

人類文明史、傳染病、數學

謝英恆

國立中興大學應用數學系

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Y. H. Hsieh



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各學院相關性

- 人類文明史：文學院
- 傳染病：農學院，生命科學院，獸醫學院
- 數學：理學院，工學院
- 社管學院？

內容提要

1. 傳染病對人類的重要性
2. 改變歷史的傳染病
3. 傳染病數學模式的歷史
4. 流感之數學模式

Time for 774 deaths to occur due to:

SARS - November, 2002 – July, 2003

HIV – 6 hours

TB – 3 hour

註:

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

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Culprits or victims of **Avian flu**?

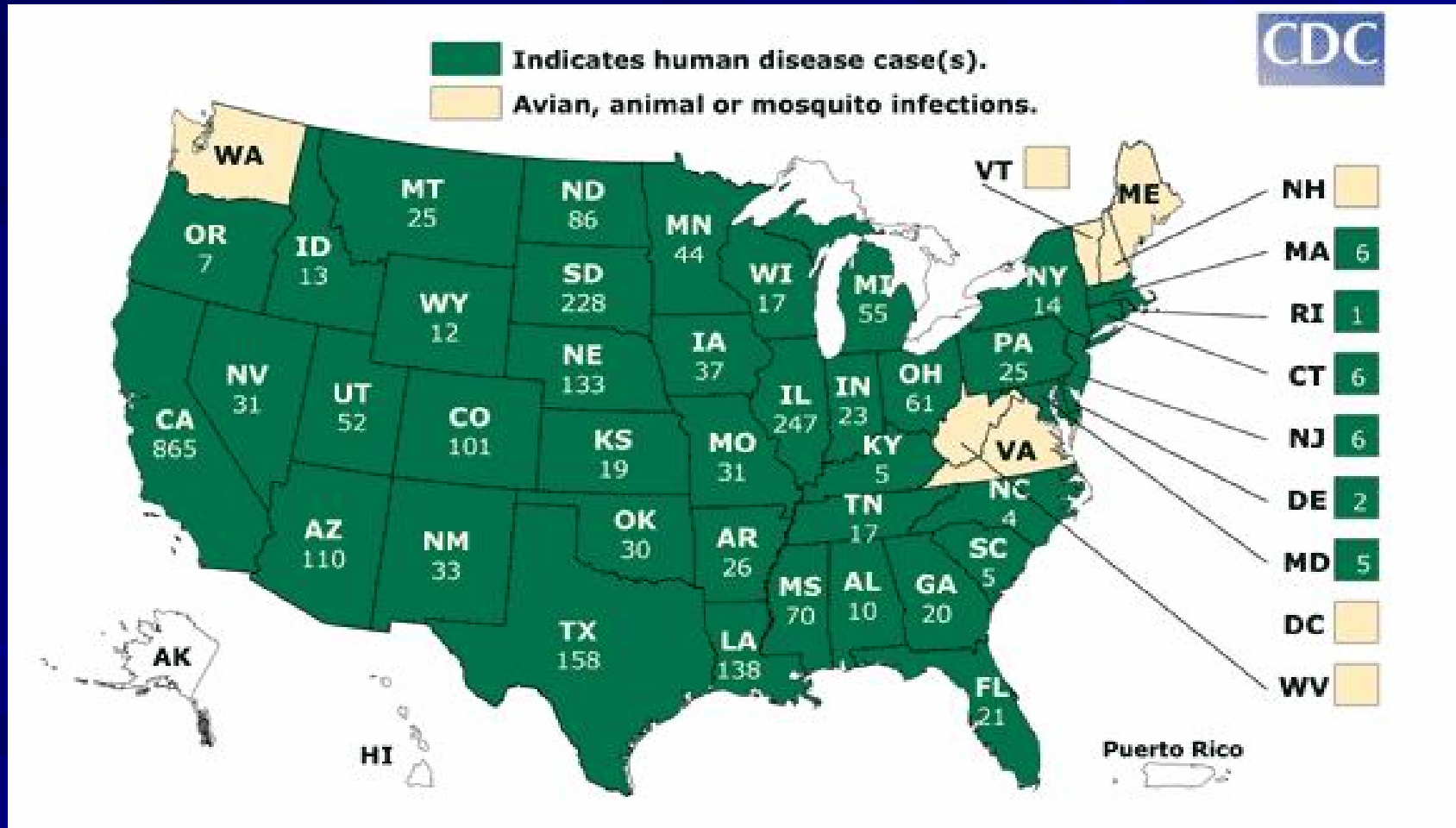
牠們是**禽流感(H5N1)**的罪魁禍首,還是受害者?



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West Nile Virus (西尼羅河病毒) in U.S.

