You know something’s happening, but you don’t know what it is, do you, Mr. Jones?
—BOB DYLAN

Ballad of a thin man
General patterns of infection

- **Acute**
  - Rhinovirus
  - Rotavirus
  - Influenza virus

- **Latent**
  - Herpes simplex virus

- **Persistent: asymptomatic**
  - Lymphocytic choriomeningitis virus
  - JC virus

- **Persistent: pathogenic**
  - Human immunodeficiency virus
  - Human T-lymphotropic virus
  - Measles virus SSPE
Acute infections

- Rapid onset of viral reproduction
- Short but possibly severe course of disease
- Production of large numbers of virus particles
- Immune clearance
The course of a typical acute infection

Rapid and self-limiting

- Virus growth
- Establishment of infection
- Innate defenses
- Induction of adaptive response
- Adaptive response
- Memory

Threshold level of virus required to activate adaptive immune response

Entry of virus

Duration of infection

Virus cleared

Principles of Virology, ASM Press
Incubation period

- Initial period before symptoms of disease are obvious
- Viral genomes are replicating
- Host is responding
- Virus may or may not be transmitted
Incubation periods of some viral infections

<table>
<thead>
<tr>
<th>Disease</th>
<th>Incubation period (days)¹</th>
</tr>
</thead>
<tbody>
<tr>
<td>Influenza virus</td>
<td>1–2</td>
</tr>
<tr>
<td>Rhinovirus</td>
<td>1–3</td>
</tr>
<tr>
<td>Ebola virus</td>
<td>2–21</td>
</tr>
<tr>
<td>Acute respiratory disease (adenoviruses)</td>
<td>5–7</td>
</tr>
<tr>
<td>Dengue</td>
<td>5–8</td>
</tr>
<tr>
<td>Herpes simplex</td>
<td>5–8</td>
</tr>
<tr>
<td>Coxsackie virus</td>
<td>6–12</td>
</tr>
<tr>
<td>Poliovirus</td>
<td>5–20</td>
</tr>
<tr>
<td>Human immunodeficiency virus</td>
<td>8–21</td>
</tr>
<tr>
<td>Measles</td>
<td>9–12</td>
</tr>
<tr>
<td>Smallpox</td>
<td>12–14</td>
</tr>
<tr>
<td>Varicella-zoster virus</td>
<td>13–17</td>
</tr>
<tr>
<td>Mumps</td>
<td>16–20</td>
</tr>
<tr>
<td>Rubella</td>
<td>17–20</td>
</tr>
<tr>
<td>Epstein-Barr virus</td>
<td>30–50</td>
</tr>
<tr>
<td>Hepatitis A</td>
<td>15–40</td>
</tr>
<tr>
<td>Hepatitis B and C</td>
<td>50–150</td>
</tr>
<tr>
<td>Rabies</td>
<td>30–100</td>
</tr>
<tr>
<td>Papilloma (warts)</td>
<td>50–150</td>
</tr>
</tbody>
</table>

¹Until first appearance of prodromal symptoms.
Inapparent acute infections

- Successful infections, no symptoms or disease
- Sufficient virus particles produced to spread in the population
- How do we know?
- Well adapted pathogens
  - >90% of poliovirus infections inapparent
Acute infections are common public health problems

- Serious epidemics affecting millions each year (influenza, norovirus, Zika virus)
- Acute infection are difficult problems: by the time you feel ill, the infection may be over and has spread
Which of the following do acute infections and incubation periods have in common?

1. The virus is not replicating
2. No symptoms are visible
3. Immune defenses are engaged
4. The immune system does not respond
5. All of the above
Viruses that cause acute infections

- Influenza virus
- Poliovirus
- Measles virus
- Rotavirus
- Norovirus
- West Nile virus
Influenza

• Types: A, B, C

• A, B cause similar disease; C mostly inapparent or mild upper respiratory tract illness

• Only A cause pandemics

• Antigenic variation

Influenza transmission

- Droplets produced by coughing, sneezing, talking
- Direct contact with infected individuals
- Contact with contaminated surface, touch mouth, eyes, nose

Uncomplicated influenza

- Incubation period 1-5 days, depending on dose, immune status of host
- Abrupt onset: headache, chills, dry cough
- High fever, myalgias, malaise, anorexia
- Fever peaks within 24 hr, 38° - 40°C
- Fever declines day 2-3, gone by day 6
- Symptoms may differ in children, elderly
Uncomplicated influenza

- As fever declines, respiratory signs intensify
- Cough changes from dry to productive
- Cough, weakness can persist 1-2 weeks
- Virus replicates throughout the tract, depending on sialic acid receptors for strain
How is influenza diagnosed?

