

Vaccinations in Primary Immunodeficiency Disorders

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Speaker Disclosure

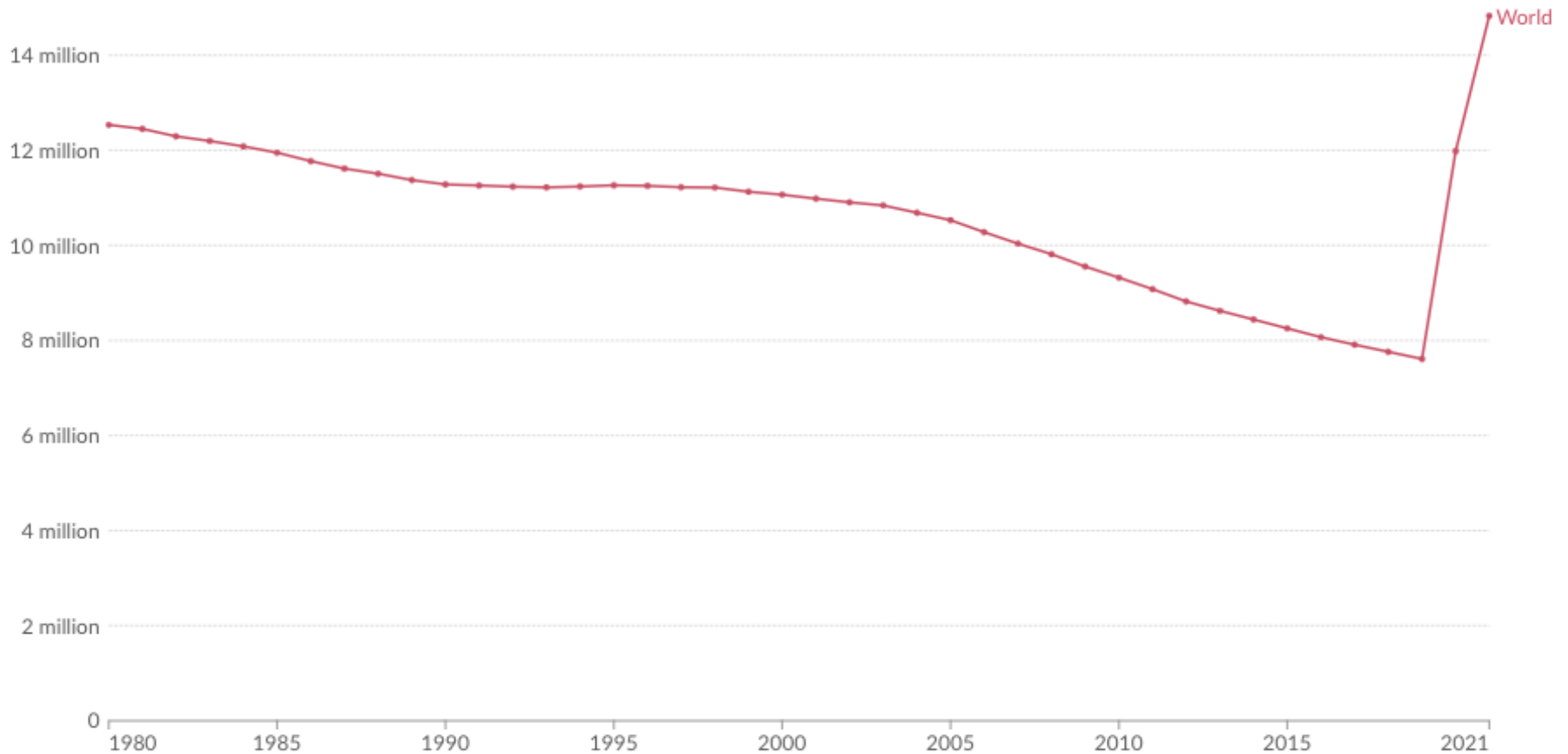
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- Research funding:
 - NHLBI
 - Jeffrey Modell Foundation
- No conflicts related to vaccines

Background

- Vaccination remains one of the most life-saving public health measures in history.