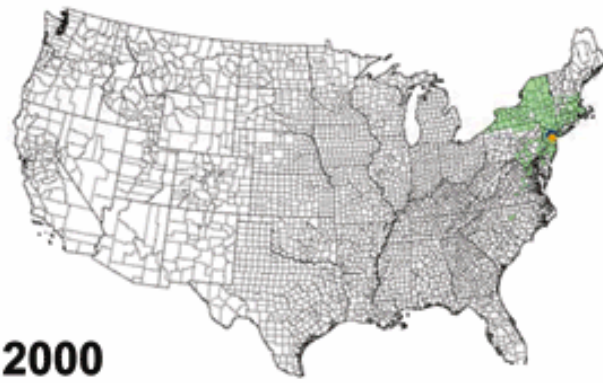
2799 cases/102 deaths (1999-2005)



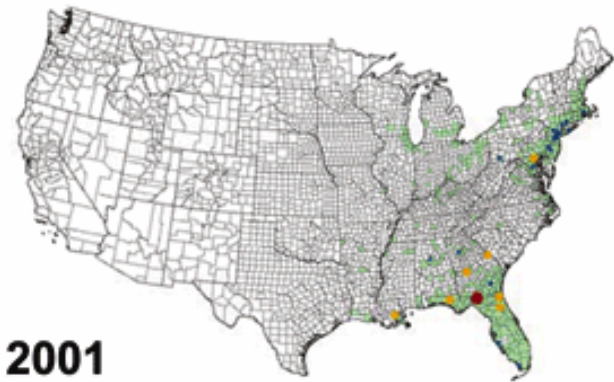
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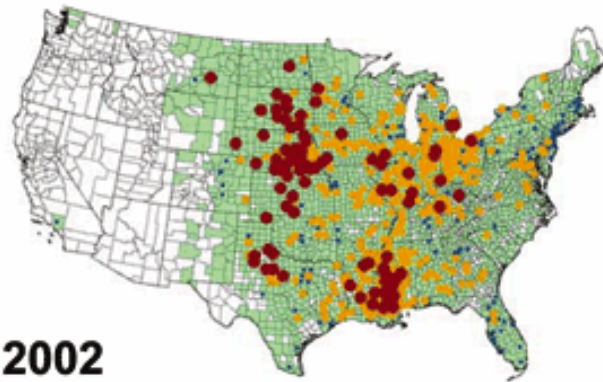
1999



