Vaccines

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Major historic population-level mortality factors

• War

• Famine

• Infectious Disease
  – Prevention
  – Cure
  – Management
Causes if death in the 20th century
Infectious Disease

Mortality rate

Prevention
* vaccines

Cure
* antibiotics

Management
* symptomatics
Why Vaccinate?
***HERD effect

If only SOME get vaccinated...

...the virus spreads.

Healthy, non-vaccinated  Healthy, vaccinated  Not-vaccinated, sick, contagious

If MOST get vaccinated...

...spreading is contained.

Healthy, non-vaccinated  Healthy, vaccinated  Not-vaccinated, sick, contagious
Why vaccinate?

• PROTECTION from infectious disease
• Reduction of the severity of infectious disease
• Protection of the community
• Eventual eradication of the disease

SUMS UP TO:

REDUCTION IN THE BURDEN, MORBIDITY, MORTALITY DUE TO INFECTIOUS DISEASE
PRE-VACCINE ERA ESTIMATED ANNUAL MORBIDITY IN THE U.S.

**DECREASE**

- **DIPHTHERIA** 100%
  - Pre-vaccine era: 21,053
  - Current: 0
- **H. INFLUENZA** 99%
  - Pre-vaccine era: 20,000
  - Current: 243
- **HEPATITIS A** 91%
  - Pre-vaccine era: 117,333
  - Current: 11,049
- **HEPATITIS B** 83%
  - Pre-vaccine era: 64,232
  - Current: 11,269
- **MEASLES** 99%
  - Pre-vaccine era: 530,217
  - Current: 61
- **MUMPS** 99%
  - Pre-vaccine era: 162,344
  - Current: 982
- **PERTUSSIS** 89%
  - Pre-vaccine era: 200,752
  - Current: 21,291
- **PNEUMOCOCCAL DISEASE** 74%
  - Pre-vaccine era: 16,069
  - Current: 4,167

***2014 data; CDC***
What is a vaccine?

• The deliberate stimulation of the adaptive arm of the immune system.

• Vaccines work by:
  - mimicking what happens during natural infection without causing illness

• Vaccines use altered versions of microorganisms (e.g. bacteria, viruses) to trigger an immune response
IMMUNITY

a.k.a. Acquired Immunity

VACCINES

Innate immunity

- Epithelial barriers
- Neutrophils
- Macrophages
- Complement
- NK cells

Adaptive immunity

- Dendritic cells
- B cells
- T cells
- Antibodies

Hours

- 0
- 12

Days

- 1
- 7
Specific Resistance (Immunity)

- Responds to threats on an individualized basis

Acquired Immunity

- Produced by prior exposure or antibody production

Active Immunity

- Produced by antibodies that develop in response to antigens (Immune response)
  - Naturally acquired immunity
    - Develops after exposure to antigens in environment
  - Induced active immunity
    - Develops after administration of antigen to prevent disease

Passive Immunity

- Produced by transfer of antibodies from another person
  - Induced passive immunity
    - Conferred by administration of antibodies to combat infection
  - Natural passive immunity
    - Conferred by transfer of maternal antibodies across placenta or in breast milk

Innate Immunity

- Genetically determined—no prior exposure or antibody production involved
During a natural infection:

The immune system recognizes a pathogen as foreign and responds to it.

A PATHOGEN (an agent that causes a PATHology) that causes an immune response is known as an ANTIGEN.

Antigens can be SOLUBLE or breakdown products of intact molecules or whole cells.

Produced after uptake by ANTIGEN-PRESENTING CELLS (directly or indirectly): e.g. macrophages, dendritic cells, and B-cells.
Immunologic Memory

**First exposure to antigen**

**Clonal expansion**

**Memory cells are long-lived, continue to reproduce**

**Second exposure to antigen**

**Stronger and more rapid response**

Antigen

Effector cells carry out immediate response; short-lived

**Primary response**

**Secondary response**

![Graph showing primary response](image1)

![Graph showing secondary response](image2)
Passive versus Active Immunity

**ACTIVE:**

The body is actively engaging a natural pathogen and In the process produces antibodies, and T-cells specific to Antigens from the pathogen; LONG-LASTING IMMUNITY, But may need boosting.

**PASSIVE:**

Antibodies to pathogens or pathogen products (e.g. toxins) are administered to people; provided through placental transfer, Breastfeeding.