- Influenza-like illness, ILI
- Fever at least 100°F
- Cough OR sore throat
- No other known cause
- Rapid lab tests: poor accuracy
- PCR, viral culture, serology
Seasonal influenza

U.S. WHO/NREVSS Collaborating Laboratories National Summary, 2004-05 through 2007-08

http://www.cdc.gov/flu/weekly/fluactivitysurv.htm
Influenza Positive Tests Reported to CDC by U.S. Public Health Laboratories, National Summary, 2015-2016 Season

http://www.cdc.gov/flu/weekly/
Pneumonia and Influenza Mortality for 122 U.S. Cities
Week Ending March 19, 2016

http://www.cdc.gov/flu/weekly/
Influenza statistics, US

- 35-50 million cases (CDC estimate)
- 3,000 - 49,000 deaths (range past 31 yr)
Complications of influenza

- Primary viral pneumonia
- Secondary bacterial pneumonia
- Myositis - generalized muscle pain
- Cardiac involvement
- Reye syndrome
Interventions for influenza

- Non-pharmaceutical
- Antiviral drugs
  - Tamiflu (oseltamivir)
  - Relenza (zanamavir)
  - Flumadine (rimantadine)
- Vaccine
Which of the following is characteristic of uncomplicated influenza?

1. Transmission may occur via respiratory droplets
2. Incubation period is 1-5 days
3. Fever peaks within 24 hr
4. Coughing and weakness can last for 2 weeks
5. All of the above
Poliomyelitis - poliovirus
Poliovirus pathogenesis
Pathogenesis of poliomyelitis

- Humans are only known reservoir
- Spread by fecal-oral transmission
- Peaks during warm months in temperate climates
- Complication: post-polio syndrome
  - 30-40 year interval
  - 25-40%
  - Not an infectious process
Poliomyelitis—United States, 1950-2007

Cases

Inactivated vaccine

Live oral vaccine

Last indigenous case
Measles

- Measles virus, *Paramyxoviridae*
- One of the most contagious human viruses ($R_0 = 15$)
- Population between 300,000 - 500,000 required to maintain virus
Measles pathogenesis

• One viral serotype, infection confers life-long protection
• Transmitted by inhalation of respiratory secretions
• Period of maximum contagiousness 2-3 days before rash
• Nearly all infected individuals show signs of disease
Uncomplicated measles

- Fever, 38.3°C or above
- Respiratory symptoms: coryza, cough
- Conjunctivitis
- Koplik spots
- Rash from face to extremities
Measles complications

- Acute postinfectious encephalitis (1/1,000)
- Bronchitis, pneumonia, ear infection
- Fatality 1-2/1000 (28% poor nutrition)
- Subacute sclerosing panencephalitis (SSPE)
- Immunosuppression leading to secondary infections (main cause of death in Third World children)
Measles prevention

- US: 3-4 million/yr, 400-500 deaths, 48,000 hospitalizations, 1,000 chronic disability from encephalitis
- Endemic transmission stopped 2000 by vaccine
- MMR: measles, mumps, rubella vaccine
- Wakefield 1998 report lead to decreased MMR immunization, outbreaks in UK, Ireland
- US outbreaks, imported
vaccine licensed
Measles Cases and Outbreaks
January 1 to March 20, 2015*

178 Cases reported in 17 states and the District of Columbia: Arizona, California, Colorado, Delaware, Georgia, Illinois, Michigan, Minnesota, Nebraska, New Jersey, New York, Nevada, Pennsylvania, South Dakota, Texas, Utah, Washington

4 Outbreaks representing 89% of reported cases this year

U.S. Measles Cases by Year

*Provisional data reported to CDC’s National Center for Immunization and Respiratory Diseases
Number of Reported Measles Cases with onset date from Aug 2015 to Jan 2016 (6M period)

Data source: surveillance DEF file
Data in HQ as of 7 March 2016

The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted lines on maps represent approximate border lines for which there may not be full agreement. ©WHO 2016. All rights reserved.
Which of the following is a good reason to get measles vaccine?

