Emerging and Re-emerging Viral Infections

Prof. Alison Kesson

alison.kesson@health.nsw.gov.au

Emerging and Re-emerging Viral Infections

- What are they
- Why do they occur
- How to diagnose them
- Therapeutic options
- Infection Prevention and Control

Infectious Disease Threats

- The rapid pace of microbial evolution enables pathogens to overcome human defences, exploit human behaviours, and elude control efforts across our highly connected world.
- Though the incidence of endemic diseases that are major killers of children and young adults has declined significantly since the 1990s—respiratory tract and diarrheal diseases, vaccine-preventable diseases, HIV/AIDS,—new threats continue to emerge and spread.
- Emerging and re-emerging infections (EIDs) have become more evident in recent years.

2002	Dengue	Americas
2002	SARS CoV	Worldwide
2005	Chikungunya virus	India
2006 2008	Rift Valley fever	East Africa
2009 – 2010	H1N1 Influenza A	Worldwide
2010	Dengue	Americas
2012 – ongoing	MERS – CoV	Middle East
2013 – 2014	Dengue	Southeast Asa
2015 -2016`	Zika	Pan-Americas
2013 2016	Ebola	West Africa
2013 2015	Chikungunya virus	Americas
2016	Yellow fever	Africa
2018	Nipah	India
2018 – 2020	Ebola	Africa
2019 -2020	Dengue	Americas
2019 - ongoing	SARS CoV2	Worldwide

Definitions

- An “emerging infection” is either a new infection that has never occurred before or a known infection that has a recent increase in prevalence.

- A “re-emerging infection” is a familiar infection that recurs. Influenza A pandemics (1918, 1957, 1668, 2009) are examples of re-emerging infections.

Why do they occur?

- The occurrence of EIDs is influenced by a variety of factors
  - Human behaviours
  - Microbial adaptation
  - Ecology – vector ecology
  - Globalisation of food supply
  - Public health infrastructure
- Often associated with
  - Increases in human population – increased urbanisation
  - Overcrowding in cities with poor sanitation – poor management of water and sewage systems
  - Increased exposure of people to microbial carrying vectors
  - Fast and intense international travel
  - Changes in handling or processing food

