Debate: "Public schools should ban unvaccinated children from attendance when district herd immunity thresholds fall below CDC guidelines"

Introduction

Wednesday, May 13th

Holly Stessman
Outline for class

• Today’s objectives
  – History of virology (ex. smallpox)
  – How do vaccinations work?
  – How are vaccinations administered in the U.S.?
  – What is "herd immunity"?
From where did human viral disease arise?

**Guns, Germs, and Steel**
Jared Diamond (1997)

- Eurasian cultivation of livestock living in close proximity to the largest variety of domesticated mammals in the world
- Smallpox, influenza, and measles are thought to have crossed species

http://www.pbs.org/gunsgermssteel/index.html
The history of smallpox

- The facts:
  - Earliest evidence ~1570 BC
  - Two forms: Variola major and Variola minor
  - Progression: Viral infection enters through the nose or throat, spreads to lungs and lymphatic system covering the body (starting with hands and face) in pustules
- Disease course:
  - Incubation period – 7-10 days
  - Initial symptoms – 2-4 days
  - Rash – 9 days **
  - Pustules/scabs – 11 days **
  - Scabs resolve and fall off
- How it spreads: Pustules are filled with smallpox viral DNA; if punctured, they are highly infectious

http://www.nature.com/nri/journal/v2/n7/images/nri845-i1.gif
Smallpox: Conqueror of the Americas

• 1520 – Smallpox arrives in the Americas on a Spanish ship sailing from Cuba carried by an infected African slave
• 1520 to 1528 – Smallpox devastates the Inca Empire, killing the Emperor Huayna Capac and unleashing a bitter civil war that distracts and weakens his successor, Atahuallpa.

Why were these diseases so devastating to newly discovered populations?

• 1713 – Smallpox epidemic in South Africa renders the native people incapable of resisting European colonization
• 1789 – Smallpox epidemic wipes out large numbers of aboriginals in Australia and New Zealand
The history of smallpox

http://www.nature.com/nri/journal/v2/n7/images/nri845-i1.gif
Variolation for smallpox immunity

- 15th century China – “nasal insufflation”
- Africa and India
- 1670 Turkey
- 1721 England
- 1721 America
- Late 19th century – the tradition persists in the Sudan despite being outlawed in many countries

Lady Mary Wortley Montagu
Rev. Cotton Mather
The history of smallpox

http://www.nature.com/nri/journal/v2/n7/images/nri845-i1.gif
Edward Jenner (1749–1823): The Father of Immunology

• Prior to vaccination -> inoculation (variolation)

• Observation: dairy maids who have had cowpox (similar to smallpox but much milder) do not contract smallpox

• Hypothesis: cowpox conferred immunity to smallpox

What was Jenner’s hypothesis?
Jenner’s vaccine experiments (1796)

The word “vaccine” comes from Latin vacca (cow)
The history of smallpox

http://www.nature.com/nri/journal/v2/n7/images/nri845-i1.gif
The history of smallpox
“Modern” smallpox vaccination

What complications might be associated with using a live virus?
“Second-generation” smallpox vaccines

Post-eradication smallpox vaccine stores were created using cell lines like Vero ———>

– Developed in 1962 by Japanese researchers
– Kidney epithelial cells
– Host: African green monkey

What are the advantages to using cell lines for vaccine production?

What characteristics might you want a cell line used for vaccine development to have?
The history of smallpox

- Why might conservation be a great attribute for eradication?
- What does a high degree of conservation tell you about the properties of this viral genome?

http://www.nature.com/nri/journal/v2/n7/images/nri845-i1.gif
The discovery of viruses

1892 — Dmitri Ivanovsky
  — non-bacterial pathogen infecting tobacco plants

1898 — Martinus Beijerinck
  — tobacco mosaic virus

• Virus (from the Latin word for venom or poison)
• 5000+ viruses described in detail
• Virus particles (virions)
  — Genetic material (DNA or RNA)
  — Envelope of lipids
  — Protein coat
Viral genomes

Nucleic Acid

DNA

Single Stranded

Smallpox

Double Stranded

HIV

RNA

Single Stranded

Positive

Negative

RNA → DNA

http://homepage.usask.ca/~vim458/vetvirol/sample/terms.html
The properties of a viral genome

Example: HIV
Properties:
- Spherical (diameter ~120 nm)
- ssRNA genome with 7 structural landmarks and 9 canonical genes (19 proteins)

