

Avian influenza



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Avian Influenza



- Mild and highly pathogenic (1 gm infects 1 M birds)
- First recognized in Italy in 1878
- Extremely contagious in birds
- Rapidly fatal (100%, same day symptoms first appear)
- Virus killed by:
 - Heat: (56° C, 3 hrs; 60° C 30 min)
 - Disinfectants: (e.g. formalin and iodine compounds)
- Survives at cool temperatures:
(in contaminated manures: 22° C, 4 days; 0° C, >30 days)

Types of Influenza Virus

- Three types: A, B, C
- Influenza Type A can infect: People, birds, pigs, horses, seals, whales and others
- Influenza Type B: Human virus
 - Not classified according to Subtype
 - Cause human epidemics but not pandemics
- Influenza Type C cause mild illness in humans
 - Not classified according to subtype
 - Do not cause epidemics or pandemics

Subtypes of Influenza A

- Subtypes defined by different antigens in humans, animals and birds
 - H (haemagglutinin): HA – 15 variations
 - N (neuraminidase): NA – 9 variations
- 15 subtypes of influenza virus infect birds
 - *Examples*
 - H1N1, H1N2, H3N2 (common human)
 - H7N7 (avian 2003, The Netherlands)
 - H5N2 (avian vaccine)
 - H5N1 (current avian)

Subtypes of Influenza A

❖ Human:

- Highest hemagglutinin (H) is H3
- Subtypes: H1N1, H1N2, H2N2, H3N2

❖ Animals:

- Lowest hemagglutinin is H5
- H5, H7 and H9 subtypes

Avian Influenza A Viruses

- ❖ Infect respiratory and gastrointestinal tracts of birds
 - Genetic reassortment occurs frequently
 - Can cause morbidity and mortality in domestic poultry
- ❖ Avian influenza A viruses are shed in the respiratory tract and in feces
 - Can survive at low temperature and low humidity for days to weeks
 - Can survive in water
 - Can survive on surfaces
 - Disinfection of the environment is needed

Low Vs. High Pathogenic Avian Influenza

- ❖ Low Pathogenic Avian Influenza Viruses (LPAI):
 - May not cause any illness in wild birds
 - Associated with mild illness in domestic poultry
 - Can evolve into highly pathogenic viruses
 - Associated with poultry outbreaks worldwide
 - Subtypes: H9
- ❖ High Pathogenic Avian Influenza Viruses (HPAI):
 - May not cause any illness in wild birds
 - High mortality in domestic poultry
 - High risk of disease in people
 - Subtypes: H5, H7

Antigenic Drift

- Point mutations in the hemagglutinin gene cause minor antigenic changes to HA
 - Continuous process
 - Immunity against one strain may be limited
- Antigenic drift produces new virus strains that may not be recognized by antibodies to earlier influenza strains
- This is one of the main reasons why people can get the flu more than one time (Seasonal epidemics)
- One or two of the three virus strains in the influenza vaccine are updated:
 - 6-8 months process
 - Targeted at high-risk (inactivated)

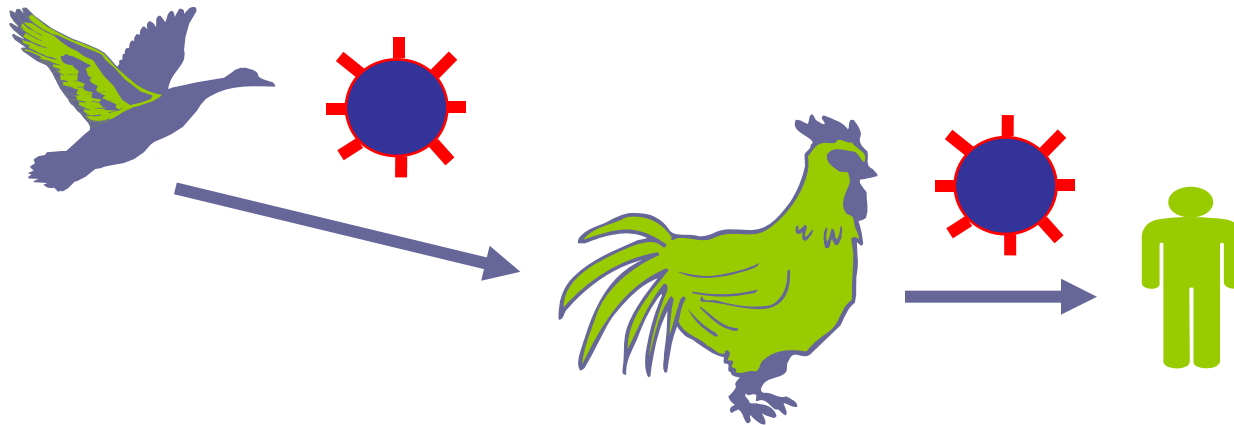
Antigenic Shift

- New influenza virus that can infect humans and has (new HA subtype \pm NA) through:
 - Genetic reassortment (human and animal viruses)
 - Direct animal (poultry) to human transmission
- If most people have little or no protection against the new virus:
 - Spread easily from person to person
 - Pandemic (worldwide spread) may occur

