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流感之流行病學及臨床表徵

何謂流感

- 由流感病毒感染所造成的呼吸道疾病
- 流感病毒可分為A，B，C三型

Antigenic type	A	B	C
RNA segments	8	8	7
Surface glycoproteins	Hemagglutinin (1-16) Neuraminidase (1-9)	Hemagglutinin Neuraminidase	HEF: hemagglutinin esterase fusion protein
Genetic variability	Drift and shifts	Drifts	Drifts
Human Disease	Pandemic, epidemic, sporadic	Epidemic, sporadic	Sporadic
Known hosts	Humans, swine, horses, poultry, sea mammals, several avian species	Humans	Humans, swine

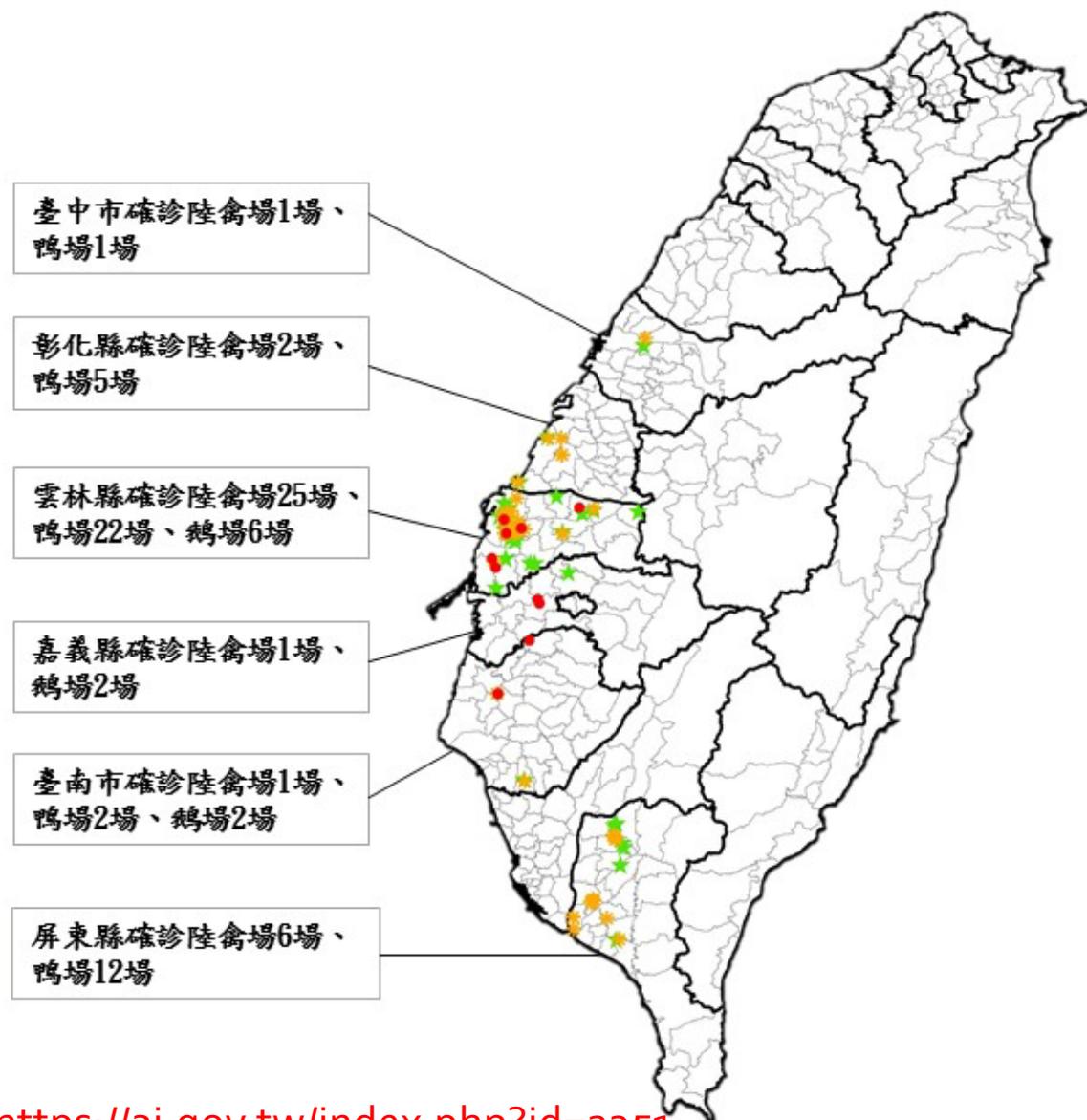
台灣重要的流感病毒：禽與人

- Seasonal flu:
 - A型：2009 H1N1, H3N2
 - B型：yamagata、victorial lineage
- 新型A型流感
 - Poultry:
 - Most common, but low pathogenic: H6N1
 - High pathogenic
 - H5 subtype: H5N2, H5N3, H5N8
 - Human:
 - H7N9

107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：107.10.6

資料更新時間：下午6時



★ 確診陸禽場

✳ 確診鴨場

● 確診鵝場

禽場高病原性禽流感案例共88例

陸禽場： 36例

水禽場： 52例

H5N2：陸禽33場、鴨40場、鵝10場

H5N8：鴨1場

H5高病原：陸禽3場、鴨1場

禽場低病原性禽流感案例共23例

陸禽場： 22例

水禽場： 1例

屠宰場確診禽流感案例共10例

陸禽場： 10例

水禽場： 0例

備註：

1.本圖不含低病原、屠宰場及理貨場確診案例。

2.理貨場低病原性禽流感案例1例。

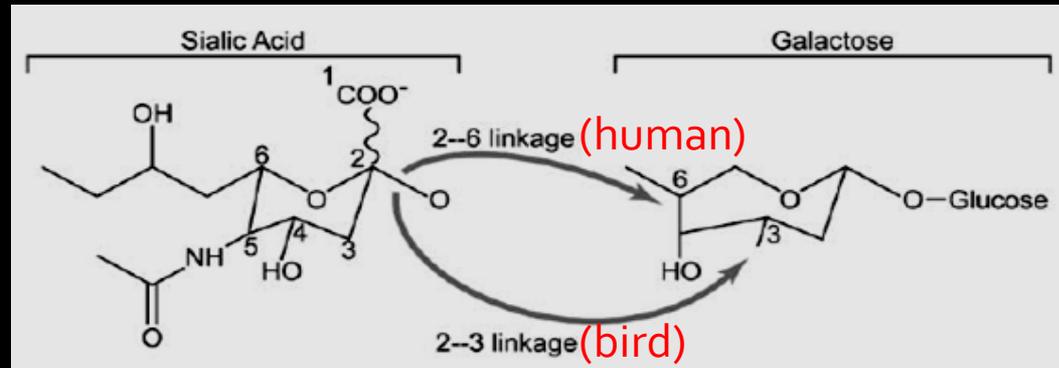
3.屠宰場確診案例，屠體依法銷燬，並依「家禽(批發)市場、家禽理貨場及屠宰場發生禽流感案例處置流程」進行防疫處置。

為什麼A型流感會造成世界大流行

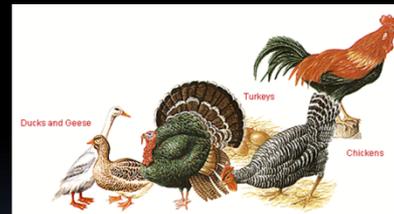
- 決定A型流感antigenicity的兩大抗原：
 - Hemagglutinin: especially
 - H1 – H16
 - Neuraminidase
 - N1 – N9
- 在大自然界中，A型流感病毒以水禽為天然宿主，經由下列兩種方式跨越物種的感染
 - Reassortment
 - Accumulation of mutation

為什麼A型流感會造成世界大流行

- Species barrier的原因：



- 如何造成 reassortment：
 - 豬的角色
 - Both receptors



Evolution of New Influenza Virus

- cross infection of human & avian influenza in pigs
- leading to reassortment of genes and new strains

