INFLUENZA PANDEMICS – LESSONS FOR COVID-19

Preparing for epidemics in South Africa – human and animal

NSTF Discussion Forum
25-26 February 2021

Pandemic and Epidemic Diseases (WHO)

- Chikungunya
- Cholera
- Crimean-Congo haemorrhagic fever
- Ebola virus disease
- Hendra virus infection
- **Influenza (pandemic, seasonal, zoonotic)**
- Lassa fever
- Marburg virus disease
- Meningitis
- MERS-CoV
- Monkeypox
- Nipah virus infection
- **Novel coronavirus (2019-nCoV)**
- Plague
- Rift Valley fever
- SARS
- Smallpox (eradicated)
- Tularaemia
- Yellow fever
- Zika virus disease

Latest Disease Outbreak News (DONs)

•Ebola virus disease – Guinea
17 February 2021

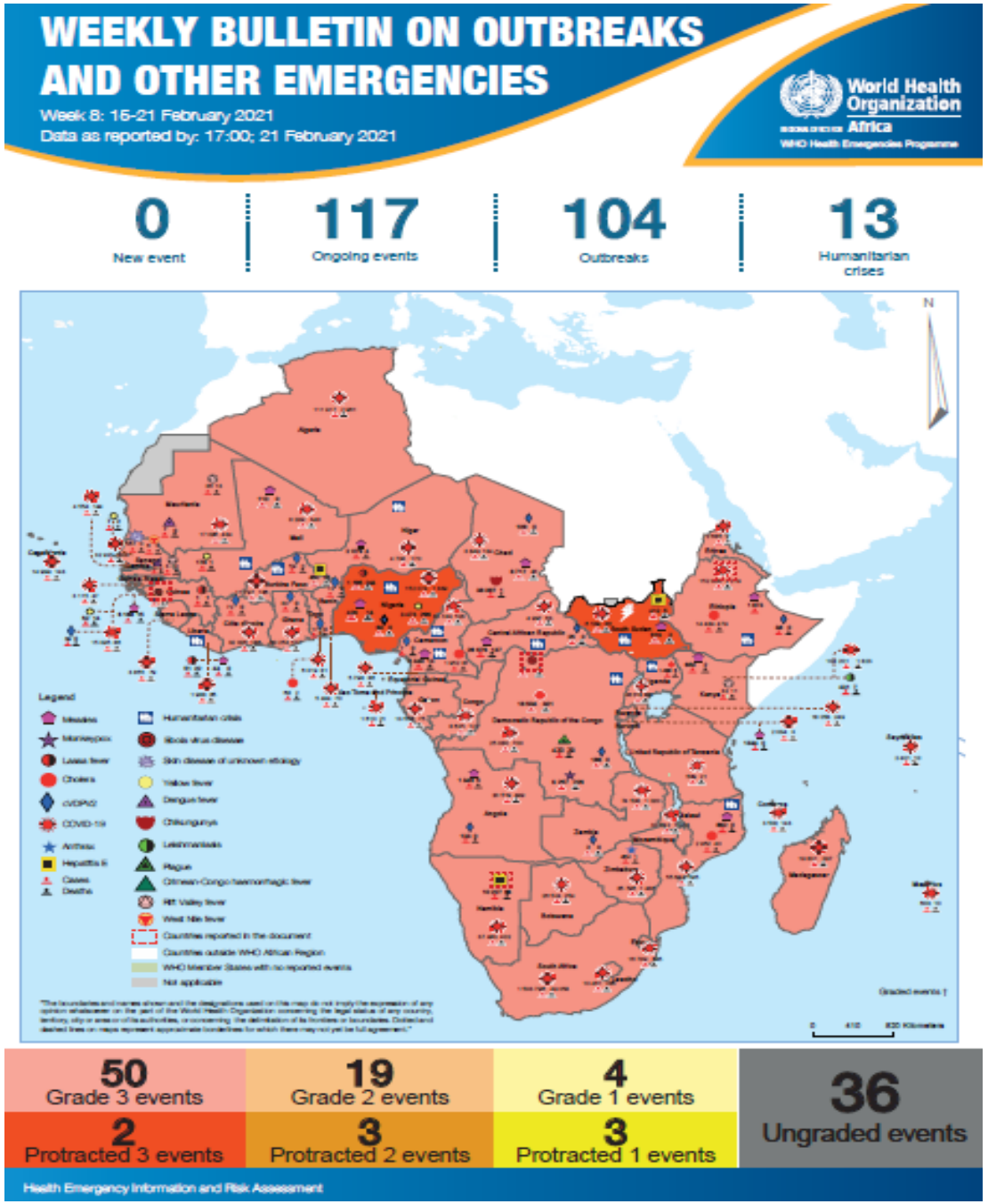
•Rift Valley fever – Kenya
12 February 2021

