

EMERGING VECTOR-BORNE DISEASES: YELLOW FEVER AS A PARADIGM

INTERNATIONAL CONFERENCE ON
EMERGING INFECTIOUS DISEASES

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TYPICAL ARTHROPOD-VERTEBRATE CYCLE

INFECTED ARTHROPOD FEEDS ON SUSCEPTIBLE VERTEBRATE



INCUBATION PERIOD, VIREMIA



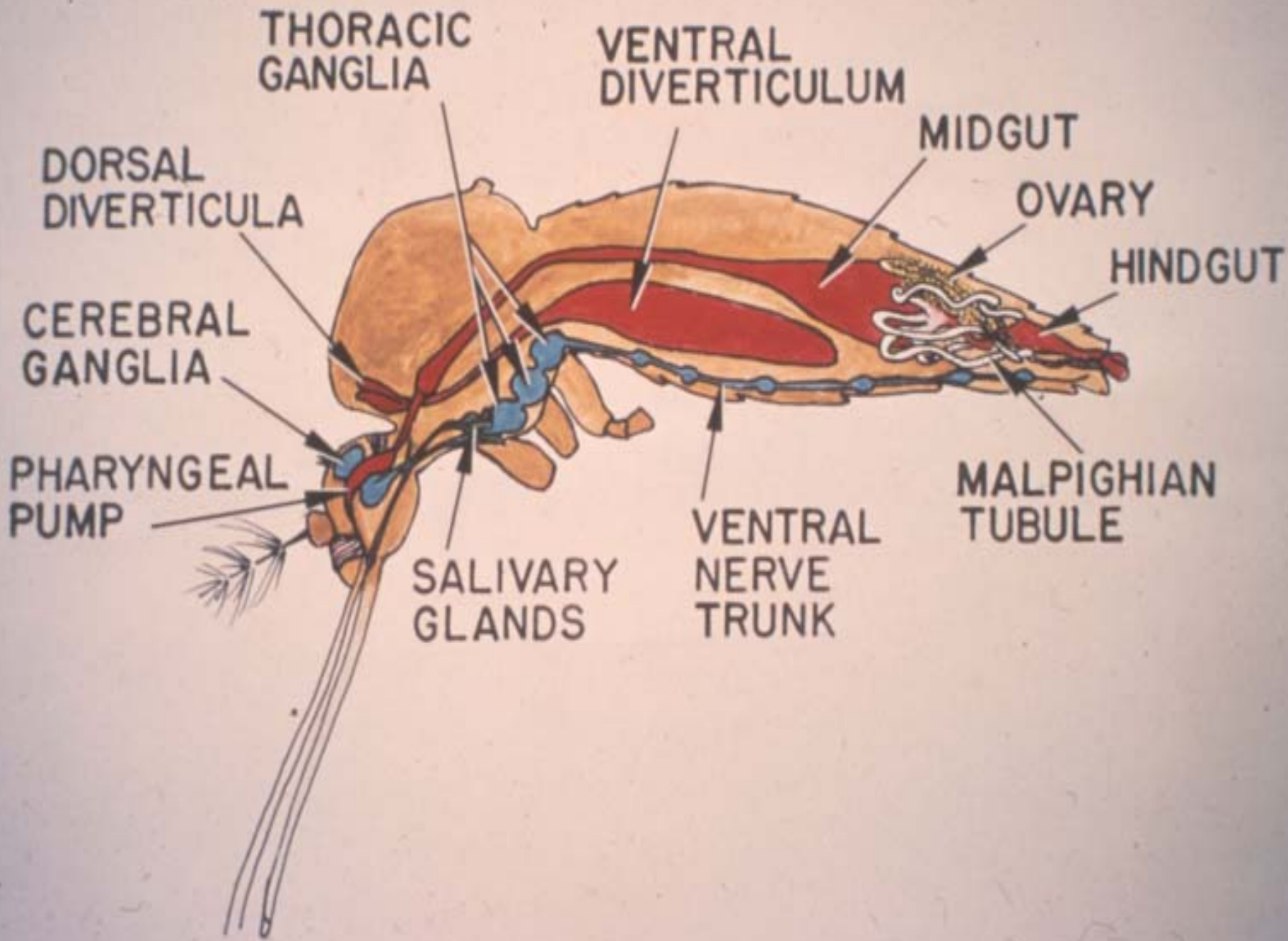
UNINFECTED ARTHROPODS FEED ON VIREMIC VERTEBRATE



