

Civilization, Infectious Diseases, and Mathematical Modeling

人類文明史、傳染病、數學建模

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Outline

1. Infectious disease and **Human civilization**
2. Infectious diseases that **changed human history**
3. History of **infectious disease modeling**
4. Example of modeling of infectious diseases



Time for 774 deaths to occur in 2003 due to:

SARS - November, 2002 – July, 2003

HIV – 6 hours

TB – 3 hour

Note:

1. HIV and TB highly correlated
2. 11% of ADI (AIDS-defined illness) deaths due to TB.



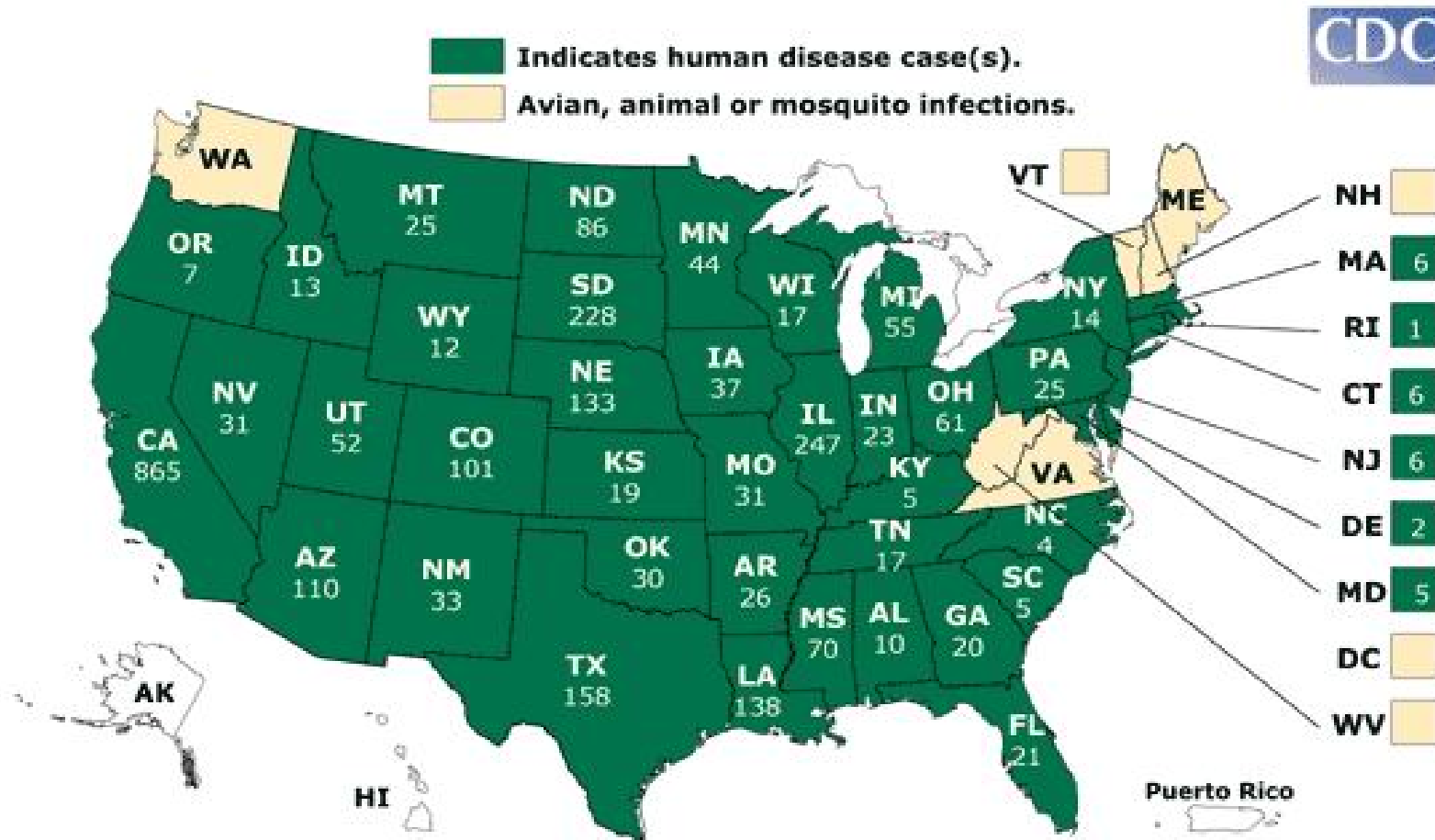
Indonesia 2005

Culprits or victims of **Avian flu**?

