Emerging and Reemerging Viral Infectious Diseases

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Learning Objectives

1. Ecology of Emerging & Re-emerging Diseases
2. Public Health Relevance
3. Relevant host-vector-pathogen interactions
4. Ecological, Epidemiological, and Clinical Characteristics
5. Current Approaches to Surveillance
Emerging Infectious Diseases: Historical Context

• 1340: Bubonic Plague “Black Death”: 75 million deaths
  - 30-60% of European population killed
• 1500s: Smallpox to the Americas: 10-15 million deaths
  - End of Aztec civilization
• 20th Century: HIV/AIDS: >50 million deaths

Fig 1: Illustration from the Toggenburg Bible of those afflicted by the Bubonic Plague
Why Emerging Infectious Disease? 1*

- Multiple explanations for the emergence and reemergence of infectious diseases:
  - Climate change
  - Injudicious and widespread use of antimicrobials
  - Bioterrorism (‘weaponization’ of pathogens)
  - Mobile human populations
  - Environmental modification (Legionnaires disease)

*Superscript references can be found at the end of this module
Why Emerging Infectious Disease?

Continued:

- Human population encroachment on wilderness (vector populations)
- Concentration of human populations
- Dispersal of vectors (and pathogens) through trade, transport, migration
- Immuno-compromised populations
The State of Emerging Infectious Diseases

- Analysis of 335 “EID Events”: 1940 to 2004
- Control for geographic and historical reporting bias
- EIDs dominated by zoonoses (60% of EIDs)
  - 71.8% of zoonoses arise in wildlife
- Viral EIDs: 25% of all EIDs
- Vector borne EIDs: 23% of EIDs: significant recent rise
- Threat of EIDs is increasing
- Non-random geographic distribution of EIDs

The State of Emerging Infectious Diseases Continued.

- Antimicrobial resistant EIDs: 20.9% of EIDs
  - attributable to increase in antimicrobial use
- Zoonotic EID events correlate with geographic wildlife diversity
  - No correlation with population growth
- Zoonotic non wildlife EIDs: predicted by human population density/growth
- Vector borne EIDs: No correlation with rainfall, human population or wildlife diversity
- Human population density independent predictor of EID events

This graphic demonstrates the geographic distribution of detected EIDs portraying the trend that EIDs are largely detected once they have reached Europe and the US, while their geographic origins are shown in the following slide. The size of each circle is proportional to the number of EID events.
Fig 3: Global EID Risk Distribution: a) zoonoses from wildlife, b) zoonoses from non-wildlife, c) drug resistant pathogens, d) vector borne pathogens. Jones et al.

This slide demonstrates the regions at most risk for the development of EIDs based on the historical sample in this study. The upper left box (a) shows zoonotic pathogens from wildlife. Box b (upper right) zoonotic pathogens from non-wildlife. Box c (lower left box) drug resistant pathogens, and lastly box d (lower right hand box) demonstrating vector borne pathogens.
Selected Emerging Viruses of Public Health Significance

- SIV/HIV
- Viral Hemorrhagic Fevers
  - Filoviruses
  - Arenaviruses
  - Bunyaviridae
- Flaviviruses (Yellow Fever, Dengue, West Nile)
- Emerging Respiratory Pathogens
  - SARS
  - Avian Flu
Lentiviruses: SIV and HIV

- SIV/HIV: retroviruses (RNA viral genome converted to DNA via enzyme reverse transcriptase)
- Simian Immunodeficiency Viruses (SIVs) are the origin of Human Immunodeficiency Viruses (HIV 1,2)
- Origin of HIV 1: SIVcpz (Chimpanzee: \textit{Pan troglodytes troglodytes})
- Origin of HIV 2: SIVsm (Sooty Mangabee: \textit{Cercocebus atys})
- SIVcpz/SIVsm cause no discernable disease in their hosts
- SIVcpz and SIVsm have existed for millennia

HIV-1 and HIV-2 are direct descendants from SIVcpz (Chimpanzee) (Cameroon, Gabon, DRC, central Africa) and SIVsm (Sootey Mangabey) (Sierra Leone, Liberia). SIVcpz and SIVsm have existed for thousands of years and no longer cause discernable disease in their hosts. However, these same viruses cause lethal immunodeficiency in other primates, particularly Asian Macaques. It is likely that humans have had contact with these viruses for an extensive period of time. However, HIV is likely a fairly new pathogen as HIV was not carried to the New World with the estimated 10 million slaves that were forcibly transported to the Americas. Evidence suggests that HIV developed within the past 100 years. It is unknown what behavioral, societal or biological factors contributed to the emergence of these cross species transmission events in the last century. It is as well unknown if these factors are still in existence and could therefore contribute to the emergence of further epidemic or pandemic subtypes of HIV.
Lentiviruses: SIV and HIV $^{4,5}$