Winning the Fight against Infectious Diseases in the 20th century



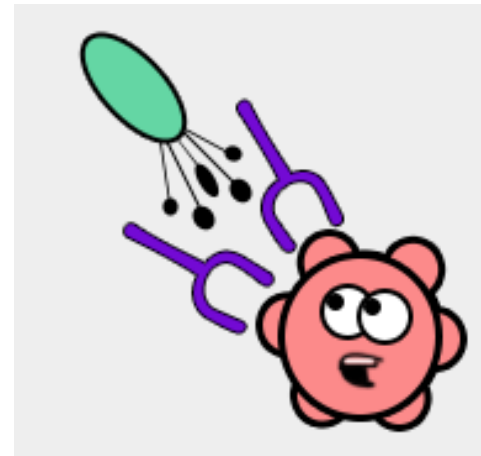
Armstrong GL *et al.*, JAMA 1999

How vaccines work

- By presenting bacterial/viral particles to the immune system, immune memory develops

Adaptive Immune cells (T-cells, B-cells) recognize the foreign particles

The immune system produces immune proteins (antibodies) and Killer T-cells to clear infectious particles




Types of Vaccines


	Viral	Bacterial
Inactivated (killed)	Inactivated influenza Poliovirus (Salk) Rabies vaccine HPV vaccine	DTAP/TDAP Pevnar/Pneumovax Haemophilus (Hib) Menactra / Menveo
Live-attenuated (weakened)	Rotavirus (Rotateq) MMR Varicella Intranasal influenza (flumist) Yellow fever Oral poliovirus (not in US/Canada)	BCG (outside US) Oral typhoid vaccine

