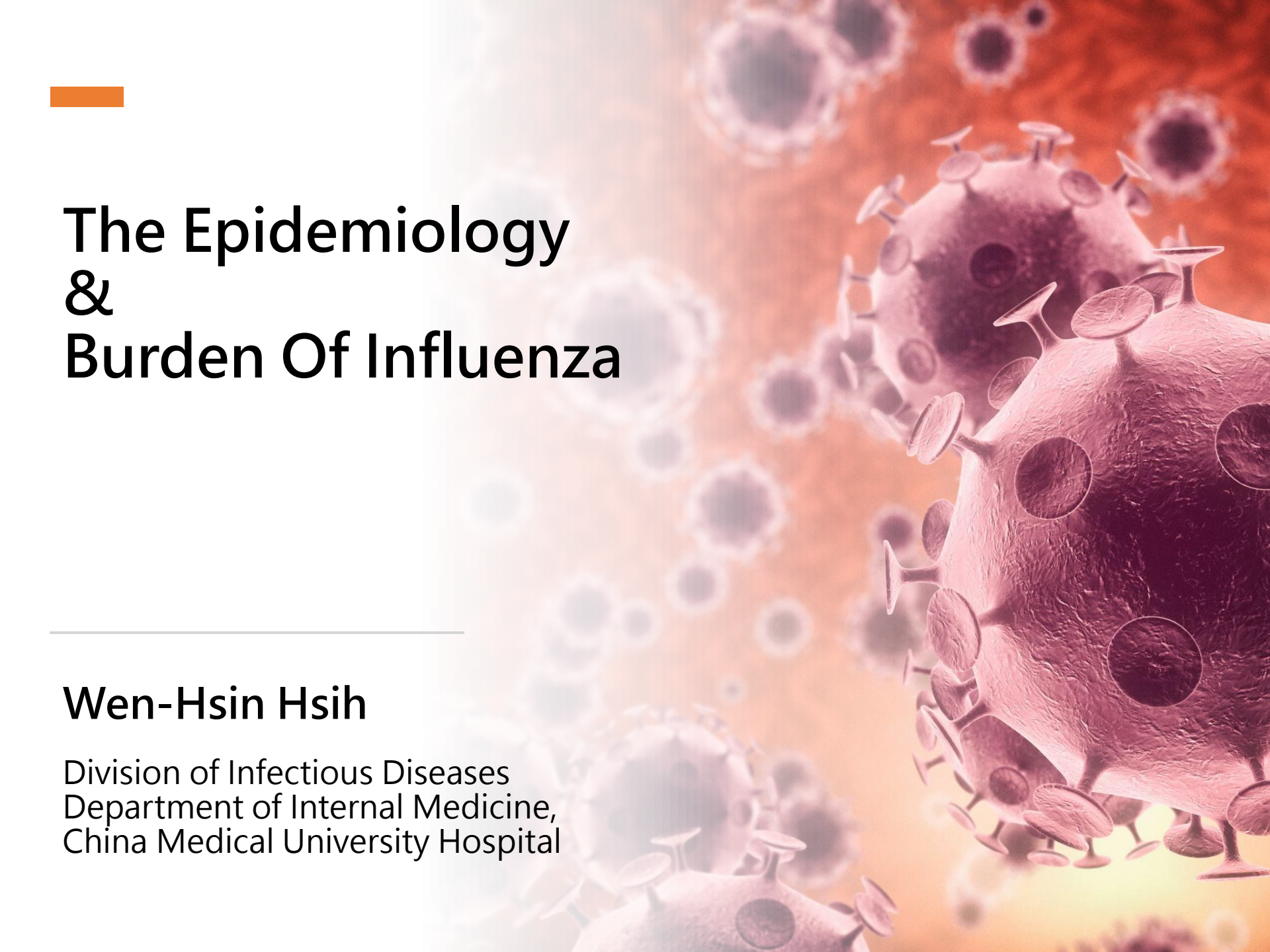
The Epidemiology & Burden Of Influenza



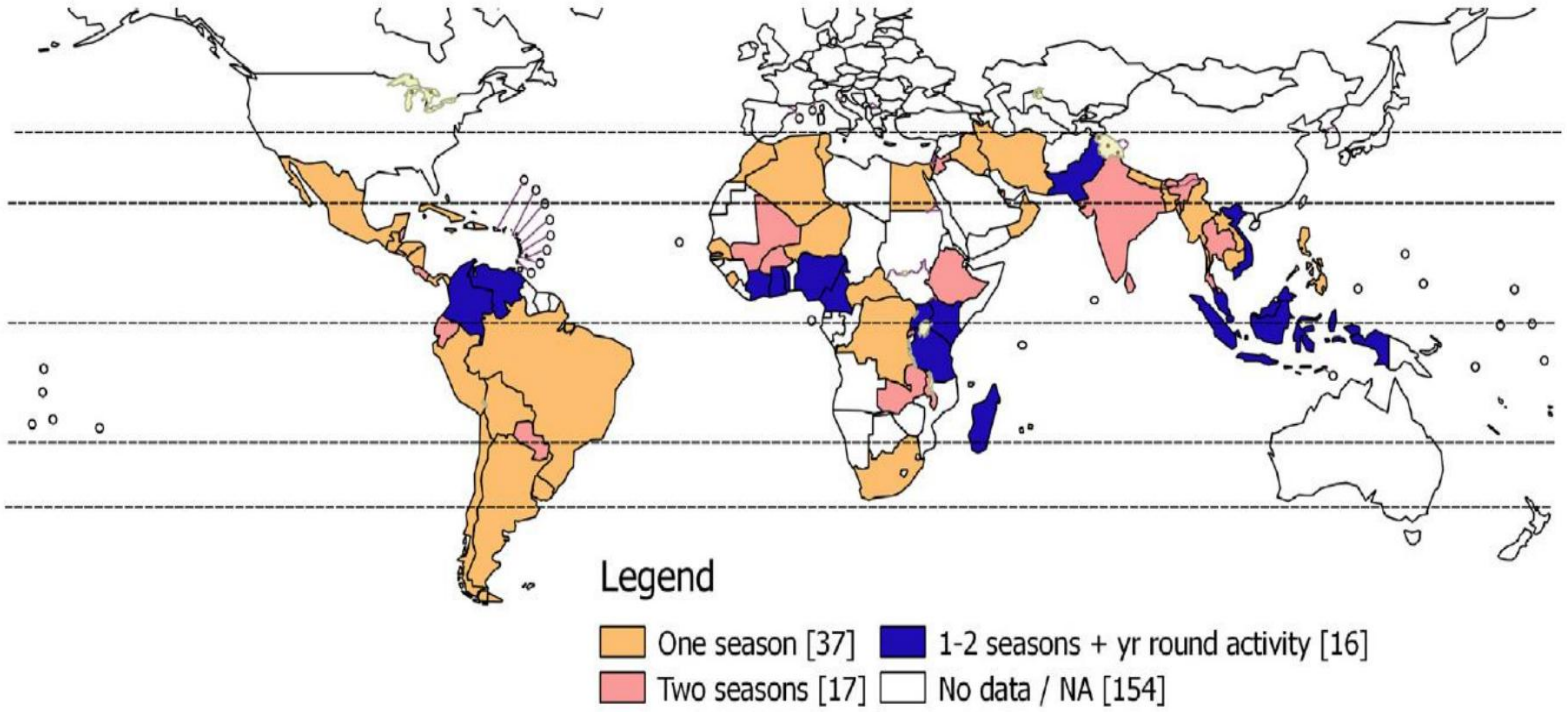
Wen-Hsin Hsih

Division of Infectious Diseases
Department of Internal Medicine,
China Medical University Hospital

Outlines

- Overview of viral structure, classification, host range
- Antigenic variation
- Epidemic & Pandemic influenza
- Emergence of pandemic viruses from animals
- Disease impact and complications

Influenza Activity In The World

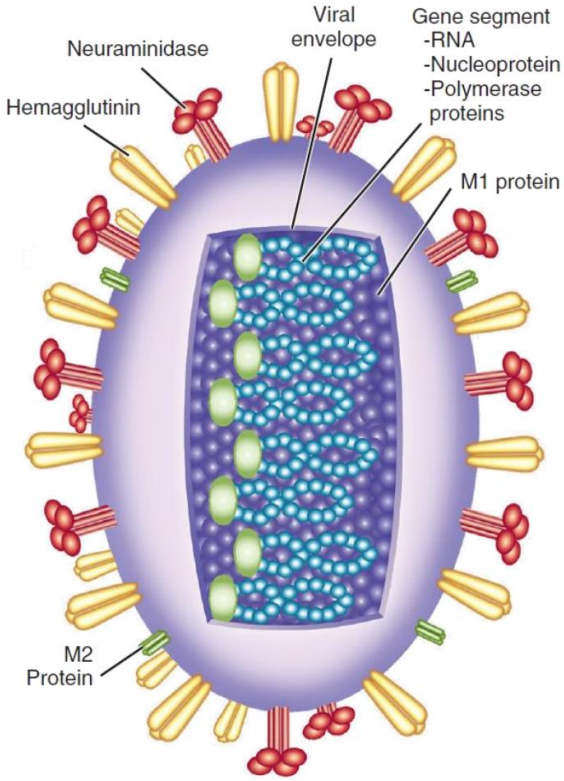


Worldwide, 3-5 million cases of severe illness and about 290000 to 650000 deaths

https://www.who.int/news-room/fact-sheets/detail/influenza-(seasonal)

Influenza Classification

- Orthomyxoviridae family 正黏液病毒科
- 基因體含8段(A、B型)或7段(C、D型)單股RNA
- Enveloped RNA virus； Approximately 80–120 nm in diameter



