

# 2017: What's Hot in Pediatric Infectious Diseases?

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# Objectives/Outcomes

- By the end of this interactive session the participants should be able to:
  - Complete this sentence: “The coolest findings related to peds ID published in the past year were...”
  - Determine which of these cool findings apply to their practice

# Question 1

The March 2017 *E. coli* O157:H7 outbreak was associated with what food?



## Multistate Outbreak of Shiga toxin-producing *Escherichia coli* O157:H7 Infections Linked to I.M. Healthy Brand SoyNut Butter (Final Update)



Posted May 4, 2017 11:45 AM EST

Although the outbreak investigation is over, illnesses may continue for some time. The recalled SoyNut Butter products have long shelf lives and may still be in people's homes or in institutions. People who don't know about the recalls could continue to eat the products and get sick. The recalled products are listed on the [Recalls & Advice to Consumers](#) page.

### Highlights

- Although the outbreak investigation is over, illnesses may continue for some time. The recalled SoyNut Butter products have long shelf lives and may still be in people's homes or in institutions. People who don't know about the recalls could continue to eat the products and get sick.
- Several products were recalled as a result of this investigation.
  - The recalled products are listed on the [Recalls & Advice to Consumers](#) page.
  - CDC recommends that consumers do not eat, and childcare centers, schools, and other institutions do not serve, any of the recalled products.
  - Even if some of the product was eaten or served and no one got sick, throw the rest of it away. Put it in a sealed bag in the trash so that children, pets, or other animals can't eat it.
- CDC, multiple states, and the U.S. [Food and Drug Administration](#) (FDA) investigated a multistate outbreak of Shiga toxin-producing *Escherichia coli* O157:H7 (STEC O157:H7) infections.
  - Thirty-two people infected with the outbreak strains of STEC O157:H7 were reported from 12 states.

### At A Glance

- Case Count: **32**
- States: **12**
- Deaths: **0**
- Hospitalizations: **12**
- Recall: **Yes**

### More Information

- [Recall and Advice to Consumers and Institutions](#)
- [Signs & Symptoms](#)
- [Key Resources](#)
- [Shiga Toxin-Producing \*E. coli\* and Food Safety](#)
- [Diaper-Changing Steps for Childcare Settings](#)



# Canadian Food Inspection Agency



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## Updated Food Recall Warning - I.M. Healthy brand SoyNut Butter products recalled due to *E. coli* O157:H7

<b>Recall date:</b>	March 10, 2017
<b>Reason for recall:</b>	Microbiological - <i>E. coli</i> O157:H7
<b>Hazard classification:</b>	Class 1
<b>Company / Firm:</b>	Directa Distribution, Healthy Planet Canada, Koyo Foods Inc., Tree of Life Canada
<b>Distribution:</b>	National
<b>Extent of the distribution:</b>	Retail
<b>Reference number:</b>	11254, 11255, 11273, 11274

# Question 2

What led to the pediatric zombie apocalypse during the summer of 2016?



# Question 2

Not to be confused with the zombie outbreak where 33 people were intoxicated with a synthetic cannabinoid and appeared like zombies



## ORIGINAL ARTICLE

### “Zombie” Outbreak Caused by the Synthetic Cannabinoid AMB-FUBINACA in New York

Axel J. Adams, B.S., Samuel D. Banister, Ph.D., Lisandro Irizarry, M.D., Jordan Trecki, Ph.D., Michael Schwartz, M.D., M.P.H., and Roy Gerona, Ph.D.

N Engl J Med 2017; 376:235-242 | [January 19, 2017](#) | DOI: 10.1056/NEJMoa1610300

# Pokemon Go → Zombies

**PLOS** | CURRENTS  
OUTBREAKS

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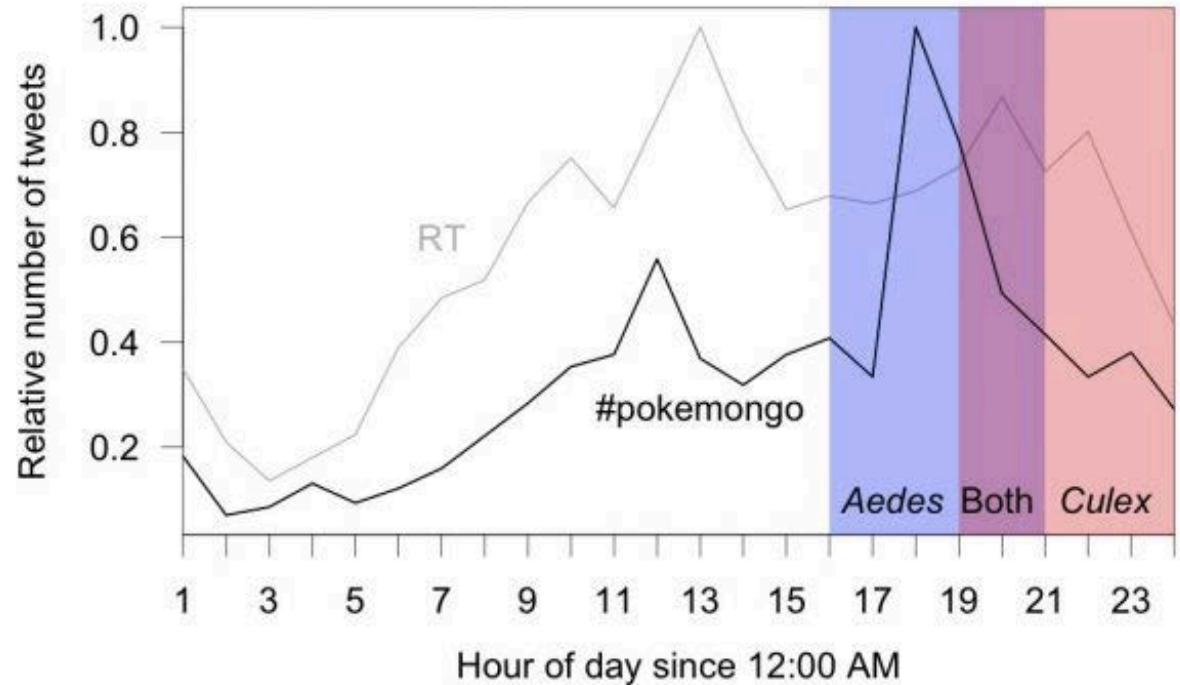
## Pokémon Go and Exposure to Mosquito-Borne Diseases: How Not to Catch 'Em All