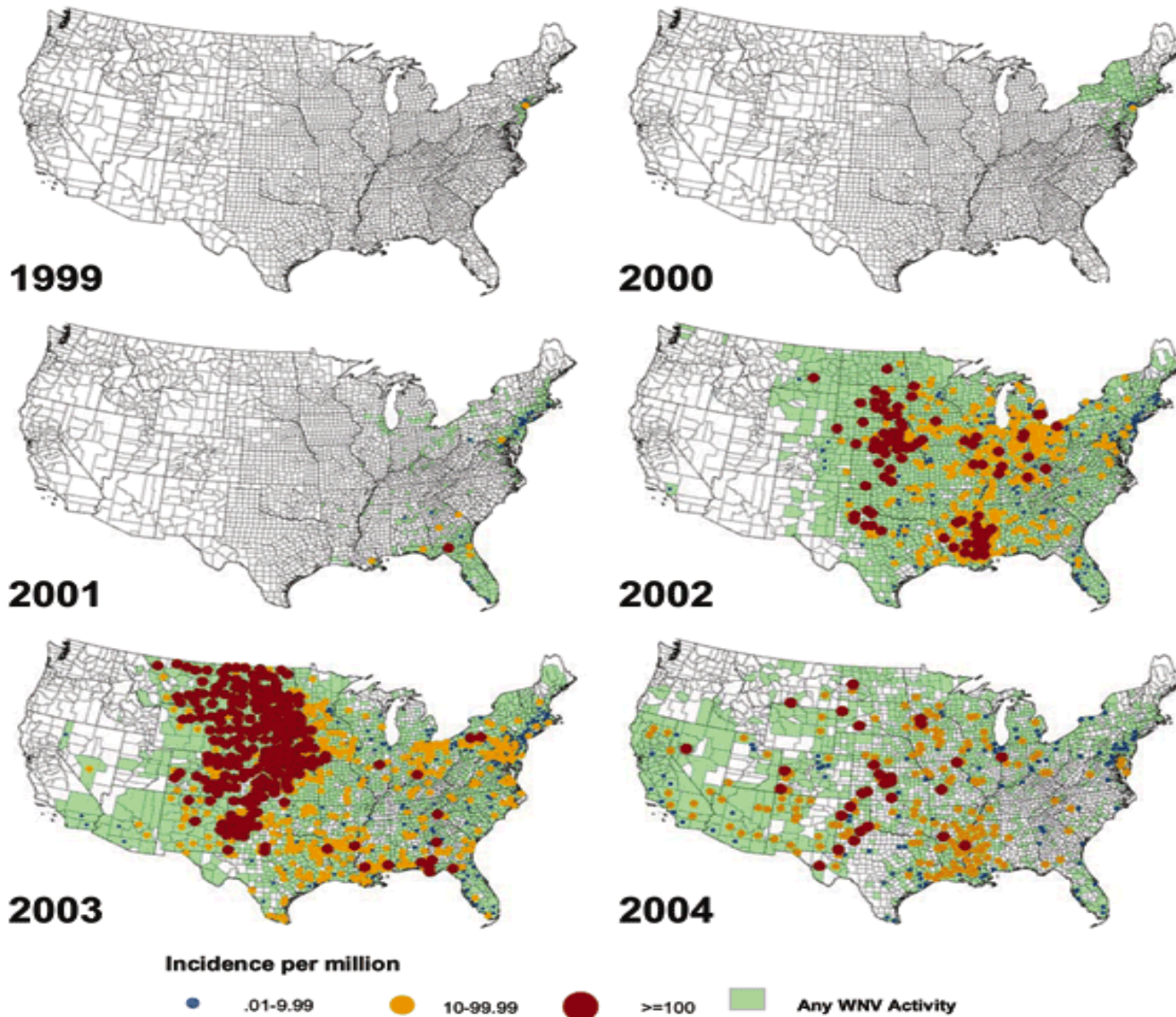
牠們是禽流感(H5N1)的罪魁禍首,還是受害者?



West Nile Virus (西尼羅河病毒) in U.S. 2799 cases/102 deaths (1999-2005)