INCUBATION PERIOD= ESCAPE FROM MIDGUT, VIRUS IN HEMOLYMPH, INFECTION OF SALIVARY GLANDS



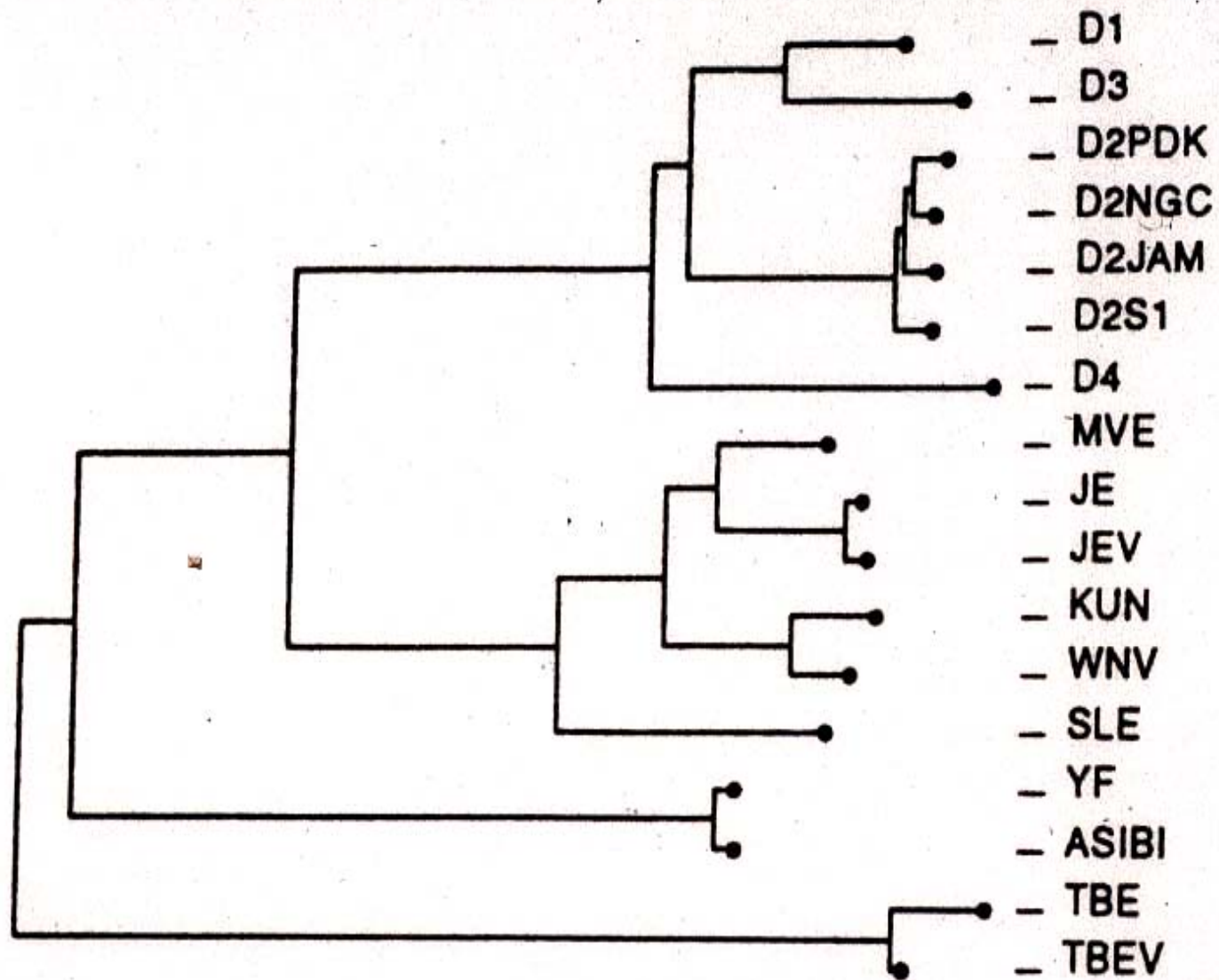
REPEAT





SYLVATIC VIRUSES, 1996

◆ Europe	51
◆ North America	108
◆ South America	154
◆ Africa	150
◆ Asia	105
◆ Australasia	70