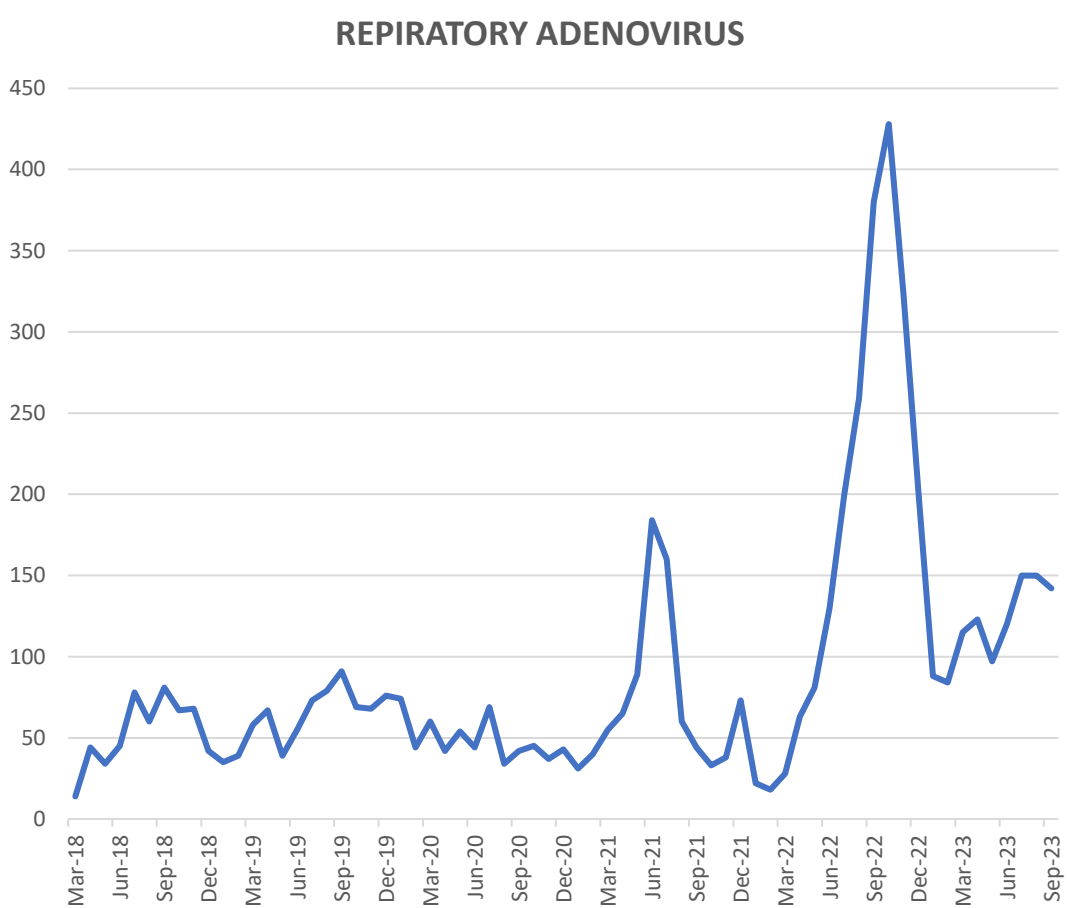
Zoonotic Infections

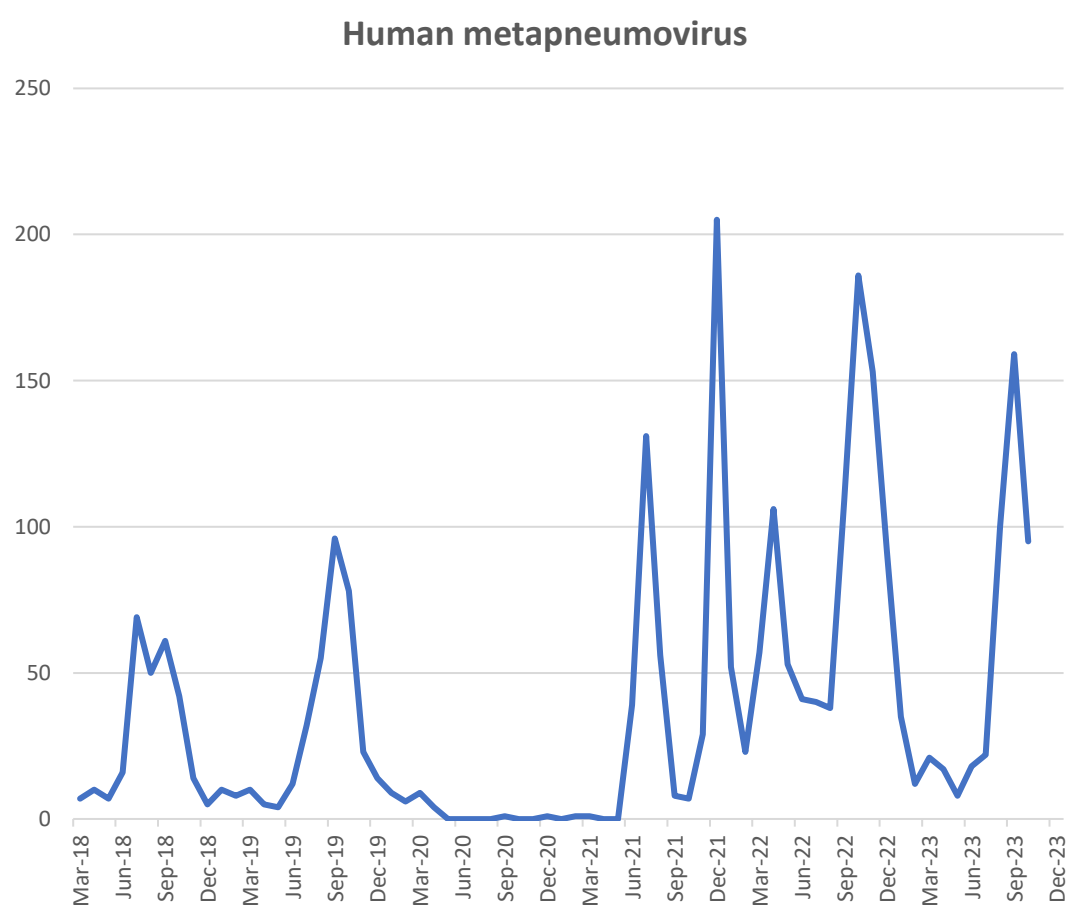
- Zoonotic pathogens are responsible for many severe human infections
  - Avian influenza A(H7N9) virus
  - Middle East respiratory syndrome (MERS) in Saudi Arabia;
  - Monkeypox in the Central African Republic
  - Zika outbreak in the Americas