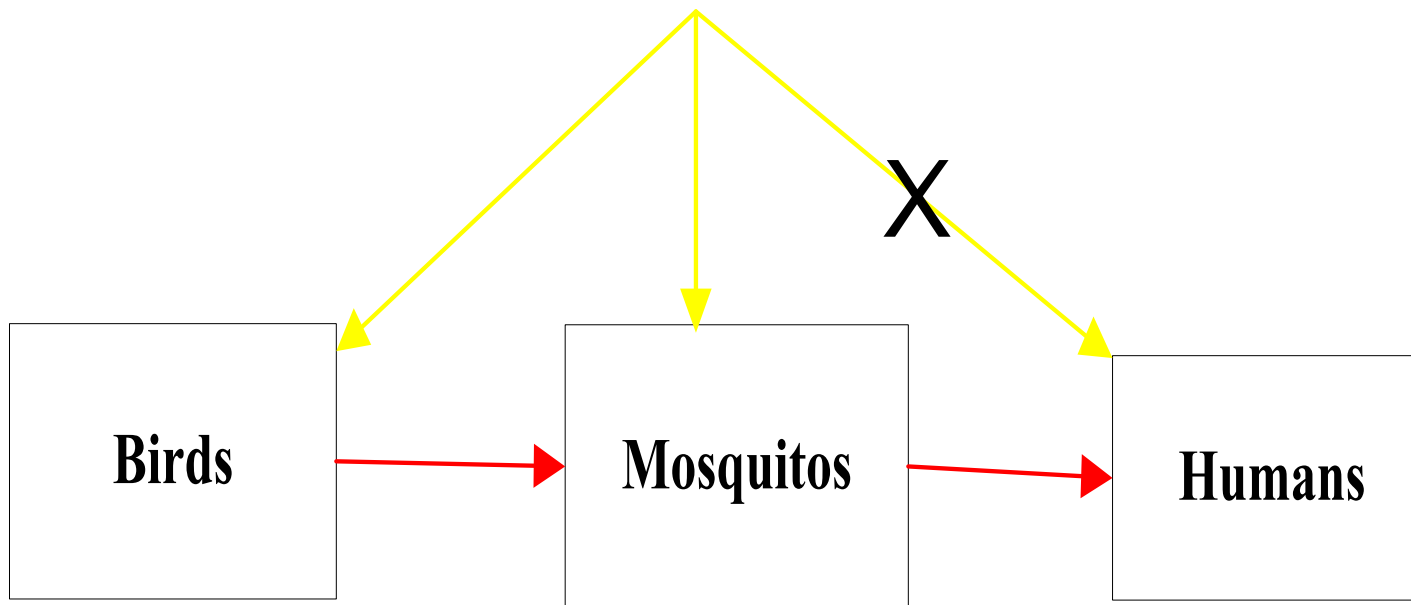


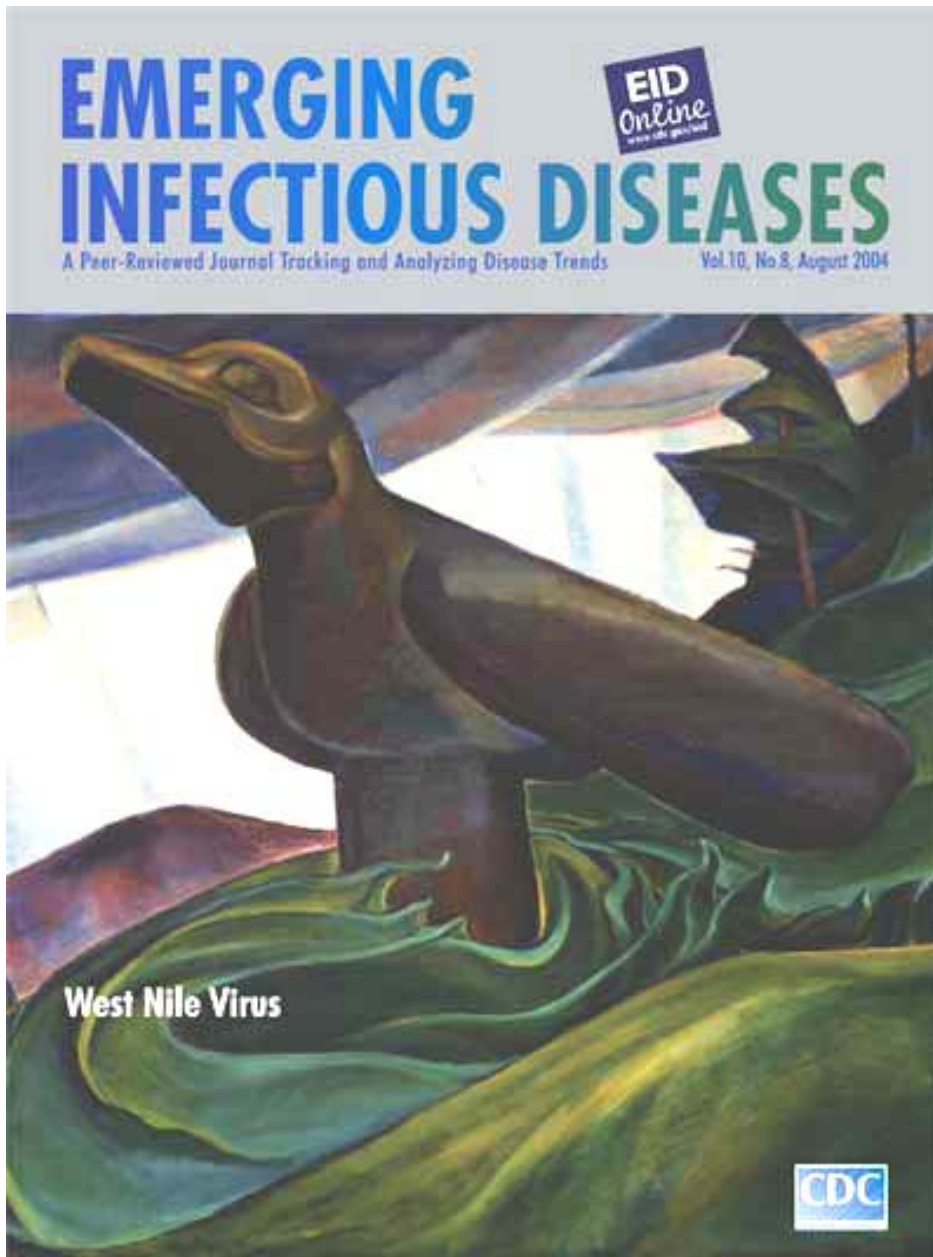
“Time changes everything!”



Mathematical model to control West Nile Virus (WNV)

Which species to cull (撲殺)?





Did Alexander
the Great (亞歷山
大大帝) died of
WNV in 323 BC
at age of 32?

-Marr and Calisher, *EID* 2003

Big Raven (1931) by Emily Carr



Application of Phylogenetic Analysis (基因系統發生分析)

- **Rebuttal** by Galli, Bernini, and Zehender (*EID*, 2004):

the **most recent common ancestor (MRC)**
for WNV can be dated back to **8th**
century (1,159 years ago) only



Priority List of Global Epidemics (全球疫情) (As Compiled by WHO 2000)

1. Drug resistant virus or microbe (抗藥性病毒或微生物) including: TB super-strain (超級變種) or multi-drug resistant (MDR) TB strains in Russia and China
2. TB (肺結核)
3. Dengue fever (登革熱)
4. HIV/AIDS (愛滋病)
5. Flu/Avian flu (流行性感冒/禽流感)



Infectious Diseases that Changed History (BC or “Before Christ”)

1350 BC - Egyptian-Hittite (西台國) war :
Egyptian prisoners passed on smallpox (天花) to people of Hittite, including their king and heir who both died, leading to the fall of the Hittite Empire.



Diseases that Changed History (BC II)

1314 BC -In the Bible, the Book of Exodus (聖經出埃及記) describes the plague (瘟疫) that Moses (摩西) brought down upon Egypt. But did Moses led his people out of Egypt to escape from the plague?

1157 BC -The mummy (木乃伊) of King Ramses V shows scars on his face and skin, perhaps indications of **smallpox** .



Infectious Diseases that Changed History (AD or After Death)

2nd century A.D. –Roman-Parthia (安息國, an Iranian civilization originating in the northeastern part of modern Iran) war brought smallpox (or some say measles) back to Rome, causing the famous **Plague of Antonine** (安東大瘟疫, 165-180 AD)。



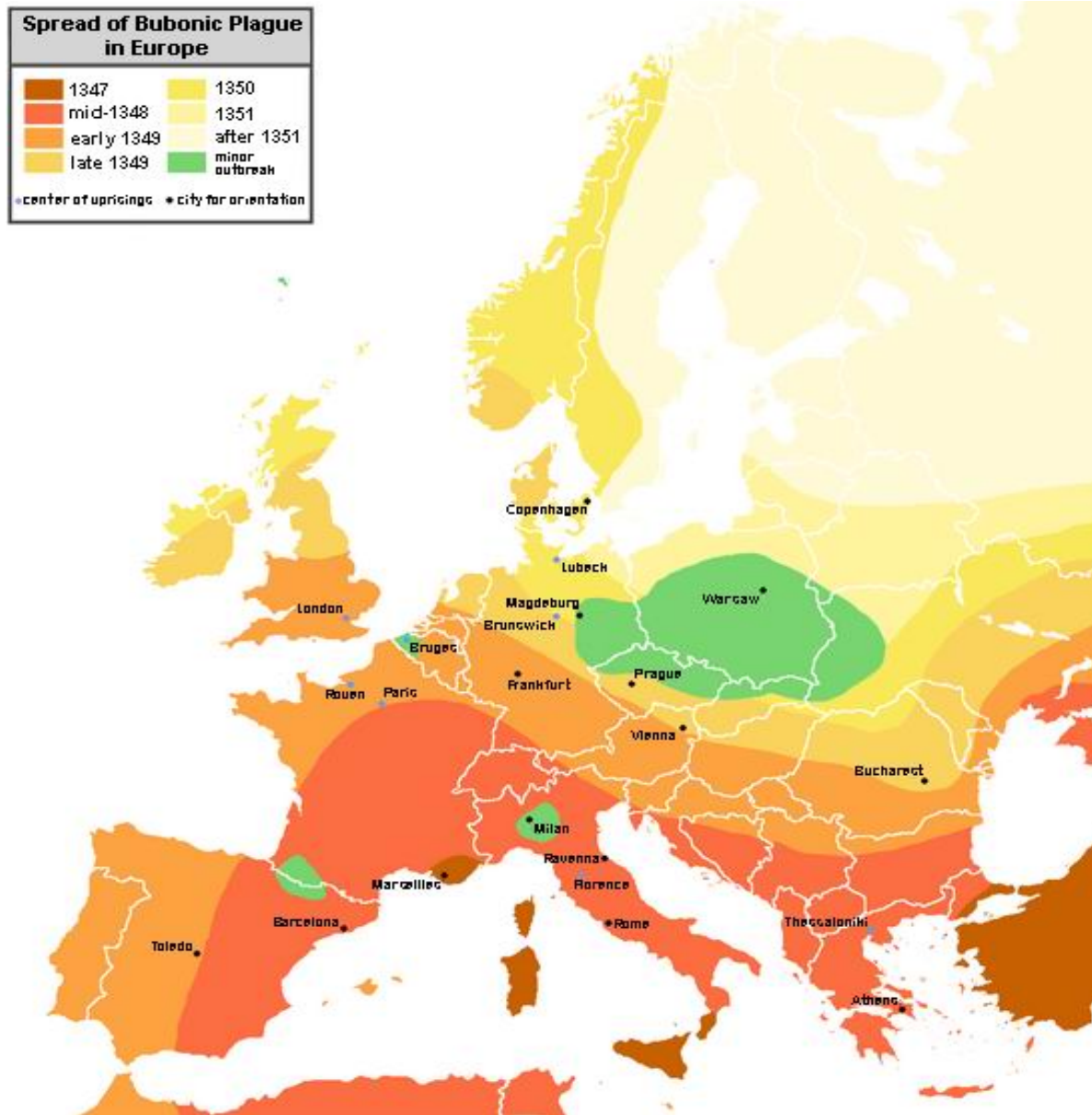
Diseases that Changed History (AD II)

