WHY IS THIS IMPORTANT?

- The world is facing challenges from both new diseases and re-emerging ones.
- Methods of management and prevention can be developed by understanding the dynamics of disease.
- Understanding how once dormant diseases are now re-emerging is critical to controlling the damage such diseases can cause.
GIROLAMO FRASCATORO
Speaking About Syphilis

- “There will come yet other new and unusual ailments in the course of time. And this disease will pass away, but it later will be born again and be seen by our descendants.”
- This quote was written 450 years ago.

INFECTIOUS DISEASE

- Infectious disease has played a prominent role in world history.
  - The Black Death in the Middle Ages killed millions in Europe.
  - Measles destroyed the South American Aztec civilization.
  - Smallpox destroyed indigenous peoples of North and South America.

INFECTIOUS DISEASE

- More than 30 new diseases have been identified in the past 30 years, including:
  - Legionnaire’s disease
  - Acquired Immune Deficiency Syndrome (AIDS)
  - Hepatitis
  - Nipah virus infection
INFECTIOUS DISEASE

- More than 30 new diseases have been identified in the past 30 years, including:
  - Hemorrhagic fevers
  - Severe Acute Respiratory Syndrome (SARS)
  - Creutzfeldt-Jacob disease (CJD)
  - Avian influenza

RE-EMERGING INFECTIOUS DISEASE

- Some diseases are re-emerging after being dormant for more than one hundred years.
  - Tuberculosis
  - Cholera

RE-EMERGING INFECTIOUS DISEASE

- Many of these diseases were thought to be controlled through antibiotics.
  - In some cases the re-emerging disease is resistant to antibiotics.
- In recent years, falling living standards and decline of infrastructure in some countries has aided the re-emergence of some infectious diseases.
EMERGING INFECTIOUS DISEASES

- Emerging infectious diseases are those whose incidence has increased over the past 30 years.
- Some are diseases that have never been seen before.
- Some were previously documented but without a known etiology.

### Emerging Infectious Diseases

<table>
<thead>
<tr>
<th>Disease</th>
<th>Infectious Agent</th>
<th>Year</th>
<th>Contributing Factors</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Lassa fever</td>
<td>Arenaviridae</td>
<td>1969</td>
<td>Urbanization and consequent increased rodent population; increased nosocomial transmission</td>
<td></td>
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<tr>
<td>Ebola hemorrhagic fever</td>
<td>Filoviridae</td>
<td>1977</td>
<td>Unknown reservoir; nosocomial transmission</td>
<td></td>
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<tr>
<td>Legionnaires’ disease</td>
<td>Legionellae pneumophila</td>
<td>1977</td>
<td>Cooling and plumbing systems</td>
<td></td>
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<tr>
<td>Lyme disease</td>
<td>Borrelia burgdorferi</td>
<td>1982</td>
<td>Environments that favor tick and deer populations</td>
<td></td>
</tr>
<tr>
<td>AIDS</td>
<td>HIV</td>
<td>1983</td>
<td>Global travel, intravenous drug abuse, multiple sexual partners</td>
<td></td>
</tr>
<tr>
<td>Cholera</td>
<td>Vibrio cholera 0139</td>
<td>1992</td>
<td>New strain of bacteria with increased virulence</td>
<td></td>
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<tr>
<td>Hantavirus pulmonary syndrome</td>
<td>Bunyaviridae</td>
<td>1993</td>
<td>Encroachment into rodent territories</td>
<td></td>
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<tr>
<td>Cryptosporidiosis</td>
<td>Cryptosporidium parvum</td>
<td></td>
<td>International travel; contaminated water supplies</td>
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<tr>
<td>Diphtheria</td>
<td>Corynebacterium diphtheriae</td>
<td></td>
<td>Interruption of immunization program due to political changes</td>
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<tr>
<td>Influenza</td>
<td>Influenza virus</td>
<td></td>
<td>Genetic re-assortment</td>
<td></td>
</tr>
<tr>
<td>Malaria</td>
<td>Plasmodium species</td>
<td></td>
<td>Drug resistance; inadequate mosquito control</td>
<td></td>
</tr>
<tr>
<td>Pertussis</td>
<td>Bordetella pertussis</td>
<td></td>
<td>Refusal to vaccinate; decreased vaccine efficacy; waning immunity in adults</td>
<td></td>
</tr>
<tr>
<td>Rabies</td>
<td>Rhodovirus</td>
<td></td>
<td>Breakdown in public health measures; travel; changes in land use</td>
<td></td>
</tr>
<tr>
<td>Tuberculosis</td>
<td>Mycobacterium tuberculosis</td>
<td></td>
<td>Antibiotic resistance; increased immunocompromised populations</td>
<td></td>
</tr>
<tr>
<td>Yellow fever</td>
<td>Flavivirus</td>
<td></td>
<td>Urbanization; insecticide resistance</td>
<td></td>
</tr>
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EMERGING INFECTIOUS DISEASES

