

Yellow Fever Lecture Notes Harvard, 1963

Evolution of Public Health Administration Methods for Prevention of Yellow Fever

See what is Yellow Fever?

Before 1900 -

- (1) Quarantine
- (2) Firing Cannon
- (3) Flight
- (4) Vaccine

Sanarelli (1897) Bacillus Icteroides (Wasdin and Gettings PHS confirmed 1899)

- (4) Anti Amaryl Serum (Monte. 1900)
- (6) Havana - 1900 - Thorough cleaning of city - Havana - 1901
  - (a) Attack on breeding places of all mosquitoes attack on infected adults.
  - (b) Fumigation (s) of infected houses and
  - (c) isolation and screening of cases.

Gorgas surprised at success-credited victory to fumigation

Evolution of Public Health Methods in Prevention of Yellow Fever

- (1) What is Yellow Fever?

causation

vector

animal host

clinical

pathology

immunology

epidemiology

wave-like phenomenon

like measles

But some endemic areas some enzootic areas

distribution

Havana 1901 double victory Yellow fever and malaria (firsts)

Gorgas 1902: "I look forward in the future to a time when yellow fever will have disappeared entirely as a disease of mankind."

Panama - repeated fumigation

(s) All houses Panama failed, Gorgas concentrated on anti-larval work

Aedes aegypti for yellow fever -

Separated yellow fever from malaria

Anophelines natural foci

Aedes aegypti - artificial foci - artefacts never on ground - never in forests in Americas -

Attack on Aedes aegypti breeding very expensive - weekly inspection of every building, house, yard, compound, and boat

Panama success; O. Cruz - Rio de Janeiro

Liceaga Joe White

Overall Observation

(a) Reduction (not eradication) of Aedes aegypti in large endemic centers led to (i) Disappearance of yellow fever from endemic centers - rapid. (ii) disappearance of yellow fever from all of tributary areas - more slowly - (x) epidemiology of control confirmed Aedes aegypti as only vector, man as only victim

(b) Endemic centers were few and could be known by rapid surveys and consultation with local physicians

1909 Gorgas reiterated belief in eradicability of yellow fever

Definition of eradication

1913-14 Rose to Asia

May 1915 yellow fever commission, W C Gorgas: Committed to eradication of Y.F.

1916 survey Ecuador Peru Colombia Venezuela and coast of Brazil -

Only endemic center was Guayaquil

Noguchi introduced vaccine

Program - Ecuador Peru Guatemala (Brazil) Honduras, El Salvador Nicaragua and Mexico - Bacaramanga Colombia - 8 countries succeeded - Brazil

Brazil - 1923

Endemic centers - capital cities North Brazil - Weekly visits each house  
Pouring out water, removing trash, destroying containers, puncturing roof gutters, fishing water jars and cisterns.

Rockefeller Foundation repeated experience of Com. F. A. 1919-1922

1925 victory in sight - African - Study begun.

1926 Revolution

1924 Virus to monkeys

1927/1928 Victory in sight

Lengthened cycle and attempt at Aedes aegypti eradication

Rio outbreak 1928

Widespread dissemination

3 years to dominate

As we look back - first decade of Rockefeller Foundation work, including Noguchi's results were a failure -

1928-29 Public Health Administration in Rio turned the page back to 1901 - put faith in fumigation (flit rather than (s)) Lost almost a year -

Hindle and Aragao Vaccine 1930 - Rockefeller Foundation accepted yellow fever as major commitment in Brazil - FLS in direct charge

Obvious that Aedes aegypti regression curve flattened (lengthened cycle gave yellow fever in Recife 0.8 actually 26%)

Obvious that yellow fever regression to zero was only apparent.

FLS

Learn to think like Mata mosquito

Decided to make Aedes aegypti reports, the end product of yellow fever expenditures as certifiable as the bank account.

