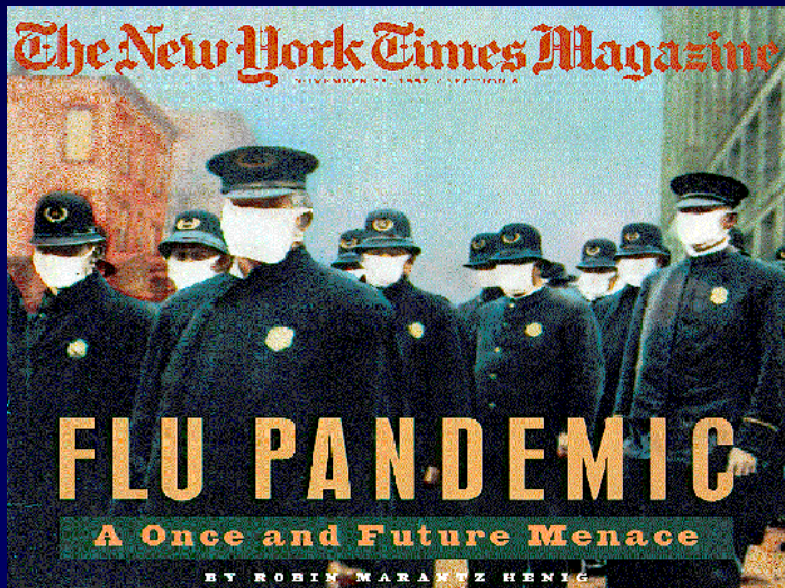
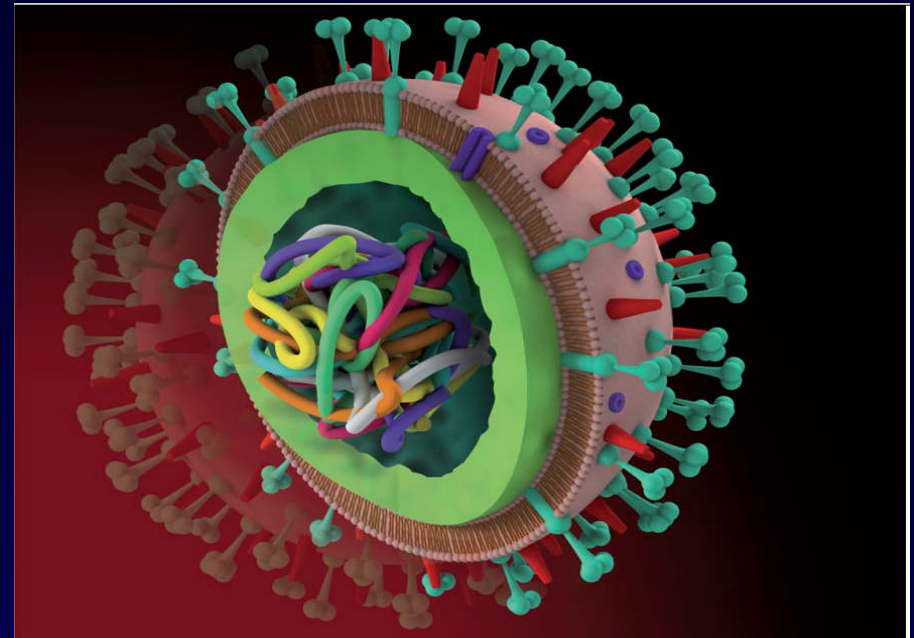


Avian Influenza



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CAREC/PAHO/WHO



Influenza Pandemic

- ✓ An influenza pandemic (or global epidemic) occurs when a new influenza virus subtype appears, against which no one is immune.
- ✓ This may result in several simultaneous epidemics worldwide with high numbers of cases and deaths.
- ✓ With the increase in global transport and urbanization, epidemics caused by a new influenza virus are likely to occur rapidly around the world.