- 25-35% of the 60 million deaths worldwide that occur each year are due to infectious disease.
- Established, emerging, and re-emerging diseases continue to affect worldwide societies.
- Four patterns of transition have been identified in emerging diseases.
- All four transition mechanisms contribute to rapid spread of emerging and re-emerging diseases.

EMERGING INFECTIOUS DISEASES

- First transition (also referred to as crowd transition)
  - Occurs when people begin to live in much closer proximity to one another
  - Proximity between populations allows for easy transmission of disease

EMERGING INFECTIOUS DISEASES

- Second transition
  - Neighboring civilizations made contact with each other through war or trade
  - Contact allowed the exchange of pools of infectious organisms and vectors between populations.
EMERGING INFECTIOUS DISEASES

- Third transition
  - Worldwide exploration and colonization led to the identification of new populations
  - Newly identified populations came into contact with pathogens never seen before within their cultures.

EMERGING INFECTIOUS DISEASES

- Fourth transition – this is happening today. The ongoing causes are:
  - Global urbanization
  - Increase in population density
  - Poverty
  - Social upheaval
  - Travel
  - Long distance trade
  - Technology development
  - Land clearance
  - Climate change

ENVIRONMENT AND INFECTIOUS DISEASE

- Humans continue to encroach on uncultivated environments.
- This can create an increased risk of contact with new pathogens.
- Examples of diseases encountered as a result of this encroachment are:
  - Hanta virus
  - Dengue fever
**FOOD-BOURNE INFECTION VECTORS**

- As populations grow, there is an increased pressure to produce more meat.
- This has led to the emergence and spread of infections from farm animals to humans
  - *Salmonella* species
  - “Mad cow” disease
  - *E. coli* O157:H7

**GLOBALIZATION AND TRANSMISSION**

- Changing patterns in human behavior and changing ecology contribute to the emergence of infectious disease in two ways:
  - Increased opportunity for animal-to-human transfer because of greater exposure.
  - Increased opportunity for the transmission from one human to another once a person is infected.

- Genetic changes in pathogens can occur through a process known as re-assortment.
  - An example of this is avian influenza.
- Modern air travel disperses pathogens worldwide very rapidly.
- Increasing numbers of immunocompromised hosts presents an increasing number of potential targets.
HURDLES TO INTERSPEcies TRANSFER

- A pathogen must overcome two major hurdles to replicate successfully in a human host
  - Must adapt in such a way that it can replicate in human cells
    - This can be a complex problem for the pathogen.
  - Must be able to configure itself so that it can be easily transmitted from one human to another

Some diseases have overcome the first hurdle but not the second one.
- Hanta virus
- Nipah virus
- Avian influenza

Overcoming these two hurdles requires:
- Extensive genetic mutation
- Genetic re-arrangement
- Genetic re-assortment
- These changes are easier for viruses, which are prone to mutation because of the lack of fidelity in replication (especially RNA viruses).
SARS

- SARS became readily transmissible in the 1990s.
- First documented case was identified in mainland China.
- It is transmitted by droplet aerosol and fomites deposited on the respiratory mucosal epithelium.
SARS: Pathogenesis

- SARS is an infection of the lower respiratory system and symptoms include fever, malaise, and lymphopenia of T cells.
- Twenty to thirty per cent of patients infected with SARS require intensive care and approximately 10% will die.
- The pathogenesis of SARS is due to a high viral load in the lower respiratory tract.

