Virology and tropical medicine: then, now, and whither

Thomas P. Monath M.D.

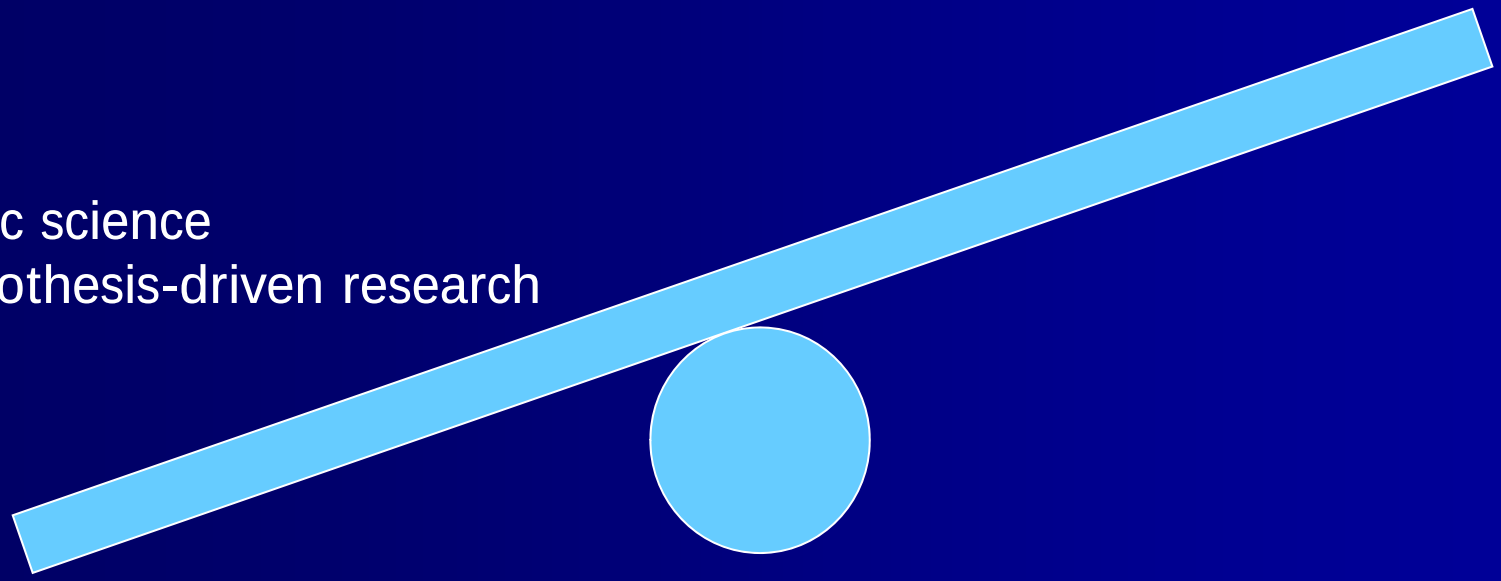
Topics

Arbovirology

- ‘Then’
  - Exploration of viruses in the Natural World
  - Pre-armed with knowledge
- ‘Now’
  - Exploration of virus structure and viruses in the world of the Cell
  - Smarter but more vulnerable in a changing world
- ‘Whither’
  - Striking a balance: Back to Basics

The Past

Exploration
Ecological and epidemiological studies
Virus isolation



Basic science
Hypothesis-driven research

Rockefeller Foundation
Virus Research

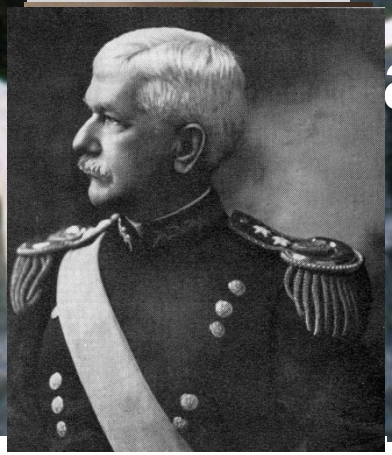
1913 RF Founded "Well-being of man…"

1916-18 1st Yellow Fever Commission (YF eradication, Gen. as)

2nd YF Commission, Africa

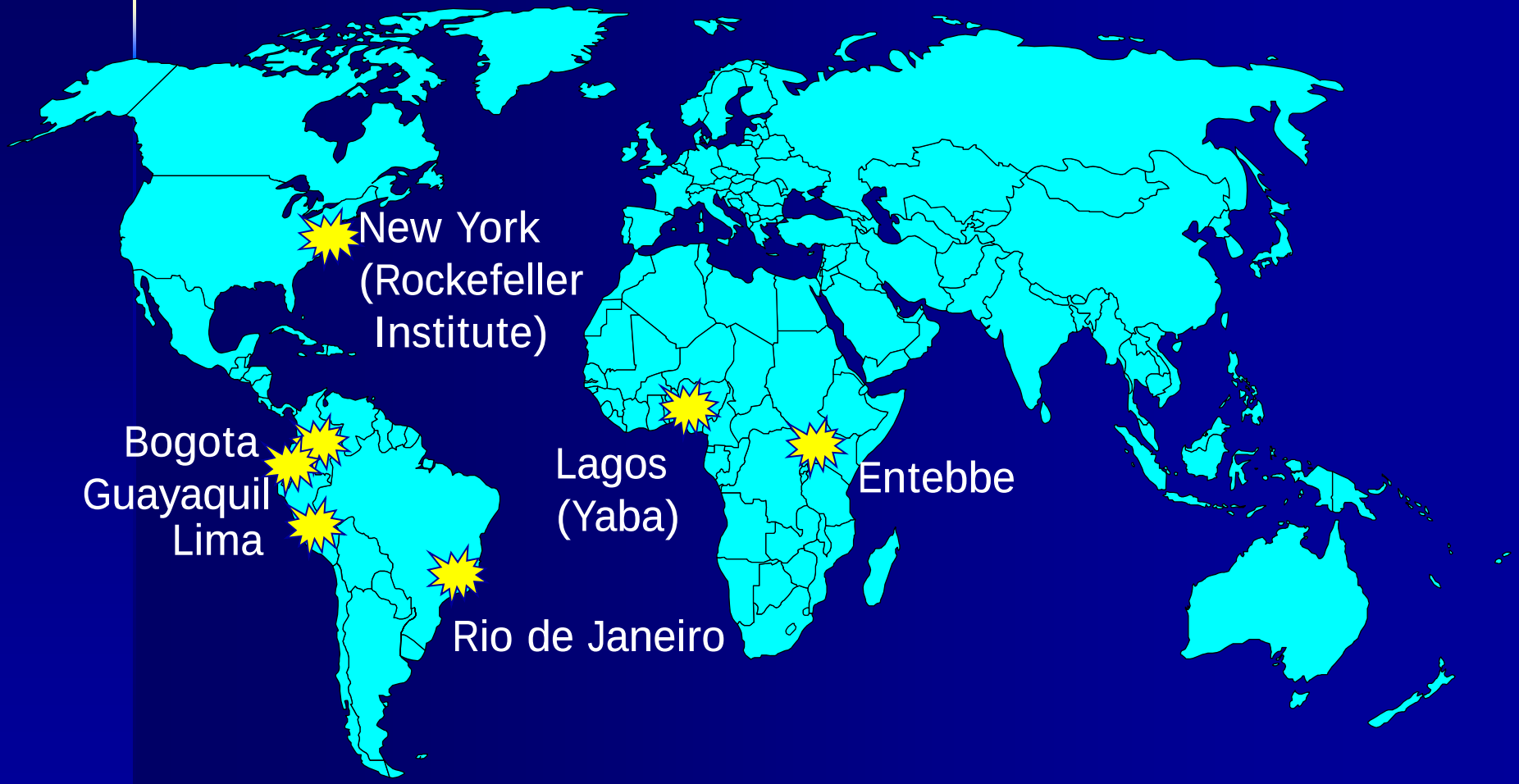
3rd 'West Africa YF Commission' (virus isolated 1927)

New York Virus Laboratory opened (Wilbur Sawyer)

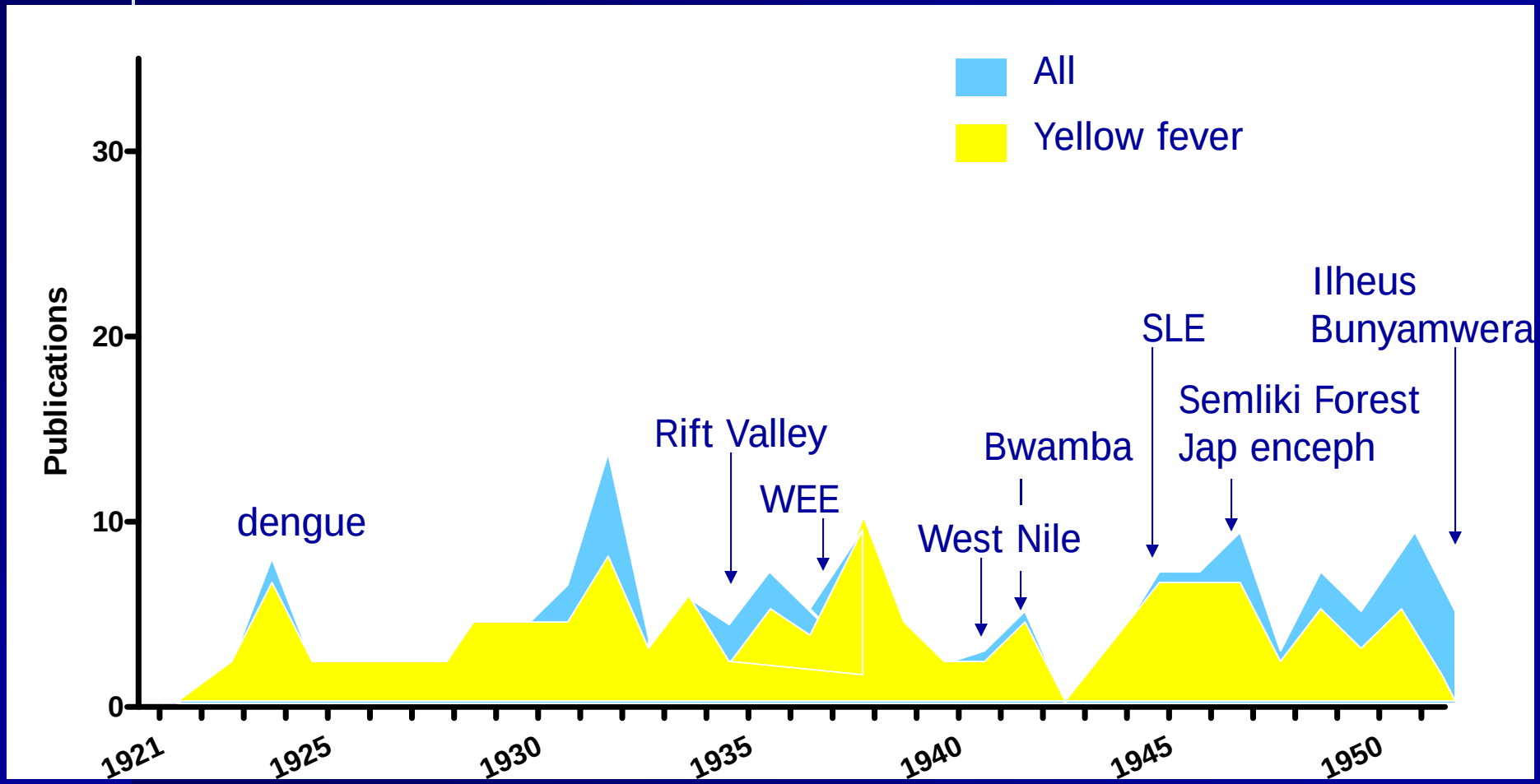


William C Gorgas
President 1909-10

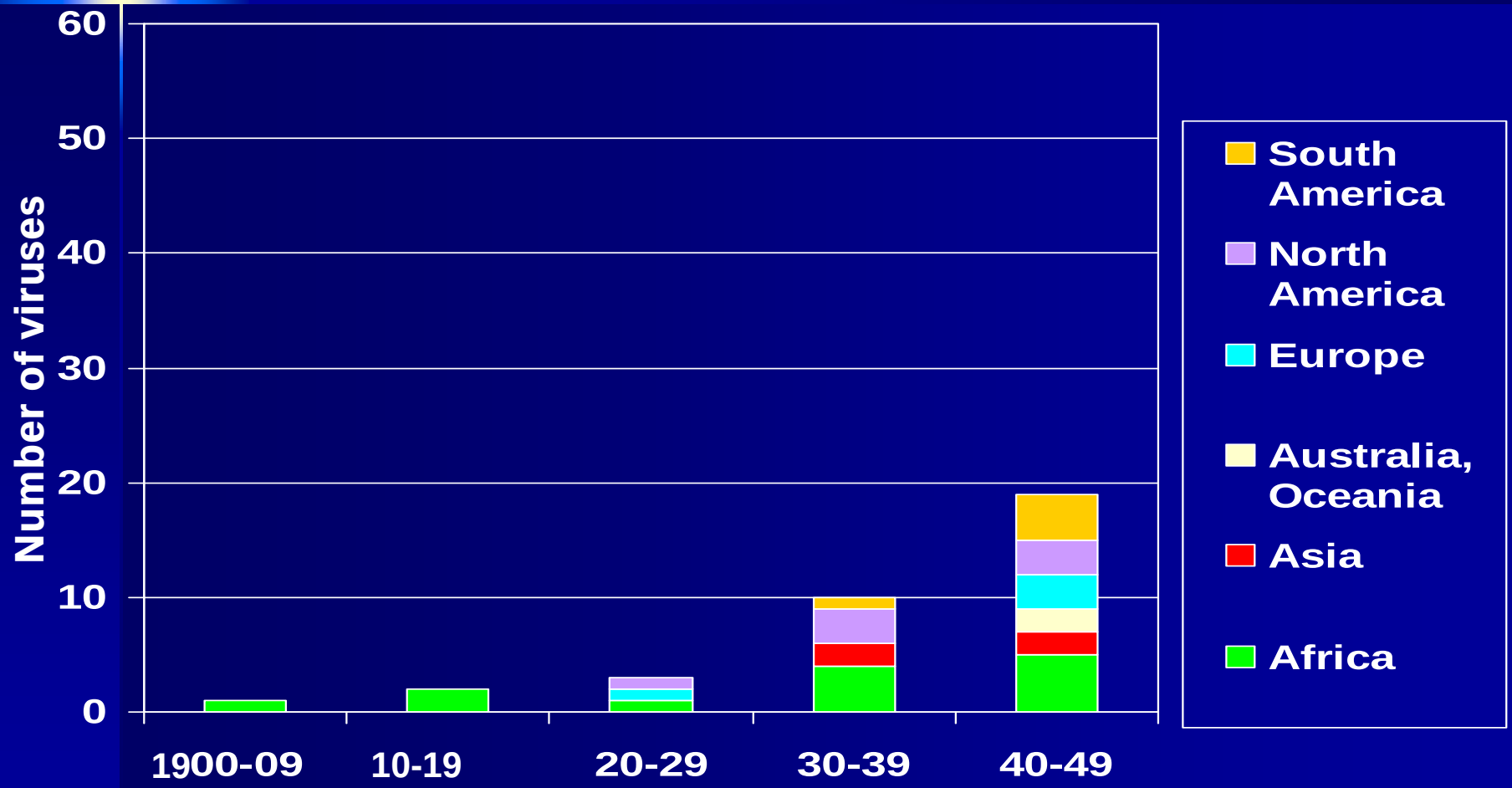
Rockefeller Foundation Yellow Fever Research 1918-45



Am J Trop Med
Arbovirus research—the early years
Dominated by YF



Arboviruses by initial year of isolation and continent, 1900-49



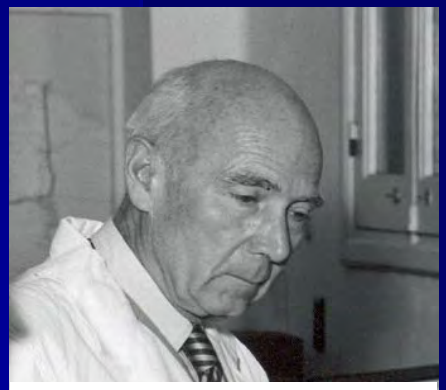
Rockefeller Foundation
Virus Research

1939-45 YF programs wind down, overseas staff repatriated

1935-45 Evolution of thought regarding virus ecology (Hammon & Reeves); new techniques for virus classification (Casals)

1945 Richard Moreland Taylor becomes Director, RF NY Laboratories. Staff directed to ‘sort out’ 30-odd ‘new’ viruses recovered during YF investigations

Taylor seeks advice of Thomas Rivers Jr and Joe Smadel on direction of future Rockefeller virus research



RM Taylor

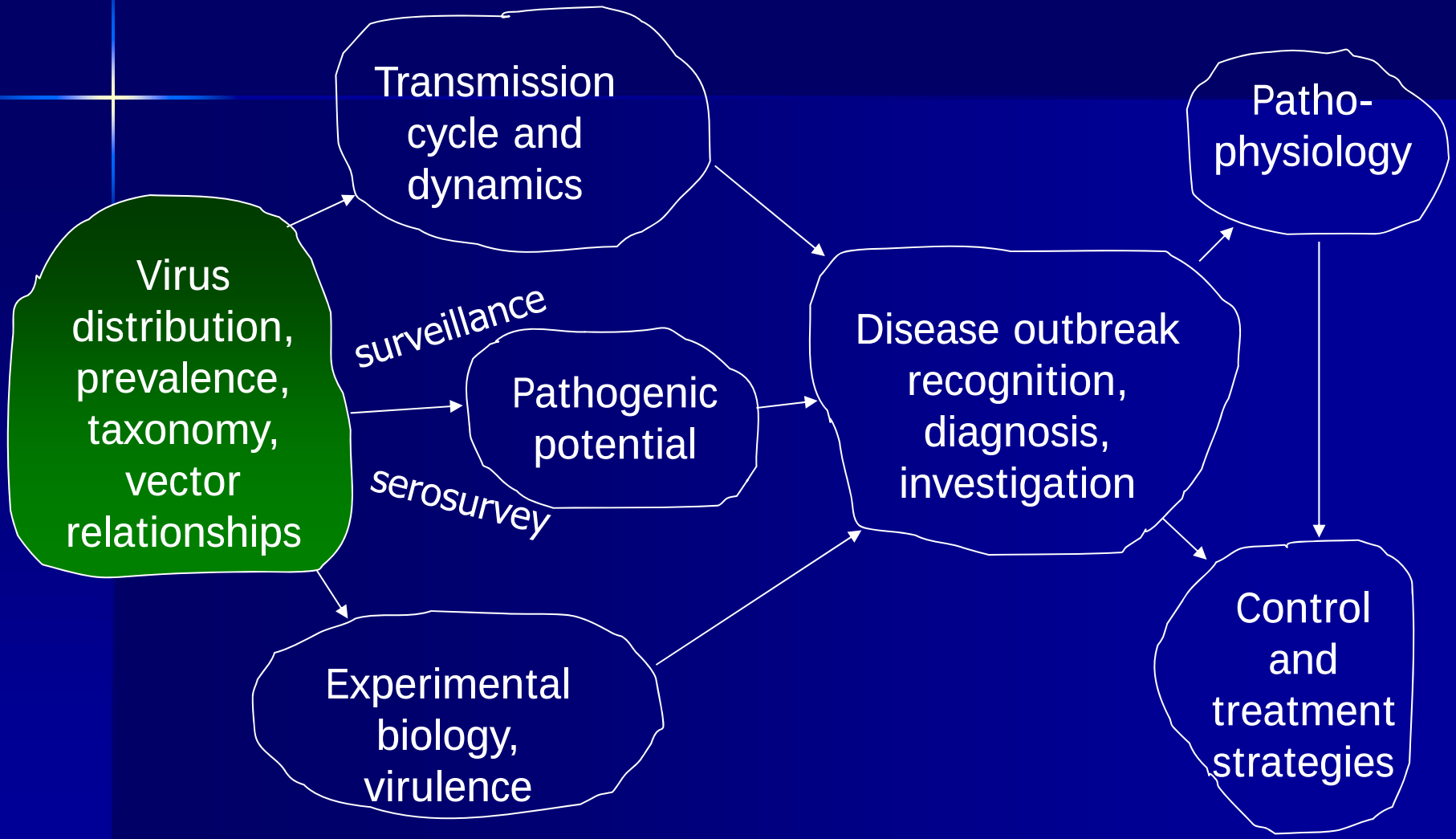
"...the liaison between the field and the laboratory should be consistent and effective."