Artificially manufactured, in animals (horses) or Through genetic engineering (bioreactors)

**SHORT-ACTING IMMUNITY**

**VACCINES:** involve active immunity, **ANTIVENINS:** involve passive immunity
Long-lasting protection; multiple effector mechanisms activated; LAG TIME

Rapid protection
Short, transient duration
Antigen-Antibody Binding and its Consequences

- **Agglutination**: Abs cause antigens to clump together.

- **Opsonization**: Antigen is coated with Abs to enhance uptake by antigen-presenting cells, and to enhance digestion therein.

- **Neutralization**: Abs inactivate microbes by blocking their attachment to host cells.

- **Complement activation**: bacterial lysis.

- **Fc Receptors**
Question

• Why is memory important for effective control of microorganism invasion?
VACCINES: BASIC CONCEPT

Deliver to the body some part or all of the microorganism that **IMITATES** the pathogen but is not pathogenic.

- Induce protective immune response

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*Entire organism*
- live (attenuated)
- killed

**LPS**
**Surface proteins**
**Intracellular proteins**
**Polysaccharide**
**capsular**
**Toxins**
The protective outcomes of a vaccine that activates the adaptive immune response

- T-cell activation, resulting in memory T-cells

- B-cell activation, resulting in memory B-cells and the production of highly-specific antibodies (neutralizing, opsonizing, destroy microorganism via complement pathway/ADCC)

- Toxin-neutralizing antibodies
How Vaccines Work

1. A vaccine activates various immune cells because it contains part of the germ called an antigen that stimulates the body's immune response. An antigen by itself or in a vaccine has little to no disease-causing ability.

Immune Response to a Vaccine
Vaccines help the body acquire immunity against many disease-causing germs and cancers. A vaccine contains killed or weakened forms of a derivative of an infectious germ. The vaccine has little or no disease-causing ability, but its presence in the body still provokes an immune response. This activates various immune cells that learn from the vaccine to recognize and destroy the germ.

2. The first immune cells that encounter the vaccine are called antigen-presenting cells. Each antigen-presenting cell displays an antigen, then displays on its surface a small piece of that antigen that can be recognized by T cells.

3. When antigen-specific helper T cells encounter an antigen-presenting cell, they become activated and send a chemical messenger to other immune cells e.g., B cells and killer T cells. The chemical messenger helps these immune cells become activated.

4. Once stimulated by the antigen and the chemical message from the helper T cells, the B and killer T cells divide and transform into specialized immune cells that fight back against that specific antigen. Also, a small but important fraction of the B and T cells transform into memory cells that react quicker when they encounter the same antigen again.

Immune Response after Vaccination
An exposure to a germ after vaccination stimulates the memory B and memory T cells, which recognize the antigen from the germ and respond quickly and effectively to prevent disease.

Activated memory B and memory T cells respond faster and more efficiently against future infection by the same antigen.

Memory T cells encounter and recognize the antigen displayed on the surface of the antigen-presenting cells that initiate the immune response against the germ. This activates memory T cells.

Memory B cells produce a molecule called an antibody that recognizes and binds to the antigen on the germ or cells infected with the germ.

Activated killer T cells bind to and destroy any cells that contain the germ's antigen.

Antibodies bind to antigens on the germ to prevent infection, as well as to the cells infected with the germ to mark them for killing.
Types of vaccines

- Live vaccines
- Live attenuated vaccines
- Inactivated (killed vaccines)
- Toxoids
- Polysaccharide and polypeptide (cellular fraction) vaccines
- Surface antigen (recombinant) vaccines
- Recombinant vaccines
- DNA/Adjuvants
- Cellular “Vaccines”***
Live vaccines

Benefits:
Live microorganisms provide continuous antigenic stimulation giving sufficient time for memory T- and B-cell production
Excellent, quick, and durable immune response

Risks:
Can cause disease, especially in immunocompromised people

Examples: Variola (smallpox) - NOT MADE from variola virus (SP), but from the related VACCINIA (cowpox) live virus which SHARES SOME ANTIGENS with smallpox virus, but is NOT PATHOGENIC TO HUMANS (refer to the story of Jenner/cowpox/smallpox)

Gives cross-immunity to Smallpox
Live attenuated vaccines

***Attenuated microorganisms are grown in hosts different from the natural ones (e.g. animals, eggs, cultured cells), and as a consequence of mutations, when introduced back into the original host, they will not grow as well as the natural strain and will not cause disease to the natural level