SARS: Host Response & Treatment

- Patients with SARS have elevated levels of cytokines and chemokines.
- There is a prolonged immunological impairment during the disease.
- Therapy includes antiviral drugs but they are only effective if given during the first few days of the infection.

WEST NILE VIRUS

- West Nile virus is caused by an arbovirus (RNA viruses).
- The virus is carried in the saliva of mosquitoes and is transmitted through bites.
- West Nile virus is a member of the Japanese encephalitis group.
- Birds are the primary hosts and the infection is spread from bird to bird by mosquitoes.
WEST NILE VIRUS

- Humans and animals such as horses are incidental hosts
  - They can be infected by mosquitoes carrying the virus.
  - The illness can also be transferred through blood transfusions and transplantation.

WEST NILE VIRUS: Pathogenesis

- Most infected people are asymptomatic unless the infection causes an invasive neurological disease called West Nile Fever.
  - Symptoms include fever, headache, myalgia, and anorexia.
  - Severe infection can cause profound fatigue, myocarditis, pancreatitis, and hepatitis.
  - Particularly severe cases can result in encephalitis or meningitis and death.

VIRAL HEMORRHAGIC FEVER (VHF)

- Emerging infectious diseases classified as VHF include the conditions caused by the Ebola, Marburg, and Yellow fever viruses.
  - VHF, in particular that caused by Ebola and Marburg, is frequently fatal.
  - All of the viruses are single-stranded enveloped RNA viruses.
**VHF: Pathogenesis**

- These viruses are transmitted in diverse ways including both arthropod and rodent vectors.
  - All of the hemorrhagic viruses can be transmitted directly from human to human.
- Symptoms include fever, bleeding, and circulatory shock.

**VHF: Pathogenesis**

- Fatality rates average between 5-20% for all of these viral infections.
  - The Ebola death rate is between 50 to 90%.
- Outbreaks of VHF are often in small remote areas.
- There is currently no successful therapy for VHF infection.

**RE-EMERGING INFECTIOUS DISEASES**

- A number of diseases we once thought were no longer a threat to humans have bounced back in recent years.
- All of them present important challenges to health care workers today.
- Two good examples of re-emerging infectious disease are:
  - Tuberculosis
  - Influenza
TUBERCULOSIS (TB)

• An estimated 2 billion people worldwide are infected with tuberculosis.
• *Mycobacterium tuberculosis* is the causative agent for TB.
• Each year eight million people worldwide are infected with TB.
• It is estimated that 2 million deaths occur worldwide per year.

TUBERCULOSIS (TB)

• TB is still the leading killer of young adults worldwide.
• Minority populations in the US are affected disproportionately by TB.
  • It is nine times more frequent among foreign-born individuals living in the US than in native-born people.

TUBERCULOSIS (TB)

• Antibiotics developed in the 1950s slowed the spread of TB, but by the year 2000, the incidence began to rise.
• Possible causes of the increase in TB:
  • HIV/AIDS epidemic
  • Increased poverty, IV drug abuse, and homelessness
  • Increased immigration of infected individuals
  • Increased elderly population, especially those in long-term care facilities
  • Failure of patients to complete antibiotic treatments.
INFLUENZA

- Influenza is caused by an RNA virus that:
  - Contains eight separate segments of nucleic acid
  - Has high mutation rates that continuously change its characteristics
  - Has two surface glycoproteins, hemagglutinin and neuraminidase, both of which occur in several subtypes.
- The virus has a stable reservoir in aquatic birds.

INFLUENZA

- Several influenza pandemics have occurred throughout history.
  - 1918 - Spanish flu
  - 1957 - Asian flu
  - 1968 - Hong Kong flu
  - 2009 - Swine flu
- Spanish flu in 1918 was the most devastating, causing an estimated 50 million deaths worldwide.