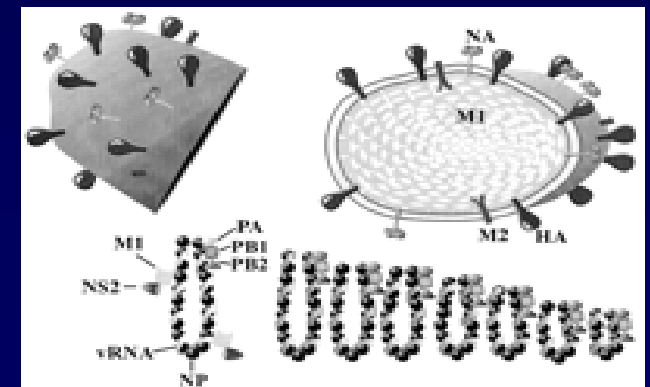
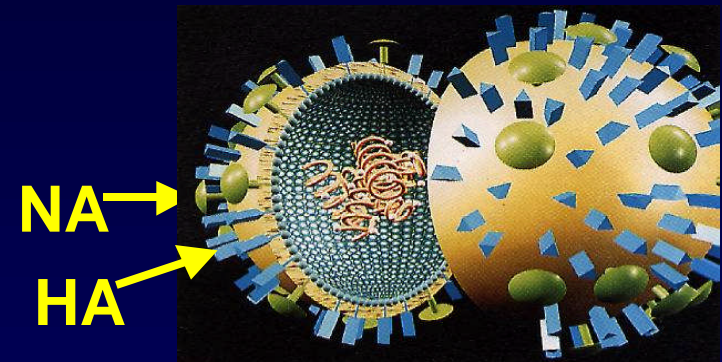
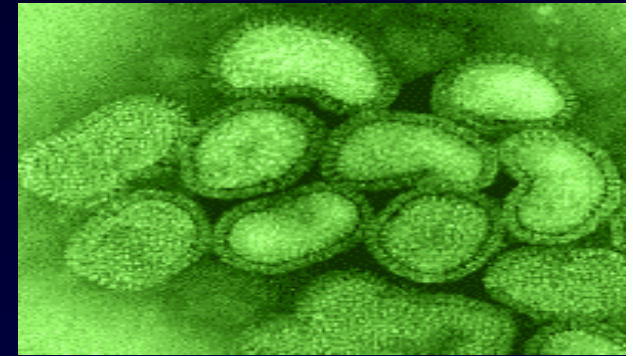
The Virus

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Influenza Virus Characteristics

- ✓ Family: *Orthomyxoviridae*
Genera: Influenza A, B, C and Thogotovirus
Many subtypes (16HA, 9NA)
- ✓ Viral particles: 80-120 nm, spherical/ovoid, lipid envelop with two prominent glycoproteins
- ✓ Genome: 8 ssRNA genome segments are package in the Core.



Influenza A

- ✓ Multiple species
 - ✓ Mammalians
 - ✓ Avian
- ✓ Most virulent group
- ✓ Classification by surface antigens into subtypes
 - ✓ Hemagglutinin (H or HA)
 - ✓ Neuraminidase (N or NA)



Influenza A HA and NA Subtypes

H1			N1
H2			N2
H3			N3
H4			N4
H5			N5
H6			N6
H7			N7
H8			N8
H9			N9
H10			
H11			
H12			
H13			
H14			
H15,16			

Evolutionary pathways of Influenza A Virus

- ✓ Antigenic Drift
 - ✓ Point mutations leading minor antigenic changes with generation of new variants, which account for the annual nature of flu epidemics.
- ✓ Antigenic Shift
 - ✓ Genetic reassortment among animal and human influenza when two or more strains infect the same cell generating a new subtype with pandemic potential.



Influenza Type B

- ✓ No animal reservoirs
- ✓ Low rate of antigenic drift
- ✓ Co-circulation of multiple distinct lineages

Then

- ✓ No antigenic drift
- ✓ No pandemic threats



Influenza C

- ✓ Humans and swine
- ✓ Different pattern of surface proteins
- ✓ Rare
 - ✓ Mild to no symptoms
- ✓ By age 15, most have antibodies



Influenza Clinical Manifestations

More frequent

- ✓ Fever
- ✓ Sore Throat
- ✓ Cough
- ✓ Myalgia
- ✓ Nasal Congestion
- ✓ Rhinorhea
- ✓ Pharyngitis

