Vaccines and Public Health

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The Plan

- History of Vaccines
- Immunity 101
- 20th Century Vaccines
- Epidemiology 101
- Safety of Vaccines
- 3 Common Vaccine Controversies

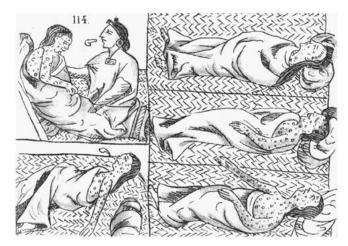
History of Vaccines

Smallpox, Variolation, and Jenner, Oh my!

Smallpox

- Smallpox is believed to have appeared ~10,000 BC
- Earliest (1570 1085 BCE)
 - Skin lesions on mummies
 - Egypt, Asia, India, China...
- Europe (5th 7th Century)
 - Epidemics → decline of the Roman Empire
 - Spread -> Crusades, discovery of West Indies and the Americas, slave trade
- 1st examples of biological warfare (French-Indian War)





Europe, 18th Century



- "The Great Pox"
- 400,000 deaths/year
- Case Fatality Rate (CFR)
 - Adults: 20 60%
 - Infants: 80 98%
- Survivors
 - Blindness
 - Disfiguring scars
 - · Became immune to the disease

Inoculation/Variolation

· Africa, India, China



- Problems with this:
 - Disseminated smallpox
 - Transmission of other blood born disease (Syphilis)
- Turkey → Europe (18th C)
 - · Lady Mary Montague (1721)
 - Royal Physician

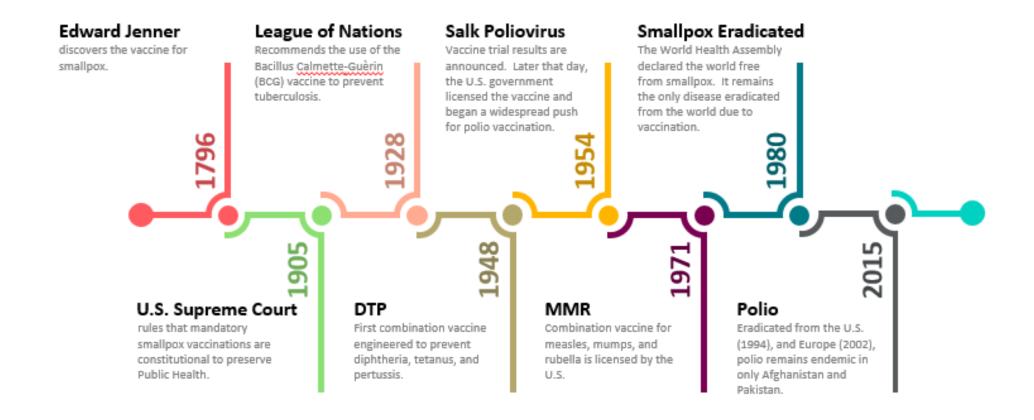
- Trial variolation on prisoners, orphaned children
- 2-3% patients
 - · Died from disease
 - Became a source of outbreak
 - Suffered from diseases transmitted (TB, syphilis)
- CFR was 10x **lower** than actual disease
- \rightarrow New world
- Ben Franklin a proponent (Philadelphia Outbreak, 1747)

Dr. Edward Jenner

- First person to confer scientific status on vaccination
- Inoculated as a child
- Dairymaids: "I shall never have smallpox for I have had cowpox."
 - Theory
 - If cowpox protects against smallpox, can we use cowpox as a deliberate mechanism of protection against smallpox?
 - May 14, 1796: Inoculated an 8-year-old boy with fresh cowpox
 - · Mild fever, discomfort, loss of appetite
 - · July 1796: Inoculated the boy with smallpox → No Disease Developed
- Spread of vaccination as credible: mostly word of mouth
 - Used during major outbreaks







Vaccines are among the 20th century's most successful and cost-effective public health tools for **preventing** disease and death. - DE Department of Public Health

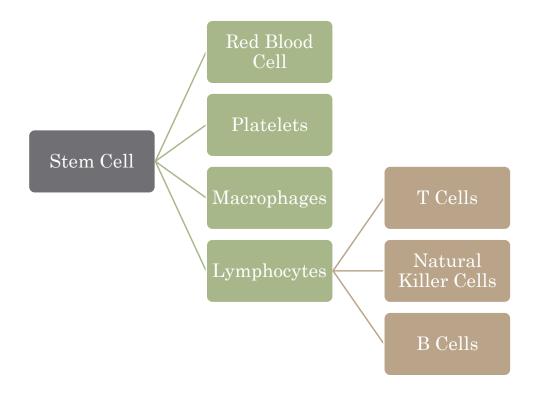
History of Vaccines – www.historyofvaccines.org/timeline

Immunity 101

Or, "My Body Can Do What, Now?"