scale divisions 5%

HISTORY OF YELLOW FEVER 1.1

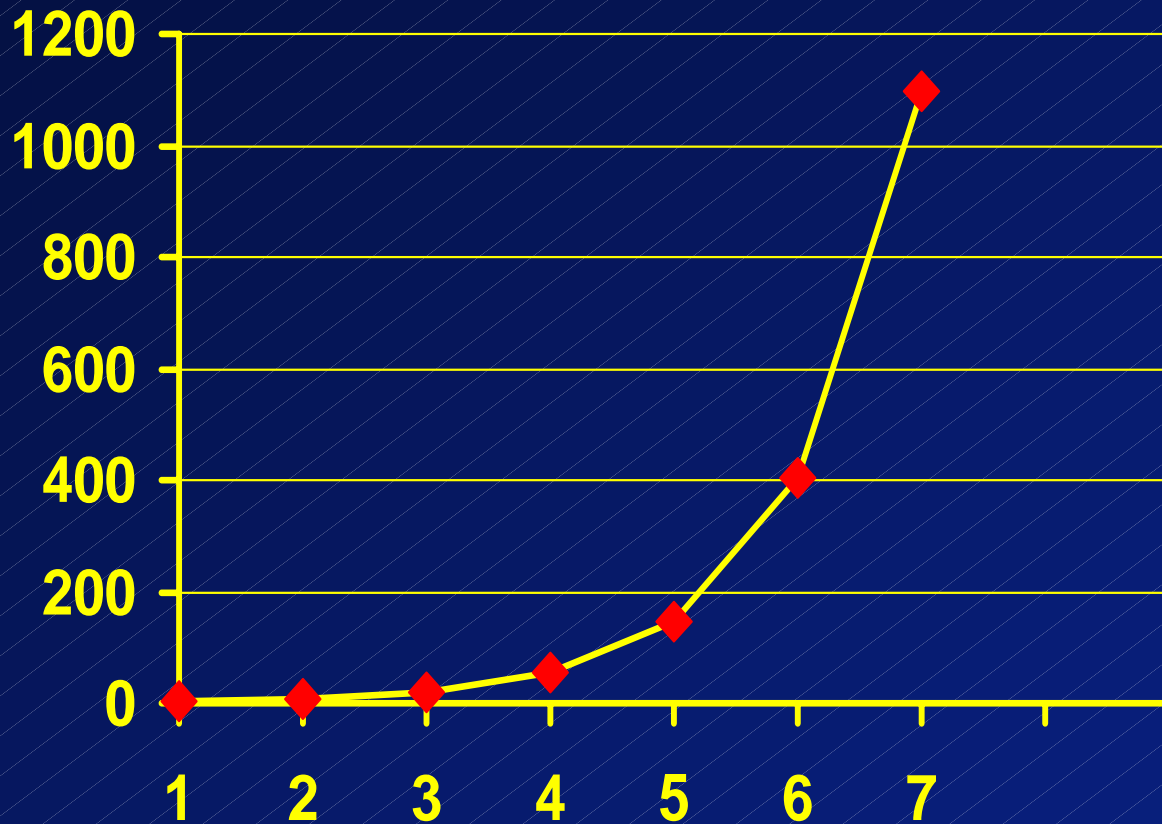
SOME SPECULATIONS

- ◆ 3,000-4,000 yrs ago YF virus emerged in the African forest as a distinct phylogenetic lineage
- ◆ Prototypical YF virus transmitted by *Aedes* (*Stegomyia*) mosquitoes among canopy dwelling primates, or perhaps prosimians





EXPONENTIAL GROWTH



$$dy/dx = ay$$

$$y = be^{ax}$$

HISTORY OF YELLOW FEVER 1.2

- ◆ 3,000-4,000 yrs ago YF virus emerged in the African forest as a distinct phylogenetic lineage
- ◆ Prototypical YF virus transmitted by *Aedes* (Stegomyia) mosquitoes among canopy dwelling primates
- ◆ A forest mosquito, *Ae.* (Stegomyia) *aegypti* adapted to human villages evolving toward a lighter colored, highly anthropophilic race
- ◆ YF virus became adapted to *Ae. aegypti* mosquitoes and became a village and later an urban problem
- ◆ Travel and transport, particularly the slave trade took the mosquito and the virus to the Americas and Europe

They are a Dieing on our right hand & on our Left, we have it oposit us, in fact, all around us, great are the number that are Calld to the grave. To see the hurst go by, is now so common, that we hardly take notice of it, in fine we live in the midst of death. When I se the Metropolis of the United States depopulated it is too distressing and afecting a sean for a person young in Life to bear.