From Birds to Human

**Migratory
water birds**

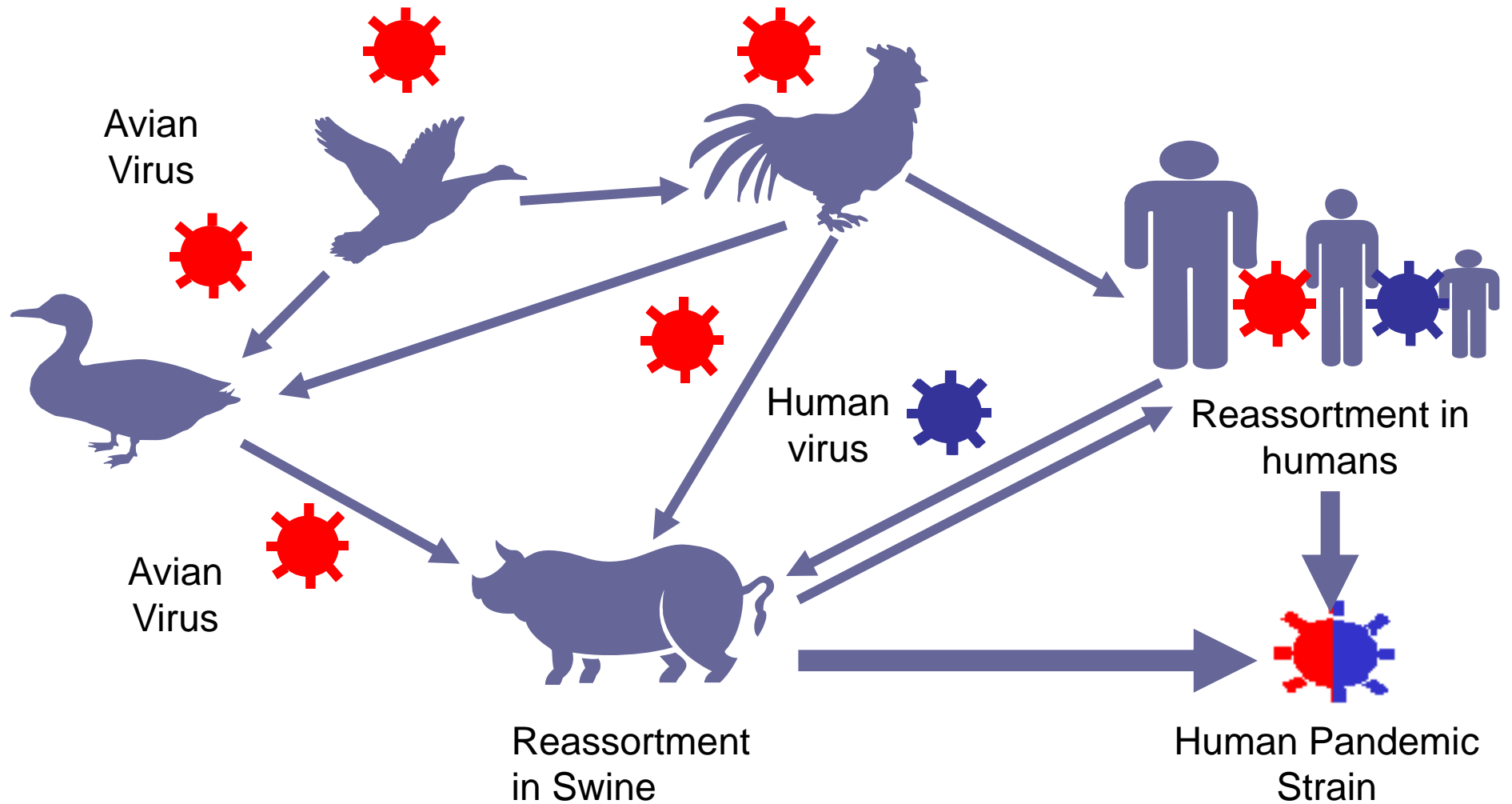
Domestic birds



- **Hong Kong
1997/2003, H5N1**
- **HK, China
1999, H9N2**
- **Netherlands
2003, H7N7**
- **Vietnam &
Thailand
2004, H5N1**
- **Indonesia
2005, H5N1**

