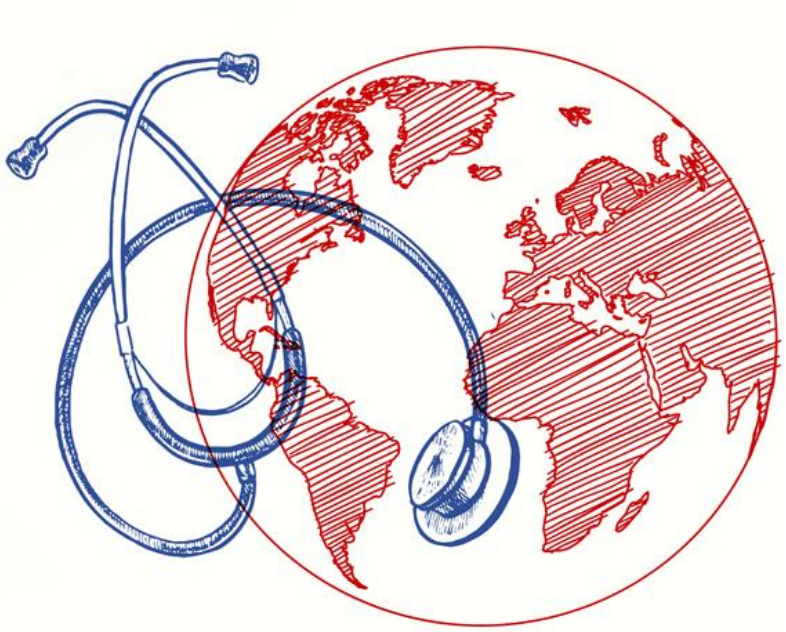
Global Health Cast 62

March 29, 2024



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What we talk about today

- Severe acute respiratory distress syndrome related to COVID can damage heart even when SARS-CoV-2 does not affect heart tissue
- New cancer therapy sees brain tumor almost disappear in five days
- Types of side effects of vaccines
- COVID, COVID vaccination and myocarditis

Circulation

ORIGINAL RESEARCH ARTICLE

Virus-Induced Acute Respiratory Distress Syndrome Causes Cardiomyopathy Through Eliciting Inflammatory Responses in the Heart

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BACKGROUND: Viral infections can cause acute respiratory distress syndrome (ARDS), systemic inflammation, and secondary cardiovascular complications. Lung macrophage subsets change during ARDS, but the role of heart macrophages in cardiac injury during viral ARDS remains unknown. Here we investigate how immune signals typical for viral ARDS affect cardiac macrophage subsets, cardiovascular health, and systemic inflammation.

METHODS: We assessed cardiac macrophage subsets using immunofluorescence histology of autopsy specimens from 21 patients with COVID-19 with SARS-CoV-2–associated ARDS and 33 patients who died from other causes. In mice, we compared cardiac immune cell dynamics after SARS-CoV-2 infection with ARDS induced by intratracheal instillation of Toll-like receptor ligands and an ACE2 (angiotensin-converting enzyme 2) inhibitor.

RESULTS: In humans, SARS-CoV-2 increased total cardiac macrophage counts and led to a higher proportion of CCR2$^+$ (C-C chemokine receptor type 2 positive) macrophages. In mice, SARS-CoV-2 and virus-free lung injury triggered profound remodeling of cardiac resident macrophages, recapitulating the clinical expansion of CCR2$^+$ macrophages. Treating mice exposed to virus-like ARDS with a tumor necrosis factor α–neutralizing antibody reduced cardiac monocytes and inflammatory MHCII^{lo} CCR2$^+$ macrophages while also preserving cardiac function. Virus-like ARDS elevated mortality in mice with pre-existing heart failure.

CONCLUSIONS: Our data suggest that viral ARDS promotes cardiac inflammation by expanding the CCR2$^+$ macrophage subset, and the associated cardiac phenotypes in mice can be elicited by activating the host immune system even without viral presence in the heart.