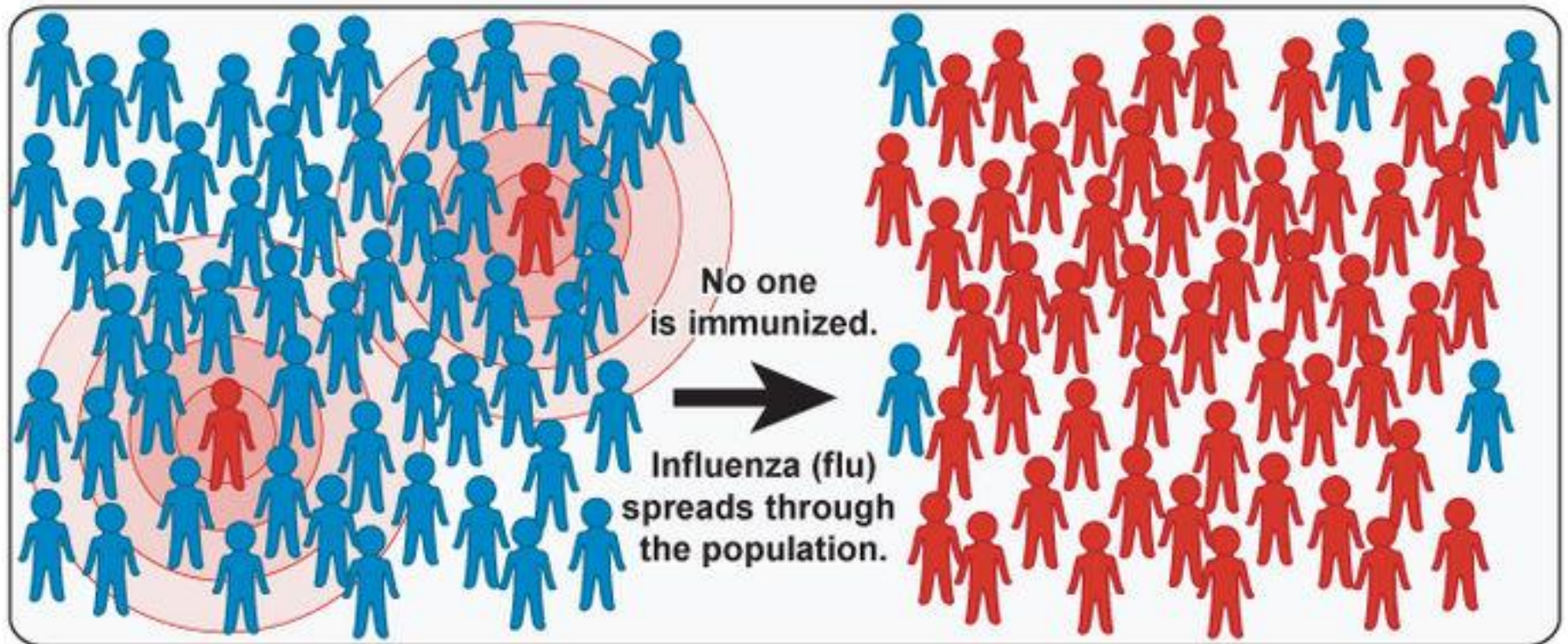
Vaccines & Public Health

- Vaccination prevent disease spread through “herd immunity”