Thomas Milton Rivers
Rockefeller Institute

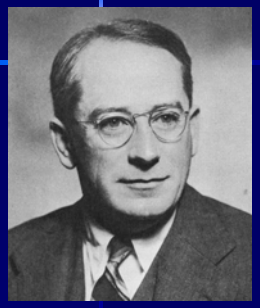
"....the Far East, particularly India, as well as ....Africa, may be important areas"... to investigate

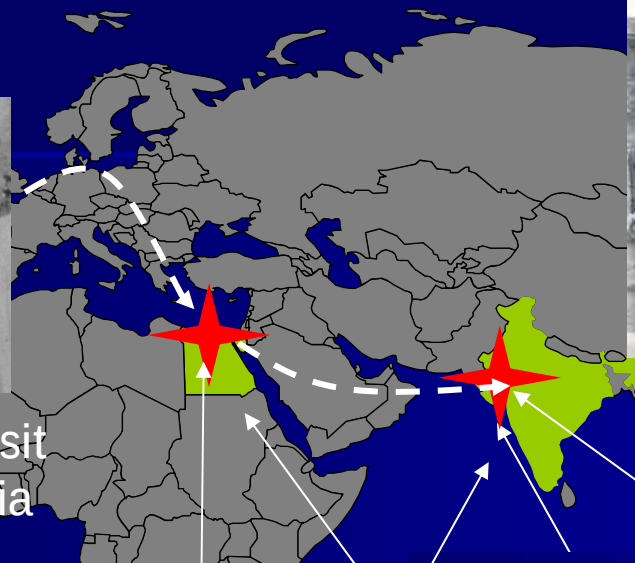
Joseph E Smadel
Formerly RF IHD; US Army

A model for arbovirus research



Rockefeller Foundation
Virus Research





Poona lab

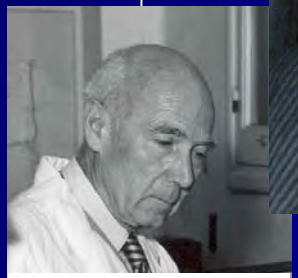
1951 Smith and Theiler visit NAMRU-3 (Cairo) and India

Agreement with US Navy (NAMRU-3) to conduct joint studies, share expenses

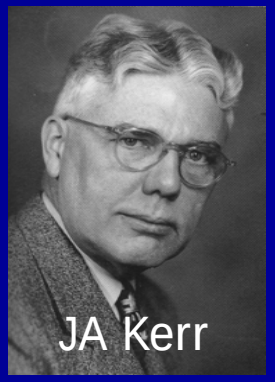
1952 Taylor spearheads Cairo effort; Theiler becomes Director NYVL

Telford H Work
President 1970

H Johnson



RM Taylor

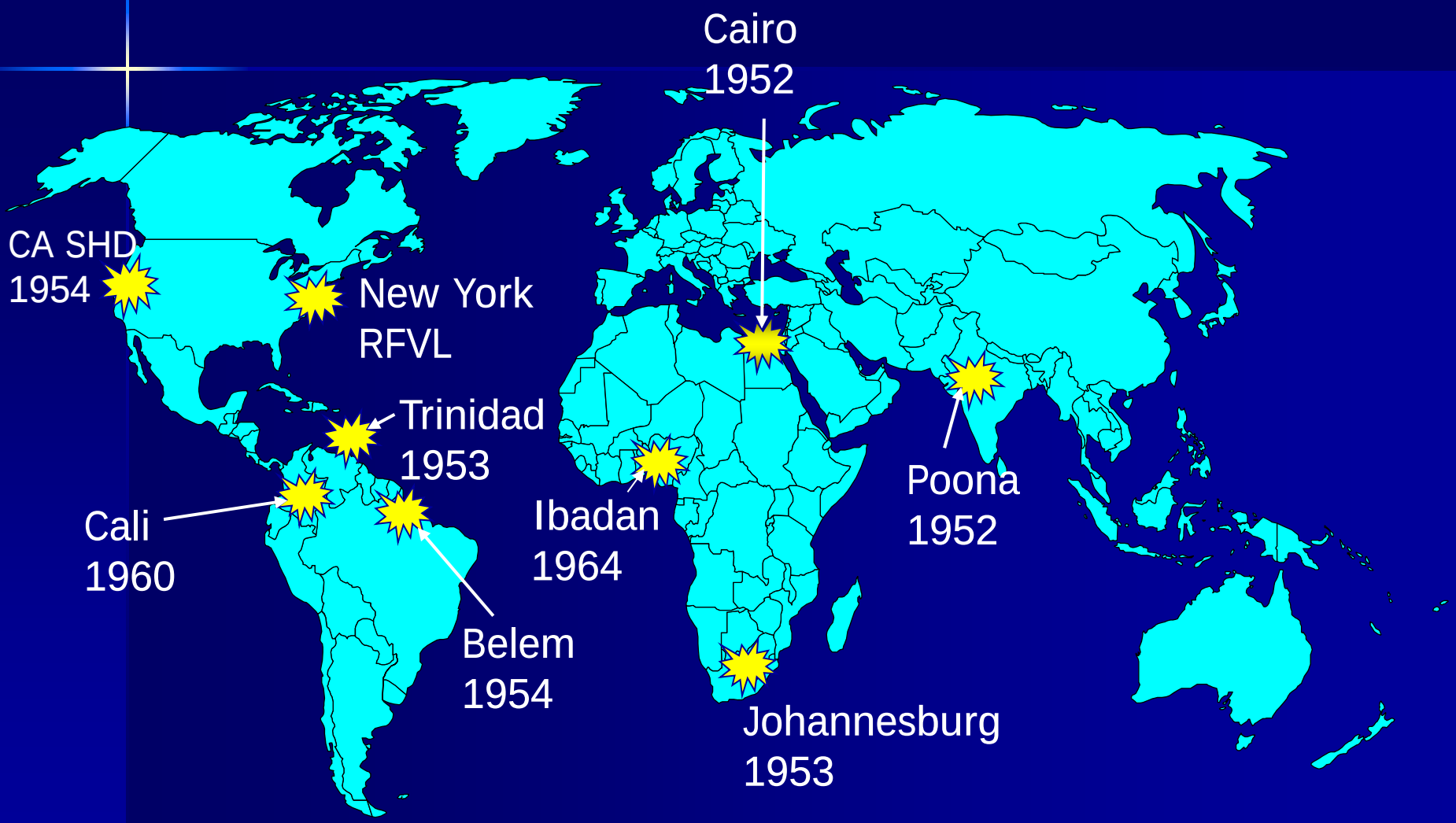


JA Kerr

Kerr and
n
a lab

Rockefeller Foundation Virus Program

Period: 1951-71 Cost: $30 million

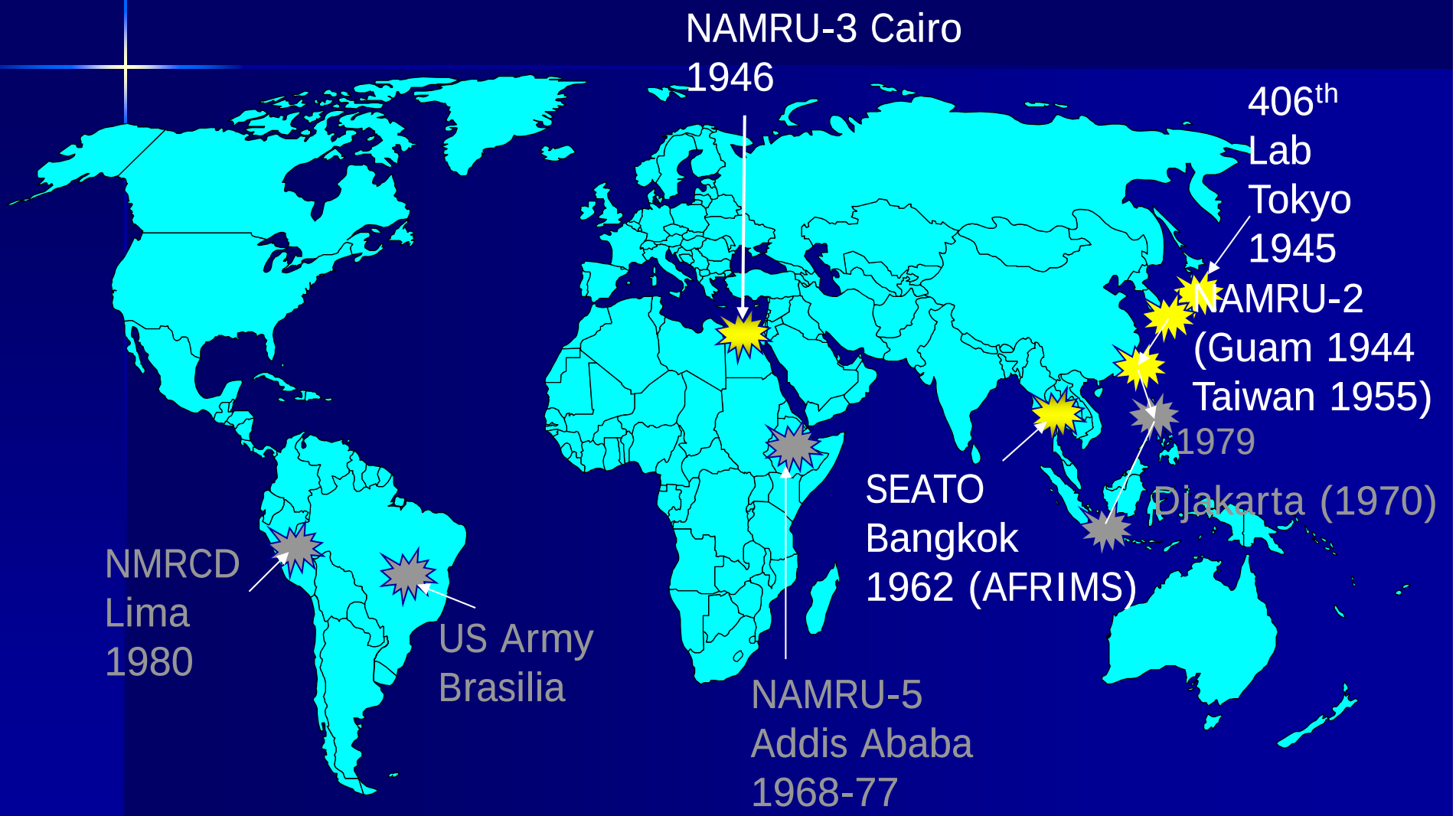


Inst Evandro Chagas-Rockefeller Virus Laboratory, Belem

Ottis and Calista Causey

- Establishe
- 50 distinct
- Routine us on
- Sentinel m
- Concept o odcutters Trans-Ama
- Forest car
- Establishe y (1964)
- First isolat
- Rabies-rel

Military Overseas Laboratories



406th Medical Laboratory Tokyo

ECOLOGIC STUDIES OF JAPANESE ENCEPHALITIS VIRUS IN JAPAN

Scherer, W.F, et al

PARTS I - IX

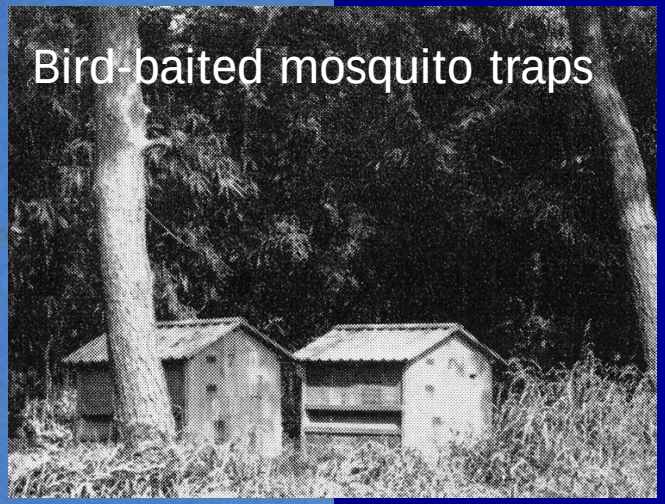
Department of Virus and Rickettsial Diseases,
406th Medical General Laboratory,
U.S. Army, Japan

Reprinted from the American Journal of Tropical Medicine and Hygiene, Vol. 8, No. 6, November 1959

pp. 644–722.

W Scherer
President 1981

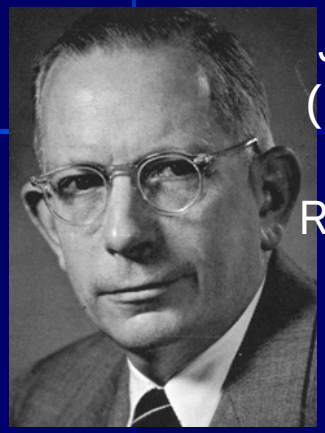
E Buescher



Bird-baited mosquito traps

HE McLure

NIH Overseas Research Units

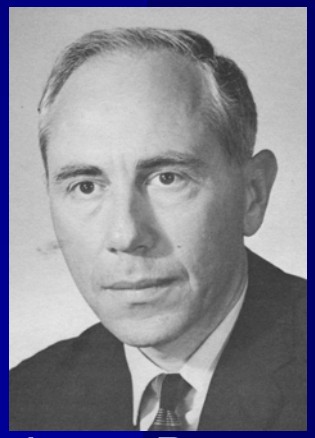


Joseph B Smadel
(1906-1963) Chief
Virology and
Rickettsiology, NIH

Middle America Research Unit (MARU)

