## NYU Langone Health

## What? Me Worry? Measles...here, there \& everywhere

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## Objectives

- Review history and pathogenesis of Measles disease
- Discuss the epidemiology of Measles in the US \& NYS.
- Describe the current Measles outbreak in the NY metro area
- Review Measles disease and Measles prevention
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## History of Measles

- Imagine an apparently infectious disease with these symptoms: high fever, eye inflammation and eye/nose discharge, labored breathing and coughing, vomiting and diarrhea, loss of appetite and lethargy, and hardening of nose and footpads...name this disease!
- Hint \#1: it's name suggests an imbalance of humors
- Hint \#2: it is caused by a single-stranded RNA virus of the family Paramyxoviridae
- Hint \#3: this disease is highly contagious via inhalation, and while morbidity and mortality may vary, it is often very high


## History of Measles

- Imagine another infectious disease that causes fever, loss of appetite, nasal and eye discharges, irregular erosions in the mouth, the lining of the nose, and the genital tract, and diarrhea....name this disease!
- Hint \#4: it is caused by an enveloped single-stranded RNA virus in the Paramyxoviridae family
- Hint \#5: The fatality rate for this disease can approach $100 \%$ in susceptible populations
- Hint \#6: This disease is spread by direct contact, drinking contaminated water, and is airborne



## History of Measles

- Disease \#1 - Canine Distemper
- Disease \#2 - Rinderpest, the 2nd infectious disease ever to be globally eradicated. And you thought smallpox was the only one! (me too...)
- So what you ask?
- Rinderpest has been known since the beginning of recorded history. This may have been one of the ten plagues recorded in Exodus 9. Has caused animal "plagues" repeatedly around the world for millennia.
- Rinderpest Virus is very closely related to Canine Distemper Virus, and...


## History of Measles

- Measles!
- Measles is believed to have possibly originated as a mutation of Rinderpest virus sometime between 5000 $B C$ and 500 AD
- NOT a true zoonosis; only humans get measles
- First described medically in 910 AD by a leading Persian physician and philosopher, Rhazes, who worked at the Baghdad Hospital in ancient Iran. European physicians began describing measles in their medical writings in the mid-1600s.


## Pathogenesis of Measles

- In a susceptible person, Measles Virus (MV) binds to two different receptors in human cells
- CD150, which is expressed by - or sticks out of - dendritic cells (which are designed to capture and bring antigens to lymphocytes) as well as B- and T- lymphocytes themselves
- PVRL4, or poliovirus receptor-like 4, which is expressed by several types of respiratory epithelial cells, particularly columnar epithelial cells common in the upper respiratory tract.
- After binding, the virus enters these cells, replicates, lyses the cell, and releases more virus.


## Pathogenesis of Measles

- Nasal mucosa - primary site of infected epithelial cells
- Creates ideal method for spreading the virus to others
- As disease progresses, increasing viral load is present in the tonsillar region, the trachea and bronchi, exacerbating viral spread when patients cough
- Rarely, and by uncertain mechanisms, MV can enter the brain and cause panencephalitis, affecting both white and grey matter
- Infection of lymphocytes creates transient immunosuppression, leading to opportunistic infections such as pneumonia and gastroenteritis


## Pathogenesis of Measles

- Infection of the entire respiratory tract infection causes edema and loss of cilia function, resulting in secondary bacterial pneumonia ... name another viral disease that does this to people
- Invasion of virus into lymphoid cells spreads it throughout the body, into skin, creating rash, Koplik spots, and conjunctivitis
- Immune memory cells often get depleted by MV infection, often for weeks to months following infection
- Eventually immune system cell counts normalize, but patients may lose immune memory (e.g., TB skin test reverts to negative)


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## Measles Epidemiology

- History is rife with examples of outbreaks of Measles
- Because disease creates life-long immunity, populations generally need to be large to support ongoing transmission in perpetuity ~ 500,000 some authors suggest, so that there are always new people to infect.
- Outbreaks affected larger medieval cities, or when imported, disease-naive populations, often catastrophically
- Experts suggest that pre-1963, there were 30 million cases and 2 million deaths per year globally from measles


## Measles Epidemiology - USA

- Reportable disease in the US starting in 1912!
- In the $20^{\text {th }}$ century, several million infections, 400-500 deaths - per year. The first half of the century had more deaths.
- Improved sanitation, and later the introduction of antibiotics reduced the death rate but not the disease incidence (population grew...)
- Outbreaks somewhat seasonal (winter/spring), worse every 2-3 years, but overall steady rates


