Lecture 18 – Immunization & Vaccines

The production of a state of immunity in a subject - a way of preventing infectious disease symptoms by boosting the immune response.

1. Passive immunization: provides transient immune protection by transfer of antibodies or lymphocytes, or other means of assisting the immune response
   - natural: placental transfer (IgG) and breastfeeding (IgA)
   - artificial: antibody/serum therapy (snake bite/diphtheria). These antibodies are typically obtained from horses. **What the advantages and disadvantages of this source of Ab?**

2. Active immunization: provides long-lasting immunity (memory)
   - natural (get sick)
   - artificial—Vaccination (vacca = latin for cow).

Case Study - Smallpox (Variola virus) Lethality rate 30% (European) - 90% (Native American).
1000 BC – documented cases.
1567 AD – Powdered smallpox scabs used intra-nasally as vaccine.
1721 AD – Variolation introduced in England – scratching skin with sample from scabs (1/1000 mortality rate)
1800 AD – Jenner uses cowpox to vaccinate against smallpox
1940 AD - Vaccinia virus (similar to variola virus) used in current vaccines (1/10⁶ mortality)
1977 AD – Smallpox eradicated globally.

2. Vaccination

Vaccine: a vehicle containing a form of an antigen that is administered to induce memory B and T cells specific for that antigen. Generally protect against disease, not infection.

B-cell vaccine: Introduction of a B-cell epitope to produce antibodies that interfere with pathogen life-cycle (neutralizing antibodies). Note this also requires the formation of Tₘ cells.

T-cell vaccine: Presentation of antigens on MHC I to stimulate formation of Tₜ memory cells.

Adjuvant: Increase immunogenicity of the antigen by causing inflammation.
   i. Aluminum salts (Alum)
   ii. MF59: oil-water emulsion
   iii. AS04: Alum + lipopolysaccharides.

Booster shots - Measles 9 months 15 months 5 yrs.

What do booster shots do?

Properties of a Useful Vaccine?

- Immunogenic
- Safe
- One dose
- Cheap
- Stable
- No needle
Some theoretical considerations for vaccine development:

i) Acute versus chronic disease.

ii) Time course of disease versus timing of secondary response: shorter incubation period of the disease may not allow rapid memory response and, therefore, disease may not be inhibited.

Which pathogen A, or B should you make a vaccine against?

How would you provide protective immunity against a pathogen with a short incubation period (e.g. Ebola)?

Importance of High Levels of Vaccination - Herd Immunity.

Reported Measles Cases, United States, 1960-1996

Cervical Cancer – Herpes Papillomavirus (HPV) 99% of cases. Vaccine Cervarix – 99% effective.

Historical Rates of one dose (3 recommended)

- 2007 – 25%
- 2011 – 53%
- 2012 – 53%
<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Target</th>
<th>Strengths (+) and Weaknesses (-)</th>
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<tbody>
<tr>
<td>Denatured (inactive) toxins/sub-units</td>
<td>Toxin (e.g. diphtheria, tetanus)</td>
<td>- Not so effective</td>
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<td></td>
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<td>- 100% inactivation, reproducible</td>
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<tr>
<td>Killed organism</td>
<td>Bacteria (Typhoid) &amp; Viruses (Salk polio)</td>
<td>- 100% inactivation required</td>
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<tr>
<td>Surface carbohydrate + carrier protein (conjugate vaccine)</td>
<td>Bacteria (H. influenza)</td>
<td>- reproducible</td>
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<td>- stable carrier protein</td>
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<td>- produce Ab response against carrier</td>
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<tr>
<td>Capsid proteins</td>
<td>Virus (HepB, HPV)</td>
<td>- TC response required, weak antigen presentation (DC only)</td>
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<tr>
<td>purified or recombinant</td>
<td></td>
<td>- limited production of antigen</td>
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<tr>
<td>Attenuated virus</td>
<td>Virus (Sabin polio, mumps, measles)</td>
<td>- revert back to original pathogen virus</td>
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<tr>
<td>i) natural non-infectious virus e.g. cowpox</td>
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<td>make safer deletions very difficult to revert.</td>
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<td>ii) passage on non-human host.</td>
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<td>iii) recombinant</td>
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<tr>
<td>Viral vector encoded</td>
<td>Virus (HepB)</td>
<td>- Virus &amp; insert antigen from pathogen (safe)</td>
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<tr>
<td></td>
<td></td>
<td>- Virus → vaccine</td>
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