This pandemic (大疫情) led to 3 million-7 million deaths. According to physicians' record, 1/4-1/3 Romans died in this pandemic, including , Lucius Verus, who died in 169, and his co-regent who ruled until 180, **Marcus Aurelius Antoninus** of the movie “the Gladiator” (神鬼戰士).

This pandemic lasted over 300 years and happened at the height of the Roman Empire, and was prelude (前奏) to the fall (and split) of the Empire.



Diseases that Changed History (AD III)



Bubonic plague in Europe or Black Death (鼠疫或黑死病)



Diseases that Changed History (AD IV)

1346-1350: Mongolians attacking Crimea (克里米亞) brought the plague to Europe, resulting in 25 millions deaths out of 100 millions Europeans, but also brought about the Renaissance (文明復興, 14th-16th century)

1665–1666: Great Plague of London (倫敦大瘟疫) killed 1/6 of Londoners, but led to Sir Isaac Newton (牛頓), his writing of calculus (微積分), and his discovery of gravity.



Diseases that Changed History (New World)

1520 - **Smallpox** in Mexico: **Cortez** (克提茲) took 600 men to Mexico to invade the Aztec (阿茲提克) Empire and brought smallpox which has **never occurred** in the American continent before the Europeans came. **Half** of 3.5 millions Aztecs (阿茲提克人) died. Within one decade (十年), the population of Mexico decreased from 30 million to 3 million.



Diseases that Changed History (New World II)

1530 – Smallpox was again brought by the Europeans to **Peru (秘魯)**, **Inca (印加) king** and his heir were both infected and died, which led to a civil war (內戰) among the successors. **Pizarro** was able to take 180 men and took control of the kingdom.



Intermission / 中場休息

		5	4	3			1	
1					2			
7								9
	8						2	
3								6
	2						3	
2								8
			9					7
	4			8	1	5		



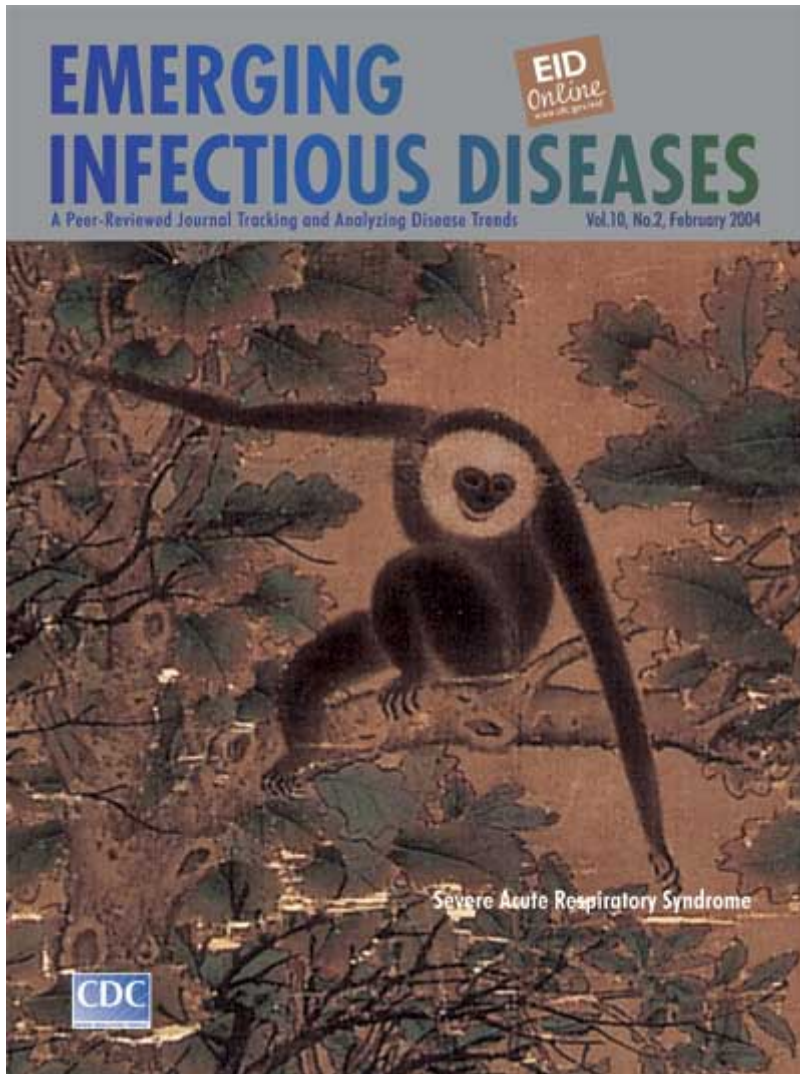
Modern Diseases that Changed History

1917-1921 - Typhus in Russia (傷寒): 2.5 millions died, which partially led to the Russian revolution.

1918-1920 - World-wide influenza (流行性感冒): 40 millions died in 12 months around the world. 1/3 U.S. population infected, 675,000 died (2.5% mortality compared to <0.1% for all other flu epidemics).



Modern Diseases that Changed History (II)

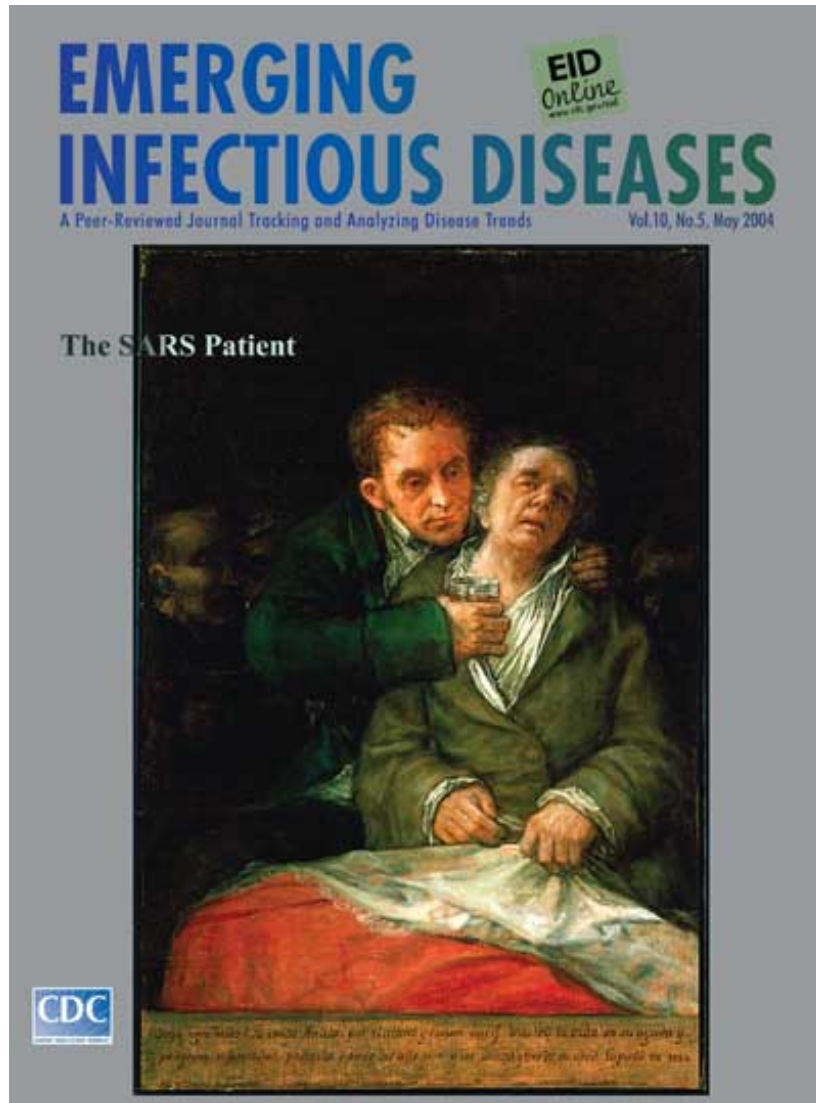


1981 - World-wide AIDS
(愛滋病): 20 millions death
so far, 40 millions living
with HIV at the end of
2005.

劉松年(1174–1224)



2003 – SARS: 8098 cases, 774 deaths world-wide.



Taiwan SARS (Hsieh et al. 2005):

480 cases, 85 deaths

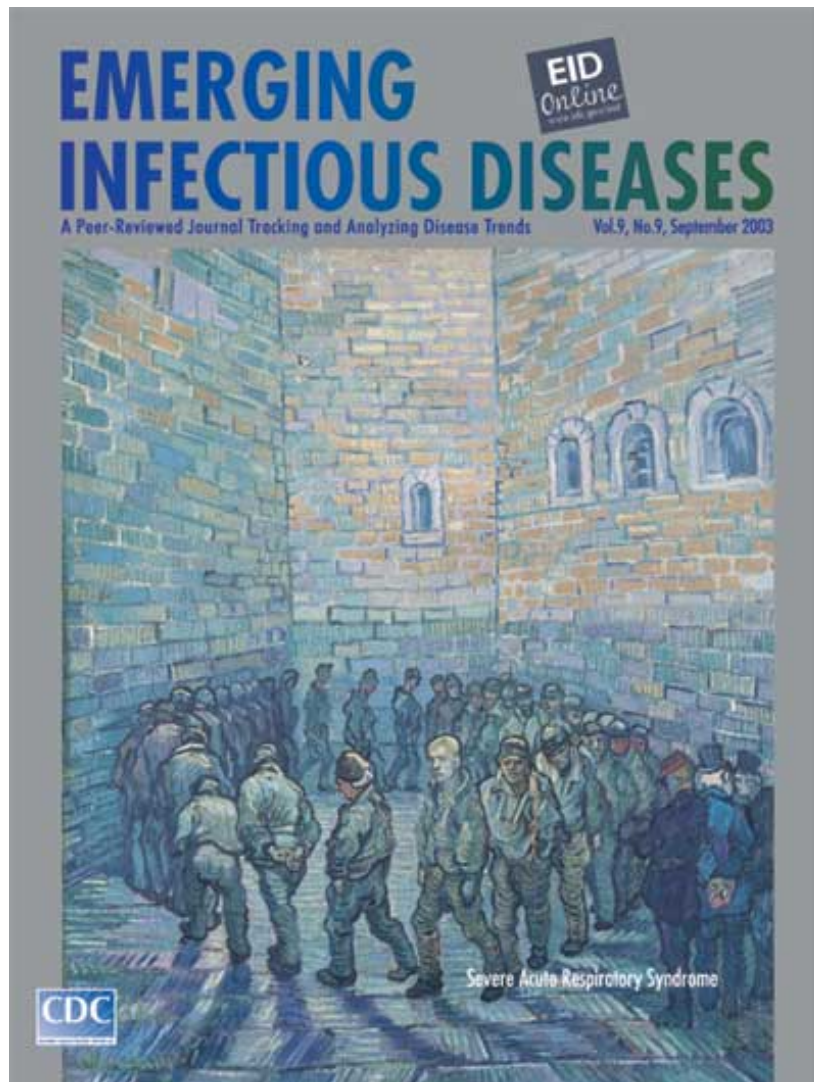
Healthcare workers:

134 cases, 13 deaths

Self-portrait with Doctor Arrieta (1820) by the painter Goya (1746–1828)



Present - World- wide TB (肺結核): one new infection per 5 seconds, 6-8 millions new infections every year, 2 million deaths per year.