- Human contact with SIVs is likely longstanding (> 1000 years) through hunting and butchering of Non-Human Primates (NHPs) for food
- Despite longstanding human SIV exposure: epidemic HIV only emerges only in last 60 years
- No HIV brought to the New World with >10 million African slaves
- Unclear mechanism of cross species transmission and origin of epidemic HIVs
- 11 individual cross species transmission events documented (HIV-1 subgroups M,N,O and HIV-2 subgroups A-G) in mid twentieth century
SIV and HIV:

- Cross species transmission events may be ongoing
- 33 species of Non-Human Primates (NHPs) harbor their own SIV species
- Hunting and butchering of NHPs for food common in central Africa
- SIVs isolated from bushmeat prepared for human consumption
- Ancestral strains of HIV-1 persist in wild chimps
- Precedent of laboratory worker acquired SIV infection
- 12 of 16 SIVs capable of infecting human lymphocytes in vitro

Fig 4: Bushmeat: Source: www.bonoboincongo.com
SIV and HIV: Human SIV Exposure

- Cameroonians (HIV 1 & 2 -) with reported history of high, medium and low levels of exposure to NHPs and bushmeat tested for presence of SIV antibodies
- Findings:
  - 17.1% reactive in high exposure group
  - 7.8% exposure in low exposure
  - 2.3% in the general population
- Conclusion: Humans are exposed and possibly infected with SIVs
- Implications: blood supply safety, further emerging zoonotic lentiviral epidemics/pandemics


Although a significant portion of the general population is positive for SIV antibodies, no SIV viral nucleic acid has been isolated from human blood. This may indicate that the SIVs that have produced antibody responses in humans, are non productive or at least not capable of producing chronic infection.
Viral Hemorrhagic Fevers (VHFs)

- Enveloped RNA viruses of diverse families
- May be arthropod borne with multiple, different animal reservoirs
- Symptoms and disease severity vary widely
- Precedent of international travel transporting viruses into non-endemic countries
- Precedent for nosocomial outbreaks involving healthcare workers and laboratory personnel
Distinct VHF Families

- Filoviridae
  - Ebola
  - Marburg
- Arenaviridae
  - Lassa Hemorrhagic Fever
  - South American Hemorrhagic Fevers
- Bunyaviridae
  - Rift Valley Fever
  - Crimean Congo Fever
VHF: Clinical Factors

- Initial symptoms nonspecific - incubation period of 2-14 days
- Severe sore throat, abdominal pain, progressive fever, vomiting and diarrhea (bloody), easy bruising and bleeding
- Conjunctival injection and non-pruritic torso rash
- Multi-organ hemorrhage and failure with widespread necrosis and microvascular thrombosis
- Uncontrolled activation of systemic inflammatory and coagulation pathways
- Ebola and Marburg: most severe with mortality 25-100%
VHF: Filoviridae: Ebola

- Ebola (5 species)
  - Sudan
  - Zaire
  - Ivory Coast
  - Reston Agent
  - Uganda
- First appearance in 1976
- Sporadic outbreaks

Fig 5: Electron micrograph of Ebola virus:
Photo Source: Dr. F.A. Murphy
VHF: Ebola: Documented Outbreaks\(^9\)

- Zaire sp.: 9 outbreaks
  - Mortality: 57-88%
- Sudan virus: 4 outbreaks
  - 50% case fatality rate
- Ivory Coast: two individuals (one survived)
- Uganda: 1 outbreak (2005)
  - Different symptom profile: 31% case fatality rate
- Reston Agent: No documented epidemics in humans
  (epidemic in captive laboratory primates)
VHFs: Filoviridae: Marburg $^9,^{10}$

- All isolates considered single species
- Varying pathogenicity (mortality ranging from 21-80%)
- Responsible for 1967 outbreak in Europe
- Outbreaks in 2000 in Democratic Republic of the Congo and 2005 in Angola

Figure 2: Electron micrograph of Marburg Virus.  
Photo Source: Centers for Disease Control and Prevention
VHFs: Ebola and Marburg: Epidemiology