NOVEMBER 15, 2016 · DISCUSSION

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**AUTHORS**

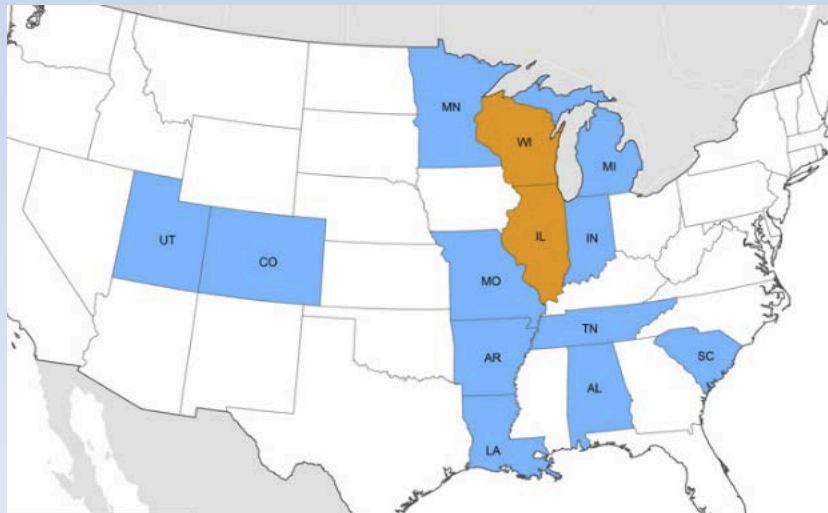
Rachel J. Oidtman | Rebecca C. Christofferson | Quirine A. ten Bosch | Guido Espana  
Moritz U. G. Kraemer | Andrew Tatem | Christopher M. Barker | T. Alex Perkins





# Question 3

- What's the connection?



# Multi-state Outbreak of Seoul Virus



Updated: April 25, 2017

## Highlights

CDC assisted health officials in investigating an outbreak of Seoul virus infection that has infected 17 people in 7 states. Investigations by CDC and partnering state and local health departments indicated that potentially infected rodents could have been distributed or received in Colorado, Delaware, Georgia, Illinois, Idaho, Iowa, Minnesota, Missouri, New Jersey, Pennsylvania, South Carolina, Tennessee, Utah, and Wisconsin.

The investigation included testing of rats and humans. In addition to testing provided by CDC for rats and people linked to ratteries with confirmed infections, commercial testing for rats was also available. In an initial evaluation, the test kits developed by the commercial laboratory IDEXX\* yielded test results with similar accuracy to those of the CDC test.

As part of a health monitoring program, rat owners and breeders may wish to seek proof of a rat's infection status prior to admitting new animals into existing colonies.

*\* Names of commercial companies are provided for information purposes only and do not constitute an endorsement by CDC or the Department of Health and Human Services.*

## At A Glance

Number of laboratory-confirmed recent human cases of Seoul virus: 17

Number of states reporting laboratory-confirmed Seoul virus positive results for humans or rats: 11:  
CO, GA, IA, IL, MN, MO, PA, SC, TN, UT, WI

## FAQs

[FAQs: Seoul virus](#)

## Resources

# Connection to Practice

## Statement

### Statement from Chief Medical Officer of Health on Seoul Virus Infection

March 1, 2017 3:00 P.M. | Ministry of Health and Long-Term Care

Today, Dr. David Williams, Ontario's Chief Medical Officer of Health, issued a statement following the identification of three human cases of Seoul virus infection linked to rat exposure in Ontario:

"The Ministry of Health and Long-Term Care, in collaboration with public and animal health partners at a variety of government levels, are investigating three human cases of Seoul virus infection in Ontario. All three individuals had prolonged contact with rats. No serious health outcomes have been reported for the cases.

The ministry and its partners are investigating the source of the illnesses including links to a multi-state investigation in the United States involving ratteries. As of February 24, 2017, the Center for Disease Control and Prevention is investigating a similar Seoul virus outbreak associated with rat exposure that involves 16 positive human cases and ratteries located in 15 states.

To date, laboratory testing of rats from some Ontario ratteries have identified positive results for Seoul virus. Further testing of rats is ongoing.