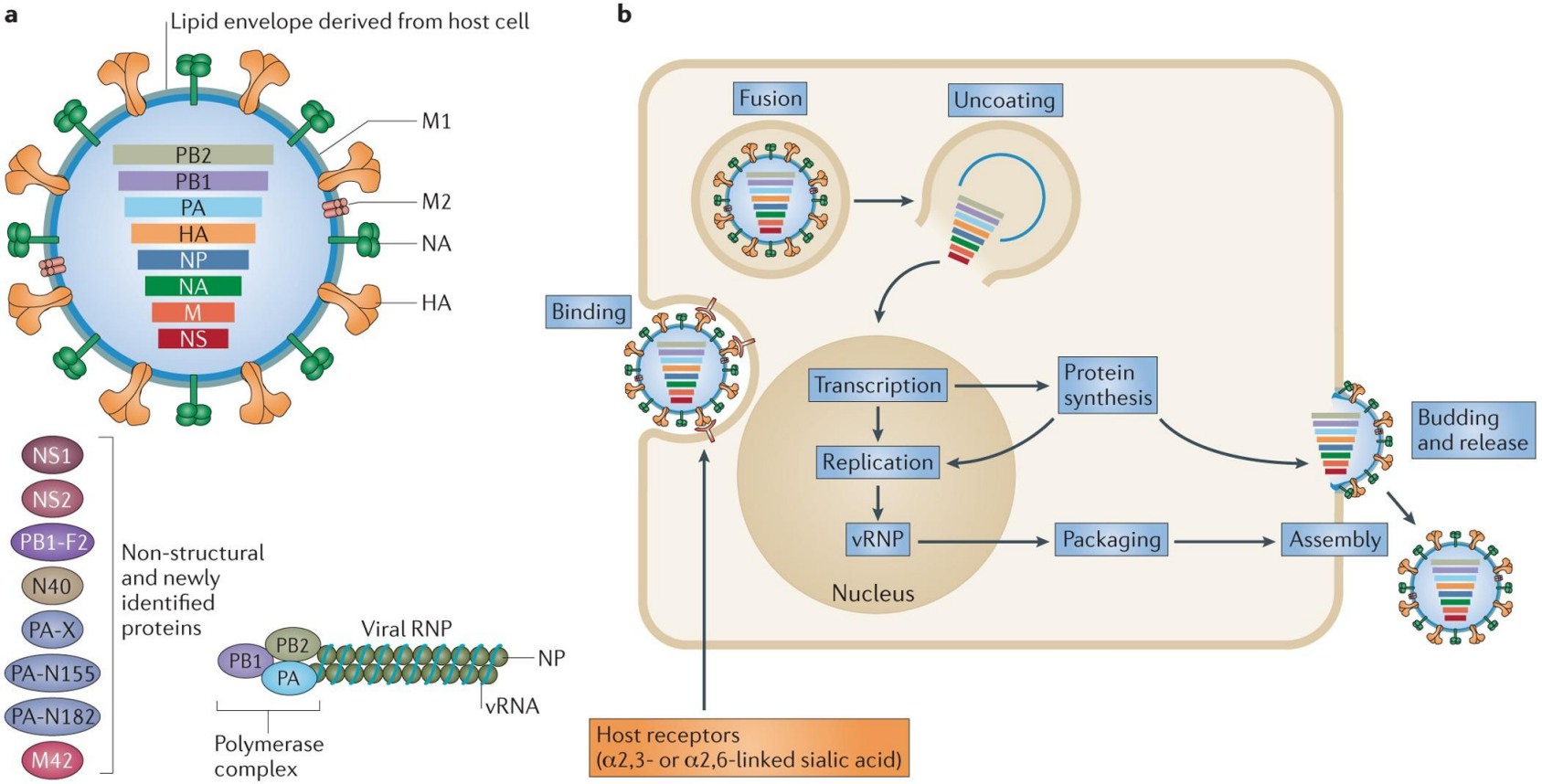
Exp Rev Anti-Infect Ther 2016;14:365. Principles and Practice of Infectious Diseases 8th, Mandell, Douglas, Bennett

Influenza Classification

A	人畜共通，會感染人類、哺乳動物與鳥類
B	只會感染人類
C	感染人類和豬，感染人類後不造成明顯臨床症狀
D	目前僅主要感染牛隻，對人類是否有致病性仍未知

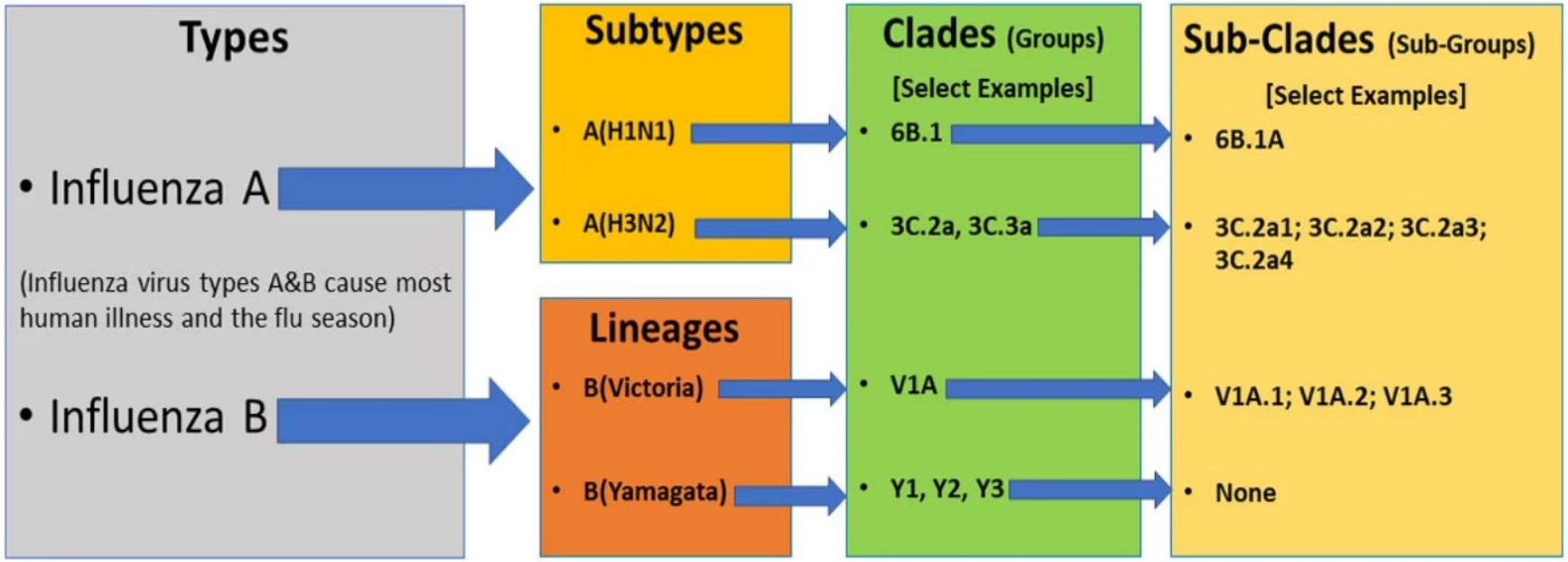
Exp Rev Anti-Infect Ther 2016;14:365. Principles and Practice of Infectious Diseases 8th, Mandell, Douglas, Bennett

Structure and Life Cycle Of Influenza A Viruses



Nature Reviews | Microbiology

Human Seasonal Influenza Virus



- Subtypes in influenza A virus
  – 18 hemagglutinin (HA) & 11 neuraminidase (NA)
- Lineages in influenza B virus: Victoria and Yamagata

https://www.cdc.gov/flu/about/viruses/types.htm

Interpretation



Taiwan CDC 流感防治與疫苗接種政策

Interpretation



新型A型流感
(Novel Influenza A Virus Infections)

定義：偶發出現感染人類的其他A型流感病毒亞型。

排除條件：排除每年週期性流行的季節性流感（A/H1N1 及 A/H3N2)。

初期傳播：通常很少經由人與人之間傳播。



基因重組



跨越物種障礙，導致人類無免疫力

案例印證：2009年 H1N1 新型流感即是經過基因重組後，突破傳播限制，最終造成大流行。



大流行流感
(Pandemic influenza)

形成要件：
1. 演化出新型流感病毒。
2. 人類群體完全無免疫力。
3. 具備有效人傳人的能力。

最終結果：導致全球規模的爆發與大流行。

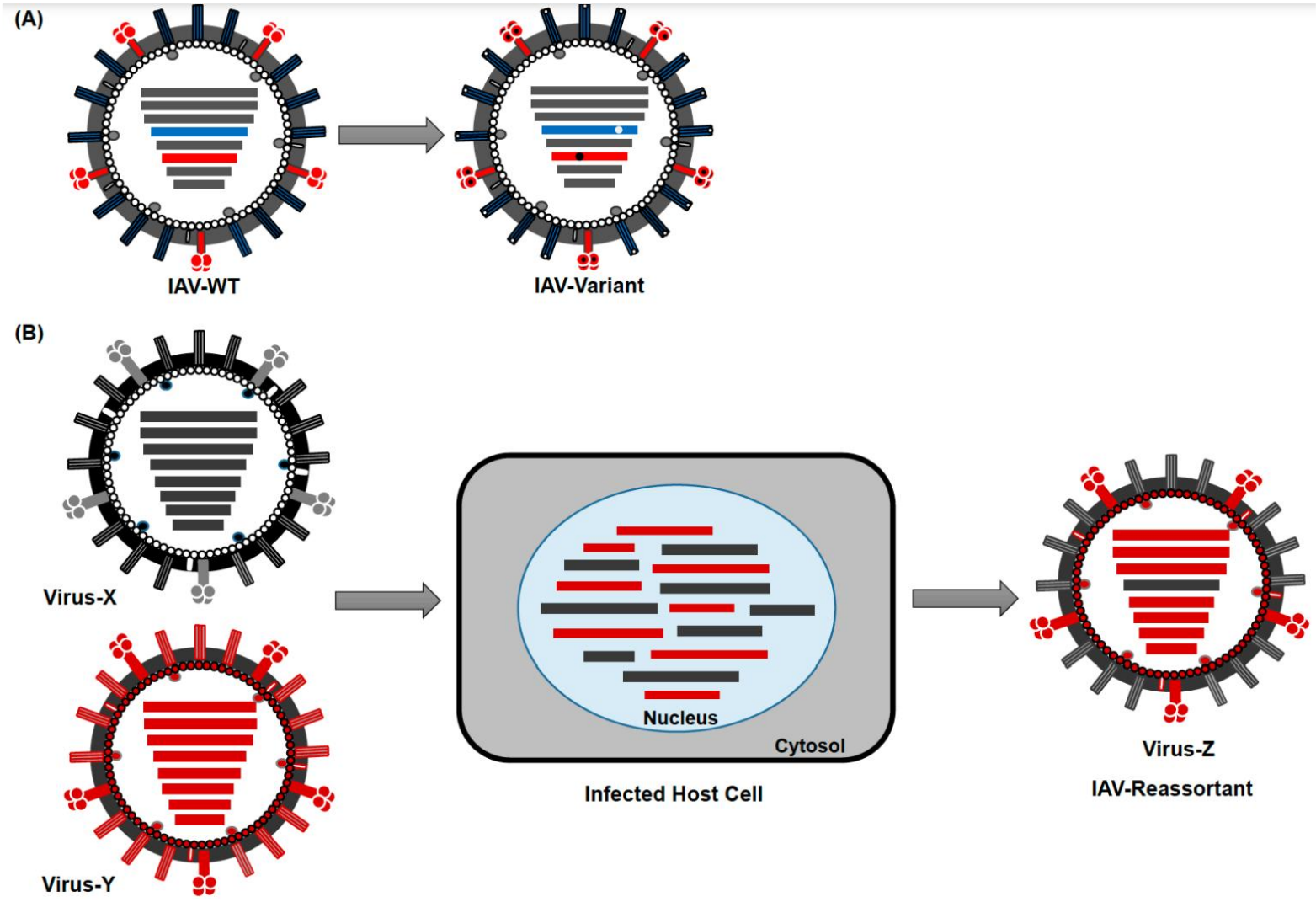
Taiwan CDC 流感防治與疫苗接種政策

Differences among Influenza A, B and C Viruses

	Influenza A	Influenza B	Influenza C
Genetics	8 gene segments	8 gene segments	7 gene segments
Natural host range	Humans, swine, equine, birds, marine, mammals	Humans only	Humans and swine
Epidemiology	Antigenic shift and drift	Antigenic drift only; two main lineages cocirculate	Antigenic drift only; multiple variants
Clinical manifestations	May cause large pandemics with significant mortality in young persons	Severe disease generally confined to older adults or persons at high risk; pandemics not seen	Mild disease without seasonality