Benefits:
Live attenuated microorganisms provide continuous antigenic stimulation giving sufficient time for memory T- and B-cell production
Excellent and quick immune response that is very durable minimizing boosters

Risks:
Even though the causative microorganism has been “attenuated”, it can still revert to the original form and cause disease

Can cause disease, especially in immunocompromised people

Examples: Tuberculosis (BCG), Measles, Mumps, Oral Polio (Sabin vaccine), Rubella (“German” measles), Yellow Fever, Typhoid, Plague, INTRANASAL INFLUENZA (FluMist™)
Inactivated/Killed Vaccines

***Attenuated microorganisms are grown in hosts different from the natural ones (e.g. animals, eggs, cultured cells), and as a consequence of mutations, when introduced back into the original host, they will not grow as well as the natural strain and will not cause disease to the natural level

Benefits along with some disadvantages:
Stable storage
Do not revert to original virulent form
Produces mainly antibody response, often require boosters
Adjuvants*** are often needed in preparation to co-stimulate immune response (aluminum hydroxide/phosphate)
Short-lasting

Risks:
Allergic response to adjuvants, stabilizer (to improve storage life: magnesium sulfate) and preservative chemicals (prevent contamination: thimerosal, phenoxyethanol), and trace formaldehyde (byproduct of purification process of microorganisms)

Examples: Diptheria, tetanus, hepatitis A/B, papillomavirus, inactivated polio (Salk), injectable Influenza (FluZone™), meningococcus, pneumococcus, rabies
Case study: Sabin vs. Salk polio vaccines

Sabin Polio Vaccine (oral), attenuated

- Attenuated by passage in foreign host (monkey kidney cells)
- Selection to grow in new host makes virus
- Less suited to original host

- Grows in epithelial cells
- Does not grow in nerves
- No paralysis
- Local gut immunity (IgA) evoked
- Reversion to wild-type is possible
Salk Polio Vaccine (killed) injected

Killed by exposure to formaldehyde

No reversion to wild-type is possible
Polio vaccine illustrates the pluses and minuses of live/attenuated vs. killed vaccines

**US: Sabin attenuated vaccine**

~10 cases vaccine-associated polio per year =

1 in 4,000,000 vaccine infections

**Scandinavia: Salk dead vaccine**

- No gut/mucosal immunity
- Cannot wipe out wild-type virus

• REASONS? NEXT SLIDE.....
Live virus generates a more complete immune response

Killed (Salk) Vaccine
- Serum IgG
- Serum IgM
- Serum IgA

Live (Sabin) Vaccine
- Serum IgG
- Serum IgM
- Serum IgA

Nasal and duodenal IgA

Days

Vaccination

Reciprocal virus antibody titer

4
8
96

Vaccination

48
96
Toxoid Vaccines

- Are prepared by detoxifying the exotoxins of some bacteria rendering them antigenic but not pathogenic. Heat or chemical treatment renders toxin non-functional.

- The antibodies produced in the body as a consequence of toxoid administration neutralize the toxic moiety produced during infection rather than act upon the organism itself.

Benefits/Disadvantages:
- Does not cause disease that it intends to prevent
- Stable and long-lasting protection
- Immunity is built against the toxin
- Adjuvant (e.g. alum precipitation) is used to increase the potency of vaccine. May cause allergies.
- Boosters needed
- Immunity against the microorganism producing toxin is weak

Examples: Diptheria toxin, Tetanus toxin, Botulism toxin, Pertussis toxin, snake Venom, other anti-venins
Polysaccharide/polypeptide (Cellular fraction) Vaccines

- They are prepared from extracted cellular fractions of a killed/inactivated microorganism cell wall.
- Their efficacy and safety appear to be high.
  - Need adjuvants
  - Boosters often required
- Examples: pneumococcus (PS in the capsule of bacterium), meningococcus salmonella, hepatitis B (polypeptide),
Surface antigen vaccines (recombinant DNA vaccines)

- Immune response is initiated against a component that is found on the surface of a microorganism in large concentration and high level (ideally).
- The best antigen candidates are proteins with the following characteristics:
  - ideally on the surface
  - stimulate B- and T-cells (are highly immunogenic)
  - induce Abs that can elicit complement/ADCC killing and/or can effectively neutralise pathogen/host cell interactions
- Immune cells primed by vaccine can rapidly detect and respond to pathogen
- B-cells react by proliferating and secreting Ab
- Abs bind complement
- Antigen-presenting cells more easily take up and process pathogen offering more antigenic epitopes via class II MHC