INFLUENZA: Virulence Factors

- The severity of infection depends on the virus and host’s overall health.
- Virulence is determined by gene constellations – clusters of genes that are constantly mutating.
- These mutations influence virulence and mean there is always the potential for increased virulence in future strains.
AVIAN INFLUENZA

- Avian influenza is potentially the most devastating re-emerging disease in the world today.
  - It can be transmitted from animal hosts to humans
  - The infection mutates very rapidly
  - It is capable of spreading at an alarming rate
  - Fortunately, it is not yet easily transmitted between humans.

AVIAN INFLUENZA

- It is more deadly than any other form of influenza.
  - It could be 10 times more dangerous than the Spanish flu.
  - It could have a 50% mortality rate.
  - Avian influenza is resistant to amantadine and rimantadine.
  - It can be easily transmitted to pigs and can use the pig as an “incubator.”
PRIONS AND PRION DISEASES

- These infectious diseases are not caused by microorganisms.
- They are caused by infectious proteins called prions.
- Diseases are called transmissible spongiform encephalopathies (TSE).

PRION HYPOTHESIS

- Prions are proteins normally found on nerve cells and are known as PrP\text{c} (prion protein cellular).
- Infectious prions are folded improperly and are known as PrP\text{sc} (prion protein scrapie).
  - They are routinely found in scrapie (a neurological disease of sheep).

PRION HYPOTHESIS

- Abnormally folded PrP\text{sc} prions:
  - Aggregate into fibrous structures in the brain, referred to as a plaque.
  - Disrupt the cell membrane, causing cell death.
  - Convert normal prions into abnormal prions.
**PRION HYPOTHESIS**

- Prions are practically indestructible.
  - They can withstand cooking.
  - They can withstand autoclaving.
  - They are resistant to strong alkali treatment.
  - They are resistant to disinfectants.
  - They can survive in soil for years.
- Inactivation requires autoclaving in an alkali solution (bleach containing 2% chlorine) for one hour.

**TSE**

- Infective prions can be ingested with prion-containing material.
- These prions can move through the intestinal wall rapidly and enter lymph nodes where they incubate
  - They are picked up by peripheral nerves and moved to the spinal cord and brain.
- Infectious prions can be transmitted between species
  - Incubation time is significantly longer when they cross between species.

**TSE**

- Prions produce transmissible spongiform encephalitis (TSE).
  - It is a neurodegenerative disease.
  - It can affect cattle and humans.
  - There is no test for it in live organisms.
  - There is no treatment.
  - There is no cure.
TSE

- Symptoms include:
  - Lack of coordination
  - Staggering
  - Slurred speech
  - Dramatic mood swings
  - Paralysis
  - Death within one year of symptom onset

TSE

- “Mad cow” disease was first seen in Britain in 1984
  - By the year 2000, there were 180,000 confirmed cases in cattle in Britain.
  - The infection in cattle has been attributed to sheep brain supplement included in cattle feed.

TSE

- First human case documented in Britain was in 1996.
  - To date, there have been more than 120 cases documented in humans.
  - Estimates of the number of new cases in the next few decades vary from a few hundred to 150,000.
BIOLOGY OF TSE

- Biological characteristics of the illness include:
  - A long incubation time
  - Plaque deposits in the brain
  - No antibody response
  - No inflammatory response

- There are five forms of this infection seen in humans:
  - Kuru
  - Creutzfeldt-Jacob disease (CJD)
  - Variant CJD (vCJD)
  - Gerstmann-Sträussler-Scheinker syndrome (GSS)
  - Fatal familial insomnia (FFI).
- The different forms affect different areas of the brain.
In the US, there are new regulations for blood donations.

There are bans on blood donors who resided in the United Kingdom for three or more months between 1980 and 1996.

These bans also apply to anyone residing in Europe for five or more years.

These bans also apply to anyone receiving a blood transfusion in the United Kingdom between 1980 and the present.