Principles and Practice of Infectious Diseases 8th , Mandell, Douglas, Bennet

Antigenic drift and Antigenic shift

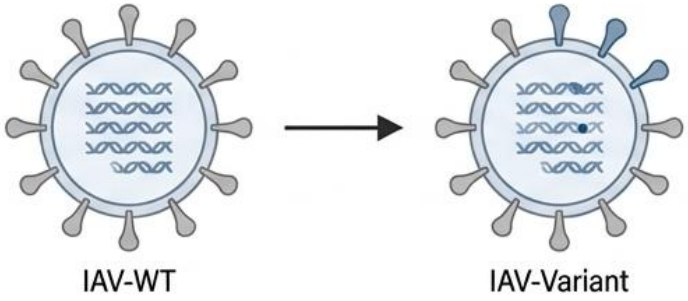


Viruses 2018. doi:10.3390/v10090497

The Mechanisms of Immune Evasion and Viral Evolution

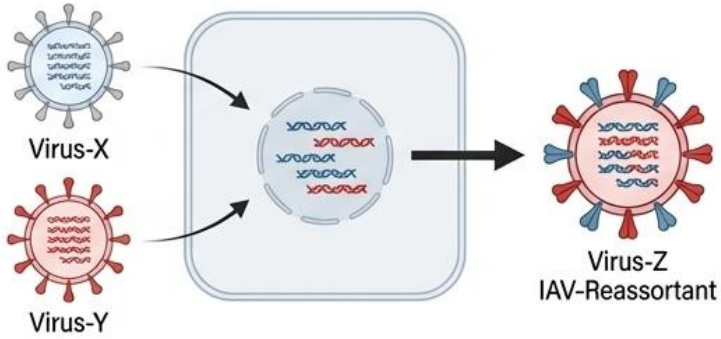
Antigenic Drift

- **Mechanism:** Gradual accumulation of point mutations in HA and NA genes.
- **Virus Types:** Occurs in Influenza Types A & B.
- **Epidemiological Result:** Drives annual, seasonal inter-pandemic outbreaks. Evades partial population immunity.

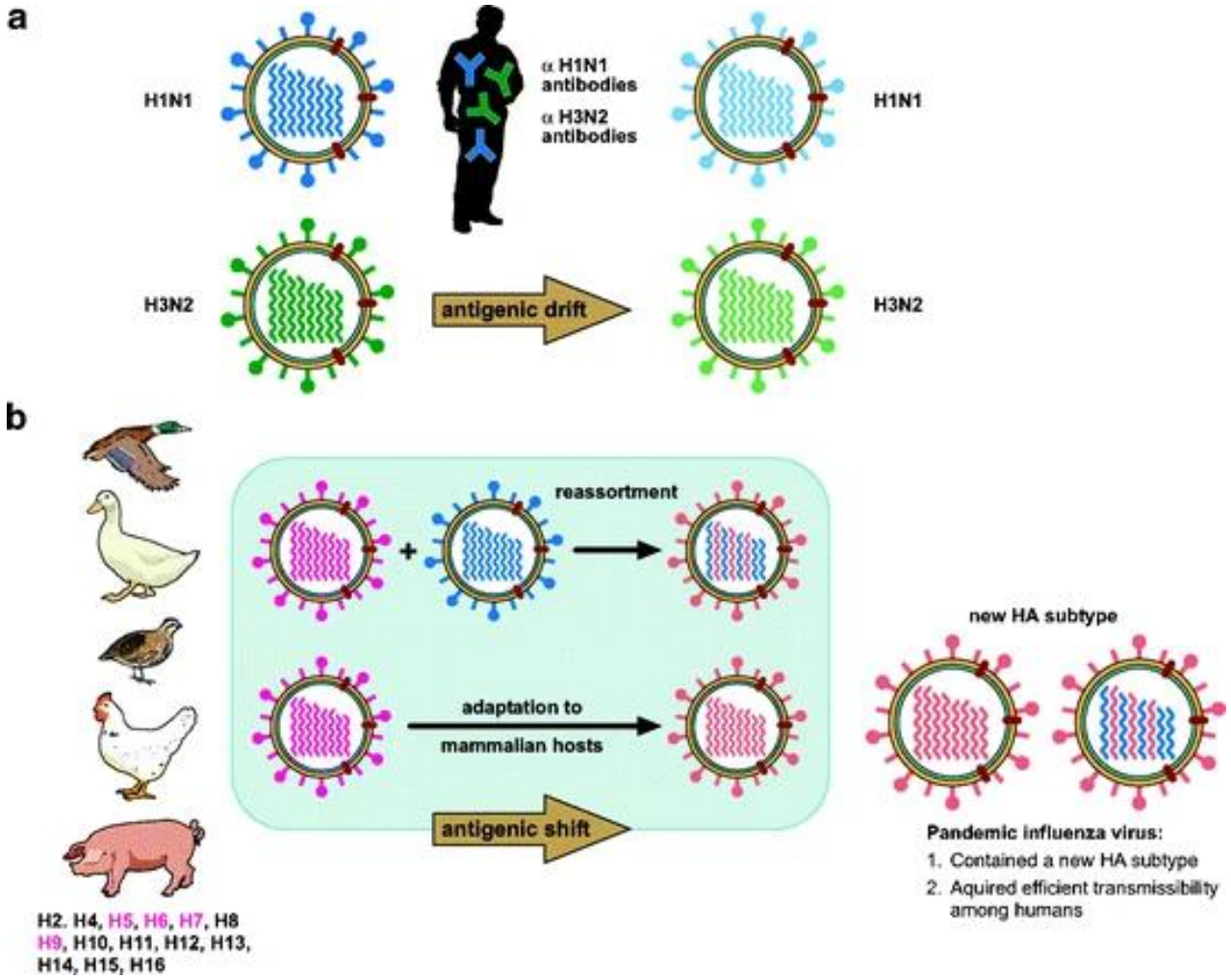


Antigenic Shift

- **Mechanism:** Direct introduction from an animal host, or sudden exchange/reassortment of gene segments (with or without a new NA subtype).
- **Virus Types:** Exclusive to Influenza Type A.
- **Epidemiological Result:** Introduces a completely novel HA subtype. The population lacks immunity, resulting in global pandemics.



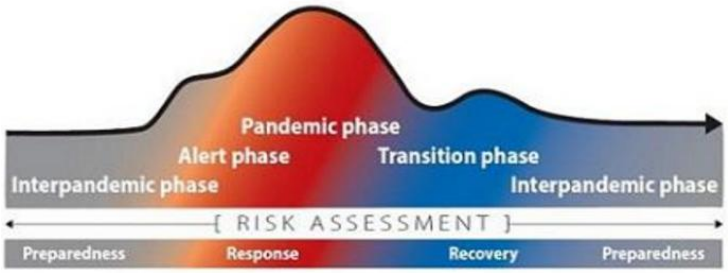
Antigenic Drift and Antigenic Shift of Influenza Virus



Yen, H. L., & Webster, R. G. (2009). Pandemic influenza as a current threat. *vaccines for pandemic influenza*, 3-24.

	Epidemic	Pandemic
Geographic Scope	Confined to a specific location (city, town, or country). Represents an increase in frequency above baseline in a given time period.	Global spread of human influenza.
Virology & Immunity	Predominantly caused by a single established strain of influenza virus.	Caused by a new influenza subtype (antigenic variant) toward which the population has little or no prior immunity.
Disease Kinetics & Staging	Begins abruptly, reaches a sharp peak in 2 to 3 weeks, and lasts 5 to 6 weeks.	Progresses through four distinct levels of activity: interpandemic, alert, pandemic, and transition.
Population Impact (Attack Rates)	Estimated at 10% to 20% in unvaccinated populations (can reach as high as 40% to 50%).	Widespread human transmission facilitated by the complete lack of baseline population immunity.

WHO Pandemic phases



Principles and Practice of Infectious Diseases 2020, 9th ed

WHO Influenza Pandemic Phases

表 0-1. WHO 流感大流行疫情等級

等級	狀況	階段
Phase 1	沒有動物流感病毒感染至人類。	動物感染為主 少數人類感染
Phase 2	動物流感病毒在野生或飼養動物間傳播，已造成人類感染，具大流行潛在威脅。	
Phase 3	動物或人類-動物流感重組病毒造成人類散發病例或小型聚集，但尚未發生人傳人及持續性社區流行。	
Phase 4	動物或人類-動物流感重組病毒已能人傳人，並發生持續性社區流行。	持續人傳人
Phase 5	在單一WHO區域*內，有2個(含)以上國家發生持續性社區流行。	廣泛性人類感染
Phase 6	在其他WHO區域內，有國家發生持續性社區流行。	
Post-peak	監視資料顯示多數國家之大流行狀況已降至高峰之下。	可能再次流行
Post-pandemic	監視資料顯示病毒活動在多數國家回復至季節性流感狀況。	季節型態活動

WHO Pandemic Influenza Phases (2009)
行政院衛生署疾病管制局
https://www.cdc.gov.tw/uploads/files/4c6e5d73-12a1-4b7a-b9a1-486c0c118629.pdf

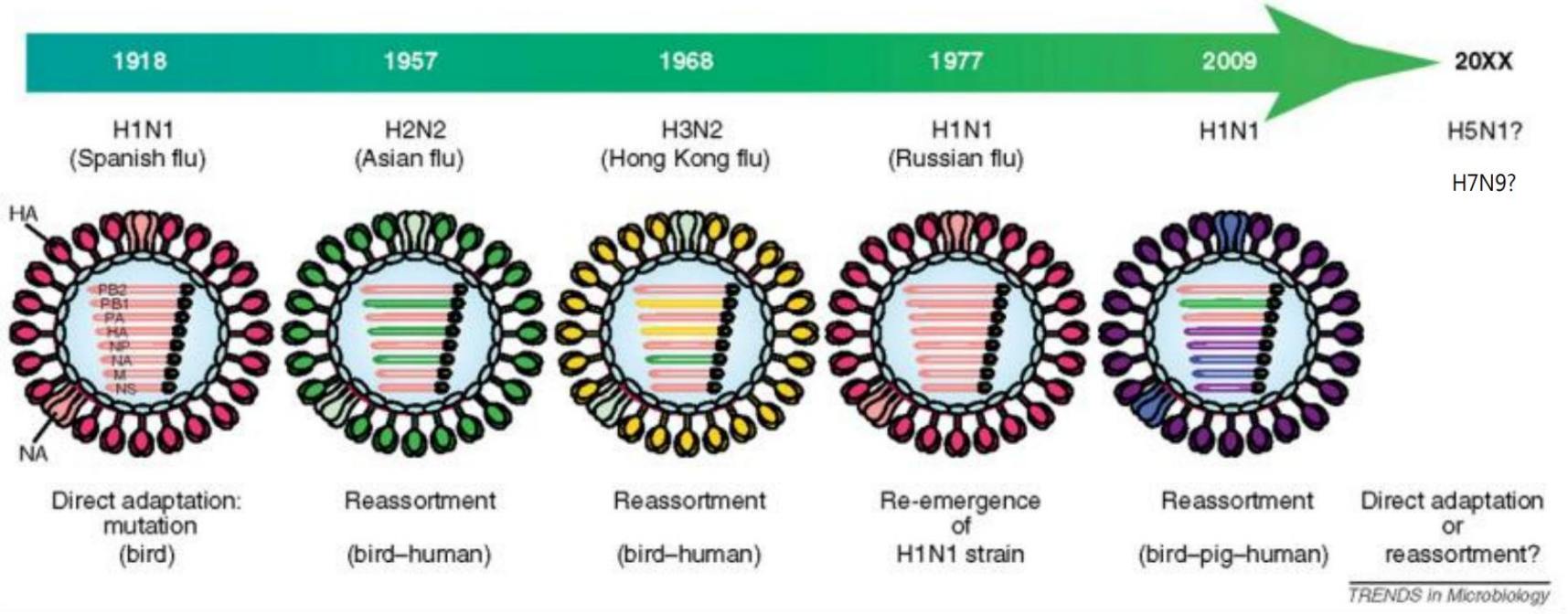
流感大流行的要件及威脅性

- 大流行之要件
  - 有一株新型流感病毒可在人體內複製並進而引起疾病
    人類對此病毒幾乎無免疫力
  - **病毒可有效人傳人**
- 大流行之威脅性
  - 依**病毒傳播的難易度**及**臨床嚴重程度評估**
  - Pandemic Severity Assessment Framework (PSAF)