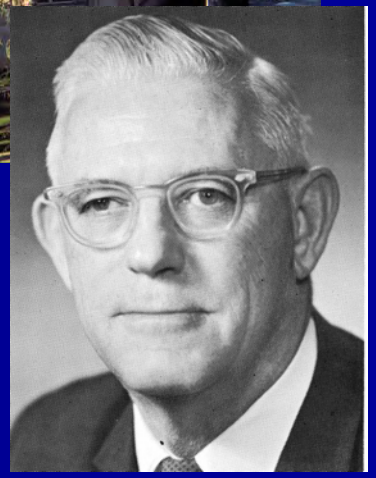
1962
Pacific
Research
Section

1957
MARU



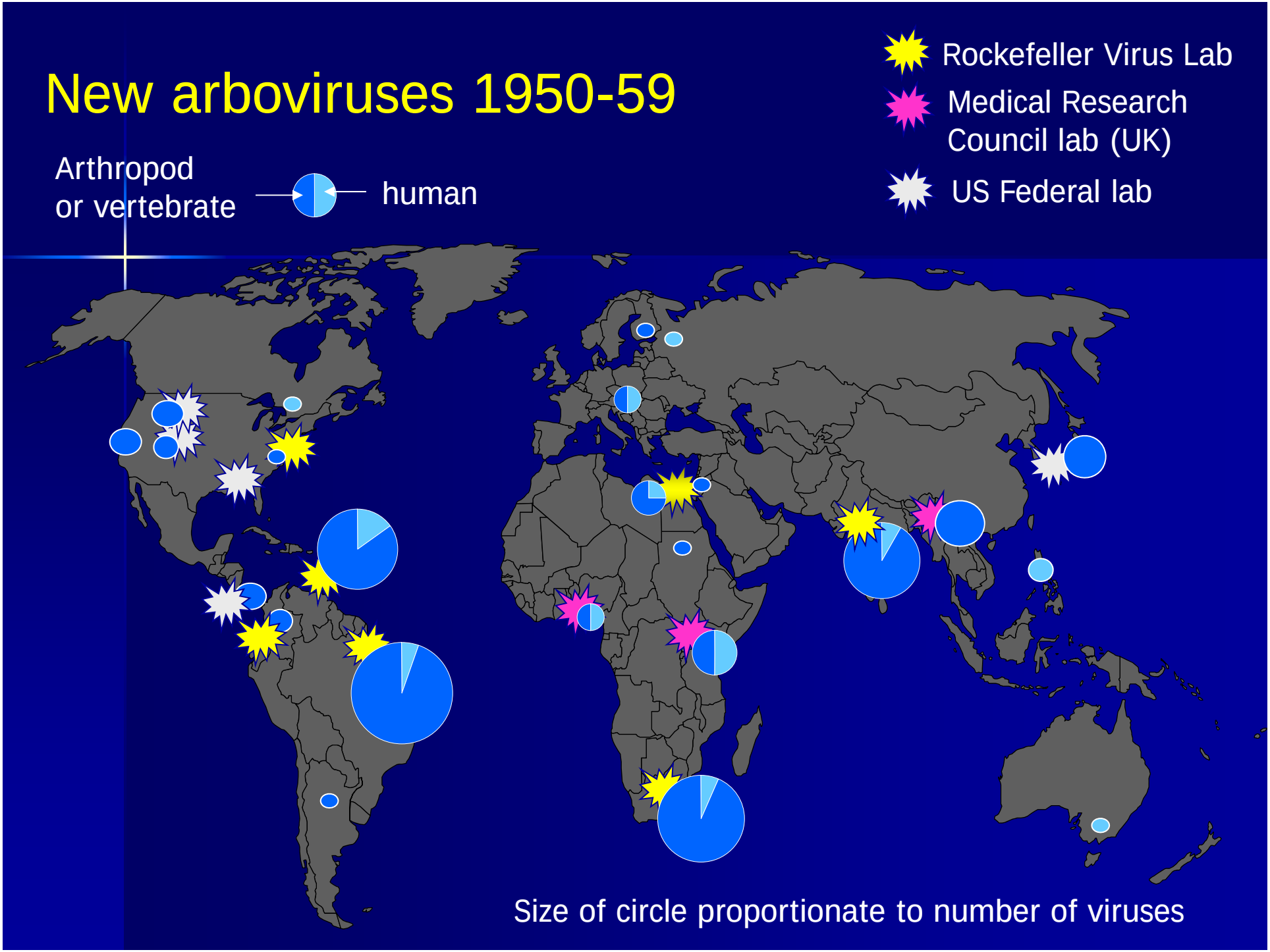
Leon Rosen
President 1976

Alexis Shelokov
Director 1957-61

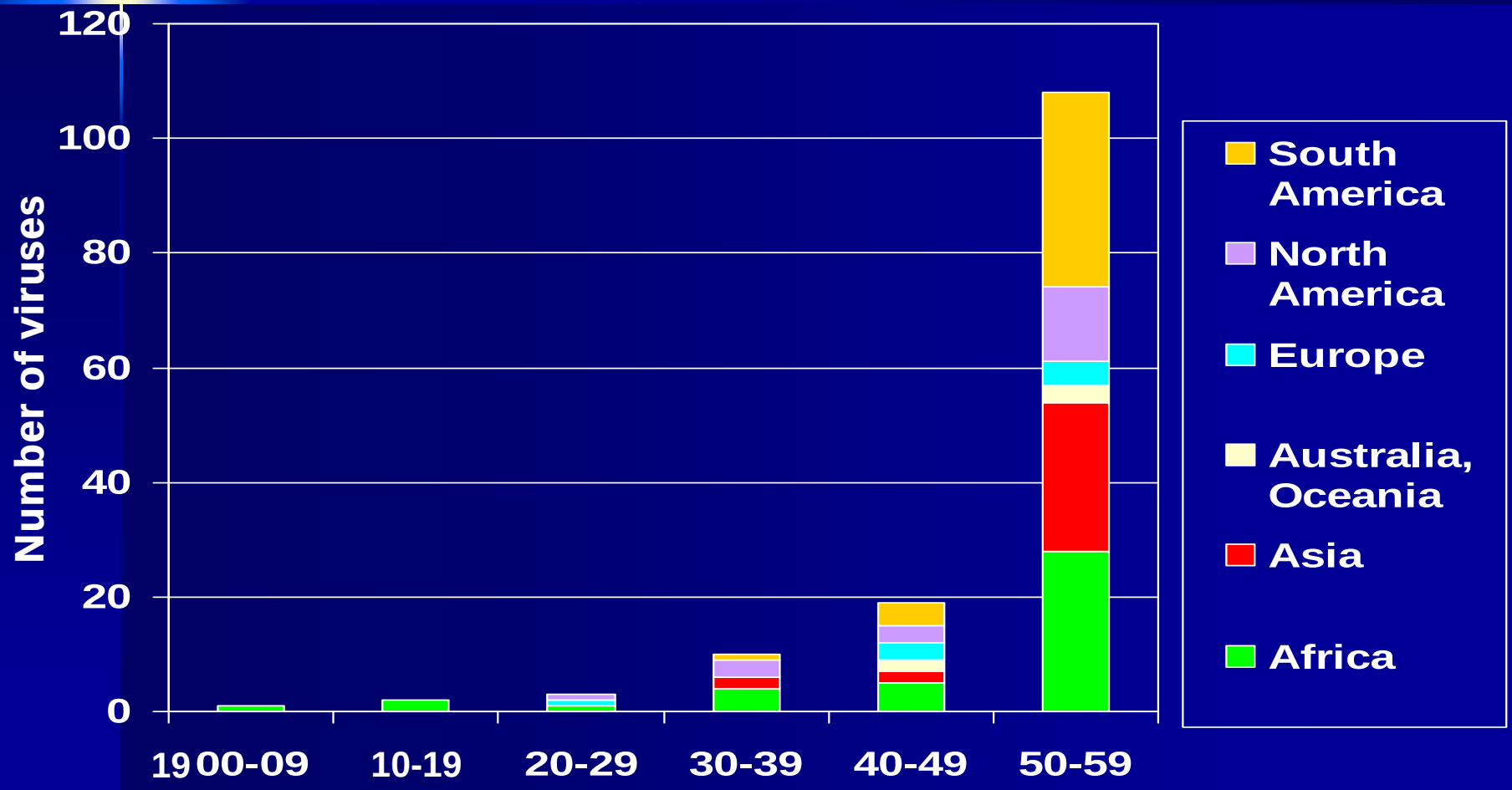


Henry Beye
Director 1961-64

New arboviruses 1950-59



Arboviruses by initial year of isolation and continent



Serological classification 1950s

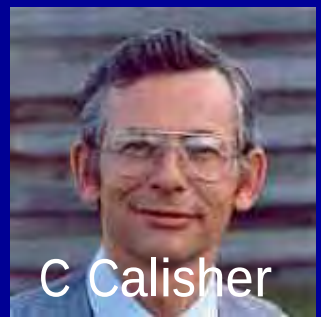
Jordi Casals-Ariet 1911-2004

- Antigenic groupings defined by HI, CF, neutralization
- e.g., Group A, B, C viruses

J Casals

D Clarke

Robert E Shope
President 1980



C Calisher

TECHNIQUES FOR HEMAGGLUTINATION AND HEMAGGLUTINATION-INHIBITION WITH ARTHROPOD-BORNE VIRUSES

D. H. CLARKE AND J. CASALS

The Rockefeller Foundation Virus Laboratories, New York, N. Y.

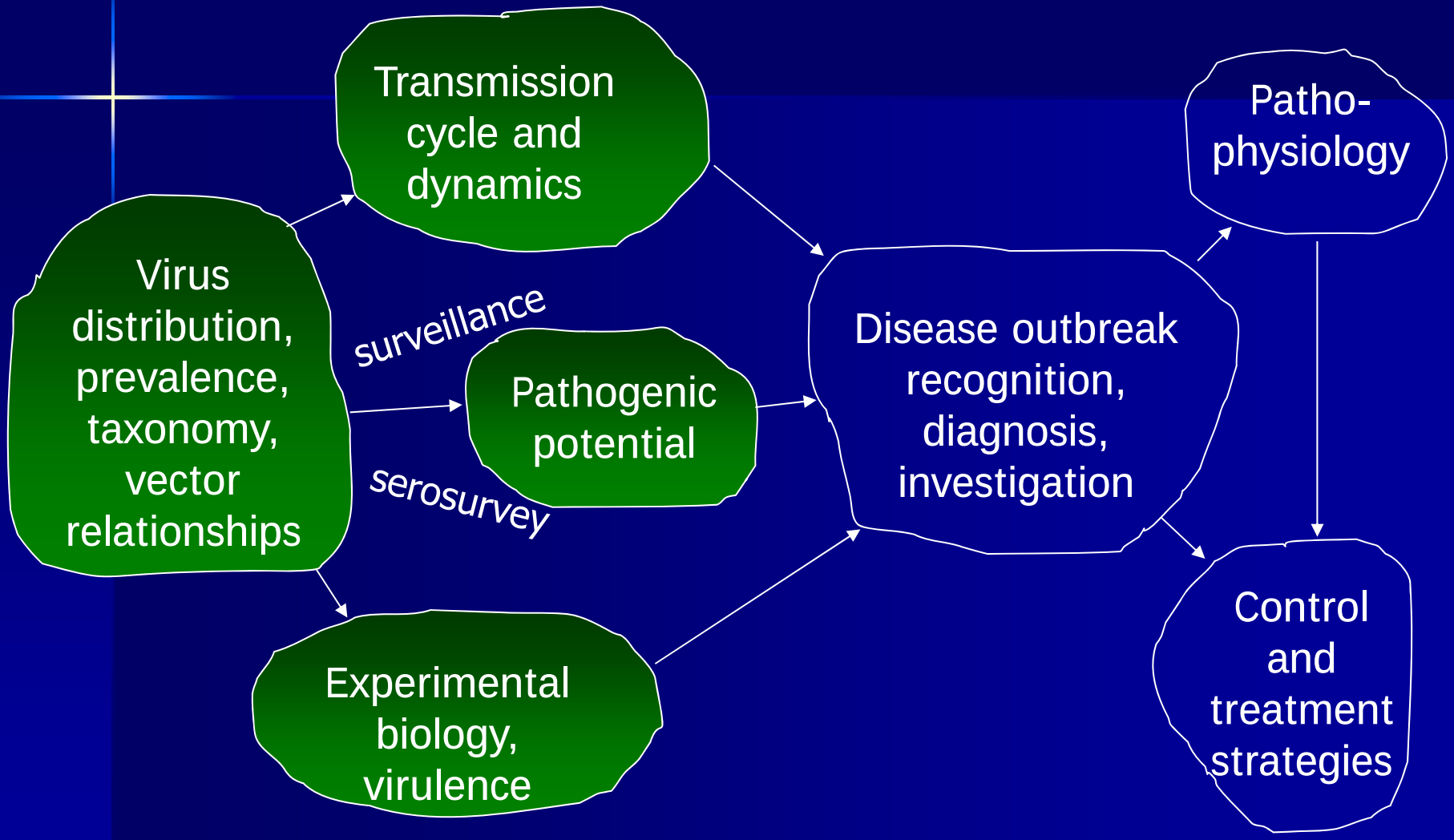
ANTIGENIC CLASSIFICATION OF ARTHROPOD-BORNE VIRUSES

Proc. 6th Int. Congr. Trop. Med. and Malar., 5: 34-47, 1959

JORDI CASALS

The Rockefeller Foundation Virus Laboratories, New York, N.Y.

A model for arbovirus research



Origins of ACAV

- Three precedent meetings to plan the international investigation of arthropod-borne viruses
- First meeting: September 19, 1958 (6th ICTM, Lisbon)
  - 50 attendees concerned with arthropod-borne viruses
  - Recommendations:
    - Designation of reference labs
    - Provision of reagents
    - Coordination of work among field laboratories

Meeting of group interested in arthropod-borne viruses ICTM, Lisbon, 1958

As the day ended, someone suggested the meeting should select a name for this field of study and for the specific viruses that were included. I thought, "Oh boy, now we will really have some turmoil." Then, someone got the floor and I was stunned to hear him say, "Bill, tell us about the derivation of terms used for these viruses in your laboratory." I did and ended with, "Arboviruses." Immediately someone made a motion that this meeting and the WHO should accept that name and make it official worldwide. I held my breath and saw a hand wave. It was Dr. Anatol Smirodintsev from Russia. I thought, "Here we go—Russia vs. the U.S.A." Anatol said, "The proposed name 'Arboviruses' has nothing to do with trees but 'arbor' does." I said, "What if we take out the second 'r' and call it 'Arbovirus'?" He said, "I like it. Accept that change and move for its acceptance by this group and after it's approved, I also move that we terminate this meeting." It was approved with no further discussion.

Reeves WC J Vector Ecol 2001;*26*:1-6

Origins of ACAV

- Second meeting: November 17-19, 1958 (WHO, Geneva)
  - Recommendations formalized
  - Expectation of strong US Government support
- Third meeting: March 12, 1959 (Washington DC)
  - Program objectives presented to Commission on Viral Infections (CVI), AFEB
  - W. McD. Hammon (Chair, CVI) recommends

    "That the CVI inquire from the RF whether it might be interested in calling a gathering to consider the ... coordination... of American groups working on arthropod-borne viruses..."

Gould House meeting
October 11-12, 1959 Ardsley-on Hudson

- Convened, chaired by Robert Morison

  Director of Medical & Natural Sciences,
  Rockefeller Foundation

R S Morison
1906-1986

Gould House

Meeting on Arthropod-borne Viruses

Gould House, Ardsley-on-Hudson, New York

October 11-12, 1959

- Exchange of information
- Serological reagents
- Central reference laboratory
- Cooperation, coordination of investigators and agencies
- Ecological problems of viruses

Sunday, Oct

9 a.m

2 p.

[illegible] considerations; a. What should be expected of field laboratories? b. Methods of helping them to obtain necessary sera for groupings? - Discussion leader: Dr. Edward L. Buescher.

Monday, October 12

9 a.m. Chairman: Dr. William C. Reeves

What should be expected of central reference laboratories? Discussion leader: Dr. Max Theiler.

Personnel and training - Discussion leader: Dr. W. McD. Hammon

Gould House meeting
October 11-12, 1959 Ardsley-on Hudson
18 scientists and administrators

- Exchange of information:
  - Subcommittee on Exchange of Information
  - Taylor (Chair), Scherer, Work
  - Information Exchange and Arbovirus Catalogue

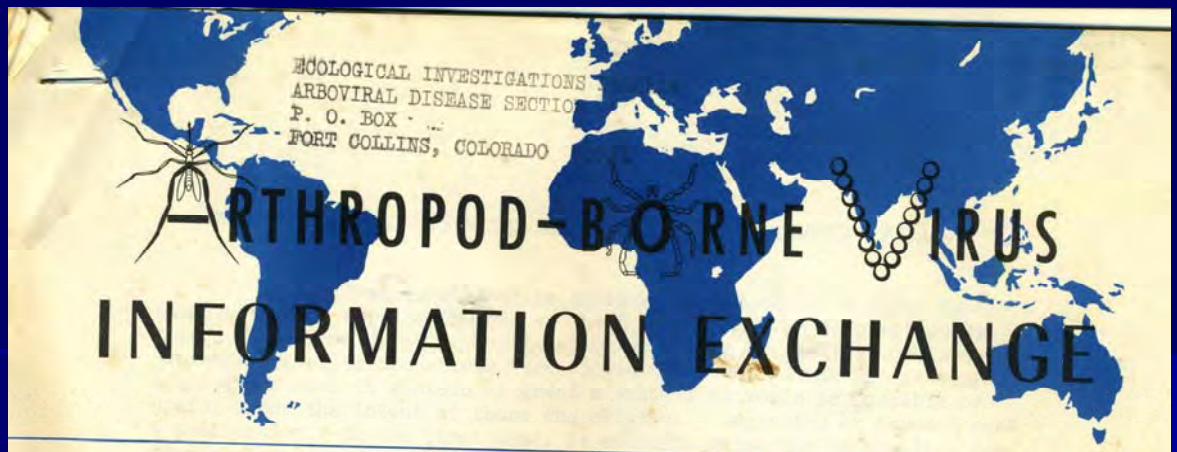
Richard M Taylor

William F Scherer

Telford H Work

First edition of the Info Exchange

April, 1960



Number One

April 1960

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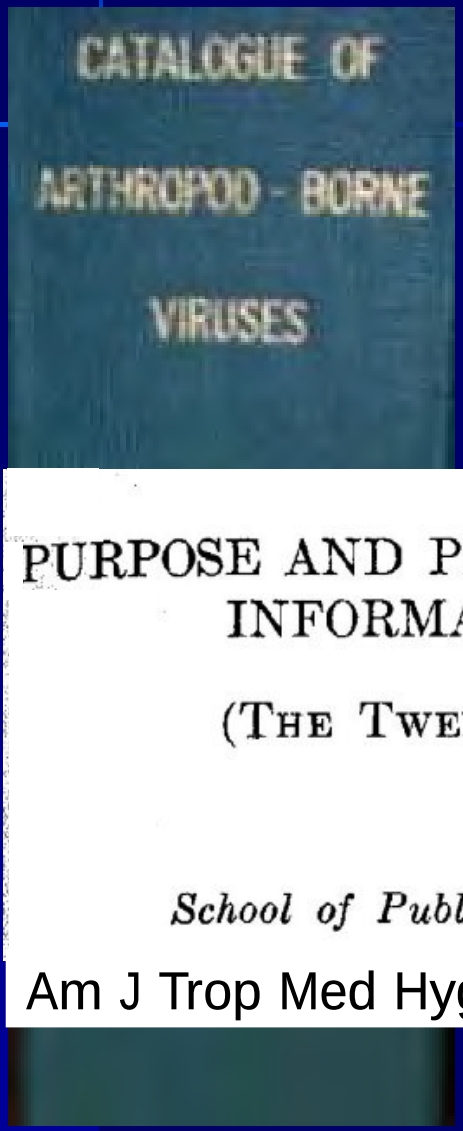
First Arbovirus Catalogue 1960



PURPOSE AND PROGRESS IN CATALOGUING AND EXCHANGING INFORMATION ON ARTHROPOD-BORNE VIRUSES

(The Twenty-sixth Charles Franklin Craig Lecture)

R. M. TAYLOR

School of Public Health, University of California, Berkeley, California

Am J Trop Med Hyg 1962;11:167-174

First RM Taylor Award, ACAV 1966

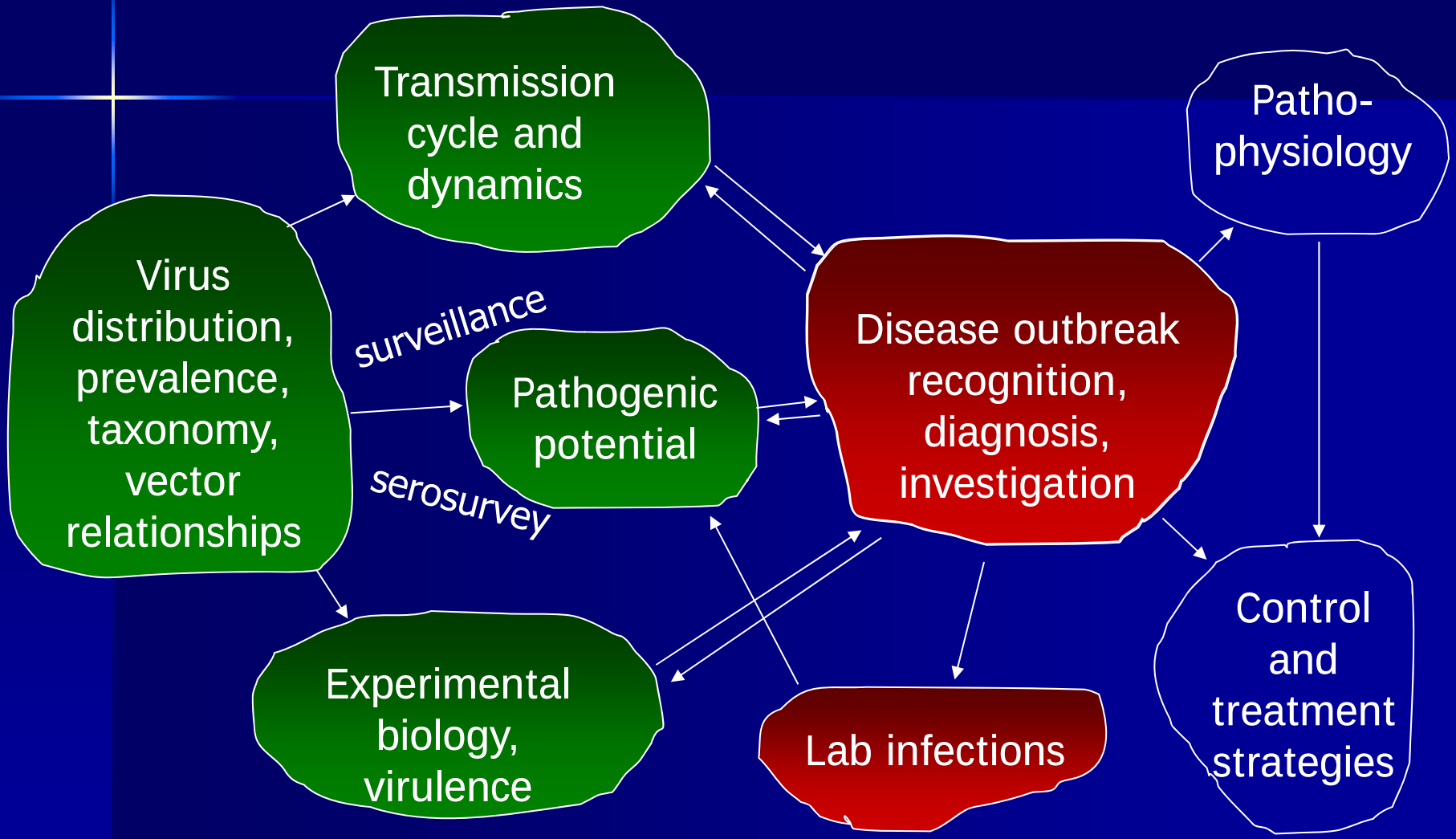
'For outstanding contributions to arbovirology throughout his or her career'