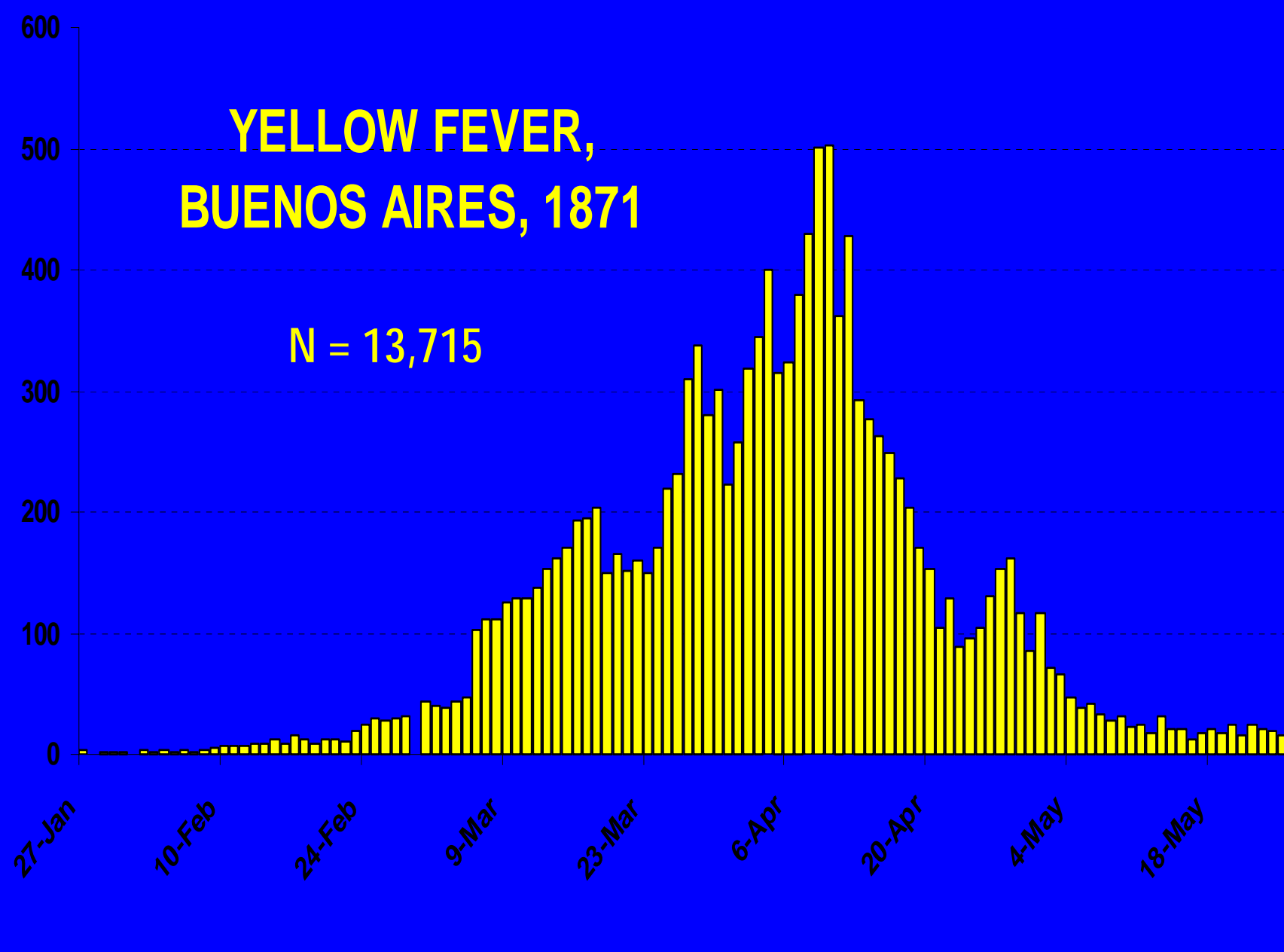
Isaac Heston, age 22 years, Philadelphia, 1793.

