Lecture 15: Measles
A bit of Measles history

- Measles infection was distinguished from smallpox as early as the 9th century by an Arab physician by the name of Abu Becr Razi (the Doctor of Baghdad).

- However, there is no record of repeated epidemics identified as measles until the 11th and 12th centuries.

- Measles was first mentioned as a childhood disease in 1224.

- The Danish physician Peter Panum is generally given credit for illuminating the basic principles of measles infection and epidemiology during his trip to the Faroe Islands in 1846 during a measles epidemic.

- Estimated to have killed about 200 million worldwide in the last 150 years.
A bit of virology

- Family Paramyxoviridae, Genus Morbilivirus
- It is 100-200 nm in diameter, with a core of single-stranded RNA, and is closely related to the rinderpest and canine distemper viruses.
- Two membrane envelope proteins are important in pathogenesis. They are the F (fusion) protein, which is responsible for fusion of virus and host cell membranes, viral penetration, and hemolysis, and the H (hemagglutinin) protein, which is responsible for adsorption of virus to cells.
- There is only one antigenic type of measles virus. Although studies have documented changes in the H glycoprotein, these changes do not appear to be epidemiologically important (i.e., no change in vaccine efficacy has been observed).
- Measles virus is rapidly inactivated by heat, light, acidic pH, ether, and trypsin. It has a short survival time (<2 hours) in the air, or on objects and surfaces.
**Epizootic relatives - Rinderpest**

- Rinderpest is the most dreaded bovine plague -- a highly infectious viral disease that can destroy entire populations of cattle and buffalo.

- In regions that depend on cattle for meat, milk products and draft power, rinderpest has caused widespread famine and has inflicted serious economic and political damage.
  
  - Three European “pandemics” in the 18th century
  - An epidemic in the 1890s wiped out 80-90 percent of all cattle in sub-Saharan Africa. (Also took out a lot of wild bovids – about 90% of them)
  - More recently, another rinderpest outbreak that raged across much of Africa in 1982-84 is estimated to have cost at least $500 million.

Source: UN & FAO (fao.org)
**Epizootic relatives - Rinderpest**

- Rinderpest is mainly spread by direct contact and by drinking water that has been infected by the dung of sick animals.
  - It can also be transmitted in the breath and can infect wild animals and pigs as well as cattle.

- Clinical signs include: a high fever; red patches with discharge from around the eyes, nose and mouth; frothy saliva from the mouth; constipation followed by diarrhea. After a few days, the infected animal dies.
  - Rinderpest can be prevented with vaccination but spreads easily among non-vaccinated herds through livestock trade and pastoral migrations.
  - Rinderpest is reportable, and a worldwide eradication effort for 2010 (was 2004) is underway

- Thought to have shaped society in the Nuer people of Sudan in the 1930s
  - Had been pastoralists, cattle as bride prices, Rinderpest changes the price, makes horticulture part of society (Evans-Pritchard research)

Source: UN & FAO (fao.org)
Epizootic relatives – Canine distemper

- Nervous system, respiratory, gastrointestinal; fatal (CDV)
- Vaccine developed in the 1960s reduced a lot of transmission from domestic dogs
- People can catch subclinical CDV – measles vaccine protects against it
- Carnivores transmit by secretions and aerosol
- Introduced into Southern Europe from Peru in the mid 18th century, descendant of Rinderpest.
- Can infect Canids, Mustelids, Pinnipeds, Mephitids, Vivverids, Procyonids
- Domestic dogs give it to Wild dogs and Lions
  - Wild dogs (*Lycaon pictus*) – about 5500 left
    - 49 of 52 in a subpopulation killed in 2 months by CDV in 2000
  - Serengeti – 15- 20% lions died in 1994 of CDV - maybe
Another “Kill Fluffy” issue – but there are vaccines
Epizootic relatives – Canine & Phocine distemper
Overfishing, climate change and crowding

• CDV affects Pinnipeds
  – Caspian seals (the world’s smallest seal)
  – a series of CDV epidemics over the last 10 years has each seen up to 10,000 animals die – out of a total population of only 120,000.

• PDV affects seals
  – PDV was first identified in 1988 as the cause of death of 18,000 harbour seals (Phoca vitulina)
  – and 300 grey seals (Halichoerus grypus) along the northern European coast.
  – Later, epidemics of CDV in Baikal seals in Siberia from domestic dogs (probably)
  – In 2002, an epidemic of PDV along the North Sea coast resulted in the deaths of 21,700 seals, estimated to be 51% of the population.
  – A third virus, Porpoise distemper virus, caused another outbreak in harbor seals

• Feline distemper is not related to these viruses
  – don’t destroy Fifi yet

http://en.wikipedia.org/wiki/Phocine_distemper_virus
Back to people: Measles symptoms

- Disease caused by the measles virus is typically marked by a prodrome of fever, conjunctivitis, coryza, and cough which is followed by the development of a rash of flat macules which first appear on the head and then move to the chest, trunk, and limbs. These macules typically fuse resulting in large blotches that can be slow to fade.
- Children get complications like diarrhea

- According to the WHO, the yearly global incidence of measles is estimated to be 50 million cases, of which 1.5 million are fatal.
  - Healthy populations 1 death per thousand cases
  - Developing nations around 10% mortality
  - In immunocompromised people upto 30% mortality

- Two serious complications of measles infection are acute postinfectious encephalitis, which occurs in about 1 in every 1,000 cases (15% mortality), and subacute sclerosing panencephalitis (SSPE), which occurs in about 1 in every 300,000 cases (fatal).
Measles treatment

- There is no standard antiviral treatment for measles although ribavirin (1-fl-D-ribofuranosyl-1,2,4-triazole-3-carboxamide) has been shown to decrease viral replication in vivo and might decrease the severity of acute measles.