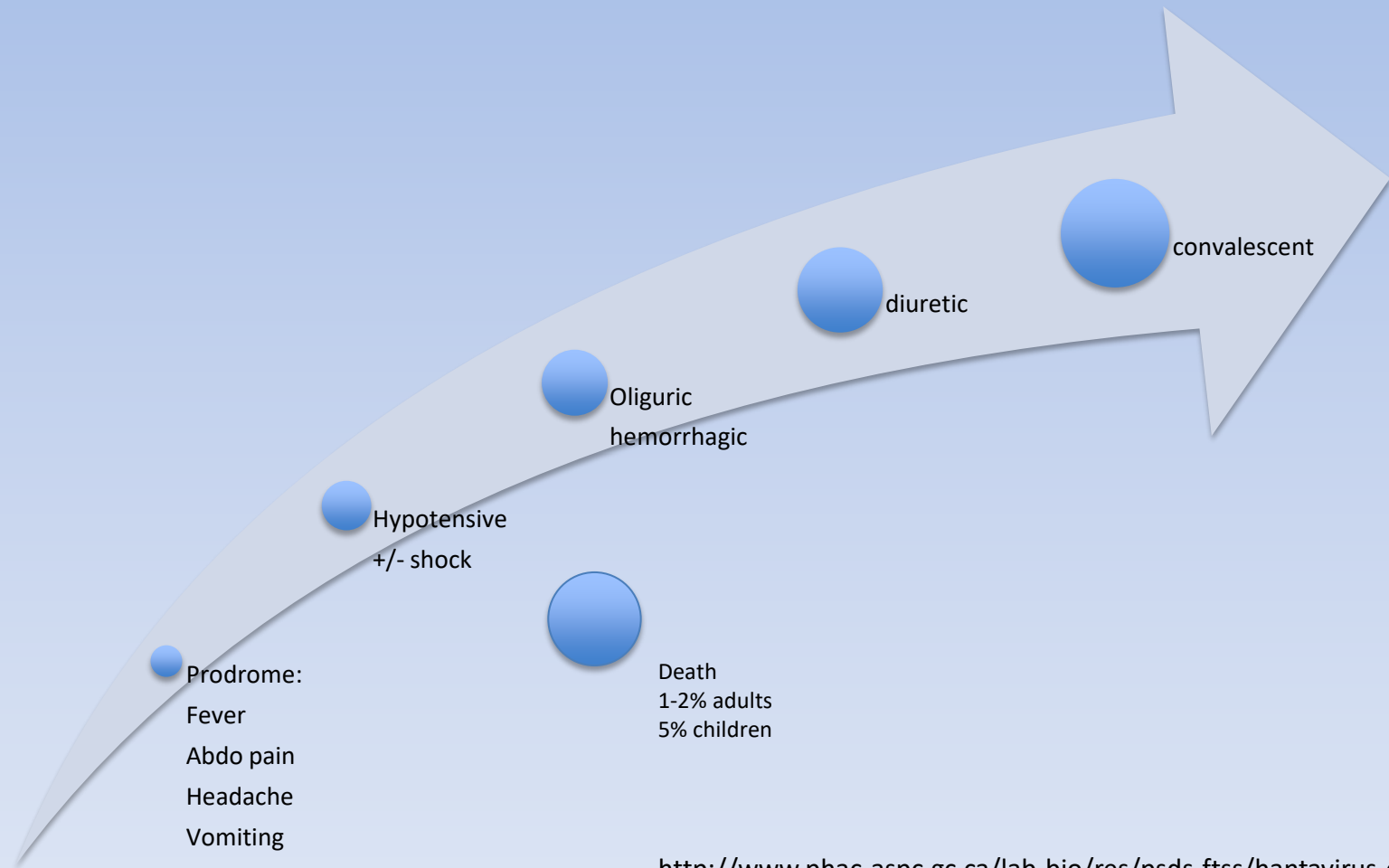
Seoul virus is a type of hantavirus that can be transmitted from rats to people through bite wounds or exposure to urine, feces, saliva or contaminated bedding.

The health risk to Ontarians is considered low and Seoul virus is not spread from person to person.

# Think about Seoul Virus if there is contacts with rats

- Contact with urine, droppings, saliva from infected rats
  - Inhalational
  - Via cuts/abrasions
  - Into mucous membranes
  - Bites
- Infected rats shed virus for their entire life but are asymptomatic

# Think about Seoul Virus if there are compatible symptoms



<http://www.phac-aspc.gc.ca/lab-bio/res/psds-ftss/hantavirus-eng.php>  
Yoo KH, Choi Y. Pediatr Nephrol. 1994 Oct;8(5):540-4.