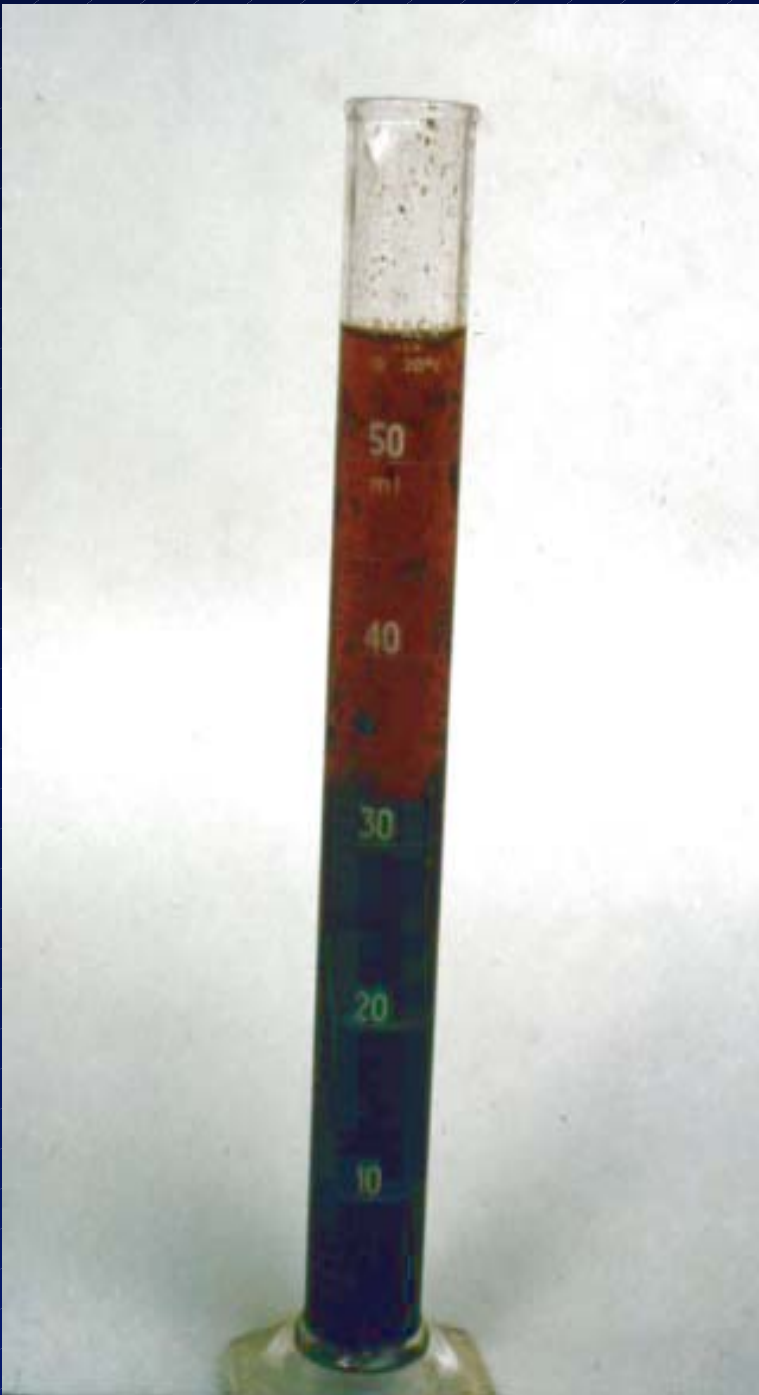
Ten days before his death from yellow fever.