Richard M. Taylor Award Recipients

★ **Presidents of ASTMH**

- Richard M Taylor, 1966
- Jordi Casals, 1968
- ★ W McD Hammon, 1970
- ★ William C Reeves, 1973
- Roy W Chamberlain, 1975
- Pedro Galindo, 1977
- Wilbur Downs, 1979
- Ottis and Calista Causey, 1980
- ★ Telford Work, 1981
- Thomas H G Aitken, 1984
- Harry Hoogstral, 1984
- ★ Karl M Johnson, 1987
- ★ Robert E Shope, 1987
- James Hardy, 1990
- ★ Thomas Monath, 1994
- ★ Scott Halstead, 1999
- ★ Leon Rosen, 2000
- ★ Philip K Russell, 2000
- Frederick A. Murphy, 2002

A model for arbovirus research



Robert Hanson

Subcommittee on Arbovirus Laboratory Safety (established 1964)

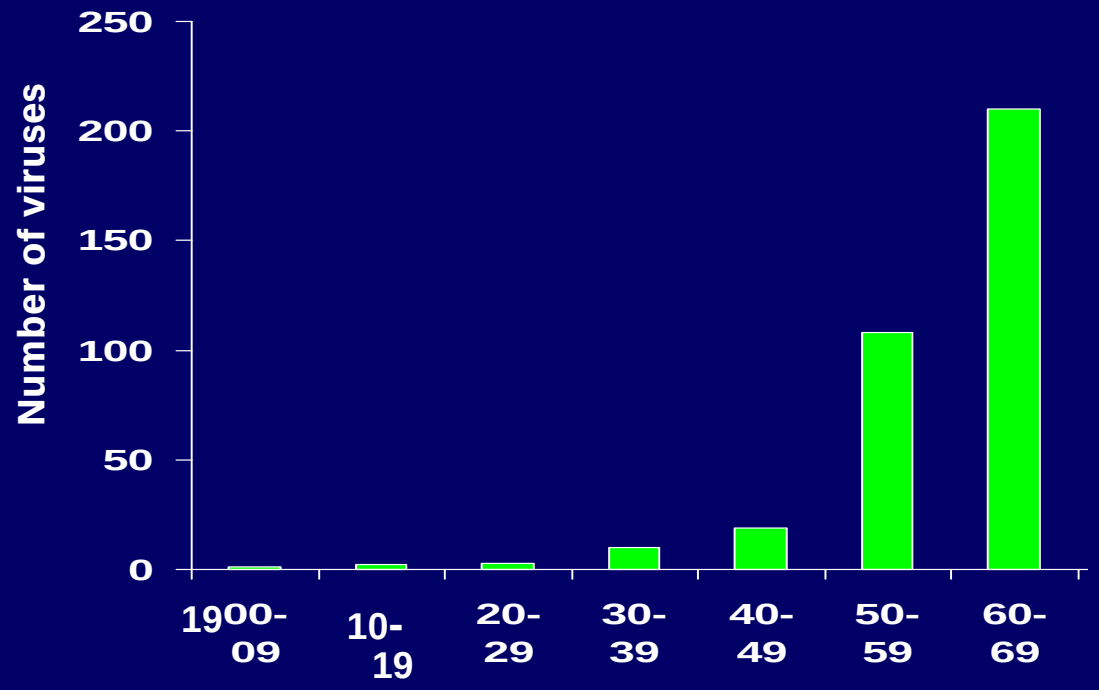
ACAV Meeting, Nov 4 1965, New Orleans

c. Laboratory Infections. (Dr. Hanson) A letter requesting information on viruses used, numbers of workers involved, immunization status, etc., was sent to most of the 180 recipients of the Information Exchange. Thirty per cent have now responded.

Last Fall when we found VE virus in materials collected in Mexico and I had a laboratory infection, I became very interested in the subject of VE laboratory infections and wanted immediately to inquire about the experiences of others with this virus. However, when a Subcommittee on Laboratory

Bill Scherer

Arboviruses by year of isolation



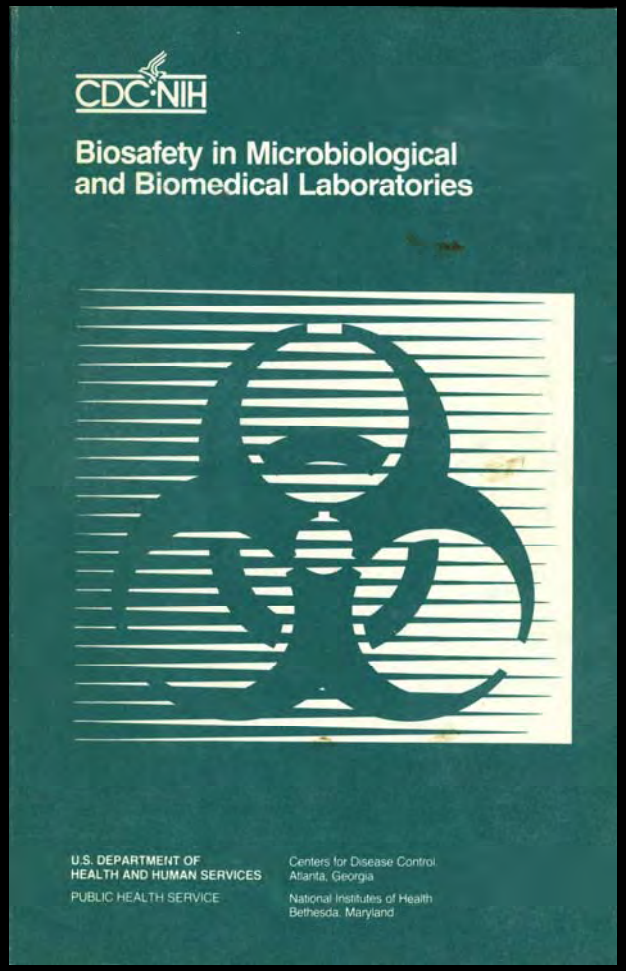
LABORATORY SAFETY FOR ARBOVIRUSES AND CERTAIN OTHER VIRUSES OF VERTEBRATES*

THE SUBCOMMITTEE ON ARBOVIRUS LABORATORY SAFETY OF THE AMERICAN COMMITTEE ON ARTHROPOD-BORNE VIRUSES†

SALS
WF Scherer, Chair
GA Eddy
TP Monath
TE Walton

Classification of 411 Catalogued arboviruses according to Biocontainment Level (majority were BL3)

The recommendations were incorporated in CDC/NIH Guidelines



1361

Total infections to date (deaths)

1
39
4
5
10
1
5
3 (1)
150 (1)
7 (2)
11
22
6
3
4
4
13
18
38 (8)
4
37 (2)
133
22
5

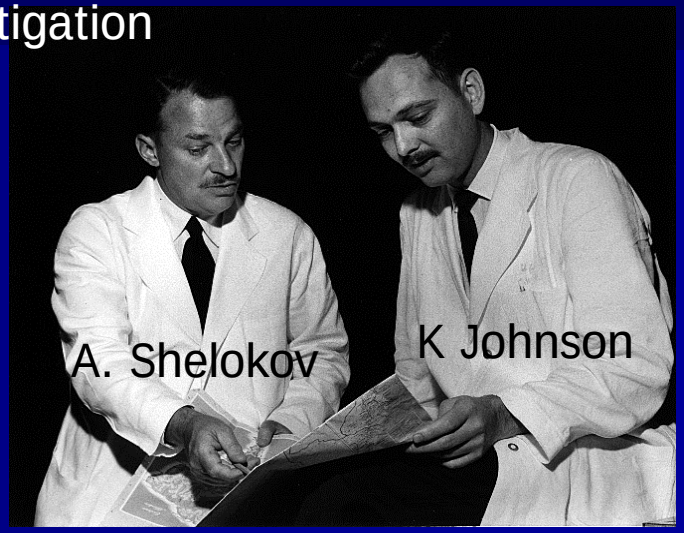
Arboviruses as Emerging Infections

1950-54	Hemorrhagic fever with renal syndrome (Korean Conflict)
1950-54	Yellow fever in Central America
1953	Argentine HF
1954-56	First dengue HF outbreaks (Thailand, Philippines)
1957	Kyasanur Forest disease (India)
1963	Bolivian HF
1967	Marburg HF (Europe)
1969	Lassa fever (Nigeria)
1969	Venezuelan equine encephalitis
1976	Ebola (Sudan, Zaire)
1981	Dengue HF in the New World
1993	Hantavirus Pulmonary Syndrome
1999	West Nile

Bolivian HF

1962 McKenzie (MPH, Berkeley, student of W Reeves) sees HF cases

1963 MARU organizes field investigation



Bolivian HF

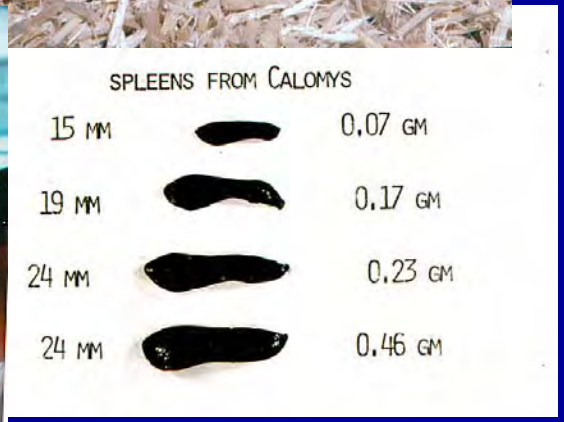
San Joaquin, Beni Province 1963-64

Calomys callosus

Field laboratory

Karl M Johnson
President 1984

Freeze drying 1st Machupo isolate



SYMPOSIUM ON SOME ASPECTS OF HEMORRHAGIC FEVERS IN THE AMERICAS*

Presented at the Annual Meeting of

AMERICAN SOCIETY OF TROPICAL MEDICINE AND HYGIENE

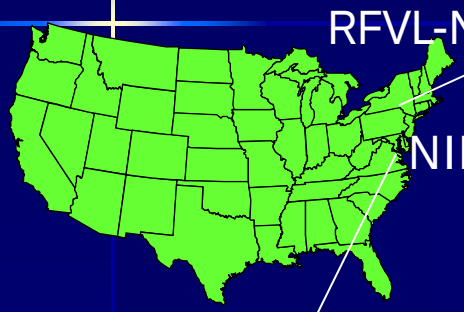
New York City, 5 November 1964

Hemorrhagic fevers in the Americas: A perspective	**Dr. Alexis Shelokov**
Junín and Tacaribe work in HeLa cells	**Dr. Sonja Buckley**
Serological studies on Junín and Tacaribe viruses	**Dr. Jordi Casals**
Junín and Tacaribe plaque production in rhesus monkey kidney cell monolayers	**Dr. J. R. Henderson & Dr. Wilbur G. Downs**
Properties of Machupo virus	**Dr. Patricia A. Webb**
Immunologic studies of Junín, Tacaribe, and Machupo viruses	**Dr. Ned H. Wiebenga**

EPIDEMIOLOGY OF MACHUPO VIRUS INFECTION:

I. Pattern of human infection, San Joaquín, Bolivia, 1962–64	**Dr. Ronald B. Mackenzie**
II. Ecological and control studies of hemorrhagic fever	**Dr. Merle L. Kuns**
III. Significance of virological observations in man and animals	**Dr. Karl M. Johnson**

Virus kinships: the value of virus explorations



1963- Junín antigenically related to Tacaribe

5

Wilbur G Downs
VP, 1968

1

1963- Johnson et al. isolate Machupo virus from a sick human

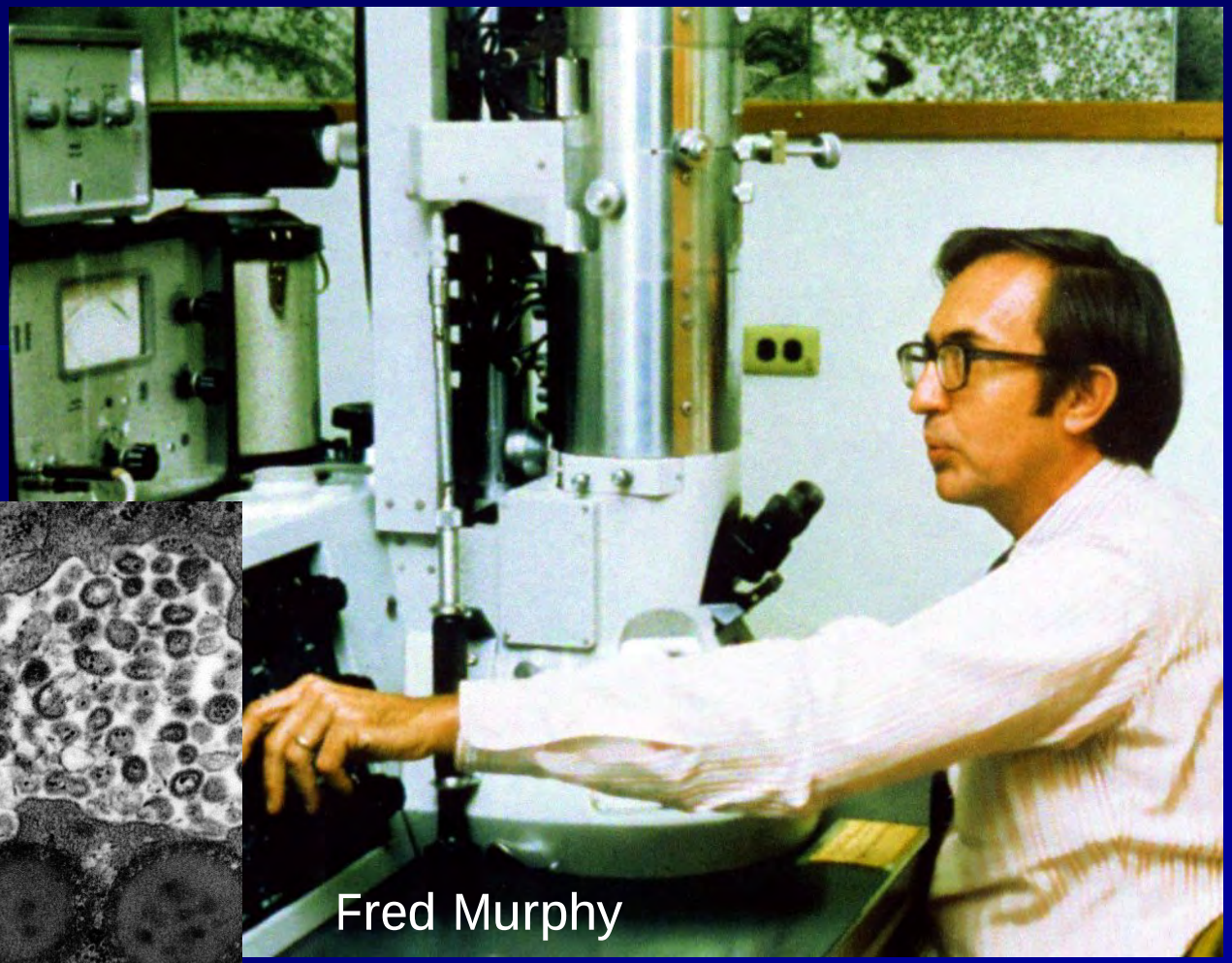
4

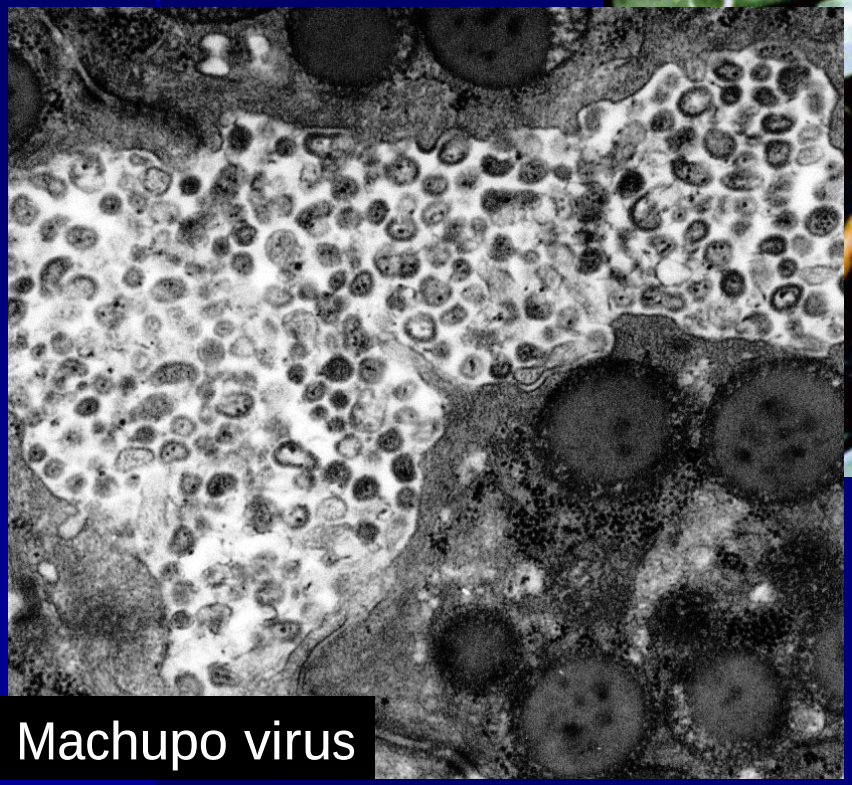
1962 -Sera from patients with VHF in Bolivia react with Junín antigen

3

1958- Junín virus isolated from sick humans

2





The *Arenaviridae*

BHF Investigations

FIELD

- Rodent reservoir/vector
- Rodent splenomegaly marker
- Risk factors for human infection
- Control strategy

LABORATORY

- Antigenic and morphologic relationships
- Infection dynamics and disease in rodent host
- Pathogenesis
- Diagnostic methods

Arboviruses as Emerging Infections

1950-54	Hemorrhagic fever with renal syndrome (Korean Conflict)
1950-54	Yellow fever in Central America
1953	Argentine HF
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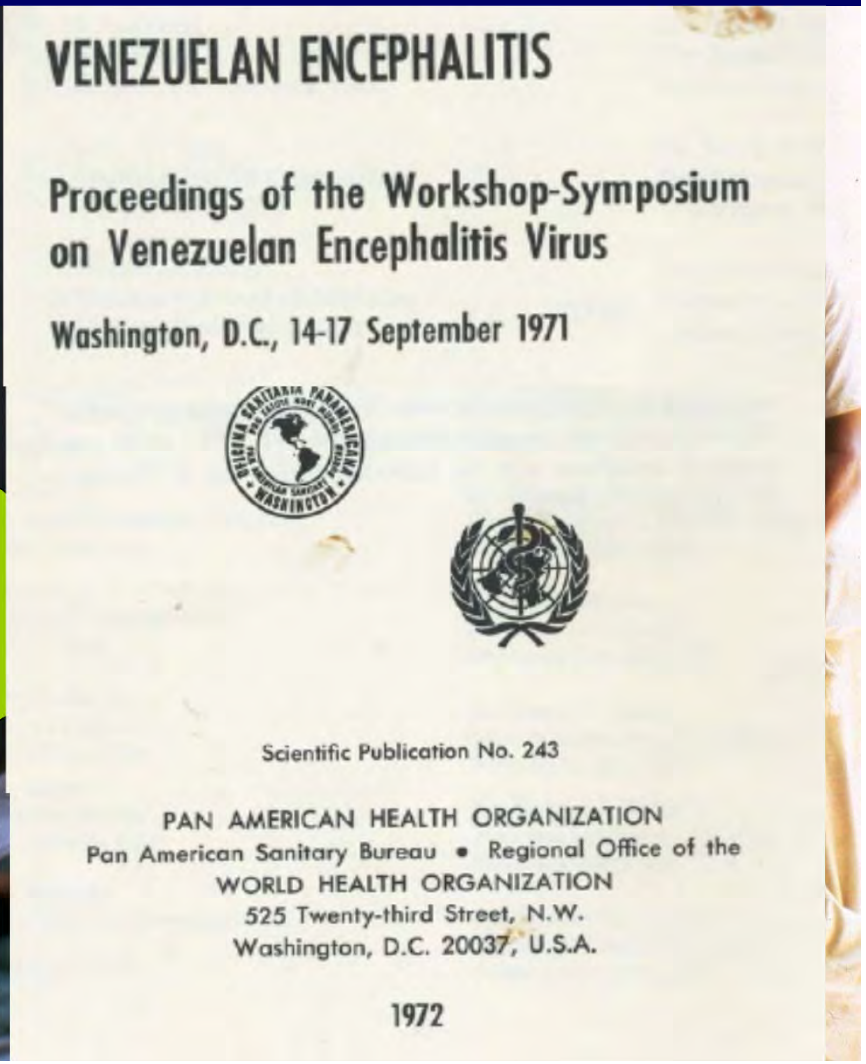
1969	Lassa fever (Nigeria)
1969	Venezuelan equine encephalitis
1976	Ebola (Sudan, Zaire)
1981	Dengue HF in the New World
1993	Hantavirus Pulmonary Syndrome
1999	West Nile

VEE invades Central America, Mexico and the US, 1969-72

50-100,000 equid cases
>30,000 human cases


VENEZUELAN ENCEPHALITIS

Proceedings of the Workshop-Symposium on Venezuelan Encephalitis Virus

Washington, D.C., 14-17 September 1971

Scientific Publication No. 243

PAN AMERICAN HEALTH ORGANIZATION
Pan American Sanitary Bureau • Regional Office of the
WORLD HEALTH ORGANIZATION
525 Twenty-third Street, N.W.
Washington, D.C. 20037, U.S.A.

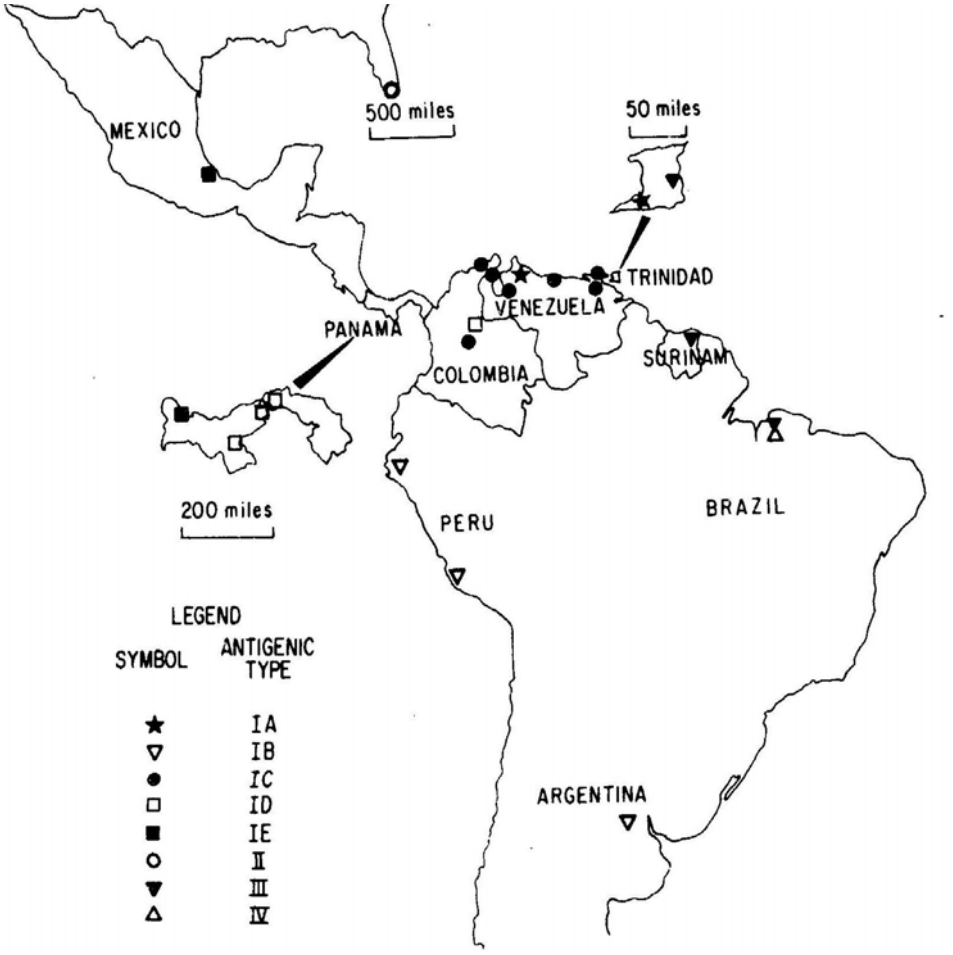
1972

AMERICAN JOURNAL OF EPIDEMIOLOGY

Vol. 89, No. 3
Printed in U.S.A.

ANTIGENIC VARIANTS OF VENEZUELAN EQUINE ENCEPHALITIS VIRUS: THEIR GEOGRAPHIC DISTRIBUTION AND EPIDEMIOLOGIC SIGNIFICANCE[1]

NATHANIEL A. YOUNG[2] AND KARL M. JOHNSON

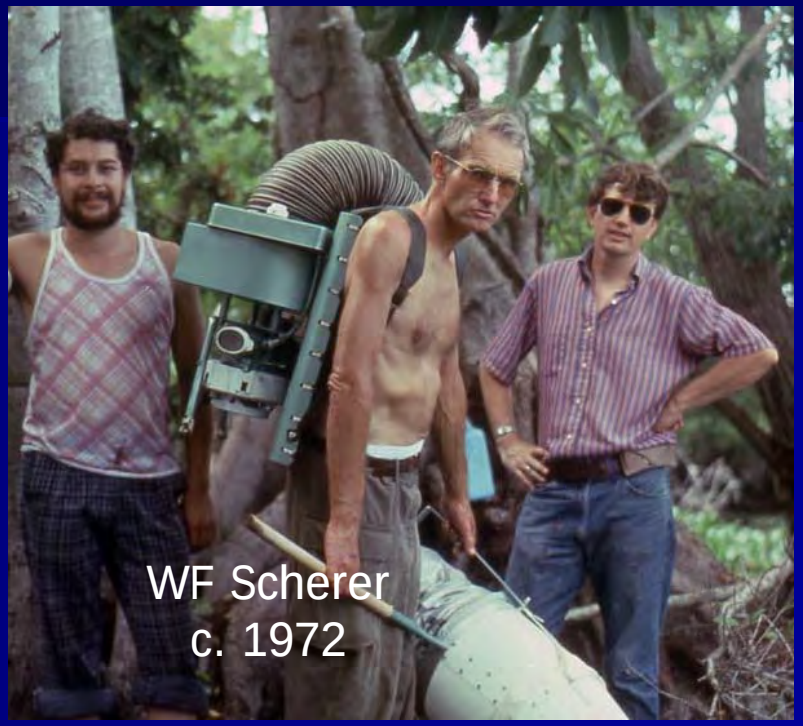


N Young

Karl Johnson

Persistence and reemergence of epizootic VEE subtypes—an enigma

- Intensive field studies in Central America (Scherer group) and Ecuador (CDC, Ft Collins) after the 1969-72 outbreaks yielded only enzootic subtype viruses
- Speculation that epizootic subtypes arise by mutation



WF Scherer
c. 1972

AMERICAN JOURNAL OF EPIDEMIOLOGY

Vol. 104, No. 1
Printed in U.S.A.

SEARCH FOR PERSISTENT EPIZOOTIC VENEZUELAN ENCEPHALITIS VIRUS IN GUATEMALA, EL SALVADOR AND NICARAGUA DURING 1970–1975[1, 2]

W. F. SCHERER, J. V. ORDONEZ, R. W. DICKERMAN AND J. E. NAVARRO

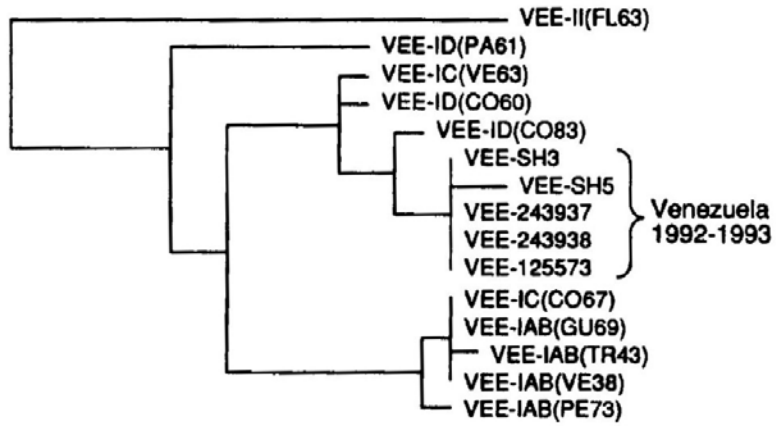
Evolution of epizootic from enzootic strains

Proc. Natl. Acad. Sci. USA
Vol. 92, pp. 5278–5281, June 1995
Microbiology

Emergence of a new epidemic/epizootic Venezuelan equine encephalitis virus in South America

(molecular evolution/epidemiology/emerging virus)

REBECA RICO-HESSE*†, SCOTT C. WEAVER‡§, JULIETA DE SIGER¶,

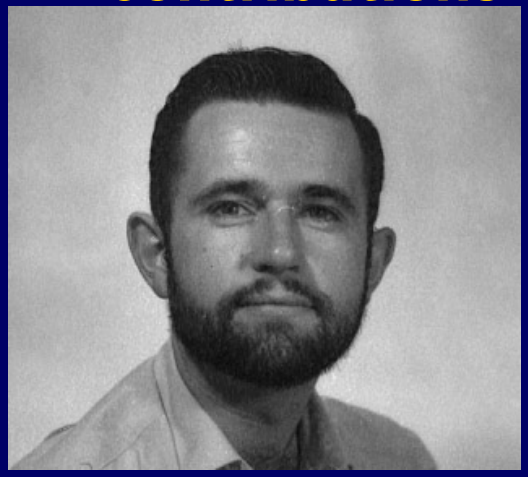


R Rico-Hesse

S Weaver

Dalrymple-Young Award, ACAV

Mid-career investigator who has made outstanding contributions to arbovirology

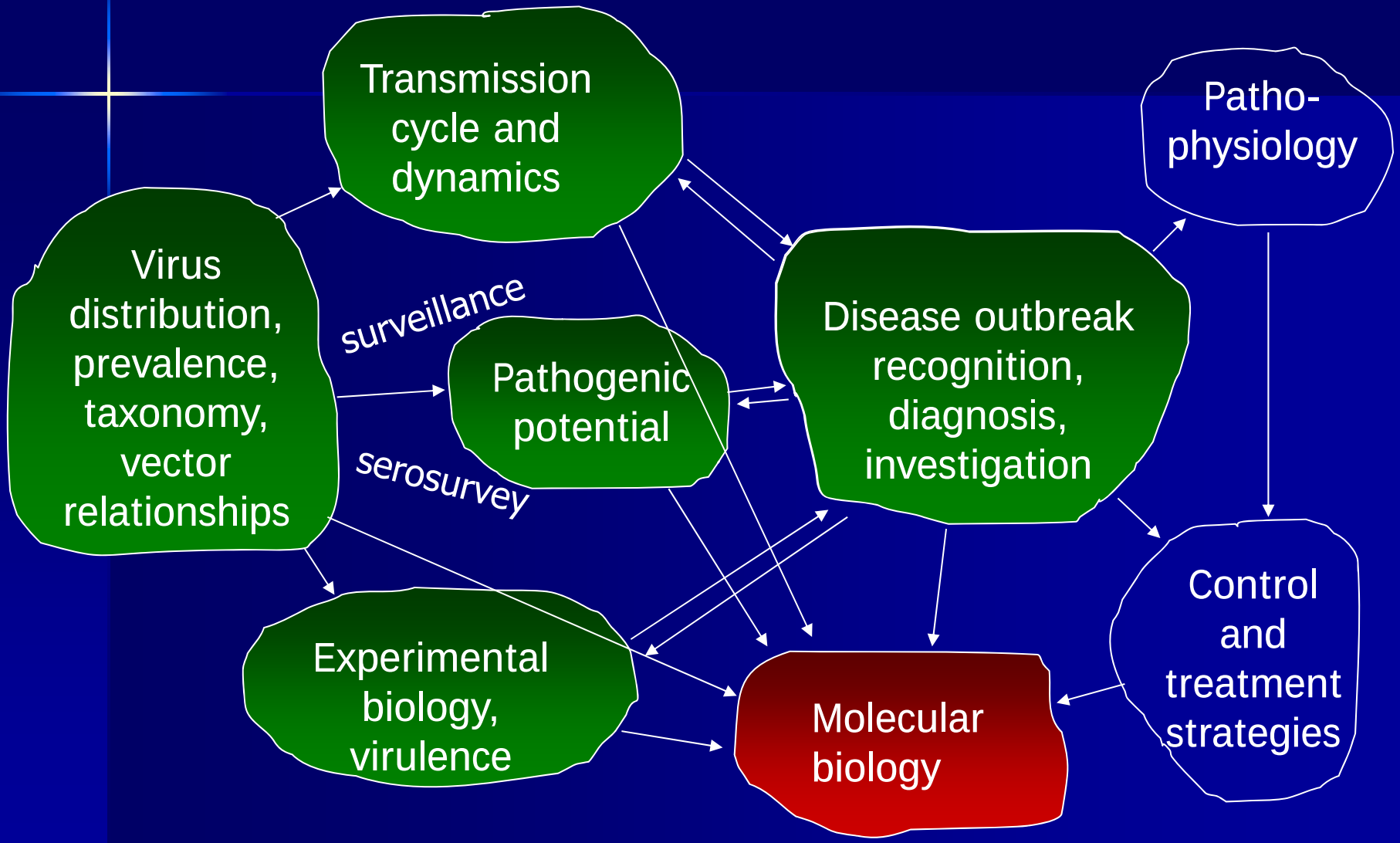


Nat Young 1937-1979

Joel Dalrymple 1939-1992

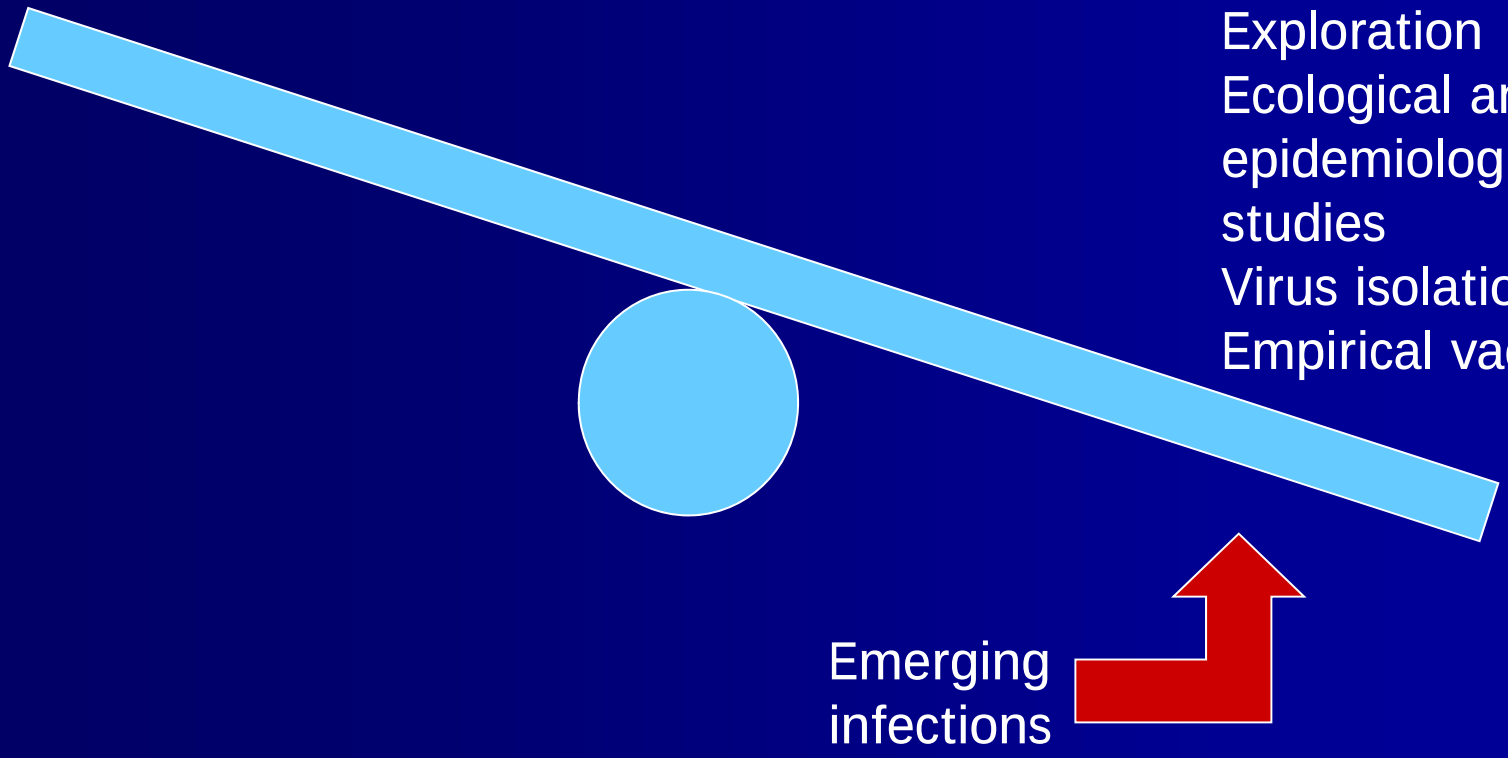
David H L Bishop	1982
Thomas P Monath	1984
Barry J Beaty	1988
Connie Schmaljohn	1996
Stuart T Nichol	1999
Scott C Weaver	2002

A model for arbovirus research



The Present

Basic science
Molecular virology
Hypothesis-driven research
Surveillance and diagnosis by specific molecular probes
Rationally designed vaccines

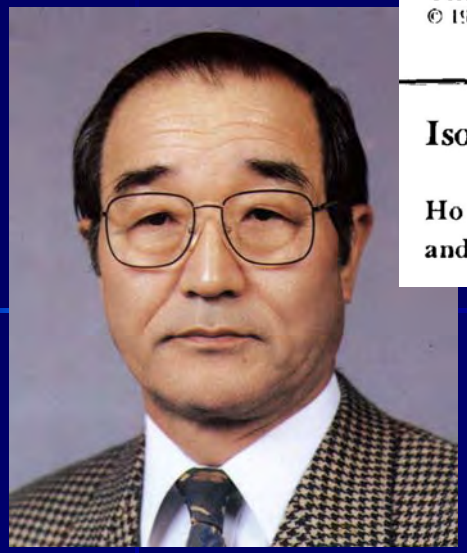


Arboviruses as Emerging Infections

1950-54	Hemorrhagic fever with renal syndrome (Korean Conflict)
1950-54	Yellow fever in Central America
1953	Argentine HF
1954-56	First dengue HF outbreaks (Thailand, Philippines)
1957	Kyasanur Forest disease (India)
1963	Bolivian HF
1967	Marburg HF (Europe)
1969	Lassa fever (Nigeria)
1969	Venezuelan equine encephalitis
1976	Ebola (Sudan, Zaire)
1981	Dengue HF in the New World
1993	Hantavirus Pulmonary Syndrome
1999	West Nile

Hemorrhagic fever with Renal Syndrome
Nephropathia epidemica

Ho Wang Lee



THE JOURNAL OF INFECTIOUS DISEASES • VOL. 137, NO. 3 • MARCH 1978
 0022-1899/78/3703-0010$01.02

Isolation of the Etiologic Agent of Korean Hemorrhagic Fever

Ho Wang Lee, Pyund Woo Lee,
and Karl M. Johnson*

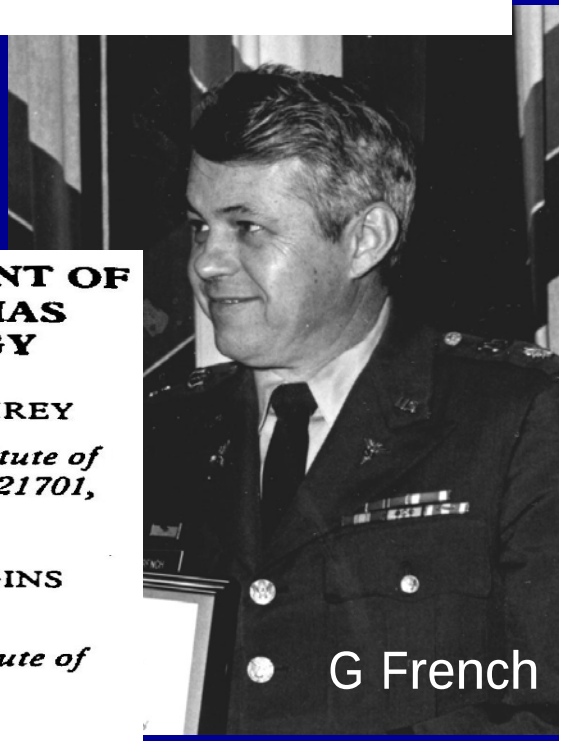
From the Department of Microbiology, Korea University College of Medicine, Seoul, Korea; and the Middle America Research Unit, Balboa Heights, Canal Zone

KM Johnson

Korean Hemorrhagic Fever: Propagation of the Etiologic Agent in a Cell Line of Human Origin

GEORGE R. FRENCH*
RICHARD S. FOULKE
ORVILLE A. BRAND
GERALD A. EDDY
U.S. Army Medical Research Institute of Infectious Diseases, Frederick, Maryland 21701
HO WANG LEE

SCIENCE, VOL. 211, 6 MARCH 1981



G French

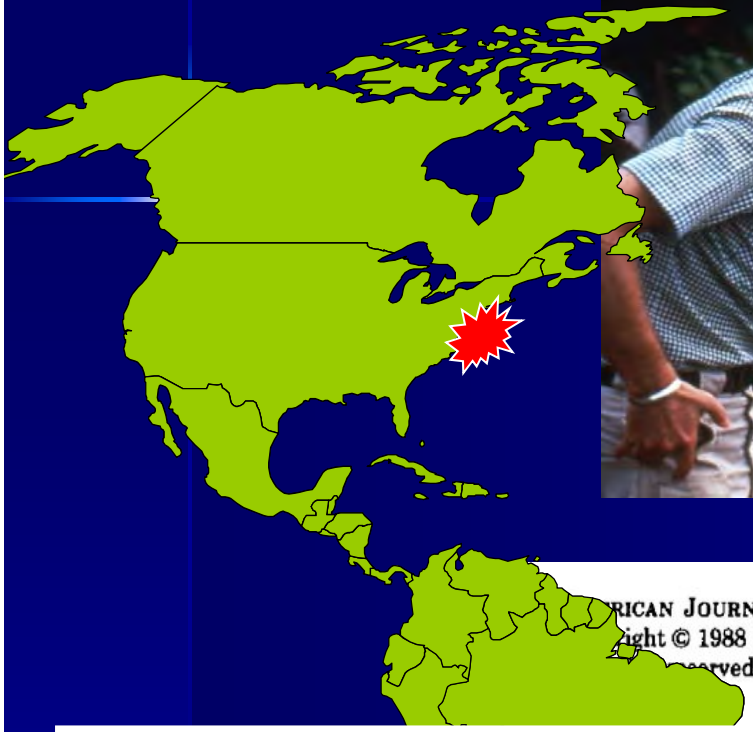
HANTAAN VIRUS, AETIOLOGICAL AGENT OF KOREAN HAEMORRHAGIC FEVER, HAS BUNYAVIRIDAE-LIKE MORPHOLOGY

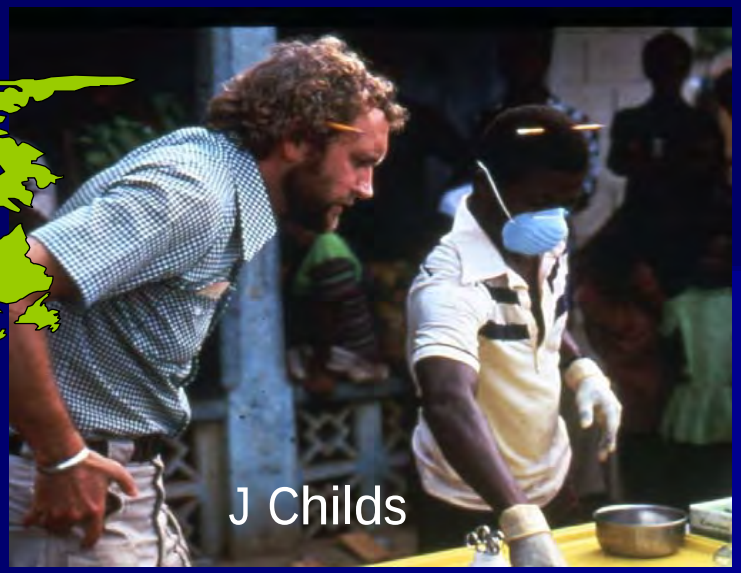
JOHN D. WHITE FRANCES G. SHIREY
Pathology Division, U.S. Army Medical Research Institute of Infectious Diseases, Fort Detrick, Frederick, Maryland 21701, U.S.A.

GEORGE R. FRENCH* JOHN W. HUGGINS
ORVILLE M. BRAND
Virology Division, U.S. Army Medical Research Institute of Infectious Diseases, Fort Detrick

HO WANG LEE
Institute for Viral Diseases, Korea University, Seoul, Korea

THE LANCET, APRIL 3, 1982





RICAN JOURNAL OF EPIDEMIOLOGY
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rved

Vol. 127, No. 4
Printed in U.S.A.

N Engl J Med. 1984;310:1325-6.

Prospect Hill virus: serologic evidence for infection in mammologists,

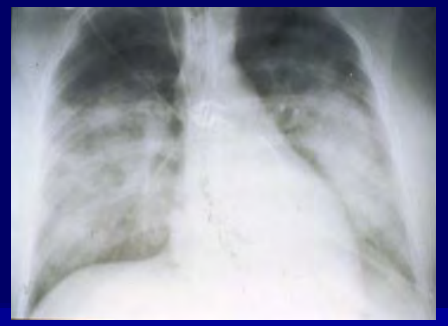
Yanigahara R, Gadjusek C, Gibbs CJ Jr, Traub R

The NEW ENGLAND JOURNAL of MEDICINE

Volume 330:949-955 April 7, 1994 Number 14

Hantavirus Pulmonary Syndrome: A Clinical Description of 17 Patients with a Newly Recognized Disease

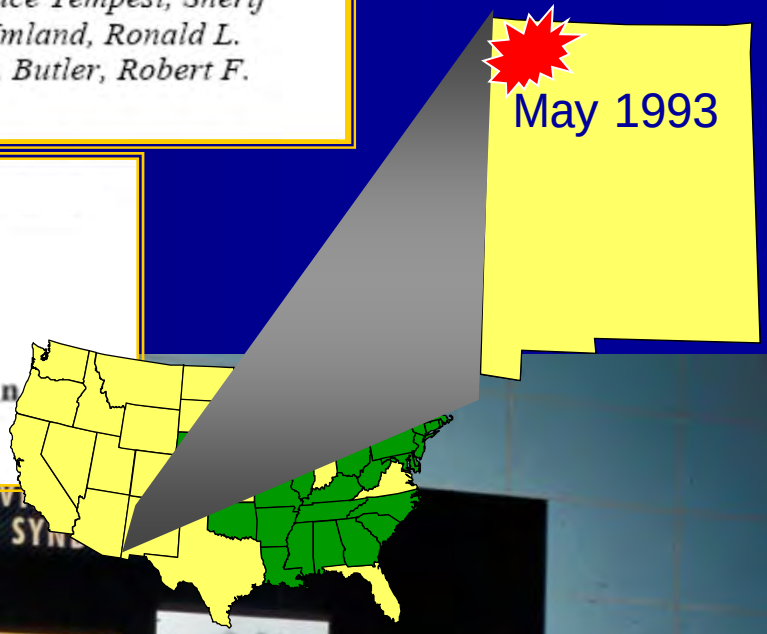
Jeffrey S. Duchin, Frederick T. Koster, C.J. Peters, Gary L. Simpson, Bruce Tempest, Sherif R. Zaki, Thomas G. Ksiazek, Pierre E. Rollin, Stuart Nichol, Edith T. Umland, Ronald L. Moolenaar, Susan E. Reef, Kurt B. Nolte, Margaret M. Gallaher, Jay C. Butler, Robert F. Breiman, for The Hantavirus Study Group



Lancet. 1994 Apr 23;343(8904):1037-8.

Retrospective diagnosis of a 1983 case of fatal hantavirus pulmonary syndrome.

Zaki SR, Albers RC, Greer PW, Coffield LM, Armstrong LR, Khan AS, Khabbaz R, Peters CJ.