New low level approach Aedes aegypti house capture yellow fever viscerotomy

Aedes aegypti eradication 1933 but viscerotomy already 1931 - endemic yellow fever and jungle yellow fever

Endemic yellow fever liquidated 1934

Jungle yellow fever 1932 - 1933

Then 1934 to 1940 Wave, Vaccine 17 D 1936

Fch vaccine - Basis of choice

Mass vaccination      Small Pox

Eradication of Aedes aegypti - Spread of USA, etc.

Introduction of DDT

Local Resistance DDT

Anopheles gambiae

Yaws

Small Pox

Malaria

Yellow Fever Lecture Notes - Harvard 1962

Yellow Fever and Eradication concept

Big news in Yellow Fever

U.S. joins up in war against Aedes aegypti 3 questions What is Aedes Aegypti?  
Eradication? Yellow Fever?

1. What is Aedes aegypti?

3 slides - urban vector of yellow fever and other viruses

2. What is eradication?

Eradication is the most important justification of International Health -

Evolution from notification and quarantine to

Eradication and seeking out seedbeds of infection.

Yellow fever aided in discrediting Eradication; contributed greatly to  
Rehabilitation.

What is Eradication?

Definition Ex radix

Eradication an absolute

Does not recur in absence of preventive measures unless reintroduced:

Local state national regional global

Eradicate Error

Eradicate Hunger

Congenital syphilis

What is Yellow Fever?

Yellow Fever - as human disease

Onset - fever headache

body pains - active congestion

nausea - anxiety

Fever and pulse disproportional

24 hour lull after 48 to 72 hours

fever, albuminuria -

passive congestion, hemorrhage

icterus, anuria

Death - 4 to 7 days (Range 3 to 10)

Mortality 50 to 60% of classical cases - Real mortality based on infection

5 to 10% - mild cases

Picture of Severe infection

followed by severe intoxication

Symptoms per se not diagnostic

Course and timing important.

Death or complete recovery - 2 slides pathology 2

Permanent immunity - no second attack

Epidemiological Data:

Short incubation period

Short period infectivity

no carrier state

No chronic cases

Vector Aedes aegypti - external incubation 9 to 12 days (Davis 4 days)  
Infected for life - no transovarian infection -  
Effective infection 6 weeks

#### Etiology

Small virus - not known to exist in nature except in unbroken chain of acute vertebrate infections (Primates and marsupials) caused by bite of previously infected mosquito vector.

First arbovirus - more intensive study than any other virus  
Monkeys Marsupials \ best prototype  
Chick Embryos - Very young chicks  
Mouse brain - tissue culture  
Viscerotropic ) Viscera -  
Neurotropic ) C.N. - Yellow fever encephalitis may be fatal.  
Different incubation periods

Virus variable in cultures  
17 D vaccine mutant  
(Non-reproducible)

All strains homologous!  
Neutralization Test - in practice very reliable in spite of B. virus group overlap.

Distribution of endemic yellow fever  
Before 1900  
American 1900 to 1931 Slide America  
Africa 1900 to 1931 Slide Africa

Yellow fever as a Zoonosis Jungle Yellow Fever  
Primary in primates of forest - Marsupials -  
Man accidental infection - no different from Aedes aegypti yellow fever

#### Hosts

All primates apparently hosts  
When infected  
Susceptibility varies but susceptibility not correlated with enzootic efficiency -  
Americas - catus - spider Some susceptible  
howler - marmosets  
Africa - Bush babies monkeys None susceptible  
Asia - Rhesus and Cynomologus All susceptible

Vectors (Haemogogus spegazzini 3 slides 3  
( equinus  
Americas ( mesodentatus  
( Aedes aucocelenus  
( Sabethes chloropterus

Africa Aedes africanus  
Aedes simpsoni

Asia Aedes albopictus

Enzootic and ) Same factors of relationship virus vector non-immune host  
Epizootic ) as govern endemic and epidemic Aedes aegypti human yellow fever.