Pandemic Severity Assessment Framework (PSAF)

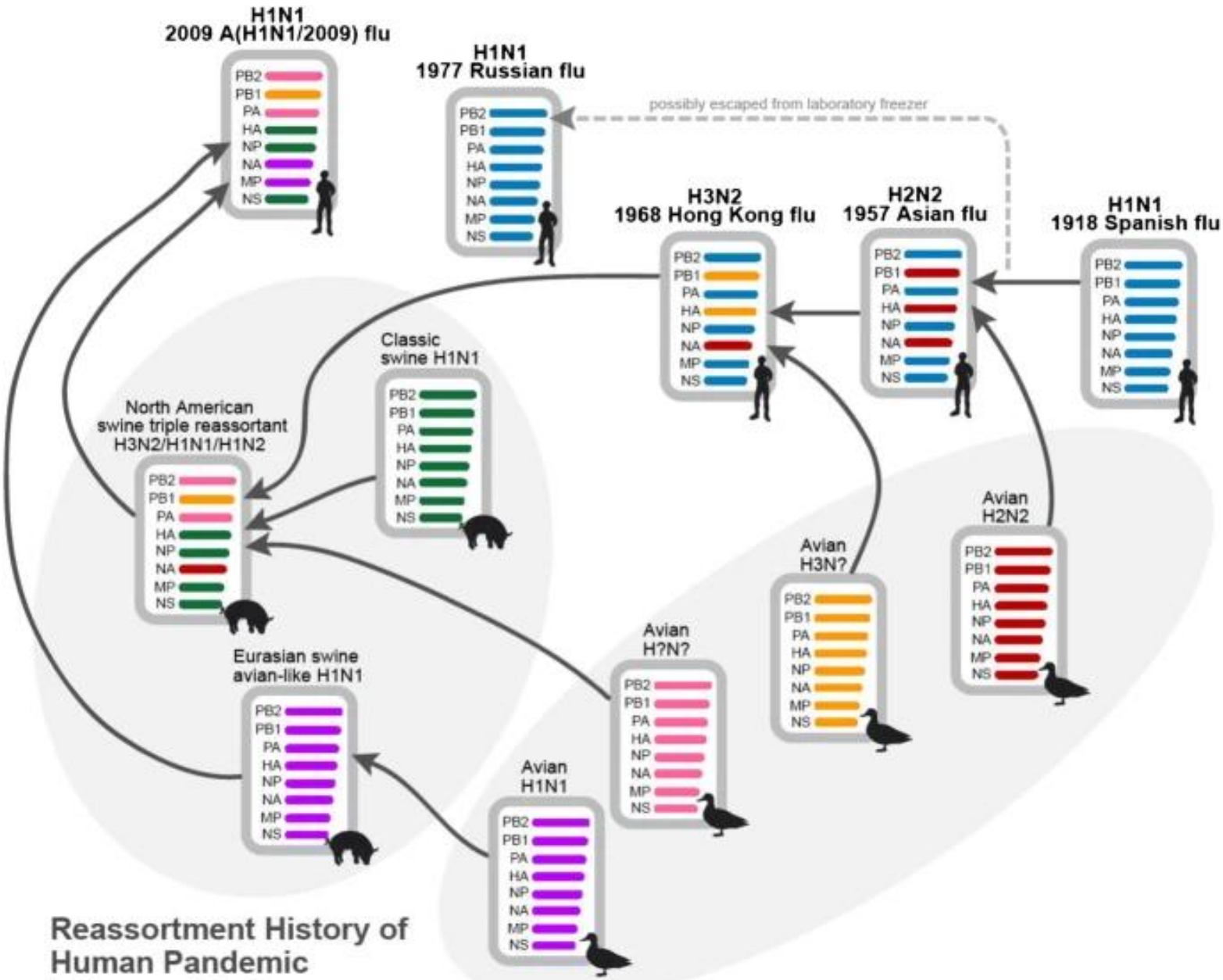
歷史事件	Severity of pandemic	PSAF
1918 西班牙流感	Very high severity (very severe to extreme pandemic)	D
1957 亞洲流感	High severity (severe pandemic)	B
1968 香港流感	Moderate to high severity (moderate to severe pandemic)	B
2009 H1N1流感	Low to moderate severity (mild to moderate pandemic)	A

流感大流行的歷史



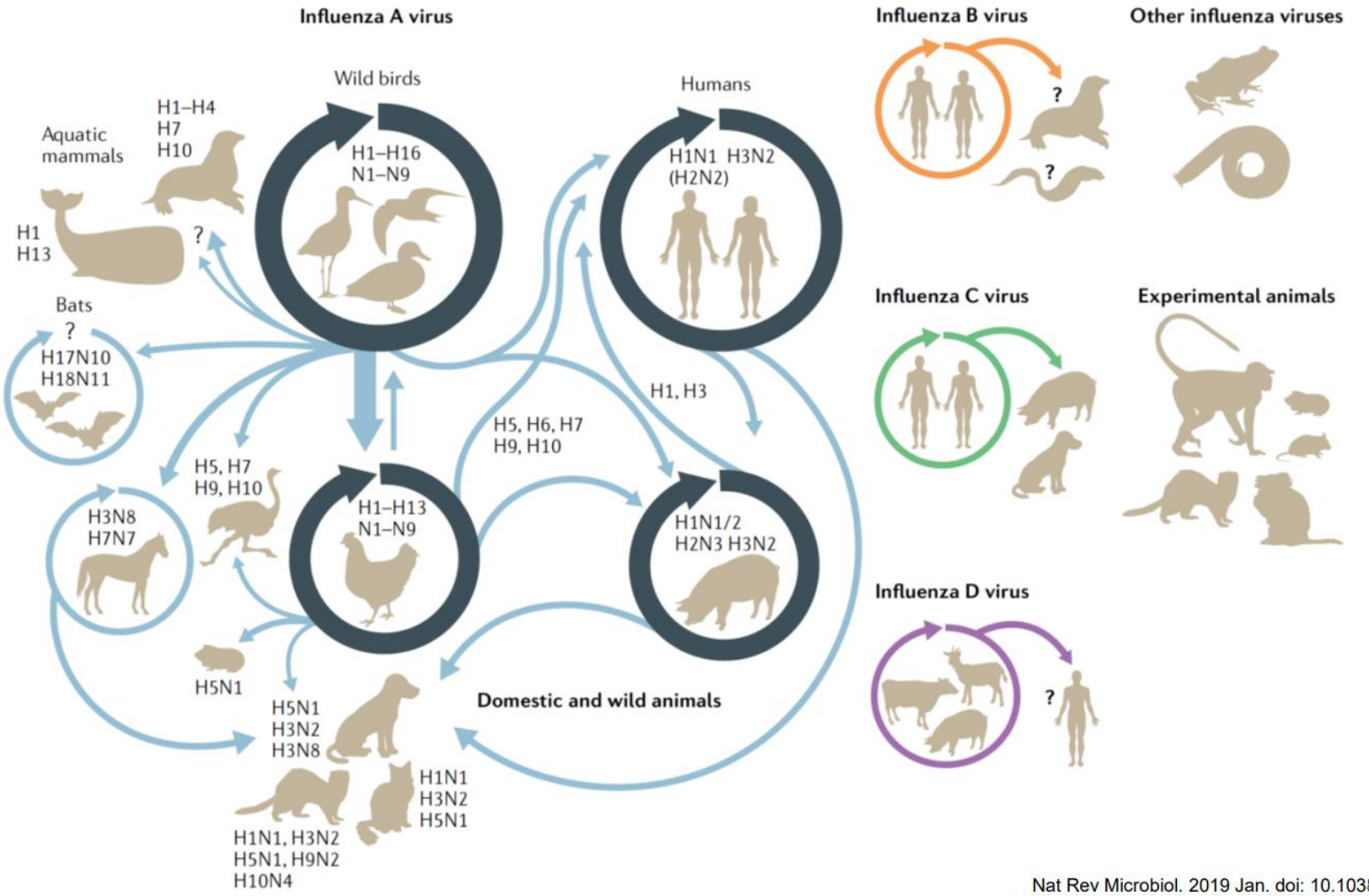
4~5千萬人死亡 | 逾200萬人死亡 | 100萬人死亡 | 70萬人死亡 | 超過1.8萬人死亡

Taiwan CDC, 2023流感防治與疫苗接種政策_公版



Curr Infect Dis Rep 2018 Aug. doi: 10.1007/s11908-018-0642-9

Ecology of Influenza Viruses



Nat Rev Microbiol. 2019 Jan. doi: 10.1038/s41579-018-0115-z

H5N1、H5N6、H6N1、H7N2、H7N3、H7N4、H7N7、H7N9、H9N2、H10N7 和 H10N8

LPAIV / HPAIV

Low Pathogenic Avian Influenza Viruses (LPAIV)

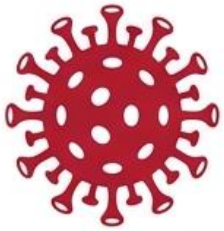


Maintained in wild aquatic birds



Almost without developing severe clinical signs of the disease.

Highly Pathogenic Avian Influenza Viruses (HPAIV)



Restricted to H5Nx, H7Nx

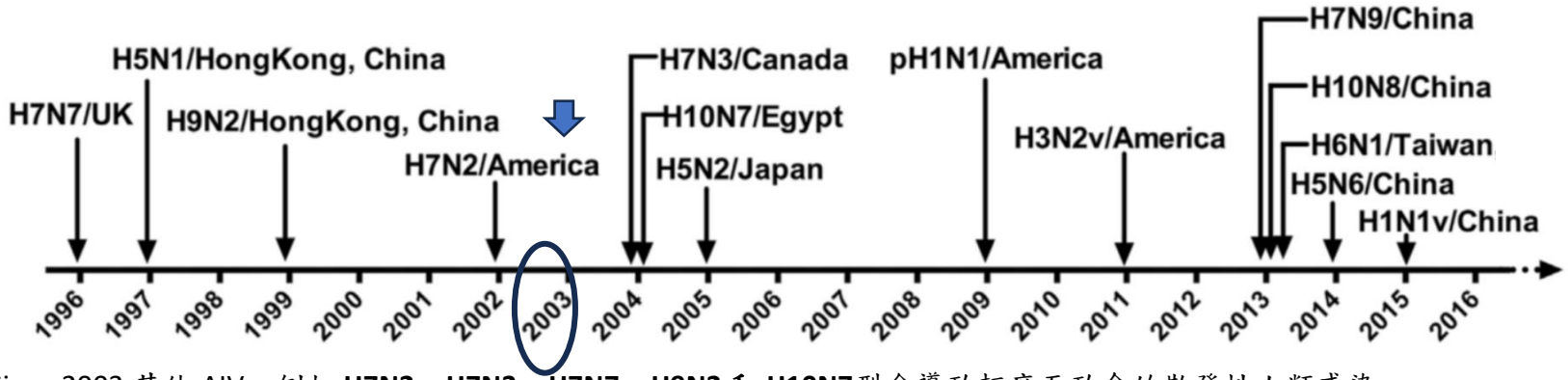


Cause up to 100% mortality in several bird species.