Future: Influenza/Avian flu (流感/禽流感), Bioterrorism (生恐戰) after 911???

The Prison Courtyard (1890) by Vincent van Gogh (1853–1890)



Diseases that Changed History (本土版)

1796 - 吳沙「開蘭」: 吳沙 and others started farming in Ilan, but was repelled by hostile native Taiwanese (原住民).

The next year, **smallpox epidemic** occurred in Ilan with many deaths. 吳沙 took the initiative to try to treat the natives, winning the goodwill of the local people. They were allowed to settle and farm in Ilan.

1918-1920 - In Taiwan, **42,000-62,000** deaths during the **flu pandemic** (Hsieh and Chan 2008).



Definition Of
MATHEMATICAL EPIDEMIOLOGY
(數理流行病學)

“The application of mathematics* to the study of **infectious disease** epidemiology”

“數學*在傳染病流行病學上之應用”

In “Infectious Diseases of Humans” by Anderson and May, 1991

*Note that ”mathematics” includes but not limited to **statistics**.



History of Infectious Disease Modeling

1760 - Daniel Bernoulli: mathematical (ODE) model to study effectiveness of inoculation (種痘) against smallpox (天花).

Early 1900's - Empirical study of smallpox (Farr and Brownlee 1906), discrete-time model of infectious diseases (Hamer 1906), continuous-time modeling of malaria (瘧疾, Sir Ronald Ross 1911, Ross was 1902 Nobel Laureate in Medicine).

1930 - **Net reproductive value** (R. A. Fisher, *Genetic Theory of Natural Selection*)



Why Mathematical Epidemiology Now?

- Cleaner environment (衛生環境的進步): for example, polio (小兒麻痺) first emerged in Europe in 19th century, first major outbreak in US in 1916)
- More and Faster Globalization (全球化): HIV 1959? WNV 1999, SARS 2003)
- Modern advances in (生物科技) science and technology on understanding of infectious diseases (Molecular biology 分子生物學: Is 1918 flu epidemic due to a strain of swine flu?)



Purposes (目的) of Mathematical Modeling

- Reconstruct history (重建歷史), design simple model, and “predict” future
- Study sensitivity (敏感度) to parameters changes
- Compare effectiveness of control strategies (防治策略之功效)
- Design more refined models (修改模式) to improve accuracy

-Fred Brauer, at “Current Science of SARS Symposium”



Albert Einstein:

- Models should be as simple as possible, but not more so.



The **KISS** method

KeeP **I**t **S**imple and **S**tupid

-from An anonymous mathematical biologist



Fig. **Residuals** of 3/12-5/25 probable SARS cases (true cumulative number values minus predicted values) fitted by **exponential model with series autocorrelation in the error structure** (Hsieh and Chen, BMJ, June 21, 2003)

