Measles

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No conflicts of interest to declare.

Will mention off-label use of vitamin A.

No politicians were harmed in making this presentation.

A Little History

- Recognized two millennia ago.
- Recognized as a contagious disease in 1846 during an outbreak in the Faroe Islands.
- Propagated in cell culture in 1953.
- Live-attenuated vaccine went into use in US in 1963.
- Formalin-killed vaccine given to less than 1 million in US 1963-67, but proved to provide only brief protection.
- Declared "eliminated" (no sustained transmission) in US 2000.

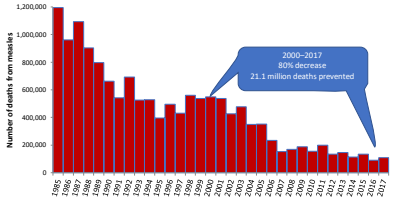
The Virus

- RNA virus
- Family Paramyxoviridae
- Relatives: Canine distemper, rinderpest
- Can infect monkeys, but humans are the main host.
- R_0 12-18 – an average case in a susceptible population will infect 12-18 others via airborne transmission.

Global Epidemiology

- **Measles is still commonly transmitted (endemic or large outbreaks) worldwide.**
- **Measles remains a leading cause of vaccine-preventable infant mortality.**
- **Great progress has been made toward measles elimination.**
- **From 2000-2017:**
  - Reported measles incidence decreased 83%, from 145 to 25 cases per million persons
  - Annual estimated measles deaths decreased 80% (21.1 million deaths prevented)
  - Every dollar spent on measles vaccine saves $58 later.

Number of Lives Saved by Measles Vaccine Globally



Source: MMWR: Nov 30, 2018 / Vol. 67 / No. 47

But the News Is Not Rosy

- Global first dose vaccine coverage plateaued at 85%, well below the level needed for herd immunity.
- Four regions experienced massive outbreaks in 2017.
- Venezuela, Germany, Russia lost control of measles.
- Surveillance is inadequate.
- Over 89,000 children died of measles in 2016.

https://www.who.int/immunization/global_vaccine_action_plan/SAGE_GVAP_Assessment_Report_2018_EN.pdf

Durrheim DN et al. J Infect Dis 2019, 220: 1870

Recent Deaths in the Congo from Viral Disease

Ebola: 2236

Measles: > 6000

Measles Outbreak in Samoa

In 2013, 90% of babies in Samoa got MMR at one year of age.

In 2018, two children died after receiving MMR that was mixed with anesthetic instead of diluent (error by nurse).

Anti-vaccine groups seized the opportunity. Robert Kennedy Jr. flew to Samoa to campaign against vaccination.

The government stopped its vaccination program.

Vaccination rate fell to 34% IN 2018 (vs 99% in nearby islands).

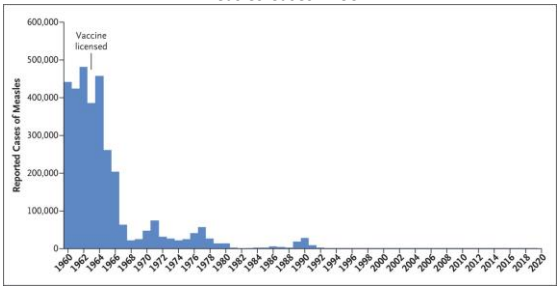
https://en.wikipedia.org/wiki/2019_Samoa_measles_outbreak

- A person with measles arrived in Samoa in August, 2019.
- By January 6, 2020, there were 5697 confirmed cases of measles (>2% of the population).
- 83 have died, mostly young children.
- Government declared a state of emergency, closed all schools.
- Curfews imposed; Christmas celebrations and public gatherings banned.
- Unvaccinated families had to display a red flag in front of their homes.
- Vaccination rates went back up.
- RFK Jr. attributed the outbreak to "defective vaccine, "absent evidence.