- ✓ Laringotracheitis
- ✓ Bronchiolitis
- ✓ Pneumonia

Others

- ✓ Vomiting
- ✓ Abdominal pain
- ✓ Otitis media



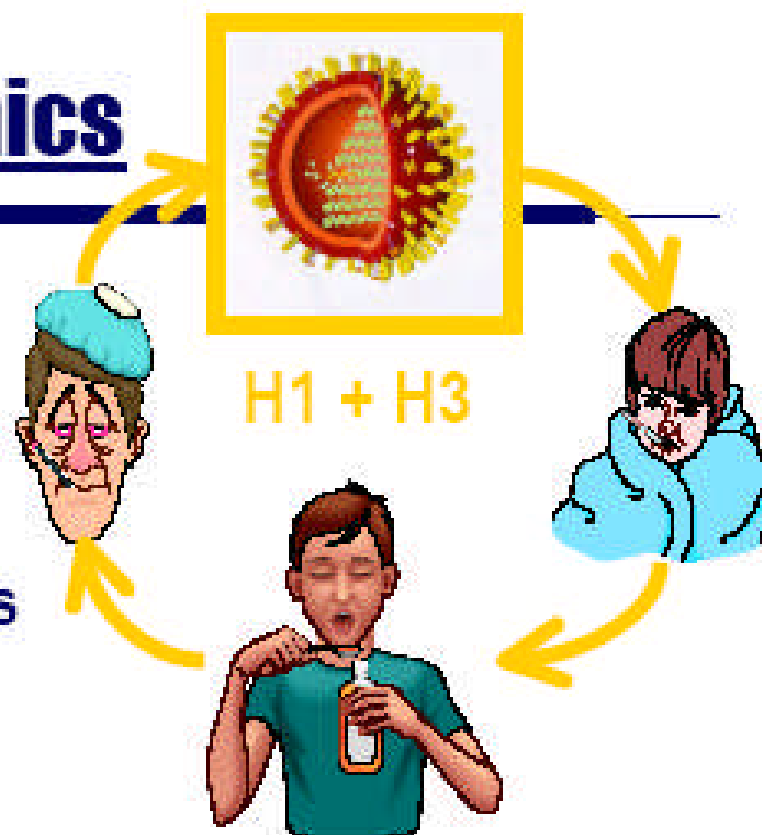
Epidemiology

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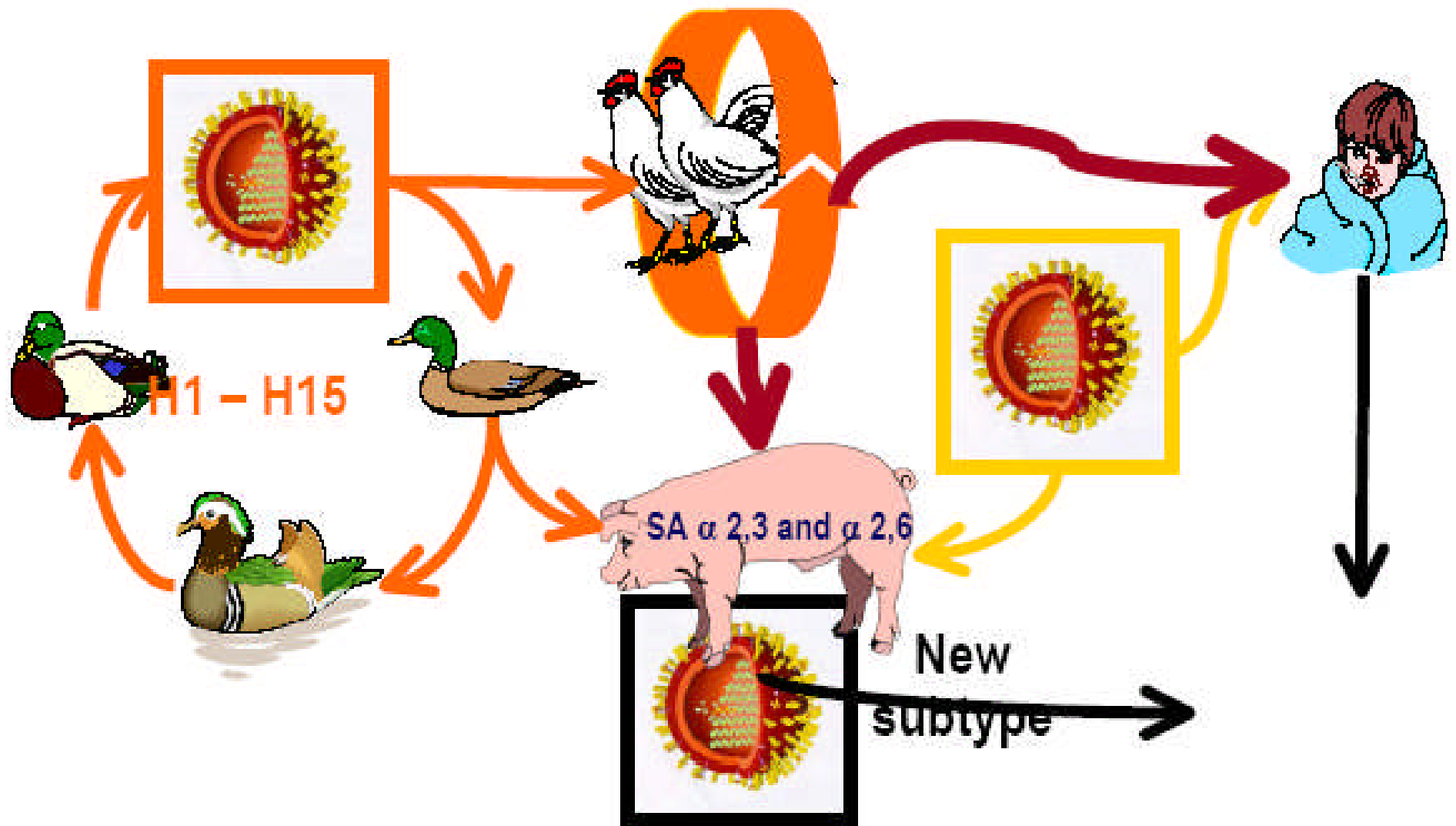