YELLOW FEVER, BUENOS AIRES, 1871

N = 13,715

DEATHS/DAY





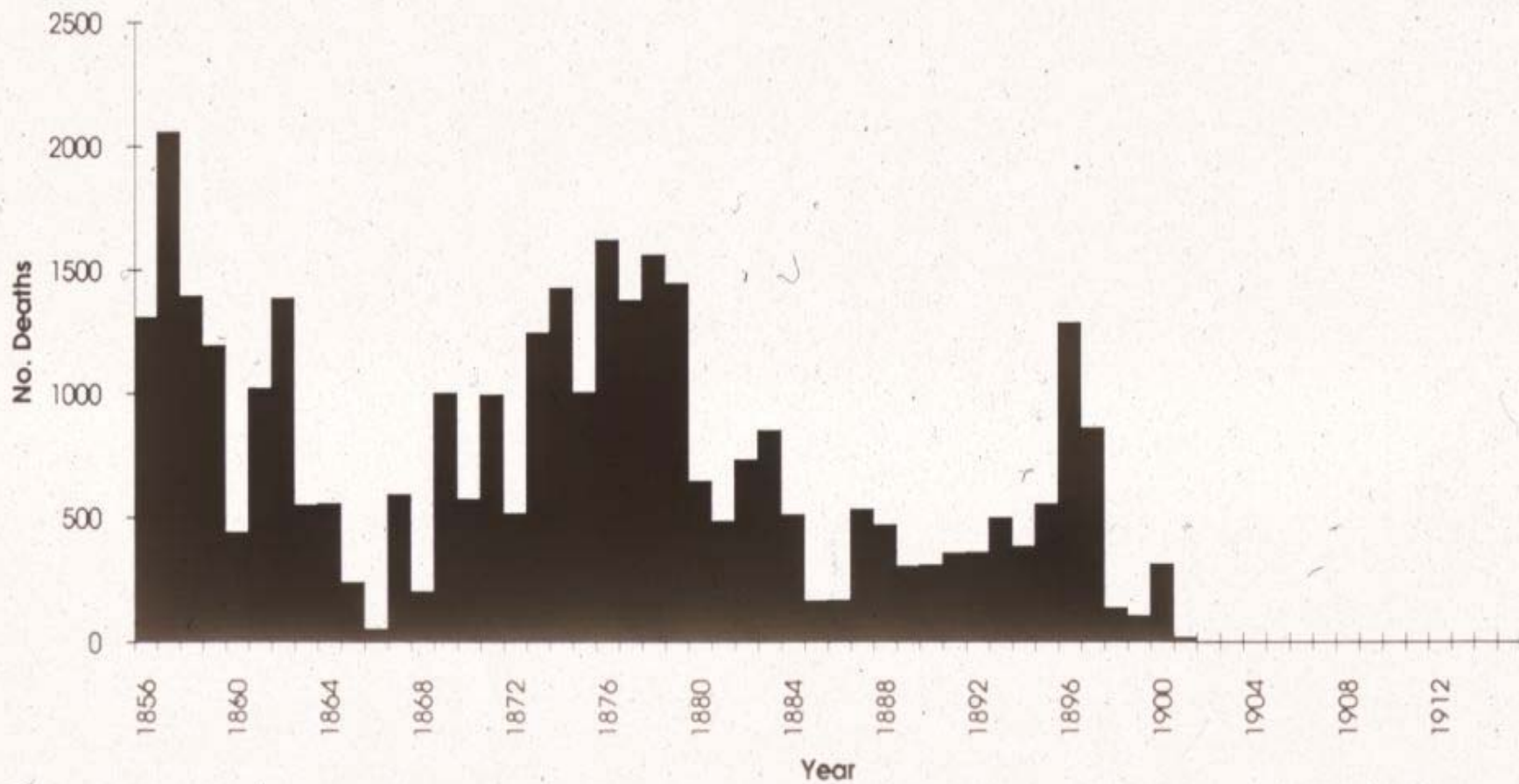
**VOMITO NEGRO
YELLOW FEVER**

HISTORY OF YELLOW FEVER 2

- ◆ 1648: first description of *xekik* epidemic in Yucatan
- ◆ YF virus adapts to new genus of mosquito and American monkeys in forest
- ◆ Major epidemics of YF in cities throughout Americas
- ◆ 1793: Philadelphia with 10% of 40,000 population
- ◆ Multiple introductions of YF to Europe (but never Asia)
- ◆ 1898: Spanish American war and Cuban occupation