 = not immunized but still healthy


 = immunized and healthy

 = not immunized, sick and contagious




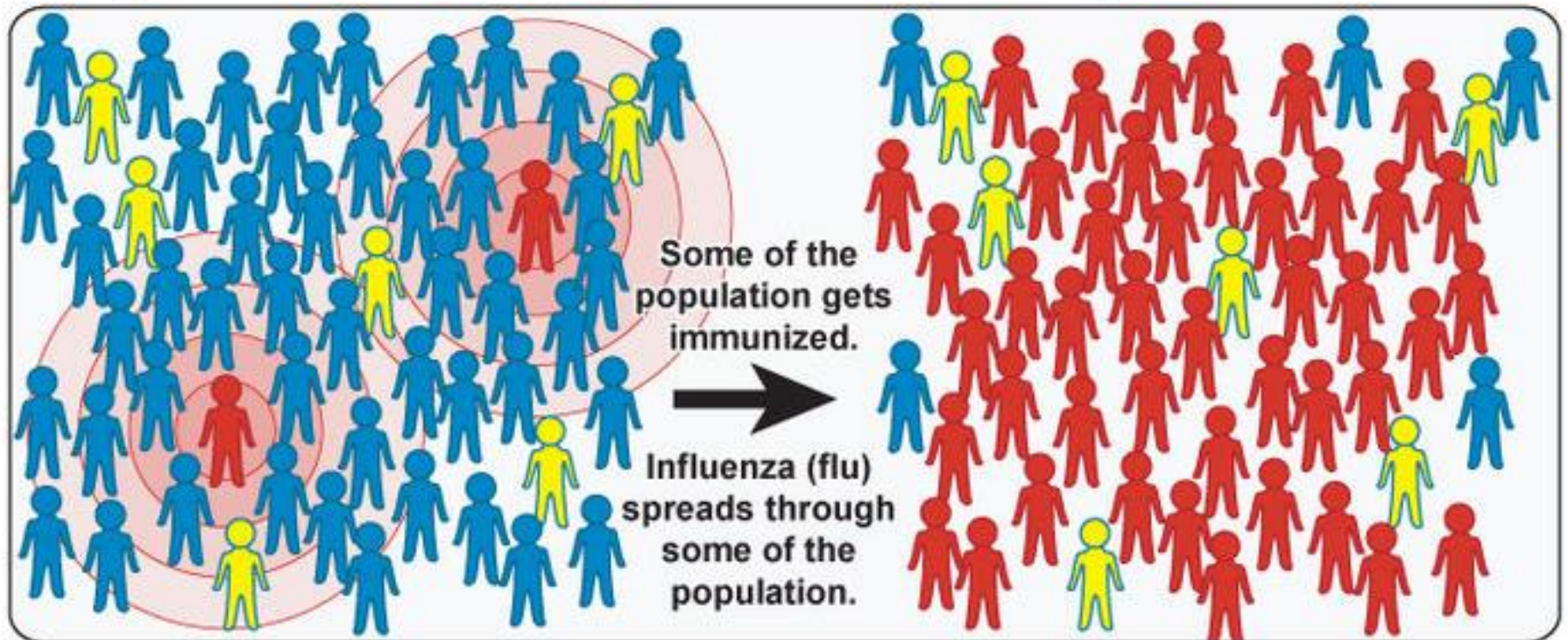
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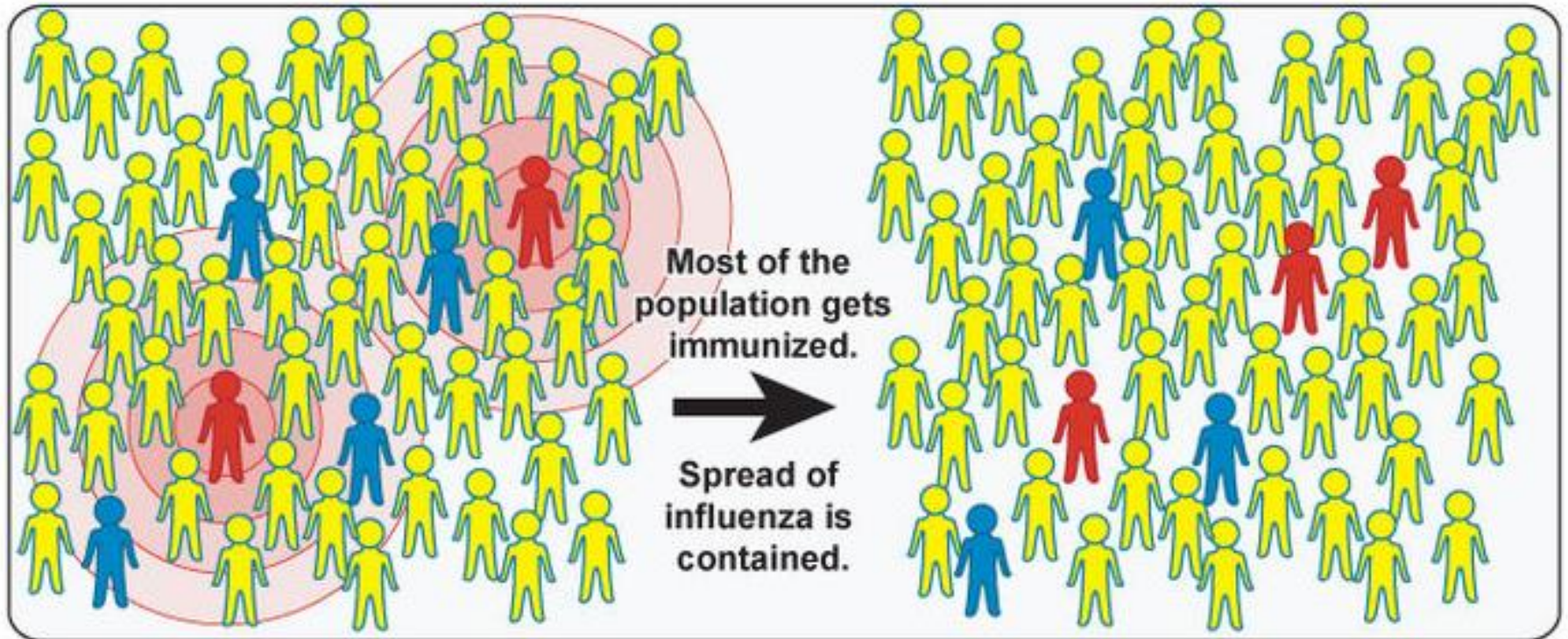
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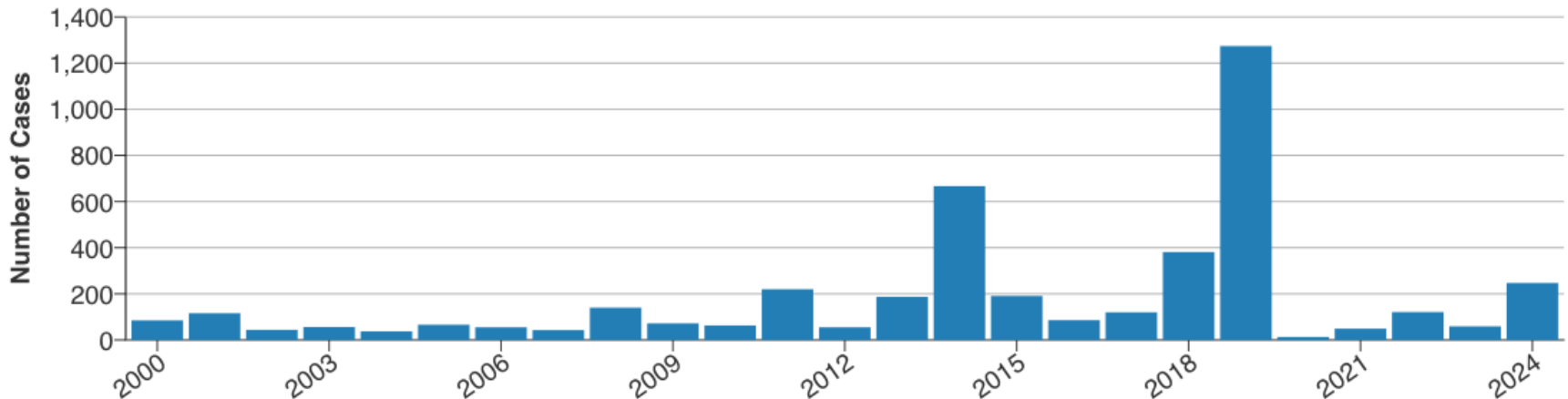