S Nichol

Hantaviruses in the New World

Red= associated with HPS

Bloodland Lake

Sin Nombre

El Moro Canyon

Limestone Canyon

New York

Monongahela

Prospect Hill

Muleshoe

Black Creek Canal

Bayou

Cano Delgadito

Maporal

Rio Segundo

Choclo

Calabazo

Rio Mamore

Anajatuba

Rio Mearim

Castelo dos Sonhos

Juquitiba

Araraquara

Laguna Negra

Oran

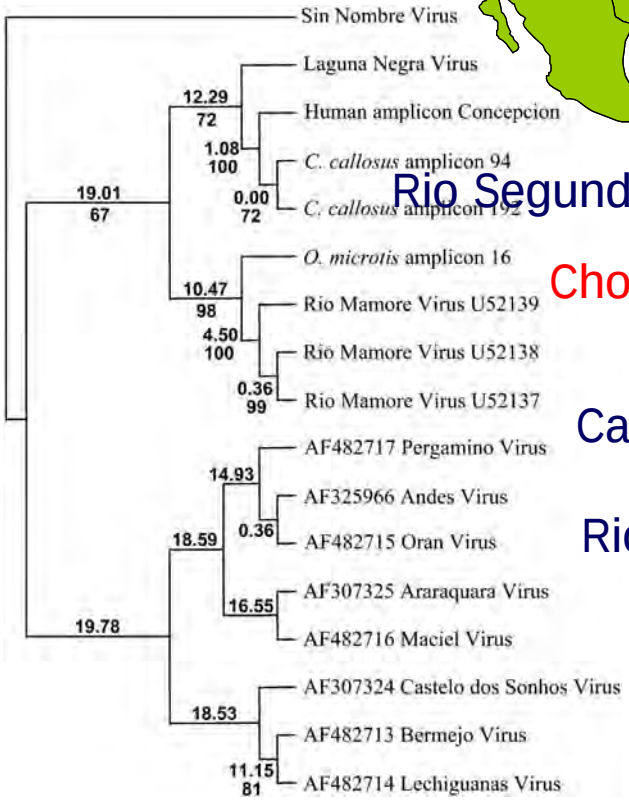
Maciel

Bermejo

Pergamino

Lechiguanas

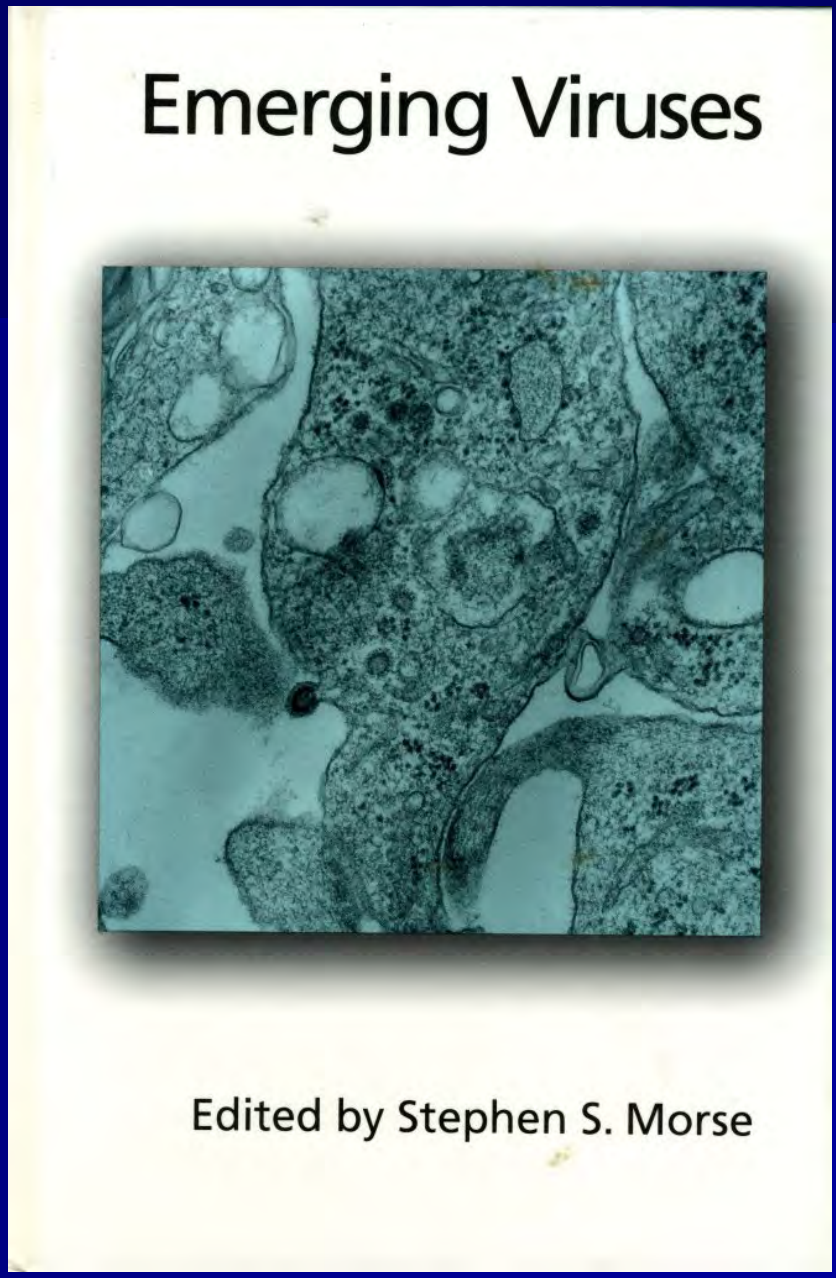
Andes



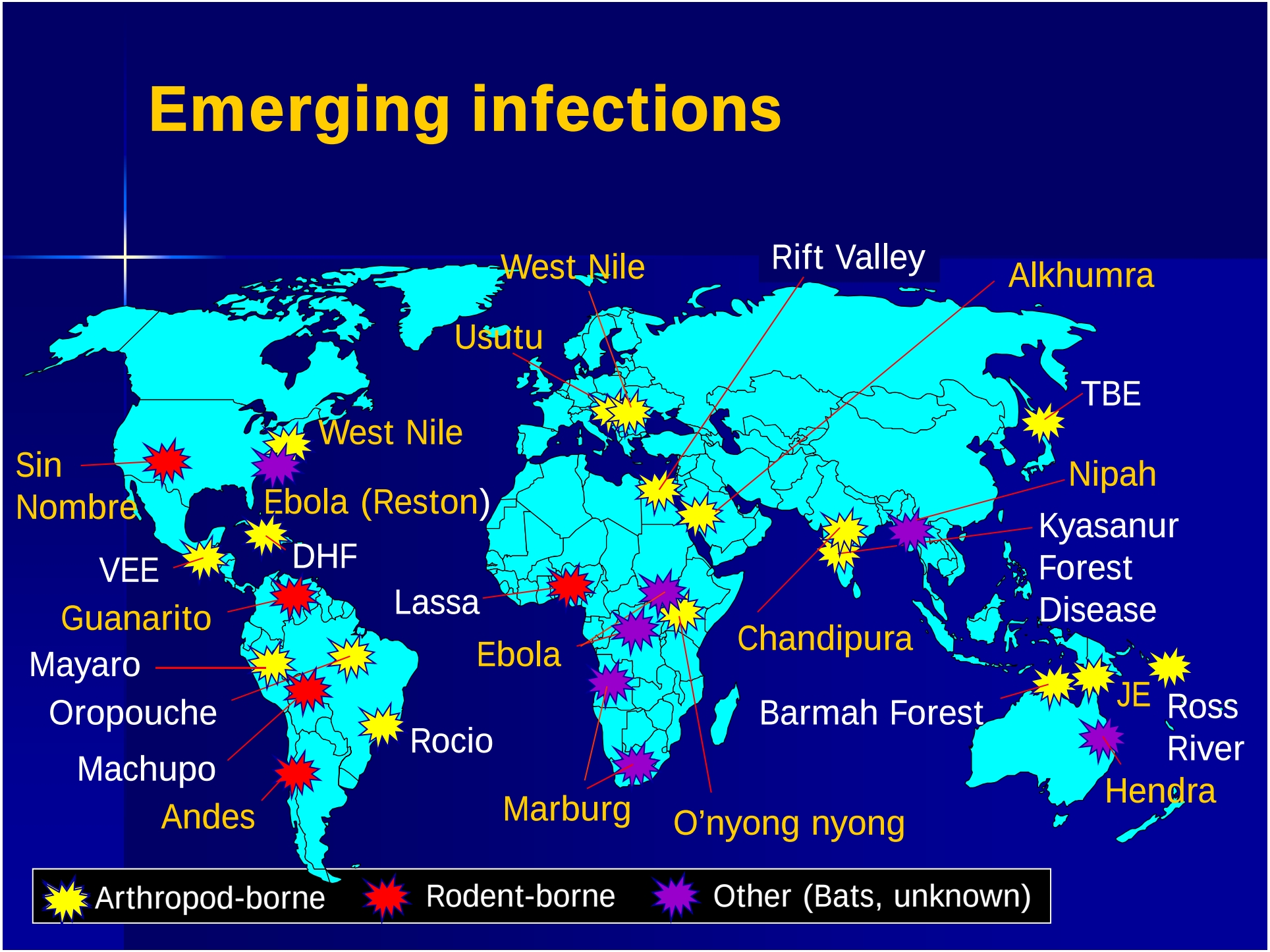
Lessons learned

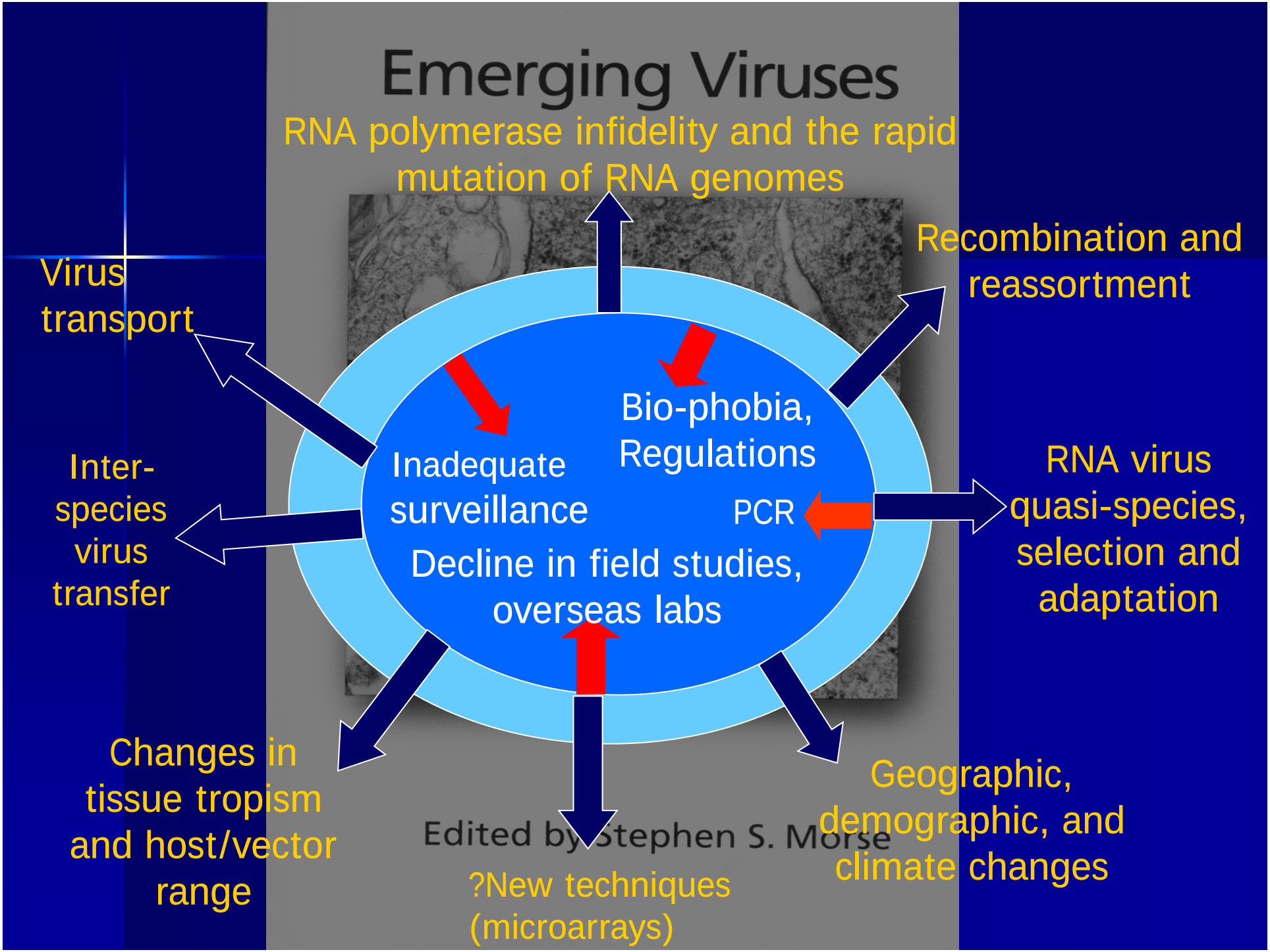
- 1970s: etiology of HFRS-- an important zoonosis -- identified; laboratory methods developed
- 1980s: Field evidence for presence in New World
  - No serious attempts to define virus distribution, prevalence
- 1990s surprised by human disease outbreak
  - Dramatic diversity and wide distribution of virus group

Emerging infections: conceptualization and reality

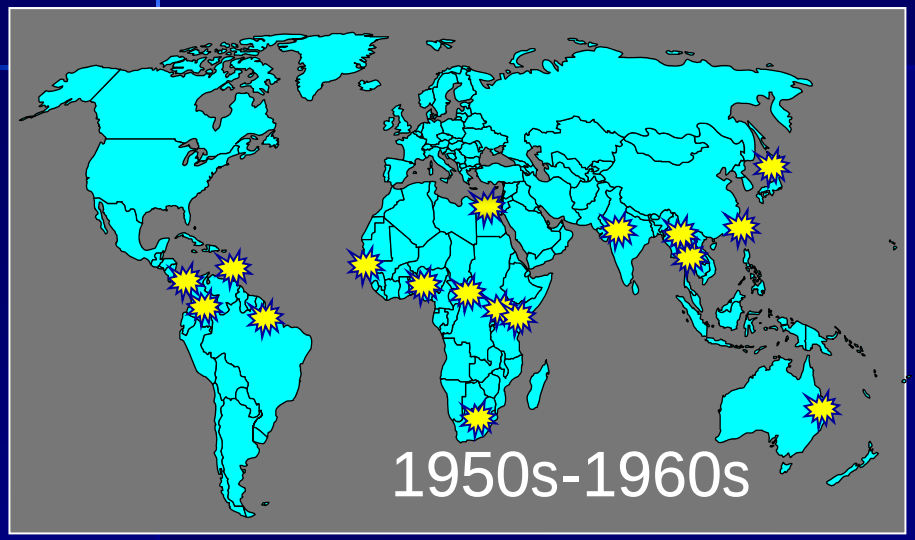


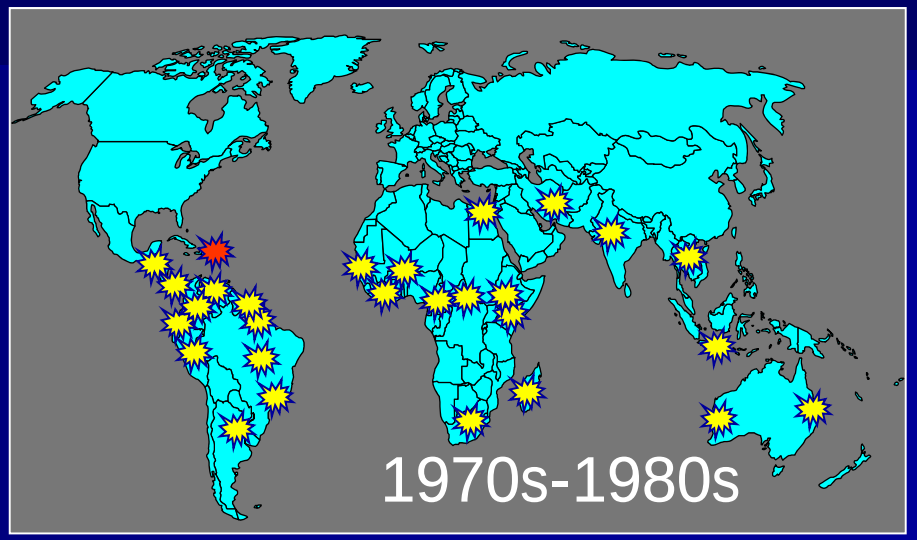
Emerging infections

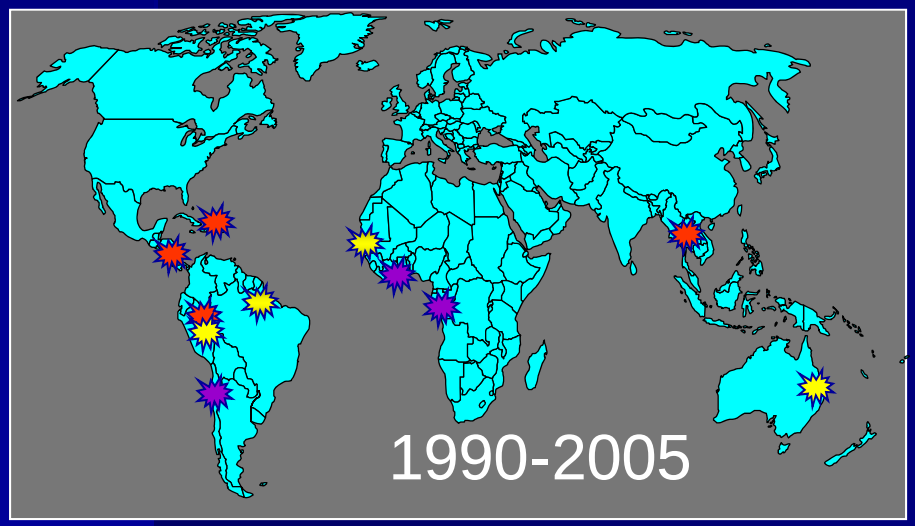



Emerging Viruses
RNA polymerase infidelity and the rapid mutation of RNA genomes
Virus transport
Recombination and reassortment
Inter-species virus transfer
RNA virus quasi-species, selection and adaptation
Changes in tissue tropism and host/vector range
Geographic, demographic, and climate changes
?New techniques (microarrays)
Bio-phobia, Regulations
Inadequate surveillance
PCR
Decline in field studies, overseas labs
Edited by Stephen S. Morse

Longitudinal field research programs in tropical arbovirology

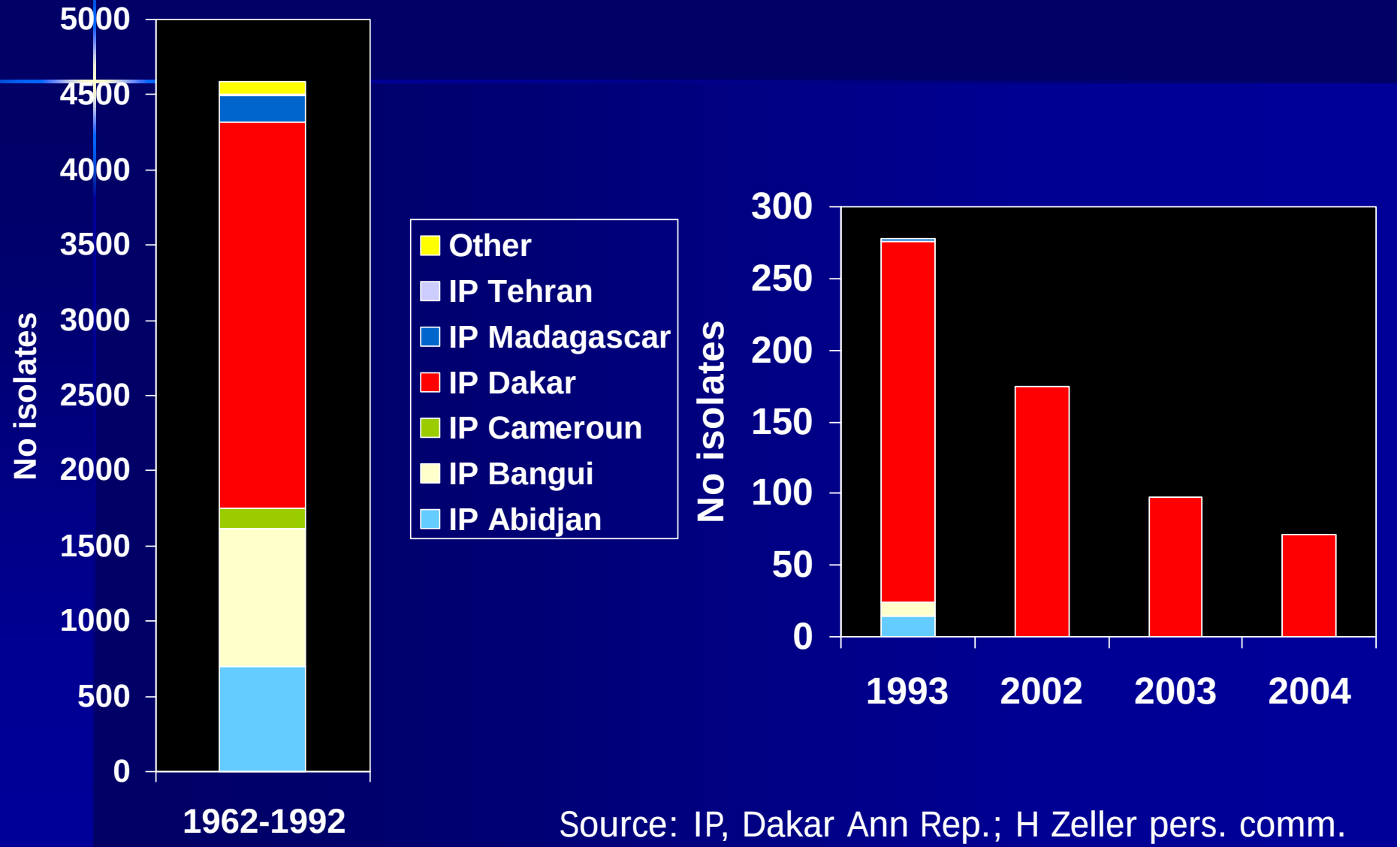






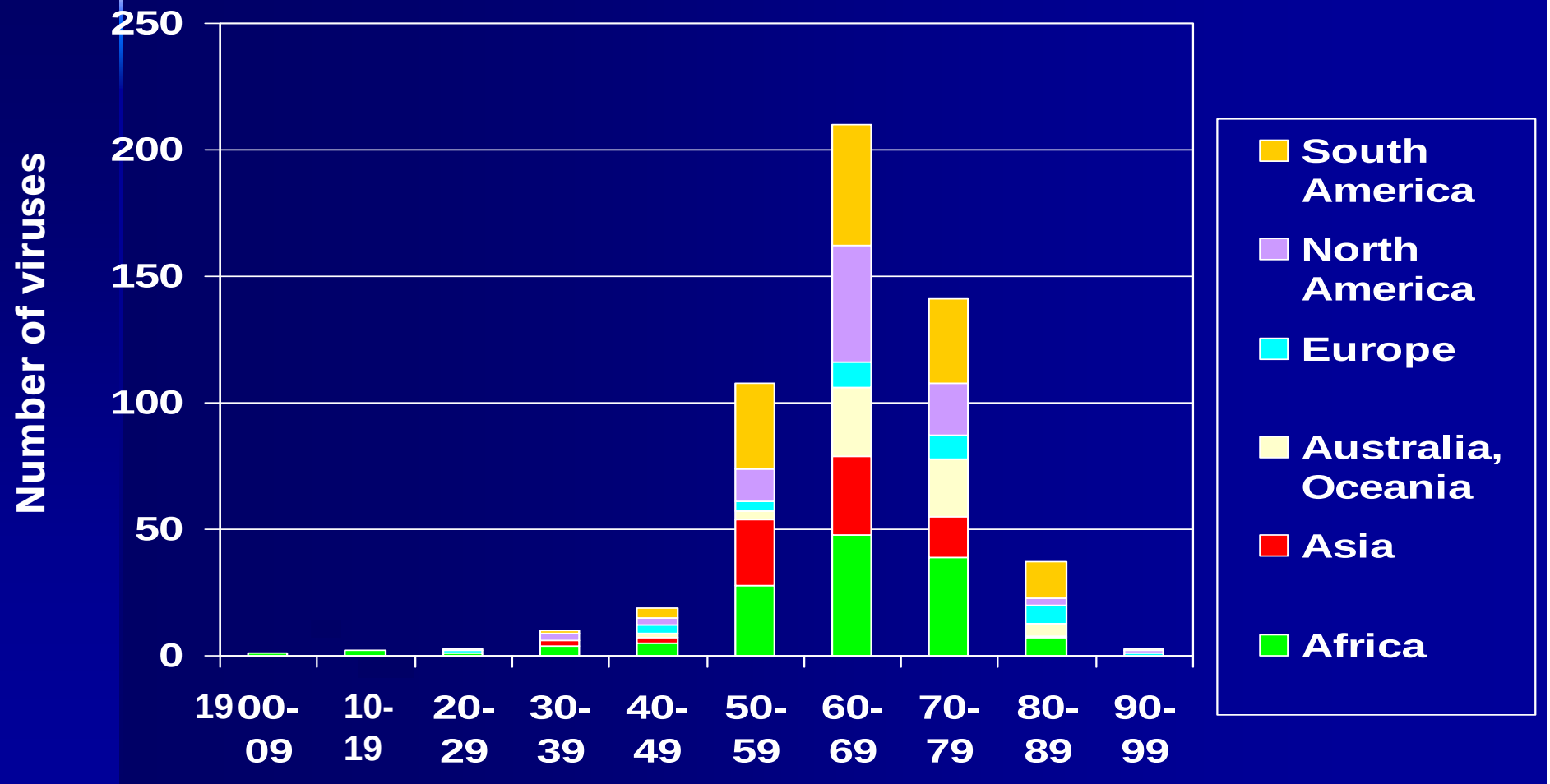
- Limited field research (dengue)
- Limited field research (VHFs)
- General arbovirology

Arboviruses identified Institut Pasteur, Dakar



Source: IP, Dakar Ann Rep.; H Zeller pers. comm.

Arboviruses (n=534) by initial year of isolation and continent



Limited funding for arbovirus field work

- Lack of visionary leadership
- Competes with funding for basic science
- Feeling that important information has already been obtained
- Importance of results may not be evident immediately
- Political and logistic barriers
- Directed to situations in which emergencies/threats do not exist
- Emphasis on disease surveillance rather than viruses ‘in search of a disease’
- Pejorative language
  - ‘Fishing expedition’
  - ‘Stamp collecting’
  - ‘old-fashioned’

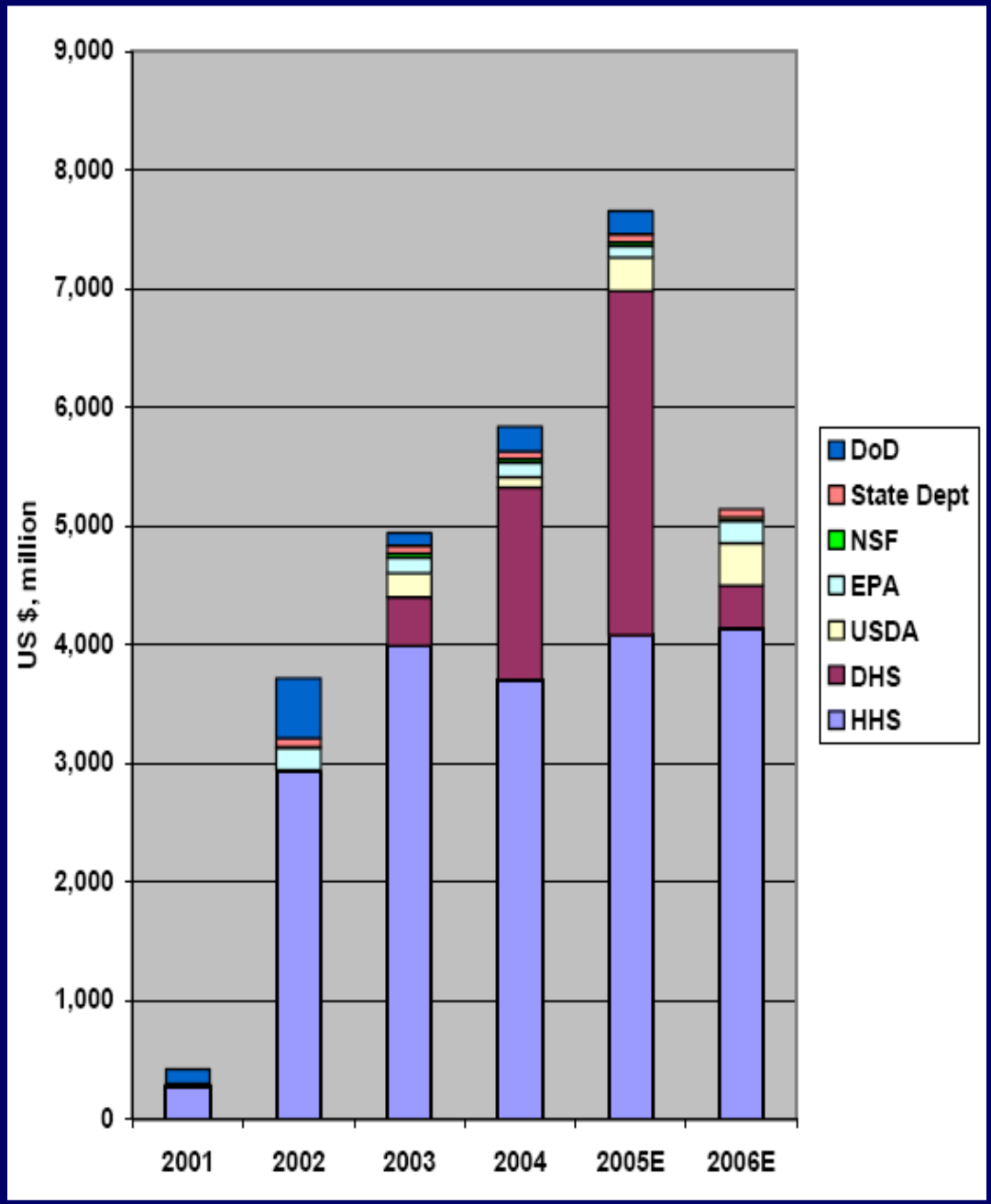
World Reference Center for Emerging Viruses and Arboviruses

NIAID maintains the World Reference Center for Emerging Viruses and Arboviruses at the University of Texas Medical Branch at Galveston

- c. 1995 YARU collection of >4000 virus stocks moved with Tesh and Shope to UTMB
- Funded at $4.4m (2003-2010) by NIAID
- While an important historical collection, it no longer functions as a Reference Center
  - Virtually no new viruses submitted for study by foreign collaborators
  - Virtually no reference viruses exported to foreign investigators

Biotrerr

- Decreased biodefense
- Select Agent Regulations
- Regulations extended to international partners
- Increasing prohibitions export and of viruses



ACAV Meeting March 1965

4. Report on Discussions with USPHS and USDA Regarding Importation Arboviruses: Regulations and Problems. Dr. Scherer contacted Dr. John ighes, USPHS, and Dr. Reisinger of USDA regarding regulations for importing id distributing viruses. The USPHS has no control of interstate shipment f U.S. viruses, but USDA has. Both control interstate shipment of exotic iruses, and their importation. The regulations are not excessively restric- ive, and are subject to the interpretation of these two men. They realize heir limitations in the area of the arboviruses, and are now relying upon r. Buescher and others for guidance. They anticipate using the ACAV com- ittee and subcommittees for help in deciding on the issuance of permits for importation and interstate transportation. Both men seem cooperative.

Value of active arbovirus surveillance and exploration

- Isolation and characterization of pathogenic agents in advance of recognition of significant disease
  - West Nile (Uganda, 1937)...Outbreaks Israel,

Am. J. Trop. Med. Hyg., 73(3), 2005, pp. 566–570

AN OUTBREAK OF CHANDIPURA VIRUS ENCEPHALITIS IN THE EASTERN DISTRICTS OF GUJARAT STATE, INDIA

MANDEEP S. CHADHA,* VIDYA A. ARANKALLE, RAMESH S. JADI, MANOHAR V. JOSHI, JYOTSNA P. THAKARE, P. V. M. MAHADEV, AND A. C. MISHRA

National Institute of Virology 20-A, Dr. Ambedkar Road, Pune, Maharashtra, India

  - Chandipura (India, 1965)....Outbreaks, India
  - Toscana (Italy, 1971)... Outbreaks Europe
  - Hendra (Australia, 1995)... Nipah emergence

Value of active arbovirus surveillance and exploration

- Identify existing viral fauna
- Evaluate pathogenic potential of new agents
  - Antigenic/genomic relationships
  - Serological evidence for infection
  - Laboratory markers of virulence
  - Vectors and hosts
  - Diagnostic tools
- Targeted study of indicator ‘emerging’ viruses
  - Factors determining cyclic changes in transmission
  - Influence of ecological change and climate
  - Predictive modeling

Value of active arbovirus surveillance and exploration

- Risk assessment during periods of rapid ecological change
  - Tropical deforestation
  - Reduction in biodiversity
  - Hydroelectric projects
  - Urbanization
  - Human migration
  - Global warming

POLICY FORUM

PUBLIC HEALTH

Pathogen Surveillance in Animals

T. Kuiken,[1] F. A. Leighton,[2] R. A. M. Fouchier,[1] J. W. LeDuc,[3] J. S. M. Peiris,[4] A. Schudel,[5] K. Stöhr,[6] A. D. M. E. Osterhaus[1]*

December 1, 2005 latimes.com : World News

Print

3 Species of Fruit Bat Found to Harbor Deadly Ebola Virus

■ Tests by scientists in Gabon and Congo detect traces of the pathogen. Human infection may have occurred through eating the animals.

By Alex Raksin, Times Staff Writer

Researchers working in Gabon and Congo have identified three species of fruit bat as the long-sought reservoirs of one of the deadliest known human pathogens, the Ebola virus.

The team tested more than 1,000 bats and other animals before tracing the virus to fruit bats, which are commonly eaten by people in Central Africa, according to a report in today's issue of the journal Nature.

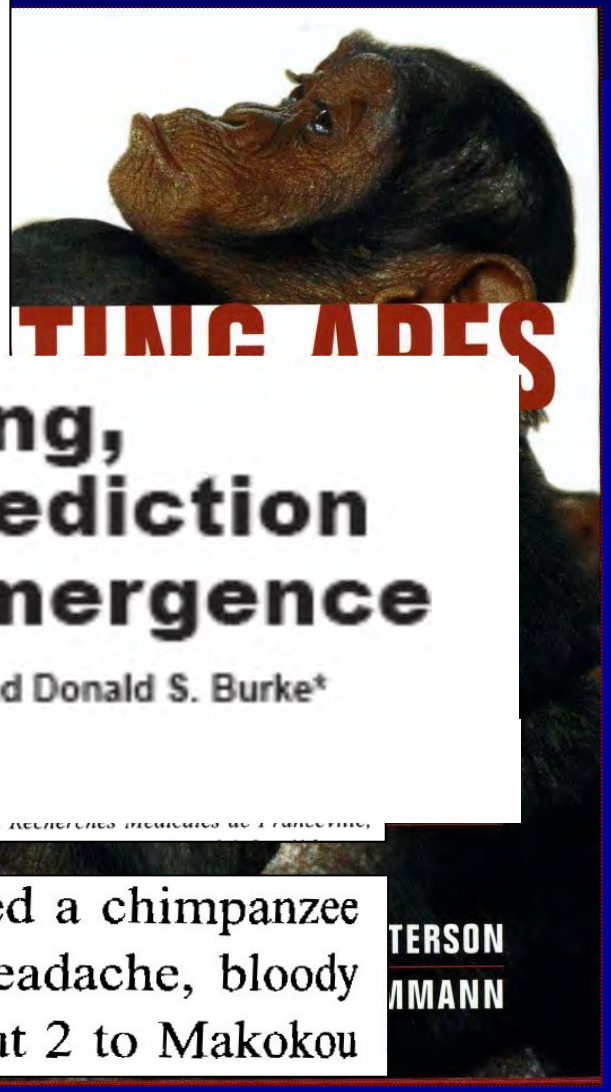
Méthode

design and implement a global animal surveillance system for zoonotic pathogens that gives early warning of pathogen emergence

Passive surveillance: the 'Bush Meat' Method

Table 6. Bush meat highly prized by humans, northeastern Gabon.

Group	Species
Primates	*Cercopithecus* species (monkeys)
	Pan troglodytes (chimpanzee)
	Gorilla gorilla
Artiodactyls	*Potamochoerus porcus* (bush pig)



Bushmeat Hunting, Deforestation, and Prediction of Zoonotic Disease Emergence

Nathan D. Wolfe,* Peter Daszak,† A. Marm Kilpatrick,† and Donald S. Burke*

Emerg Infect Dis 2005;11:1822

Alain-Jean Georges, Eric M. Leroy, Andre A. Renaut,

Eighteen people who had skinned and chopped a chimpanzee cadaver that they found became ill (fever, headache, bloody diarrhea). They were evacuated from Mayibout 2 to Makokou

Unexplored virus groups

- Marked speciation/diversity
- Wide host range
- History of ‘species jumping’
- Human and animal disease reported
- Wide geographic range
- Little/no information on transmission and human infection

- Orbiviruses, Seadornaviruses
- Paramyxoviruses
- Rhabdoviruses
- Filoviruses
- Phleboviruses
- Hantaviruses

Reoviridae

Seadornavirus

Phytoreovirus

BANNA
KADIPIRO
LIAO NING

Rotavirus

Orbivirus

AFR HORSESICKNESS
CHANGUINOLA
ORUNGO
BLUETONGUE
YUNNAN

Mycoreovirus

Aquareovirus

EYACH
CTF

Coltivirus

Orthoreovirus

Oryzavirus

Figivirus

Cypovirus

Hantaviruses in the New World

Red= associated with HPS

Bloodland Lake

Sin Nombre

El Moro Canyon

Limestone Canyon

New York

Monongahela

Prospect Hill

Muleshoe

Black Creek Canal

Bayou

Cano Delgadito

Maporal

Rio Segundo

Choclo

Calabazo

Rio Mamore

Anajatuba

Rio Mearim

Castelo dos Sonhos

Juquitiba

Araraquara

Laguna Negra

Oran

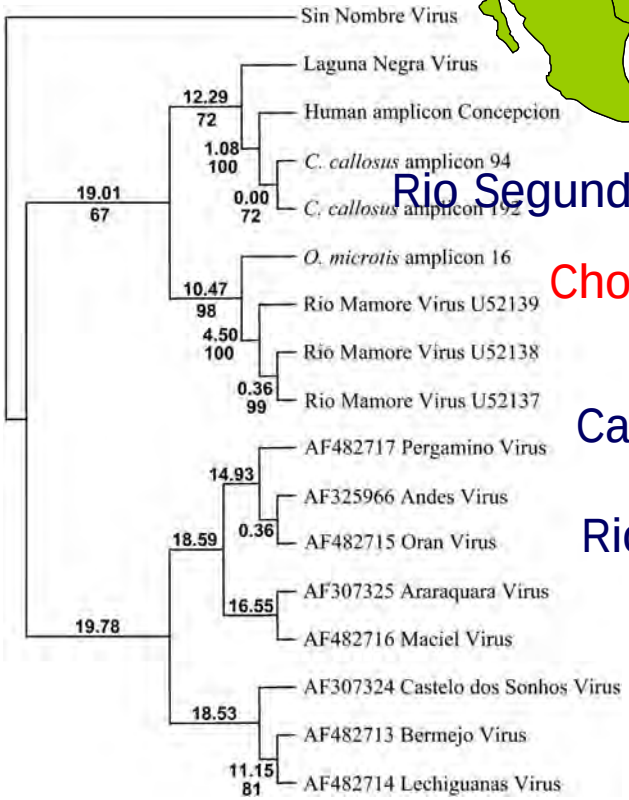
Maciel

Bermejo

Pergamino

Lechiguanas

Andes



Solutions

- Provide leadership in defining priorities for field research
- Engage and fund scientists in the tropics at the forefront of virus emergence
- Support and adequately fund longitudinal field research on selected pathogens
- Redefine Global Surveillance to include the ‘silent world’ of viruses circulating in nature
- Include virus isolation in addition to broad (virus family/genus) molecular probes, and apply to human illness, wildlife samples, arthropod pools
- Link field research to carefully designed experimental studies of virus-vector-host interactions

Solutions

- Priority given to areas undergoing rapid ecological change
- Develop and apply new serological tools for comprehensive retrospective mapping of virus exposure
- Determine pathogenic potential (serological surveys, diagnosis)
- Re-instate and adequately fund regional Reference Centers
- Develop Bio-Banking
- Develop policies and procedures to facilitate the exchange of specimens, reagents, and information

108TH CONGRESS
1ST SESSION

S. 871

To provide for global pathogen surveillance and response.

IN THE SENATE OF THE UNITED STATES

APRIL 10, 2003

Mr. BIDEN (for himself, Mr. LUGAR, Mr. KENNEDY, Mr. HAGEL, Mr. DOMENICI, and Mr. FEINGOLD) introduced the following bill; which was read twice and referred to the Committee on Foreign Relations

---

A BILL

To provide for global pathogen surveillance and response.

1 *Be it enacted by*

2 *tives of the United St*

Donald S Burke
President 1996

(6) To establish "lab-to-lab" cooperative relationships between United States public health laboratories and established foreign counterparts.

... detect and quickly contain infectious disease outbreaks or bioterrorism agents before they can spread.

The EDEN Project

Emerging Diseases in a Changing European Environment

- West African and European project focus
- Indicator human diseases, e.g. TBE, Rift Valley fever sensitive to environmental changes
- Describe epidemiological cycles
- Intrinsic and extrinsic factors triggering or modulating emergence
- Predictive models
- Definition of environmental changes favoring emergence

ICTDR NETWORK

International Centers for Tropical Disease Research

- Hantavirus Ecology and Research, Chile (Greg Mertz, UNM)

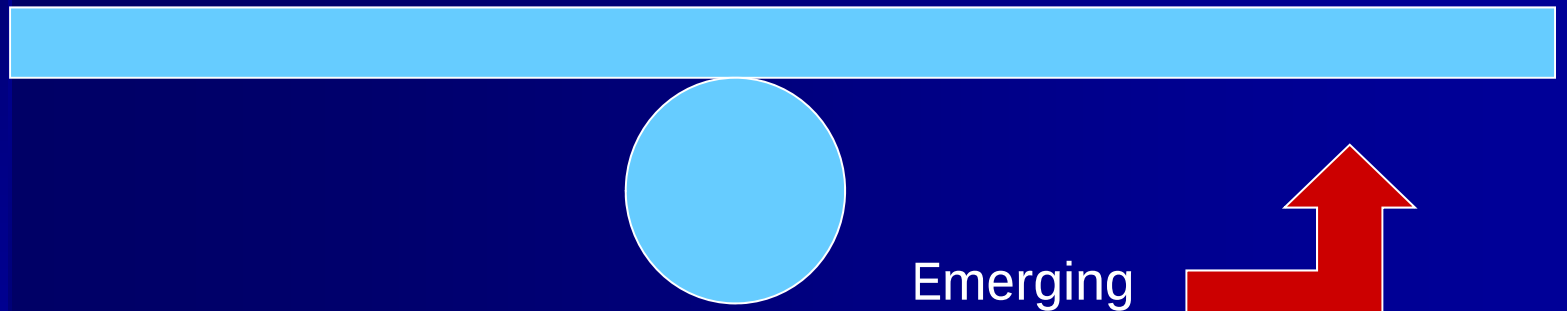
The consequences of inaction

- Continued surprises
- Retrospective and reactionary
- Static reference and reagent collections
- Limited capacity for surveillance
- Reliance on human disease
- Finding only what we look for
- Increasing regulations and restricted international collaborations
- Incomplete information on disease ecology

Back to Basics

Basic science
Molecular virology
Hypothesis-driven research
Surveillance and diagnosis by specific molecular probes

Exploration
Ecological and epidemiological studies
Virus isolation
Surveillance of wild-life
Active reference collections



Emerging infections

Thanks to:

- Martine Jozan
- Many, many colleagues who provided photographs

Apologies to:

- Those whose photos I couldn’t show (you will be in the Archives!)