Influenza 1: Annual epidemics

- Influenza A (15 major subtypes) and B viruses
- Globally between 0.5 – 1 million death per year plus hospitalizations and disease
 - US: 36k death; hospitalizations; outpatient visits; disease
 - Data on severe outbreak from developing countries but very evidence on annual impact of influenza
- Minor changes in virus surface protein require annual adaptation of influenza vaccine

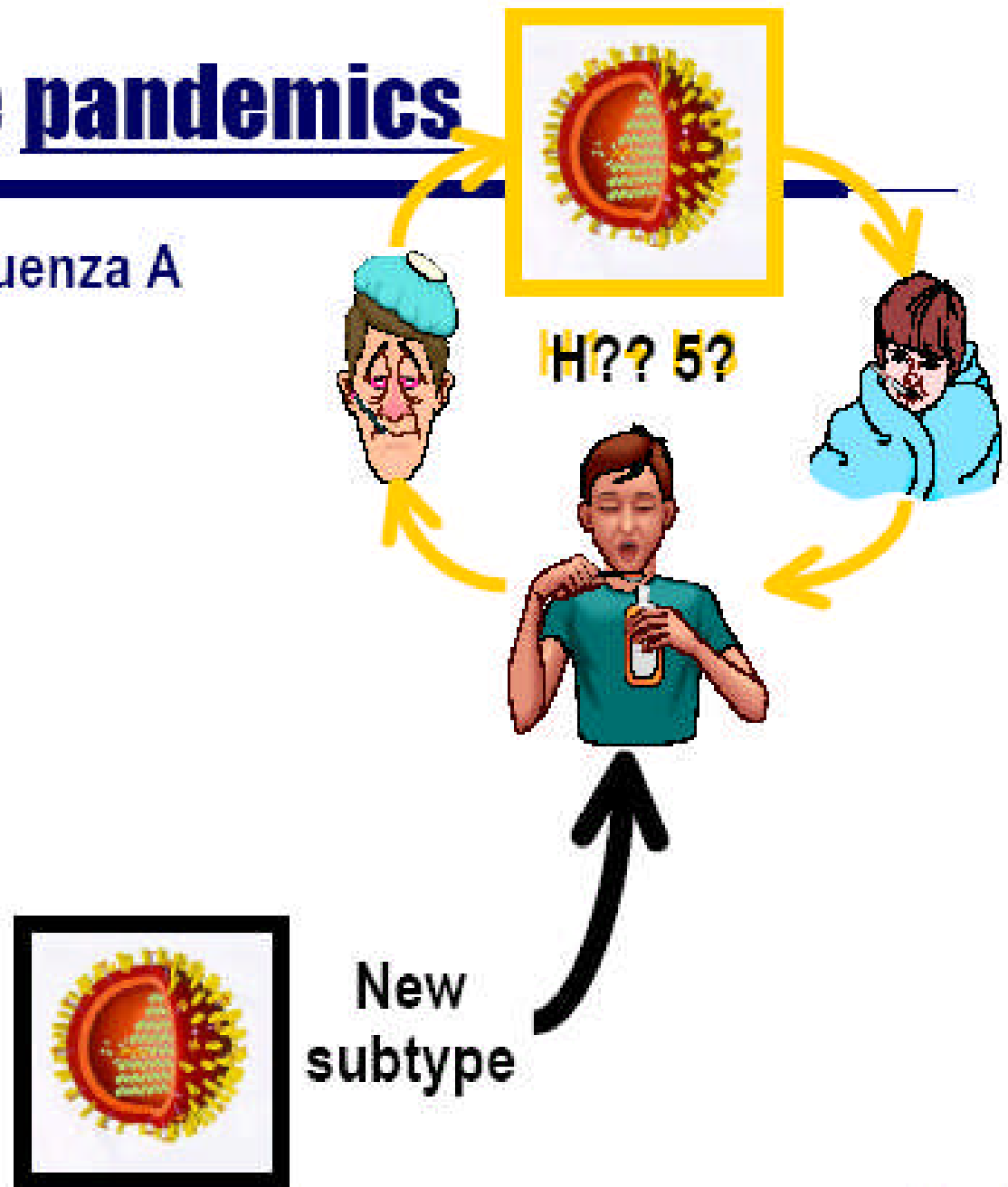


Influenza 2: Rare pandemics

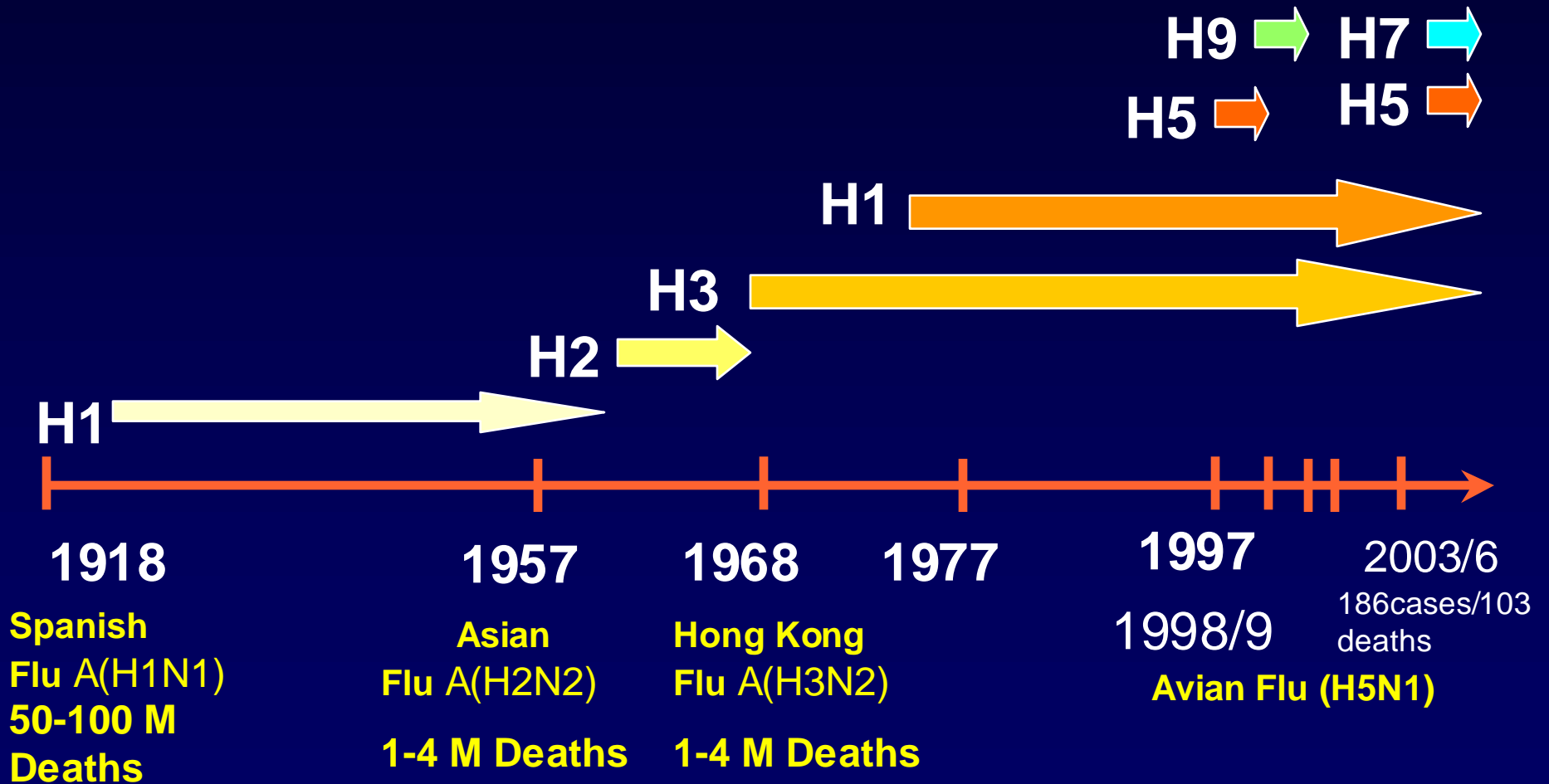


Influenza 2: Rare pandemics

- Emergence of new Influenza A subtype
- No immunity



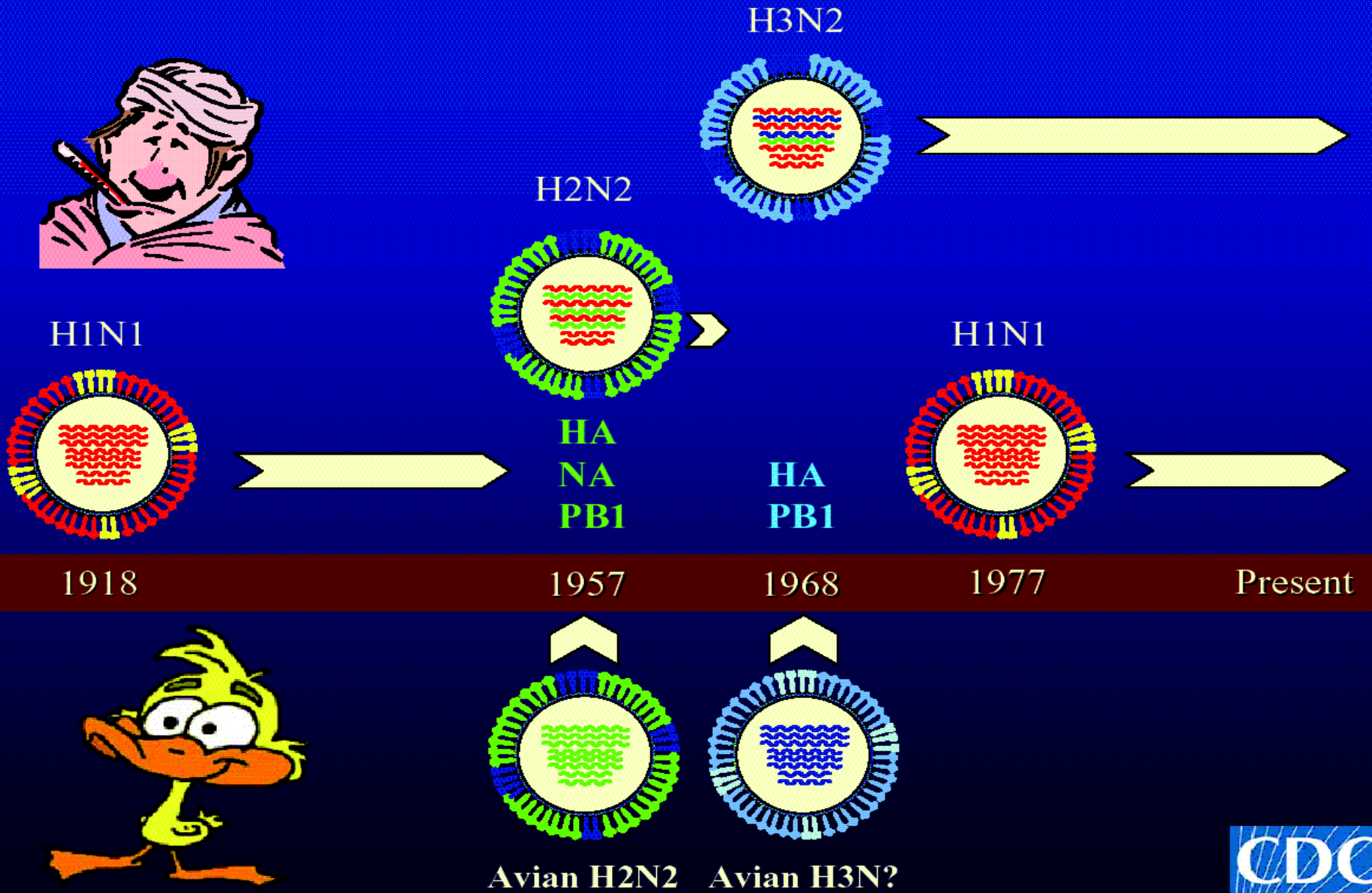
Timeline of Emergence of Influenza A Viruses in Humans