The importance of selecting surface-expressed antigens accessible to the immune system for vaccine development
Surface antigen vaccines (recombinant DNA vaccines)

- Examples: Hepatitis B Surface Ag, Human Papilloma Virus L1 protein
- Gene is cloned into yeast
- Grown in yeast in bioreactors and expressed
- Purified

Advantages:

- Very quick production
- Large quantities
- Free from infectious pathogen to which immunity is sought
- Need to identify best antigens
- Adjuvants are often needed
- Boosters required

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Fig. 16.1: (A) Hepatitis B virus–Dane particle (42 nm particle); (B) Production of hepatitis B surface antigen (HBsAg) in yeast cells (Trp–Tryptophan, ADH–Alcohol dehydrogenase).
Recombinant DNA-modified vectors

- Genetic material is cloned from the pathogenic organism to another bacterial/viral organism that is not pathogenic (or will be rendered non-pathogenic during process of production)

- The non-pathogenic organism will express the antigens expressed by the cloned DNA

- Expressed on an intact organism, the antigens of the organism to which immunity is sought, an adjuvant effect is achieved and often good cellular responses are induced

- The “carrier“organisms are usually live viruses
Recombinant DNA-modified vectors

- Examples of live *engineered* vectors:
  Vaccinia, polio, adenovirus, HIV, salmonella, oral streptococcus
DNA/Adjuvant Vaccines

• Plasmid DNA vectors expressing antigens are often used

• Conventional adjuvants (aluminum OH/PO$_4$) or short single-stranded DNA (consisting of repeated Cytosine/Guanine tracts) are co-administered
CpG oligonucleotide adjuvants activate Pattern Recognition Receptors (e.g. Toll-like Receptors) and amplify the ability of antigen-presenting cells to take up and/or express exogenously-administered antigen(s)
Questions

1. What type of vaccine would you design to prevent a bacterial disease that has an acute course but is quite deadly in the population?

2. What type of vaccine would you design to control the spread of a virus from a few infected cells in a person's body, so that very few if any other cells get infected?
Specific Resistance (Immunity)

- Responds to threats on an individualized basis

Acquired Immunity

Produced by prior exposure or antibody production

Innate Immunity

Genetically determined—no prior exposure or antibody production involved

Active Immunity

Produced by antibodies that develop in response to antigens (Immune response)

- Naturally acquired immunity
  
  Develops after exposure to antigens in environment

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Passive Immunity

Produced by transfer of antibodies from another person

- Induced passive immunity
  
  Conferred by administration of antibodies to combat infection

- Natural passive immunity
  
  Conferred by transfer of maternal antibodies across placenta or in breast milk
Passive Immunity

• Naturally involves the transfer of existing antibodies from mother to fetus (trans-placental) and later via breast-feeding (colostrum)

• Offers a short window of Ab-based protection against organisms to which mother has a good Ab titer

• Abs are low-avidity IgA

• Abs are removed from circulation within 14 days

***Potential for transfer of maternal IgE (allergies)
Passive Immunity

- Can also be a “Quick and Crude” Solution for emergency, for which no other approach exists.

- Antibodies to antigen/organism raised in animals.

- Purified serum often used.

- Antibody-mediated protection used mainly for neutralization of toxins/venins.

Diagram:
- Tetanus toxoid
- Immunized horse
- Immune horse serum (tetanus antitoxin)
- Patient at risk of tetanus
- Patient protected
Passive Immunity

- **Advantages**
  - immediate protection (chiefly Ab-mediated)

- **Disadvantages**
  - transient protection (short-lived)
  - potential for serum sickness
  - no immune memory established
    (no antigenic stimulus)
  - potential for anti-antibody responses by host
    resulting in loss of effect over time
    (host Abs neutralize the serum Abs)
<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>
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<td>Killed organism</td>
<td>Bacteria (Typhoid) &amp; Viruses (Salk polio)</td>
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<td>Surface carbohydrate + carrier protein (conjugate vaccine)</td>
<td>Bacteria (H. influenza)</td>
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<td>Attenuated virus</td>
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<td>+Never pathogenic - Incomplete immune response (some Ab isotypes not present; IgA, IgD)</td>
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Vaccines: what is still needed?