Respiratory Infections

- Respiratory infections - dynamic areas for emerging and reemerging diseases.
- newly recognized pathogens IN 21ST century
  - human metapneumovirus (identified in 2001)
  - the coronavirus associated with SARS (identified in 2003)
  - human bocavirus (identified in 2005)
  - pandemic influenza A(H1N1) (identified in 2009)
  - Middle Eastern novel coronavirus (identified in 2012)
  - Two additional coronaviruses (NL63 and HKU1)
  - Novel human polyomaviruses KI and WU
  - Rhinovirus groups C
  - Parechoviruses
- although in some instances the role of these agents as pathogens is still being clarified.

CHW - prevalence



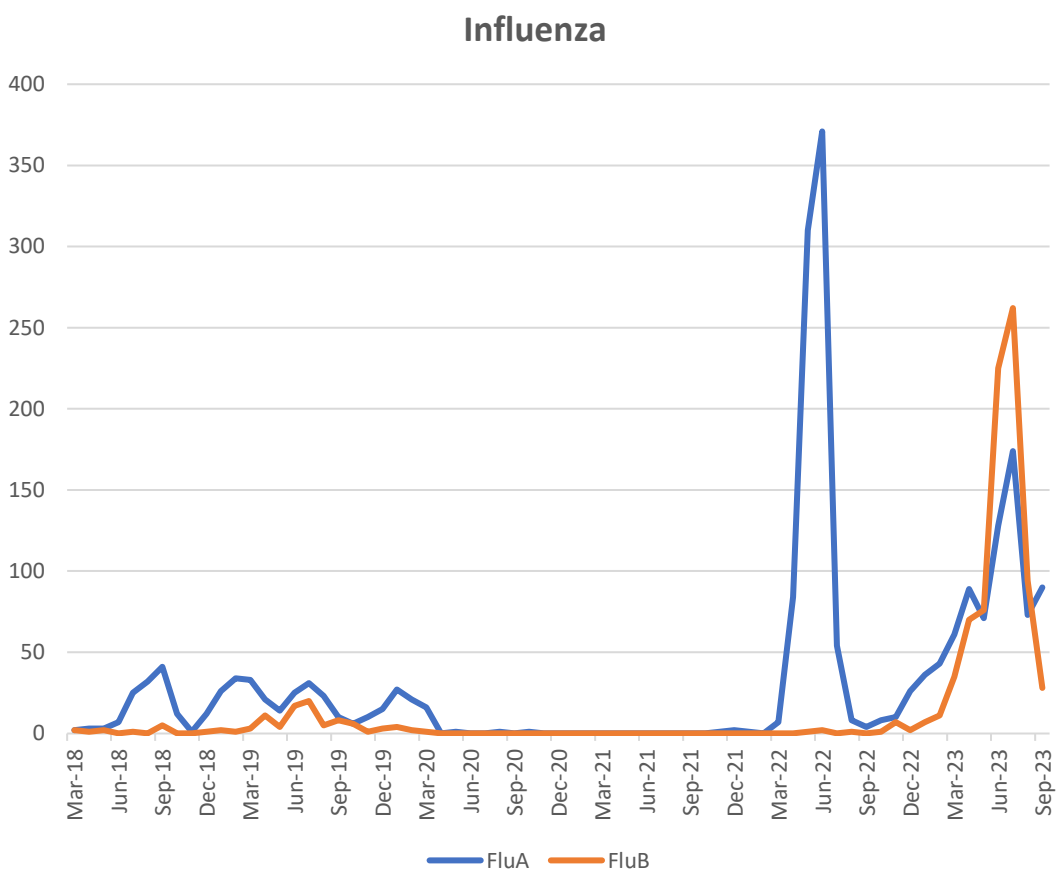


Influenza

- Influenza viruses are one of the most challenging infectious diseases for clinicians, public health and agricultural officials.
- The viruses are constantly changing - drift and shift , spread rapidly in populations, and can cause significant illness.
- Of the four main types of influenza viruses—A, B, C, D—only influenza A viruses circulate in multiple animal (birds and pigs) and human reservoirs, sometimes spilling over to cause illness in other species and adapting and exchanging genes (shift) to generate new influenza viruses with potential to cause pandemics.

Influenza

- In the last 100 years, there have been four antigenic shift events leading to re-assorted influenza A viruses that have caused pandemics in humans – 1918 (H1N1) , 1957 (H2N2), 1968 (H3N2) , 2009 (H1N1).
- Global laboratory surveillance for influenza viruses circulating in humans is in place through the WHO's Global Influenza Surveillance and Response System (GISRS).



Norovirus

- Following the introduction and use of rotavirus vaccines, noroviruses have also become the leading cause of medically attended acute gastroenteritis
- In March 2012, a new GII.4 norovirus strain, named GII.4 Sydney, was identified in Australia and subsequently spread to the United States, the United Kingdom, and a number of other countries
- GII.4 norovirus outbreaks have been associated with higher rates of hospitalization and mortality compared with outbreaks caused by other genotypes.
- New variants of the GII.4 genotype have emerged every 2 to 4 years over the last 2 decades, likely driven by escape from population immunity.

Vector-borne diseases

- Vector-borne pathogens are predominately zoonoses, and vectors (mosquitos and ticks) frequently bridge the gap between humans and animal reservoirs that rarely come into direct contact, an especially important contribution to pathogen emergence.
- The mosquito *Aedes aegypti*, transmits dengue, yellow fever, chikungunya, and Zika viruses
- Sometimes humans remain dead-end hosts, as happens with West Nile virus but with dengue and Zika viruses, the pathogens have gained the ability to be vectored between humans.
- Vaccines in widespread use against vector-borne pathogens are yellow fever and Japanese encephalitis viruses

Ebola and Marburg Haemorrhagic Fevers

- Ebola and Marburg viruses cause rare, severe, and often-fatal diseases in humans and non-human primates.
- Symptoms include fever, headache, joint and muscle aches, sore throat, and weakness, followed by diarrhea, vomiting, and stomach pain. Some patients also exhibit a rash, red eyes, hiccups, and internal and external bleeding.
- There is no licensed vaccine or standard treatment for Ebola or Marburg, and treatment is supportive.
- Haemorrhagic fever outbreaks typically result from a single or small number of spillover events from the virus reservoir with subsequent chains of human-to-human transmission.
- The case-fatality proportion for patients managed in biocontainment units in Europe and the United States was 18.5% (versus 40%–70% in West Africa), highlighting the importance of critical care and advanced organ support.

How do you diagnose them?