The Immune System: A Primer

- Antigen anything that causes an immune system response
 - · Grass, pollen, flu
- Pathogen disease causing antigen



Types of Immunity

INNATE

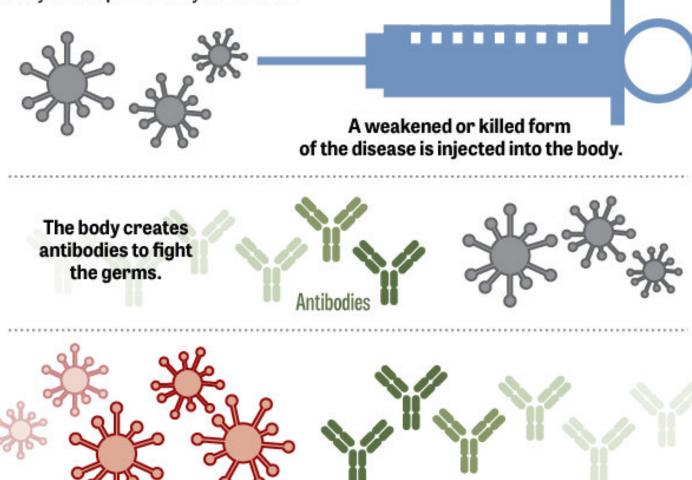
- Non Specific (Immediate)
- Physical Barriers
 - Skin
 - · Chemicals in Blood
 - Macrophages & NK Cells
- Maternal Protection for Fetus

ADAPTIVE

- Antigen-Specific (Takes Time)
- 1. T- & B-Cells Recognize Antigen as foreign
- 2. T- & B-Cells Differentiate make specific **antibody**
- 3. Copy/Paste → army of immune cells specific to that antigen
- Memory keep some cells for later
 Next time an antigen is in the body, the response is MUCH faster

HOW DO VACCINES WORK?

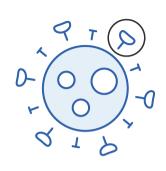
Vaccines reduce the risk of infection by working with the body's natural defenses to safely develop immunity to disease.



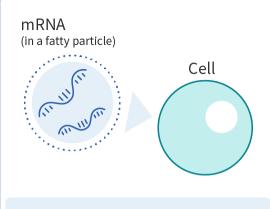
If the actual disease germs ever attack the body, the antibodies return to destroy them.

(MLive.com)

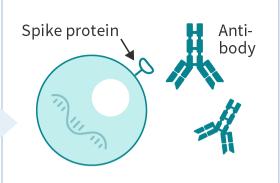
mRNA Vaccines



The RNA vaccine contains messenger RNA, which contains an instruction to make a SARS-CoV-2 spike protein.



For messenger RNA (mRNA) to enter the muscle cell at the injection site, it is packaged inside a very small fatty particle.



Messenger RNA instructs cells to produce a coronavirus spike protein.

The body's defence system recognises the spike protein as foreign and begins to protect itself against it.

#coronavirus

Source: Finnish Institute for Health and Welfare 2020

Types of Vaccines

Type	What is it?	Examples	
Live Attenuated	Weakened version of living pathogen that cannot cause disease	Measles, mumps, rubella, polio (oral), yellow fever	
Inactivated ("killed")	Pathogen has been killed with chemicals, heat, or radiation	Cholera, flu, hepatitis A, plague, polio (IM), rabies	
Subunit	Includes antigens that best stimulate the immune system	Hepatitis B, pertussis, pneumonia	
Toxoid	Inactivated toxins from bacteria	Diphtheria, tetanus	
Conjugate	Antigens linked to sugars	H. Influenzae type B, pneumonia	
DNA	DNA	Flu, herpes, HIV	
mRNA	Messenger RNA	COVID-19	

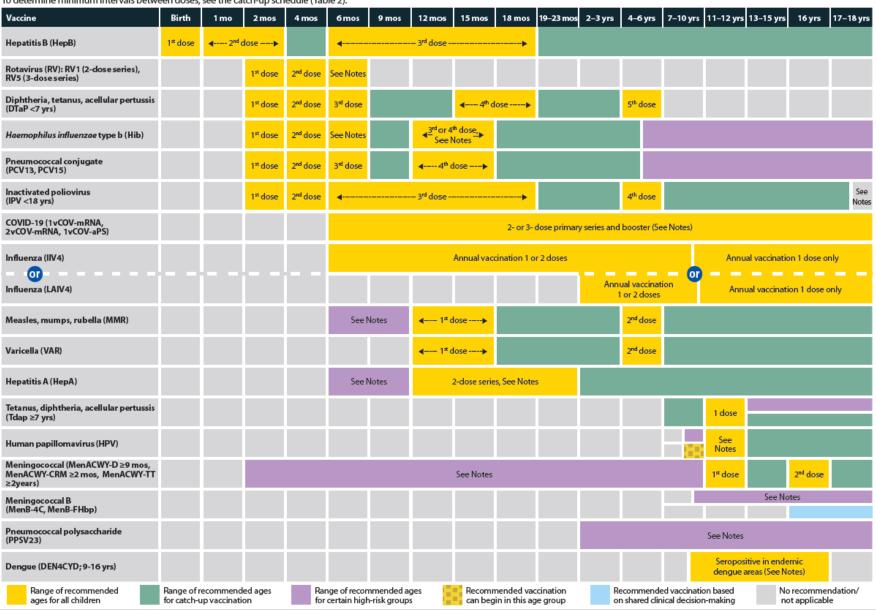
20th Century Vaccines

Or, "Why I hated the doctor when I was little."

See Addendum for new or updated ACIP vaccine recommendations

 Table 1
 Recommended Child and Adolescent Immunization Schedule for ages 18 years or younger, United States, 2023

These recommendations must be read with the notes that follow. For those who fall behind or start late, provide catch-up vaccination at the earliest opportunity as indicated by the green bars. To determine minimum intervals between doses, see the catch-up schedule (Table 2).