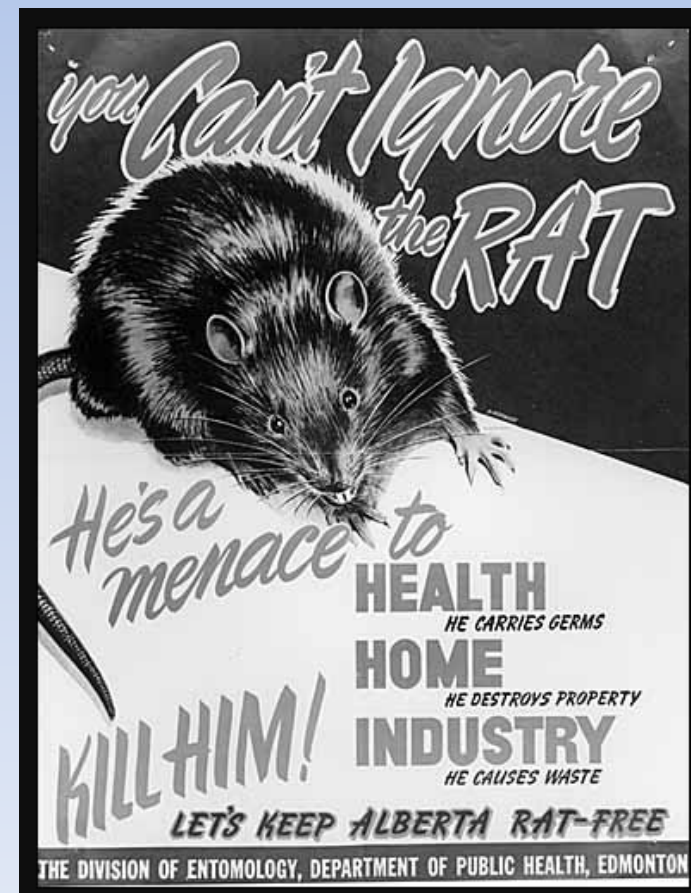
# Look for evidence of Seoul Virus

DISEASE PHASE	Incubation (2-4 weeks)	Prodrome (3-5 days)	Hypotensive (1-2 days)	Oliguric (3-5 days)	Diuretic (wks-months)	Convalescence (wks-months)	
CLINICAL FINDINGS		<ul style="list-style-type: none"> <li>Fever</li> <li>Malaise</li> <li>Myalgia</li> <li>Anorexia</li> <li>Headache</li> <li>Eye pain</li> <li>PUUV only</li> <li>Somnolence</li> <li>Dizziness</li> <li>Other CNS</li> <li>Sudden myopia</li> <li>Vision Loss</li> <li>Other ophthalmological</li> </ul>	<ul style="list-style-type: none"> <li>Thirst</li> <li>Restlessness</li> <li>Hypotension</li> <li>Narrow pulse pressure</li> <li>Tachycardia</li> <li>Cold skin</li> <li>Mental confusion</li> </ul>	<ul style="list-style-type: none"> <li>Oliguria</li> <li>Anuria</li> <li>Renal insufficiency</li> <li>Resolution of petechiae</li> <li>Resolution of flushing</li> <li>Hypertension or normotension</li> <li>Back pain</li> <li>Nausea/ vomiting</li> <li>Severe hemorrhage</li> <li>Pulmonary edema</li> </ul>	<ul style="list-style-type: none"> <li>Clinical improvement with the onset of diuresis</li> <li>Complications</li> <li>Hypotension</li> <li>Visceral hemorrhage</li> <li>Pulmonary symptoms</li> <li>CNS symptoms</li> </ul>	<ul style="list-style-type: none"> <li>Muscular weakness</li> <li>Lack of stamina</li> <li>Hypostenouria</li> <li>Polyuria</li> </ul>	
		<ul style="list-style-type: none"> <li>Petechiae</li> <li>Conjunctival injection</li> <li>Subconjunctival hemorrhage</li> <li>Other hemorrhage</li> </ul>	<ul style="list-style-type: none"> <li>Flushing of face/torso</li> <li>Abdominal pains</li> <li>nausea/vomiting</li> </ul>				
LABORATORY FINDINGS	Hantavirus RT-PCR	Anti-hantavirus IgM and IgG antibodies				Anti-hantavirus IgG Abs	
		<ul style="list-style-type: none"> <li>Thrombocytopenia</li> <li>Leukocytosis</li> <li>Elevated CRP</li> <li>Proteinuria</li> <li>Hematuria</li> </ul>	<ul style="list-style-type: none"> <li>Elevated aPTT</li> <li>Elevated PT</li> <li>Increased AST</li> <li>Hypoalbuminemia</li> </ul>	<ul style="list-style-type: none"> <li>Elevated CK</li> <li>Elevated uric acid</li> <li>Decreased magnesium</li> <li>Decreased corrected serum calcium</li> </ul>	<ul style="list-style-type: none"> <li>Electrolyte abnormalities</li> </ul>		
IMAGING FINDINGS		<ul style="list-style-type: none"> <li>Renal U/S</li> <li>Decreased cortico-medullary differentiation</li> <li>Parenchymal edema/ increased echogenicity</li> <li>Sinus narrowing</li> <li>Enlargement</li> </ul>	<ul style="list-style-type: none"> <li>Other U/S</li> <li>Ascites</li> <li>Pleural effusion</li> <li>Increased gall bladder wall thickness</li> <li>Hepatosplenomegaly</li> <li>Pancreatic edema</li> </ul>	<ul style="list-style-type: none"> <li>Pulmonary HRCT</li> <li>Atelectasis</li> <li>Pleural effusion</li> <li>Intralobular+ interlobular septal thickening (esp in the lower lungs)</li> <li>Ground glass opacity</li> <li>Hilar+ mediastinal lymphadenopathy</li> </ul>			
			<ul style="list-style-type: none"> <li>Chest X-ray</li> <li>Atelectasis</li> <li>Pleural effusion</li> <li>Frank pulmonary edema</li> </ul>				

Figure 1. Clinical course of HFRS and findings by disease phase (Lednicky, 2003; Bi et al., 2008; Kanerva et al., 1996; Paakkala et al., 2011; Brorstad et al., 2010; Kim et al., 2007). Puumala virus (PUUV), central nervous system (CNS), antibodies (Abs), c-reactive protein (CRP), activated partial thromboplastin time (aPTT), prothrombin time (PT), aspartate transaminase (AST), creatine kinase (CK), ultrasound (U/S), high resolution computed tomography (HRCT).

Unless you live in Alberta...

Question 4 – Will Seoul Virus be seen  
in Alberta?



<http://www.archivesalberta.org/odd/rat.jpg>



## Calgarians with pet rats face potential \$5,000 fines in rat-free Alberta

CALGARY — The Canadian Press

Published Monday, Feb. 27, 2012 5:51PM EST

Last updated Thursday, Sep. 06, 2012 11:47AM EDT



Phil Merrill, a Rat and Pest Specialist with Alberta Agriculture, on a farm near Oyen, Alberta on October 06, 2015.

(Chris Bolin for The Globe and Mail)

## On the frontlines of Alberta's war against rats

**JUSTIN GIOVANNETTI**

ALSASK, SASK. — The Globe and Mail

Published Thursday, Nov. 26, 2015 8:23PM EST

Last updated Friday, Nov. 27, 2015 12:56AM EDT

“Some in Alberta question whether the province is truly rat-free. Mr. Merrill explains that what the status means is that the province has no breeding rat population. Hundreds of rats do come into Alberta on commercial trucks from the U.S. and other provinces, but they’re always alone and die alone.” Alberta’s war on rats started in 1950 when the rodents were first found in the border hamlet of Alsask, Sask. With the Rockies to the west, badlands to the south and vast forests to the north, Alberta had never had rats. But after two centuries of slow progress west from the port cities of the East Coast, rats had finally arrived at Alberta’s doorstep. With a post-Second World War government that wielded significant resources, understood agriculture and feared the damage that rats could do to crops and buildings, the Alberta government created the rat patrol.”

Globe and Mail article549545

Globe and Mail article27504057

## Question 5

What is SSPE and how commonly is it seen?