•Ebola virus disease – Democratic Republic of the Congo
10 February 2021

•Influenza A (H3N2) variant virus – United States of America
5 February 2021

•Middle East respiratory syndrome coronavirus (MERS-CoV) – The Kingdom of Saudi Arabia
1 February 2021

Africa is prone to Epidemics and Pandemics



Responding to Epidemics and Pandemics

- Known pathogen without a licensed intervention e.g Chikungunya, West Nile
- Known pathogen with a licensed intervention e.g. Ebola, Cholera, Yellow Fever, Influenza
- Unknown/ emerging pathogen e.g. SARS, MERS-CoV, Nipah Virus, **Covid-19**

WHO: Emergency Response Framework Outbreak for Covid-19

- Coordination
- Preparedness
- Surveillance
- Case management
- Infection Prevention and Control
- Laboratory
- Logistics
- Risk Communication and Community Engagement
- Continuity of Essential Services
- Vaccination

Research is critical during Epidemic Outbreaks & Post Epidemic Outbreaks

- Development of better risk modelling
- Prevention and surveillance for countries at risk of serious infectious disease outbreaks
- Identifying research gaps and priorities for priority diseases at country level
- Research, especially country-owned, should be part of pandemic preparedness, with overall objective of strengthening Biosecurity and Research Infrastructure
- In the context of ONE health – critical to leverage on existing networks, platforms and Experts from academia, industry, healthcare, veterinary care, regulatory agencies, food safety and agriculture, philanthropic organizations and international organisations
- **Optimise development of new health interventions such as vaccines, therapeutics and rapid diagnostic tools.**

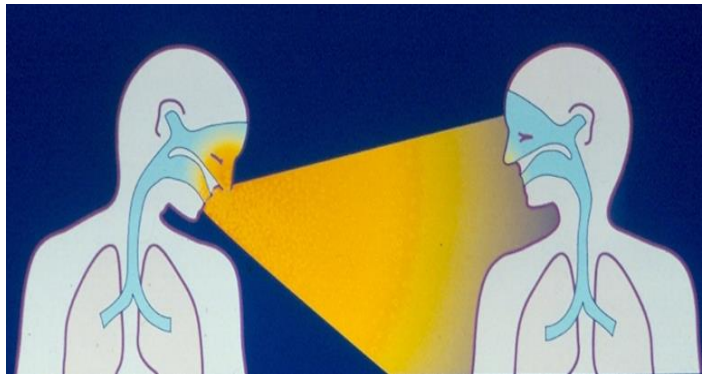
GLOPID-R - INTERNATIONAL NETWORK OF FUNDERS INVESTING IN RESEARCH TO ANTICIPATE AND FIGHT CRITICAL INFECTIOUS DISEASE OUTBREAKS

Global Research Collaboration for Infectious Disease Preparedness – *Anticipating future disease outbreaks*

GloPID-R – Network of Funding Organisations

- Facilitate exchange of information in outbreak situations
- Establish a response plan and a strategic agenda for a coordinated and rapid research response
- Address scientific, legal, ethical and financial challenges to a rapid response
- Connect infectious disease research networks
- Support public health decision-making

Influenza: How well are we prepared for the next pandemic?