- Disease burden in comparison to HIV/Malaria/Tb is small
- Total number of identified cases <3000
- Increasing frequency of outbreaks in sub-Saharan Africa
- Significant ongoing outbreaks in wild (endangered) non human primate species (chimpanzees)
- Unknown natural reservoir: primates likely secondarily infected (bats suspected to be reservoir)
- Diagnosis: Currently ELISA viral antigen or PCR based field techniques (antibody response can be muted)

Viral hemorrhagic fevers, including Ebola and Marburg have been implicated in several epidemics amongst endangered non-human primate species including gorillas and chimpanzees. Surveillance for primate illness has been suggested as a method for detecting emerging VHF epidemics prior to significant human infections.

ELISA: Enzyme Linked Immunosorbency Assay is a method for detecting antigens and antibodies specific to particular pathogens in blood or other body fluids. PCR: Polymerase Chain Reaction is a laboratory method for amplifying potentially minute amounts of viral nucleic acid from body fluids.
VHF: Ebola and Marburg: Transmission $^{9,13,14}$

- Person-person spread: contact with infected fluids
- Corpse preparation a risk factor for exposure
- Sexual transmission: documented but likely rare
- Droplet infection via mouth or eyes
- Aerosol spread documented in animals (likely minimal role of respiratory spread in epidemics)
- No evidence for mosquito or arthropod spread
- Animal to human transmission: dead primates butchered and eaten
VHF: Ebola and Marburg: Transmission

- **Nosocomial Transmission:**
  - Syringe reuse/contaminated blood products
  - Explosive and exponential outbreaks
  - Exposure during procedures and care giving
  - Exposure during preparation of bodies for burial
  - Extremely variable rates of health care worker infection

- **Epidemic “burnout”:**
  - Short incubation period
  - Precipitous progression of disease and death
  - Extreme clinical manifestation and symptoms
  - Limited means of transmission
VHFs: Ebola and Marburg: The Reservoir Hunt $^{13,14}$

- Traditionally infectious disease causes mild or no disease in reservoir species
- Primates succumb to HF after infection
- No definite reservoir or vector identified
- Epidemic and vector control hampered by lack of clear reservoir animal
- Evidence for fruit bats as possible reservoirs (asymptomatic hosts)
  - Experimentally infectable
  - Bats strongly present in epidemic environments
  - ~5% of 3 species of fruit bat have Ebola IgG in epidemic and non-epidemic areas
VHFs: Ebola and Marburg: Infection Control

  - [www.cdc.gov/ncidod/dvrd/spb/mnpages/vhfmanual.htm](http://www.cdc.gov/ncidod/dvrd/spb/mnpages/vhfmanual.htm)
- Universal precautions are sufficient to prevent transmission –
  - N-95 masks or respirators
  - Gowns, face shield, rubber boots, double glove
  - Triton X decontamination of all medical, laboratory equipment and surfaces
- Private rooms with negative pressure for patients (if available)
- Restrict access to infected or exposed patients
VHFs: Ebola and Marburg: Infection Control

- **Low Resource Isolation:**
  - limit access to suspected cases
  - separate from general patient population
  - isolate early
  - limit staff in isolation area
  - isolated toilet
  - changing room
  - adequate ventilation
  - screened windows

- **Low Resource Waste Disposal**
  - 1/10 and 1/100 bleach solutions after cleaning with soap solution for reusable equipment
  - liquid waste, laboratory samples, and used disinfectants: discard in isolated latrine
  - solid waste, disposable medical equipment: burned (diesel fuel)
  - cleaning and waste disposal staff: personal protective equipment
VHF: Vaccine Development

- Pan-filovirus vaccine under development
- Live attenuated viruses risk possibility of reversion to pathogenicity
- Adenovirus vector expressing multiple filoviral antigens
- Inoculation of nonhuman primates at 1,000 times lethal dose
- 100% protection against infection by 2 species of Ebola virus and 3 Marburg virus subtypes
- Utility for biodefense and epidemic preparation: early epidemics typically undifferentiated

VHF: Ebola and Marburg: Treatment

- Treatment:
  - Supportive care
    - Respiratory support
    - Reversal of coagulopathy
  - Limited role for convalescent sera
  - No role for ribavirin
  - Post-exposure prophylaxis for exposed patients:
    Research underway
    - Interferons: Research underway