Key Words: acute respiratory distress syndrome ■ CCR2 ■ macrophage ■ SARS-CoV-2

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Intraventricular CARv3-TEAM-E T Cells in Recurrent Glioblastoma

Summary

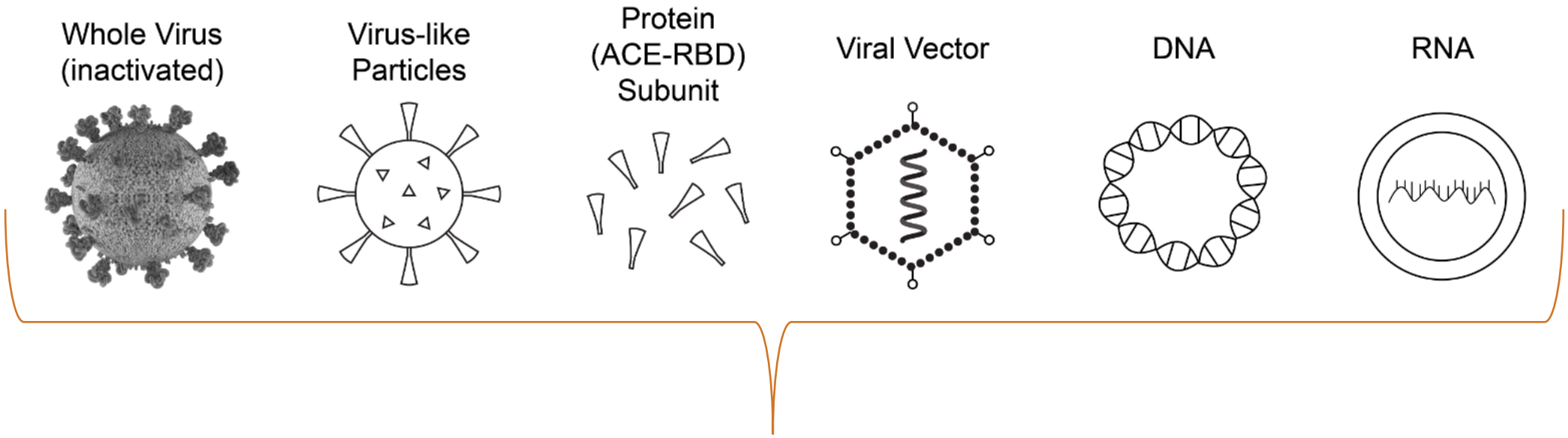
In this first-in-human, investigator-initiated, open-label study, three participants with recurrent glioblastoma were treated with CARv3-TEAM-E T cells, which are chimeric antigen receptor (CAR) T cells engineered to target the epidermal growth factor receptor (EGFR) variant III tumor-specific antigen, as well as the wild-type EGFR protein, through secretion of a T-cell–engaging antibody molecule (TEAM). Treatment with CARv3-TEAM-E T cells did not result in adverse events greater than grade 3 or dose-limiting toxic effects. Radiographic tumor regression was dramatic and rapid, occurring within days after receipt of a single intraventricular infusion, but the responses were transient in two of the three participants.

Types of Side Effects of Vaccines

1. Reactogenicity
2. Anaphylaxis
3. Technical errors
4. Vaccine-specific side effects

SARS-CoV-2 Vaccine platforms: Vaccine-specific AE

Coincidental or Causal association? Frequency?



