Vaccines of the Future

Changing the way we will practice medicine forever.
Why Vaccines?

• Striking reductions of infection and disease
• Enables the body to marshal its defenses
• Avoids the problem of drug resistance
• Promises applications beyond infectious diseases
• Cheaper for large population healthcare
The body of man [is] God’s drug-store and [has] in it all liquids, drugs, lubricating oils, opiates, acids, and anti-acids, and every sort of drug that the wisdom of God thought necessary for human happiness and health. —*Autobiography of A. T. Still*
Vaccines have a long history

- Smallpox scarification
- The success of Edward Jenner
- Louis Pasteur and his discovery of attenuation
- The cell-culture revolution
- Inactivated vaccines
- Genetic engineering
Smallpox

A public health milestone

Worldwide cooperation

Roadmap for further infectious disease eradication
Vaccine Approval Process

1. Recognize the disease and identify the etiologic agent
2. Attempt to grow the agent in the laboratory
3. Establish an animal model for the disease
4. Identify an immunologic correlate for immunity to the disease – Usually a serum antibody
5. Choose antigen (in laboratory)
6. Prepare candidate vaccine following Good Manufacturing Practice
Vaccine Approval Process (Cont.)

- 6. Evaluate candidate vaccine for ability to protect animal model
- 7. Prepare protocol for human studies
- 8. Phase 1 human trials - Safety and immunogenicity using small group
- 9. Phase II trials – Safety and immunogenicity using relatively larger group
- 10. Phase III trial – Efficacy and safety
- 11. Long and complicated process
  - Usually takes 10-15 years
  - Many vaccine candidates fail for every success
Emerging Next Generation Technologies

- Viral vector vaccines
- Dendritic cell vaccines
- DNA vaccines
- The power of antibodies
- Immune-boosting molecules
- Nanoparticle vaccines
Viral Vector Vaccines

- Genes are put in non-disease causing viruses
- Viral vectors “transfect” the cell
- The cell degenerates and presents proteins
- The body responds to this as it does any foreign substance
- The immune system recognizes the proteins and prepare long-lived memory cells
Dendritic Cell Vaccines

- Dendritic cells orchestrate the body's immune response.
- They grab foreign bodies in the blood and present them to other immune cells to trigger a powerful immune response.
- Infections, like HIV, hijack these important immune system responses and use the dendritic cells to cross the mucosa.
DNA Vaccines

- These vaccines use the microbes genetic material.
- Cells take up the material.
- Cells secrete antigens, display the on their surfaces.
- Body’s own cells become vaccine-making factories.
The Big Three

- Malaria
- Tuberculosis
- Human Immunodeficiency Virus
Malaria
Malarial Vaccines Pose Unique Challenges

- Large eukaryotic genomes
- Complex life cycles
- Antigenic variations
- Lack of lifelong protection resulting from natural infection
- Immune evasive techniques
- Special consideration for formulation and delivery in developing nations
Malaria Vaccines

- Anti-parasitic immunity and anti-toxic immunity
- Complex life cycle
- Vaccine should have therapeutic value and prevent further transmission
- Thirty antigens currently being researched
- May require an antigen “cocktail” for wider success
Tuberculosis – A Killer
TB Case Rates, * United States, 2014

- White: ≤ 3.0 (2014 national average)
- Blue: >3.0

*Cases per 100,000.
Tuberculosis Vaccines

- Bacille Calmette-Guerin (BCG) – one of the first vaccines to be developed
- Requires a T-cell response
- Twelve TB vaccines currently in development
- Next generation vaccines will be designed to induce sterilizing immunity
Human Immunodeficiency Syndrome

First HIV vaccine trial in 1987
Lack of Natural immunity
Variability of HIV types
Lack of correlates of protective immunity
Lack of animal model that reliably predicts vaccine efficacy
Preventative and therapeutic vaccines in development
**Issues Related to Influenza Vaccines**

