

## BACKGROUND

- Myocarditis = inflammation of heart muscle
- Pericarditis = inflammation of tissue overlying the heart
- Often occur together (myopericarditis)
- Often caused by viral infection
- Can occur after vaccination
  - Smallpox vaccine
  - Inactivated influenza vaccine
  - Others?

## OBJECTIVE

Review and describe reports of myopericarditis after vaccination received by the Vaccine Adverse Event Reporting System (VAERS).

## METHODS

### Identified reports

- Searched VAERS (January 1, 1990–December 31, 2018)
  - Medical Dictionary for Regulatory Activities (MedDRA) codes
  - Preferred Terms (PTs) that could indicate myopericarditis: “myocarditis”, “coxsackie carditis”, “pericarditis”, “pericardial effusion”, and “pericardial effusion”; others

### Reviewed reports

- Met existing case definition,<sup>1</sup> or were physician-diagnosed
- Serious report; non-serious report with medical records

### Stratified by age

- Sex
- Seriousness
- Diagnosis (case definition or physician)
- Time to onset of symptoms

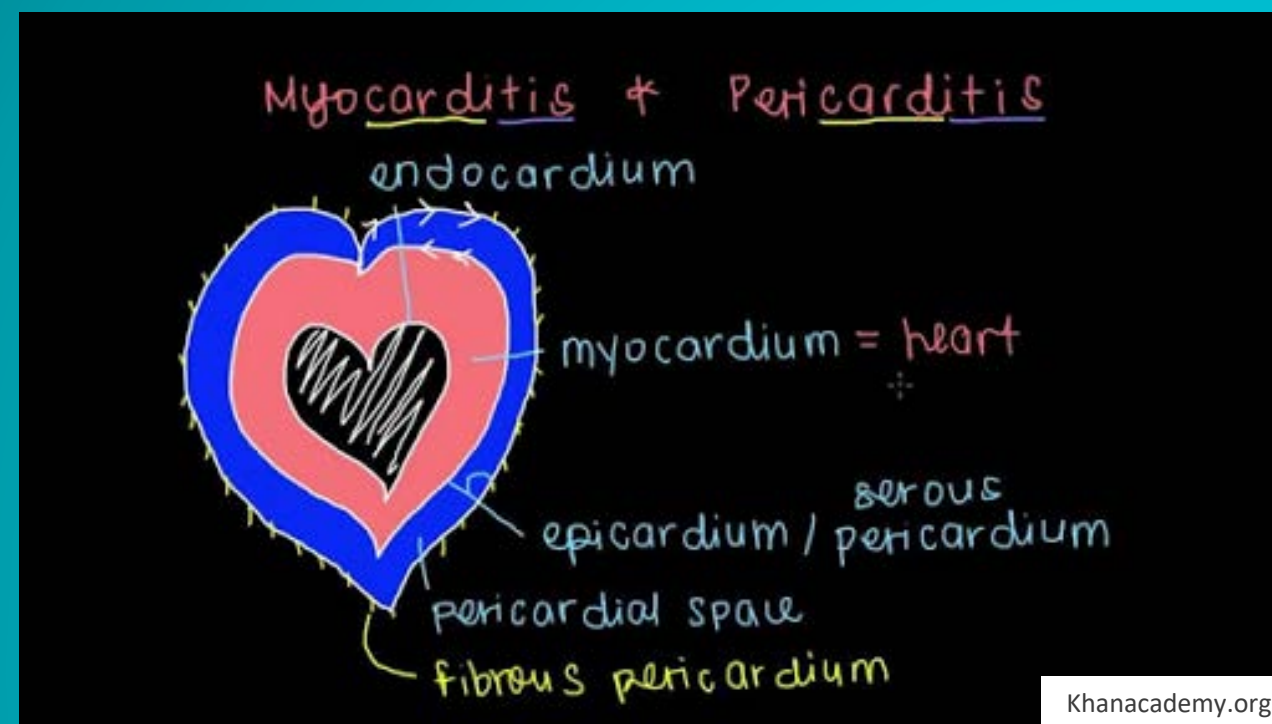
### Estimated rates

- Smallpox (2014–2018)
- Influenza (2014–2018)