Yellow fever distribution after 1932

Americas slide  
Africa slide

Yellow fever and eradication

Eradication concept after Pasteur

Yellow Fever before 1900 - no cure, no prevention, safety in flight

Mississippi Valley 1878

US Yellow Fever Commission 1879

Carlos Finlay 1881

Reed et al 1900

Gorgas Havana 1901

US Army Commission

Key Center Eradication - Aedes aegypti Reduction in large cities only

Gorgas 1909

Rockefeller Foundation chartered 1913

Threat of Panama Canal

Rockefeller Foundation Yellow Fever Eradication

1915 - 1925 success

1925 African Adventure

1928 Pub - Virus to Asian Monkeys

Transmission Non-Aedes aegypti

But 1926 - military epidemic - surprise - led to attempt to eradication

Aedes aegypti Parahyba

1928 - Rio de Janeiro

1929 - Socorro and Guasapati

Yellow Fever 1928 - 1931 Slide

Recife 1929 - Not able to withstand Bombardment with virus

Situation Brazil end of 1929

Yellow fever program had failed! Eradication concept discredited

Anopheles gambiae - 1930 missed

Why cause (1) Inadequate attack on Aedes aegypti?

(2) Unknown mechanism of survival?

Both Aedes aegypti and yellow fever virus survived below threshold of visibility!

Reorganization: FLS personally responsible - From the top

FLS 3 months - maps, itinerary, routine oiling foci.

Learn to think like inspector SFA 52 - Explosion in Nichteroy

Search for low level incidence - lowering thresholds of visibility -

(a) Viscerotomy for yellow fever

(b) Adult captures for Aedes aegypti

Results showed (a) Inadequate attack on Aedes aegypti; but because of limited area of attack on Aedes aegypti, not in Key Centers

With lowered thresholds Visibility

(a) 1931 - Endemic silent yellow fever NE BR.

Key center method not applicable

(b) 1932 - yellow fever without Aedes aegypti - Key

Center method not applicable

1933 Jungle yellow fever Brazil, Bol., Colombia, Venezuela

(c) 1933 - Aedes aegypti disappears port cities  
Importance over shadowed by jungle yellow fever, etc.  
Rockefeller Foundation Yellow Fever eradication then had failed because of  
2 unknown mechanisms of survival!

Silent endemic yellow fever eliminated by village and rural anti-Aedes aegypti  
measures - the end of Aedes aegypti yellow fever August 1934 but not eradicated.

Roots of yellow fever infection in forests - 1933

How important is jungle yellow fever?

What measures should be taken?

In spite of previous non-recognition

jungle yellow fever important in its own right - young mans disease

the engaged young mans disease 1932 - Sta Cruz de la Sierra - Aedes aegypti

(Attacks both sexes and all ages among Indians in forest

House and Work / Forest.

Attacks mostly adult men - lumber and chicleiros and materos

1934 - 1940 Cel. Ponce 7 slides

1935 - Teofile Otoni

1936 - Figueira - Cambara

1938 - Infectious cases Rio

Retrospective - Rio 1928 - Socorro, Guasapati 1929. Slide endemic area and towns

Not only was jungle yellow fever a threat to cities and towns but was important  
for rural populations - no cure, no prevention - stay out of infected forest  
and starve. - Estimated 15000 cases Brazil 1938!

Measures taken

(a) Aedes aegypti eradication for cities as permanent protection of entire  
urban populations

(b) Vaccination for individual protection - Rural populations

Vaccination First

Finlay believed he was giving mild infections ! (Protected; did not protect;  
infected)

Killed virus vaccine Rio - 1929

Later animal tests

serum virus 1931

modified viruses

tissue culture and serum - Heterologous Sera

Fch neurotropic - Syarification - Failed in Brazil

17-D 1936 - 1937 5 slides

Use in field 1937 - 1942

Reduced antigenicity

Serum Hepatitis

Postvac Encephalitis

Post-Vac Encephalitis with Fch Neurotropic vaccine Costa Rica 1951 Nigeria 1952

Choice of vaccines

Vaccination

Americas - Rural areas - Travelers

Africa - Urban and rural



Aedes aegypti Eradication Second

Eradication not planned Slide  
Careful administration  
Complete coverage  
Oiling of foci  
Adult captures for missed mother foci

Eradication discredited 1929; recommendation to decentralize to local health units.