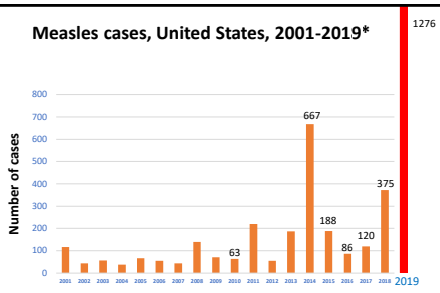
US Epidemiology Before Vaccine

- **Each year, measles caused an estimated 3 to 4 million cases**
  - 48,000 hospitalizations
  - 1,000 cases with encephalitis
  - 400 to 500 deaths
  - SSPE risk: 1 per 11,000 (all die) – but rate may be higher

Measles Cases in US

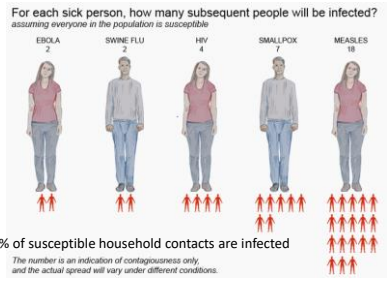


Strebel PM and WA Orenstein. Measles. *New Engl J Med* 2019; 381: 4.



30 states reported 1172 cases as of August 1; ¾ of cases are in New York state

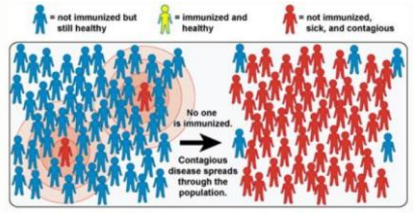
*Source: Morbidity and Mortality Weekly Report (MMWR), Notifiable Diseases and Mortality Tables



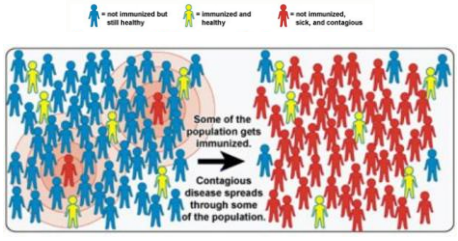
75-90% of susceptible household contacts are infected

https://www.abc.net.au/news/2014-07-30/ebola-virus-explainer/5635028

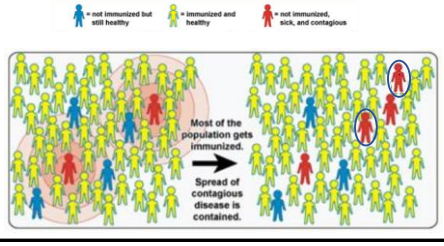
Rapid spread of disease in a nonimmune population



Spread is slowed but extensive in partly-immune population



Minimal transmission in a mostly-immune population
Even the non-immune are partly protected



Simulation: 1000 people and one with measles

Scenario 1
Nobody vaccinated.
15 people infected, then 225, then everybody.
Only 3 generations before entire population is infected.

Scenario 2
50% vaccinated, vaccine efficacy 95%.
$R = R_0 \times .5 / .95 = 7.9$.
Virus spreads efficiently, but takes 4 generations to infect nonimmune population.
A few of the vaccinated people get infected, but outbreak ends before most are infected.

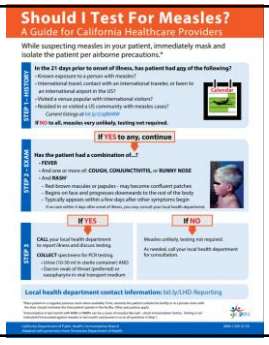
Scenario 3
95% vaccinated, vaccine efficacy 95%
$R = R_0 \times .05 / .95 = 0.79$.
Outbreak terminates with minimal spread.

Measles Symptoms

- Incubation period is 10-14 days (range, 7-21)
- Begins with fever, cough, runny nose, conjunctivitis.
- Red, watery eyes
- Rash appears on day 2-4 and begins on the head/neck.
- Rash progresses over 2-4 days and may become confluent.
- Tiny white spots inside the mouth appear 1 day before onset of rash and disappear after 2-3 days.
- Infectiousness begins about 3 days before onset of rash
- May have otitis, bronchitis, pneumonia, mastoiditis, diarrhea, encephalitis.

Measles Rash

Koplik's Spots



Should I Test For Measles?
A Guide for California Healthcare Providers

While suspecting measles in your patient, immediately mask and isolate the patient per airborne precautions.*

STEP 1 – HISTORY
In the 21 days prior to onset of illness, has patient had any of the following?
- Known exposure to a person with measles?
- International travel, contact with an international traveler, or been to an international airport in the US?
- Visited a venue popular with international visitors?
- Resided in or visited a US community with measles cases?
Current listings at bit.ly/caphcMV
If NO to all, measles very unlikely, testing not required.