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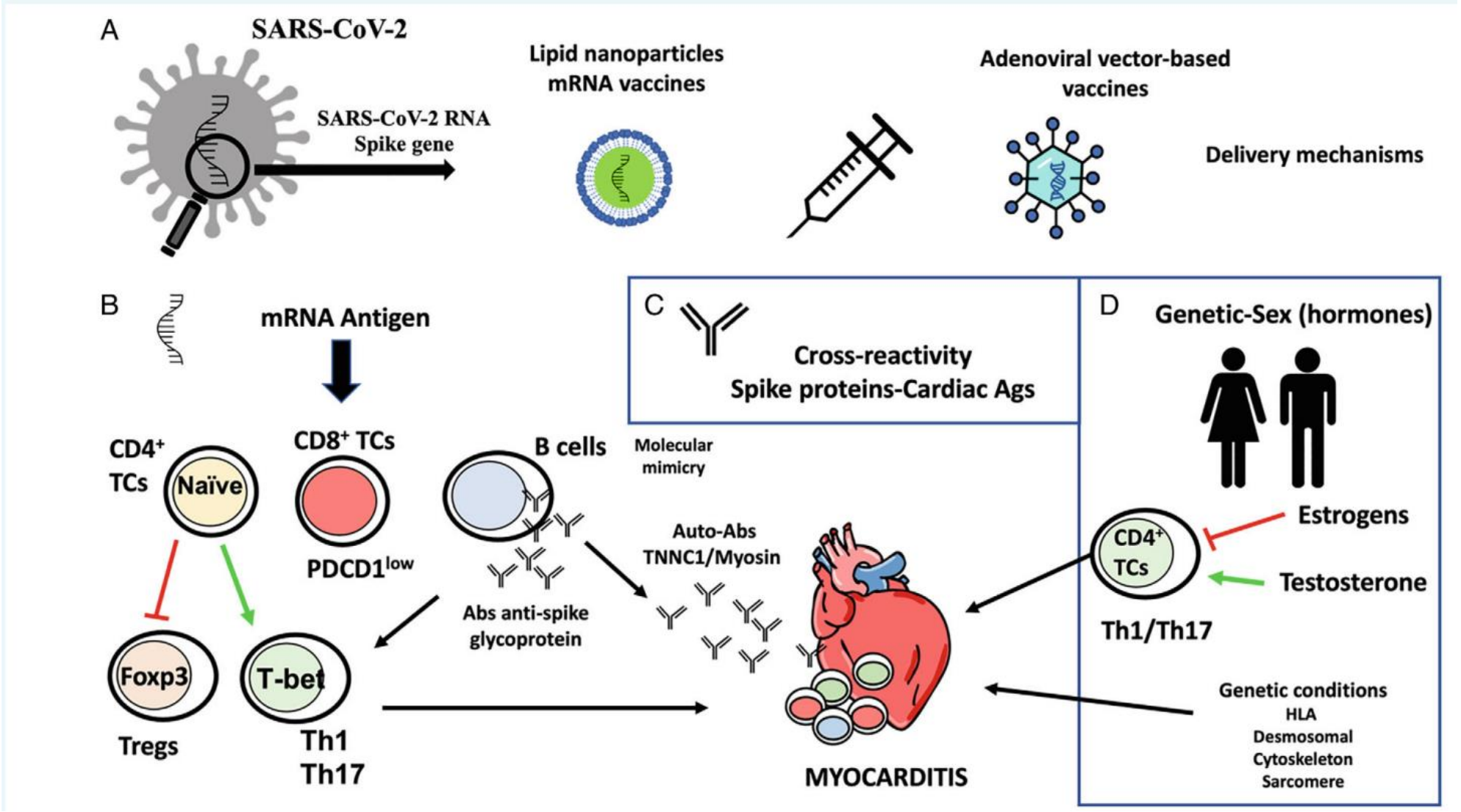
1. Facial Paralysis: causal relation, but protection by vaccine
2. Vaccine Induced Thrombocytopenia and Thrombosis (VITT)
3. **Myocarditis**

Table 4 Clinical characteristics of vaccination-related myocarditis

Symptoms	Signs
Chest pain or pressure, may be respiratory-dependent	Elevated troponins (peak between 48–72 h after symptom onset)
Shortness of breath	C-reactive protein elevation
Palpitations	Minor pericardial effusion on transthoracic echocardiography
Malaise	Cardiac inflammation on cardiac magnetic resonance imaging
General weakness and fatigue	Electrocardiographic changes (most commonly subtle and non-specific):
	Mild diffuse ST-segment changes
	PQ segment depressions
	Non-specific ST-segment changes
	Sinus tachycardia
	Supraventricular or ventricular arrhythmias (very rare)
Subfebrile or febrile temperatures	Clinical signs of heart failure and severe arrhythmias are very rare

Myocarditis, COVID19 & COVID19-vaccination: Pathogenesis



Heidecker B et al., European Journal of Heart Failure (2022) REVIEW ARTICLE doi:10.1002/ejhf.2669

Table 2 VAERS Reporting Rates of Myocarditis (per million doses administered) after mRNA vaccine, days 0–7

Vaccine	Age (years)	Males			Females		
		Dose 1	Dose 2	Booster	Dose 1	Dose 2	Booster
Pfizer	5–11	0.2	**2.6**	0	0.2	0.7	0
Pfizer	12–15	**5.3**	**46.4**	**15.3**	0.7	**4.1**	0
Pfizer	16–17	**7.2**	**75.9**	**24.1**	0	**7.5**	0
Either	18–24	**4.2**	**38.9**	**9.9**	0.6	**4.0**	0.6
Either	25–29	1.8	**15.2**	**4.8**	0.4	**3.5**	2.0
Either	30–39	1.9	**7.5**	1.8	0.6	0.9	0.6
Either	40–49	0.5	**3.3**	0.4	0.4	1.6	0.6
Either	50–64	0.5	0.7	0.4	0.6	0.5	0.1
Either	≥65	0.5	0.3	0.6	0.1	0.5	0.1