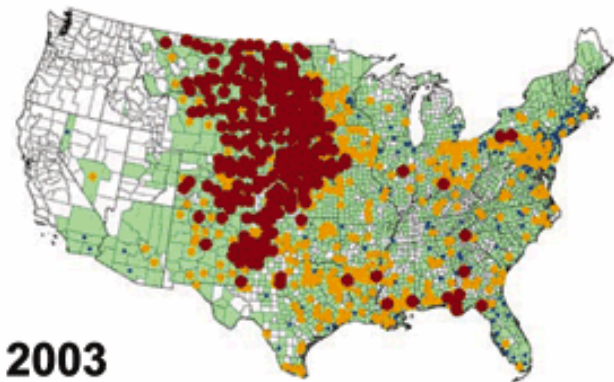
2000



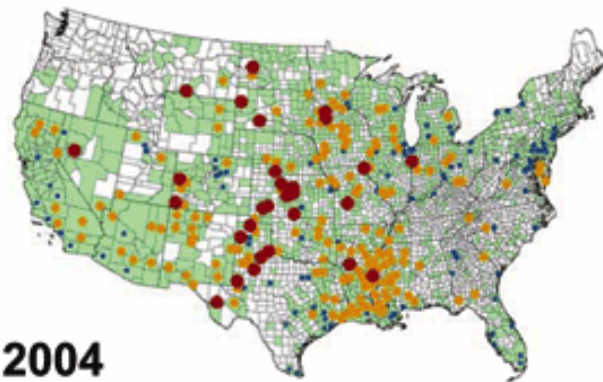
2001



2002



2003



2004

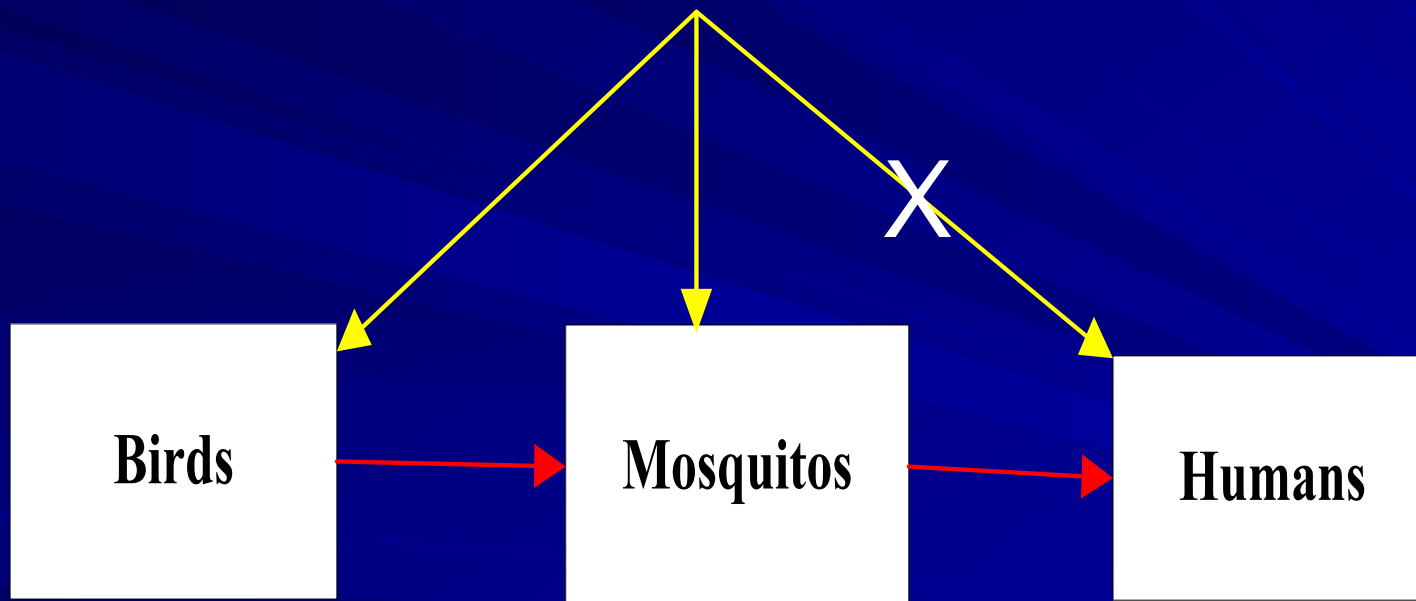
Incidence per million



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防止 West Nile Virus (西尼羅河病毒)

Which species to cull (撲殺)?

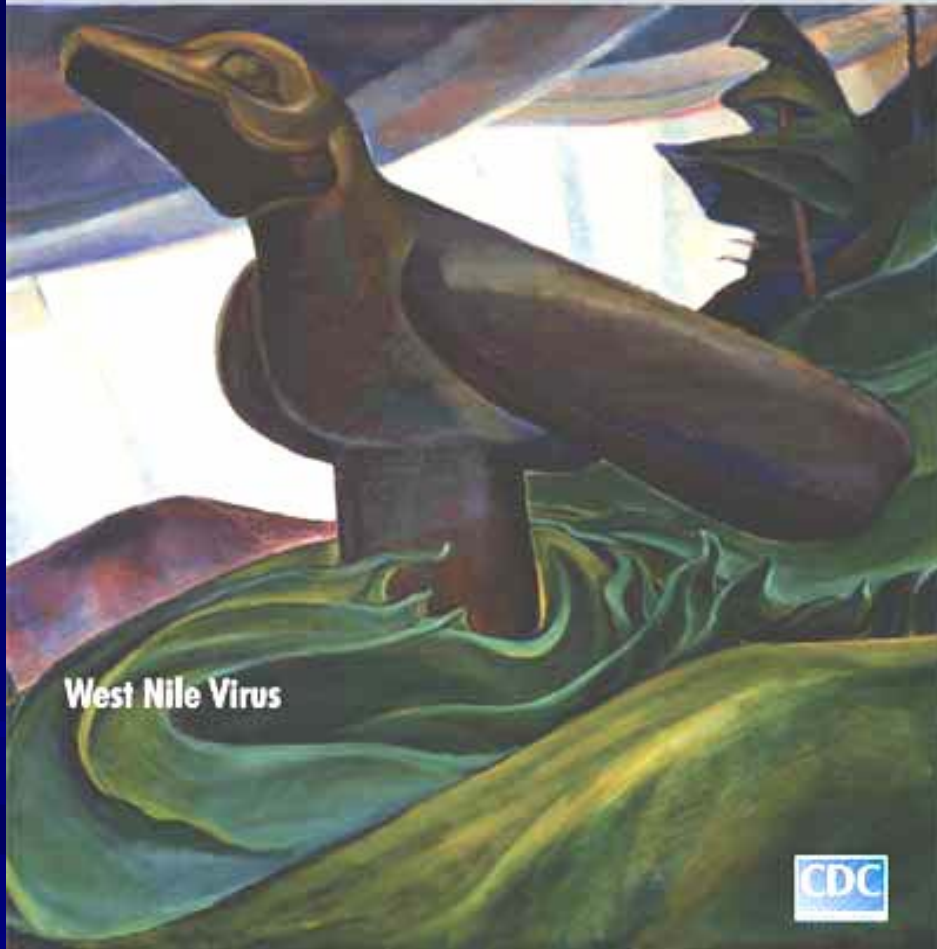


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EID
Online
www.cdc.gov/eid

A Peer-Reviewed Journal Tracking and Analyzing Disease Trends

Vol. 10, No. 8, August 2004



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

-Marr and Calisher, *EID* (新
興傳染病) 2003

Big Raven (1931) by Emily Carr

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Phylogenetic Analysis (基因系統發生分析)

- Galli, Bernini, and Zehender (*EID*, 2004):
the **most recent common ancestor (MRCA)**
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):

TB super-strain (超級變種) or multi-drug resistant (MDR) TB strains in Russia and China in 2004