IF YES to any, continue

STEP 2 – EXAM
Has the patient had a combination of...?
- FEVER
- And one or more of: COUGH, CONJUNCTIVITIS, or RUNNY NOSE
- And RASH†
- Red-brown macules or papules - may become confluent patches
- Begins on face and progresses downwards to the rest of the body
- Typically appears within a few days after other symptoms begin

IF YES | IF NO

STEP 3
CALL your local health department to report illness and discuss testing.
COLLECT specimens for PCR testing.
- Urine (10-50 ml in sterile container) AND
- Dacron swab of throat (preferred) or nasopharynx in viral transport medium

Measles unlikely, testing not required.
As needed, call your local health department for consultation.

Local health department contact information: bit.ly/LHD-Reporting

http://eziz.org/assets/docs/IMM-1269.pdf

Testing for Measles

Preferred samples are urine in a cup and throat swab in Universal Viral Transport.

- Send to Santa Clara County Public Health Lab for measles PCR (order as miscellaneous reference test in HC).
- IgM is unreliable and should be avoided.
- IgG is for assessing immune status.
- Do NOT send suspect cases to the lab.
- Form:

https://www.sccgov.org/sites/phd-p/programs/Lab/Documents/Lab%20Forms/gen-submittal-form.pdf

Wrong Specimen

A Local Case

- 8 month old child exposed to measles during flight home from Asia (family was called by county to inform them of exposure).
- 6-9 days after exposure, she developed cough and runny nose.
- 11 days after exposure, developed high fever (103) and papular rash on face, which spread to trunk, plus red eyes and cough.
- ED notified prior to patient's arrival, and patient was placed in airborne isolation on arrival. No additional exposures.
- PCR positive for measles virus.
- Admitted; treated with vitamin A, fluids, antibacterials for secondary pneumonia.
- An exposed adult on the same flight became ill. Additional transmissions were avoided because he had also been notified to watch for symptoms of measles.

Treatment of Measles

No specific antiviral, and none is likely.

Hydration.

High-dose vitamin A for children with severe measles.

Treatment of secondary bacterial infections.

Prevention of Measles

- Immediate airborne isolation
- Postexposure prophylaxis with vaccine (up to 72 hours)
- Postexposure prophylaxis with immune globulin (up to 6 days) – then vaccinate 8 months later
- Never let a good crisis go to waste

What to do with a suspected measles case

- Institute airborne precautions or put the patient in a closed room in clinic.
- Contact your infection prevention/infection control or ID team.
- Order tests as noted four slides prior. Remember that?
- Contact county Public Health for approval (call the after-hours health officer on call if evening/weekend/holiday).
- Accompanying family members or visitors should be screened for symptoms.
- When the patient exits, the patient should wear a mask and be escorted out.
  - If your patient is being sent home and measles is suspected, the patient should be instructed to isolate at home until cleared by either ID or Public Health.
  - Note that measles does not necessarily require hospitalization. Need for hospitalization is based on the clinical needs of the patient.

Measles Vaccine

- Live attenuated; contraindicated in pregnancy and in most immunocompromised patients.
- Can cause a rash but will not transmit to others.
- Available ONLY as MMR.
- One dose 93% effective, two doses 97% effective.
- Immunity is generally lifelong (but may fade for mumps).
- Approximately 92-94% vaccination rate required for effective herd immunity (R<1).

(late 2018, New York)

Current Outbreak: Vaccination Status

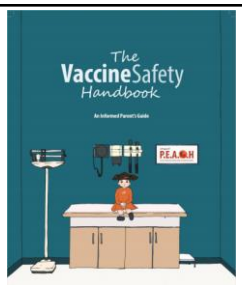
Age Group	# Cases	0 Doses	1 Dose	2 Doses	Unknown
< 1 Year	15	15 (100%)	0	0	0
1-3 Years	21	20 (95%)	1 (5%)	0	0
4-18 Years	47	42 (89%)	0	2 (4%)	3 (6%)
19 + Years	19	8 (42%)	1 (5%)	1 (5%)	9 (47%)
Totals	102	85 (83%)	2 (2%)	3 (3%)	12 (12%)

Table 1. Comparison of the Risk of Complications Associated with Measles and the Risk of Serious Adverse Events after Measles Vaccination.*

Complication or Serious Adverse Event	Risk after Natural Disease†	Risk after Vaccination‡
Otitis media	7 to 9 per 100	0
Diarrhea	8 per 100	0
Pneumonia	1 to 6 per 100	0
Subacute sclerosing panencephalitis	4 to 11 per 100,000	0
Encephalitis	0.5 to 1 per 1000	<1 per 1,000,000
Death	Approximately 1 per 1000 (1 to 15 per 100 in developing countries)	0
Febrile seizure	—§	1 per 3000
Thrombocytopenic purpura	—§	1 per 30,000
Anaphylaxis	0	2 to 14 per 1,000,000

* Information is from the Institute of Medicine[35] and Pless et al.[36]
† Risk is expressed as the number of events per number of cases of measles.
‡ Risk is expressed as the number of events per number of vaccine doses administered.
§ Complication has been described in measles case reports, but the risk is not well quantified.