- Virus spreads via water droplets, and small particle aerosols when coughing or sneezing
- Virus enters the body through nose, mouth and eye

Virus Classification

RNA virus

Family: **ORTHOMYXOVIRIDAE**

Genus: **Influenza virus** **Influenza C virus**

Types: **Type A** **Type B** **Type C**

Specificity: **Man** **Animal** **Man** **Man**

Kingsbury D. W., Virology, IInd edition, New York, 1990, 1076-87

Virus Nomenclature

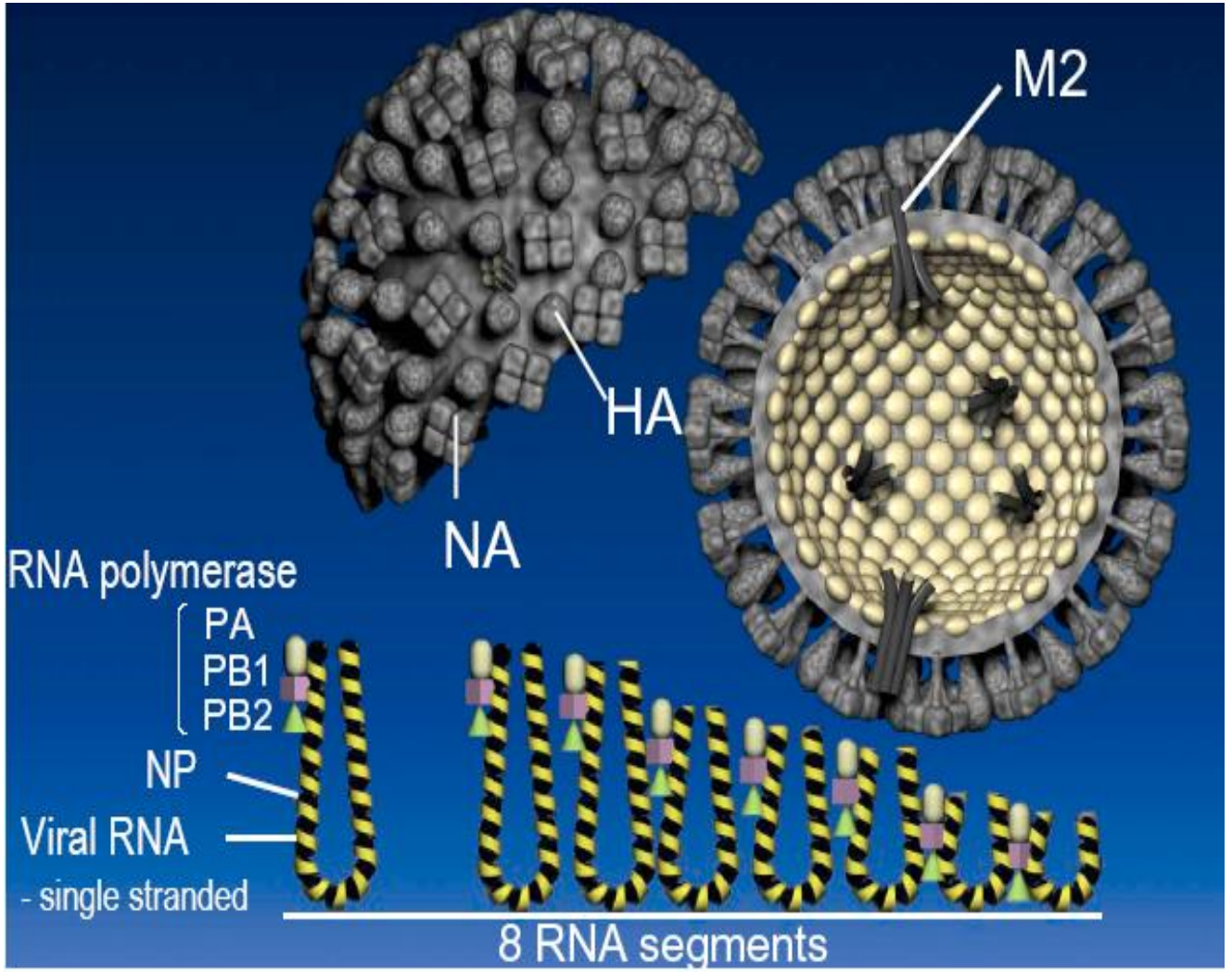
A/California/10/78 [H1N1]