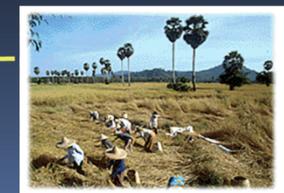
Transmission of avian influenza virus by stool



New flu virus
Spread by aerosol



Transmission of human flu to pigs by aerosol



為什麼A型流感會造成世界大流行

- 一旦跨越物種，變成可以在人與人之間有效率的傳遞並造成感染
 - 新型流感
 - 由於整個人類族群沒有抵抗力（herd immunity），所以可以導致大流行
 - 經過一段時間後，稱為人流感（或季節流感）

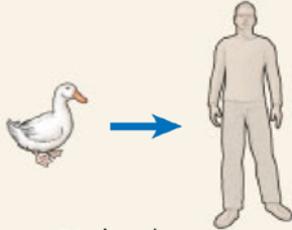
1918 "Spanish influenza"

1957 "Asian influenza"

1968 "Hong Kong influenza"

Next pandemic influenza

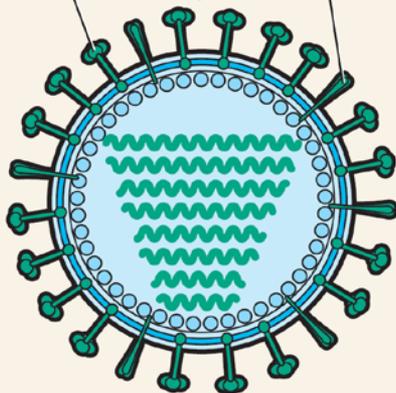
H1N1 influenza virus



Bird-to-human transmission of H1N1 virus

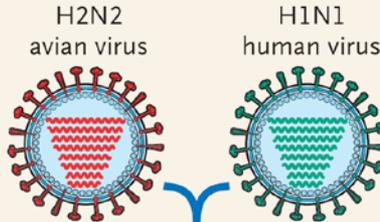


Hemagglutinin Neuraminidase

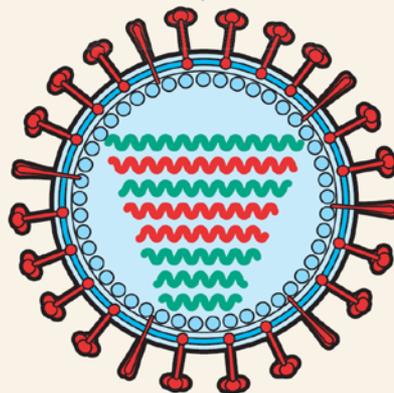


All 8 genetic segments thought to have originated from avian influenza virus

H2N2 influenza virus

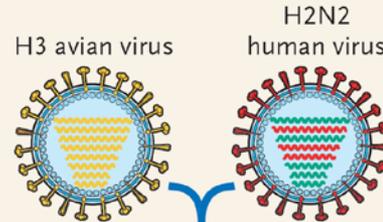


Reassortment

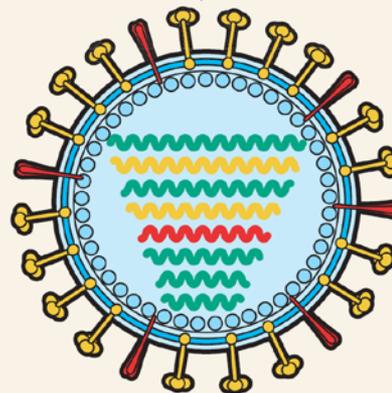


3 new genetic segments from avian influenza virus introduced (HA, NA, PB1); contained 5 RNA segments from 1918

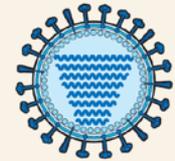
H3N2 influenza virus



Reassortment

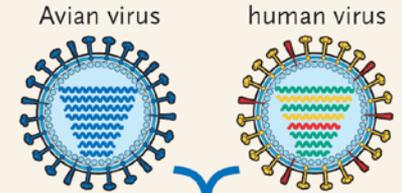


2 new genetic segments from avian influenza virus introduced (HA, PB1); contained 5 RNA segments from 1918



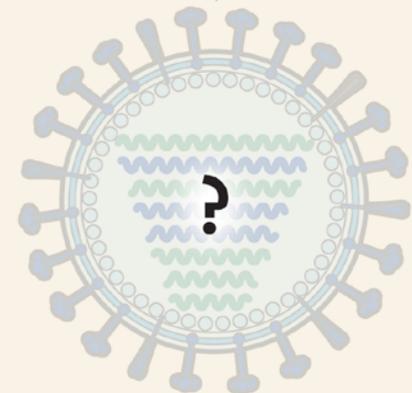
Avian virus

or



Avian virus

H3N2 human virus



All 8 genes new or further derivative of 1918 virus

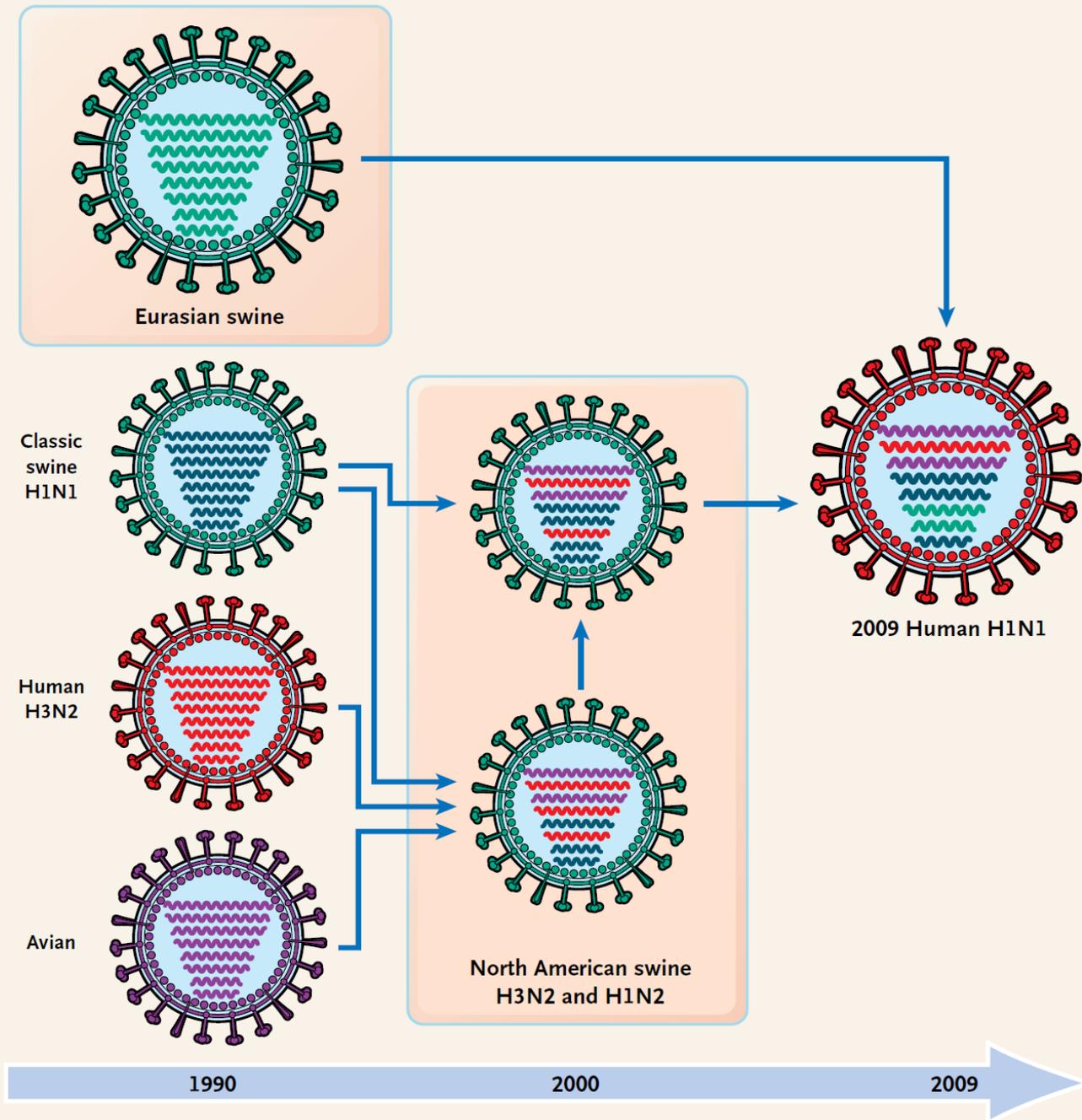


Figure 1. History of Reassortment Events in the Evolution of the 2009 Influenza A (H1N1) Virus.

Trifonov V, et al. N Engl J Med 2009

流感與一般感冒(Cold)的症狀比較

症狀	流感	一般感冒
發作期 (Onset)	突然	漸進
發燒 (Fever)	常見, 且溫度高 (超過 38.3°C); 維持 3 至 4 天	少見
咳嗽 (Cough)	有時會很嚴重	乾咳
頭痛 (Headache)	明顯	少見
肌肉痛 (Myalgia)	常見, 通常嚴重	輕微
疲勞 (Fatigue) 虛弱 (Weak)	維持 2 至 3 週	輕微
極度疲乏	明顯	少見
胸部不適感	常見	輕至中度
鼻塞 (Stuffy nose)	偶爾	常見
打噴嚏 (Sneezing)	偶爾	經常
喉嚨痛 (Sore throat)	偶爾	常見

DAYS AFTER
INOCULATION

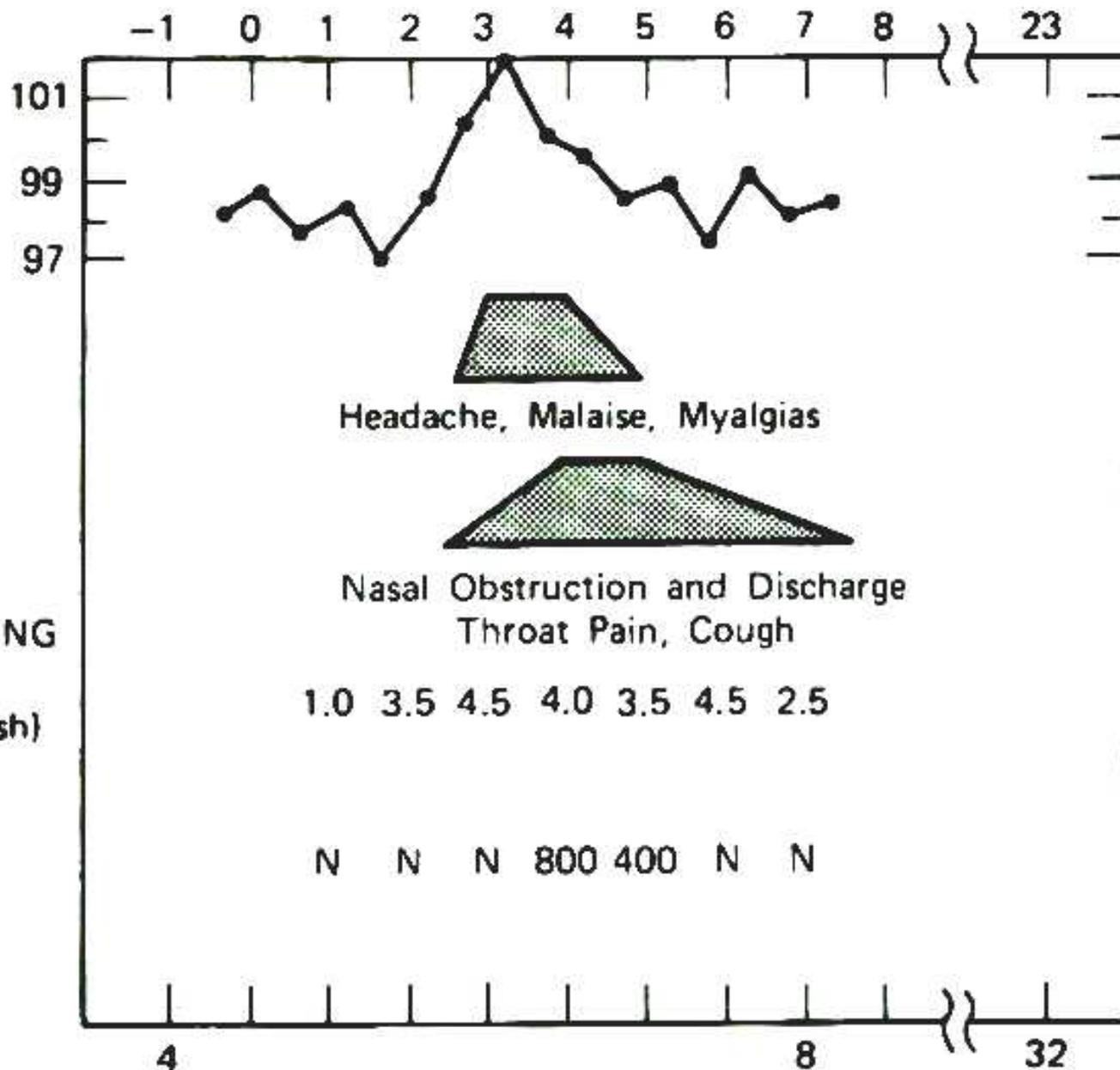
TEMP. °F

ILLNESS

VIRUS SHEDDING
(log₁₀ TCID₅₀
per ml nasal wash)

INTERFERON
(IU per ml
nasal wash)

ANTIBODY
(HI reciprocal
titer)



流行性感冒的臨床表現：Lab. Data

- Laboratory findings
 - Leukopenia
 - Lymphopenia
 - Thrombocytopenia
 - Abnormal liver function
 - Abnormal renal function
 - hyperglycemia

流行性感冒的診斷

- 臨床症狀與病史：Cluster
- Rapid antigen test
- Virus isolation
- RT-PCR
- Specific antibody reaction
- Microarray

類流感的定義：

- 必須符合下列各項：
 - 突發性高燒(>38 °C)
 - 沒有已知的其它原因
 - 下列兩項呼吸道症狀中，至少有一項：
 - 乾咳
 - 喉嚨痛

WHO. Clinical Management of Pandemic (H1N1) 2009 Virus Infection.
WHO Document 2009;Sep. 17.

流行性感冒的併發症

- 肺炎：
 - 病毒性肺炎
 - 細菌性肺炎(續發性感染)
 - *S. pneumoniae*, *S. aureus*
- 腦炎：
- 其他併發症：
 - 腹瀉
 - 腎衰竭
 - 心肌炎

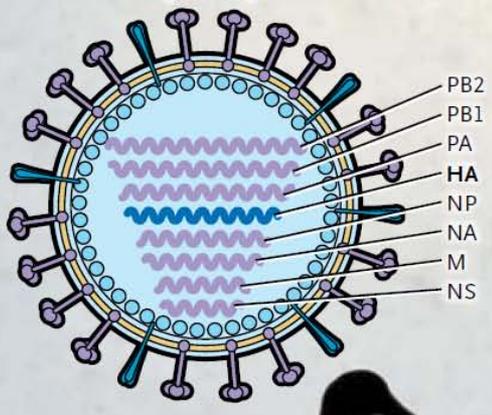
流行性感冒的死亡率與危險因子

- 死亡率：
 - 大約 0.3% - 1%
- 死亡的危險因子：
 - < 5歲, > 65歲
 - 使用aspirin的青少年
 - 懷孕婦女
 - 肥胖
 - 有重大的潛在性疾病