- The big three:
  - HIV
  - Malaria
  - Tuberculosis
Challenges for vaccine development

-In the developed world
  - **Cost of development**: facilities, regulations, litigation
  - **Market size**: only given once, 57% bought by public sector
  - **Litigation costs**: National Vaccine Injury Compensation Program

-In the developing world
  - Storage and transportation conditions
    - UV protection
    - The ‘cold chain’ / Freeze watch label
  - Syringe use
    - Auto-disposable syringes *eg. Solo-shot syringe*
    - Needle free methods
  - **Cost**
    - GAVI: Unicef, WHO, Gates, NGOs
Everything you need to know 😊

- https://www.youtube.com/watch?v=zQG0cOBi6s

- https://www.youtube.com/watch?time_continue=2&v=7MaIT5w5NWQ

- ....continue to next slides for a summary, practical application, and for your interest.....
SUMMARY

AND

PRACTICAL APPLICATIONS

(For your information only)
## Types of vaccines

<table>
<thead>
<tr>
<th>Live vaccines</th>
<th>Live Attenuated vaccines</th>
<th>Killed Inactivated vaccines</th>
<th>Toxoids</th>
<th>Cellular fraction vaccines</th>
<th>Recombinant vaccines</th>
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<tr>
<td>• Smallpox variola vaccine</td>
<td>• BCG</td>
<td>• Typhoid oral</td>
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<td>• Diphtheria</td>
<td>• Meningococcal polysaccharide vaccine</td>
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<td>• Salk polio</td>
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</table>
• Deep subcutaneous or intramuscular route (most vaccines)
• Oral route (Sabin polio, oral BCG vaccine)
• Intradermal route (BCG vaccine)
• Scarification (smallpox vaccine)
• Intranasal route (live attenuated influenza vaccine FluMist™)
Immunization schedules

• Primary vaccination
  – One dose vaccines (BCG, variola, measles, mumps, rubella, yellow fever)
  – Multiple dose vaccines (polio, DPT, hepatitis B)

• Booster vaccination
  To maintain immunity level after it declines after some time has elapsed (DT, MMR).
Periods of maintained immunity due to vaccines

- Short period (months): cholera vaccine
- Two years: TAB vaccine
- Three to five years: DPT vaccine
- Five or more years: BCG vaccine
- Ten years: yellow fever vaccine
- Solid immunity: measles, mumps, and rubella vaccines.
Levels of effectiveness

• Absolutely protective (100%): yellow fever vaccine
• Almost absolutely protective (99%): Variola, measles, mumps, rubella vaccines, and diphtheria and tetanus toxoids.
• Highly protective (80-95%): polio, BCG, Hepatitis B, and pertussis vaccines.
• Moderately protective (40-60%) TAB, cholera vaccine, and influenza killed vaccine.
Are vaccines effective?

Recommended Immunization Schedule for Persons Aged 0–6 Years—UNITED STATES • 2008
For those who fall behind or start late, see the catch-up schedule

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<th>Vaccine ▼</th>
<th>Age ▶</th>
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<td>Influenza</td>
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<td>Influenza (Yearly)</td>
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<td>Measles, Mumps, Rubella</td>
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<td>MMR</td>
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<td>Varicella</td>
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<td>Varicella</td>
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<td>Hepatitis A</td>
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<td>HepA (2 doses)</td>
<td>HepA Series</td>
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<td>Meningococcal</td>
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<td>MCV4</td>
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This schedule indicates the recommended ages for routine administration of currently licensed childhood vaccines, as of December 1, 2007, for children aged 0 through 6 years. Additional information is available at www.cdc.gov/vaccines/recs/schedules. Any dose not administered at the recommended age should be administered at any subsequent visit, when indicated and feasible. Additional vaccines may be licensed and recommended during the year. Licensed combination vaccines may be used whenever any components of the combination are indicated and other components of the vaccine are not contraindicated and if approved by the Food and Drug Administration for that dose of the series. Providers should consult the respective Advisory Committee on Immunization Practices statement for detailed recommendations, including for high risk conditions: http://www.cdc.gov/vaccines/pubs/ACIP-list.htm. Clinically significant adverse events that follow immunization should be reported to the Vaccine Adverse Event Reporting System (VAERS). Guidance about how to obtain and complete VAERS form is available at www.vaers.hhs.gov or by telephone, 800-822-7967.
The annual ritual of flu vaccines...