17 Diseases

Children (birth - 7 years)

- Hepatitis A & B
- Rotavirus
- Hemophilus influenza type b
- Diphtheria, tetanus & pertussis
- Pneumococcal
- Polio
- Measles, mumps & rubella
- Varicella











Yearly

- Flu
- COVID-19

Teens

• HPV

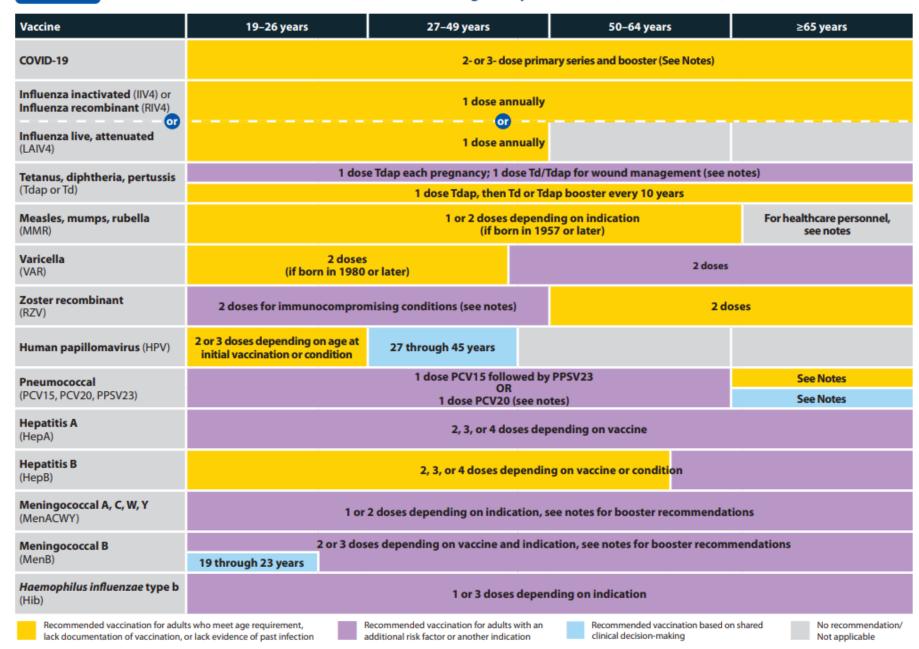


http://www.cdc.gov/vaccines/schedules/downloads/child/0-18yrs-child-combined-schedule.pdf

Table 1

See Addendum for new or updated ACIP vaccine recommendations

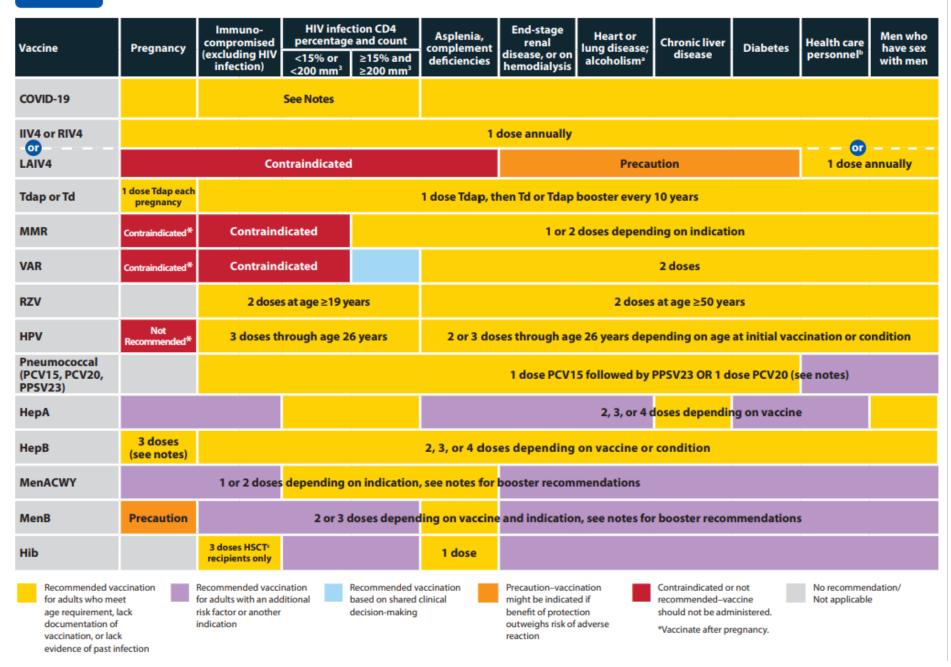
Recommended Adult Immunization Schedule for ages 19 years or older, United States, 2023



- Boosters (2-4)
- 2 new vaccine
 - Zoster
 - HSV

Table 2

Recommended Adult Immunization Schedule by Medical Condition or Other Indication, United States, 2023



Epidemiology 101

Or, "There is a reason I did not major in math."

Endemic

• Disease exists permanently in a particular region or population

Epidemic

- An outbreak of disease that attacks many people at the same time and may spread through communities
- Cases are over and above the "normal" case rate of an endemic disease
- Flu epidemic, Cholera, Ebola

Pandemic

- An epidemic that spreads around the world
- SARS, Swine Flu, Zika, COVID-19
- Way more likely in the era of fast transportation

Infection Exposure

- Incubation
 - Time it takes to show symptoms after infection
- Contagious
 - Time disease can spread to others

Disease	Incubation	Contagious
Chickenpox	10-21 days	6-7 days
Measles*	8-12 days	4 days before and after rash
Diphtheria	2-5 days	Sore throat – antibiotic for 4 days
Flu	1-2 days	Symptoms

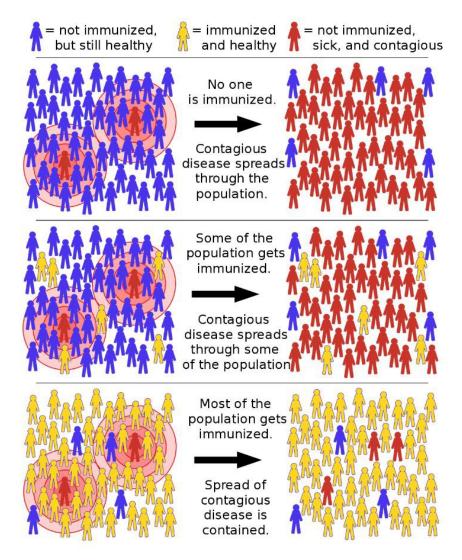
^{*}The most contagious disease (90% of contacts). It was declared eliminated from the US in 2000 (no endemic transmission); in 2016 came close to losing that declaration