What general classes of genes might you expect to be encoded by the HIV genome?
- Structural proteins for new viral particles (gag, pol, env)
- Ability to infect cells
- Produce new copies of virus
- Cause disease
- Reverse transcriptase
Types of immunity

Innate Immunity:
- Epithelial barriers
- Phagocytes
- Dendritic cells
- Plasma proteins
- NK cells

Adaptive Immunity:
- Naive B cell
- Naive T cell
- Antibodies
- Effector T cells

Natural

Artificial

http://missinglink.ucsf.edu/lm/immunology_module/prologue/objectives/obj02.html
The immune response to viral infection
Immune response to vaccines

http://www.saburchill.com/IBbiology/chapters04/011.html
# 0-18 years vaccination schedule (U.S.)

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Birth</th>
<th>1 mo</th>
<th>2 mos</th>
<th>4 mos</th>
<th>6 mos</th>
<th>9 mos</th>
<th>12 mos</th>
<th>15 mos</th>
<th>18 mos</th>
<th>19-23 mos</th>
<th>2-3 yrs</th>
<th>4-6 yrs</th>
<th>7-10 yrs</th>
<th>11-12 yrs</th>
<th>13-15 yrs</th>
<th>16-18 yrs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hepatitis B (HepB)</td>
<td>1st</td>
<td></td>
<td></td>
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<td></td>
<td></td>
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<td></td>
<td>3rd dose</td>
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<tr>
<td>Rotavirus (RV) RV1 (2-dose series); RV5 (1-dose series)</td>
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<td>2nd</td>
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</tr>
<tr>
<td>Diphtheria, tetanus, &amp; acellular pertussis (DTaP: &lt;7 yrs)</td>
<td>1st</td>
<td>2nd</td>
<td>3rd</td>
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<td>4th</td>
<td>5th</td>
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<tr>
<td>Tetanus, diphtheria, &amp; acellular pertussis (Tdap: ≥7 yrs)</td>
<td>1st</td>
<td>2nd</td>
<td>3rd</td>
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</tr>
<tr>
<td>Haemophilus influenzae type b (Hib)</td>
<td>1st</td>
<td>2nd</td>
<td>3rd</td>
<td>3rd or 4th</td>
<td>3rd or 4th</td>
<td>4th</td>
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<tr>
<td>Pneumococcal conjugate (PCV13)</td>
<td>1st</td>
<td>2nd</td>
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<tr>
<td>Pneumococcal polysaccharide (PPSV23)</td>
<td>1st</td>
<td>2nd</td>
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<td>4th</td>
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</tr>
<tr>
<td>Inactivated poliovirus (IPV: &lt;18 yrs)</td>
<td>1st</td>
<td>2nd</td>
<td></td>
<td></td>
<td>3rd</td>
<td>4th</td>
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<tr>
<td>Influenza (IIV; LAIV) 2 doses for some: See footnote 8</td>
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<td></td>
<td>Annual vaccination (IIV only) 1 or 2 doses</td>
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<tr>
<td>Measles, mumps, rubella (MMR)</td>
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<td></td>
<td>1st</td>
<td>2nd</td>
<td>1st</td>
<td>2nd</td>
<td>1st</td>
<td>2nd</td>
<td>1st</td>
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</tr>
<tr>
<td>Varicella (VAR)</td>
<td></td>
<td></td>
<td>1st</td>
<td>2nd</td>
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<tr>
<td>Hepatitis A (HepA)</td>
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<td></td>
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<td>2nd dose series. See footnote 11</td>
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</tr>
<tr>
<td>Human papillomavirus (HPV2: females only; HPV4: males and females)</td>
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<tr>
<td>Meningococcal (Hib-MenCY ≥ 6 weeks; MenACWY-D ≥ 9 mos; MenACWY-CRM ≥ 2 mos)</td>
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</tr>
</tbody>
</table>

- **Range of recommended ages for all children**
- **Range of recommended ages for catch-up immunization**
- **Range of recommended ages for certain high-risk groups**
- **Range of recommended ages during which catch-up is encouraged and for which it is not recommended**