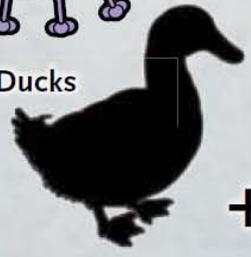
M2 ion channel Viral polymerase genes

NS-1

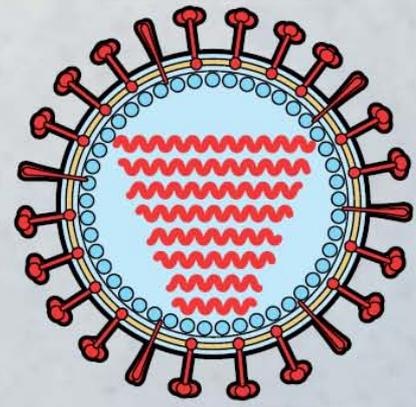
ZJ12-like
(H7N3)



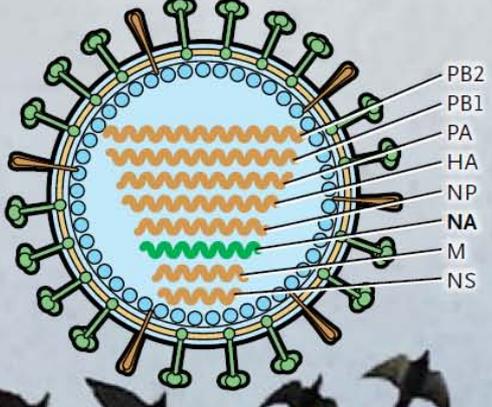
Ducks



BJ16-like
(H9N2)



KO14-like
(H7N9)



Bramblings



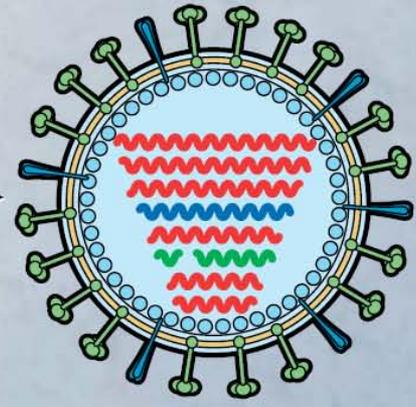
燕雀

Wild birds



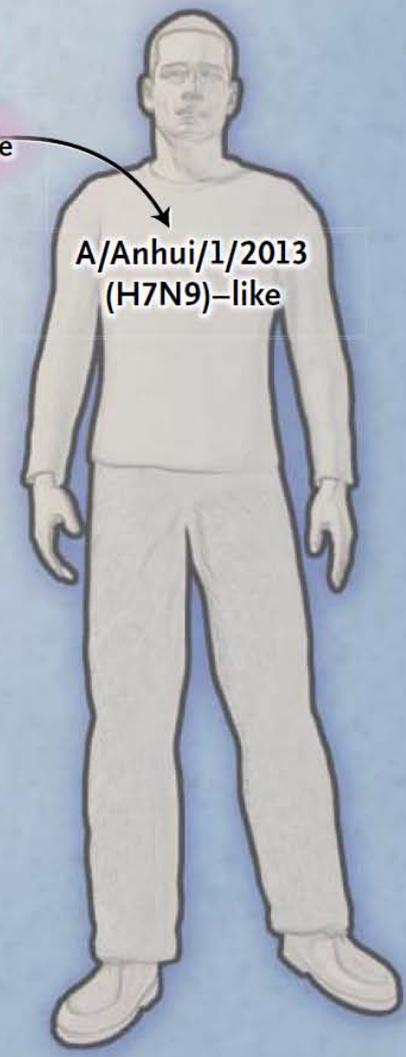
Possible intermediate host?

Reassortant avian-origin
(H7N9)



Unknown host

A/Anhui/1/2013
(H7N9)-like



Clinical Manifestation of H7N9 Infection

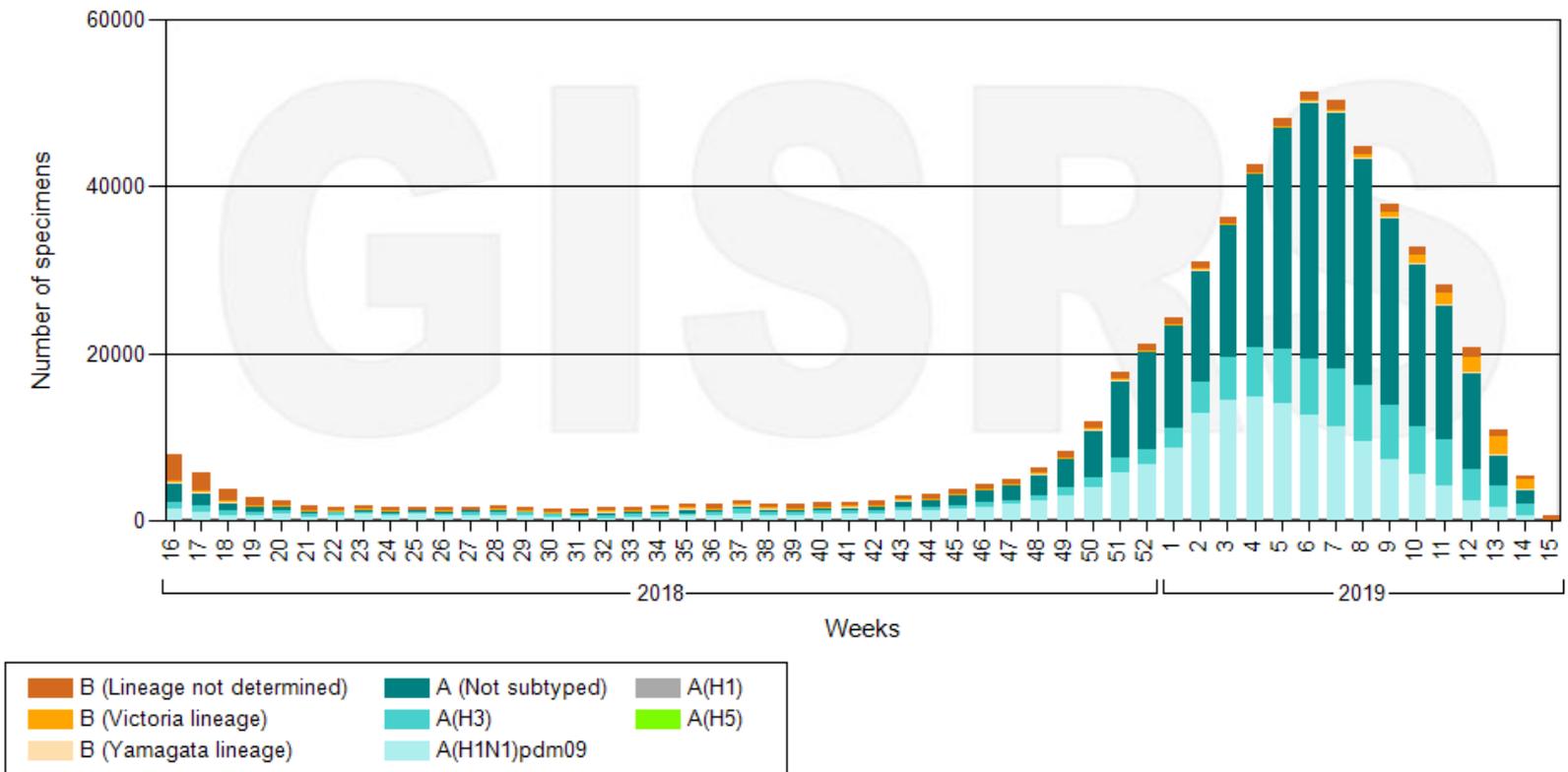
- Initial presentation:
 - Fever, cough, headache, myalgia, chills, malaise
 - No upper airway symptoms
- Progression:
 - 5–7 (3–14) days later, persistent high fever
 - Dyspnea, hemoptysis, pneumonia, ARDS, septic shock, multi-organ (?) failure
 - Decrease of viral load: 15–20 days after onset
- Laboratory findings:
 - Leukopenia/lymphopenia; CK, GPT, Cre, LDH, CRP 上升
 - Leukocytosis, marked elevation of cytokines while ARDS