"I hate it when we’re not sure we’re inoculating against the right strain of flu virus."
The case of the flu

Influenza virus A (B, C)

Infects respiratory tract
- Cells killed by virus or immune response

Immune mediators: Interferons mainly
- fever
- muscle aches
- headaches
- fatigue

Adaptive immunity: Humoral & cell-mediated responses
clear infection & create immune memory, but:

- Yearly outbreaks, in spite of previous infections
- Yearly vaccination needed
**Influenza A**

- **Viral Spread**
  - Infected person sneezes or coughs
  - Micro-droplets containing viral particles inhaled by another person
  - Penetrates epithelial cells lining respiratory tract

- **Influenza kills cells that it infects**
  - Can only cause acute infections
  - Cannot establish latent or chronic infections

- **How does it evade immune extinction?**
  - Antigenic drift
  - Antigenic shift: reassortment
Influenza A virus

- RNA core: 8 segments
- Protein capsid: w/RNA polymerases
- Envelope

- 2 major glycoproteins:
  - Hemagglutinin (HA) subtypes: 1, 2, 3...16
  - Neuraminidase (NA) subtypes: 1, 2...9

Size = 80-120nm
The influenza virus life cycle:

HA - mediates entry,
- main target of humoral immunity
NA - mediates release
The adaptive immune response to influenza

a Antibody-mediated immunity
- Influenza virus
- HA-specific antibody
- Block viral attachment
- Plasma membrane
- Sialic-acid receptor
- Epithelial cell
- Prevent release of new virions
- NA-specific antibody
- NA protein
- Infected epithelial cell
- Prevent release of viral particles
- M2-specific antibody
- M2 protein

b Cell-mediated immunity
- Infected cell
- MHC class I
- NP peptide
- TCR
- Perforin
- Cell lysis
- Antiviral activity
- IFNγ
- TNF
- CD8+ T cell

Nature Reviews | Immunology
The influenza virus life cycle:

HA - mediates entry, main target of humoral immunity
NA - mediates release

Antigenic drift:
- Viral RNA polymerases don't proofread reproduction
- Point mutation changes in HA/NA change antigenicity
The 1918 Spanish Influenza Flu Pandemic

- Population lacked immunity to new H1N1 strain: 40 million deaths in <1 yr!

- Today widely circulating human viruses: H1, H2, H3

- Birds are predominant host for all H1-H16/ N1-N9 strains

Antigenic shift and flu pandemics

Shift - Reassortment: viral gene segments randomly reassociate
-Achieved by co-infection of a single cell with these viruses

How does this happen?
1. Virus shed in bird feces gets into pigs drinking water
2. Humans handle and/or cough on the pig
   = New virus: segments from human birds & pigs virus

China: Guangdong Province
-breeding ground: proximity of humans, pigs, birds:
- H5N1: 50% lethal, no human-human transmission yet
How are flu vaccines made?

The trivalent influenza vaccine

1. CDC/WHO experts gather to decide which strains to target.

2. Virus reassortment in cell culture

3. 300 million fertilized eggs are cleaned and inoculated with reassorted virus

4. Viral fluid from eggs is harvested, centrifuged and filtered. Virus is inactivated with formalin

5. Purified inactivated virus from each strain is combined and packaged into doses
How are vaccines made?

The influenza vaccine

WILD TYPE INFLUENZA VIRUS (virulent) AS RECOMMENDED BY WHO EACH YEAR.

TWO GENES FROM THE WILD TYPE VIRUS CONFER SURFACE H&N ANTIGENS TO TRIGGER IMMUNE RESPONSE.

REASSORTANT VIRUS FORMS THE BASIS OF THE LIVE ATTENUATED INFLUENZA VACCINE.

SIX GENES FROM THE MASTER STRAIN CONFER NON-VIRULENT PROPERTIES.

COLD ADAPTED MASTER STRAIN (non-virulent).
An alternative production approach:

1. Genetic engineering of virus
2. Growth in tissue culture cells
McCarthyism in the 21st Century
The anti-vaccination hyperbole

• Just like all medicaments, vaccines do have side effects, and can cause reactions in some people, just like........
To think about…..

Anti-vaccine activists, Web 2.0, and the postmodern paradigm – An overview of tactics and tropes used online by the anti-vaccination movement

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Article has been distilled into: