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 infection**
  - Rhinovirus
  - Rotavirus
  - Influenza virus

- **Persistent infection, smoldering**
  - Lymphocytic choriomeningitis virus

- **Persistent infection, latent**
  - Herpes simplex virus

- **Persistent infection, slow**
  - Measles virus SSPE
  - Human immunodeficiency virus
  - Human T-lymphotropic virus
The course of a typical acute infection

Virus growth

Establishment of infection

Induction of adaptive response

Adaptive response

Memory

Threshold level of virus required to activate adaptive immune response

Duration of infection

Entry of virus

Virus cleared

Principles of Virology, ASM Press
Incubation period

- Initial period before symptoms of disease are obvious
- Viral genomes are replicating
- Host is responding (cytokines with global effects)
  - Fever, malaise, aches, pains, nausea
Table 5.1  Incubation periods of some common viral infections

<table>
<thead>
<tr>
<th>Disease</th>
<th>Incubation period (days)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Influenza</td>
<td>1–2</td>
</tr>
<tr>
<td>Common cold</td>
<td>1–3</td>
</tr>
<tr>
<td>Bronchiolitis, croup</td>
<td>3–5</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>Enterovirus disease</td>
<td>6–12</td>
</tr>
<tr>
<td>Poliomyelitis</td>
<td>5–20</td>
</tr>
<tr>
<td>Measles</td>
<td>9–12</td>
</tr>
<tr>
<td>Smallpox</td>
<td>12–14</td>
</tr>
<tr>
<td>Chickenpox</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>Mononucleosis</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>
<tr>
<td>AIDS</td>
<td>1–10 yr</td>
</tr>
</tbody>
</table>

*Until first appearance of prodromal symptoms.
Inapparent acute infections

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

- Serious epidemics affecting millions each year (polio, influenza, measles)
- Acute infection are difficult problems: by the time you feel ill, the infection may be over and has spread
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

<table>
<thead>
<tr>
<th>Site of replication</th>
<th>Clinical manifestation</th>
<th>Virus</th>
</tr>
</thead>
<tbody>
<tr>
<td>Turbinate “baffles”</td>
<td>Rhinitis (common cold)</td>
<td>Rhinovirus, coronavirus, parainfluenza virus, respiratory syncytial virus</td>
</tr>
<tr>
<td>Tonsillar lymphoid tissues</td>
<td>Pharyngitis</td>
<td>Influenza virus, adenovirus, herpes simplex virus, Epstein-Barr virus</td>
</tr>
<tr>
<td>Palate</td>
<td>Laryngitis</td>
<td></td>
</tr>
<tr>
<td>Tongue</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Esophagus</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cervical lymph node</td>
<td>Tracheitis</td>
<td>Parainfluenza virus, respiratory syncytial virus, influenza virus, adenovirus</td>
</tr>
<tr>
<td>Trachea</td>
<td>Bronchitis</td>
<td></td>
</tr>
<tr>
<td>Bronchi</td>
<td>Bronchiolitis</td>
<td></td>
</tr>
<tr>
<td>Bronchioles</td>
<td>Bronchopneumonia</td>
<td></td>
</tr>
<tr>
<td>Bronchial lymph node</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alveolus</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alveolar macrophage</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
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
Pneumonia and Influenza Mortality for 122 U.S. Cities
Week Ending March 15, 2014

% of All Deaths Due to P&I

Epidemic Threshold
Seasonal Baseline

Weeks

http://www.cdc.gov/flu/weekly/
Data from the Influenza Hospitalization Surveillance Network (FluSurv-NET), a population-based surveillance for influenza related hospitalizations in children and adults in 13 US states. Incidence rates are calculated using the National Center for Health Statistics’ (NCHS) population estimates for the counties included in the surveillance catchment area.

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
Poliomyelitis - poliovirus
Poliovirus pathogenesis
<table>
<thead>
<tr>
<th>Phase of Infection</th>
<th>Incubation</th>
<th>Systemic</th>
<th>Neural</th>
<th>Recovery</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Clinical</strong></td>
<td>Headache</td>
<td>Headache</td>
<td>Headache</td>
<td>Nausea</td>
</tr>
<tr>
<td><strong>Temp. F.</strong></td>
<td>103</td>
<td>102</td>
<td>101</td>
<td>100</td>
</tr>
<tr>
<td><strong>Concentration X Standard</strong></td>
<td>10,000</td>
<td>1,000</td>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td><strong>Alimentary Tract</strong></td>
<td>Virus in Feces</td>
<td>Virus in Throat Secretions</td>
<td>Antibody in Throat Secretions</td>
<td></td>
</tr>
<tr>
<td><strong>Lymphatic and Blood</strong></td>
<td>Virus in Blood</td>
<td>Serum Antibody</td>
<td>Virus in Tonsils and Peyer's Patches</td>
<td></td>
</tr>
<tr>
<td><strong>Central Nervous System</strong></td>
<td>Virus in CNS</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Exposure</th>
<th>Days</th>
</tr>
</thead>
<tbody>
<tr>
<td>7 days</td>
<td>5 days</td>
</tr>
</tbody>
</table>

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

- Inactivated vaccine
- Live oral vaccine
- Last indigenous case
Measles

- Measles virus, *Paramyxoviridae*
- One of the most contagious human viruses
- 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
Thanks, Anti-Vaxxers. You Just Brought Back Measles in NYC.