Complication of H7N9 Infection

- Usual complication
 - Pneumonia, ARDS
 - Rhabdomyolysis
 - Acute renal failure
 - Encephalopathy
 - Superimposed bacterial infection / sepsis
- Mortality rate:
 - $45/135 = 33.3\%$

Global circulation of influenza viruses

Number of specimens positive for influenza by subtype



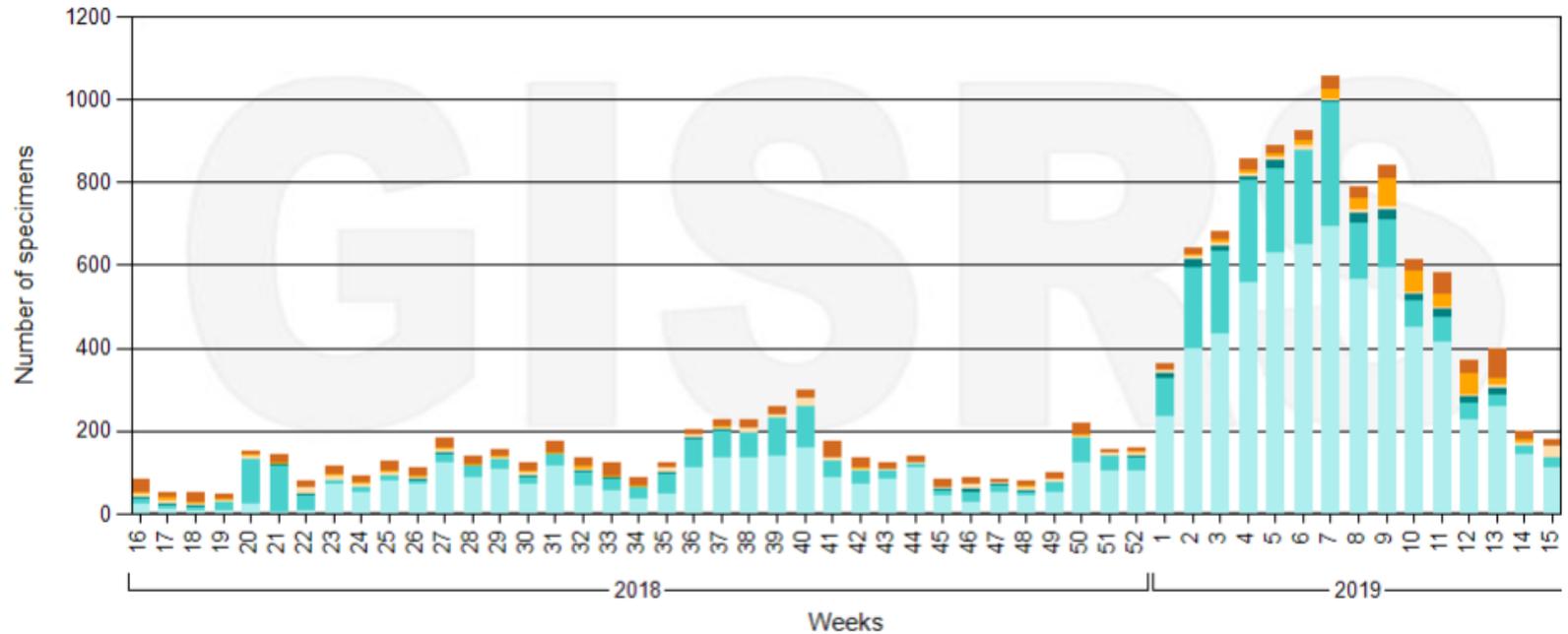
Influenza Laboratory Surveillance Information

generated on 18/04/2019 07:33:27 UTC

by the Global Influenza Surveillance and Response System (GISRS)

South-East Asia Region of WHO

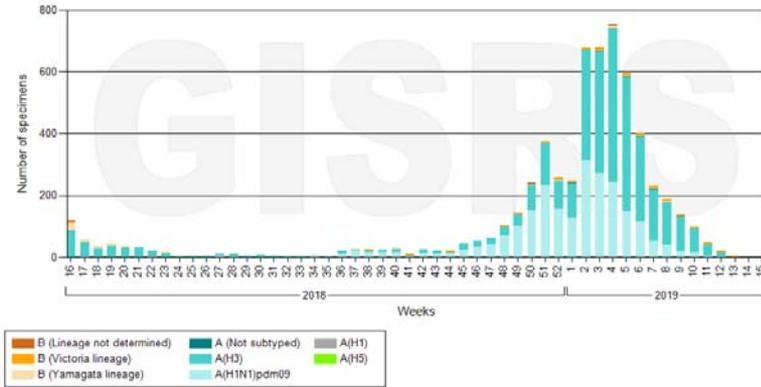
Number of specimens positive for influenza by subtype



Japan

Japan

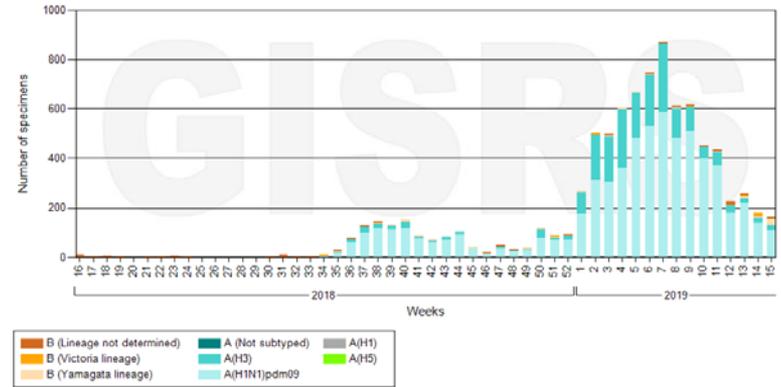
Number of specimens positive for influenza by subtype



India

India

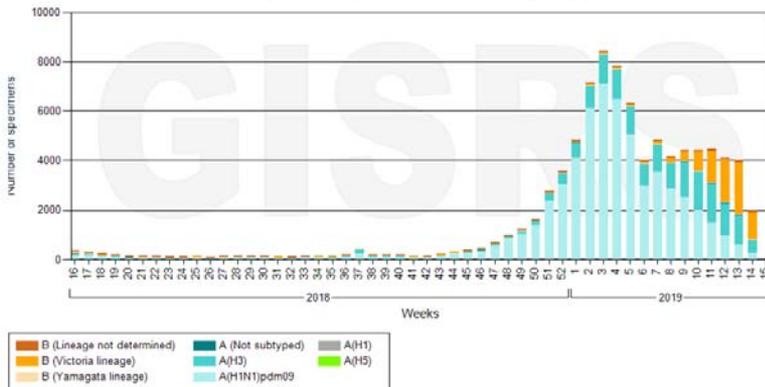
Number of specimens positive for influenza by subtype



China

China

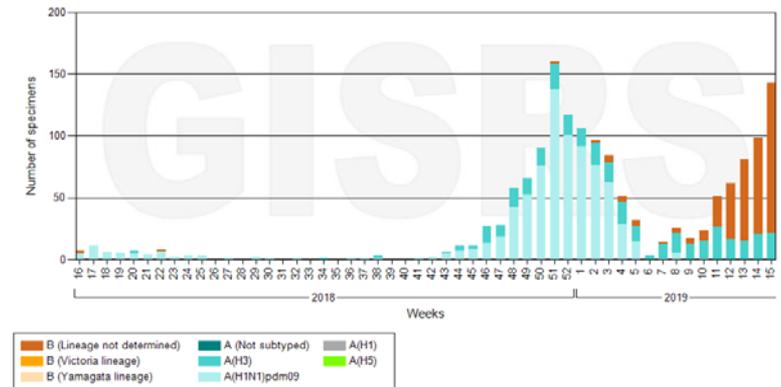
Number of specimens positive for influenza by subtype