Ribavirin is an anti-viral medication useful in treating some viral infections (Lassa) it has not been shown to be useful in Ebola Marburg or HIV infections. Interferon is a man-made molecule (cytokine) that plays a central role in the immune response to viral infection.
VHFs: Reston Agent

- Considered an Ebola species
- Possible animal reservoir- Philippine Islands
- Outbreak amongst non-human primates in quarantine facilities in US leading to widely fatal hemorrhagic fever in captive primates
- Unclear human pathogenicity
- Unclear role of airborne or droplet spread in primate outbreaks
VHF: Filoviridae: Marburg and Ebola - Summary Points

- Potential for global spread via transportation networks
- Limited large scale epidemic potential given short incubation period, severity of illness and limited transmission patterns
- Likely bat reservoir species
- Potential for impact on non-human primate populations
- Concerning for severe illness in returned travelers from central Africa (and the Philippine Islands?)
- Limited treatment options
- Concern for development as bioterrorism agents
VHFs: Arenaviruses

- Enveloped RNA viruses
- Hemorrhagic disease is typical
- Generally rodent transmitted disease
- Rodents have no apparent illness
- Incidental human infection via contact with infected rodent urine or feces
- Contact with infected material typically from agricultural work or rodent infestation of homes or other buildings
- Documented nosocomial and person to person spread
VHF: Arenaviruses

- Hemorrhagic febrile syndrome
- Variable case infection and mortality rates
- Old World Arenavirus:
  - Lassa Fever (West Africa)
- New World Arenaviruses:
  - South American Hemorrhagic Fevers

Fig. 5: New World Arenavirus particles budding out of an infected cell: Source CDC
Arenaviruses: Lassa Fever

• Localized to West Africa although travel has resulted in cases in Europe and North America
• Discovered in 1969
• Likely asymptomatic/mild disease in ~80% of infected
• Can manifest outbreaks with case fatality rates of 50%
• Estimated 100-300,000 cases/year in West Africa
• Significant contribution to population mortality in selected communities in Nigeria, Sierra Leone
• Diagnosis: ELISA for Lassa IgM or Lassa Antigen, PCR
  - substantial population with prior exposure (IgG)

IgM and IgG are two types of antibodies produced by B cells to combat infection. IgM (Immunoglobulin M) is typically produced early in infection and as the infection progresses the antibody response shifts and IgG (Immunoglobulin G) antibodies become prominent. IgG responses are typically more specific to the pathogen antigens than IgM responses. The IgG response may be lifelong and as such IgG positivity may reflect prior exposure, rather than acute infection, which is typically suggested by the presence of IgM. Acute and convalescent sera is another means for detecting acute infection. Serum is drawn at the onset of illness and antibody response and then is measured again after several days. An interval increase in the IgM or IgG response during this time is suggestive of acute infection.
Arenaviruses: Lassa Fever: Transmission

- Vector: Rodents: *Mastomys* genus
- Transmission occurs with human contact or inhalation of infected rodent urine and feces
- *Mastomys* sometimes consumed as food source
- Nosocomial transmission via contact with infected medical equipment

Fig 6.: Lassa virions (arenavirus).
Source: CDC
Arenaviruses: Lassa Fever: Clinical Notes

- Incubation period lasts 1-3 weeks
- Symptoms:
  - High Fever
  - Retrosternal Pain
  - Neurologic Deficits
  - Liver inflammation
  - Conjunctivitis
  - Vomiting
  - Hemorrhage
  - Sore throat
- Complications: Deafness (may occur with mild or serious infection)
- Prognosis: Mortality: 15-20% of symptomatic cases but only ~1% of overall cases
Lassa Fever: Prevention and Treatment

Prevention:
• Safe food storage
• Rodent control
• Wet down surfaces prior to sweeping
• Lassa vaccine (?)