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Origin of Pandemic Viruses that Emerged in the 20th Century



The Source

CAREC/PAHO/WHO



The Source



- ✓ Influenza A are perpetuated in the wild birds, predominantly in waterfowl. Migratory waterfowl spread to domestic birds.
- ✓ Viruses remain in evolutionary stasis with minimal changes and producing asymptomatic infection.
- ✓ After transfer to a new host, either avian or mammals, influenza viruses undergoes rapid evolution.

Animal Transmission



- ✓ Avian influenza A viruses can infect a variety of domestic and wild avian species:
 - ✓ chickens, turkeys, ducks, geese quail, pheasants, psittacines, gulls, shore birds, seabirds, eagles and others.
- ✓ Virus is shed in respiratory secretions

Animal Transmission – (Cont'd)

- ✓ Spread by aerosol, shared drinking water, fomites and feces of infected animals.
- ✓ Influenza A remains viable at moderate temperatures:
 - ✓ 4 days in water at 22°C over 30 days at 0°C



Avian Influenza

- ✓ Pathogenicity based on genetic features and/or severity of disease in domestic poultry:
 - ✓ Low pathogenic AI (LPAI)
 - ✓ H1 to H15 subtypes
 - ✓ Highly pathogenic AI (HPAI)
 - ✓ Some H5 or H7 subtypes
 - ✓ LPAI H5 or H7 subtypes can mutate into HPAI



Human Transmission

- ✓ Previously considered non-pathogenic for humans.
- ✓ 1997, Hong Kong:
 - ✓ 18 humans infected, 6 died
 - ✓ H5N1 virus linked to outbreak in live bird market and area farms
- ✓ 2003, the Netherlands:
 - ✓ 83 confirmed cases in humans, 1 death
 - ✓ H7N7 strain