Korea

Republic of Korea

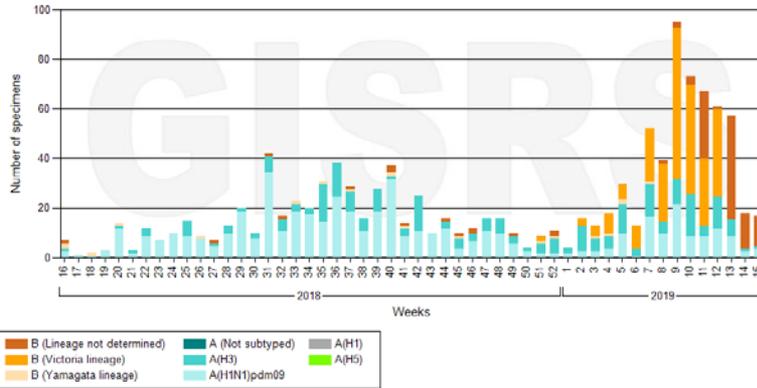
Number of specimens positive for influenza by subtype



Thailand

Thailand

Number of specimens positive for influenza by subtype



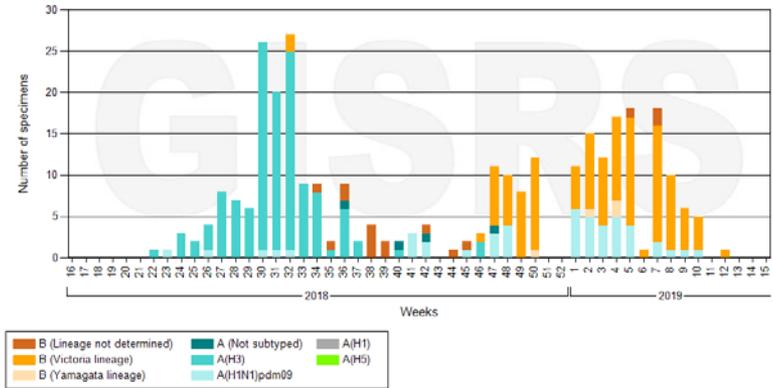
Data source: FluNet (www.who.int/fluinet)_GISRS

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Philippines

Philippines

Number of specimens positive for influenza by subtype



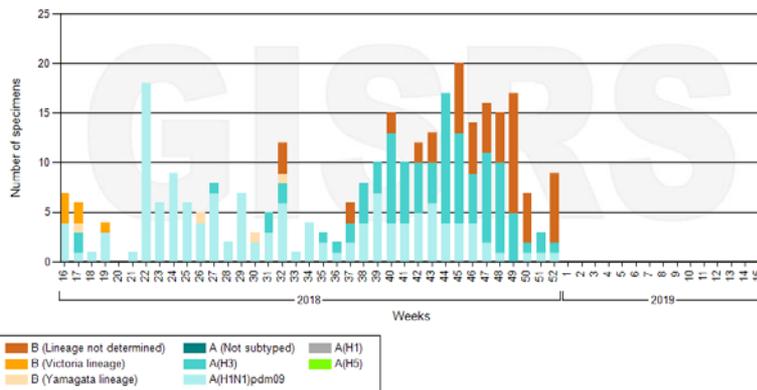
Data source: FluNet (www.who.int/fluinet)_GISRS

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Viet Nam

Viet Nam

Number of specimens positive for influenza by subtype



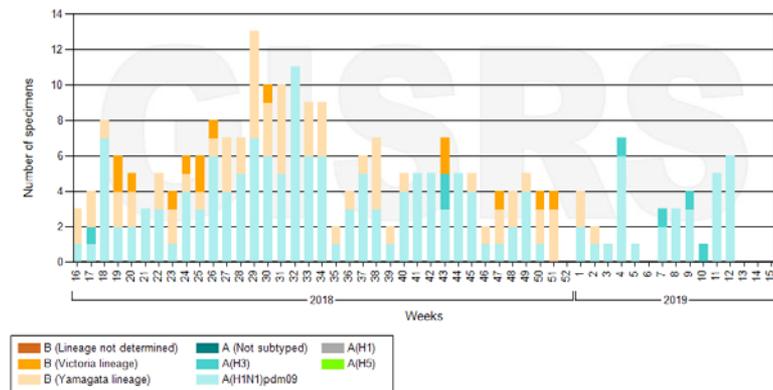
Data source: FluNet (www.who.int/fluinet)_GISRS

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Cambodia

Cambodia

Number of specimens positive for influenza by subtype



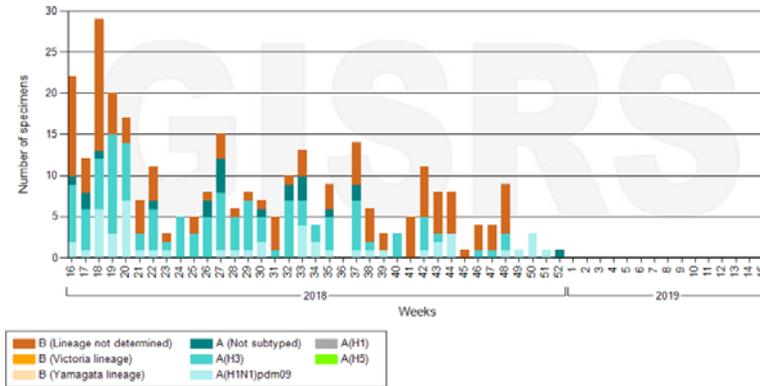
Data source: FluNet (www.who.int/fluinet)_GISRS

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Indonesia

Indonesia

Number of specimens positive for influenza by subtype



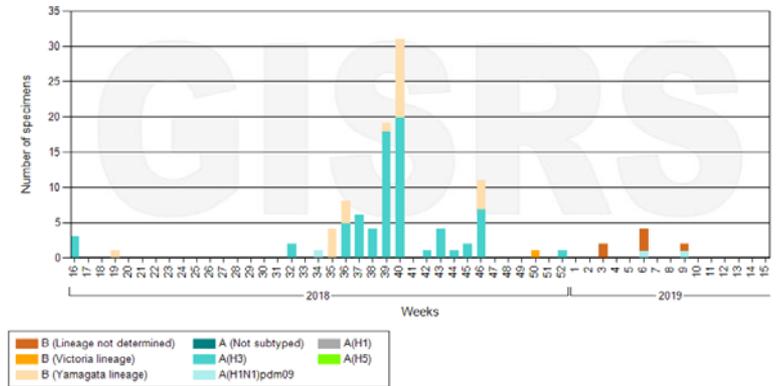
Data source: FluNet (www.who.int/fluinet), GISRS

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Myanmar

Myanmar

Number of specimens positive for influenza by subtype



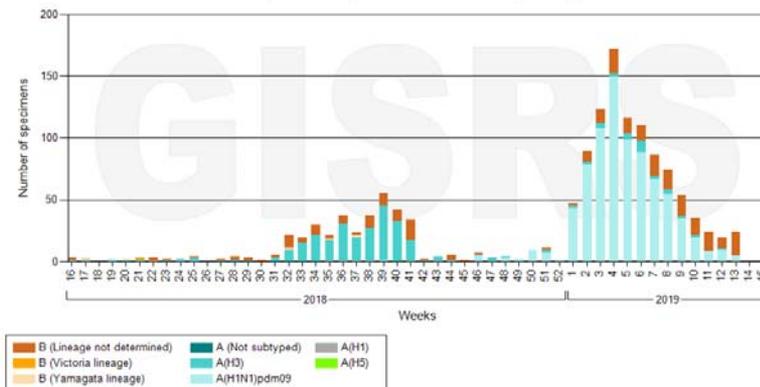
Data source: FluNet (www.who.int/fluinet), GISRS