2. TB (肺結核)
3. Dengue fever (登革熱)
4. HIV/AIDS (愛滋病)
5. Flu (流行性感冒)

改變歷史的傳染流行病 (西元前) (Infectious diseases in History)

1350 BC-埃及與西台國(Hittite)戰爭：埃及戰俘可能把天花傳給西台人。連西台國王與其繼承人都得病去世，導致西台國滅國。

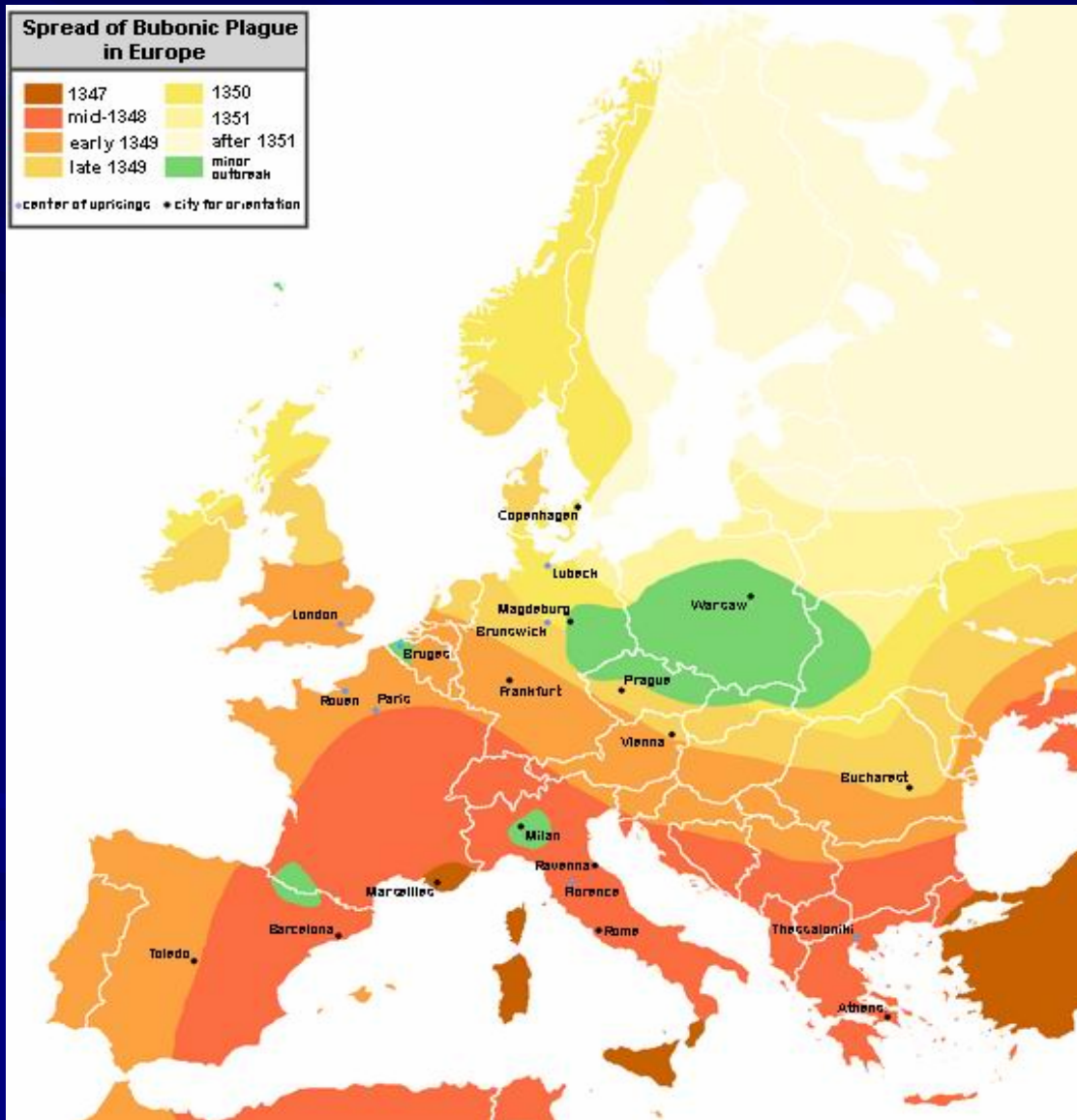
1314 BC-The Book of Exodus (聖經出埃及記) describes the plagues (瘟疫) that Moses (摩西) brought down upon Egypt. 摩西是否為逃避瘟疫而帶猶太人的祖先離開埃及。

1157 BC-埃及拉姆色斯五世(Ramses V)的木乃伊之臉上及皮膚有天花感染的跡象。他死後不久，埃及的新帝國瓦解。

改變歷史的傳染流行病(西元後-I)

2nd century –羅馬人與安息國(Parthia)作戰，把中亞流行的天花帶回羅馬，導致史上有名的安東大瘟疫(Plague of Antonine)。這場瘟疫死三百萬至七百萬人，根據當時醫師記載，有1/4-1/3的羅馬人死於這場瘟疫，包括羅馬皇帝奧瑞利亞斯(Marcus Aurelius 神鬼戰士)。這場瘟疫延續了三百多年。對當時日正當中的羅馬帝國打擊很大，最後只好東遷為東羅馬帝國。