1. There is a 1/1000 chance of acute post-infection encephalitis
2. There is a 1-2/1000 chance of death from measles
3. Each infected person spreads measles virus to 15 others
4. Immunosuppression can lead to secondary infections
5. All of the above
In a 24 hour period...

- About 200,000,000 people have gastroenteritis
- The amount of diarrheal water passed equals the volume of water passing over Victoria Falls in 1 minute

65,280,000 liters/min
Norovirus

- *Caliciviridae*
- (+) strand RNA virus
- Cause 50% of all food-borne outbreaks of gastroenteritis (23 million/yr US)
Known Causes of Foodborne Illness Outbreaks, U.S., 2006–2010

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>Estimated number of illnesses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Norovirus</td>
<td>5,461,731</td>
</tr>
<tr>
<td><em>Salmonella</em>, nontyphoidal</td>
<td>1,027,561</td>
</tr>
<tr>
<td><em>Clostridium perfringens</em></td>
<td>965,958</td>
</tr>
<tr>
<td><em>Campylobacter</em> spp.</td>
<td>845,024</td>
</tr>
<tr>
<td><em>Staphylococcus</em> aureus</td>
<td>241,148</td>
</tr>
<tr>
<td><strong>Subtotal</strong></td>
<td></td>
</tr>
</tbody>
</table>
• Fecal-oral spread
• Retain infectivity passing through stomach
• Blunting of villi in proximal jejunum
• Basis for vomiting, diarrhea not known
Enteric bacteria promote human and mouse norovirus infection of B cells
Clinical and epidemiological features

- Affects all ages
- Year round, peaks in cold weather
- Outbreaks often occur in semi-closed environments (nursing homes, hospitals, cruise ships), military, schools, recreational activities (sports events, camping trips, travel) that favor person-to-person spread
Clinical and epidemiological features

• Incubation period 10-51 hr
• Symptoms: Sudden onset of vomiting (more common in children), diarrhea (more common in adults), stomach pain
• Duration of illness: 28-60 hr; longer in immunocompromised or with underlying illness
• 30% asymptomatic infections
How contagious is norovirus?

Just a very small amount - as few as 18 viral particles - of norovirus on your food or your hands can make you sick.

That means the amount of virus particles that fit on the head of a pin would be enough to infect more than 1,000 people!

SOURCE: Journal of Medical Virology, August, 2008
Clinical and epidemiological features

- Viral shedding peaks 1-3 days after illness onset, may persist for 56 days

- Transmission: Fecal–oral; aerosol–vomitus; contact with fomites; food, water, or environmental contamination; foods can be contaminated at the source (oysters, raspberries) or during preparation by food handlers

- Immunity: short term homologous only; reinfection with other strains may occur, or later in life
Clinical and epidemiological features

• Treatment: Supportive to prevent dehydration
• Reservoir: Humans, but evidence for animal reservoir
• Vaccine in early development
• Not usually serious, but can be in persons with underlying illness
Real life ‘Airplane!’ Entire flight sickened by norovirus

Wednesday, December 28, 2011

Holiday travel can not only be a hassle but can you get sick – and in a recent case among Air New Zealand crew members, seriously ill. According to a report last week in Scientific American, recent studies have shown just how easily the cruise ship gastrointestinal bug, norovirus, can be transmitted to travelers on planes.