Contagious

Herd Immunity

- When many are immunized, there is little opportunity for outbreak
- Some are not eligible for vaccines
 - Infants
 - · Pregnant women
 - Immunocompromised
 - Allergies

Disease	Herd Immunity Threshold
Measles	92-95%
Pertussis	92-94%
Diphtheria	83-86%
Rubella	
Smallpox	80-86%
Polio	



https://www.theguardian.com/society/ng-interactive/2015/feb/05/-sp-watch-how-measles-outbreak-spreads-when-kids-get-vaccinated

From the training course titled "Smallpox: Disease, Prevention, and Intervention". The Centers for Disease Control and Prevention and the World Health Organization. Slide 17. Retrieved 13 March 2015

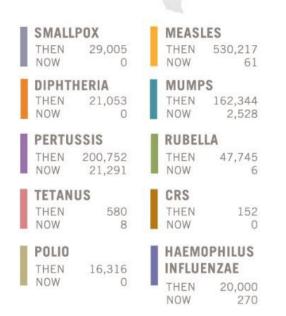
Death due to...

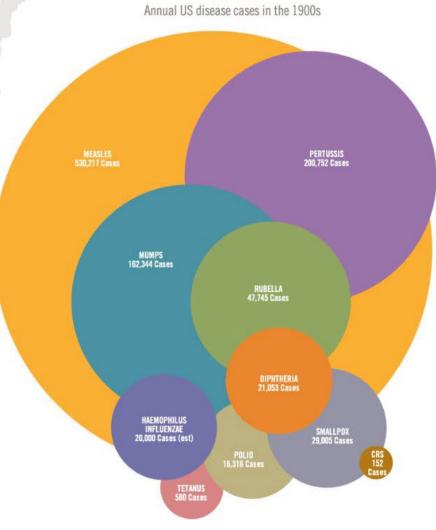
Disease	Cases	Deaths	Vaccine	Cases (2006)	Deaths (2004)
Diphtheria	21,053	1,822	1943	0	0
Measles	530,217	440	1960s	55	0
Mumps	162,344	39	1940s	6584	0
Pertussis	200,752	4,034	1941	15,632	27
Polio (paralytic)	16,316	1,879	1955	0	0
Rubella	47,745	17	1969	11	0
Smallpox	29,005	337	1798	0	0
Tetanus	580	472	1949	41	4

Vaccines available before 1980

VACCINES WORK

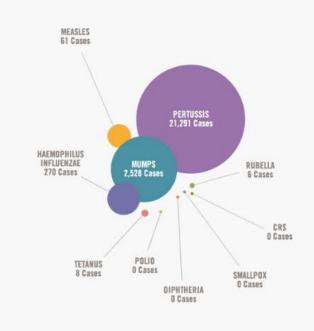
These bubbles are sized according to the annual number of disease cases in the US during the 1900s versus 2010. We've come so far. It's a reminder that while disease rates are low, most diseases haven't disappeared. This is why we continue to vaccinate.







US disease cases in 2010



^{9.} Centers for Disease Control and Prevention (CDC). Parents Guide to Childhood Immunizations. http://www.cdc.gov/vaccines/pubs/parents-guide/default.htm. Accessed August 15, 2011.

10. CDC. Impact of Vaccines in the 20th & 21st Centuries. http://www.cdc.gov/vaccines/pubs/pinkbook/downloads/appendices/G/impact-of-vaccines.pdf. Updated January 2011. Accessed August 15, 2011.

If vaccines are so amazing, why do I need a booster shot?

- An additional dose of a vaccine needed to periodically "boost" the immune system.
- Immunology 101 "memory" cells
 - If enough time has passed since vaccination, and the pathogen in question can cause disease rapidly, it may spread faster than the immune system can respond
 - Tetanus, Pertussis, Influenza (kind of)
 - HPV? Chicken pox? Diphtheria?
 - Immunocompromised people ask a doctor!
- If the disease is a slow-moving one, the immune system will be able to respond before the disease "takes over"

But how do we know they're safe?

Because we test them. A lot.

The Vaccine Life Cycle

safety at every phase

GUIDE

ACIP

ADVISORY COMMITTEE ON IMMUNIZATION PRACTICES

BLA

BIOLOGICS LICENSE APPLICATION

CDC

CENTERS FOR DISEASE CONTROL AND PREVENTION

FDA

FOOD AND DRUG ADMINISTRATION

IND

INVESTIGATIONAL NEW DRUG APPLICATION

VACCINE

safety + effectiveness

safety is a priority during vaccine development + approval

PHASE 1 PHASE 2 PHASE 3 safety effectiveness

IND SUBMITTED BASIC RESEARCH DISCOVERY PRE-CLINICAL

STUDIES

CLINICAL STUDIES / TRIALS

Drug Trial Phases

- Phase 0
 - 10-15 subjects
 - What does drug do to body?
 - What does body do to drug?
 - Absorption, distribution, metabolism, removal/excretion
- Phase I
 - Screening for safety
 - Safe dosage, common side effects
- Phase II
 - **Efficacy** does it do what it's supposed to do?
 - Less common side effects
- Phase III
 - Confirmation of efficacy, monitor side effects, compare it to common treatment

Before a new vaccine is ever given to people, extensive lab testing is done that can take several years. Once testing in people begins, it can take several more years before clinical studies are complete and the vaccine is licensed.