- Lack of life-long immunity following infection/vaccination

- Invariable drift of seasonal influenza strains requiring “timetable” approach to vaccine development

- Imprecision in predicting seasonal strain

- Inability to stockpile vaccines for several years

- Potential for emergence of pandemic strain
Is a Universal Influenza Virus Vaccine on the Horizon?
The Common Cold

Rhinovirus presents a moving target

Cannot be grown in the laboratory

Genomes of viral types have been determined

Minor illness that may not require expensive treatment
**GAS Vaccines**

Frequent cause of both mild and severe infections

M protein–based and non–M protein–based vaccines

Twenty-five vaccine candidates in development
STD’s Fall to Vaccines

Gonorrhea
Syphilis
Chlamydia
Herpes, Type 1
Other Areas of Interest

- Methicillin-resistant Staph. Aureus (MRSA)
- Respiratory syncytial virus
- Ebola virus
- Typhoid
- Cholera
- Chlamydia
- Klebsiella pneumonia
- Herpes simplex I and II
- Rabies
- Shigellosis
- Hepatitis C and E
- Pseudomonas aeruginosa
- Clostridium difficile
- Ebstein-Barr virus
Diabetes mellitus

Bacillus Calmette-Guerin (BCG)
Phase II clinical trials

Eliminates WBCs that destroy problematic Beta cells

Trials for both new and longstanding patients

Already FDA approved
Cholesterol vaccines

Affects 74 million people

Targets PCSK9 protein

Even better when combined with statins
**Hypertension Vaccines**

Pathogenesis is multifactorial

Targeting angiotensin-II

May provide lasting effects for 6-9 months
Alzheimer's Disease

Imbalance between production and clearance of amyloid B and tau proteins

Plaque formation may begin 15-20 years before symptoms

Future vaccines may be more effective in prevention than treatment

DNA vaccines may promote body’s T-cell activity
A Vaccine to Combat the Nicotine Habit
Drug Addiction – Treated with Vaccines?

Cocaine

Heroin

Methamphetamine
Obesity in the Crosshairs

Worldwide health problem

Current treatment modalities insufficient

Poor patient compliance

Ghrelin protein a target
Rheumatoid Arthritis

- Current therapies only treat symptoms and slow the progression of the disease
- New vaccine targets specific rheumatoid arthritis antibodies
- Personalized immunotherapy prepared for each patient
- Treatment teaches the patient’s immune system to ignore naturally occurring peptide identified as “foreign”
Preventive Cancer Vaccines

- Biological response modifiers
- Preventative vs. therapeutic
- Microbes associated with cancer
  - Human Papilloma Virus (HPV)
  - Hepatitis B
  - Hepatitis C
  - Epstein-Barr virus
  - Helicobacter pylori
**Therapeutic Cancer Vaccines**

- Intended to treat cancers that have already developed
- Body loses ability to “see” cancer cells as dangerous
- First cancer treatment approved in 2010 for metastatic prostate cancer
- Weakened or killed cancer cells as antigens
- Adjuvants may augment antigen immune response
Potential Cancer Vaccine Targets

- Brain tumors (especially glioblastomas)
- Breast cancer
- Cervical cancer
- Colorectal cancer
- Kidney cancer
- Lung cancer
- Lymphoma
- Melanoma
- Pancreatic cancer
Vaccines for Allergies?

Allergen-specific immunotherapy currently in use
Producing allergens in recombinant form
Reduction of IgE reactivity
Phase III studies for grass and ragweed vaccines
Dental Caries Vaccine – A Possible Option

Irreversible microbial disease of the calcified tissues of the teeth

*Streptococcus mutans*

Mucosal immune response can influence pathogenesis

Lack of strong economic interest
Not more Needles? Alternatives to Injectables

- Tablets
- Patches
- Jet injectors
- Inhalers
- Nasal sprays
- Edible vaccines
Challenges to Vaccine Development

- Pathogen characteristics
- Host characteristics
- Who pays for all this?
- How do we define efficacy?
- Vaccine safety concerns