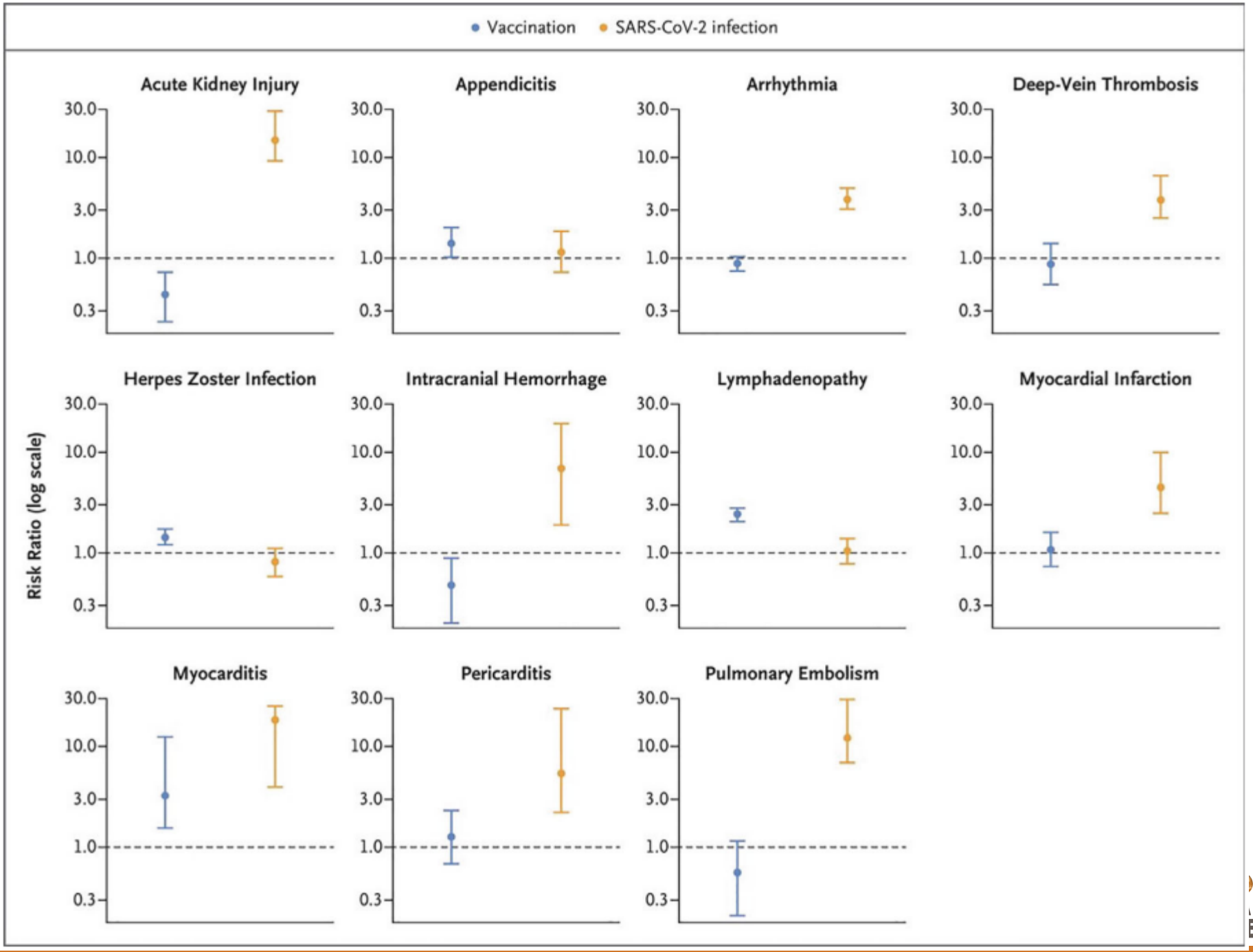
Either means either Pfizer or Moderna mRNA vaccine administered. Data as of 26 May 2022.
Bold numbers indicate rates that exceed calculated baseline rate in the population of 0.2–2.2 per million population.
Data presented at the Advisory Committee of the Immunization Practices Committee, June 2022.

Table 3 Prevented hospitalizations and excess vaccination-related myocarditis cases with different COVID-19 vaccines[35]

Age and sex groups	Hospitalizations prevented	Excess vaccine-related myocarditis cases
All 18–39 years old		
mRNA-1273 vaccine (Moderna®)	2982	33
BNT162b2 mRNA (Pfizer-BioNTech®)	2820	24
Males 18–39 years old		
mRNA-1273 vaccine (Moderna®)	1903	68
BNT162b2 mRNA (Pfizer-BioNTech®)	1799	47

Risk of complications after COVID-19 vaccine vs infection: national study in Israel

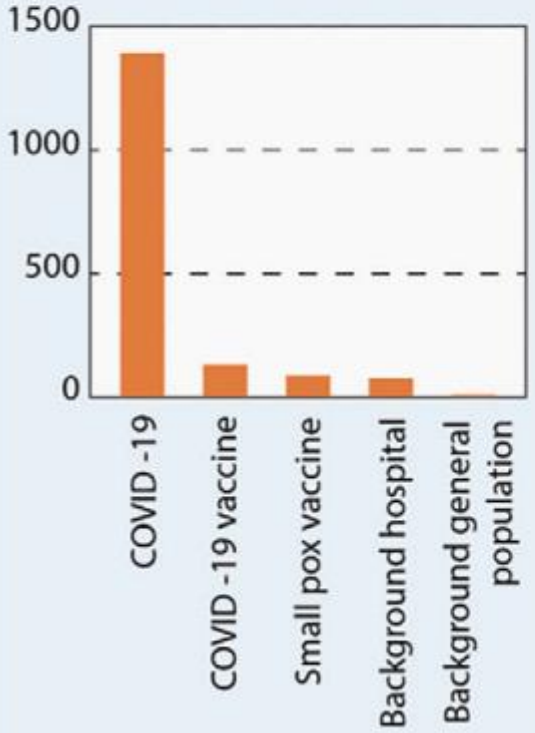
Each cohort had >800 000 individuals.



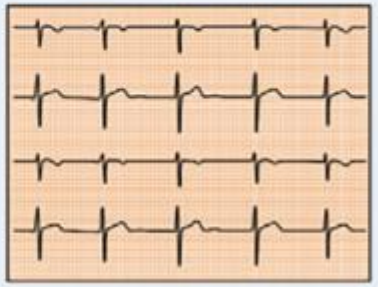
Summary: COVID, COVID vaccination and Myocarditis

Incidence

Cases of Myocarditis in 1 Million Subjects



Diagnosis



Therapy

Heart Failure Therapy
Immunosuppression
(e.g. steroids, NSAIDS)

Summary

- Highest incidence of myocarditis in young men after 2nd dose of vaccine (106 cases/million).
- Incidence of myocarditis in COVID-19 (1500/million).
- Diagnosis: CMR and EMB
- Treatment: Heart failure medication and immuno-suppression.

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SARS-CoV-2 Vaccine platforms: Vaccine-specific AE

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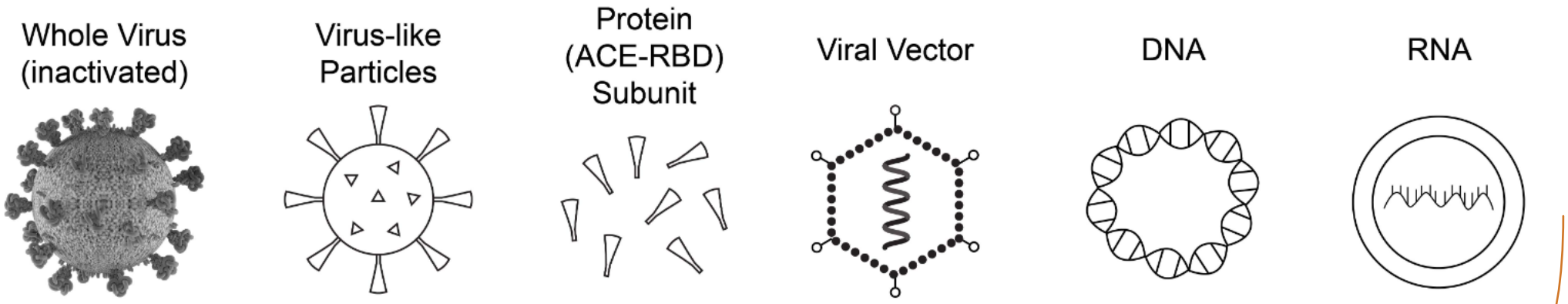

1. **Facial Paralysis: causal relation, but less with vaccine (protection)**
2. **VITT: Adeno-vector COVID19 vaccines**
3. **Myocarditis: causal relation, but less with vaccine (protection)**

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