Herd Immunity is Critical for Immunocompromised Patients

Roughly 500,000 children in the US cannot receive vaccines because of age or medical conditions

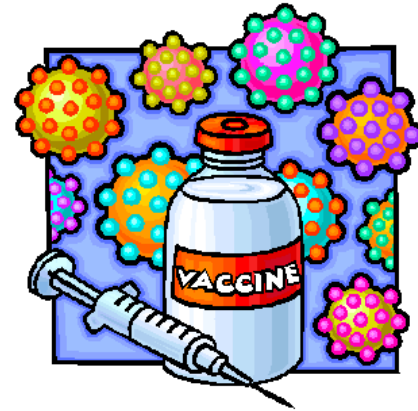
Herd immunity requires high vaccination rates

Annual US Measles Cases



Diagnostic use of vaccines

- Vaccine responses inform us about person's immune system.
 - You need functional T-cells and B-cells to respond to different vaccines



- Many types of PID can impair or prevent vaccine response.

Vaccination in special populations

- **Vaccines may be less effective or sometimes harmful in immunocompromised patients**
 - Primary Immunodeficiency
 - Bone marrow / cord blood transplant recipients
 - Solid organ transplant recipients
 - Uncontrolled HIV patients
 - Patients on immunosuppressive medications



Risk of Live Vaccines in PID

- Live-vaccine associated disease can occur in severe forms of immunodeficiency.

BCG vaccination in patients with severe combined immunodeficiency: Complications, risks, and vaccination policies

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Persistent systemic rotavirus vaccine infection in a child with X-linked severe combined immunodeficiency

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Clinical and Experimental Immunology

ORIGINAL ARTICLE

doi:10.1111/cei.12421

Vaccine-associated varicella and rubella infections in severe combined immunodeficiency with isolated CD4 lymphocytopenia and mutations in *IL7R* detected by tandem whole exome sequencing and chromosomal microarray

Vaccines in patients with PID

Recommendations for live viral and bacterial vaccines in immunodeficient patients and their close contacts

Medical Advisory Committee of the Immune Deficiency Foundation

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*** New vaccine guidelines in development by AAAAI
Primary Immunodeficiency Committee**

Vaccines in patients with PID

In Severe T-cell defects:

SCID, Complete DiGeorge syndrome, NEMO, MHC II deficiency, related disorders

Live vaccines strictly contraindicated

(Rotateq, MMR, Varicella, BCG, Oral polio, Oral typhoid)