Yellow Fever Deaths in Havana, 1856-1915



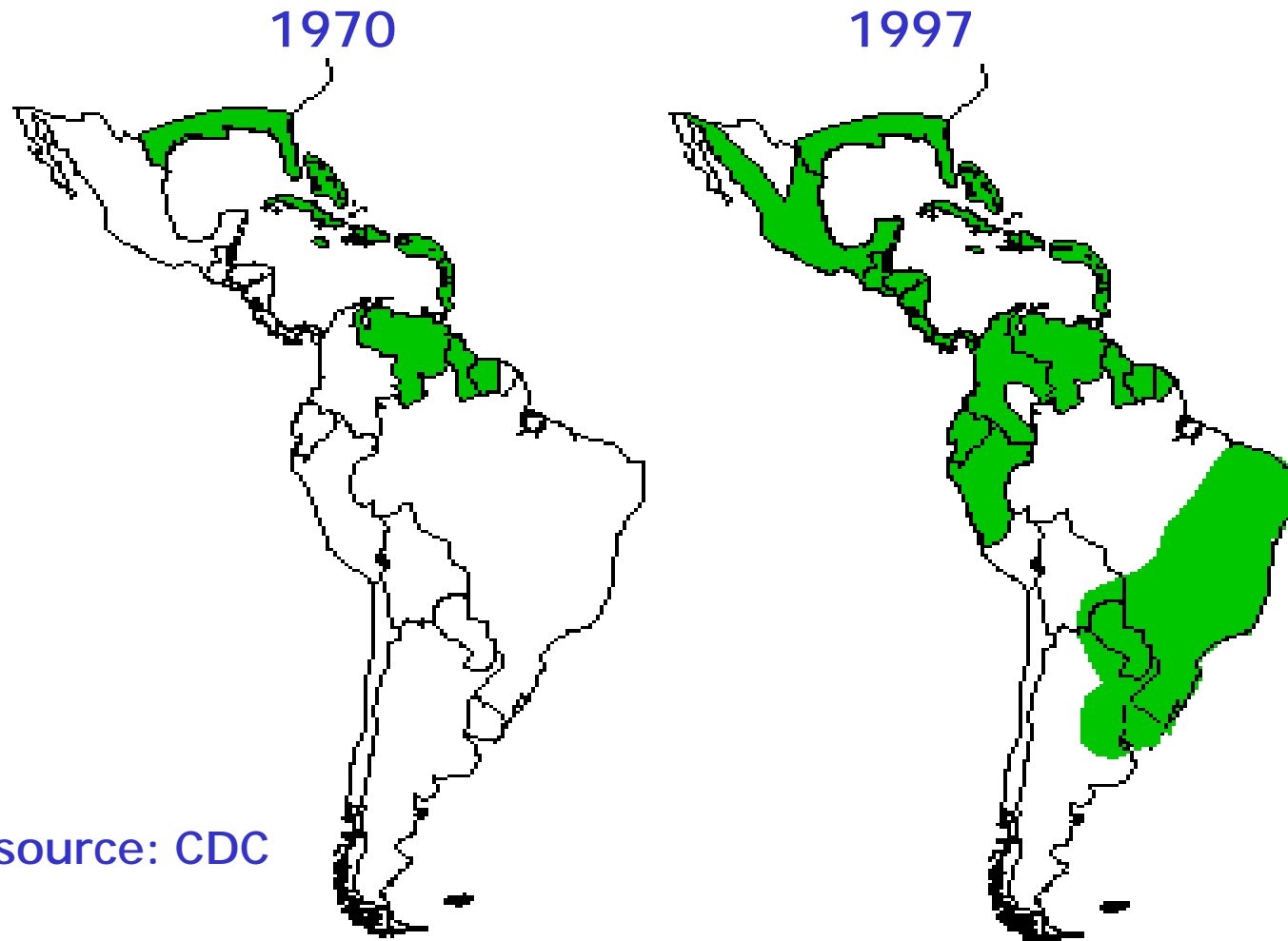


LAB INFECTIONS YF VIRUS: ROCKEFELLER EXPERIENCE

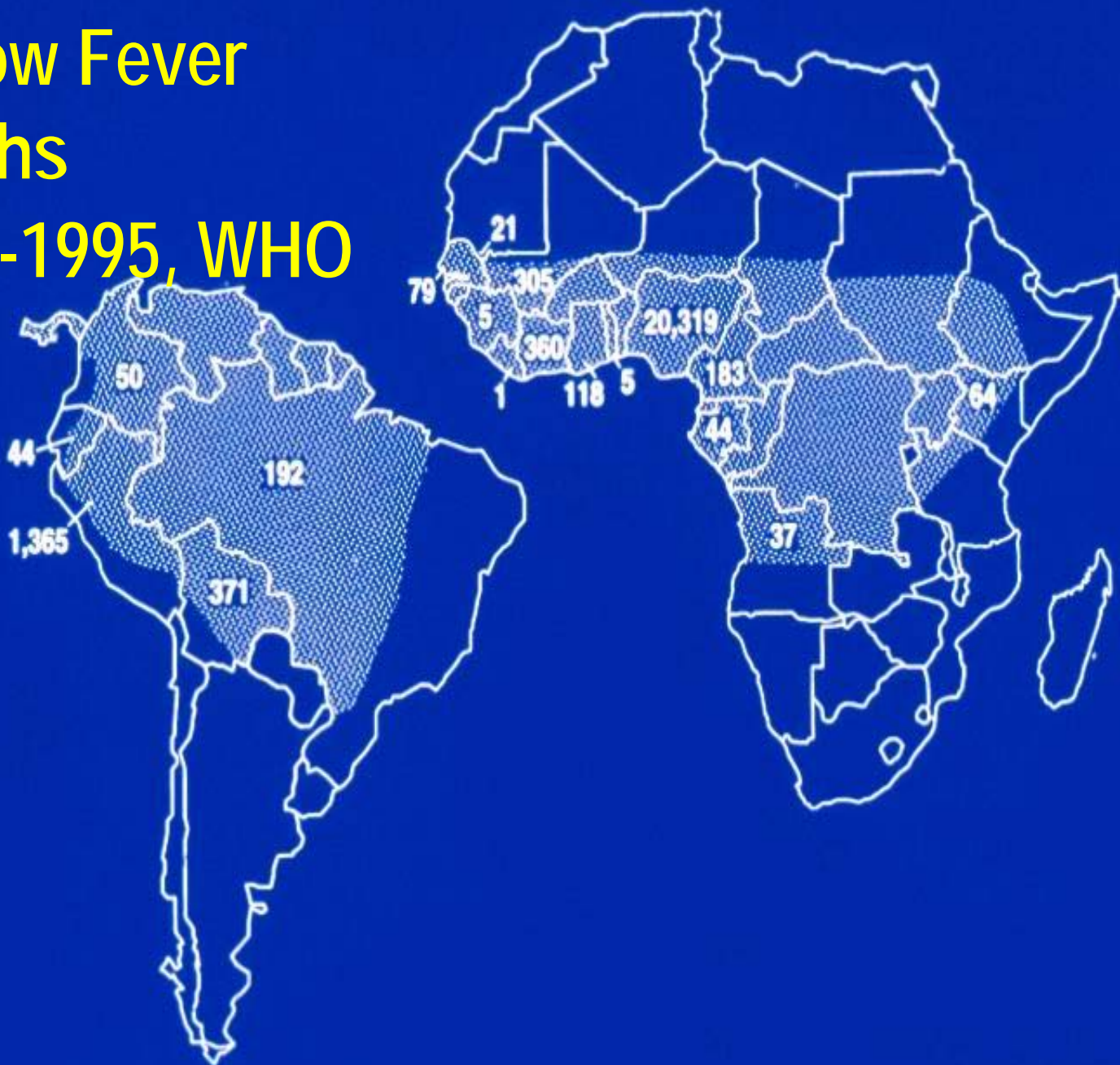
Vaccine	Workers	Cases	Dead
Before	55	16	5
After	189	0	0

After May 1931 the International Health Division used
17D yellow fever vaccine in their staff

Distribution of *Aedes aegypti* in the Americas 1970-1997



Yellow Fever Deaths 1986-1995, WHO





YELLOW FEVER
Santa Cruz, Bolivia



YELLOW FEVER, 2002

- ◆ 47yo petroleum engineer on 5 day fishing trip to Amazon; no YF vaccine, malaria prophylaxis, DEET, mosquito net.
- ◆ Mar 10 fever and severe headache. Wbc 3.3; platelets 158,000; SGOT 35; BUN 11
- ◆ Mar 12 develops nausea and vomiting and admitted with temp of 104⁰ F. Wbc 2.3; platelets 103,000; BUN 21
- ◆ Mar 13 photophobia. Wbc 1.4; BUN 34; SGOT 8598
- ◆ Mar 14 progression of liver failure, renal failure, shock
- ◆ Mar 16 death after intubation and extensive blood contamination of physician