Migrator
y birds

Reassortment (in Animals and
Humans)



Prerequisites for a Start of a Pandemic



- The first two of three prerequisites have been met:
 - A novel virus
 - Virus must be able to replicate in humans and cause disease
 - New virus must be efficiently transmitted from one human to another

- Virus can improve its transmissibility via two mechanisms:
 - Adaptive mutation
 - Genetic reassortment
(can take place in humans without prior adaptation in another mammalian species, such as the pig)

HPAI H5N1

- Is probably the most worrisome for human health
- Have a unique capacity to infect humans and cause severe disease
 - In 1997 in Hong Kong
 - In February 2003 in Hong Kong
 - Since mid-January of this year, in Viet Nam and Thailand

Public Health Risk

- ❖ Emergence of a new influenza virus
 - ❖ Highly pathogenic
 - ❖ Rapid spread from person-to-person
- ❖ Influenza Pandemics 20th Century:
 - ❖ 1580 -1900: 28 pandemics
 - ❖ 1918-19 “Spanish flu” 20 - 40 million deaths A (H1N1)
 - ❖ 1957 “Asian flu” 1 - 4 million deaths A (H2N2)
 - ❖ 1968 “Hong Kong flu” 1 - 4 million deaths A (H3N2)

Morbidity/Mortality

- Morbidity: Up to 100%
- Mortality: 90%
- Varies greatly depending on
 - Virulence and strain
 - Avian species and susceptibility of host
 - Environmental conditions
 - Secondary infections
 - Vaccination history
- Some species show few or no signs
 - Carrier state may exist

Animal Transmission

- Direct contact with feces and respiratory discharges
- Contamination of the environment

- Feed, water
- Equipment
- Human clothing



- Contaminated or incompletely inactivated vaccines

Animal Transmission

- Survives for long periods in the environment
- Incubation period: 2-15 days
 - ✓ 5-6 days average
- Migratory birds, feral pigeons
 - ✓ Contamination of poultry feed

Human Transmission

- Mild conjunctivitis
 - ✓ Virus shed in ocular secretions for 4-7 days
 - ✓ Avoid contact with avian species during this time
- Lab workers and vaccination crews most at risk
- No cases from handling or consuming poultry products
- No human-to-human spread

Environmental Factors

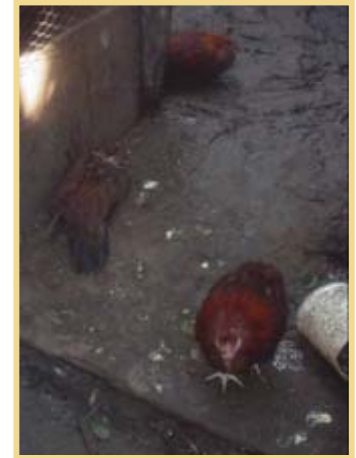
- Crowding index:
 - Easy spread from person to person through:
 - Droplet spread
 - Touching objects with flu viruses then touching mouth and nose
 - Pass on the flu before sickness (1 day before symptoms)
- Speed of travel:
 - Means of transport: World is becoming so small

Host

- ❖ Lack of immunity:
 - Antigenic shift: Pandemic
 - General health and immune system of the individual
- ❖ Very high case fatality of the Avian Influenza:
 - In animals: up to 100%
 - In humans: up to 80% or even more

Clinical Signs

- Drop in egg production
- Numerous deaths within (24-48 hours)
- Deaths continue for (7-10 days)



Clinical Signs

- Edema of head, especially around eyes
- Greenish-dark watery diarrhea
- Respiratory and neurological signs
- Signs vary with species and virulence



Post Mortem Lesions

- Edema of the head and neck
- Edema, hemorrhage, necrosis or ulceration of lymphoid tissue
- Lesions vary with species and virulence



Sampling

- Before collecting or sending any samples, the proper authorities should be contacted
- Samples should only be sent under secure conditions and to authorized laboratories to prevent the spread of the disease
- Samples may be zoonotic

Clinical features in Humans

- Eye infections
 - Reddening, excessive tearing, edema of lids, conjunctivitis, subconjunctival hemorrhage
 - Usually transient, cornea not affected
 - Lab workers and vaccination crews most susceptible
 - No human to human spread

Diagnosis

- Laboratory Tests
 - Virus isolation
 - Virus characterization
 - To determine virus strain and pathogenicity
 - Serology
 - No strain information, so limited value
 - May be used post-vaccinal to confirm immune response