HOW A NEW VACCINE IS DEVELOPED, APPROVED AND MANUFACTURED

Food and Drug Administration (FDA) sets rules for the three phases of clinical trials to ensure the safety of the volunteers. Researchers test vaccines with adults first.



Does this vaccine seem to work? Are there any serious side effects?

> How is the size of the dose related to side effects?



short-term side effects?

How are the volunteers' immune systems responding to the vaccine?



HUNDREDS or THOUSANDS of VOLUNTEERS

How do people who get the vaccine and people who do not get the vaccine compare?

Is the vaccine safe?

Is the vaccine effective?

What are the most common side effects?

• It's safe and effective FDA licenses the vaccine only if: Benefits outweigh risks



Manufacturers must test all lots to make sure they are safe,

pure and potent. The lots can only be released once FDA reviews their safety and quality.



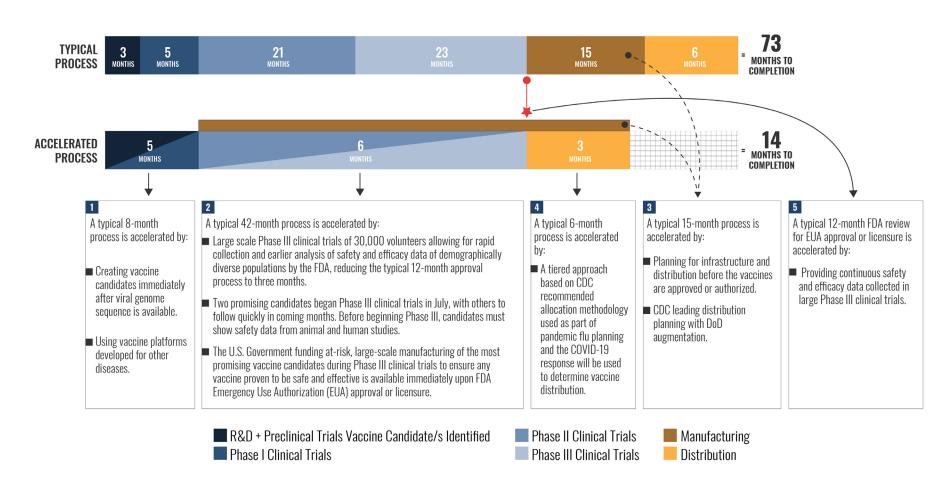
The FDA inspects manufacturing facilities regularly to ensure quality and safety.

FOR MORE INFORMATION, VISIT HTTP://WWW.FDA.GOV/CBER

If the FDA licenses a vaccine, experts may consider adding it to the recommended immunization schedule.



MISSION: Deliver 300 million doses of safe and effective vaccine by 1 January 2021.



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safety at every phase

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INVESTIGATIONAL NEW DRUG APPLICATION

> BASIC RESEARCH

VACCINE

DEVELOPMENT

safety
is a priority
during vaccine
development
+ approval

DISCOVERY PRE-CLINICAL STUDIES PHASE 1 PHASE 2 PHASE 3

effectiveness safety +

effectiveness

CLINICAL STUDIES / TRIALS

FDA REVIEW Vaccines and Related Biological Products Advisory Committee

Full Agency Approval



The Vaccine Life Cycle

safety at every phase

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VACCINE

safety is a priority during vaccine development + approval

BASIC RESEARCH DISCOVERY PRE-CLINICAL STUDIES

PHASE 1 safety

PHASE 2

PHASE 3

effectiveness safety + effectiveness

CLINICAL STUDIES / TRIALS

4 APPROVAL OF INEW VACCINE FDA REVIEW

ACIP REVIEW

Advisory Committee on **Immunization Practices**

Full Agency Approval



Advisory Committee on Immunization Practices (ACIP)

HOW A VACCINE IS ADDED TO THE U.S. RECOMMENDED IMMUNIZATION SCHEDULE

The Advisory Committee on Immunization Practices (ACIP) is a group of medical and public health experts. Members of the American Academy of Pediatrics (AAP) and American Academy of Family Physicians (AAFP) are among some of the groups that also bring related immunization expertise to the committee. This group carefully reviews all available data about the vaccine from clinical trials and other studies to develop recommendations for vaccine use.

When making recommendations, ACIP considers:



How safe is the vaccine when given at specific ages?
How well does the vaccine work at specific ages?
How serious is the disease this vaccine prevents?
How many children would get the disease the vaccine prevents if we didn't have the vaccine?

ACIP recommendations are not official until the CDC Director reviews and approves them and they are published.

