The Struggle with Infectious Disease
Lecture 2
Today

• Smallpox
  – History and impact
  – Development of a vaccine
  – Eradication program

• Immunity and Immunization
Smallpox

• One of the oldest and most devastating infectious diseases

• First recorded occurrence about 3000 years ago in Egypt, India or China following trade routes

Mummified remains of Ramses V; died 1157 BC with smallpox lesions
Smallpox

• There is an ancient Hindu god *Sitala*: god of smallpox
• Known as ‘the cool one’ she carried water to soothe the raging fever
• Sopona: the Yoruba god thought to cause smallpox

• Yoruba is part of current day Nigeria

Sopona  by James Gathany (photo), CDC.
Smallpox

• Returned to Europe along trade routes
• Probably primary cause of infectious death in the Roman Empire
  – Antoine Plague AD 165
• Introduced into Africa in 1500’s and 1600’s and the Americas in the 1500’s
Smallpox

• While Bubonic plague reshaped Europe, Smallpox depopulated the New World
• It remained present in populations throughout Eurasia
  – Because of the long time of exposure (~3000yrs) Eurasians had developed an equilibrium with the disease.
  – Resistant individuals had been selected in an evolutionary sense ...they could become carriers
Smallpox

• Because Americans had not encountered the disease they had no immunity

• Rapid spread and high mortality decimated the population.
  – Over 90% of the native population of Hispaniola was dead within 40 years of Columbus’s arrival
Smallpox

- 300 million deaths worldwide in 20th century
- 60 Million Europeans
- 5 reigning monarchs in 18th Century
- 1967: 15 million cases & 2 million deaths (WHO)
Smallpox in the 20th Century

- Up to 30% mortality
- Up to 80% mortality in children under 5
- 1/3 of survivors were blind
Concept of the Day: Immunity

Take home message:

• The body has a complex immune system to combat invaders that may be pathogenic
• To be even more effective the system has a memory that allows rapid and effective response to invaders it has seen before
• There are two parts to the immune system:
  – External protection
  – Internal destruction
External Protection

• Skin
  – Provides physical barrier

• Mucosa
  • Nose
  • Mouth
  • Intestinal Tract
  – Detect and attempt to remove foreign objects
Internal System

- Detects foreign cells
  - Self identification molecules
- Marks foreign cells
  - Antibodies
- Destroys foreign cells and removes them
  - Variety of techniques depending on type of invader
Nonspecific Response

1. Bacteria and other pathogens enter wound.
2. Platelets from blood release blood-clotting proteins at wound site.
3. Mast cells secrete factors that mediate vasodilation and vascular constriction. Delivery of blood, plasma, and cells to injured area increases.
4. Neutrophils secrete factors that kill and degrade pathogens.
5. Neutrophils and macrophages remove pathogens by phagocytosis.
6. Macrophages secrete hormones called cytokines that attract immune system cells to the site and activate cells involved in tissue repair.
7. Inflammatory response continues until the foreign material is eliminated and the wound is repaired.
The defense process is different for each different type of pathogen.

It keeps a few cells necessary to fight an infection for the next time.

This speeds the response next time.
Cell Mediated Immune Response

University of Illinois at Chicago http://www.uic.edu/classes/bios/bios100/lecturesf04am/lect23.htm
Antibody Mediated Response
Antigen Presentation

1. Antigen enters dendritic cell.
2. Enzyme inside cell breaks antigen into pieces.
3. Antigen pieces bind to MHC protein inside endoplasmic reticulum.
4. The MHC-antigen complex is transported to the cell surface via the Golgi apparatus.
5. The MHC protein presents the antigen on the surface of the cell membrane.

Major histocompatibility (MHC) protein
• The most common disease-causing microbes are bacteria, viruses, and parasites. Each uses a different tactic to infect a person, and, therefore, each is thwarted by different components of the immune system.

• Most bacteria live in the spaces between cells and are readily attacked by antibodies. When antibodies attach to a bacterium, they send signals to complement proteins and phagocytic cells to destroy the bound microbes. Some bacteria are eaten directly by phagocytes, which signal to certain T cells to join the attack.

• All viruses, plus a few types of bacteria and parasites, must enter cells of the body to survive, requiring a different kind of immune defense. Infected cells use their major histocompatibility complex molecules to put pieces of the invading microbes on their surfaces, flagging down cytotoxic T lymphocytes to destroy the infected cells. Antibodies also can assist in the immune response by attaching to and clearing viruses before they have a chance to enter cells.
- Parasites live either inside or outside cells. Intracellular parasites such as the organism that causes malaria can trigger T cell responses. Extracellular parasites are often much larger than bacteria or viruses and require a much broader immune attack. Parasitic infections often trigger an inflammatory response in which eosinophils, basophils, and other specialized granule-containing cells rush to the scene and release their stores of toxic chemicals in an attempt to destroy the invaders. Antibodies also play a role in this attack, attracting the granule-filled cells to the site of infection.
Lymphatic System

• The body’s lymphatic system allows a path external to the blood stream for immune cells to be produced, transported activated and removed

• Allows combat of extracellular infections
Lymphatic System

- Lymph nodes act as active sites for immune response
- There is rapid exchange of cells between the lymphatic system and the blood stream
Memory

• The key element here is the ability of the immune system to remember and reactivate in response to an invader.