Viruses 2018. doi:10.3390/v10090497

Animal-to-Human Transmission of Influenza A

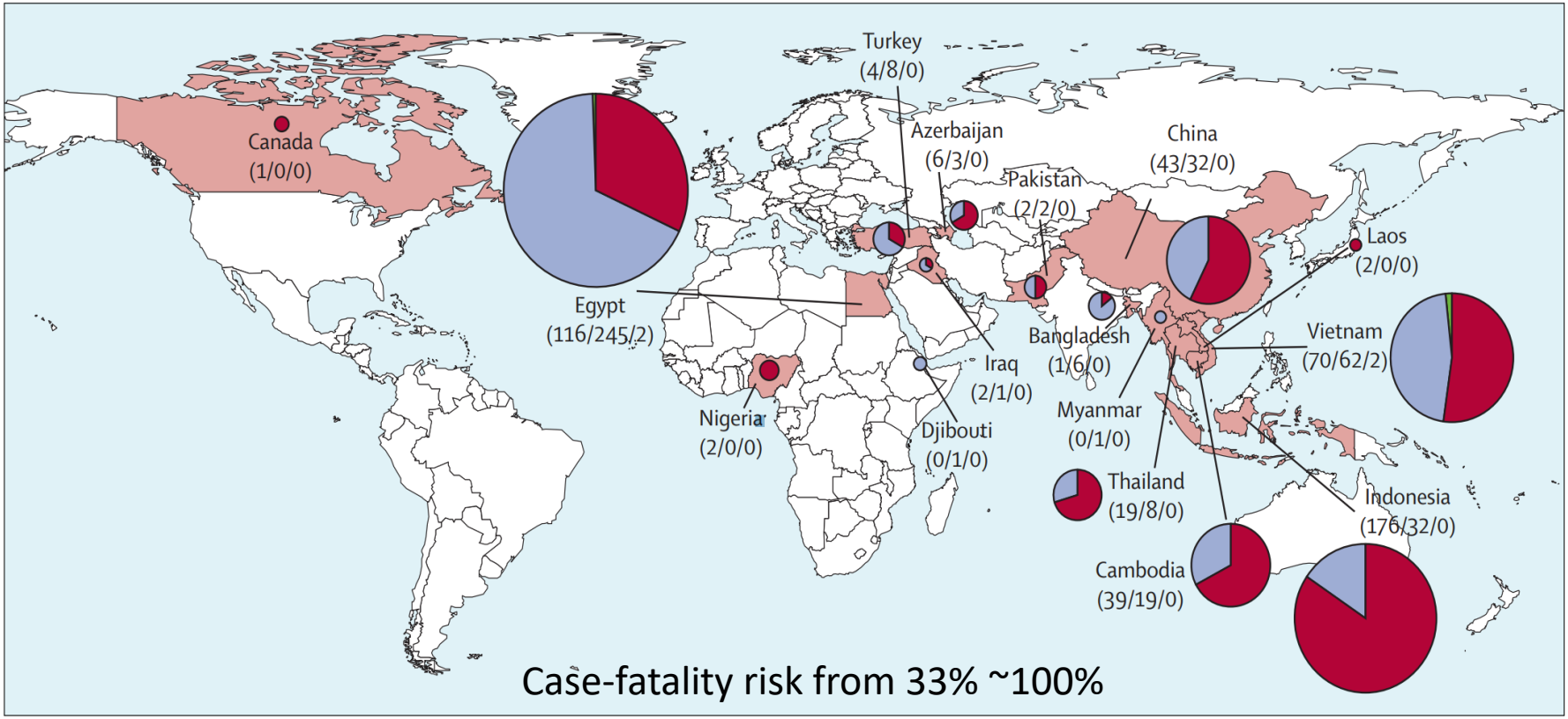
Year	Subtype	Source of infection	Symptoms
1976	H1N1	Swine to human	Respiratory (200/1)
1977	H7N7	Seal to human	Conjunctivitis
1993	H1N1	Swine to human?	Mild respiratory
1995	H7N7	Avian to human	Conjunctivitis
1997	H5N1	Avian to human	Respiratory
1999	H9N2	Avian to human	Mild respiratory



Since 2003,其他 AIV，例如 **H7N2**、**H7N3**、**H7N7**、**H9N2** 和 **H10N7**型會導致輕度至致命的散發性人類感染
Since 2013, **H5N6**、**H6N1**、**H7N4**、**H7N9**、**H9N2**、**H10N8**跨越物種屏障進行感染人類誘發無症狀至致命感染

Occup Med (Lond). 2002 Aug, doi: 10.1093/occmed/52.5.241. Clin Chest Med 2017;38:59

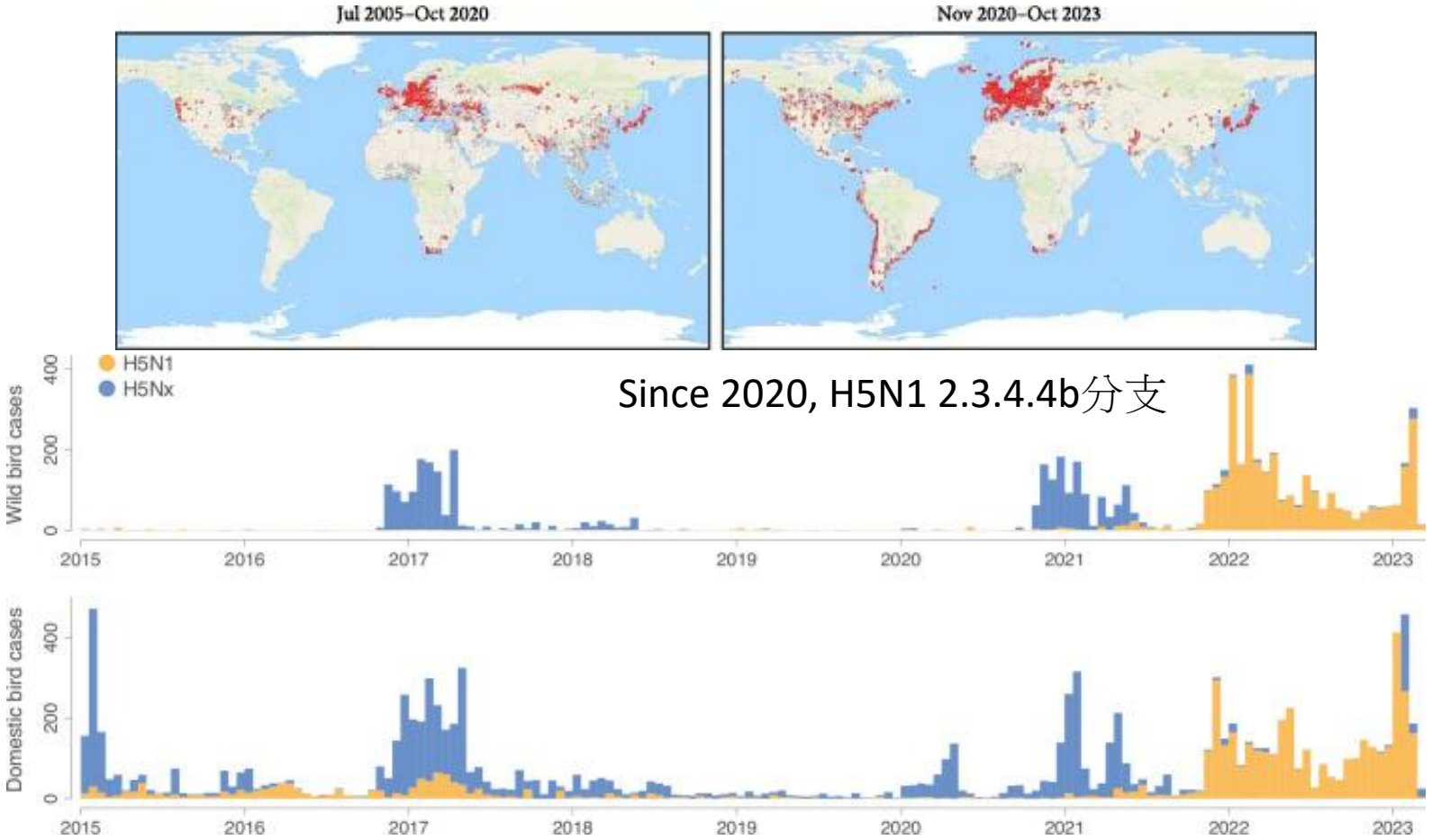
Geographic Distribution Of Human H5N1 Infection by Outcome, May, 1997, to April, 2015



Total Cases (2003–2026): Since 2003, there have been nearly 1,000 confirmed human cases of H5N1 worldwide, with a high case fatality rate of nearly 50%.

Lancet Infect Dis 2016; 16: e108
World Health Organization

Novel Epidemiologic Features of High Pathogenicity Avian Influenza Virus A H5N1 2.3.3.4b