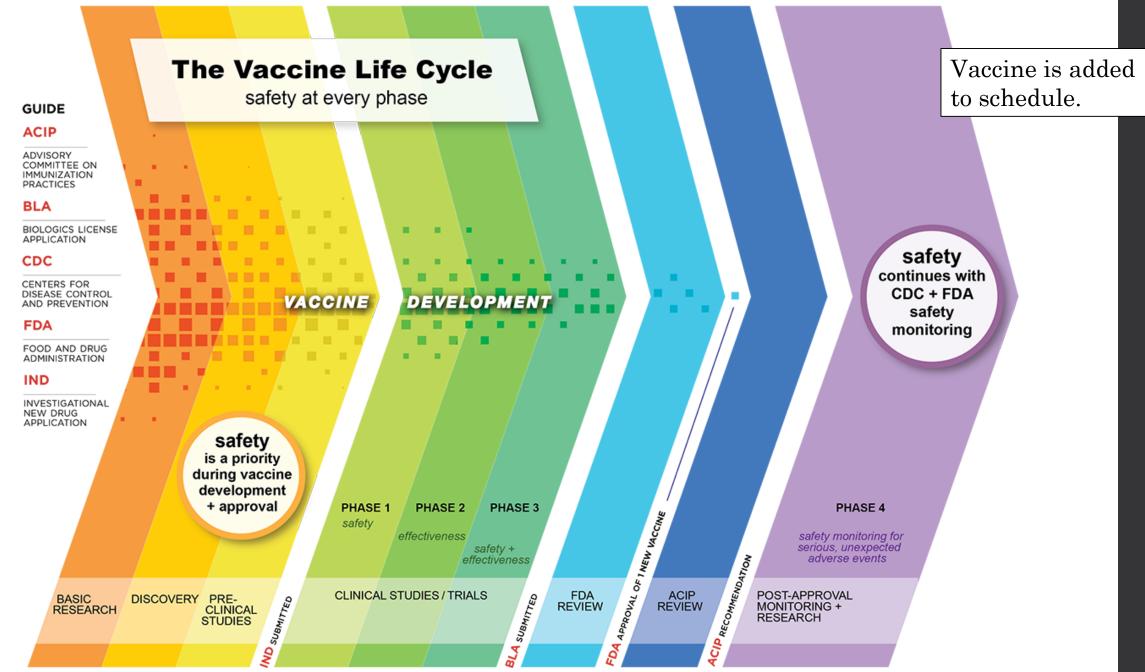
These recommendations then become part of the United States official childhood immunization schedule.

New vaccine to protect your child against a disease is added to the schedule.

FOR MORE INFORMATION, VISIT HTTP://WWW.CDC.GOV/VACCINES

After being added to the U.S. Recommended Immunization Schedule, health experts continue to monitor the vaccine's safety and effectiveness.

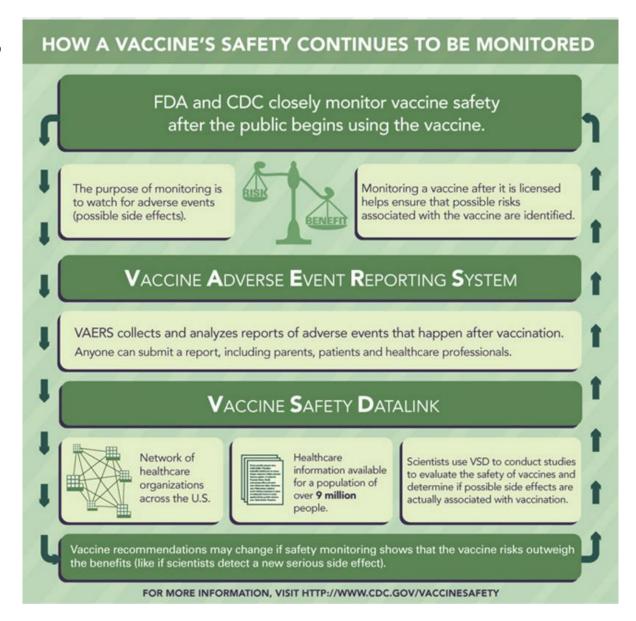
- Chair
- Exec. Secretary
- 15 voting members
- 8 ex-officio members
- Liaisons from 26 health-related professional organizations



https://www.cdc.gov/vaccinesafety/ensuringsafety/history/index.html

"Phase IV Trial"

- Continuous Monitoring
- VAERS
- Datalink



Vaccine Controversies

The "Anti-Vax Movement"

1. Vaccines cause autism

Quick answer: No. Just, no.

Long Answer:

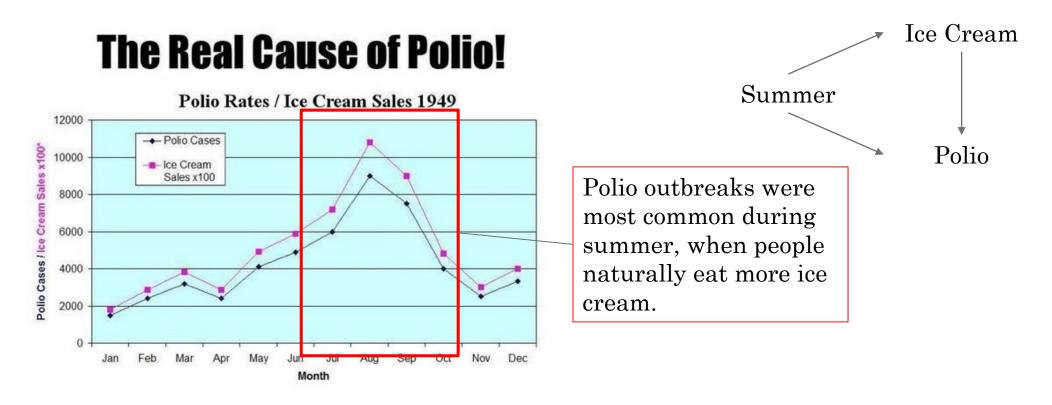


- In 1998, Dr. Andrew Wakefield published a study in the British Medical Journal, *The Lancet*
- In it, he claimed that "the onset of behavioral symptoms was associated, by the parents, with MMR vaccination in 8 of the 12 children"

"The most damaging Medical Hoax of the last 100 years"

- Why was it bad?
 - Manipulated Evidence
 - Reports of 8 out of 12 children
 - Retrospective data: Parents/Physicians linked the start of their behavior symptoms to MMR vaccination
 - Bowel symptoms, endoscopy findings, biopsy → "autistic entercolitis"
 - Suggested connection between autism and gastrointestinal issues was real, but did not prove an association between triple vaccine and autism
 - Press Conference
 - Wakefield "thought it prudent" to use single vaccines instead of the MMR triple vaccine until the triple vaccine could be ruled out as an autism trigger
 - Major health scare in the UK

Correlation Does Not Imply Causation



In the late 1940s, before there was a polio vaccine, public health experts in America noted that polio cases increased in step with the consumption of ice cream and soft drinks.