Treatment:
• Ribavirin (early treatment improves survival)
• Supportive care
• Correction of coagulation abnormalities, resuscitation

Fig.: 7 African Countries endemic for Lassa Fever
Ribavirin for Lassa Fever

• Sierra Leone, 1986
• Study of therapy/prognostic factors in Lassa Fever
• Findings:
  - Elevated aspartate aminotransferase (AST) > 150 IU/L at admission associated with 55% mortality rate
  - Viremia ≥ 10(3.6) TCID50 per milliliter on admission associated with a case-fatality rate of 76%
• Intravenous ribavirin within first 6-7 days of fever associated with reduced mortality (5-9% vs 55-76%)

Lassa Fever: Effective therapy with ribavirin. McCormick JB, King IJ, Webb PA. 
Arenaviruses: South American Hemorrhagic Fevers (HFs)

- Viruses:
  - Machupo (Bolivia HF)
  - Junin (Argentine HF)
  - Guanarito (Venezuelan HF)
  - Sabia (Brazilian HF)
- As with other arenaviruses:
  - rodents serve as vector
  - significant hemorrhage
  - rural populations and farmers frequently infected
  - documented nosocomial & occupational spread (Machupo/Sabia)

Fig 6: Victim of Bolivian Hemorrhagic Fever. Photo Source: www.medicineworld.org
Arenaviruses: South American HFs $^{21,22}$

- Case infection rate of 50% of exposed (overall)
- Mortality: 15-30% of those infected (overall)
- Symptoms similar to Lassa Fever with significant neurologic manifestations
- Live, attenuated Junin virus vaccination in Argentina: reduced incidence to less than 100 cases per year
- Significant success with vector control efforts
VHF: Bunyaviruses

- Enveloped RNA viruses
- Largest family of viruses with >200 species
- Diagnosis: Antigen detection and serological tests available although virus isolation and PCR useful
- Most bunyaviruses require an arthropod vector (exception: Hanta)
- Humans are usually dead end hosts
VHF: Bunyaviruses

- Crimean Congo Hemorrhagic Fever
  - Bulgaria, Yugoslavia, former Soviet Union, China, Middle East, Pakistan, and sub Saharan Africa
  - Infection rate: 20-100% with case fatality rate: 15-30%
  - Most severe bleeding and ecchymoses of VHF
  - Transmitted via tick bite (*Hyalomma* genus) or exposure to aerosols or fomites of slaughtered livestock
  - Nosocomial outbreaks documented
  - Human vaccine available
  - Vector control efforts of primary importance
VHF: Bunyaviruses

- Rift Valley Fever
  - South Africa, Kenya, Uganda, Sudan, Egypt, Mauritania
  - Appears as epizootics in sheep, cattle, camels, goats
  - 1% infection rate of exposed with mortality rate of 50%
  - Retinal vasculitis that may cause blindness
  - Transmission: mosquito or contact with infected livestock blood
  - No interhuman transmission documented
  - Animal (sheep and cattle) vaccine available to break transmission cycle
Flaviviridae

- Wide range of clinical symptoms (including hemorrhagic fever)
- RNA viruses
- Insect borne (arthropod borne)
- Main human pathogens:
  - Yellow Fever
  - Dengue
  - West Nile Virus
  - Encephalitic Viruses (Japanese, St Louis, Tick Borne Encephalitis)
Flaviviridae - Transmission

- Human to human transmission noted for Dengue, Yellow Fever, and West Nile
- Humans are typically dead end hosts
- Animal infection as well, but likely dead end (NHP)
- Tick and mosquito vectors

Fig 6: Aedes sp mosquito taking a blood meal. Photo Source: www.aedesmosquito.com
Flaviviruses: Yellow Fever $^{25,26,27}$

- Single serotype RNA virus
- Yearly incidence: 200,000 cases (90% in Africa) with 30,000 deaths
- Distribution: Sub-Saharan Africa, South America, Central America, Caribbean
- Possible differences in mortality and epidemic incidence between African and South American Yellow Fever
- *Aedes* sp. mosquitoes infect primates & humans
Yellow Fever: Distribution

Fig 7: Yellow Fever distribution in South America and Africa (red areas).
Photo Source: www.geo.arc.nasa.gov
Yellow Fever Transmission Cycles

- **African Yellow Fever (Old World)**
  - Jungle: Virus circulation between NHPs (no effect) and humans (dead end hosts)
  - Intermediate: Small simultaneous epidemics in many small villages
  - Urban Yellow Fever: Human-human transmission can occur in populated/urban areas (mosquito transmission)

- **South American Yellow Fever (New World)**
  - Introduction of virus from Africa within 500 years
  - Haemagogus and Sabethes species of mosquito
  - S. American monkeys die following infection
  - Similar jungle and urban transmission cycles to that of African YF (no intermediate cycle)
Yellow Fever: Clinical Points