Strebel and Orenstein, NEJM



P.E.A.C.H.

Parents **E**ducating and **A**dvocating for **C**hildrens' **H**ealth

Who are they?

https://s3.amazonaws.com/assets.forward.com/downloads/measles-vaccine-peach-magazine-pdf-brooklyn-1554905824.pdf

A SLICE OF PIE
Parents Informed & Educated
Making PIEs Out of PEACH:
MMR Edition
Bringing Current and Reliable Vaccine Information to Frum Families

https://www1.nyc.gov/assets/doh/downloads/pdf/a-slice-of-pie

- Measles vaccine is safe and effective.
- Measles vaccine does not cause autism; that claim has been disproven.
- I recommend this vaccine for myself and my family.
- There are some people who the CDC says should not get the vaccine. You (your child) are not one of them.
- Measles vaccine protects you (your child) and also the entire community, especially immunocompromised children.
- Measles is now required for school.
- Debunk immunology myths from the internet.

https://www.shotsforschool.org/

https://www.cdc.gov/vaccines/hcp/conversations/downloads/vacsafe-mmr-color-office.pdf

Peter J. Hotez, MD, PhD
Dean, National School of Tropical Medicine

Author of "Vaccines Did Not Cause Rachel's Autism"

https://twitter.com/PeterHotez

Why the Fuss over a "Routine" Childhood Disease?

Mortality from other infections rises after a measles outbreak. Why?

- Mina et al. Measles virus infection diminishes preexisting antibodies that offer protection from other pathogens. *Science* **366**, 599-606 (2019).
- Petrova V et al. Incomplete genetic reconstitution of B cell pools contributes to prolonged immunosuppression after measles. *Sci. Immunol*. **4**, eaay6125 (2019).
- Frederick E. How measles causes the body to 'forget' past infections. *Science* **366**, 560 (2019).
- Measles infection (but not measles vaccine) "erased" the immune memory of children.

Vaccination Schedule

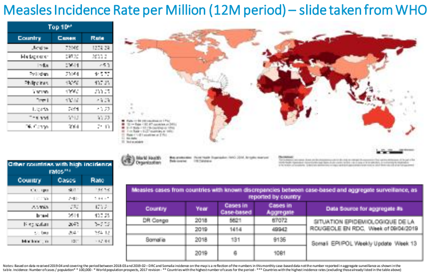
Children: Two doses of MMR, at ages 12-15 months and 4-6 years.
If a dose is given before age 1 for travel, two more doses should be given after 12 months of age.

Adults (catch-up for nonimmune): At least one dose of MMR.
If vaccinated 1963-67, may have received ineffective vaccine.

Adults (high-risk groups): Two doses of MMR at least one month apart.

Measles and Travel

Measles Incidence Rate per Million (12M period) – slide taken from WHO



Country	Year	Cases in Case-based	Cases in Aggregate	Data Source for aggregate #s
DR Congo	2018	5621	67072	SITUATION EPIDEMIOLOGIQUE DE LA ROUGEOLE EN RDC. Week of 09/04/2019
	2019	1414	49942	
Somalia	2018	131	9135	Somali EPI/POL Weekly Update Week 13
	2019	6	1081	

What to do about international travelers?

All international travelers are considered high-risk.
Our Call Center Travel Clinic addresses this.
Make sure all meet evidence of immunity for high-risk:
Positive blood test, or two doses of MMR, or born before 1957

Children may receive a dose of MMR as early as 6 months.
If they get an early dose (before 1 year), they will need two more.

Consider measles in ddx of a traveler with fever and rash.

Another Local Case

- Young adult M, immigrated 2011, with fever, sore throat, congestion for two days.
- Vaccination history unclear. No travel history obtained.
- Diagnosed with viral syndrome and sinusitis and given amoxicillin [*sic*].
- Two days later developed a rash, sent back to clinic [*sic*].
- Overseas travel noted. Patient transferred to ED with precautions taken. Masked in his car and taken through ambulance bay to airborne isolation room.
- Noted return from the Philippines two weeks prior.
- Throat swab positive for measles virus by PCR.
- 118 people exposed in clinic needed follow-up.