Inactivated vaccines likely safe but also likely ineffective

Vaccines in patients with PID

In mild to moderate T-cell defects:

Partial DiGeorge syndrome

Ataxia Telangiectasia

Cartilage Hair Hypoplasia

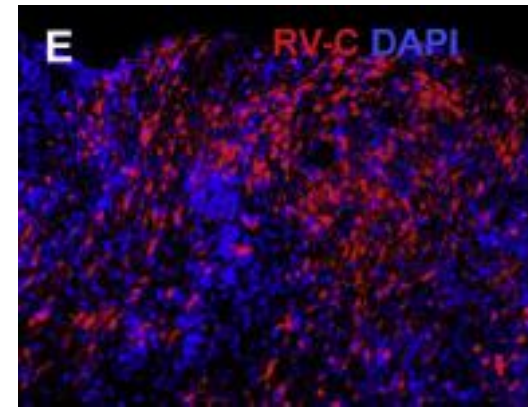
Other select forms of combined immunodeficiency

Selected live vaccines may be safe, but evaluation is required first.

Inactivated vaccines safe and may be beneficial

Complications from Rubella vaccine in CID

- Granulomatous disease described in rare patients with T-cell deficiency disorders
 - Vaccine strain Rubella isolated from lesions
 - Disorders:
 - Ataxia Telangiectasia
 - Nijmegen Breakage Syndrome
 - RAG1/2 deficiency
 - Ligase 4 deficiency
 - WHIM syndrome
 - MHC II deficiency



Perelycina L *et al.*,
J All Clin Immunol 2016

Buchbinder D *et al.*,
J Clin Immunol 2019

Vaccines in patients with PID

In B-cell deficiencies:

X-linked agammaglobulinemia

Common Variable Immunodeficiency

Most live vaccines contraindicated

- Oral polio, Oral typhoid, intranasal influenza, Yellow fever

Inactivated vaccines likely safe but may not be effective

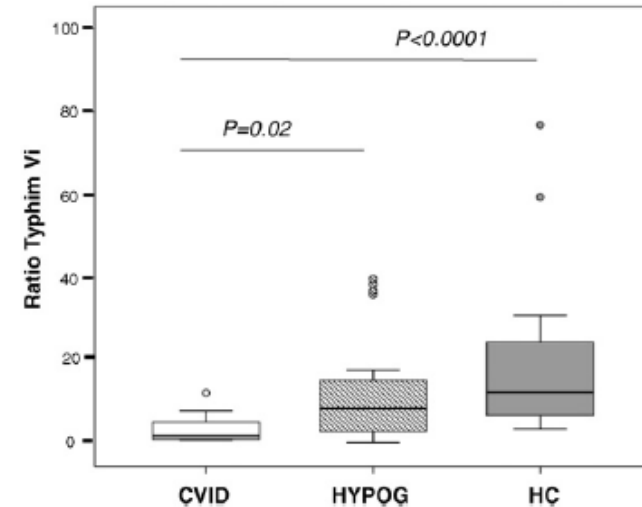
- Exceptions: Inactivated influenza, COVID-19 boosters recommended

Vaccines & Immunoglobulin replacement

- Immunoglobulin provides protection against many vaccine-preventable illnesses
 - **Exceptions:**
 - Annual influenza strains
 - Annual inactivated Influenza vaccine recommended for patients and caregivers.
 - **HPV:** inactivated vaccines recommended
 - **COVID-19** vaccines recommended

