%]) occurred in the first trimester. Most reports did not comment on mode of delivery. Of the deliveries that were reported, 2 were vaginal and 8 were cesarean section. The most common reason for cesarean section was failure to progress, in 4 deliveries. Other reasons for cesarean section were shoulder position, breech presentation, repeat cesarean, and fetal distress.

Three reports included both maternal and infant AEs and were thus considered separate events (134 total events). In the majority (83 [61.9%]) of pregnancy reports, no AE was reported. Of the pregnancy AE reports, 44 (32.8%) were in patients receiving MMR vaccine alone. The most common pregnancy-specific AE was spontaneous abortion (17 [12.7%]) (Table 6). The next most commonly reported pregnancy-specific AEs were therapeutic abortion and oligohydramnios, with 5 (3.7%) reports each. Vaginal bleeding occurred in 3 women and premature delivery occurred in 2 women. No maternal hospitalizations were reported, other than for delivery. Two reports were considered serious and involved infant outcomes. One infant, whose mother was vaccinated in the first week of gestation, was born with multiple congenital anomalies (anorectal disorder, hydrocephalus). Another infant, whose mother was vaccinated in the second week of gestation, was born at term and hospitalized for meningitis at 3 weeks of age. The infant recovered. Other congenital anomalies reported include Jacobsen syndrome, Triploidy 69XY, Turner syndrome, and 1 report of "unspecified congenital anomalies" with no other related information.

Table 6. Adverse Events in Pregnant Women Reported to the Vaccine Adverse Event Reporting System Following Measles, Mumps, and Rubella Vaccine (n = 134[a]), 1 January 2003–31 July 2013

Adverse Events	MMR Vaccine Alone, No. (%)	MMR With Other Vaccines, No. (%)	All MMR Vaccines, No. (%)
Total No. of pregnancy AE reports	44	90	134
Pregnancy-specific AEs			
Spontaneous abortion	3 (6.8)	14 (15.6)	17 (12.7)
Therapeutic abortion	2 (4.5)	3 (3.3)	5 (3.7)
Oligohydramnios[b]	3 (6.8)	2 (2.2)	5 (3.7)
Vaginal bleeding/ spotting	0 (0.0)	3 (3.3)	3 (2.2)
Preterm delivery[c]	0 (0.0)	2 (2.2)	2 (1.5)
Prolonged rupture of membranes	0 (0.0)	1 (1.1)	1 (0.7)
Postpartum hemorrhage[d]	0 (0.0)	1 (1.1)	1 (0.7)
Hyperemesis	0 (0.0)	1 (1.1)	1 (0.7)
Preeclampsia	0 (0.0)	1 (1.1)	1 (0.7)
Placenta previa	0 (0.0)	1 (1.1)	1 (0.7)
Total	8 (18.2)	29 (32.2)	37 (27.6)
Nonpregnancy specific AEs			
Rash	0 (0.0)	1 (1.1)	1 (0.7)
Urinary tract infection	1 (2.3)	0 (0.0)	1 (0.7)
Upper respiratory infection	1 (2.3)	0 (0.0)	1 (0.7)
Headache and stomach ache	0 (0.0)	1 (1.1)	1 (0.7)
Fever	1 (2.3)	0 (0.0)	1 (0.7)
Influenza infection	0 (0.0)	1 (1.1)	1 (0.7)
Pain at injection site	0 (0.0)	1 (1.1)	1 (0.7)
Total	3 (6.8)	4 (4.4)	7 (5.2)
Congenital abnormalities/major birth defects			
Jacobsen syndrome[e]	1 (2.3)	0 (0.0)	1 (0.7)
Anorectal disorder[f]	0 (0.0)	1 (1.1)	1 (0.7)
Triploidy 69XY[g]	0 (0.0)	1 (1.1)	1 (0.7)
Turner syndrome[f]	1 (2.3)	0 (0.0)	1 (0.7)
Unspecified congenital anomalies[g]	1 (2.3)	0 (0.0)	1 (0.7)
Total	3 (6.8)	2 (2.2)	5 (3.7)
Fetal/infant outcomes			
Neonatal jaundice	1 (2.3)	0 (0.0)	1 (0.7)
Meningitis at 3 wk of age[g]	0 (0.0)	1 (1.1)	1 (0.7)
Total	1 (2.3)	1 (1.1)	2 (1.5)
No AE (or no information)	29 (65.9)	54 (60.0)	83 (61.9)

Abbreviations: AE, adverse event; MMR, measles, mumps, and rubella.

[a] Includes 134 AEs in 131 reports; 3 pregnancy reports contained 2 AEs each (AE in mother and AE in infant).