### Disproportionality analysis

- Empirical Bayesian data mining<sup>2</sup>; identified PTs related to myopericarditis reported more often than expected
- Empirical Bayes Geometric Mean and its 90% confidence interval (EB05, EB95): EB05 ≥ 2.0 considered potential signal

# Myopericarditis after vaccines is rare...



## Estimated Reporting Rates

- Smallpox vaccine: 4.0 per 1,000 doses distributed
- Influenza vaccine (all types): < 0.1 per 1 million doses distributed

## Disproportionality Analysis

- EB05 ≥ 2.0 for myopericarditis-related PTs:
  - Smallpox vaccine
  - Anthrax vaccine (In 95% reports, also received smallpox vaccine)
  - Typhoid vaccine (In all reports, also received smallpox vaccine)

## Case Definition<sup>1</sup>

- **Suspected myocarditis:**
  - Dyspnea, palpitations, or chest pain of probable cardiac origin in a patient with ≥1 of the following:
    - Electrocardiogram (ECG) abnormalities beyond normal variants, not documented previously, including:
      - ST-segment or T-wave abnormalities
      - Paroxysmal or sustained atrial or ventricular arrhythmias
      - AV nodal conduction delays or intraventricular conduction defects
      - Continuous ambulatory electrocardiographic monitoring that detects frequent atrial or ventricular ectopy
    - Imaging that shows evidence of depressed left-ventricular function of indeterminate age
- **Probable myocarditis** – fulfills “suspected” criteria, plus ≥1 of the following:
  - Elevated cardiac enzymes (i.e., troponins, creatine kinase myocardial band)
  - Evidence by an imaging study (e.g., echocardiography) of depressed LV function of new onset or increased severity
  - Cardiac radionuclide imaging (e.g., gallium-67 imaging) indicating myocardial inflammation
- **Confirmed myocarditis** – histopathologic evidence (by biopsy or autopsy) of myocardial inflammation

# ... but it happens.

## 75 reports described patients who died

- Median age: 7 years (range: 8 to 80 years)
- 40 males, 35 females
- Median time to onset: 6 days after vaccination (range: 0 to 571 days)
- 61 reports = attributable to known cause (e.g., viral infection)
- 14 remaining reports
  - <1 year of age (5 reports): DTaP (4), pneumococcal conjugate (3)
  - 12 to 18 years of age (4 reports): meningococcal conjugate (2), quadrivalent HPV (1), mumps (1)
  - ≥18 years of age (6 reports): smallpox (2), influenza, not specified (2), HIV (1), live attenuated zoster (1)

## RESULTS

### Reported cases of myopericarditis, general characteristics by age group, 1990–2018

	Age group, years (%)				Total, N=708
	0 to 18, n=99	19 to 49, n=490	50+, n=85	Not reported, n=34	
<b>Sex</b>					
Male	55 (56)	439 (90)	42 (49)	23 (68)	599 (85)
Female	44 (44)	51 (10)	43 (51)	7 (21)	145 (20)
Unreported	0 (0)	0 (0)	0 (0)	4 (12)	4 (1)
<b>Seriousness</b>					
Non-serious	5 (5)	184 (38)	13 (15)	19 (56)	221 (31)
Serious, non-death	40 (40)	294 (60)	63 (74)	15 (44)	412 (58)
Serious, death	54 (55)	12 (2)	9 (11)	0 (0)	75 (11)
<b>Diagnosis</b>					
MMWR definition and MD	54 (55)	293 (60)	39 (46)	8 (24)	394 (56)
MMWR only	20 (20)	45 (9)	21 (25)	4 (12)	90 (13)
MD only	25 (25)	152 (31)	25 (29)	22 (65)	224 (32)
<b>Time to onset, days</b>					
≤7	46 (46)	111 (23)	49 (58)	3 (9)	209 (30)
8 to 14	15 (15)	263 (54)	8 (9)	14 (41)	300 (42)
15 to 29	8 (8)	62 (13)	13 (15)	1 (3)	84 (12)
30+	14 (14)	20 (4)	4 (5)	1 (3)	39 (6)
unreported	16 (16)	34 (7)	11 (13)	15 (44)	76 (11)