Vaccine Responses with Antibody deficiency

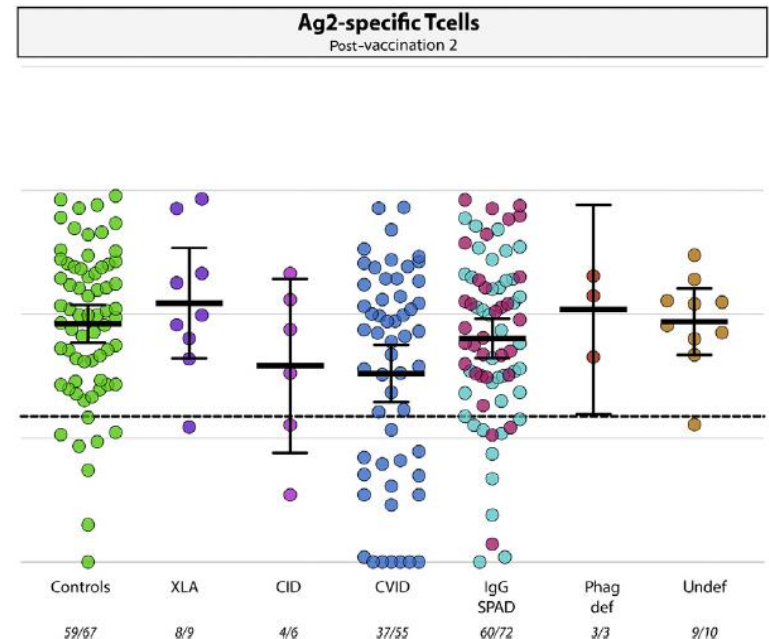
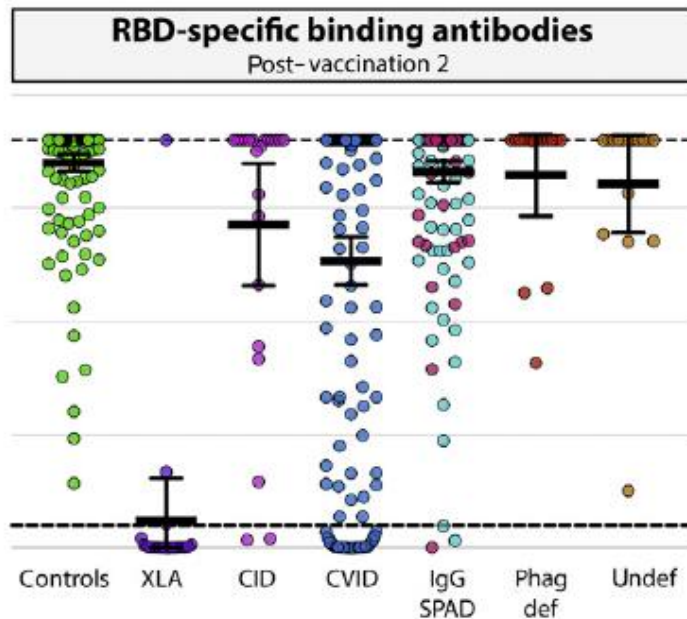
- EMPATHY study (2016)
 - 41% of patients with CVID responded to inactivated Typhoid vaccine
- Influenza vaccine studies:
 - In 3 studies, 20-30% of antibody deficiency patients had detectable responses to inactivated influenza vaccine



Sanchez-Ramon S *et al.*,
Clin Immunol 2016

COVID-19 vaccines and Immunodeficiency

- Many patients with PID have partial responses to COVID-19 vaccines and boosters
- T cell responses also identified in many patients with PID



COVID-19 vaccine recommendations for Immunocompromised patients

- Pfizer / Moderna (mRNA) vaccines:
 - 3 doses if never vaccinated (ages 6 months+)
 - At least one updated 2023-2024 vaccine, at least 8 weeks after last dose
- Novavax (age 12 yrs+)
 - 2 doses total (separated by 8 weeks) if never vaccinated
 - 1 dose 2023-2024 vaccine if previously vaccinated

Zoster vaccination for Immunocompromised adults

- Varicella-Zoster is common in patients with PID and older adults
- Shingrix is a recombinant subunit vaccine for prevention of zoster in adults
 - Approved for all adults 50+ years
 - Patients 18 yrs+ who are immunocompromised
 - Given as 2 doses separated by at least 1 month.