Measles was considered eliminated at the turn of the millennium. Now it’s back, thanks to the loons who refuse to vaccinate their children.

Of all the things to be nostalgic for, infectious diseases probably don’t make it onto many lists.

However, if you happen to pine for the good old days when measles was an active public health threat, I have good news for you. The anti-vaccine crowd is bringing it back.


Health Department Investigating Measles Outbreak in Northern Manhattan and the Bronx

Department urges all New Yorkers to make sure they are vaccinated against measles

Infants should be vaccinated at 12 months of age

March 7, 2014 – The Health Department announced today that it has identified 16 cases of measles in northern Manhattan and the Bronx. Seven adult cases and 9 pediatric cases have been identified to date. New Yorkers are urged to make sure all household members, including young children, are vaccinated. To date, there have been four hospitalizations as a result of this outbreak.

vaccine licensed
Number of Reported Measles Cases with onset date from Aug 2011 to Feb 2012

Data source: surveillance DEF file
Data in HQ as of 7 March 2012

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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
Rotavirus

• Most common cause of childhood gastroenteritis: Infect nearly every child in the world

• 25,000,000 physician visits/yr, 2,000,000 hospitalizations, 800,000 deaths

• US pre-vaccine, all children infected by 5 yr: 1 in 72 hospitalized

• High mortality in developing world due to dehydration - 5% of all mortality < 5 yr old
Global distribution of rotavirus deaths
Rotavirus
Rotavirus pathogenesis

- Transmitted by fecal-oral contamination
- $10^8 - 10^{10}$ particles/ml feces
- 10-100 virions
- Infants <24 months risk of dehydration
- Older children, adults reinfected, mild or no disease
Rotavirus pathogenesis

- Contaminated hands
- Contaminated foods
- Virions are stable on environmental surfaces
Rotavirus pathogenesis

- Incubation period 1-3 days
- Asymptomatic infections play a role in spread
- Vomiting, 4-8 days of diarrhea, fever
- Recovery complete unless electrolyte replacement not done
**Rotavirus Infection**

- **Time:**
  - 0 hpi: Contaminated food or water
  - 12 hpi: Patchy viral antigen duo<jej<ileum 4+
  - 24-72 hpi: High titers duo<jej=ileum 4+
  - 7 dpi: 0

**Diarrhea:**
- 0

**Mucosal surfaces of gastrointestinal tract**
Rotavirus vaccines

- **Rotarix**: infectious attenuated human isolate
- **RotaTeq**: human - bovine reassortant
- Both found contaminated by porcine circovirus 1

Norovirus

- *Caliciviridae*
- (+) strand RNA virus
- Cause 50% of all food-borne outbreaks of gastroenteritis (23 million/yr US) - cannot be cultured
Known Causes of Foodborne Illness Outbreaks, U.S., 2006–2010

- Norovirus: 49%
- Bacteria: 40%
- Chemicals: 6%
- Other/Multiple: 4%
- Parasites: 1%
• Fecal-oral spread
• Retain infectivity passing through stomach
• Blunting of villi in proximal jejunum
• Basis for vomiting, diarrhea not known
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) and diarrhea (more common in adults)
• Duration of illness: 28-60 hr; longer in immunocompromised or with underlying illness
• 30% asymptomatic infections
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
A Settings

- Restaurants, Catered Meals: 40%
- Retirement Centers: 25%
- Nursing Homes: 25%
- Hospitals: 10%
- Schools: 13%
- Day Care Centers: 10%
- Other: 7%
- Unknown: 5%

n=233

B Modes of Transmission

- Person-to-Person: 88%
- Foodborne: 10%
- Waterborne: 1.5%
- Unknown: 0.5%

n=5,036
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.
The happiest place on earth?

<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>
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<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!

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

www.cdc.gov/Norovirus
"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
WNV transmission cycle
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
WNV CFR 1999-2009

The bar chart shows the case-fatality ratio (CFR) per age group for West Nile Virus (WNV) from 1999 to 2009. The x-axis represents age groups in years (0-9, 10-19, 20-29, 30-39, 40-49, 50-59, 60-69, ≥70) and the y-axis represents the case-fatality ratio. The chart indicates a notable increase in the CFR with age, particularly in the ≥70 age group.
West Nile virus activity, 2012

5,387 cases
2,734 neuroinvasive
243 deaths

http://www.cdc.gov/ncidod/dvbid/westnile/
WNV prevention