# Types of vaccines

<table>
<thead>
<tr>
<th>Type</th>
<th>Component</th>
<th>Diseases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Live, attenuated</td>
<td>Live microbe weakened by growth conditions in the lab or a less dangerous relative</td>
<td>Measles, mumps, rubella, varicella, influenza (nasal), rotavirus, zoster, yellow fever</td>
</tr>
<tr>
<td>Inactivated/Killed</td>
<td>Microbe killed by chemicals, heat, or radiation</td>
<td>Polio (IPV), hepatitis A, rabies</td>
</tr>
<tr>
<td>Toxoid (inactivated toxin)</td>
<td>Toxin inactivated by formaldehyde</td>
<td>Diphtheria, tetanus</td>
</tr>
<tr>
<td>Subunit/conjugate</td>
<td>1-20 parts of a microbe that best stimulate immune response</td>
<td>Hepatitis B, influenza (injection), <em>haemophilus influenza</em> type b (Hib), pertussis, pneumococcal, meningococcal, human papillomavirus (HPV)</td>
</tr>
</tbody>
</table>
What other components are necessary for a vaccine?

- Vehicle (e.g., formaldehyde, glutaraldehyde)
- Preservatives/stabilizers (e.g., 2-Phenoxyethanol)
- Adjuvants: substances that enhance the immune response by mimicking molecules similar to pathogenic microbes (e.g., aluminum phosphate)
## National Vaccination Coverage (2103)

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>% (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>DTaP (≥4 doses)</td>
<td>83.1 (±1.3)</td>
</tr>
<tr>
<td>Poliovirus (≥3 doses)</td>
<td>92.7 (±1.0)</td>
</tr>
<tr>
<td>MMR (≥ 1 dose)</td>
<td>91.9 (±0.9)</td>
</tr>
<tr>
<td>Hib (full series)</td>
<td>82.0 (±1.3)</td>
</tr>
<tr>
<td>HepB (≥3 doses)</td>
<td>90.8 (±1.0)</td>
</tr>
<tr>
<td>Varicella (≥1 dose)</td>
<td>91.2 (±0.9)</td>
</tr>
<tr>
<td>PCV (≥4 doses)</td>
<td>82.0 (±1.3)</td>
</tr>
<tr>
<td>HepA (≥2 doses)</td>
<td>54.7 (±1.6)</td>
</tr>
<tr>
<td>Rotavirus</td>
<td>72.6 (±1.5)</td>
</tr>
<tr>
<td>Combined series</td>
<td>70.4 (±0.9)</td>
</tr>
<tr>
<td>No vaccines</td>
<td>0.7 (±0.3)</td>
</tr>
</tbody>
</table>

- Represents children aged 19-35 months
- 14,060 children from U.S., USVI, and Guam with telephone access
- 1 in 12 children not receiving their first dose of MMR on time
- High vaccination rates from 1994-2013 have saved an estimated net $1.38 trillion over the lifetimes of these children
- Underserved populations require a focused effort
- Healthy People 2020 (www.healthypeople.gov)

Elam-Evans, et al. (2014) MMWR
How does Washington rank?

<table>
<thead>
<tr>
<th>Region</th>
<th>MMR (≥1 dose)</th>
<th>DTaP (≥4 doses)</th>
<th>HepB (birth)</th>
<th>HepA (≥2 doses)</th>
<th>Rotavirus</th>
<th>Combined series</th>
</tr>
</thead>
<tbody>
<tr>
<td>U.S. (all)</td>
<td>91.9%</td>
<td>83.1%</td>
<td>74.2%</td>
<td>54.7%</td>
<td>72.6%</td>
<td>70.4%</td>
</tr>
<tr>
<td>Washington</td>
<td>93.5%</td>
<td>79.8%</td>
<td>75.0%</td>
<td>55.7%</td>
<td>76.3%</td>
<td>70.8%</td>
</tr>
<tr>
<td>Iowa</td>
<td>94.5%</td>
<td>89.6%</td>
<td>79.5%</td>
<td>57.5%</td>
<td>74.7%</td>
<td>78.3%</td>
</tr>
<tr>
<td>Michigan</td>
<td>89.2%</td>
<td>79.6%</td>
<td>82.5%</td>
<td>51.2%</td>
<td>70.1%</td>
<td>70.0%</td>
</tr>
<tr>
<td>Minnesota</td>
<td>90.8%</td>
<td>90.5%</td>
<td>63.8%</td>
<td>54.3%</td>
<td>80.3%</td>
<td>74.1%</td>
</tr>
<tr>
<td>Mississippi</td>
<td>95.2%</td>
<td>87.4%</td>
<td>79.2%</td>
<td>39.1%</td>
<td>63.2%</td>
<td>74.6%</td>
</tr>
<tr>
<td>New York</td>
<td>95.5%</td>
<td>86.6%</td>
<td>63.7%</td>
<td>48.4%</td>
<td>73.8%</td>
<td>72.2%</td>
</tr>
<tr>
<td>Texas</td>
<td>92.7%</td>
<td>81.5%</td>
<td>81.8%</td>
<td>64.2%</td>
<td>73.8%</td>
<td>72.5%</td>
</tr>
<tr>
<td>Montana</td>
<td>87.3%</td>
<td>79.0%</td>
<td>73.9%</td>
<td>46.4%</td>
<td>65.5%</td>
<td>65.4%</td>
</tr>
</tbody>
</table>
The goal of eradication