Human Transmission

- ✓ The H5N1 strain circulating in Asia appears to be highly pathogenic for humans.
- ✓ 2004-2005, SE Asia
 - ✓ 186 reported, confirmed cases
 - ✓ 105 deaths
 - ✓ Case-fatality ratio of 56%
- ✓ 90% of the case occur within the vicinity of poultry outbreaks and have had a clear history of exposure to sick poultry



Clinical Features of Avian Influenza in humans

- ✓ Incubation period 2-4 days
- ✓ Persistent fever, shortness of breath and cough are the presenting features.
- ✓ All patients present lymphopenia and severe pneumonia
 - ✓ Unusual presentations possible



Infection in Sporadic Cases

- ✓ High mortality because the virus can infect cells in multiple organs and the gut.
- ✓ The virulence of avian influenza H5N1 subtype is linked in part to the cleavage of the HA₀ by a wide range of host proteases.
- ✓ Human viral strains are cleaved by respiratory tract proteases



Characteristics of Sporadic Cases

- ✓ Healthy children and adults.
- ✓ No airborne transmission of the H5N1 virus.
- ✓ No evidence of human-to-human transmission (although it is possible in two instances)
- ✓ Only one or two base changes in the HA cleavage site can alter this ability.



Why concern?

Alarm in features of H5N1

- ✓ The unprecedented rapid spread
- ✓ The virus undergoes constant genetic changes and over time has become progressively more pathogenic to wild and domestic birds.



Why concern? (Cont'd)

- ✓ The virus expand its mammalian host range.
- ✓ This is the concern because a minor alteration in the current H5N1 strain might result in in efficient human-to-human transmission, a necessary condition for a human pandemic.
- ✓ High fatality rate in humans and animals.



Pandemic Preparedness

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- ✓ Recent experiences with highly pathogenic H5N1 avian influenza have given the world its first advance warning that another influenza pandemic may be imminent.
- ✓ Given the unpredictable behaviour of influenza viruses, no one can know in advance whether the start of a pandemic will begin gradually, or by a sudden explosion of cases.
- ✓ Opportunities to intervene by preparing strategic and operational plans



Preparing for a Pandemic

- ✓ Planning process
- ✓ Surveillance in birds and humans
- ✓ Emergency activities
- ✓ Prevention of introduction and spread of disease
- ✓ Treatment of patients



Activity	Description	Responsibility
Creation of planning group	Composed of members of all groups that will be involved in preparation for and response to a pandemic	Created through the Office of the Prime Minister as a part of general disaster plan
Development of plan	<u>Planning for:</u> Surveillance (human & animal); Emergency activities; Prevention of disease spread; Treatment of patients; Communication with the public.	Developed by the planning group



Activity	Description	Responsibility
Surveillance	<p><u>Animal</u>: test specimens from dead birds; after positive found, test birds in commercial flocks</p> <p><u>Human</u>: test specimens from a subset of patients with fever and respiratory symptoms at selected sentinel sites</p> <p><u>Lab</u>: identify, order supplies</p>	CMO, VPH director, epidemiologist, surveillance group, EPI manager
Emergency activities	<p>Maintenance of vital services;</p> <p>Mass communication;</p> <p>Culling activities for poultry</p>	Designated chief of activities with clear chain of command



Activity	Description	Responsibility
Prevention of spread of disease	<p><u>Pharmacological</u>: purchase of and plan for vaccines, antivirals, and antibiotics; registration of drugs</p> <p><u>Public health interventions</u>: educate on hygiene; order masks; review laws to restrict movement and crowding.</p>	CMO, Ministry of Health; Disaster Coordination, Office of the Prime Minister
Treatment of patients	<p>Identify separate clinic and ward facilities;</p> <p>Prepare for separate staffing;</p> <p>Organize supplies for facilities.</p>	CMO, hospital medical directors



Who makes the Plan?

National Influenza Planning Committee

- ✓ National and regional public health authorities
- ✓ Epidemiologists, virologists, biologists
- ✓ Veterinary public health leaders
- ✓ Medical, nursing, and pharmacists' societies
- ✓ Transportation, communication, public safety leaders
- ✓ Mass media leaders and experts
- ✓ NGOs



Surveillance in Humans

- ✓ Establish network of surveillance sites most likely to see influenza patients
- ✓ Use a subset of current ARI surveillance sites
- ✓ Collect throat and nasopharyngeal swabs from hospitalized patients with flu-like symptoms
- ✓ Collect serum specimens from poultry workers near wetlands