TEST REQUESTED		RESULTS	REFERENCE RANGE
MEASLES VIRUS RT-PCR ASSAY		MEASLES VIRUS RNA DETECTED	NOT DETECTED
Tested: 03/28/2019	Reported: 03/28/2019		Analyst: DTC

But wait, there's more!

Adult M with unknown immunity to measles. Exposed in clinic to a case and given MMR two days later. Two weeks later, he e-mailed his PCP c/o cold sweats, chills and aches for 3 days, with red dots on his torso. During this time, he had been in a local supermarket. He sent pictures, PCP consulted with ID, who arranged for him to come to ED next AM around 7 am to get tested (ED notified, precautions taken, no exposures). Public Health department was notified and agreed to process specimens.

Meanwhile, his employer had sent out a memo to the staff of 80 people informing them of possible exposure, with information from CDC about what to do if measles is suspected. Two pregnant coworkers were concerned that they were exposed to him. They called the Call Center and were handled by our sister facility.

Swab PCR was positive for measles vaccine virus.

Evidence of Immunity

General population
- Birth before 1957, OR
- One documented dose of MMR after 1967, OR
- Positive measles IgG

High risk
- Two documented doses of MMR after 1967, at least one month apart, OR
- Positive measles IgG, OR
- Born before 1957 (we don't use this if health-care worker)

Hot Tips

- There are no new recommendations, nor any need for "boosters".
- For most of the population, birth before 1957, OR one dose of vaccine after 1967, OR a positive serology, is sufficient.
- Some people are at higher risk, notably students, international travelers, health-care workers, close contacts of immunocompromised or nonimmune people, and people with HIV (CD4 >200).
- For them, a higher standard of immunity is recommended: Two doses of measles vaccine after 1967, at least one month apart, OR a positive measles IgG, OR born before 1957 (unless HCW).

Hot Tips 2

- If someone does not meet the criteria for immunity, you can send a measles serology (most will be positive), and vaccinate if negative, OR just vaccinate with one dose of MMR.
- There is no need for "quantitative" titers, as these do not add any value.
- See https://tinyurl.com/tlds7d7
- People who've been vaccinated but are seronegative are considered to have evidence of immunity. Exactly how well protected they are is not entirely clear. Some have antibody below the limit of detection.

Vaccination of Standard-Risk Patients – this is on ID eConsult FAQ

Status	Presumptive Immune Status	Action
Born before 1957 Served in the US military Has received a dose of measles vaccine after 1967 Legal immigrant to US after 1995 with immigrant visa or green card	Presumed Immune	No vaccination or testing required
Unknown vaccine status	Unknown	Check serology (measles IgG) and vaccinate if negative, OR give single dose MMR
Vaccinated between 1963-1967	May not be immune	Check serology (measles IgG) and vaccinate if negative, OR give one dose MMR
Never vaccinated, born after 1957	Non-immune	Vaccinate with one dose of MMR
Measles vaccination is contraindicated for pregnant persons and those with known severe immunodeficiency (malignancy, chemotherapy, congenital immunodeficiency, long-term immunosuppressive therapy, or HIV with CD4 <200)		

Take-Home Messages

- Measles vaccine is safe and highly effective, but not 100%. Because measles is so contagious, very high vaccination rates are needed to prevent ongoing transmission.
- Travelers are at risk and should be up-to-date on the vaccine (two doses). Infant travelers 6-12 months old may be vaccinated ahead of schedule.
- High-risk people born 1957 or later should have two doses of vaccine or a positive serology to confirm immunity.
- Obtain a travel history in people with a fever. Handy for typhoid, malaria, dengue, and (heaven forbid) Ebola, too.
- Communication is critical to prevent additional exposures!!!!

Online References

Information for patients asking about immunity and boosters:

https://www.cdc.gov/measles/about/faqs.html#protection

Latest CA Public Health immunization recommendations:

https://www.cdph.ca.gov/Programs/CID/DCDC/CDPH%20Document%20Library/Immunization/MeaslesRec.pdf

All the measles minutiae on the CA Public Health web site at:

https://www.cdph.ca.gov/Programs/CID/DCDC/CDPH%20Document%20Library/Immunization/Measles-Quicksheet.pdf

Santa Clara County web site with many links:

https://www.sccgov.org/sites/phd-p/diseases/measles/pages/measles-home.aspx