[b] One patient with oligohydramnios also had gestational hypertension, another had group B streptococcal infection.

[c] Patient also had a rash and elevated liver function tests after vaccination.

[d] Patient also had gestational diabetes.

[e] Maternal vaccination in the fourth week of gestation.

[f] Maternal vaccination in the first week of gestation.

[g] Maternal vaccination in the second week of gestation.

Data Mining

There were 18 data mining findings for the age group 19–44 years. All findings were either described in the manufacturer's package insert (labeled) or "not an adverse event." Labeled events included lymphadenopathy, measles, mumps, rash (morbilliform), parotid gland enlargement, parotitis, sialoadenitis, and "no therapeutic response." The 9 findings under "not an adverse event" were related to antibody testing, for example, "measles antibody positive," "measles antibody negative," and "rubella antibody test." The single unlabeled data mining finding was "osteoarthritis." Review of these cases found subjective joint swelling or an acute, self-resolving arthritis, not a chronic degenerative process. In the age group 45–64 years, there were 14 data mining findings. Five were related to antibody testing and 4 were related to rash. The remaining labeled findings were arthralgia, joint stiffness, joint swelling, lymphadenopathy, and osteoarthritis. The only data mining finding in those aged ≥65 years was arthralgia.

DISCUSSION

We conducted a comprehensive review of VAERS reports following MMR in adults aged ≥19 years, including automated analysis of reports; clinical review of serious reports, pregnancy reports, and reports of prespecified outcomes; and data mining to assess for disproportionate reporting. We did not find any unexpected or concerning patterns of AEs for MMR when given alone or with other vaccinations.

Previous studies indicate that MMR is well tolerated [3]. MMR is most commonly associated with fever (<15%), rash (5%), lymphadenopathy (5% in children, 20% in adults), and parotitis (<1%). MMR safety data in adolescents and adults are limited. A Vaccine Safety Datalink study found that children 10–12 years of age were more likely to have medically attended events after the second dose of MMR than children 4–5 years old [27]. In 2001, an MMR vaccination campaign was implemented in Costa Rica for persons aged 15–39 years in response to a large rubella outbreak [7]. More than 1.6 million doses were administered, and 981 AEs were detected using a passive reporting system (reporting rate 60/100 000 doses). The most common AEs were rash (26%), lymphadenopathy (16%), and fever (15%). In 1998, Turkish health professionals implemented an MMR vaccination program for individuals aged 20–24 years in response to a measles outbreak at a medical school [9]. Most (96%) subjects did not report AEs. The most commonly reported AEs were upper respiratory tract infections (2.3%), fever (1.9%), and anorexia (1.9%).

Our safety review is the first to focus specifically on AEs following MMR in adults aged ≥19 years. Findings are consistent with previous data that indicate MMR is well tolerated in adults. Our review has limitations. As a passive surveillance system,

VAERS is subject to reporting bias. Additionally, we are unable to determine the number of doses of MMR administered to adults during the study period because MMR vaccination coverage in adults is not available through national surveys. VAERS data do not include an unvaccinated comparison group and include incomplete data on vaccinated individuals with AEs, so we cannot determine incidence of AEs or assess risk. Due to these limitations, we are generally not able to assess whether a vaccine caused an AE.

Measles and rubella control is a global priority. In 2012, the World Health Assembly endorsed the Global Vaccine Action Plan to target measles and rubella elimination in at least 5 World Health Organization regions by 2020 [28]. Because epidemics are continuing, some European countries are considering vaccination programs targeting adults. Domestically, measles outbreaks related to imported cases are a growing problem [10]. In 2014, there were 644 cases of measles reported in the US, the largest number of cases reported in a year since the regional elimination of the disease in 2000 [29]. Therefore, adult MMR vaccination might become a domestic issue.

Based on our review of VAERS reports, we found no new or unexpected safety concerns for MMR in adults. We identified reports of pregnant women vaccinated with MMR, a group in whom the vaccine is contraindicated, which demonstrates the need for continued provider education on vaccine recommendations and screening for contraindications.

Supplementary Data

Supplementary materials are available at *Clinical Infectious Diseases* online (http://cid.oxfordjournals.org). Supplementary materials consist of data provided by the author that are published to benefit the reader. The posted materials are not copyedited. The contents of all supplementary data are the sole responsibility of the authors. Questions or messages regarding errors should be addressed to the author.

Notes

Disclaimer. The views, findings and conclusions in this report are those of the authors and do not reflect the official policy or position of the Centers for Disease Control and Prevention, the National Institute of Allergy and Infectious Diseases (NIAID), or the National Institutes of Health.

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