The elimination of such treats was recommended as part of an anti-polio diet.



So people started investigating his claims

1999

a study of 500 CHILDREN

no connection was found

2001

a study of 10,000 CHILDREN still found no connection 2002

Following Dr. Wakefield's study, here's what other more rigorous

studies found

a study from Denmark of 537,000 CHILDREN found no connection

a study from Finland of 535,000 CHILDREN once again found no connection

2012

A review of 27 cohort studies, 17 case control studies, 6 selfcontrolled case series studies, 5 time series trials, 2 ecological studies, 1 case cross-over trial covering over

> 14,700,000 CHILDREN

2005

A review of 31 studies covering more than

CHILDREN

Also found no connection

__<u>~</u>← 2004

Lancet released a statement **REFUTING** the original findings

NO LINK TO AUTISM WAS FOUND IN ANY CASE, IN ALL OF THE STUDIES.

They had conducted invasive investigations on the children without obtaining the necessary ethical clearances... picked and chose data that suited their case;

THEY FALSIFIED FACTS. 9 9

Then what?

- Wakefield was found to have undisclosed conflicts of interest
 - Paid to conduct the study by lawyers of parents
 - Received £55,000 from solicitors seeking evidence
 - Had applied for patent on a rival, single vaccine (measles)
- His co-authors withdrew their support for the interpretations
- There were **ethical** considerations:
 - Children were subjected to unnecessary invasive medical procedures (colonoscopies, lumbar punctures)
 - Bought blood samples from children at his son's birthday party
 - Acted without institutional review board approval
- Feb 2, 2010, the Lancet "fully retracted the paper from the published record"
- May 24, 2010, Wakefield's **medical license was revoked** for "serious and wideranging findings of misconduct."

https://www.healthychildren.org/English/safety-prevention/immunizations/Pages/Vaccine-Studies-Examine-the-Evidence.aspx

2. Vaccines have mercury in them.

Quick answer: Kind of.

Long Answer

• TRUE: Mercury (methylmercury) has been found to damage the nervous system

HOWEVER

- Thimerosal (the preservative used in vaccines) contains ethylmercury
 - Multiple studies have found **NO LINK** between
 - Thimerosal and autism
 - Thimerosal and neurologic issues in children

ALSO

- Thimerosal was removed from all childhood vaccines between 1999 and 2001
 - Mainly due to the studies at the time that stated Mercury was bad for everyone
 - Thimerosal is still found in some multi-dose vials of some flu vaccines
 - Single-dose vials are the general rule

https://www.cdc.gov/vaccinesafety/concerns/autism.html

3. That many vaccines at once is bad for children.

Quick answer: No, it's not.

Long Answer

Adaptive Immune System

- Passive protection from mother (transplacentally, breastmilk)
- Gradually matures during infancy
- T cells can produce a large immune response to brief stimulation
- Vaccines
 - Stimulate protective immune responses
 - · Immunological memory accumulation

Exposure

- Womb is sterile
- Bacterial exposure: birth canal, skin contact, breathing, eating, putting things in mouths, gut bacteria
- Exposure to microorganisms is CONTINUOUS

Combined Vaccine

- Decreased risk of catching disease while waiting for full immunization coverage.
- 2 injections = less pain and distress than 6
- Extra visits for more vaccines → delayed and missed coverage



So explain this!

Identified Prevalence of Autism Spectrum Disorder

Surveillance Year	Birth Year	Sites Reporting	Prevalence per 100,000	Approx.
2020	2012	11	27.6 (23.1-44.9)	1 in 36
2018	2010	11	23.0 (16.5-38.9)	1 in 44
2016	2008	11	18.5 (8.0-19.1)	1 in 54
2014	2006	11	16.8 (13.1-29.3)	1 in 59

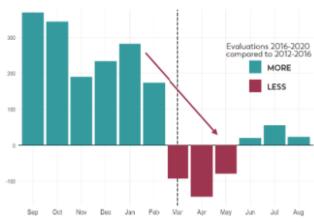
• 4x more common in boys

General population of 8 year olds in 11 states, extrapolated to the rest of the US

Autism is "increased" because...

- Awareness & Diagnostic Criteria Changed
 - 1966 (1 in 250,000) focused on children at the severe end of the spectrum
 - 1980 Autism is added to the DSM
 - Before this, many with autism were institutionalized and "invisible"
 - 1987 expanded diagnostic criteria (1 in 1,400)
 - 1991 diagnosis of Autism qualifies for special education services
 - Previously, children may have been listed as "intellectual disability"
 - 1994 definition broadens even further (includes Aspergers as mildly Autistic)
 - 2006 AAP recommends screening all children for autism between 18 and 24 months of age
 - 2010 AHA increased access to care