## Measles Epidemiology - USA

- Measles was \#1 in 1888-2011 ~ 318/100,000
- Diphtheria was \#2 in 1888-2011 ~ 237/100,000
- In modern US, new HIV cases ~ 12.3/100,000 (2016)
- In modern US, new Chlamydia ~ 495/100,000 (2016)
- In modern US, new Gonorrhea ~ 145/100,000 (2016)
- In modern US, new Syphilis ~ 27/100,000 (2016)
- In modern US, new Salmonella ~ 16.7/100,000 (2016
- In modern US, new Hep B/Hep C ~ 1.0/100,000 (2016)
- In modern US, new Measles ~ 0.03/100,000 (2016)


## Measles Epidemiology - USA

- In the pre-vaccine era, nearly everyone had measles by age 15
- Worst outcomes were usually infants/small children
- Vaccine released in 1963, single dose
- Within 5 years of vaccine use, $95 \%$ cases were being prevented; most successful vaccine preventable disease effort ever
- Two dose requirement began in 1989, and measles was declared "eradicated" in 2000.


## Measles Epidemiology - USA

- In the US, measles cases dropped dramatically after the introduction of vaccination in 1963.



## Measles Epidemiology - New York State \& NYC

- In NY, most years, cases were far more numerous in NYC than upstate, except 2018


## Annual Measles Cases - NYS + NYC, <br> Select Years (CDC data) * prelim data



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## Current Measles Outbreak - New York State \& NYC

- Current Measles Outbreak
- Rockland County = 96 cases (New Square, Spring Valley, Monsey, New City)
- New York City = 50 cases (Williamsburg, Borough Park, and Bensonhurst, Brooklyn)
- Orange County = 6 cases
- Rockland County - 8 separate index cases, all with exposures to ongoing measles outbreak in Israel
- Orange County - all cases linked to outbreak in Rockland County


## Current Measles Outbreak - New York State \& NYC



## Current Measles Outbreak - New York State \& NYC

- Measles Cases in NY State, 1997-2018* *As of 12-19-2018
- The current outbreak is the largest in New York State since the 1990's



## Current Measles Outbreak - New York State \& NYC



## Current Measles Outbreak - New York State \& NYC

- Public Health Response
- Community Outreach
- Posters
- Postings in local journals - Provider visits
- School visits
- Conference call with moms - School exclusions


## Current Measles Outbreak - New York State \& NYC

- Health Care Provider and School Support
- Advisories
- Clinical support
- Fact sheets
- Letters to school administrators
- Vaccination, Immune globulin administration



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## Measles - Clinical Review

- Course of illness explained by pathogenesis
- Inoculation of virus infects dendritic cells and lymphocytes in the respiratory tract (CD150 receptor-mediated)
- These immune system cells spread virus throughout body
- Virus transmitted to respiratory epithelium cells (PVRL4 receptor-mediated) directly and by lymphocytes. Virus spread to peripheral lymphoid tissues
- Virus spread to epithelium and keratinocytes in dermis, creating rash
- Activation of immune system creates fever, destruction of respiratory epithelium causes cough, coryza, and conjunctivitis (ocular epithelium infection)


## Measles - Clinical Review



## Measles - Clinical Review

- Measles Presentation
- Classic Presentation: Fever, rash, and the "three C's":
- Cough
- Coryza (redness and swelling of nasal mucosa)
- Conjunctivitis (red, watery eyes)
- Can also have
- Koplik spots (scattered blue-white tiny spots on a bright red background) may appear inside the mouth (think intra-oral rash)
- Malaise
- Diarrhea
- Anorexia
- Lymphadenopathy



## Measles - Clinical Review

- Measles Complications
- Children younger than 5 years of age and adults older than 20 years of age are more likely to suffer from measles complications
- Acute otitis media (ear infections) - occurs in about 1 in 10 children with measles
- Can result in permanent hearing loss
- Pneumonia - As many as 1 in 20 children with measles gets pneumonia, the most common cause of death from measles in young children
- Subacute Sclerosing Panencephalitis (SSPE) - very rare delayed condition (several years after infection), progressive and has no known cure. Most individuals with SSPE will die within 1-3 years of diagnosis, more likely if patient under 2 yrs of age when infected


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## Map of the Tisch Hospital Emergency Department c. 2018



Emergency Dept


## Inpatient Measles Case Examples

- One fine Sunday evening in late September... a toddler $<2$ y old is admitted to a very full Peds ED ... so the patient is put in the adjacent "overflow" (adult) area, in a curtained bay next to adults...
- Initial RN notes:
- Pt has rash all over body, s/p abx drops for red eyes. Has purulent bilat eye drainage $x$ 3 days, Parent reports malaise $\times 5$ days before eye drainage began. Rash began on face yesterday - still all over face, now all over body. Has runny nose.
- Initial MD notes:
- [above repeated] No wheezing or cyanosis. Pt appears to have some increased difficulty breathing. No foreign body swallowed. No sick contacts. Was in Israel 2 weeks ago. Pt vaccinated on schedule.
- What do you think?