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Nepal

Nepal

Number of specimens positive for influenza by subtype



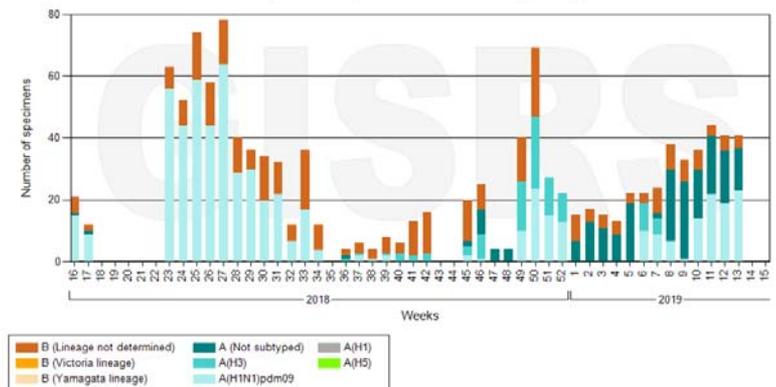
Data source: FluNet (www.who.int/fluinet), GISRS

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Cambodia

Sri Lanka

Number of specimens positive for influenza by subtype

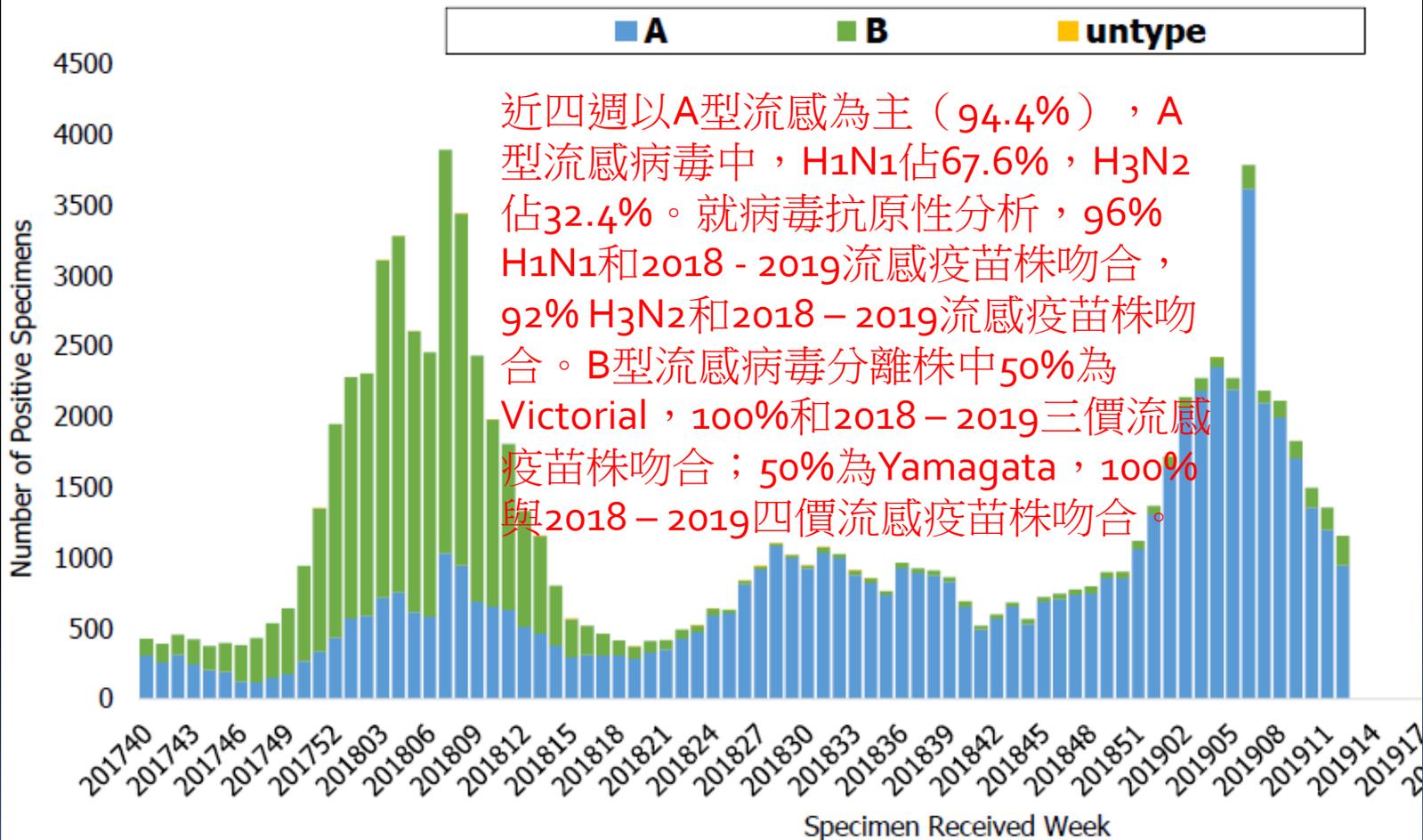


Data source: FluNet (www.who.int/fluinet), GISRS

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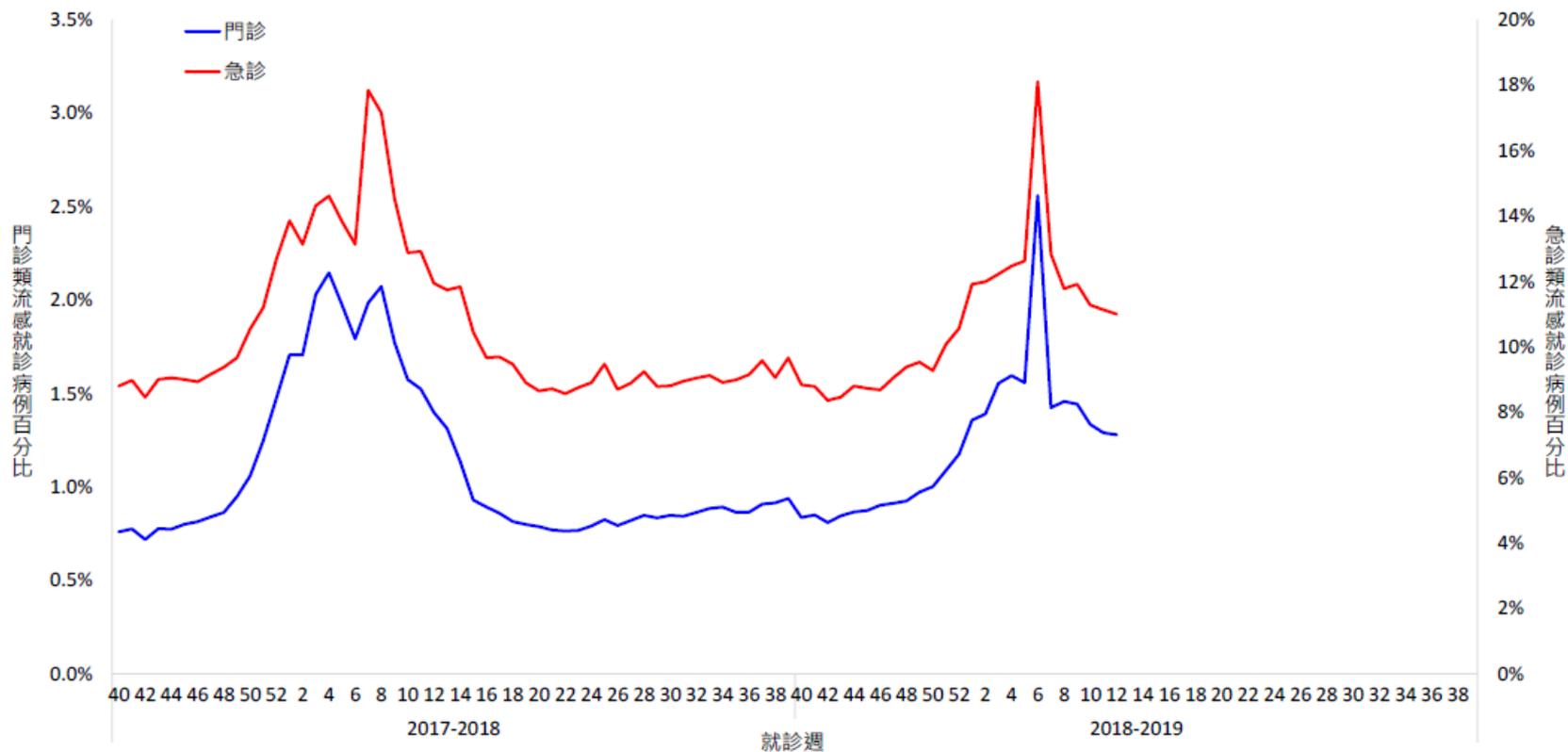
Surveillance in Taiwan CDC