1934 proposal to eradicate in Brazil

Aedes aegypti, not yellow fever, focus of attack.

Cities held on monthly cycle - 3/4 men for suburbs.  
Peripheral expansion from each eradicated center (Soper's Law)  
Interior towns, villages, rural areas -  
Cities of South Brazil, including Sao Paulo, where yellow fever never occurred.  
Paraguay Bolivia, Peru, Colombia, Venezuela, Cuba USA

1939 - Six states and Rio de Janeiro

1941 - Brazilian objective eradication!

PAHO 1942 - Bolivian resolution

1946 - Reinfestation Brazil

PAHO 1947 - PAHO resolution Brazil

First official international eradication program

Brazil carried early load

Soper's Law of Peripheral Expansion of eradication effective internationally as well as internally.

Yellow Fever Helps -

Distribution 1946 - 1953 1 slide

(a) Panama Mexico 1948-58 2 slide

1951 (b) Sto Domingo de los Colorado 5 slides

(c) Trinidad Caracas 1954 - 3 slides Trinidad and Caracas first reports since 1914 Long apparent absence no index of safety

(d) 5 to 8 countries each yr. 4 slides

(e) Since eradication 1947 resolution all countries on the mainland except Canada, USA, El Salvador, Chile Uruguay

DDT eases load; resistance of Aedes aegypti.

Soper's Law - Against USA 1954 - even though not of primary concern - Slide

1956 Aedes aegypti situation.

1958 - Brazil 1942

1959-1960 - Mexico

Mexico 1961 five year limit

1962 US joins up.

US decision - not based on increased threat Yellow Fever, Dengue, encephalitis and other viruses; but based on recognition of right of other nations which have eradicated Aedes aegypti to be protected against reinfestation from our cities and ports.

New principle in International Health practice; US joined in 5 year vote in 1962 against 2 laggard American nations in Small Pox eradication.

By-products of Aedes aegypti eradication

Anopheles gambiae Brazil 1939/40 - missed in 1930-31  
Egypt 1944/45

Rehabilitation of eradication concept  
1947 US National Malaria Eradication Program  
1950 PAHO Malaria, Yaws, Small Pox

Later WHO Malaria, Yaws Small Pox

1955 APHA endorsed eradication concept

USA - Poliomyelitis, Diphtheria, Tetanus, Whooping Cough (As Public Health problems! But experience will teach.)  
Tuberculosis Syphilis

We learned from Aedes aegypti and yellow fever

- (a) To lower threshold of visibility
- (b) to refine methods as zero is approached
- (c) the need for careful administration, meticulous checking, based on detailed records and complete coverage
- (d) the growth power of eradication through peripheral expansion.

Eradication is an increasingly useful concept as world shrinks and as Pan Am and World Health Organizations become more adept at coordinating preventive programs in all the countries of a region.

Just as part of a country cannot enjoy the benefits of eradication apart from other units, so no single country may safely relax to enjoy its own eradication efforts, so long as eradication has not been extended to those countries from which reinfection or reinfestation may come.

Yellow Fever in Africa vs Yellow Fever in America 5 cycle slides

Aedes aegypti in Americas domestic

Africa domestic and forest -

Prospect for eradication of Aedes aegypti in Africa?

Aedes (Stegomyia) simpsoni

Human to Human Vector invillages close to forest

Africa no Aedes aegypti outbreaks in central and Eastern Africa, no virus to Asia.  
FLS visit to Sudan 1936

Large outbreak in Sudan Slide. Africa endemic.

1940-

Ethiopia - 1959-60-61 62 - Simpsoni?

Still unknowns in yellow fever

Threat to Asia - greatly reduced in absence of Aedes aegypti in proximity to infected forests. (No urban yellow fever in central and Eastern Africa)

Monkeys susceptible - vectors available

Eradication of Aedes aegypti in Asia - hemorrhagic disease in Manila and Bangkok. -  
Final slide.