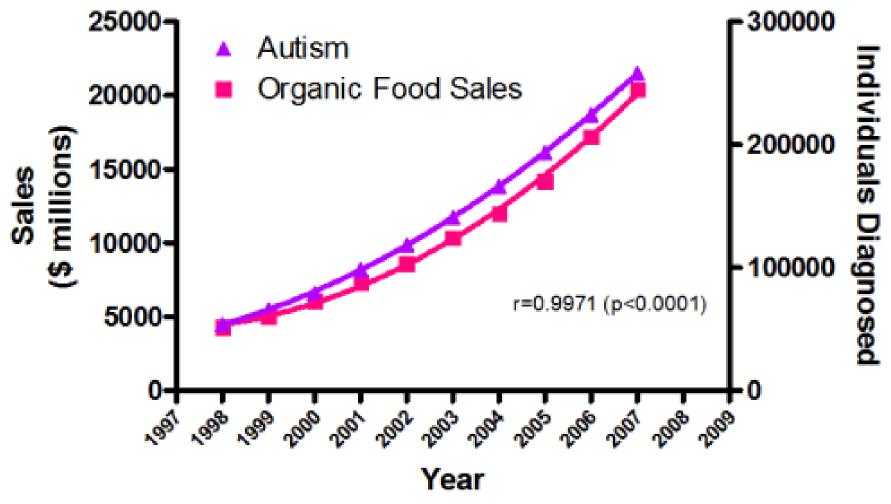
From 2016 to the beginning of 2020, **4-year-old children** had more evaluations and identifications than children aged **8-years** (when they were 4) had from 2012 through 2016.



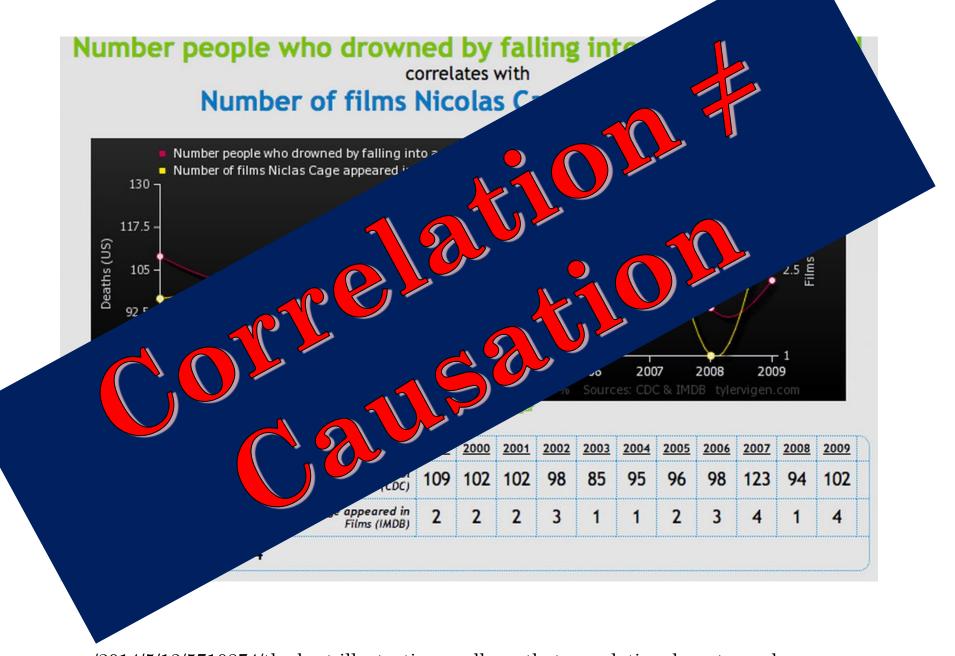
Displayed as 6 months prior and 6 months post-pandemic

Biological factors

- Older parents (especially fathers)
- Prematurity



Sources: Organic Trade Association, 2011 Organic Industry Survey; U.S. Department of Education, Office of Special Education Programs, Data Analysis System (DANS), OMB# 1820-0043: "Children with Disabilities Receiving Special Education Under Part B of the Individuals with Disabilities Education Act



Take Home Message

Vaccines are Backed by Science

- Must pass stringent Phase I, II, and III trials before it is regulated for use and are continuously monitored following licensure
- All vaccines routinely recommended for children 6 years of age or younger and marketed in the U.S. contain no thimerosal or only trace amounts
- Infants and young children who follow immunization schedules that spread out shots or leave out shots are at risk of developing diseases during the time that shots are delayed
- Vaccines keep communities healthy, and protect some of the most vulnerable in our society

American Academy of Pediatrics. (2017). American Academy of Pediatrics Emphasizes Safety and Importance of Vaccines. Retrieved from https://www.aap.org/en-us/about-the-aap/aap-press-room/Pages/American-Academy-of-Pediatrics-Emphasizes-Safety-and-Importance-of-Vaccines.aspx

Centers for Disease Control and Prevention. (2016). *Infant Immunizations FAQs*. Retrieved from https://www.cdc.gov/vaccines/parents/parentsquestions.html

U.S. Food and Drug Administration. (2015). *Thimerosal in Vaccines: Questions and Answers*. Retrieved from http://www.fda.gov/BiologicsBloodVaccines/Vaccines/QuestionsaboutVaccines/UCM070430#q5

Other Resources

- CDC.gov/vaccines
- Immunizedelaware.org
- Vaxopedia.org
- HistoryofVaccines.com



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Public Health Is Awesome!



- Bachelors from Penn State
 - Nuclear Engineering/ Engineering Mechanics
- MD from Xavier University School of Medicine
 - Aruba!
 - Atlanta and Chicago



- MPH from Arcadia
 - International internship → vaccine safety, cold chain breaks in Australia
- Delaware Academy of Medicine
 - Patient Centered Care, Immunizations, Chronic Disease, Built Environment/Environmental Health, Education, Biostatistics, Epidemiology, ...





Clearinghouse for Vaccine information

- www.immunizedelaware.org
- Info for public and providers
 - Flu season
 - · Clinic locations, dates, times
 - Types of vaccines in this season's shot
 - Specific vaccine information
 - · Links to the CDC
 - Vaccine Information Statements
 - News
 - New vaccines
 - Continuing Education
 - New controversies