## Inpatient Measles Case Study

- After 6 hours, pt is admitted to 30+ general peds inpt unit
- Three hours later...different MD adds:
- Pt partially vaccinated only, did not receive MMR. Rash on face, scalp, trunk, arms, palms, upper legs. Patient may have Measles, or Kowasaki's, or Roseola, or drug rash. RVP negative, so doubt enterovirus infection. Begin Airborne Precautions....
- Four hours later, case is reported to NYCDOH as possible Measles and later that day, Measles testing is collected, and results IgM and PCR positive the next day.
- What do you think now? What do you do now?



## Inpatient Measles Case Study

- Differential Diagnosis of Measles / Other febrile rash illnesses
- Parvovirus B19 (Fifth's Disease)
- Human Herpesvirus -6 (Roseola)
- Enteroviruses
- Streptococcal infection (Scarlet Fever)
- Adenovirus
- Infectious mononucleosis
- Influenza: "Fleasles"
- Dengue
- Drug rash
- If you have a patient presenting with a febrile rash illness, consider the patient presentation and differential carefully. If measles is a concern, enact infection control practices immediately, and immediately report the case to your local health department.
- DO NOT WAIT FOR LABORATORY CONFIRMATION TO REPORT


## Inpatient Measles Case Study

- Start with the usual - confirm the diagnosis (done)
- Characterize the case by person, place, \& time - IPC team met to review facts - time spent in ED, route of travel in the ED, Room on general peds unit, layout of ED, Peds unit
- IPC team began to gather lists of exposed staff, requested Occupational Health to verify Measles immunity for these staff ... What challenges do you think occur here?
- IPC consulted with NYCDOH
- Help define risks to other patients, visitors, staff, exposure "duration" (two hours beyond time patient was present)
- Determine extent of contact tracing to be done ... What challenges do you think occur here?


## Emergency Dept. Map

Entry to the ED
—— First Avenue


## Inpatient Pediatric Unit Map (Kimmel 8)



## Inpatient Measles Case Study

- Contacts will be patients in the Pediatric and Adult ED - in the zone where the patient was, not the entire ED; similarly, and one half of inpatient Peds unit ...Why?
- Will include family/visitors, especially on Peds unit
- Who else do we need to focus on? What would you do about "them?"
- Peds ID consulted to assist with treatment decisions for exposed pediatric patients, adult ID consulted similarly for adult exposed patients/visitors
- Who else do we need to check on? The EMS crew!


## Inpatient Measles Case Study

- Post Exposure Prophylaxis (PEP)
- For exposed individuals without evidence of immunity (priority includes pregnant women, infants <12 month and severely immunocompromised)
- May prevent or modify disease
- MMR vaccine or Immunoglobulin (IG), MMR and Ig cannot be given at the same time
- MMR vaccine
- Within 72 hours of initial exposure
- Persons age $\geq 6$ months
- Vaccination should be offered at any interval following exposure to protect from future exposures
- IG
- Within 6 days of initial exposure
- Individuals who are at risk for severe disease and complications from measles should receive IG. via IV route (not IM) for pregnant women and severely immunosuppressed
- IGIM can be given to other exposed persons without evidence of immunity -- Priority for those with intense, prolonged contact
- If vaccine is contraindicated


## Inpatient Measles Case Study

- When all was said and done...
- About 120 patients' records had to be reviewed to determine where in the ED they received care
- 58 patients/visitors exposed; many had to be called using DOH's script, took several days
-5 patients given RX (vaccine or IVIG)
- 0 visitors given $R x$ (all were vaccinated / born before 1957
- 25 staff exposed, all immune (some needed urgent titers)
-3 of 4 EMS crew quickly confirmed as immune, $4^{\text {th }}$ was left to be checked by NYCDOH
- What kinds of challenges did we face?