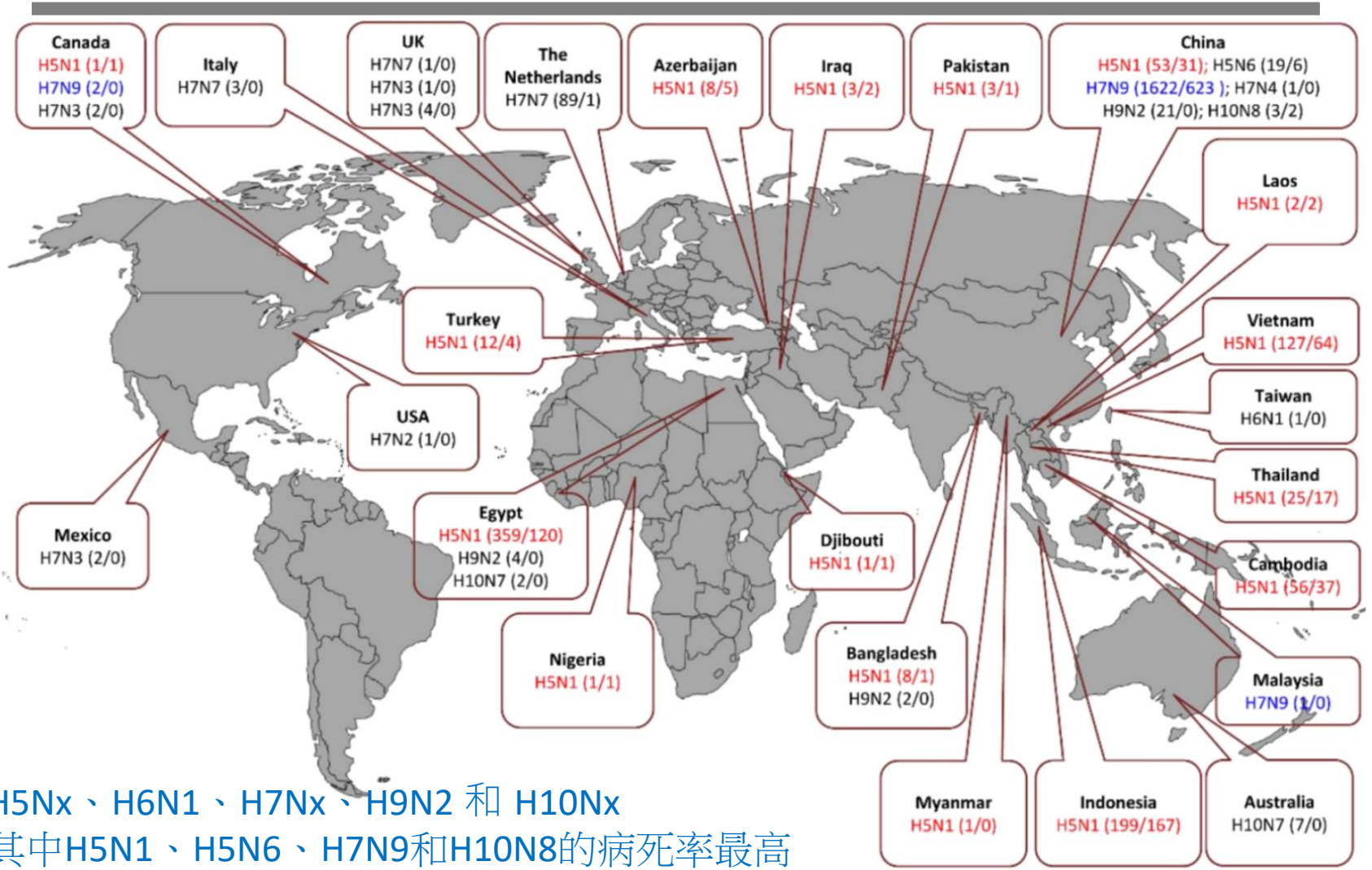
Transboundary and Emerging Diseases, Volume: 2024, Issue: 1, First published: 27 September 2024, DOI: (10.1155/2024/5322378)
eLife. 2026 Jan 28;14:RP104748. doi: 10.7554/eLife.104748

Key H5N1 Human Case Data (Through Early 2026)

- As of May 2026, sporadic cases have been reported, including in Cambodia, which reported its 4th H5N1 case of the year on April 21, 2026. Another fatal case was reported in a child from Bangladesh in the first quarter of 2026.

European Centre for Disease Prevention and Control, Solna, Sweden
www.ecdc.europa.eu
World Health Organization Avian Influenza Weekly Update Number 1029

Documented Human Cases And Fatalities Caused By Zoonotic Avian influenza viruses



H5Nx、H6N1、H7Nx、H9N2 和 H10Nx

其中H5N1、H5N6、H7N9和H10N8的病死率最高

Viruses 2018. doi:10.3390/v10090497

Lancet Infect Dis. 2017 Aug;17(8):822-832. doi: 10.1016/S1473-3099(17)30323-7. Epub 2017 Jun 2.

Confirmed Human Infections/Fatalities With LPAIV or HPAIV H7N9 per Wave

Wave	Period	Phenotype	Cases	Fatalities	Fatality rate
1	February 2013–September 2013	LPAIV	134	45	34%
2	October 2013–September 2014	LPAIV	306	131	43%
3	October 2014–September 2015	LPAIV	219	102	47%
4	October 2015–September 2016	LPAIV	114	47	41%
5	October 2016–September 2017	LPAIV/HPAIV	848	295	35%
6	Since October 2017	LPAIV/HPAIV	4	3	75%

- The human pathogenic H7N9 is derived from multiple reassortments between AIV H7N9 (NA), H7N7 (HA), and H9N2 (internal proteins coding gene segments) in domestic ducks and chickens
- 自 2013 年以來，記錄了六波 LPAIV 和 HPAIV H7N9 ，共有1625例人感染（LPAIV H7N9：1593例，HPAIV H7N9：32例），總共造成 623 人死亡（死亡率 38%），該病毒存在有限「人傳人」的能力

Viruses 2018. doi:10.3390/v10090497
World Health Organization

Avian-Originated Influenza Viruses Transmission

- Most avian originated influenza viruses, including influenza A H7N9 and H5N1, few clustering cases are reported so far.
- Human-to-human transmission is inefficient and non-sustainable.

Viruses 2018. doi:10.3390/v10090497

Avian Influenza in Taiwan

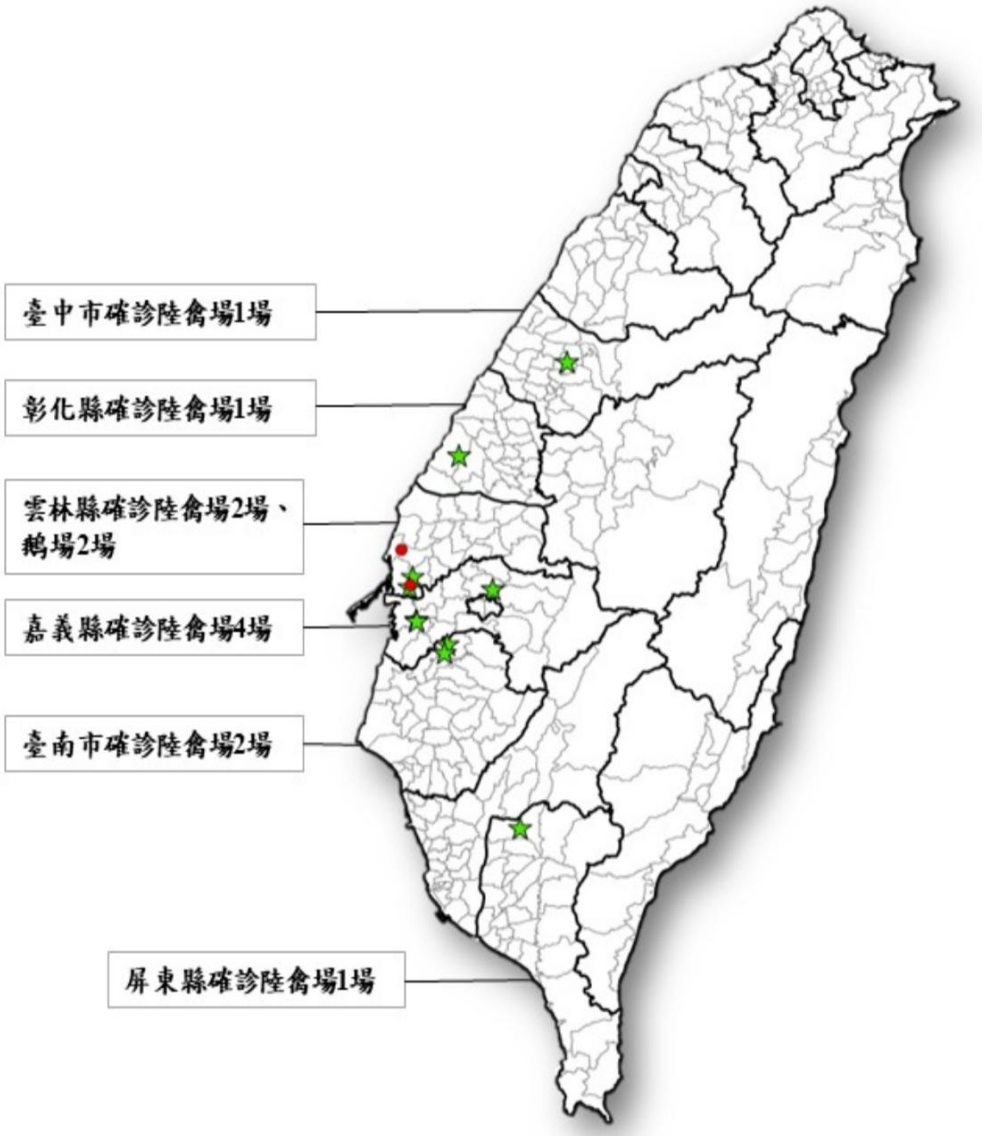
台灣在地化的禽流感主要為 H5N2 及 H5N1 亞型病毒株。
隨著病毒演化，目前在台灣禽場與環境監測中，以 H5 亞型
（特別是 H5N1 及 H5N2 的 2.3.4.4b 分支）為最主要的流行型別。

	H5N1	H5N2	H6N1
出現與時間軸	自 2022 年底首度在台檢出。	過去十多年在台灣禽場高度在地化。	2013 年發生全球首例人類感染個案；過去常在本土雞隻中被檢驗出。
病原性特徵	高病原性	早期多為低病原性，隨後演變為高病原性	地方性低病原性
流行病學現況	近年高病原性禽流感的主流病毒株；廣泛流行於禽場及候（野）鳥中；已取代過去的 H5N2 與 H5N5。	至今仍是農政單位防檢疫監控的核心重點。	屬於地方性低病原性禽流感，具跨物種感染歷史紀錄。

Taiwan CDC

115年高病原性禽流感確診及撲殺養禽場分布圖

資料更新日期：115.3.22



確診陸禽場
確診鴨場
確診鵝場
確診混養場

禽場高病原性禽流感案例共13例	
陸禽場：	11 例
水禽場：	2 例
混養場：	0例

H5N1：陸禽11場、鵝場2場

禽場低病原性禽流感案例共1例	
陸禽場：	1 例
水禽場：	0 例

屠宰場確診禽流感案例共4例	
陸禽場：	4例
水禽場：	0 例

備註：
1.本圖不含禽場低病原、屠宰場及理貨場確診等案例。
2.屠宰場及理貨場低病原性禽流感案例0例。
3.屠宰場確診案例，屠體依法銷燬，並依「家禽(批發)市場、家禽理貨場及屠宰場感案例處置流程」進行防疫處置。

農業部動植物防疫檢疫署 禽流感資訊專區

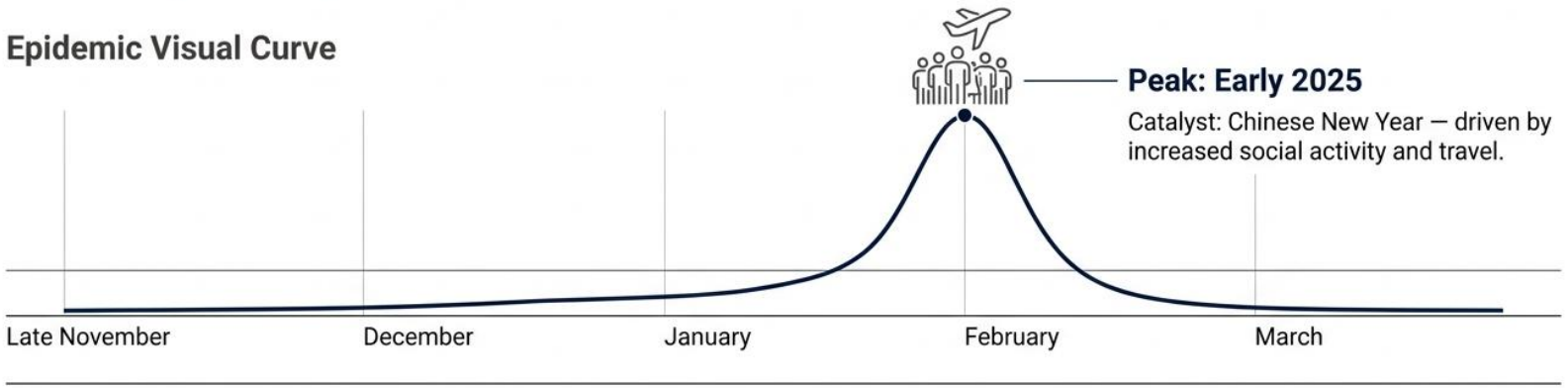
國內首例本土H7新型A型流感病例，痰液基因定序結果為H7N7，個案已於今日解除隔離，並出院返家休養