- Symptoms range from asymptomatic to life threatening shock, liver/kidney failure and hemorrhage
- Highest disease severity in elderly
- 3 distinct clinical phases:
  - **Period of Infection**: viremia, fever, acute illness (3-4 days), relative neutropenia
  - **Period of Remission**: potential recovery and clinical improvement (2 days)
  - **Period of Intoxication**: 15% progress to intoxication with hemorrhage, multi-organ failure (20% mortality)
Yellow Fever: Diagnosis and Treatment

- **Diagnosis:**
  - Can be confused clinically with Dengue, other VHF, viral hepatitis, severe malaria
  - ELISA for IgM (acute and convalescent sera) cross reactivity with other flaviviruses confuses diagnosis
  - Viral isolation: PCR, viral culture (special cases only)

- **Treatment:**
  - Supportive and symptomatic care
  - Unclear role for hyperimmune globulin
  - Animal evidence: ribavirin or interleukins
Yellow Fever Vaccination

- Effective attenuated vaccine available since 1936
- 95% vaccine seroconversion rate
- Recommended for travelers or residents of endemic areas (required for entry to some nations)
- Few adverse effects (two serious clinical syndromes)

Fig 7: Yellow Fever vaccination. Photo Source: Author
Yellow Fever Vaccine Adverse Effects

- **YEL-AND**: YF Vaccine Associated Neurotropic Disease
  - Viral presence in CSF after vaccination
  - Historically in children < 9 months but can affect adults
  - Symptoms consistent with viral encephalitis
  - Incidence: 1.8-5.1/million

- **YEL-AVD**: YF Vaccine Associated Viscerotropic Disease
  - Symptoms consistent with wild type Yellow Fever Infection with identical mortality
  - 2.2/million but higher in elderly
  - No viral mutations identified, likely determined by host susceptibility factors, immunodeficiency, thymus removal (primary vaccination, >65 years old)
Flaviviridae: Dengue Fever $^{25,28}$

- Most prevalent mosquito ($Aedes$ sp.) borne viral disease
- Greater than 100 million dengue infections yearly
- Wide range of clinical symptoms (mild to severe)
- 4 separate viruses (DEN 1-4)
- Weak cross reactivity between subtype antibodies allows multiple infections with different subtypes
- Range of symptoms from mild to severe
Dengue Fever: Clinical Points #1 \(28,29,30\)

- Symptoms: Asymptomatic to life threatening shock and hemorrhage
- Severity may be inversely proportional to age
- Incubation period of 4-7 days
- Laboratory: transaminitis (elevations in liver function tests), leucopenia, thrombocytopenia
- Symptoms:
  - Fever
  - Retro-orbital pain
  - Headache
  - Muscle and joint pain ("Break Bone Fever")
  - Rash - may be late
Dengue Fever: Clinical Points #2

- Diagnosis: clinical diagnosis or IgM ELISA with paired acute and convalescent sera
- Treatment: Supportive care, avoid NSAIDs (Reyes Syndrome), fluid replacement
- Prevention: Mosquito control, tetravalent Dengue vaccine (in development)
- Dengue Hemorrhagic Fever (DHF)
  - Severe manifestation of Dengue infection
  - Secondary exposure to different Dengue subtypes
  - Circulatory failure, hemorrhage and shock
Dengue Fever: 2 Transmission Patterns

Epidemic Dengue
- Introduction of single viral subtype as isolated event
- Large susceptible populations: explosive transmission (25-50% incidence during epidemic)
- Predominant in small islands
- Low infection risk for travelers, except in epidemics
- DHF frequency low

Hyperendemic Dengue
- Continuous transmission of multiple subtypes in same area
- Year round presence of susceptibles and mosquitoes
- Majority of Dengue infections
- 5-10% of the susceptibles are afflicted annually
- Seasonal variation
- DHF frequency higher
Flaviviridae: West Nile Virus $^{31,32,33}$

- First isolated in West Nile Province of Uganda in 1937
- 1999: 62 cases of encephalitis and 7 deaths
- WN Virus now detected across North America, Caribbean and South America
- Nearly all human infections due to mosquitoes (*Culex*)
- Virus maintained/amplified in bird-mosquito-bird cycle
- Birds usually asymptomatic, with exceptions of native bird deaths in North America (crows) and elsewhere
- Transmission documented from infected blood products and organ transplantation (screening now in place)
West Nile Virus: Clinical Points $^{32,34,35}$

- **Symptoms**
  - 80% infections asymptomatic
  - Immunity after infection thought to be life long
  - Peak in late summer/early fall (mosquito cycles)