流感陽性件數趨勢



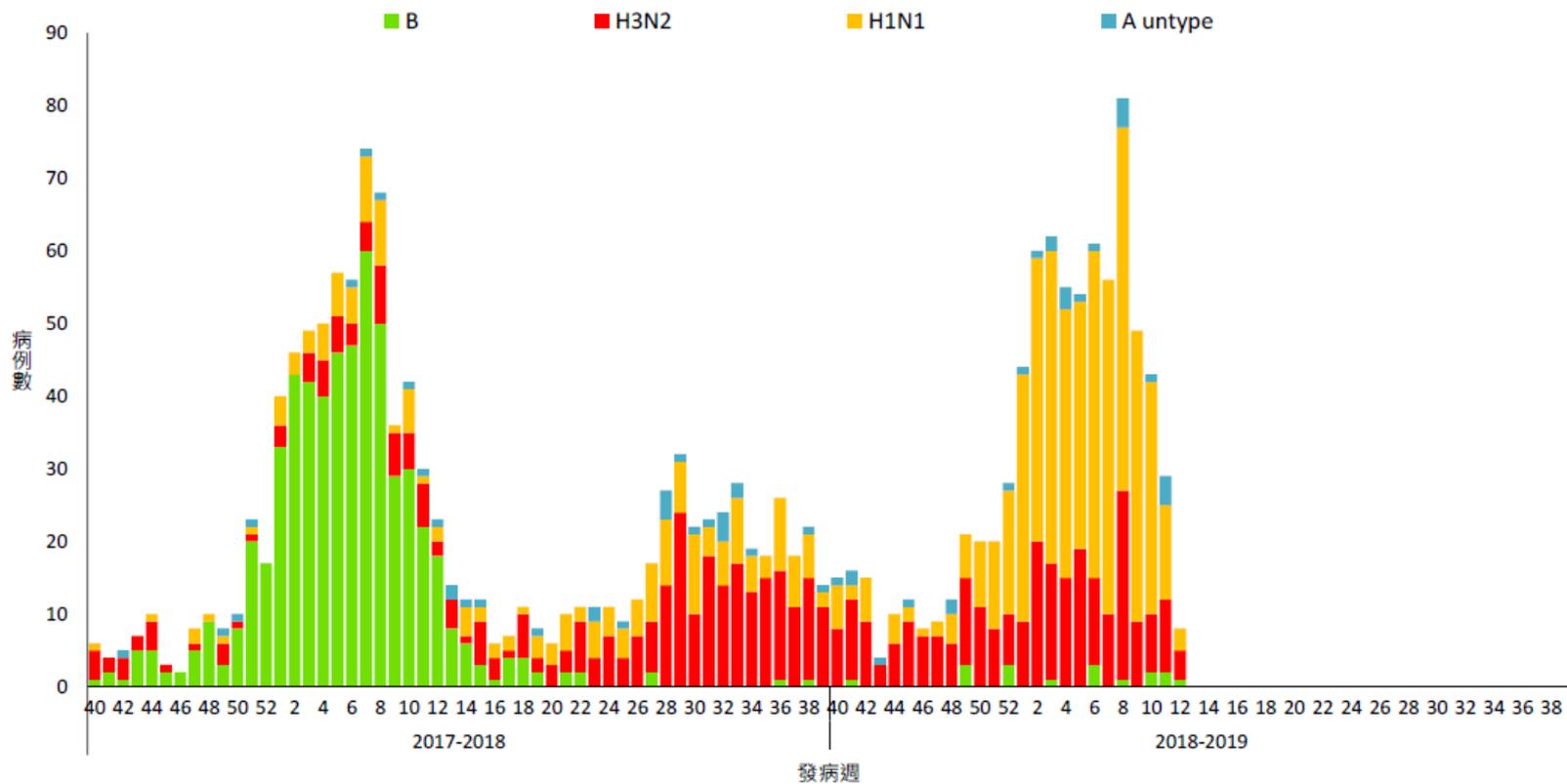
流感疫情監測：類流感病例百分比

門診及急診類流感就診病例百分比



流感監測：重症之病原性分析

流感併發重症確定病例數趨勢 - 依發病週



流感併發重症確定及死亡病例數統計

Age (years)	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
≤ 3	25	1	4.2	0.2
3 - 6	15	1	1.7	0.1
7 - 18	18	3	0.7	0.1
19 - 24	4	0	0.2	0
25 - 49	104	9	1.2	0.1
50 - 64	213	21	4.1	0.4
≥ 65	411	47	12.3	1.4

統計至108年3月25日止

流感併發重症通報定義 (1)

■ 臨床條件

- 出現類流感症狀後兩週內因併發症(如肺部併發症、神經系統併發症、侵襲性細菌感染、心肌炎或心包膜炎等)而需加護病房治療或死亡者。

■ 檢驗條件: 具有下列任一個條件

- 呼吸道臨床檢體(咽喉擦拭液等)分離並鑑定出流感病毒
- 臨床檢體分子生物學核酸檢測陽性。
- 臨床檢體抗原檢測陽性。
- 臨床檢體血清學抗體檢測陽性: 急性期與恢復期流感病毒血清抗體效價 ≥ 4 倍上升。

■ 流行病學條件

- 曾經與經實驗室證實之確定病例具有密切接觸(close contact)，即照護、同住、或與其呼吸道分泌物、體液之直接接觸

流感併發重症通報定義 (2)

- 通報定義

- 符合臨床條件。

- 疾病分類

- 可能病例：

- 符合臨床條件。

- 極可能病例：

- 符合臨床條件及流行病學條件。

- 確定病例：

- 符合臨床條件及檢驗條件。

新型A型流感通報定義 (1)

- 臨床條件：同時具有以下兩項條件
 - 急性呼吸道感染，臨床症狀可能包括發燒 ($\geq 38^{\circ}\text{C}$)、咳嗽等
 - 臨床、放射線診斷或病理學上顯示肺部實質疾病
- 檢驗條件：下列任一
 - 臨床檢體培養分離及鑑定出新型A型流感病毒(非現行於人類流行傳播之H1N1、H3N2季節性流感病毒)
 - 臨床檢體新型A型流感病毒核酸檢測陽性
 - 血清學抗體檢測呈現為最近感染新型A型流感
- 流行病學條件：發病前10日內，具有下列任一條件
 - 曾經與出現症狀的極可能或確定病例有密切接觸，包括在無適當防護下提供照護、相處、或有呼吸道分泌物、體液之直接接觸
 - 曾至有出現新型A型流感流行疫情地區之旅遊史或居住史；
 - 曾有禽鳥、豬暴露史或至禽鳥、豬相關場所
 - 在實驗室或其他環境，無適當防護下處理動物或人類之檢體，而該檢體可能含有新型A型流感病毒

新型A型流感通報定義 (2)

- 何時通報？具有下列任一個條件：
 - 符合臨床條件及流行病學條件
 - 僅符合臨床條件第(一)項及流行病學條件第(一)項
 - 符合檢驗條件。



**THANK YOU FOR
YOUR ATTENTION!**