- **Eradication** = reduction of an infection disease’s prevalence in the global host population to zero
- The only human disease to have been eradicated worldwide is **smallpox**
- Diseases identified as potentially eradicable – Guinea worm, polio, measles, mumps, rubella, lymphatic filariasis, cysticercosis, yaws

International Task Force for Disease Eradication
The goal of eradication

• Key factors in eradicating a disease
  – Epidemiologic vulnerability
  – Availability of an effective and practical intervention
  – Demonstrated feasibility of elimination

• Other factors:
  – Perceived burden of disease
  – Expected cost of eradication
  – Synergy of eradication efforts with other interventions
  – Necessity for eradication rather than control
What is the basic concept of “herd immunity”? 
Herd immunity

Vaccinated, immune
Unvaccinated, susceptible
Transmitting case
For which disease(s) does herd immunity not apply?
Diagram illustrating transmission of an infection with a basic reproduction number $R_0 = 4$ (see Table 1).

<table>
<thead>
<tr>
<th>Disease</th>
<th>Transmission</th>
<th>$R_0$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Measles</td>
<td>Airborne</td>
<td>12–18</td>
</tr>
<tr>
<td>Pertussis</td>
<td>Airborne droplet</td>
<td>12–17</td>
</tr>
<tr>
<td>Diphtheria</td>
<td>Saliva</td>
<td>6–7</td>
</tr>
<tr>
<td>Smallpox</td>
<td>Airborne droplet</td>
<td>5–7</td>
</tr>
<tr>
<td>Polio</td>
<td>Fecal-oral route</td>
<td>5–7</td>
</tr>
<tr>
<td>Rubella</td>
<td>Airborne droplet</td>
<td>5–7</td>
</tr>
<tr>
<td>Mumps</td>
<td>Airborne droplet</td>
<td>4–7</td>
</tr>
<tr>
<td>HIV/AIDS</td>
<td>Sexual contact</td>
<td>2–5</td>
</tr>
<tr>
<td>SARS</td>
<td>Airborne droplet</td>
<td>2–5</td>
</tr>
<tr>
<td>Influenza (1918 pandemic strain)</td>
<td>Airborne droplet</td>
<td>2–3</td>
</tr>
<tr>
<td>Ebola (2014 Ebola outbreak)</td>
<td>Bodily fluids</td>
<td>1.5–2.5</td>
</tr>
</tbody>
</table>
Estimated % coverage needed to prevent disease from persisting in the population

<table>
<thead>
<tr>
<th>Disease</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diphtheria</td>
<td>85%</td>
</tr>
<tr>
<td>Pertussis</td>
<td>92-94%</td>
</tr>
<tr>
<td>Polio</td>
<td>80-86%</td>
</tr>
<tr>
<td>Measles</td>
<td>83-94%</td>
</tr>
<tr>
<td>Mumps</td>
<td>75-86%</td>
</tr>
<tr>
<td>Rubella</td>
<td>83-85%</td>
</tr>
</tbody>
</table>
Current genetics work in influenza

Sequencing strains collected over a large period of time to identify the sequence of mutations that have occurred.

Gong L, Suchard M, and Bloom J (2013) *eLife*
Small group activity (~3 ppl)

Diseases
• Hepatitis B
• Diphtheria
• Polio
• Influenza
• Measles
• Human papillomavirus

Questions provided on the handout

Helpful websites
- http://www.cdc.gov/vaccines/default.htm
- http://www.historyofvaccines.org/
- http://www.vaccines.gov/