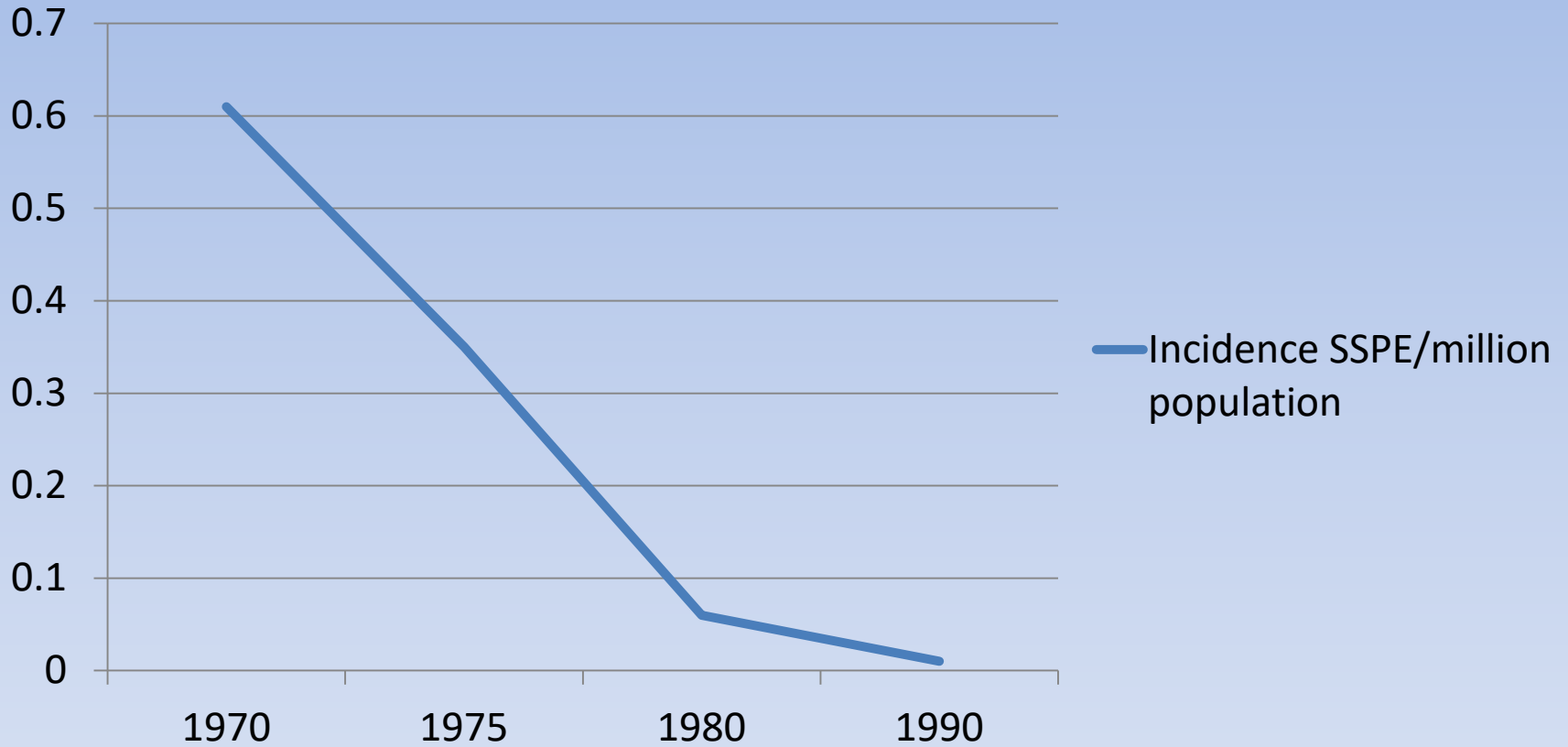
# SSPE

- Fatal, progressive degenerative disease of the central nervous system that usually occurs 7 to 12 years after natural measles virus infection
- US: 4-5 cases/year
- India: >20 million cases/year

- Redd SC, et al. Measles vaccine. In: Plotkin SA, Orenstein WA. (eds). Vaccines. 3rd ed. Toronto: W.B. Saunders Company, 1999:222-66.
- Subacute Sclerosing Panencephalitis Surveillance – United States. MMWR Weekly 1982;31(43):585-8.
- Campbell C, et al. BMC Pediatr. 2005;5:47.
- Singer C, Lang AE, Suchowersky O. *Mov Disord* 1997; **12**: 342–53.




## Incidence SSPE/million population



- Subacute Sclerosing Panencephalitis Surveillance – United States. MMWR Weekly 1982;31(43):585-8.

- Campbell C, et al. BMC Pediatr. 2005;5:47.



# SSPE may be more common than we thought

- SSPE cases 1998-2016 (in California)
- 17 cases
- 12 (71%) cases had a measles-like illness <15 months of age and measles vaccination
- SSPE diagnosed at 12y (median) (3-35 years)
- Latency = 9.5 years (range 2.5-34 years).

# SSPE relevance to practice

- Many had long-standing cognitive or motor problems prior to diagnosis
- Think about SSPE in patients with compatible symptoms, even in older patients with no specific history of measles infection
- Advocate for vaccines - SSPE demonstrates the high human cost of “natural” measles immunity

# SSPE relevance to practice: Use the CPSP Case Definition

**Table 1: Case Definition.**

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**Definite Case**

A. High titres of serum antibodies against measles virus and the presence of oligoclonal measles virus antibodies in CSF (Serum: CSF measles antibody ratio indicative of intrathecal antibody production).