RSV Vaccines and monoclonal antibodies

- Respiratory syncytial virus (RSV) is a leading cause of hospitalization in children as well as older adults



RSV Vaccines and monoclonal antibodies

- New vaccines reduce severe RSV by up to 80%

Vaccine product	Doses / intervals	Age approvals
Abryso	1 dose	60 years and in pregnant women (32-36 weeks gestation)
Arexvy	1 dose	60 years
mRESVIA	1 dose	60 years

Vaccines in patients with PIDD

In mild to moderate B-cell deficiencies:

Selective IgA deficiency

IgG subclass deficiencies

Inactivated vaccines safe and likely beneficial

Routine live vaccines may be given and are recommended.

Vaccines in patients with PIDD

In Phagocyte deficiencies:

Chronic granulomatous disease, leukocyte adhesion deficiency,

Live bacterial vaccines contraindicated

Oral polio, Oral typhoid, BCG (outside US)

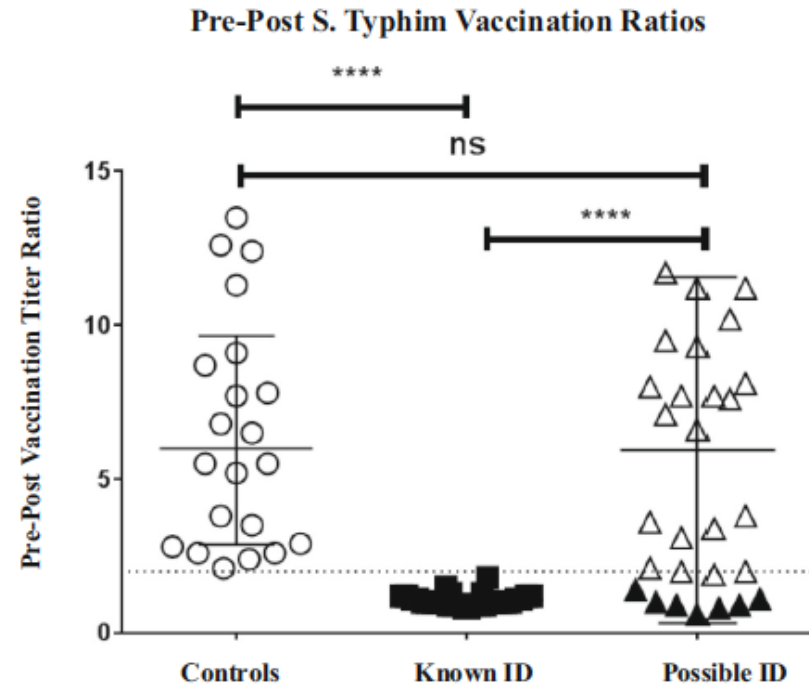
Inactivated vaccines and live viral vaccines safe and recommended

Vaccination after Bone marrow transplantation or Gene Therapy

- Current guidelines suggest resuming inactivated vaccines at 3-6 months post-BMT
 - No consensus on requirements
 - Suggestions:
 - Clinically well enough to stop IVIG for 3 months
 - Donor CD4+ T-cells ($> 200/\mu\text{L}$)
 - Donor B-cells ($> 200/\mu\text{L}$)
 - Inactivated vaccines given first

Re-testing while on IVIG/ScIG

- **Inactivated Typhoid vaccine**
 - Routes *et al*: Typhim V vaccine responses can distinguish PID patients
 - None of 26 PID patients had significant antibody response
 - Responses in 22/29 patients with hypogam without known PID



Bausch-Jurken *et al.*,
J Clin Immunol 2017

Vaccinations for Close Contacts

- Vaccinations for family members is essential to protect patients with PID
- Most live vaccines are considered **safe** for close contacts
 - MMR, Varivax: transmission very unlikely
 - If local rash occurs after varivax: cover it with a dressing and call your immunologist.
 - **EXCEPTIONS:**
 - Avoid oral poliovirus (not used in US)
 - Avoid oral typhoid vaccine (Inactivated available).

More Information



Centers for Disease Control and Prevention

CDC 24/7: Saving Lives. Protecting People.™

www.cdc.gov/vaccines/

American Academy
of Pediatrics



DEDICATED TO THE HEALTH OF ALL CHILDREN™

www2.aap.org/immunization/

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