On a recent Air New Zealand flight, a sick passenger passed norovirus along to the crew. "Not only did the crew that cleaned up the mess get sick, but on every successive flight at least one or more crew members got sick with typical symptoms of norovirus," said David Freedman, of the University of Alabama at Birmingham, at a meeting of the American Society of Tropical Medicine and Hygiene held earlier this month.
<table>
<thead>
<tr>
<th>Cruise Line</th>
<th>Cruise Ship</th>
<th>Sailing Dates</th>
<th>Causative Agent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Crystal Cruises</td>
<td>Crystal Symphony</td>
<td>11/02 - 11/21</td>
<td>Unknown</td>
</tr>
<tr>
<td>Holland America Line</td>
<td>Nieuw Amsterdam</td>
<td>10/18 - 11/07</td>
<td>Norovirus</td>
</tr>
<tr>
<td>Carnival Cruise Lines</td>
<td>Carnival Glory</td>
<td>10/09 - 10/16</td>
<td>Norovirus</td>
</tr>
<tr>
<td>Holland America Line</td>
<td>Zuiderdam</td>
<td>04/20 - 05/08</td>
<td>Unknown</td>
</tr>
<tr>
<td>Celebrity Cruises</td>
<td>Mercury</td>
<td>03/08 - 03/19</td>
<td>Norovirus</td>
</tr>
<tr>
<td>Celebrity Cruises</td>
<td>Mercury</td>
<td>02/26 - 03/08</td>
<td>Norovirus</td>
</tr>
<tr>
<td>Royal Caribbean International</td>
<td>Jewel of the Seas</td>
<td>02/22 - 03/05</td>
<td>Unknown</td>
</tr>
<tr>
<td>Celebrity Cruises</td>
<td>Millennium</td>
<td>02/22 - 03/05</td>
<td>Norovirus</td>
</tr>
<tr>
<td>Holland America Line</td>
<td>Maasdam</td>
<td>02/19 - 03/05</td>
<td>Norovirus</td>
</tr>
<tr>
<td>Celebrity Cruises</td>
<td>Mercury</td>
<td>02/15 - 02/26</td>
<td>Norovirus</td>
</tr>
<tr>
<td>Fred Olsen Cruise Lines</td>
<td>Balmoral</td>
<td>01/05 - 02/04</td>
<td>Unknown</td>
</tr>
<tr>
<td>Cunard Cruise Line</td>
<td>Queen Victoria</td>
<td>01/12 - 01/27</td>
<td>Unknown</td>
</tr>
<tr>
<td>Cunard Cruise Line</td>
<td>Queen Victoria</td>
<td>01/04 - 01/12</td>
<td>Norovirus</td>
</tr>
</tbody>
</table>
Why are noroviruses associated with cruise ships?

- Health officials track illness on cruise ships, so outbreaks are found and reported more quickly on a cruise ship than on land.
- Close living quarters may increase the amount of group contact.
- New passenger arrivals may bring the virus to other passengers and crew.
Protect Yourself from Norovirus!

- Wash your hands often
- Rinse fruits & vegetables
- Cook shellfish thoroughly
- Clean surfaces & wash laundry
- When you're sick, don't prepare food or care for others

Share this widget | More info
www.cdc.gov/Norovirus
Go to:

m.socrative.com
room number: virus

Norovirus transmission could be curbed by:

1. Covering your mouth when you sneeze
2. Washing your hands after using the bathroom
3. Using condoms during sex
4. Using mosquito-proof nets
5. None of the above
"We're pretty sure it's the West Nile Virus."
West Nile virus

- *Flaviridae*, isolated 1937, West Nile district of Uganda
- Absent from Western Hemisphere until 1999
- New York isolate identical to virus from Israeli goose
- Virus infects hundreds of birds, 37 kinds of mosquitoes, 18 other vertebrates
West Nile virus

[Diagram showing the structure of West Nile virus with labels for Membrane protein (M), Envelope (E) dimer, RNA, and Capsid (C).]
WNV transmission cycle

Birds
Culex mosquito
Primary transmission cycle
Incidental host
Horse
Human
WNV pathogenesis

- Transmitted to humans by *Culex* bite
- Incubation period 3-14 days
- 20-30% develop flu-like illness called WNV fever
- 80%: no symptoms
WNV pathogenesis

- 1/150 individuals develop neuroinvasive disease
  - Headache
  - Ocular manifestations
  - Muscle weakness
  - Cognitive impairment
  - Polio-like flaccid paralysis
  - 10% mortality
  - >50% long term neurological sequelae
West Nile Virus USA

![Graph showing the number of West Nile Virus cases in the USA from 1999 to 2013. The graph includes a table with the number of neuroinvasive disease cases, non-neuroinvasive disease cases, total cases, and deaths for each year.]
West Nile virus activity, 2012

5,387 cases
2,734 neuroinvasive
243 deaths

http://www.cdc.gov/ncidod/dvbid/westnile/
Average annual incidence of West Nile virus neuroinvasive disease reported to CDC by age group, 1999-2014

Source: ArboNET, Arboviral Diseases Branch, Centers for Disease Control and Prevention
West Nile virus disease cases reported to CDC by week of illness onset, 1999-2014

Source: ArboNET, Arboviral Diseases Branch, Centers for Disease Control and Prevention
WNV prevention