And/or

B. Measles virus antigen detected in brain tissue by biopsy or at autopsy

**Suspect Case**

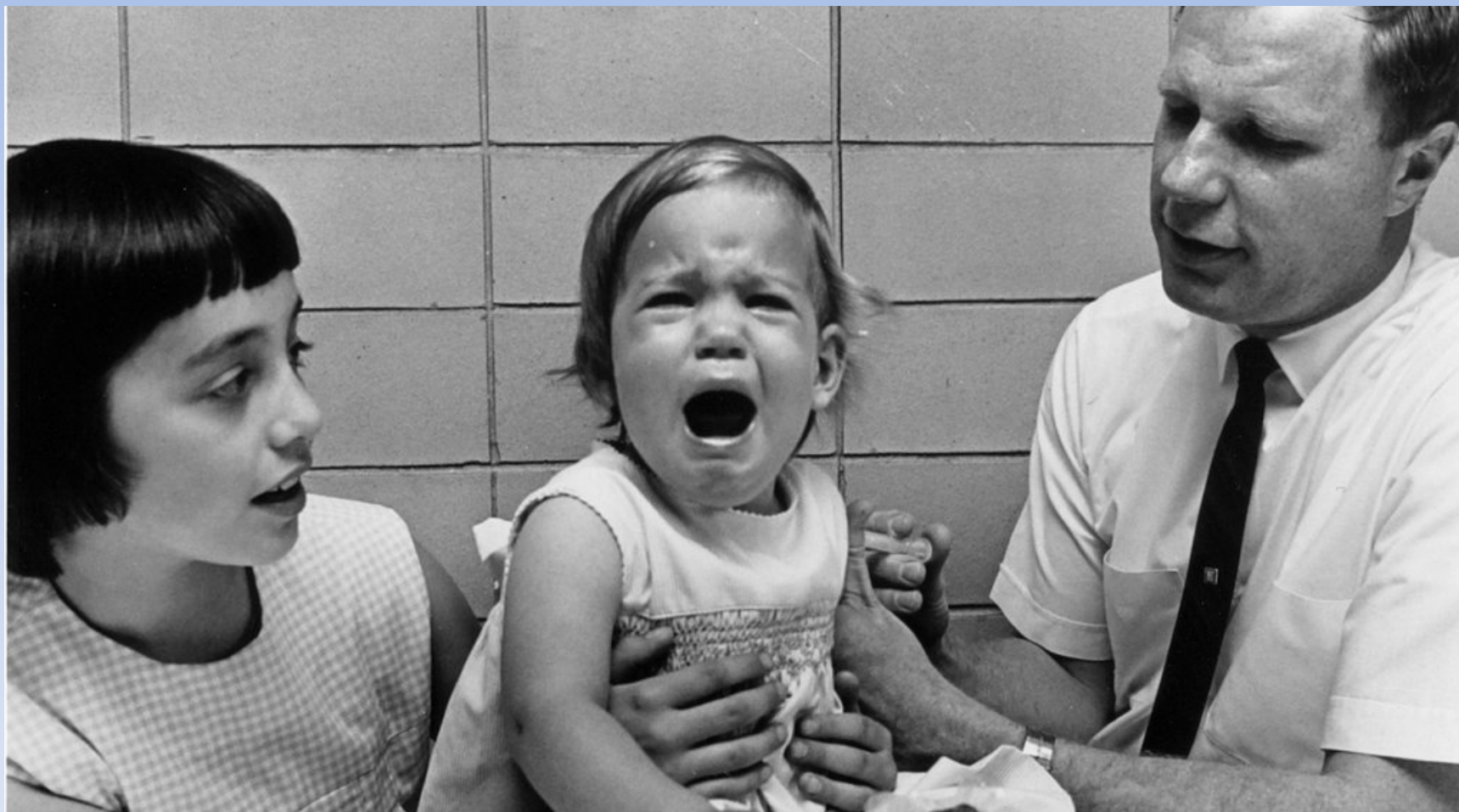
A. Typical clinical history: usually insidious onset of mental deterioration, followed (usually within a few months) by motor dysfunction, final progressive decerebration and untimely death

And

B. Typical EEG changes

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Question 6: Who are these people (and what's the connection to recent outbreaks)?





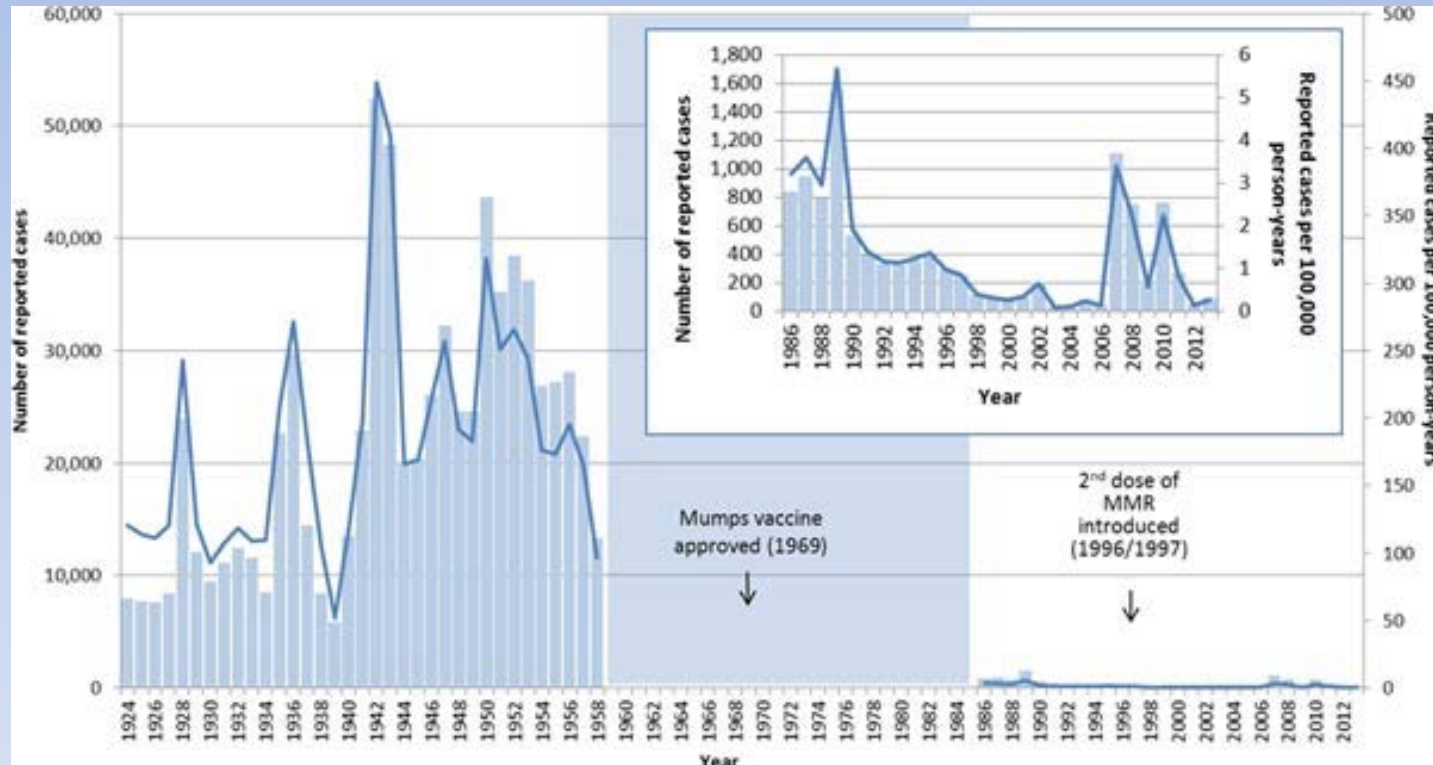
- Original mumps virus for the vaccine in North America was from Jeryl Lynn (on the left).
- In 1963 her father made the diagnosis, and swabbed her throat. He propagated the virus in the lab and the attenuated strain was used in the mumps vaccine.
- He tested it out on his younger daughter Kirsten (center) in 1966.
- 1967 the vaccine was used more widely.
- Maurice Hilleman developed or improved 40 vaccines – including 9/14 of the ones used for children today.
- There are now known to be 2 attenuated mumps strains (JL1 and JL2) depending on what cell lines the virus is propagated through.