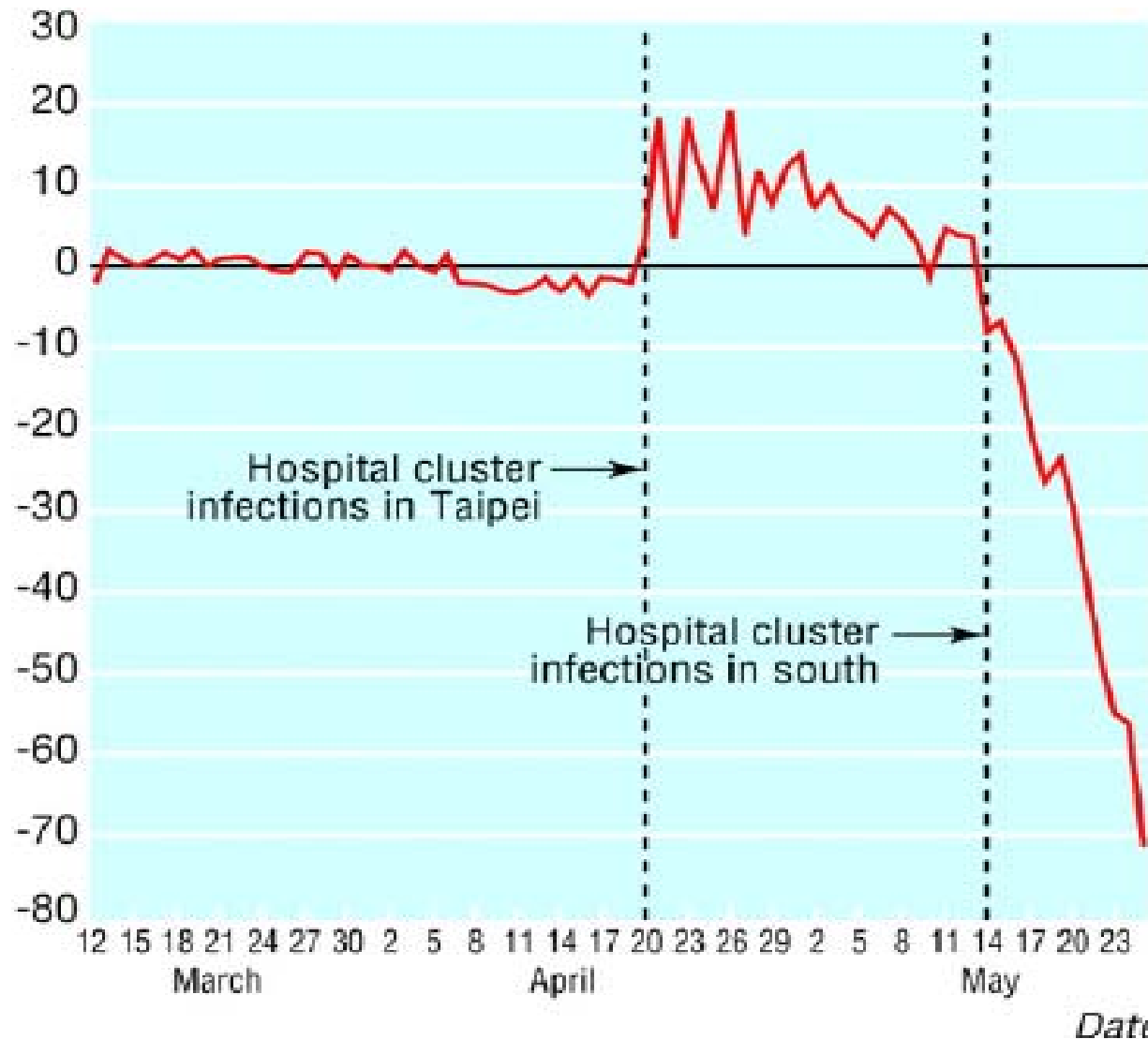
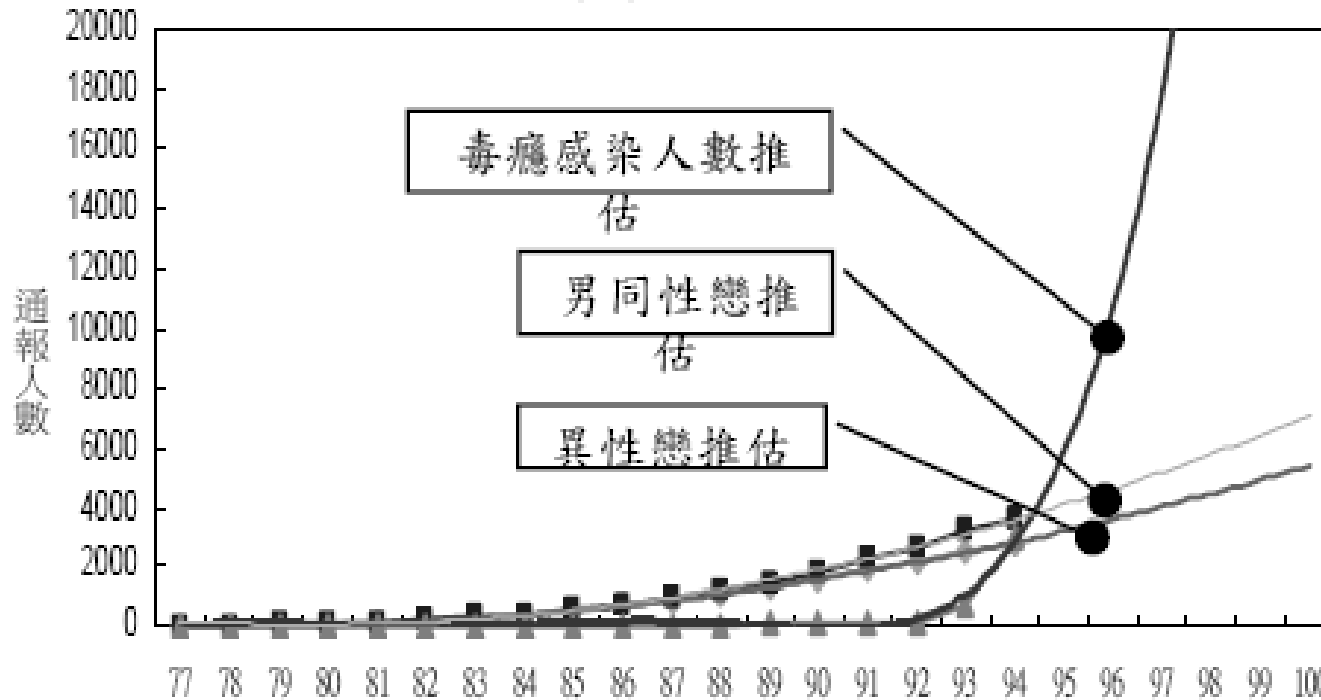


Fig. 2005 Projection of Taiwan HIV cases in 2007 by TCDC personnel using exponential curve fitting (TCDC website)



不同危險因子累積通報 感染人數推估



2007 actual HIV data: MSM:4293, IVDU: 5785



Table. Cumulative Number of Confirmed Human Cases of Avian Influenza H5N1 (WHO, December 30, 2005)

Indonesia		Vietnam		Thailand		Cambodia		Cambodia		Total	
case	death	case	death	case	death	case	death	case	death	case	death
16	11	93	42	22	14	4	4	7	3	118	61