✓A	Type, v*irus strain designation*
✓sw, eq, av	*The host of origin*
✓California	*Geographic origin*
✓10	*Laboratory strain number*
✓1978	*Year of isolation*
✓H1N1	*Subtype*

Hay A.J., Belshe B. R., Anderson E.L., Gorse G.J., Ulf Westblom T. Textbook of human virology, IInd ed., 1990:307-41

Key Medical Aspects of Influenza

- Highly infectious disease
- Acute infection of the respiratory tract
- Repeat infections (due to viral mutations)
- Transmitted by aerosol route:
  - coughing/sneezing/talking
  - contaminated handkerchiefs or hands
- Incubation period usually 2–3 days[1]



Antigenic Variation: Mutation capacity of influenza viruses

Risk - each year mutation can induce a different virus

- Mutation is frequent with Influenza A,

  less for type B, never for type C
- Mutation allows virus to escape immunity
- Involves the external antigens: HA and NA
- Two types of mutations depending on whether the RNA segment variation is small or great:
  - **Antigenic drift (**minor variations**)**
  - **Antigenic shift (**major variations**)**

Annual changes in surface proteins pose vaccination challenge

- Changes affect recognition by immune system
  - **Annual outbreaks**
  - **Antigenic drift - epidemics**
  - **Antigenic shift – pandemics**
- No broad and long lasting immunity

Betts FR, Douglas RG, Mandell G.L., Douglas R. G., Bennett J.E., Principles and practice of infectious diseases, 3rd ed., 1990;39:1306-25

Influenza Epidemics vs Pandemics

EPIDEMICS

- Regional
- Occur virtually every year
- **Every Year is Influenza Year**
- Result from antigenic drifts and waning immunity
- Influenza A and B

PANDEMICS

- Worldwide
- Occur every few decades
- **Occur at unpredictable intervals**
- Result from antigenic shifts due to genetic reassortment or **direct transmission from avian to human**
- Appearance of novel virus to which population has no immunity
- New virus is highly pathogenic
- Pandemic can occur within 4 weeks
- Influenza A only

Influenza Pandemics (1)

- 1510
- 1889 – 1890 H2N2
- 1899 – 1900 H3N2
- 1918 – 1919 H1N1 “Spanish flu”
- 1957 – 1958 H2N2 “Asian flu”
- 1968 – 1969 H3N2 “Hong Kong flu”
- **2009 – ?2010 H1N1 “Swine Flu”**

Influenza Pandemics (2)

Year	*Designation*	*Resulting pandemic*	*Death toll*
1918	H1N1 “Spanish Flu”	Devastating	50-100 million
1957	H2N2 “Asian Flu”	Moderate	1 million
1968	H3N2 “Hong Kong Flu”	Moderate	1 million

H1N1 “Swine Flu” Pandemic

- **April 12**: an **outbreak of influenza-like illness** in Veracruz, Mexico, reported to WHO
- **April 15-17**: two cases of a **new A(H1N1) virus infection** identified in two southern **California** counties in U.S.A.