“All I did, was get sick at the right time,  
with the right virus, with the right father.”

# Mumps (Canada)

Started to see mumps outbreaks late 80/s-early 90's and 2<sup>nd</sup> dose of MMR reduced this.  
But now we are seeing similar outbreaks ~10 years after 2<sup>nd</sup> dose of MMR.



Removed from Notifiable  
Disease List 1959-1986.



# Why?

1. 'Herd' immunity threshold higher in crowded settings
2. Improper storage of vaccine
3. Primary vaccine failure (78%,88%)
4. Secondary vaccine failure
5. Genetic drift

- Offitt P: [www.scientificamerican.com/article/whats-behind-the-2016-mumps-spike-in-the-u-s/](http://www.scientificamerican.com/article/whats-behind-the-2016-mumps-spike-in-the-u-s/)  
- Rota JS, et al. Clin Vaccine Immunol, 2013;20:391-396.  
- Cortese MM, et al. Clin Infect Dis, 2008;46:1172-1180.  
- Rubin S, et al. Pediatr Infect Dis J, 2016;35(7):799-801.

# Secondary Vaccine Failure

- Numerous studies have shown time after vaccination (>10 years) with declining levels of mumps virus-specific Ab and increased risk of contracting the disease

Weibel RE, et al. N Engl J Med, 1967;276:245-251.

Rota JS, et al. Clin Vaccine Immunol, 2013;20:391-396.

Cortese MM, et al. Clin Infect Dis, 2008;46:1172-1180.

Rubin S, et al. Pediatr Infect Dis J, 2016;35(7):799-801.