改變歷史的傳染流行病(西元後-II)



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

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1346-1350: 蒙古軍隊圍攻克里米亞所帶來疾病，
25 millions deaths out of 100 millions Europeans.
但也帶來文明復興(Renaissance: 14-16世紀)

1665–1666: Great Plague of London (倫敦大瘟疫)
killed 1/6 of Londoners (但造就了Isaac Newton 牛頓)。

1720–1722: Bubonic plague epidemic in Provence
(普羅旺斯), half the population of Marseilles (馬賽),
44 per cent of the population of Arles (梵谷),
and 30 percent of the population of Aix (塞尚) and
Avignon died.

改變歷史的傳染流行病(西元後-III)

1520 – Smallpox in Mexico (天花): Cortez (克提茲)帶領六百西班牙士兵入侵墨西哥將瘟疫帶到當地。 Half of 3.5 millions Aztecs (阿茲提克人) died. 十年內墨西哥原住民人口由三千萬減至三百萬。

1530 – 天花瘟疫在祕魯流行，印加國王與其繼承人都得病去世，導致內戰。Pizarro 得以順利帶領一百八十名西班牙士兵入侵祕魯。

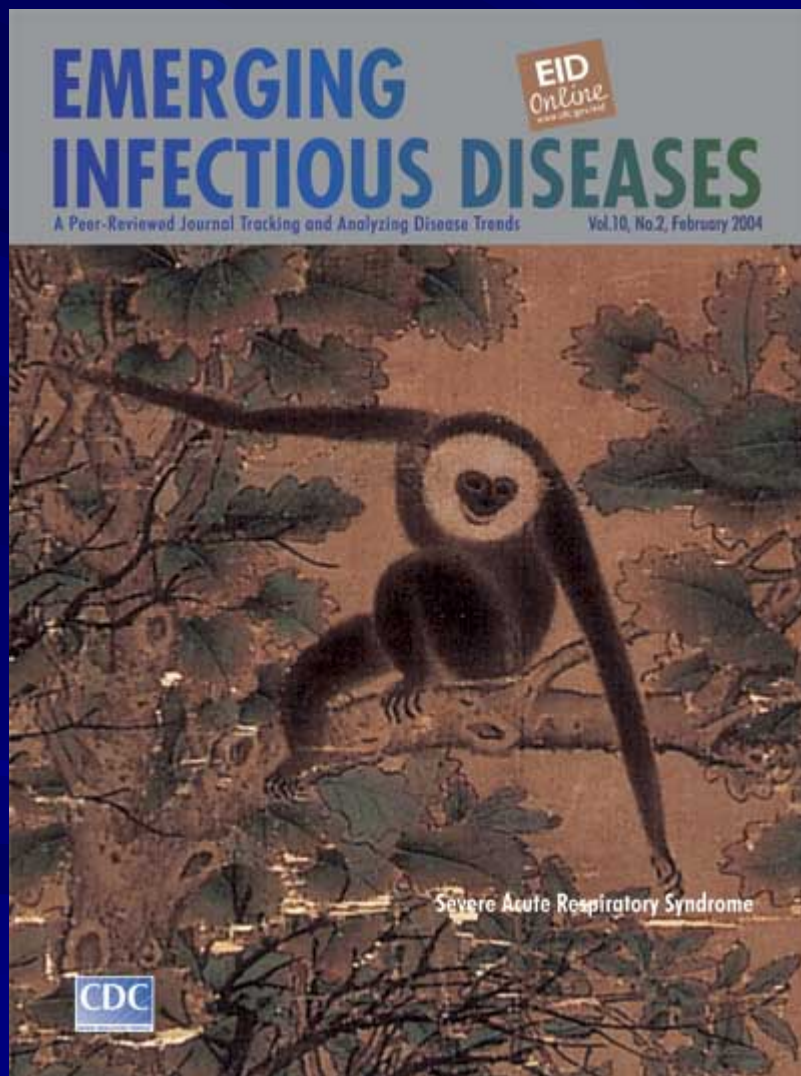
改變歷史的傳染流行病(近代版)

1850 – Cholera (霍亂) in Europe: John Snow(流行病學之父)發現水源是感染源: 倫敦為首的西方世界開始現代的都市衛生系統建設

1917-1921 - Typhus in Russia (傷寒): 2.5 millions died.

1918-1919 - World-wide influenza (流行性感冒): 40 millions died in 12 months. 1/3 U.S. population infected, 675,000 died (2.5% mortality compared to <0.1% for all other flu epidemics).