Laboratory Network

- ✓ Preparation of samples locally, plus rapid IFA test (*specificity +++; sensitivity -*)
- ✓ Send to satellite laboratory for PCR with primers that are specific for HA genes; plus serology for IgM and IgG
- ✓ Send to regional reference laboratory for genetic sequencing and sub-typing
- ✓ Send to WHO reference laboratory for confirmation



Planning for Emergency Activities

- ✓ Identify organizations and individuals whose role will be vital in an emergency
- ✓ Form a committee to develop a plan
- ✓ Establish clear command and control roles
- ✓ Establish clear roles for each organization
- ✓ Assess the current risk of an emergency
- ✓ Communicate with everyone
- ✓ *(usually plan already exists for hurricanes, etc.)*



Prevention of Spread of Disease

- ✓ Vaccines
- ✓ Prophylactic use of antivirals
- ✓ Public health interventions



Vaccines

- ✓ Pandemic influenza vaccine.
- ✓ Seasonal influenza vaccine.
- ✓ Pneumococcal vaccine.
- ✓ New vaccine production techniques.



Pandemic Influenza Vaccine

- ✓ Human pandemic strain unknown.
- ✓ Vaccine available against current H5N1 HPAI.
- ✓ Efficacy unknown (*being tested now*)
- ✓ 100,000 doses on hand.
- ✓ More vaccine only during 2nd or 3rd wave of pandemic.



Immunization Strategy

- ✓ Try to obtain vaccine, especially for 2nd and 3rd waves (there will be a shortage)
- ✓ Determine distribution method (*clinics, homes, etc.*)
- ✓ Determine age group to immunize (*not easy – normally children & elderly but Spanish flu struck young adults hardest*)



Immunization Strategy (Cont'd)

- ✓ Select occupations to immunize – e.g., *health care workers, public safety workers, politicians, essential service personnel, etc.*
- ✓ If possible incorporate seasonal flu vaccine into national schedule



Seasonal Influenza Vaccine

- ✓ H3N2 + H1N1 + Influenza B
- ✓ *Might* offer some cross protection (but probably not)
- ✓ Will prevent a dangerous disease
- ✓ Help to increase vaccine production
- ✓ Vaccinate same group as for AI
- ✓ Prevent reassortment in individual



Pneumococcal Vaccine

- ✓ Pneumonia is a major killer associated with influenza
- ✓ Available now
- ✓ Highly effective
- ✓ Expensive
- ✓ Use for all persons at high risk of pulmonary or cardiac complications



New Vaccine Techniques

- ✓ Current H5N1 virus kills chicken eggs
- ✓ Cell culture techniques
- ✓ Genetic engineering
- ✓ Direct at other antigens to produce a “universal influenza vaccine”



Antiviral Drugs

- ✓ Amantadine
- ✓ Tamiflu



Amantadine

- ✓ Blocks action of hemagglutinin
- ✓ HPAI H5N1 is resistant because of illegal use by chicken farmers
- ✓ Recent data indicating that newly evolved strains of H5N1 are susceptible to amantadine



Oseltamivir (Tamiflu)

- ✓ Blocks action of neuraminidase
- ✓ Effective against HPAI, H5N1



Tamiflu (Cont'd)

- ✓ HPAI H5N1 will probably become resistant (*single base change*)
- ✓ Both dosage and duration may need to be doubled to be effective (*10 → 40*)
- ✓ Expensive: US\$50-100 per course
- ✓ Currently in extremely short supply
- ✓ Manufactured from a Chinese herb
- ✓ 12 children reportedly died after using Tamiflu



Public Health Interventions

- ✓ Veterinary public health interventions
- ✓ Public health interventions
- ✓ Protective masks



Public Health Interventions

- ✓ Improve personal hygiene
 - ✓ *wear face masks*
 - ✓ *wash hands*
 - ✓ *disinfect surfaces*
- ✓ Quarantine cases
- ✓ Restrict movement of symptomatic persons
- ✓ Restrict mass gatherings (*cinemas, churches, etc.*)



Public Health Interventions (Cont'd)

- ✓ Close schools, day care, bars, *etc.*
- ✓ Use isolation wards in hospitals
- ✓ Use isolation rooms in homes
- ✓ *(need to ensure that laws are current)*



Protective Masks

- ✓ Infected persons should wear surgical masks.
- ✓ Healthy persons should use "N95" masks



Current Status of Preparedness in CARICOM Member States

<u>Task</u>	<u>Status</u>
Formation of committee	+++
Preparation of plan	+
Initiation of surveillance system	-
Development of lab network	---



Most Important Tasks for Preparation for Disease in Humans

- ✓ *Establishing a laboratory network*
- ✓ *Conducting simulation exercises for the safe handling of specimens*



Most Important Tasks for Preparation for Disease in Animals

- ✓ *Establishing a laboratory network*
- ✓ *Conducting simulation exercises for the safe handling of specimens*



Thank you

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