- 1. Take a history
- 2. Examine the patient

- Unique features may suggest an EID

- Stop and Think – don’t panic

- Discuss with colleagues the possibility of an EID

How do you diagnose them?

- Molecular diagnostics have recently played a significant role in the detection of the genetic material (DNA or RNA) of various pathogens in clinical samples.
- Methods have included
  - Polymerase Chain Reaction (PCR). PCR amplifies specific regions of the viral genetic material in a sample.
  - Next Generations Sequencing (NGS). NGS can sequence the entire genome of a virus present in a clinical sample.
  - Clustered Regularly Interspaced Short Palindromic Repeats and CRISPR-associated protein 9 (CRISPR-Cas9). A genome editing technology that can be used to detect and cut specific regions of viral genetic material. This can be used to develop highly specific and sensitive viral diagnostic tests, as well as to potentially develop new antiviral therapies.

Therapeutic Options

- Viruses are obligate intracellular “parasites”. They can only reelicate within a cell.
- Antiviral agents target processes unique to the virus (not the host cell) to minimise toxicity
- Antivirals are static agents i.e. they block viral replication, they do not “kill” viruses.
- Most antivirals target specific viruses, there are very few “broad spectrum” antiviral agents.

Therapeutic Options

Convalescent plasma	High titre neutralising antibodies
Fusion inhibitors	Block interactions required for fusion of some enveloped viruses
Monoclonal antibodies	Neutralising or block receptor interactions
Nucleoside analogues	Terminate DNA or RNA chain elongation
Polymerase inhibitors	Blocks viral polymerase to stop replication
Receptor decoys	Free proteins which bind to virus and act as decoy
Protease inhibitors	Inhibit cleavage of viral proteins
Translation inhibitors	Blocks translation of viral mRNAs
Endocytosis inhibitors	Target endocytosis pathways used for viral cell entry
Interferons	Upregulate host immune response
Kinase inhibitors	Modulate cellular environment
Lipidomic drugs	Target lipid biosynthesis used by some enveloped viruses

Vaccination

- Although vaccines have widely eliminated rubella and therefore congenital rubella and eradicated smallpox worldwide, vaccine-preventable diseases such as measles can reemerge even in the setting of high-functioning immunization programs.
- In many parts of the world, weak primary health care systems and limited access to the most vulnerable populations result in many children being unimmunized.
- Reduced vaccine acceptance in some affluent countries and waning vaccine immunity in the setting of high vaccination coverage have emerged as threats to protecting communities from vaccine-preventable diseases.

Infection Prevention and Control

1. Apply infection prevention and control precautions if EID suspected
   - Don appropriate PPE
   - Standard precautions should be used with ALL patients
2. Isolation as appropriate

   Contact

   Droplet

   Airborne
3. Cleaning clinical environment.
4. Waste disposal.

Conclusion

- Each emergent event teaches particular lessons:
  - HIV's emergence was long and insidious;
  - Ebola's was explosive and logistically complex;
  - Zika's dangers were unappreciated too long.
- In all cases the most critical advantage would have been early detection of the initial cases of disease.
- 2005 International Health Regulations (IHR 2005) as an international treaty that requires identification, reporting, and control of emerging threats was developed.
- IHR 2005 requires member nations to report all Public Health Emergencies of International Concern (PHEICs) to the WHO, including not only outbreaks of infectious diseases but all biological, chemical, or radionuclear threats and natural disasters.
- IHR 2005 primary goal is to improve national capacities to control threats at their source

Conclusion

- IHR 2005 requires prompt reporting of a single case of smallpox; poliomyelitis due to wild-type poliovirus; SARS; and human influenza caused by a new subtype.
- IHR 2005 primary goal is to improve national capacities to control threats at their source and encourages participation in international systems such as the WHO Global Outbreak Alert and Response Network (GOARN), which provides technical assistance during outbreak investigations, and the WHO Global Influenza Surveillance and Response System (GISRS) which tracks influenza viruses with pandemic potential.

Thank you

Questions