改變歷史的傳染流行病(現代版)



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)

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

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A Peer-Reviewed Journal Tracking and Analyzing Disease Trends
Vol. 10, No. 5, May 2004

EID
Online
www.elsevier.com

The SARS Patient



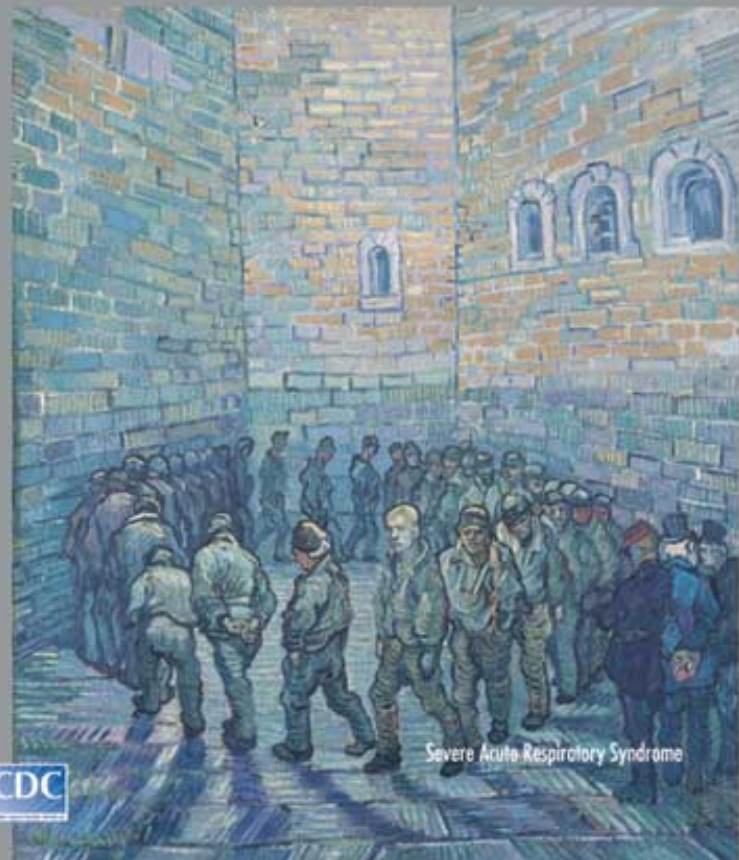
Taiwan SARS:
480 cases, 85 deaths
醫護人員:
134 cases, 13 deaths

Self-portrait with Doctor Arrieta
(1820) by 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.

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A Peer-Reviewed Journal Tracking and Analyzing Disease Trends Vol.9, No.9, September 2003



Future - 流感/禽流感, 生恐戰(Bioterrorism) ???

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

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改變歷史的傳染流行病(本土版)

西元405年-東晉發生天花瘟疫。這種疾病當時叫做「虜瘡」，顯然是外國傳來的疾病。從《晉書》的記載可知，醫學家葛洪生平共遇到五次大疫，時間與中亞的大瘟疫相近。

1334年-鼠疫在湖北爆發。

1796年-吳沙「開蘭」因受原住民的猛攻，只好暫退。次年，原住民流行天花，不少人病死。吳沙主動醫治病苦中的原住民，因此出現轉機。在不到一年的時間，墾地幾十里，接連開發了二圍、三圍。

1894年-鼠疫：中國大陸→香港→世界(包括臺灣)。

1919年-臺灣霍亂疫情：從中國福州搭船來台的日籍古董商帶進病原。

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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		

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Definition of Epidemiology (流行病學)

- **Traditional Definition:** The study of **communicable diseases** (傳染病) which is temporarily prevalent (盛行) in a community.
- **Modern Definition** (after 1950): The study of all **health-related states or phenomena** (健康相關現象) prevalent in a community and their control. (Also include non-infectious diseases such as cancer 癌症, gout 痛風, obesity 肥胖, alcoholism 酗酒 etc.)

Definition Of MATHEMATICAL EPIDEMIOLOGY (數理流行病學)

“The application of mathematics* to the study of infectious disease epidemiology”
“數學*在傳染流行病學上之應用”