發佈日期：2026-04-03

- 基因定序出型別為H7N7流感病毒，未發現抗藥性突變，對抗病毒藥物仍具敏感性，屬低病原性禽流感病毒(LPAI)
- 可能是遭候鳥或野鳥傳染，其工作的養殖場禽類採檢結果則皆為陰性
- 2013年後無新增人類病例，我國首例之H7基因分析顯示已與10-20年前的歐洲人類病例H7有顯著差異，而與國內多年來野鳥曾檢出的H7最相近，且**未發現禽傳人能力增強之相關突變**
- 全球自1959年以來已報告逾90例H7N7人類病例，並集中於2003年之前，以歐洲為主，其中僅1例死亡，絕大多數為結膜炎輕症，其後2013年義大利曾報告3例亦為結膜炎輕症

Seasonal circulation and endemic influenza in Taiwan 2024-2025

Epidemiological dynamics indicate a winter surge driven by social mobility and A/H1N1 dominance



Microbiology Split-Panel

Influenza A/H1N1

Dominant Strain (2024-2025)

H1N1pdm09

Influenza A/H3N2

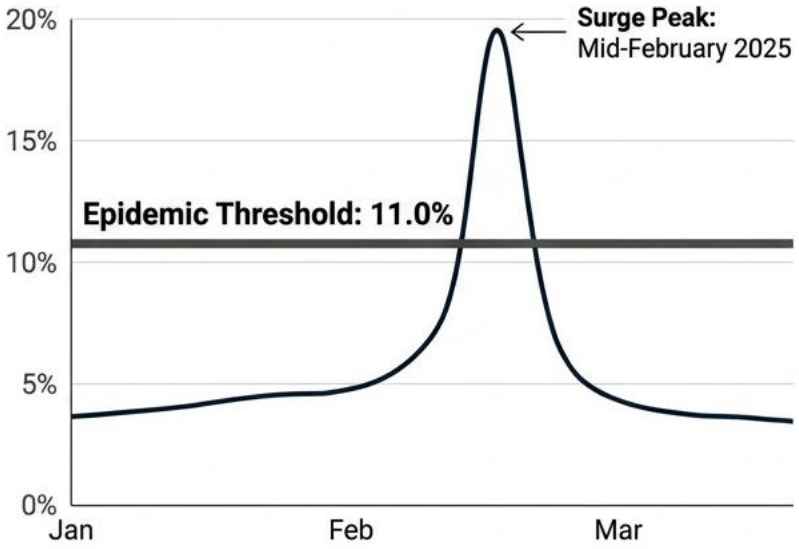
Co-circulating Strain

Taiwan CDC 2026

Seasonal circulation and endemic influenza in Taiwan 2024-2025

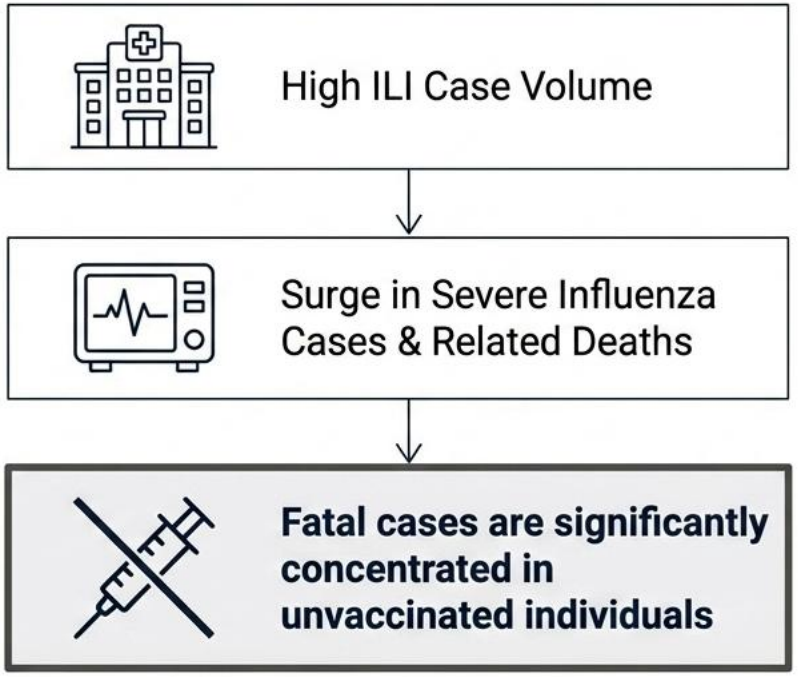
Systemic Strain Threshold Graphic

Early 2025 ER visit data



Emergency room visits for influenza-like illness (ILI) exceeded baseline epidemic limits in early 2025.

Causal Funnel: Severe Outcomes & Mortality



*Data sourced from national surveillance reports.

Taiwan CDC 2026

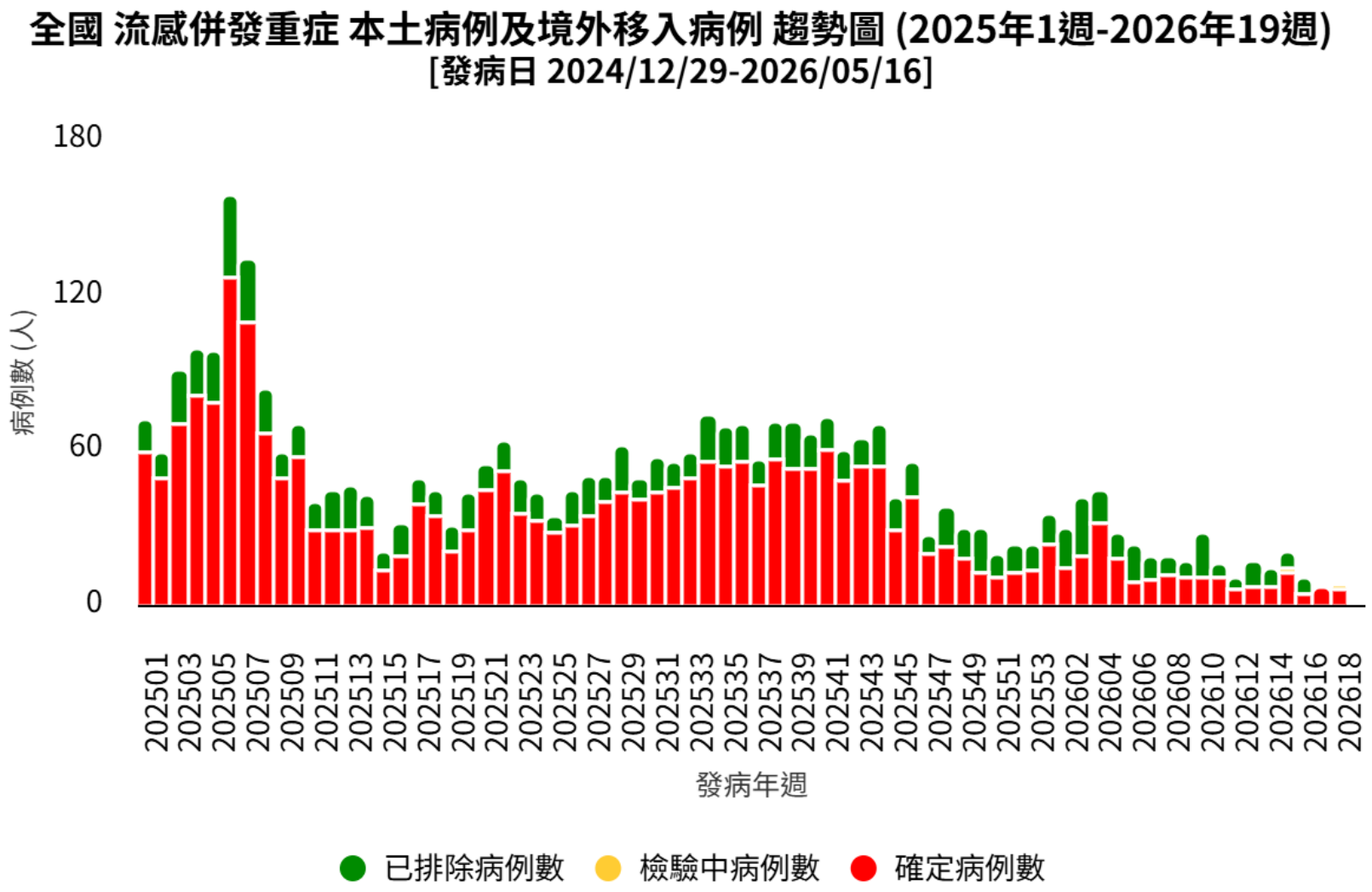
Dominant Strain Circulating Globally and in Taiwan in 2025-2026 Influenza Season



重要病毒株變異：K分支 (Subclade K)

- **抗原漂移：** 疾管署監測發現，2025年流行的K分支與WHO建議施打的流感疫苗株在抗原性上存在顯著差異，意即病毒發生了「抗原漂移」。
- **流行優勢：** 由於累積了多重基因突變，K分支已具備在人群中快速傳播的優勢。

台灣流感併發重症統計



Taiwan CDC 2026

台灣流感併發重症統計

2025-2026 流感季流感併發重症發生率及死亡率統計

年齡別	病例數	死亡數	每十萬人口 累積發生率	每十萬人口 累積死亡率
小於 3 歲	2	0	0.50	0.00
3-6 歲	5	0	0.75	0.00
7-18 歲	14	1	0.57	0.04
19-24 歲	3	0	0.21	0.00
25-49 歲	23	3	0.27	0.03
50-64 歲	46	2	0.87	0.04
65 歲以上	165	21	3.61	0.46
總計	258	27	1.11	0.12