- **West Nile Fever**
  - Self-limited febrile illness (fatigue, fever, headache, rash)
  - Indistinguishable clinically from other viral illnesses
  - Symptoms can last up to 30 days

- **Neuroinvasive Disease**
  - Only 1 in 150 infections (2-12% case fatality rate)
  - Encephalitis, meningitis, flaccid paralysis, cranial nerve palsies
  - Associated with old age, diabetes and alcohol abuse
West Nile Virus: Diagnosis & Treatment

- **Diagnosis**
  - ELISA for IgM antibody (plasma or CSF)
  - IgM may appear after 8 days of infection and may persist for 6 months
  - Viral isolation: Viral culture, PCR (not routine)

- **Treatment**
  - Supportive care
  - In vitro and animal evidence for interferon alfa efficacy
  - Ribavirin: not proven and possibly detrimental in animal models
  - Possible role for IV immunoglobulin (unstudied)
Emerging Respiratory Pathogens: SARS $^{36,37,38}$

- Severe Acute Respiratory Syndrome
- 2003: Severe, progressive respiratory infection in Hong Kong, China, Viet Nam, Singapore, Taiwan, Canada
- First ever WHO travel advisories: Guangdong Province China, Hong Kong, Taiwan, Hanoi, Singapore
- Contagion identified as a new Coronavirus
- Significant number of health care worker infections
- 9 cases due to viral research: National Institute of Virology, Beijing
SARS: WHO Case Definitions

- **Suspected Case**
  - Fever >38 deg C plus
  - Cough or respiratory distress plus
  - Contact with a SARS patient, travel/residence in affected area

- **Probable Case**
  - Suspected Case + x-ray evidence: pneumonia, or ARDS
  - Suspected Case with positive SARS diagnostic testing
  - Fatal respiratory illness with evidence of ARDS without other etiology
SARS - Epidemiology

- First cases in Guangdong Province China
- Most cases in adults with higher mortality in elderly (43% case fatality > 60 years old)
- Likely milder disease in children with no fatal pediatric cases documented
- 2003 outbreak: 8422 cases with 916 deaths (case fatality rate of 11%)
- Reservoir: Horseshoe bats harbor viruses with identical sequence to SARS/Molecular similarity to civets (cat-like animal) coronavirus
- Transmission likely via droplet (high rate of nosocomial spread) and possibly airborne
SARS: Clinical Points

• Prodromal Phase: fever, myalgias, malaise
• Respiratory Phase: 3-7 days: non productive cough, respiratory failure
• Poor Prognostic Factors
  - Diabetes
  - Acute Renal failure
  - Elevated serum LDH
  - Older age
  - Comorbid conditions

• Diagnosis:
  - Serology: ELISA (acute and convalescent sera)
  - Viral isolation: PCR

• Treatment: Supportive care (critical care and ventilatory support)
  - No proven anti-viral therapy
  - Interferon alfa may decrease symptom length (animal model)
SARS: Prevention

- Avoidance of exposure and infection control for suspected cases and contacts
- Infection control difficult as not all patients require hospitalization
- Voluntary measures to avoid exposing others
- Closing of facilities (e.g., schools, hospitals, clubs) and quarantines, travel advisories
- Strict adherence to infection control practices in hospitals (droplet and airborne precautions)
- Avoid respiratory procedures
Emerging Respiratory Pathogens: Avian Flu

- Avian Influenza H5N1 endemic among bird and poultry in Asia
- Spread via migratory birds
- Sporadic transmission to humans
- Concern for exchange of genetic material with co-infecting human influenza viruses-new epidemics
- For further information please see the GHEC Module entitled: *Emerging Infectious Disease: Focus on Avian Influenza*
Summary: Emerging and Reemerging Viral Infectious Diseases

- Multiple biological, behavioral, ecological factors contributing to the emergence and reemergence of viral infectious diseases
- Multiple EID hotspots exist globally
- SIV/HIV
- Viral Hemorrhagic Fevers
  - Filoviruses
  - Arenaviruses
  - Bunyaviridae
Summary

• Flaviviruses
  - Yellow Fever
  - Dengue
  - West Nile
• Emerging Respiratory Pathogens
  - SARS
  - Avian Flu H5N1
• Other viral pathogens not covered in this module:
  - Hanta virus
  - Hepatitis C
  - Viral Encephalitidies
  - Resistant pathogens (HIV)


References


Credits

• **Joseph U. Becker, MD:**
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