- Vitamin A supplements have been shown to decrease both the morbidity and mortality of acute measles, even if the individual is not suffering from a vitamin A deficiency.

- Finally, numerous agents have been suggested for therapeutic treatment of SSPE but it is extremely difficult to determine their efficacy because SSPE is rare and the benefits of such treatments would only be short-term.
Measles Immunization

- The measles virus was isolated in 1954 by Enders and Peebles.
- One of the first available vaccines was a formalin-inactivated vaccine. Due to the short-term immunity it induced and the risk of atypical measles after exposure to wild measles, the vaccine was discontinued in 1967.
- The first live vaccine, also prepared from the Edmonston strain (named after a young measles victim), was highly reactogenic. At the end of the 1960's, live "further attenuated" vaccines, only slightly reactogenic were produced in the United States, Japan, Yugoslavia, USSR, and China. These are the vaccines that are widely administered today.
- In 1998, a committee of WHO experts put forth an objective to eradicate measles by 2007.
- The final objective of immunization is the eradication of the disease. This ambitious goal appears feasible, particularly in light of the encouraging results of activities in North America to halt the transmission of measles.
- $R_0$ of around 18 means vaccinate 95% of population (okay, so maybe it’s not that high, but coverage goals are necessary)
- How?
Measles Immunization

- In most industrialized countries such as United States, Great Britain, and France, the measles vaccine is combined with the mumps and rubella vaccines (MMR).
- In France, combined MMR recommended at age one for boys and girls.
  - For children attending day-care centers, the vaccine is administered even earlier, at nine months, with a booster administered six months later in combination with the mumps and rubella vaccines.
- A second MMR recommended for all children between 3 and 6 years
  - Second dose addresses vaccine failures, (about 5% to 10% of vaccinated children fail to develop immunity)
- The benefits of the measles vaccine were also reduce neurological complications.
  - In France, the number of cases of encephalitis dropped from 50 per year before immunization to 33 per 545,000 cases of measles reported in 1987.
  - Van Bogaert's subacute sclerosing panencephalitis, which occurs 5 to 10 years after the infection and is always fatal, also declined from 28 cases in 1990 to less than 5 cases per annum since 1990.
Measles Immunization

- In England and Wales, measles reporting began in 1940 – lots of data.
- Before 1968, annual cases varied between 160,000 and 800,000.
- End of the 1980's, reported cases 50,000 and 100,000 per year.
  - immunization coverage was insufficient to stop the spread of the virus.
- Between 1970 and 1988, average of 13 deaths from measles every year.
- Introduction of the triple MMR vaccine in October 1998 and coverage exceeding 90%, the number of cases dropped to all time records.
  - 9,612 cases of measles reported in England and Wales in 1993.
  - Since 1988, 11 measles-related deaths have been recorded.
- In the United States an average of 503,282 cases of measles were reported between 1958 and 1962, of which 432 were fatal.
  - The incidence of measles and the number of measles-related deaths began to decline in 1965, a trend that continued over the subsequent 33 years, except during the epidemics of 1970-72, 1976-78 and 1989-91.
- In 1998, only 89 cases of measles were reported and no deaths.
  - All of the cases in 1998 were either demonstrated to be imported cases or considered as such.
Measles Immunization

• In the United States, in 1984, every dollar spent on measles immunization led to a saving of $10.3 in direct medical costs and $3.2 indirect costs.
  – Similarly, in Finland, the savings accumulated after three years of immunization already exceeded immunization costs.

• Improved measles vaccines, immunization strategies and heightened global surveillance have had a major impact on the incidence of measles over the last twenty years.
  – Before this 130 million cases yearly with about 7 to 8 million deaths.
  – As a result of immunization and an immunization rate of 80% of all infants under one year old, over a million measles-related deaths are avoided every year.
Measles Immunization

• So what’s wrong?
  – People don’t like immunizations – Professor Jones’ lecture
  – Hypothesis that Measles vaccine causes autism
    • 2005 Indiana outbreak from un-vaccinated kids
    • 2000 UK MMR autism scandal – 2006/2007 showing increase in measles in children
  – Endemic measles declared eradicated in North, Central and South America in 2002
  – Lack of vaccination pushes the average age of infection higher

• In France, measles incidence has remained high, between 50,000 and 80,000 cases per year.
  – Immunization rate among two-year-olds fluctuates between 80% and 85%.
  – Insufficient to prevent measles from spreading; > 95% is necessary
  – A shift in clinical cases now affects more adolescents and adults. Measles is a more serious illness for adults and adolescents and usually followed by more severe complications.

• Globally, measles deaths are down 60 percent, from an estimated 873,000 deaths in 1999 to 345,000 in 2005.
  – Africa has seen the most success, with annual measles deaths falling by 75 percent in just 5 years, from an estimated 506,000 to 126,000. (UNICEF)
May 1, 2008: ATLANTA, Georgia (CNN) -- Sixty-four cases of measles have been diagnosed in the United States this year, the most in seven years, according to the CDC.

- Do-able options
  - Give kids shots
  - Give dogs shots

- Save the seas
  - Wait-and-sea?

http://www.cnn.com/2008/HEALTH/conditions/05/01/measles.outbreak/index.html?eref=rss_latest