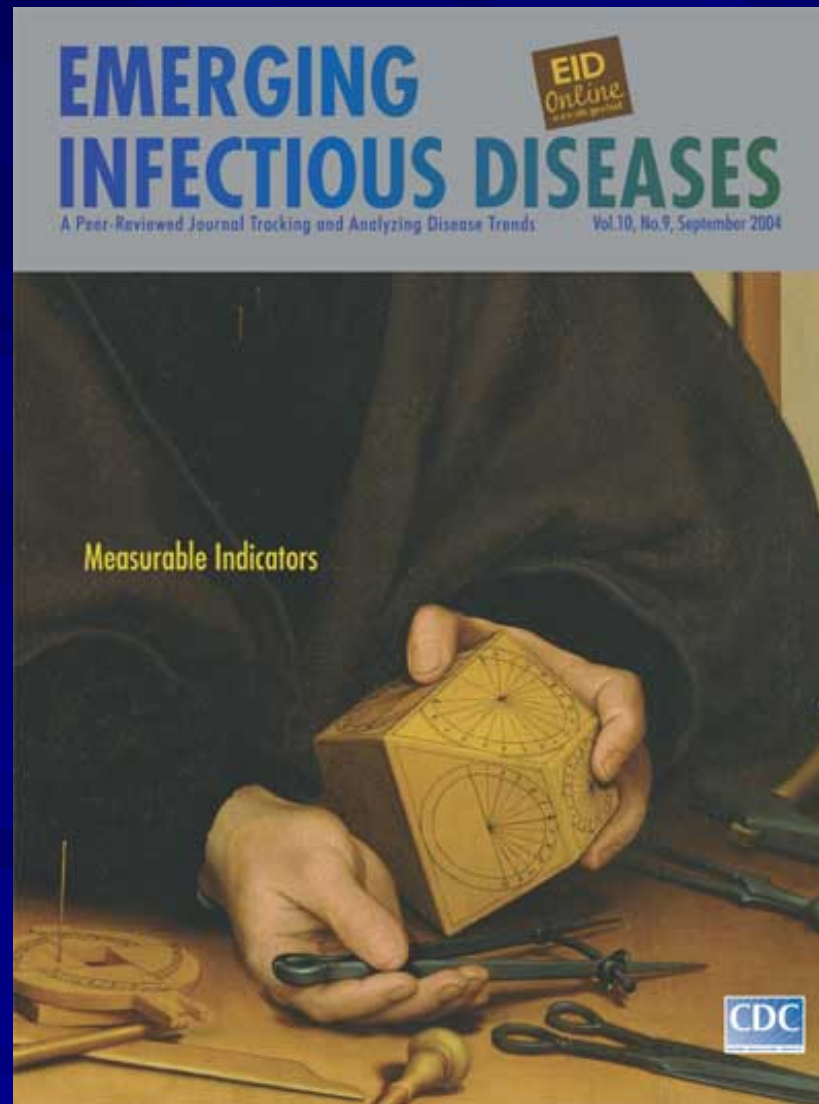
In “Infectious Diseases of Humans” by Anderson and May, 1991

*Includes but not limited to **statistics**.

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Nicholas Kratzer (mathematician and astronomer to Henry VIII) by Hans Holbein the Younger (1497–1543)



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傳染病數學模式的歷史

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

1889 - D. En'ko: discrete time model of measles (麻疹) epidemic

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, Ross 1908-1917).

1927 - Epidemic threshold (門檻) theory (Kermack and McKendrick)

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

Why Mathematical Epidemiology Now?

- (衛生環境的進步) Cleaner environment (polio小兒麻痺: emerge in Europe in 19th century, first major outbreak in US in 1916)
- More and (全球化) Faster Globalization (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”

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Albert Einstein:

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

The **KISS** method

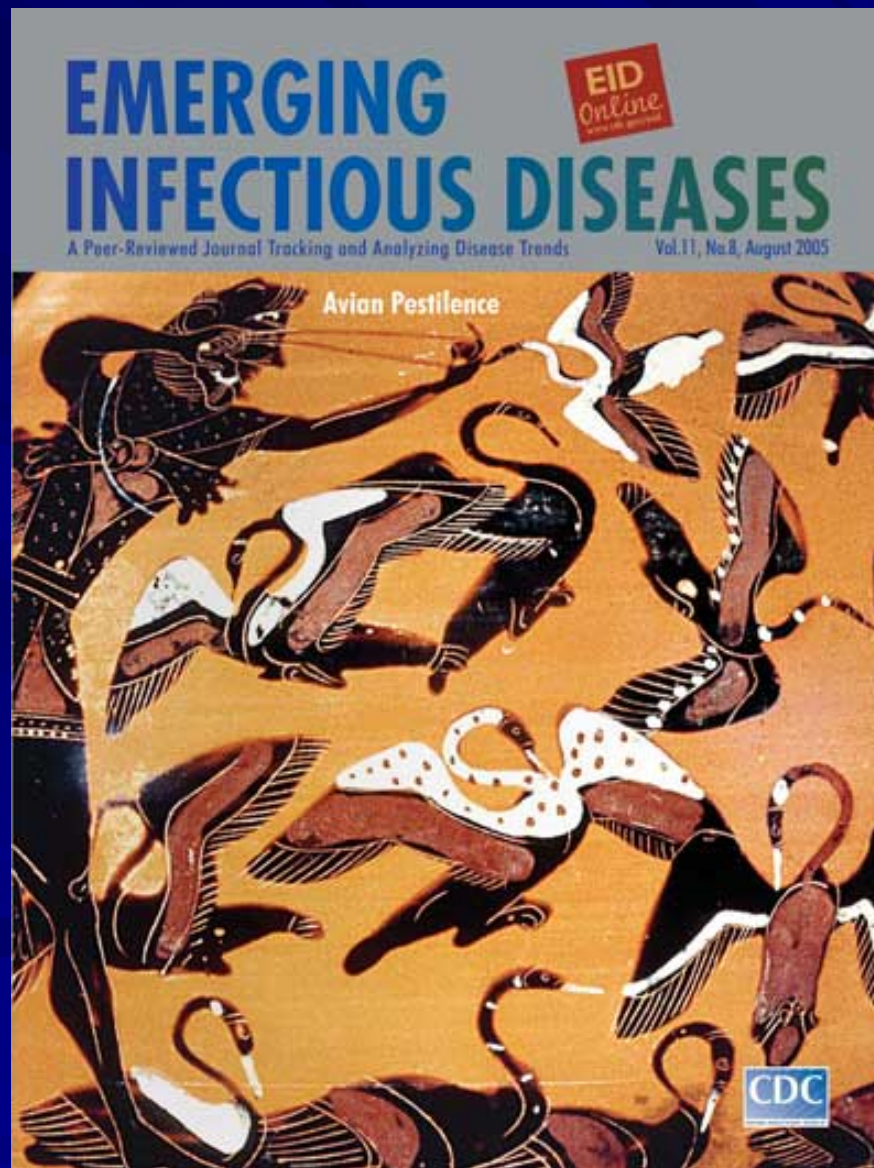
Keep **I**t **S**imple and **S**tupid

-A mathematical biologist

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

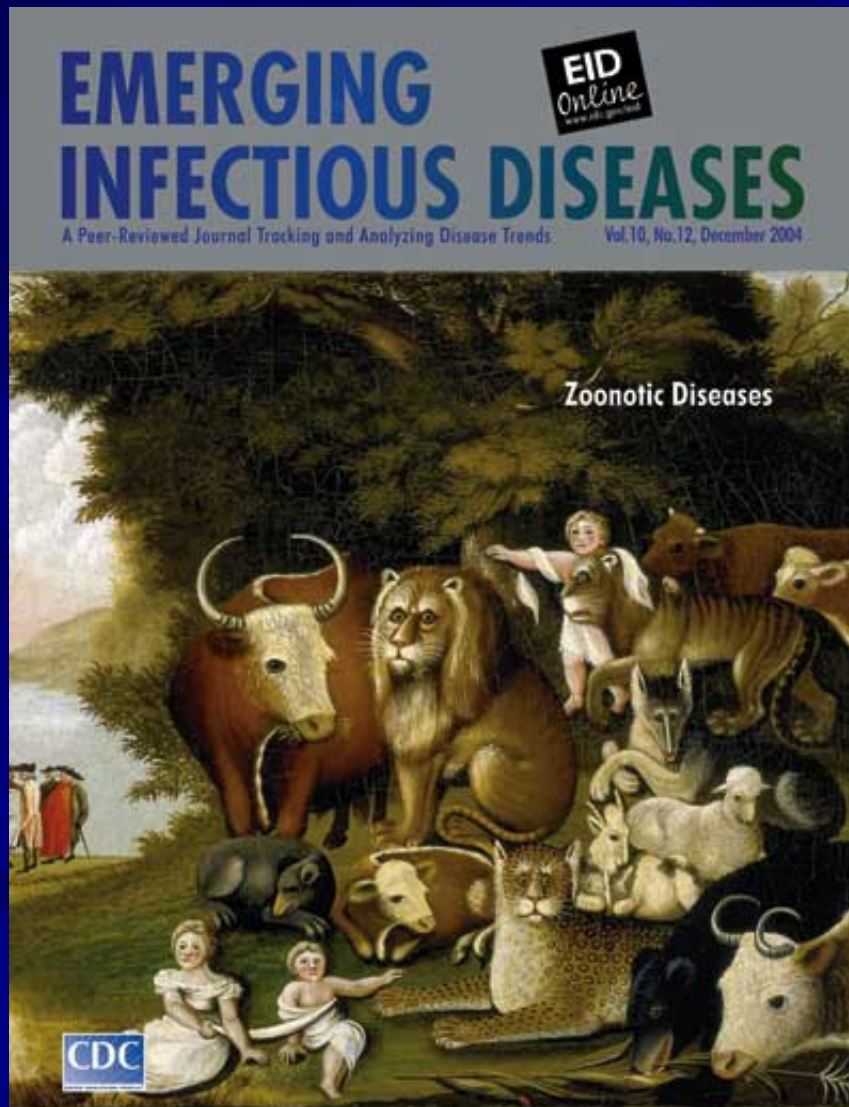
	Indonesia		Vietnam		Thailand		Cambodia		Cambodia		Total	
	case	death	case	death	case	death	case	death	case	death	case	death
Total	16	11	93	42	22	14	4	4	7	3	118	61

Herakles (Son of Zeus) and the Stymphalian Birds (circa 6th century BC)



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Peaceable Kingdom (c. 1833) by Edward Hicks (1780–1849)



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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 (same day)
- In US (CDC, 2004, using FluAid): 18-42 millions cases, 890,000-2.07 millions deaths
- In Taiwan (using **FluAid?**): **5.3 millions symptomatic cases, 14,000 deaths?**

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

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

“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

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-Chance favors the well-prepared.

-幸運總是留給準備最充分的人



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你覺得你是…
思考周全？做事認真？勇於接受挑戰？電腦高手？
如以上皆是…

誠徵 國科會研究計劃兼任研究助理

時效：隨時起聘

學歷：大學部以上

專長：具思考分析能力及熟悉電腦程式

連絡人：謝英恆老師

台中市中興大學應數系620室

Tel：04-22853949

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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

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