Prevention and Control

Recommended Actions

- Notification of Authorities
 - Federal:
 - Area Veterinarian in Charge (AVIC)
 - State veterinarian

- Quarantine all suspect animals and the premises

Recommended Actions

❖ Confirmatory diagnosis

❖ Depopulation may occur

➤ Proper destruction of

✓ Exposed cadavers

✓ Litter

✓ Animal products



Control and Eradication

- Disinfection of premises
- Delay re-introduction of new birds for 30 days
- Control insects and mice
- Limit human traffic



Disinfection

- Virus killed by:
 - Household bleach, 6%
 - Extremes in pH
 - ✓ Less than 2 or greater than 12
 - Heat
 - ✓ Boiling one minute
 - Detergents
 - Dryness
 - Ultraviolet light and sunlight

Newcastle disease Virus

- The virus is killed by common disinfectants:
 - Each strain has different sensitivities
 - Care must be taken to screen for the virus after disinfection (virus can survive for some days outside the host and for several months in eggs and for years in frozen carcasses)
- During outbreaks NCD:
 - infected flock must be slaughtered
 - carcasses must be burned
 - Affected areas may also be placed under strict quarantine

Control Measures in Birds



- Culling of all infected or exposed birds
- Quarantining & rigorous disinfection of farms
- Restriction of movement of live poultry
(Spread by bird droppings, contaminated dust and soil,
Contaminated equipments, vehicles, feed, cages and clothing –
especially shoes, mechanical transmission: Animal feet (rodents),
flies (limited evidence) and wet markets)
- Chickens, domestic ducks, turkeys, geese

Culling

- Rapid destruction of all infected or exposed birds with proper disposal of carcasses
- First line of defence for both the protection of human health and the reduction of further losses in the agricultural sector
- Prompt culling of Hong Kong's entire poultry population (1997) probably averted a pandemic
- Workers involved in the culling of poultry flocks must be protected: (proper clothing and equipment, against infection should also receive antiviral drugs)

Vaccination

- Vaccination routine worldwide
- Reduces clinical signs
- Does not prevent virus replication or shedding
- Not an alternative to good management, biosecurity or good hygiene in rearing practices

Vaccination

- Vaccine:
 - “Flu shot”: inactivated vaccine
 - Nasal-spray flu vaccine: Live attenuated Influenza Vaccine
 - Best time to get vaccinated is October or November
- Who should get vaccinated each year?
 - People at high risk for complications from the flu
 - People 50 to 64 years of age
 - People who can transmit flu to others at high risk for complications

Treatment

- Tamiflu: Oseltamivir
 - Work against influenza A & B viruses
 - If taken 48 hours of becoming ill:
 - Stops virus from bursting out of infected cells
 - Used in children over 1 year of age
- WHO have advised all health authorities to stockpile anti-viral medicines to prepare for the pandemic.

Antiviral Drug

Osetamivir (Tamiflu[®])

- Effective against all subtypes of influenza viruses A (including H5N1)
- Capsules (75 mg), Oral suspension (12 mg/ml)
- Store at 25° C, excursions permitted to 15-30° C
- 1 yr and above, symptoms within 48 hrs
- 13 yrs or older: 75 mg twice daily for five days
- Prophylaxis:
 - ✓ Close contacts: 75 mg daily for at least 7 days
 - ✓ Community contacts: 75 mg once daily up to six weeks
- Adverse reactions: Nausea and vomiting with first dose



NDC 0004-0800-85



TAMIFLU™
(oseltamivir phosphate) Capsules

75 mg

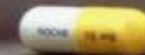
Each capsule contains oseltamivir phosphate equivalent to 75 mg oseltamivir (free base).

10 Capsules



Rx only.

To Open Lift This Flap





Influenza Vaccine Development (Seasonal Vaccine)

- Infection with virus does not provide any long lasting immunity
 - ✓ No cross-protection against other subtypes
 - ✓ Seasonal outbreaks almost every year
 - ✓ Recommendation on the composition of vaccine

- Limited production:
 - ✓ 300 million doses annually
 - ✓ Europe, North America, Australia and Japan
 - ✓ No single influenza vaccine producer in south-east Asia
 - ✓ No routine vaccination in most countries

- No one can predict pandemic subtype
- Hardly cover more than 10% of the world's population (even all producers switch to production of a pandemic influenza vaccine)
- Prototype H5N1 has been developed
- Several candidates are in various stages of development
- WHO will provide technical (support to countries for vaccine production, guide good manufacturing practices and strengthen National Regulatory Authorities)