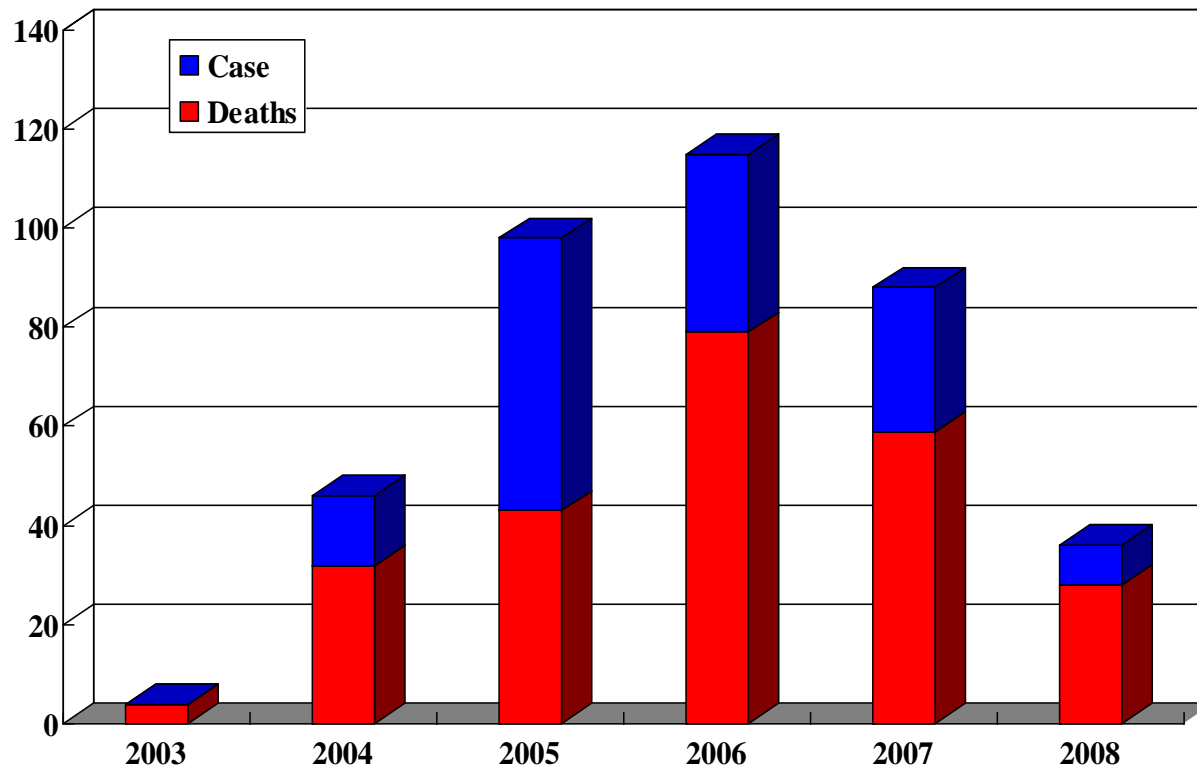


Predictions for Avian flu (H5N1) or Influenza pandemic

- United Nation bird flu envoy **David Nabarro**: 5 millions to 150 millions deaths (Sept. 30, 2005)
- WHO communications director for the communicable diseases **Dick Thompson**: 2 millions to 7.4 millions (on the same day)
- In US (CDC, 2004, using FluAid): 18-42 millions cases, 890,000-2.07 millions deaths
- In Taiwan (summer of 2005, also using **FluAid?**): **5.3 millions symptomatic cases, 14,000 deaths?**

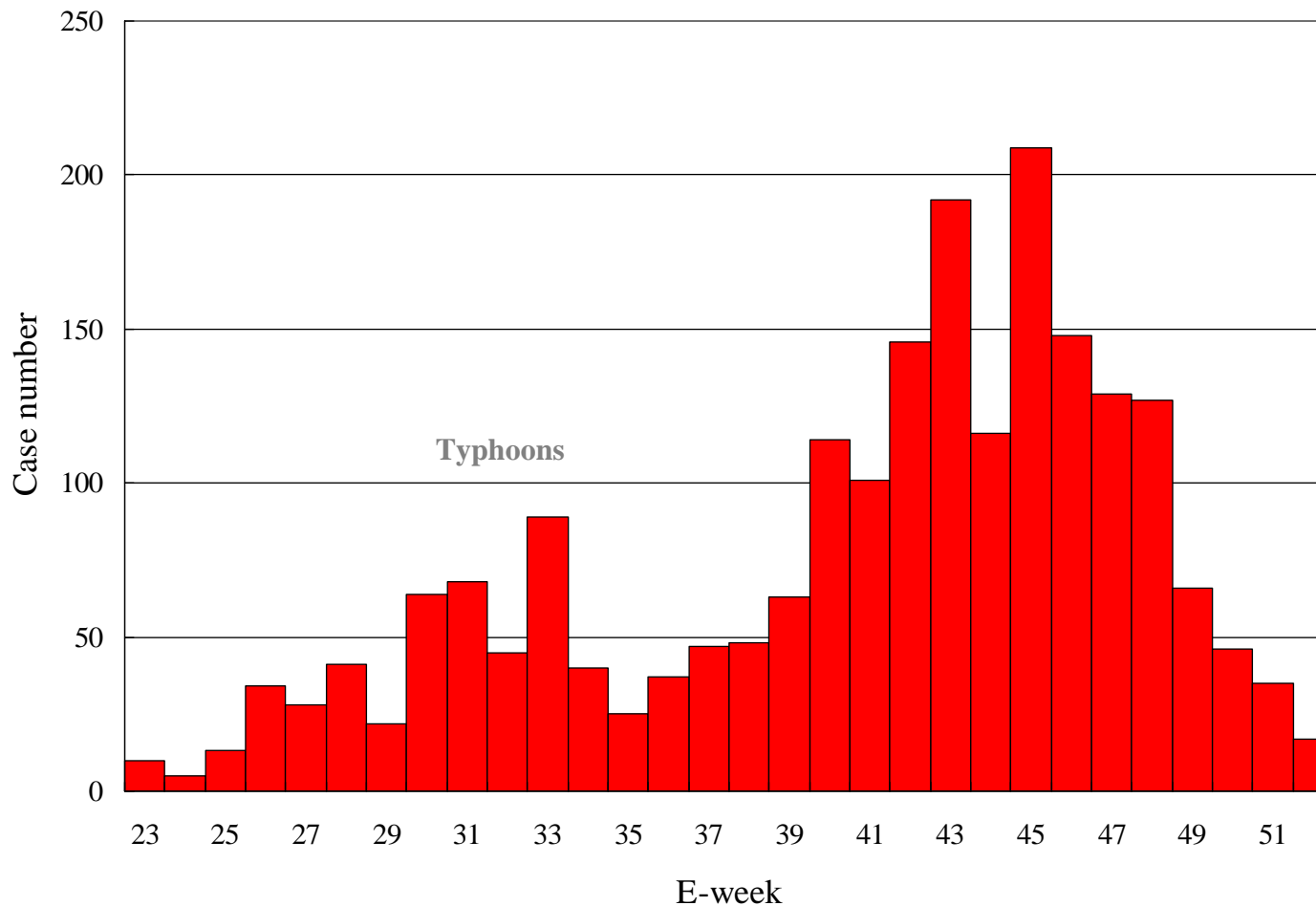


Fig. Cumulative Number of Confirmed Human Cases of Avian Influenza A/(H5N1) Reported to WHO, September 10, 2008. (Source: WHO Website)



Modeling 2-wave dengue outbreak in Taiwan, 2007: Impact of Climate Change. (Hsieh 2008)

Fig. Daily dengue (DF/DHF) case data by onset



“Mathematics is a way of thinking clearly, no more, but no less.”

– Robert M. May, Lord (勳爵) of Oxford, President of Royal Society, United Kingdom, in *Virus Dynamics* (2000 Nowak and May).



“The mathematical method of treatment (using **mathematical model of malaria transmission**) is really nothing but the application of careful reasoning (細心推理) to the problems at issue”

-Sir Ronald Ross (1911)



“I have deeply regretted that I did not proceed far enough at least to understand something of the great leading principles of mathematics; for men thus endowed seem to have an extra sense (特殊官感).”

-Charles Darwin (達爾文)



-Chance favors the well-prepared.

-幸運總是留給準備最充分的人



8	9	5	4	3	7	6	1	2
1	6	4	8	9	2	3	7	5
7	3	2	6	1	5	4	8	9
5	8	1	3	6	9	7	2	4
3	7	9	1	2	4	8	5	6
4	2	6	5	7	8	9	3	1
2	5	3	7	4	6	1	9	8
6	1	8	9	5	3	2	4	7
9	4	7	2	8	1	5	6	3