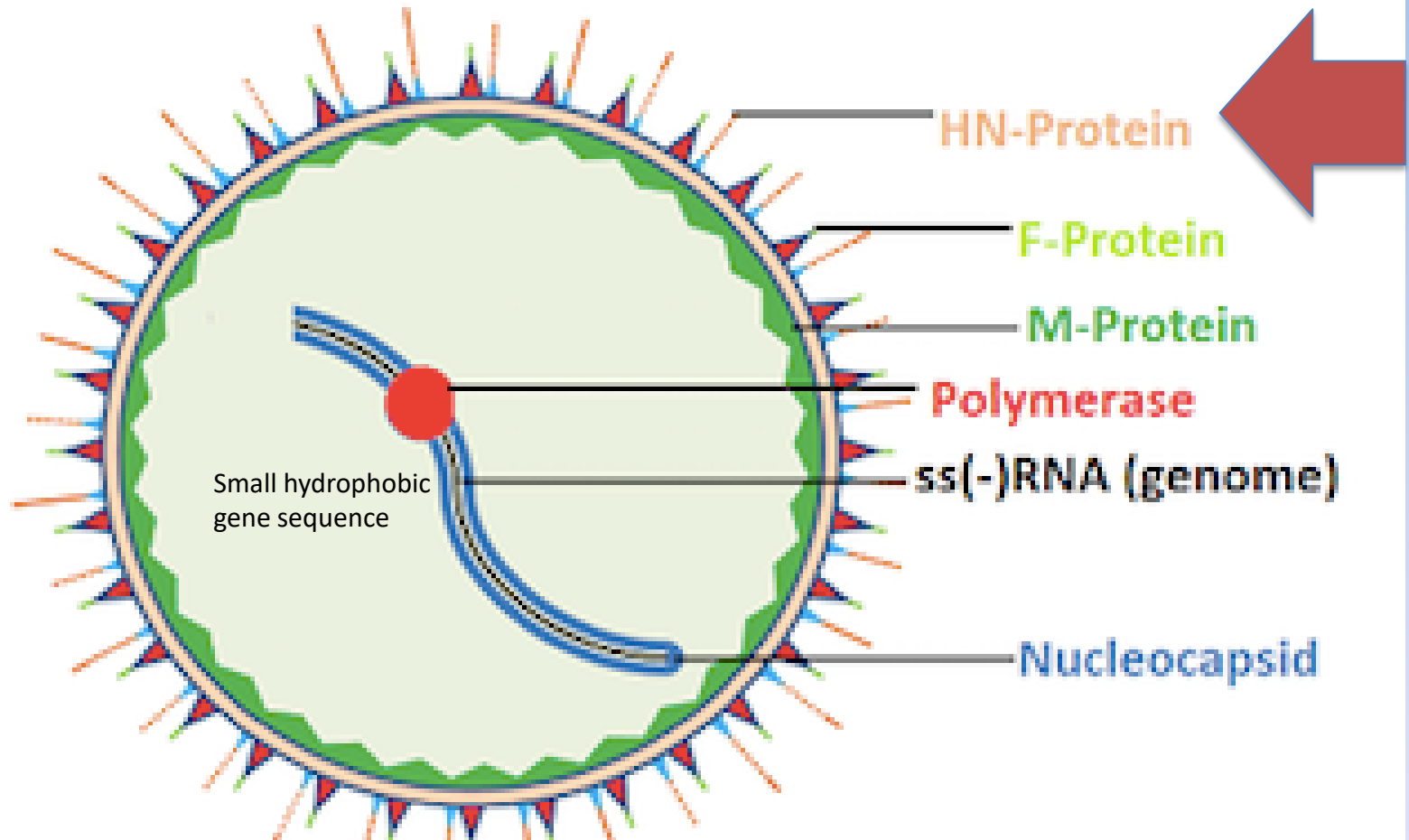
# Secondary Vaccine Failure

- Measles and rubella is rare after 2 doses of vaccine
- With mumps: quantitative (less virus specific memory B cells) and qualitative (lower avidity Ab) differences in response
  - A significant proportion of breakthrough cases after 2 doses of vaccine show both IgM and higher avidity IgG showing a response to previous vaccine that was not sufficient to prevent reinfection

# Genetic Drift

- Recent outbreaks are different genotypes from the vaccine strain
  - JL strain = genotype A
  - Outbreaks = genotypes B, C, D, G, H, I
  - 6% variation between 12 mumps genotypes

# Genetic Drift





# Genetic Drift

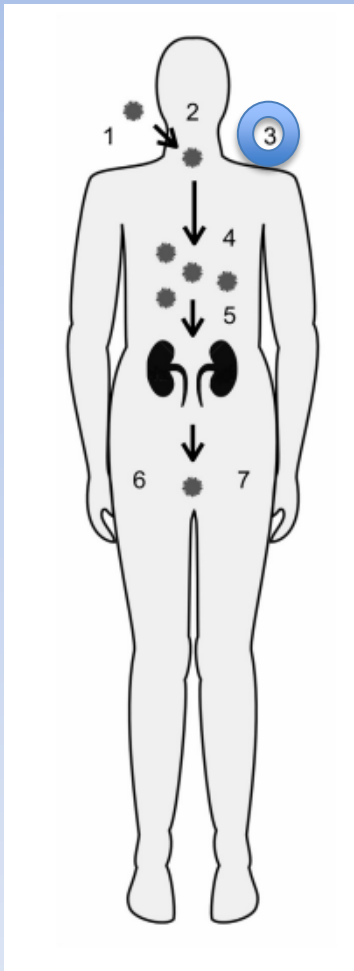
- Sera collected shortly after vaccination has been shown to neutralize a vast array of genetically disparate strains
- But if people respond to vaccination with only nominal levels of neutralizing antibody, or if antibodies have waned, some theorize that the mismatch may facilitate immune escape



# Recent Mumps Outbreaks

- Silver lining?
  - 1-15% of people with mumps develop encephalitis
  - 30% of males develop orchitis
- 2016 outbreaks: “We have not seen these complications in the 5600 cases last year, so it seems that there is some protection from serious sequelae”

# Severity of mumps and vaccinations



1. Viral Entry
2. Replication in upper respiratory tract
3. Parotitis
4. Systemic infection
5. Infection of the organs
6. Viruria
7. Orchitis/oophoritis

= Salivary loads

- Bilateral parotitis, viruria and orchitis significantly higher in unvaccinated

Salivary viral loads did not differ between twice vaccinated and unvaccinated people (n=1112). But bilateral parotitis, viruria and orchitis did. SO the risk for a systemic mumps infection is reduced with vaccination.  $P < 0.005$ .

Gouma S, et al. *Vaccine* 2016;34:1868-1873.



# Implications for practice

- Mumps outbreaks are seen even with 2 doses of vaccine – so remain suspicious especially in older teens and young adults (even with unilateral parotitis)
- Diagnosing mumps after vaccination is difficult with serology (low rates of IgM positivity) so send buccal swab for PCR

In unvaccinated people IgM is positive 5 days after illness onset and peaks 7 days post onset.  
In vaccinated there may be no IgM response or it may be transient (5% sensitivity).  
PCR 68% sensitivity – higher sensitivity closer to symptom onset.

# Question 7

What's the connection between asthma and the microbiome?

# Asthma NEJM

- [NEJM Quick Take Video Summary](#)

# Implications for Practice

- Videos are great teaching tools
- Eat dirt and have pet cows...

# New Guidelines

McCrindle BW, et al. Diagnosis, Treatment, and Long-Term Management of Kawasaki Disease: A Scientific Statement for Health Professionals From the American Heart Association. *Circulation*. 2017 Apr 25;135(17):e927-e999.

Tunkel AR et al. 2017 Infectious Diseases Society of America's Clinical Practice Guidelines for Healthcare-Associated Ventriculitis and Meningitis. *Clin Infect Dis* 2017; 64 (6): e34-e65.

Lewinsohn DM, et al. Official American Thoracic Society/Infectious Diseases Society of America/Centers for Disease Control and Prevention Clinical Practice Guidelines: Diagnosis of Tuberculosis in Adults and Children. *Clin Infect Dis* 2017; 64 (2): 111-115.



# So hopefully you can complete the following sentence:

- “The coolest findings related to peds ID published in the past year were...”
  - *E. coli* and soy nut butter
  - Pokemon GO has infection risks
  - Seoul Virus is in Canada (except Alberta)
  - SSPE is more common than we thought
  - Mumps outbreaks are likely due to waning immunity
  - Asthma and the microbiome are linked

- And it's up to you which of these you will use in your practice

# Thanks and Go Oilers!