## Measles in the Ambulatory Setting

- Seven cases identified at NYU clinics from Nov. 2018 to date
- Two cases generated significant exposures requiring postexposure evaluation \& prophylaxis.
- Immunoglobulin
- MMR
- Check immunity
- Quarantine for 21 days after exposure
- IPC involved in the follow up of both
- What about the other 5???
- IPC notified after the fact
- Patients examined outside of the clinic


## Measles in the Ambulatory Setting

## Case \# 1. Exposure date 11/13/18

4 month old female presenting with cough runny nose $\times 2$ days, fever, sore throat, nausea, vomiting, diarrhea, rashes, and ear pain. Dx - Viral URI and discharged. Returned following day with worsening fever and rash. Patient examined in the car for the $2^{\text {nd }}$ encounter. IgM and measles PCR nasal swab obtained and sent to the DOH lab. IPC notified of POSITIVE Measles results by DOH on 11/16/18 (Friday afternoon). Clinic closed for the day.

## Discuss............

- No. of exposed individuals 26 (patients \& relatives)
- Immune (i.e., had 2 doses of MMR) - 6
- Contacts requiring Immunoglobulin - 3
- $2^{\text {nd }}$ dose MMR needed/given - 5
- IgG positive titers - 1


## Measles in the Ambulatory Setting

## Case \# 2. Exposure date 12/16/18 and12/17/18

8 month old male presenting with cough and runny nose $\times 2$ days, No sore throat, rash or conjunctivitis, dx - URI. Returned the next day with worsening fever and now has rash, ear pain, conjunctivitis, $\mathrm{D} \& \mathrm{~V}, \mathrm{dx}$ - Acute viral conjunctivitis of both eyes along with fever of unspecified cause. Retuned to clinic on 12/18/18 (seen outside). Measles suspected. Parent disclosed contact with someone with Measles at a family gathering $31 / 2$ weeks ago and was given MMR prophylaxis.

- Total no. exposed - 21
- Immune contacts (i.e., had 2 doses of MMR) - 8
- Non-vaccinated contacts - 4
- Contacts given Immunoglobulin - 4
- What happened to the rest of the exposed individuals?
- Declined any intervention
- Lost to follow up


## Measles in the Ambulatory Setting

## Case \# 3-1/11/19

- Adult male presented to an ambulatory location with diffuse rash and history of subjective fever, cough, and runny nose. Negative for conjunctivitis. Onset 6-7 days ago, History of contact with friends who traveled from Hong Kong.
- Physician suspects Measles and orders IgM, no Measles PCR nasal swab was collected 1/14/19 - IgM positive, IgG negative, Remember - no PCR swab was obtained DOH verdict - False positive, further testing to be done and serum sample to CDC lab to re-test

Hong Kong does not have any ongoing Measles outbreak

- https://wwwnc.cdc.gov/travel


## Measles in the Ambulatory Setting

- Challenges
- Lack of Airborne isolation facilities
- Only one clinic has airborne isolation room in Staten Island!
- Information regarding exposures difficult to obtain in a timely manner
- First ambulatory case was an incidental finding
- Unclear workflows
- Who does what?
- Access to DOH lab to expedite testing
- Staff not familiar with the process of reporting and notification of communicable diseases
- Clinics that have recently transitioned to our institution not always familiar with IPC role in ambulatory setting


## Measles in the Ambulatory Setting - Patient Screening

Highly Infectious Communicable Disease and Emerging Pathogens Screening Algorithm

## Clinical Staff:

Patient presents with Fever \& Rash OR Fever \& Cough in the past 3 days


- Review IPC travel / screening protocol (Link to Ellucid with the information from CDC re travel notices https://www.cdc.gov/outbreaks/index.html ).
- If concern for highly infectious pathogen initiate Airborne and Contact Precautions and notify primary MD/team.
- Contact Infection Prevention and Control.
- If Suspected Measles or Chickenpox, Initiate Airborne and Contact Precautions and call IPC Department
- Continue with care as needed - OR -
- Reschedule and/or refer to primary care provider or ED

IPC Dept Tisch, LOH and KP: Regular hours: 212-263-5454, After hours/weekends: 212-263-4316,

## Measles in the Ambulatory Setting

- Strategies
- Enhanced screening of patients by intake staff - Messaging our communicable disease screening algorithm
- Targeted screening of patients when booking appointments clinic actively asking for symptoms (fever \& rash) before scheduling appointments
- ‘Side walk’ consultation - when it is safe to do, clinicians evaluating patient in a car or an alternative location to minimize exposures indoors
- Engaging the DOH in a timely manner. This will aid in expediting testing and timely prophylaxis
- Provider education - Alerts to ED \& Ambulatory clinics - 1 page educational updates to providers


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## THANK YOU!

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## Thank You