### Vaccines after which myopericarditis was most frequently reported, overall\*

Vaccine	Age group, years (%)				Total, N=708
	0-18, n=99	19-49, n=482	50+, n=81	Not reported, n=46	
Smallpox	6 (6)	387 (80)	5 (6)	19 (41)	417 (59)
Anthrax	5 (5)	158 (33)	1 (1)	6 (13)	170 (24)
Typhoid	3 (3)	85 (18)	2 (2)	2 (4)	92 (13)
Influenza, inactivated	11 (11)	34 (7)	31 (38)	2 (4)	78 (11)
Influenza, not specified	4 (4)	19 (4)	11 (14)	9 (20)	43 (6)
Hepatitis B	18 (18)	18 (4)	3 (4)	3 (7)	42 (6)
Tdap**	9 (9)	14 (3)	3 (4)	4 (9)	30 (4)
Influenza, live attenuated	3 (3)	22 (5)	0 (0)	3 (7)	28 (4)
Hepatitis A	12 (12)	10 (2)	1 (1)	3 (7)	26 (4)
Varicella	16 (16)	5 (1)	0 (0)	3 (7)	24 (3)
H. influenzae type b	22 (22)	0 (0)	0 (0)	0 (0)	22 (3)
Zoster, live attenuated	0 (0)	0 (0)	19 (23)	2 (4)	21 (3)
MMR**	13 (13)	7 (1)	0 (0)	0 (0)	20 (3)
Quadrivalent HPV**	16 (16)	3 (1)	0 (0)	0 (0)	19 (3)
DTaP**	14 (14)	0 (0)	0 (0)	4 (9)	18 (3)
Meningococcal conjugate	14 (14)	2 (0)	0 (0)	2 (4)	18 (3)
Polio, inactivated	11 (11)	4 (1)	0 (0)	1 (2)	16 (2)
Pneumococcal polysaccharide	1 (1)	8 (2)	4 (5)	0 (0)	13 (2)
Pneumococcal conjugate, 7-valent	12 (12)	0 (0)	0 (0)	0 (0)	12 (2)
Pneumococcal conjugate, 13-valent	7 (7)	1 (0)	3 (4)	1 (2)	12 (2)

\* Counts not mutually exclusive \*\* DTaP = combined diphtheria and tetanus toxoid, acellular pertussis vaccine; MMR = combined measles, mumps, and rubella vaccine; HPV = human papillomavirus vaccine; Tdap = combined tetanus and diphtheria toxoid, acellular pertussis vaccine

### Vaccines after which myopericarditis was most frequently reported, administered alone

Vaccine*	Age group, years (%)				Total, n=452
	0-18, n=40	19-49, n=303	50+, n=74	Not reported, n=35	
Smallpox	2 (5)	222 (73)	5 (7)	13 (37)	242 (54)
Influenza, inactivated	4 (10)	20 (7)	29 (39)	0 (0)	53 (12)
Anthrax	1 (3)	26 (9)	1 (1)	0 (0)	28 (6)
Influenza, not specified	2 (5)	1 (0)	9 (12)	8 (23)	20 (4)
Zoster, live attenuated	0 (0)	0 (0)	18 (24)	2 (6)	20 (4)
Tdap	1 (3)	10 (3)	2 (3)	3 (9)	16 (4)
Hepatitis B	5 (13)	7 (2)	2 (3)	0 (0)	14 (3)
Quadrivalent HPV	10 (25)	1 (0)	0 (0)	0 (0)	11 (2)
Influenza, live attenuated	1 (3)	7 (2)	0 (0)	1 (3)	9 (2)
Hepatitis A	1 (3)	4 (1)	1 (1)	1 (3)	7 (2)
Meningococcal conjugate	4 (10)	1 (0)	0 (0)	1 (3)	6 (1)
Varicella	3 (8)	2 (1)	0 (0)	1 (3)	6 (1)
MMR	3 (8)	2 (1)	0 (0)	0 (0)	5 (1)
Pneumococcal conjugate, 13-valent	0 (0)	1 (0)	3 (4)	1 (3)	5 (1)

\* MMR = combined measles, mumps, and rubella vaccine; HPV = human papillomavirus vaccine; Tdap = combined tetanus and diphtheria toxoid, acellular pertussis vaccine

## CONTACT INFO

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<sup>1</sup>MMWR (Mar 30, 2003); Considered “myopericarditis” if either case definition met <sup>2</sup> DuMouchel (*Am Stat* (1999))