Taiwan CDC

Complications Of Influenza

Pulmonary Complications



Primary influenza viral pneumonia



Secondary bacterial pneumonia

Non-Pulmonary Complications



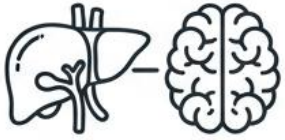
Myositis



Cardiac complications



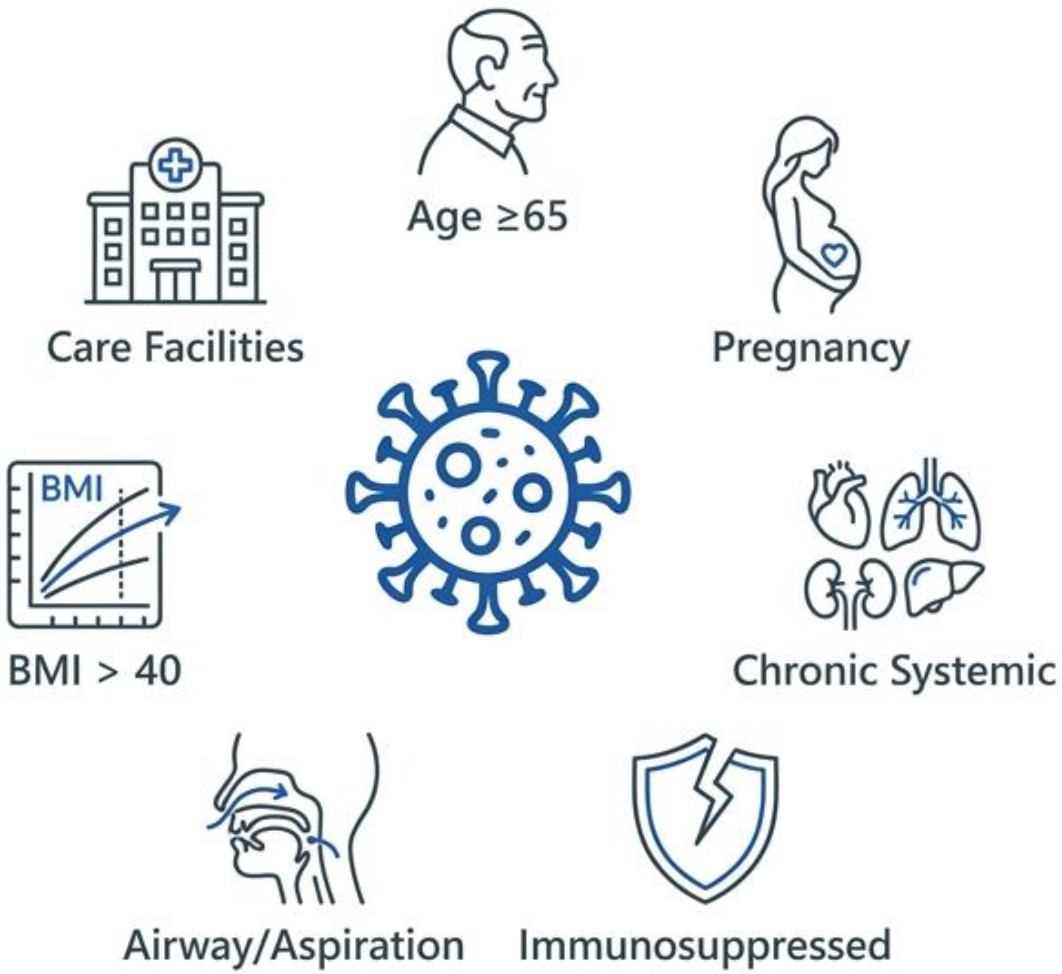
Central nervous complications



Reye syndrome

Principles and Practice of Infectious Diseases 2015, 8th,ed

Higher Risk For Influenza Complications, Adults



Principles and Practice of Infectious Diseases 2015, 8th,ed

Higher Risk For Influenza Complications, Children



Demographic

Age younger than 5 years.



Systemic

Chronic pulmonary (asthma), cardiov-ascular (excluding hypertension), renal, hepatic, hematologic, or metabolic (diabetes) disorders.



Immunological

Immunosuppressed (HIV or immunosuppressive medications).

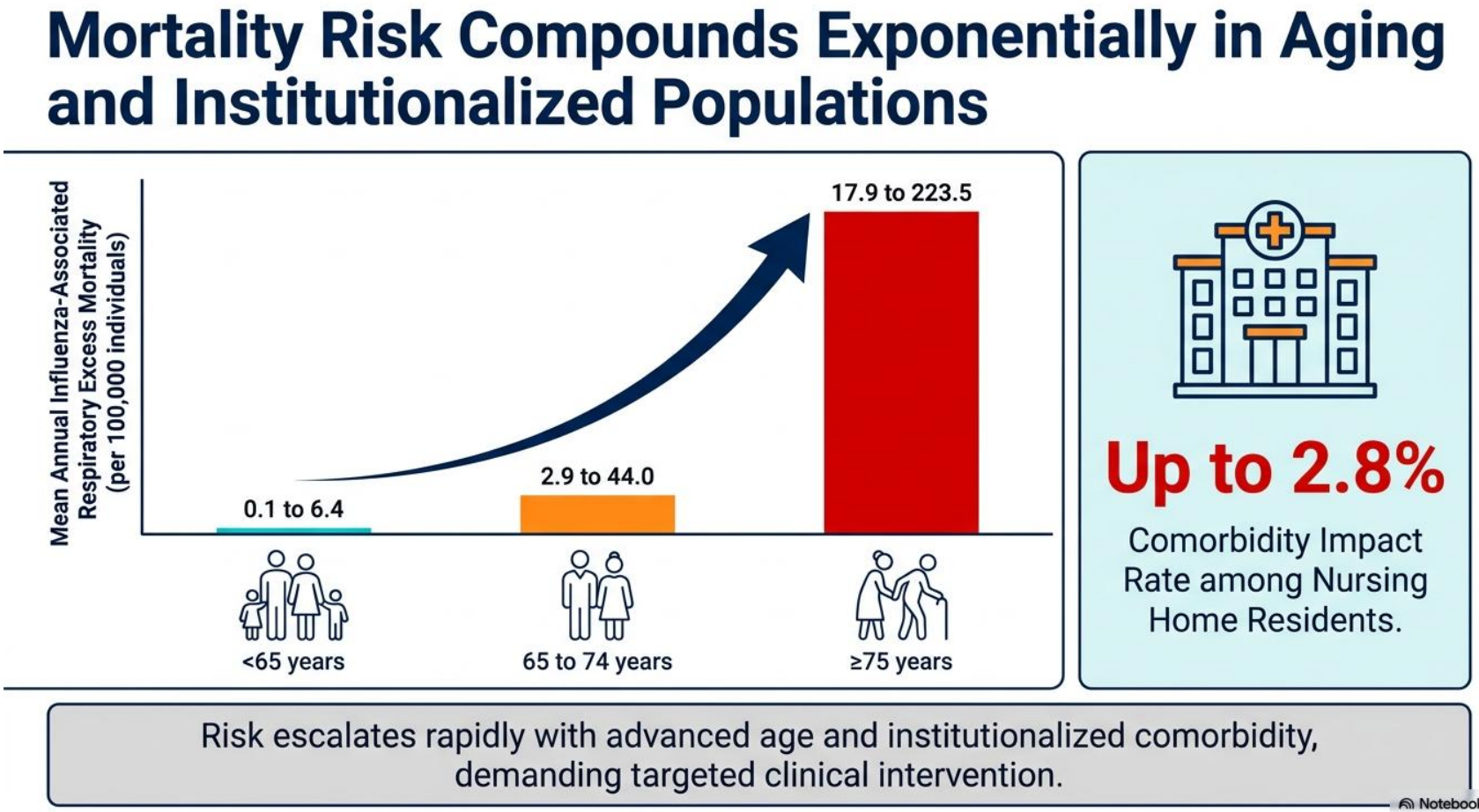


Pharmacological

Long-term aspirin therapy (Reye syndrome risk).

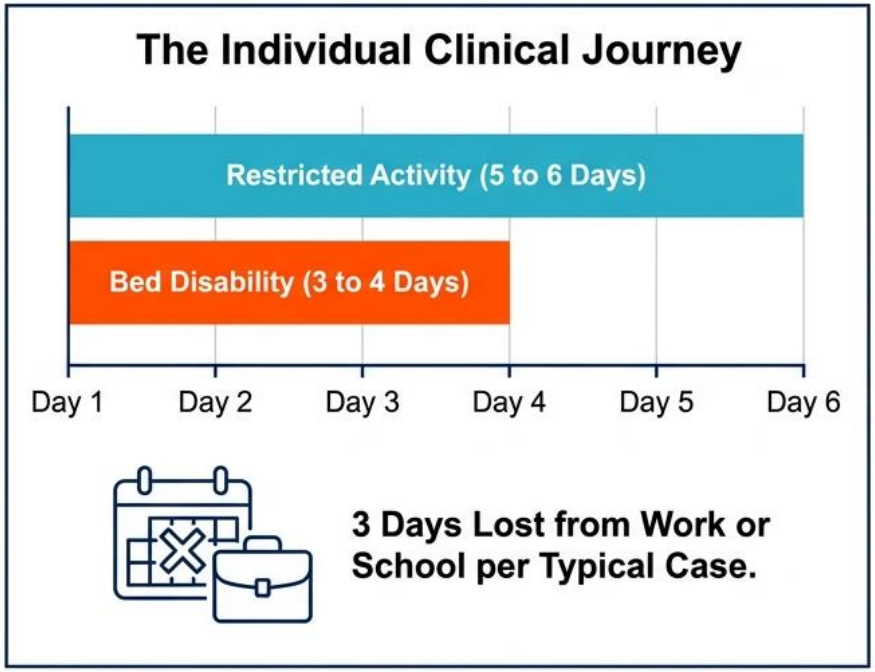
Principles and Practice of Infectious Diseases 2015, 8th,ed

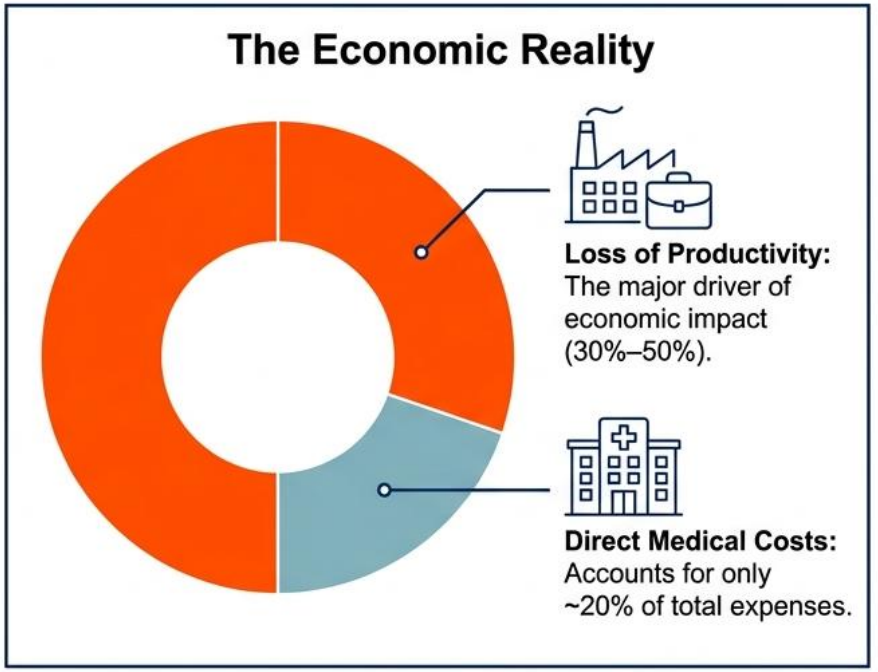
Morbidity, Mortality, & Burden Of Influenza



UpToDate Topic 7006 Version 46.0. Principles and Practice of Infectious Diseases 2020, 9th,ed

Morbidity, Mortality, & Burden Of Influenza





The true cost of the flu is hidden in the severe restriction of human output and daily functioning.

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Take Home Message

- Despite the presence of viral variants, receiving a flu vaccine can still provide a certain degree of cross-protection, thereby reducing the risk of severe illness.
- Most avian originated influenza viruses, including influenza A H7N9 and H5N1, few clustering cases are reported so far; Human-to-human transmission is inefficient and non-sustainable.

Thank you for listening.