After clearing the body of an invading organism, the B-cell retains memory of its target and rests until another infection occurs.

Genentec Inc.
What is Smallpox

• Viral infection (*variola*)
• Spread person to person via face to face contact at distances less than 2m
• Can be spread via contact with bodily fluids or contaminated objects
What is Smallpox

• The virus itself is considered to be the ‘most developed’
• Different reproduction than other pathological viruses
  – Cytoplasm not nucleus
• Contains extra proteins to help in defense and reproduction
Animal Cell

http://www.sfu.ca/~fankbone/biol/index3.html
The struggle for protection

• As early as the 12th Century in China it had been noted that children who survived smallpox did not succumb to the disease when exposed later
The struggle for protection

- ‘Variolation’ was developed as traditional Chinese medicine
- Smallpox scabs were powdered and blown into the nose
- Since this was a live virus, some people did contract the disease
The struggle for protection

- Of interest: When the Mogols invaded Southern China in the 13th century they had no immunity to smallpox and isolation and variolation became important.
1643: Fall of Ming Dynasty
Spread of Variolation to Europe

• Variolation as a prevention technique spread along trade routes and was well established in Africa, India and the Ottoman Empire by 1700

• 1717 Lady Montagu, wife of the British Ambassador in Constantinople learned of variolation

• 1721 first trial of the technique on prisoners and abandoned children
Acceptance of Variolation

- When successful, the Royal Family was treated
- Procedure became fashionable in Europe
- There was a risk: King George III lost a son to variolation
Variolation in North America

• Introduced into America by slaves
• First publicized and used in the Boston epidemic in 1721
• Due to sparse population the technique did not become particularly popular
Historical Note

• It may be that Canada remained British due to Smallpox.
• Smallpox became more prevalent due to crowded quarters and weakened immune systems
• British Army was variolated (as common practice); Revolutionary Army wasn’t
• Washington's army had to retreat from Quebec as it was so weakened by disease.
The First Vaccine

• Dr Edward Jenner a family physician in England
• He followed the ‘folklore’ that milkmaids did not get smallpox
• 14 years of observation and note talking
The First Vaccine

• 1796 Jenner inserted puss from cow pox in cuts in an 8 year old

• James Phipps subsequently survived direct exposure to smallpox
The First Vaccine

• Issues
  – The process was not understood
  – Concerns about injecting cow into people
  – No efficient way to prepare large quantities of vaccine

• The practice of vaccination developed in Europe and NA
Vaccination in Canada

• The first smallpox vaccines: end of 19th century (1886)
• Dr J.R. Fitzgerald established lab in Toronto for anti-toxin production and smallpox in 1914
• Smallpox was eradicated in Canada in 1962
Eradication of Smallpox

• Last endemic case of smallpox in Canada was in 1946
• In 1962 a 14 year old boy arrived in Toronto from Brazil with a mild form of the disease. He was isolated and no one was infected
• Europe and America were generally smallpox free by early 1950’s
Eradication of Smallpox

• Accomplished through mass vaccination
• The development of ‘herd immunity’

• Cases were still reported due to arrival of infected immigrants or visitors
  – e.g. New York 1947 (visitor from Mexico)
  – 6 million people were vaccinated in one month
  – 12 people caught the disease, 2 died
Global Eradication of Smallpox

- Properties that make smallpox amenable to eradication:
  - Disease is specific to humans
  - No intermediate host, no insect vectors
  - No sub-clinical conditions: cases can readily be identified
  - No latent state, persistence or recurrent infection
  - Only one serotype (strain)
Factors Favouring Global Eradication

AND

No social stigma (as with STD’s and HIV)
Factors Favouring Global Eradication

• Social
  – Recognised by populations worldwide as a serious problem

• Technological
  – Manufacture and transportation of vaccine
  – Communication

• Political
  – UN
  – Biological Warfare
Global Eradication of Smallpox

• Plan to eradicate smallpox proposed to the WHO in May 1958 by USSR. Approved in 1959
• By 1967 10-15 million cases were still occurring annually in more than 30 endemic countries
• January 1, 1967 WHO implemented the Intensified Smallpox Eradication Program
• Based on mass vaccination
A New Approach

• Outbreak in India in 1970 where 80% of the population was immunized (123 dead)
• Africa: Nigeria late 1966 outbreak without sufficient vaccine available. Alternate approach essential:
  – Identification
  – Isolation
  – Tracking contacts
  – Vaccination
• National centred programs
Eradication Program

Technology
- Freeze dried vaccine
- Jet injector
- Bifurcated needle

Surveillance and Tracking
- Education
- Surveillance
- Tracking
- Vaccination
Technology
Education
REWARD - RECOMPENSE

$1000

Smallpox Variola OCPA Vinuela Smittkoppar

The World Health Organization offers a reward of $1000 to the first person reporting an accident or laboratory incident confirming a smallpox or smallpox-like virus isolation. Any person who can provide this information should contact the nearest WHO office.

L'Organisation mondiale de la Santé offre une récompense de $1000 à la première personne qui peut prouver un cas de variola ou d'une variété similaire. Tout le monde qui peut fournir cette information devrait contacter le bureau le plus proche de l'OMS.
Surveillance
Tracking
Vaccination
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**LE DERNIER DIX DANS LES PAYS CONSIDÉRÉS ENRÉMICQUES EN 1967**