- ◆ Mar 22 Sherif Zaki reports positive IHC and TDOH makes case public

ARBOVIRUS DISEASES THAT MOVE AROUND

DISEASE	VECTOR	AMPLIFIER
◆ Yellow fever	<i>Ae. aegypti</i>	Human
◆ Dengue	<i>Ae. aegypti</i>	Human
◆ Chikungunya	<i>Ae. aegypti</i>	Human
◆ West Nile	<i>Cx. pipiens</i>	Birds
◆ Venezuelan EE	Multiple	Horses
◆ Rift Valley fever	Multiple	Sheep, Cattle

*He that will not apply
new remedies must
expect new evils; for
time is the greatest
innovator.*

On innovations Essays
Sir Francis Bacon, 1561-1626

MOSQUITO-BORNE FLAVIVIRUS ENCEPHALITIS

Virus	Location	Emergence
St Louis	Americas	Sewers, waste water
Japanese	East Asia	Rice paddy, pigs
West Nile	Africa, ME	Irrigation, waste water
Murray V	Australasia	Irrigation

Single clade of antigenically related viruses transmitted between birds by *Culex* mosquitoes that breed in stagnant, high-organic water

“Mixing” of JE and WN in southwest Asia

Intro of JE into N Australia, role of pigs

Intro of WN into N America