  A(H1N1) California7/2009

- **April 23**: **new influenza A (H1N1) virus infection** confirmed in several patients in **Mexico**
- **April 24**: WHO declares a public health event of international concern (**PHEIC**).
- **April 27**: WHO declares pandemic **phase 4** - sustained community transmission in Mexico
- **April 29**: WHO declares pandemic **phase 5** (2 countries affected)
- **June 11**: WHO declares pandemic **phase 6** (spread to 2 WHO regions)
- **In 9 weeks, all WHO regions** reporting cases of **pandemic (H1N1) 2009**
- **18 June 2009: 1st case in South Africa**

1918/1919 Influenza Pandemic

- One of the most deadly pandemics of communicable diseases to have affected the world
- In South Africa
  - SA was 5th hardest hit country in the world
  - Victims 20 – 40 years of age
  - 500 000 died, 62 % in the Cape
  - Pandemic overwhelmed the ability of the authorities to dispose of the corpses
  - It resulted in paralysis of the health care system

Influenza: Lessons from Past Pandemics

Key Lesson: Unpredictability

- Occur unpredictably, and not always in winter
- Great variations in mortality, severity of illness, and pattern of illness and age distribution
- Always a rapid surge in the number of cases over a brief period of time, often measured in weeks
- Pandemics tend to occur in waves with a duration of 6 - 8 weeks, subsequent waves may be more or less severe

Threat of Avian Influenza

Most Influenza pandemics originated from Avian virus

- H5N1 (1997-Hongkong)
- H7N3 (2004-Canada)
- H7N7 (1995-UK)
- H9N2 (1999-Hongkong)
- H10N7 (Egypt-2004)
- H5N1 (2003-2007)

  H5N1 (2006-2007) – thought most likely would be the cause of the next pandemic

WHO: Every Country Must Be Prepared For A Possible Influenza Pandemic

- Influenza pandemics are recurring events
- The world may be on the brink of another pandemic
- All countries will be affected
- Widespread illness will occur
- Medical supplies will be inadequate
- Large numbers of deaths will occur
  (WHO conservative estimate: 2 - 7.4 million deaths)
- Economic and social disruption will be great
- Every country must be prepared

www.who.int/csr/disease/influenza/pandemic10things/en **(March 2007)**

Possible Interventions in Case of a Pandemic

- **Non-pharmaceutical interventions**
  - Quarantine
  - Isolation
  - Screening for febrile/ respiratory illnesses
  - Social distancing
  - Hand hygiene / discouraging hand shaking
  - Wearing masks
  - Cancelling large group gatherings
  - Closing schools
  - Travel limitations / Border control …..

- **Pharmaceutical interventions**
  - Stockpiling and early use of antivirals (e.g. Tamiflu™, Relenza™)
    - Not a substitute for vaccination
  - Use of pandemic vaccines developed and manufactured after the start of the pandemic

Why vaccinate against influenza?

- Vaccination represents **first-line intervention**
- Vaccines are regarded as the “most important medical intervention for preventing influenza and reducing its health consequences “
- Primary weapon against annual epidemics
- Proven efficacy in reducing morbidity, mortality and associated respiratory disease
- Vaccine efficacy is 70–90%[1]
- Clinical effectiveness of vaccination is even higher[2]
- Cost–benefits of vaccination are firmly established[2]

[1]Monto 1996; [2] Nichol 2003

Challenges of Scaling Up Vaccine Production

- During a pandemic, vaccine may not be readily available
- Seasonal influenza vaccine production takes ≥ **6 months**!
- Process involves identification of relevant strains, growth of virus in eggs or cells, virus extraction, potency testing and clinical trials.
- Vaccine will not be available for most countries with the current production capacity
  - **How to increase pandemic vaccine manufacturing capacity?**
  - **How to ensure protection as early as possible after onset of pandemic?**

CHARACTERISTICS OF INFLUENZA PANDEMICS – LESSONS FOR COVID-19

- Novel virus
- Increased transmissibility
- +/- increased virulence
- Age shift
- Novel risk factors
- Relative non-seasonality
- Multiple waves
- Human adaptation → seasonal influenza

THANK YOU

http://www.mrc.ac.za