ENTOMOLOGY BRACH:
Overview of Activities

2 February 2004

CDC
CENTERS FOR DISEASE CONTROL
AND PREVENTION

Department of Health and Human Services (FTEs)

US Public Health Service

Centers for Disease Control and Prevention (~7,800)

National Center for Infectious Diseases (~1,070)

Division of Viral and Rickettsial Diseases

Viral and Rickettsial Zoonoses Br

Division of Vector-Borne Infectious Diseases (~150)

Arbovirus / Dengue / Bact. Zoonoses Br

Division of Parasitic Diseases (~150)

Office of the Director & Data Mngt Activity (35)

Parasitic Diseases Branch (50) + 77 = 127

Malaria Branch (47) + 19 = 66

Entomology Branch (18) + 25 = 43

CDC

CENTERS FOR DISEASE CONTROL AND PREVENTION

Entomology Physical Facilities

Five laboratories

- **-Molecular biology**
- **-Resistance/behavior**
- **-ELISAs**
- **-Chemistry**
- **-WNV**

Four insectaries

- **~1,400 sq.ft.**
- **-12 separate areas**
- **-2 infected vector areas**
- **-Emergency generator backup**
- **-24 hr Environmental monitoring**
- **-24 hr Guard/card key restricted access**

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WHO Collaborating Centers

- Malaria Sporozoite ELISAs
- Insecticide Resistance in Vectors
- Evaluation of Existing and New Insecticides
- Morphologic/Molecular Vector ID (proposed)
- Evaluation of Anti-malarial Drugs (proposed)
- Malaria Control (MB)
- Control/Elimination LF in the Americas (PDB)

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DISEASES	ACTIVITIES
Malaria	Intervention: ITNs, drugs
Chagas Disease	Insecticide resistance
Lymphatic Filariasis	Molecular studies
Leishmaniasis	Transgenics/Taxonomy
West Nile Virus	Population genetics
Trachoma	Vector surveillance
Toxoplasmosis & PCP	Vector biology

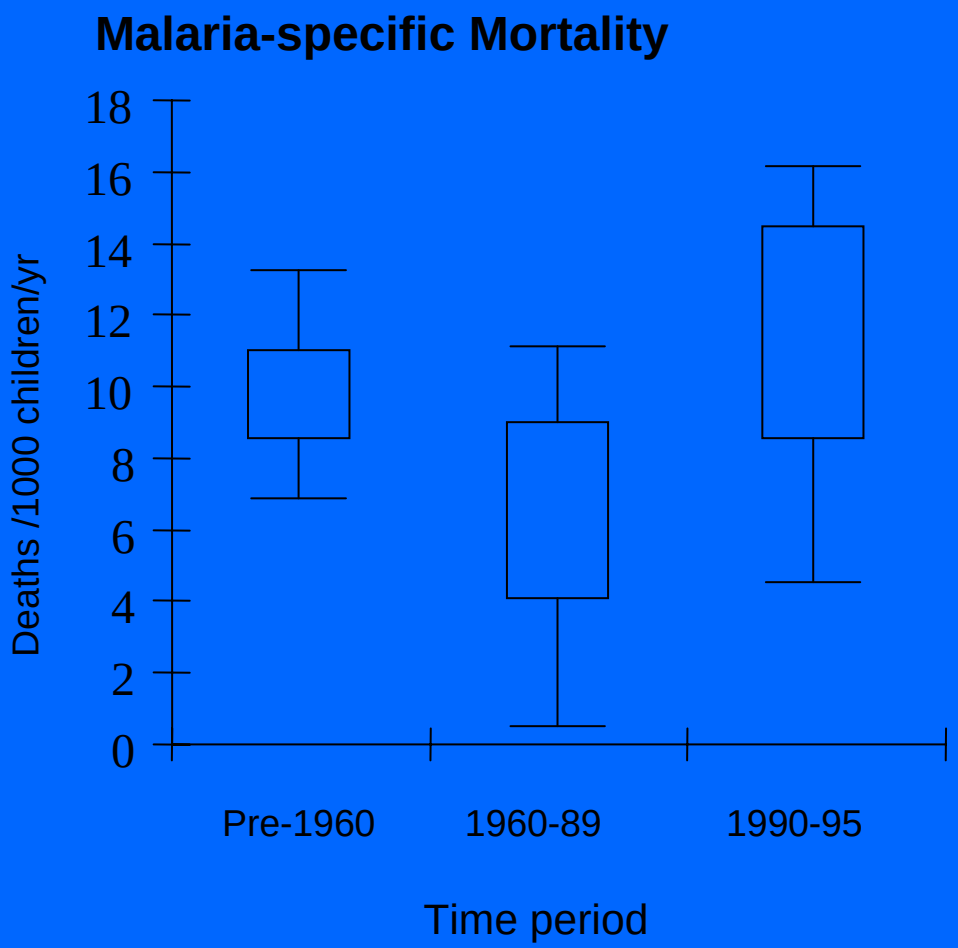
CDC's roots are in malaria AND vector control

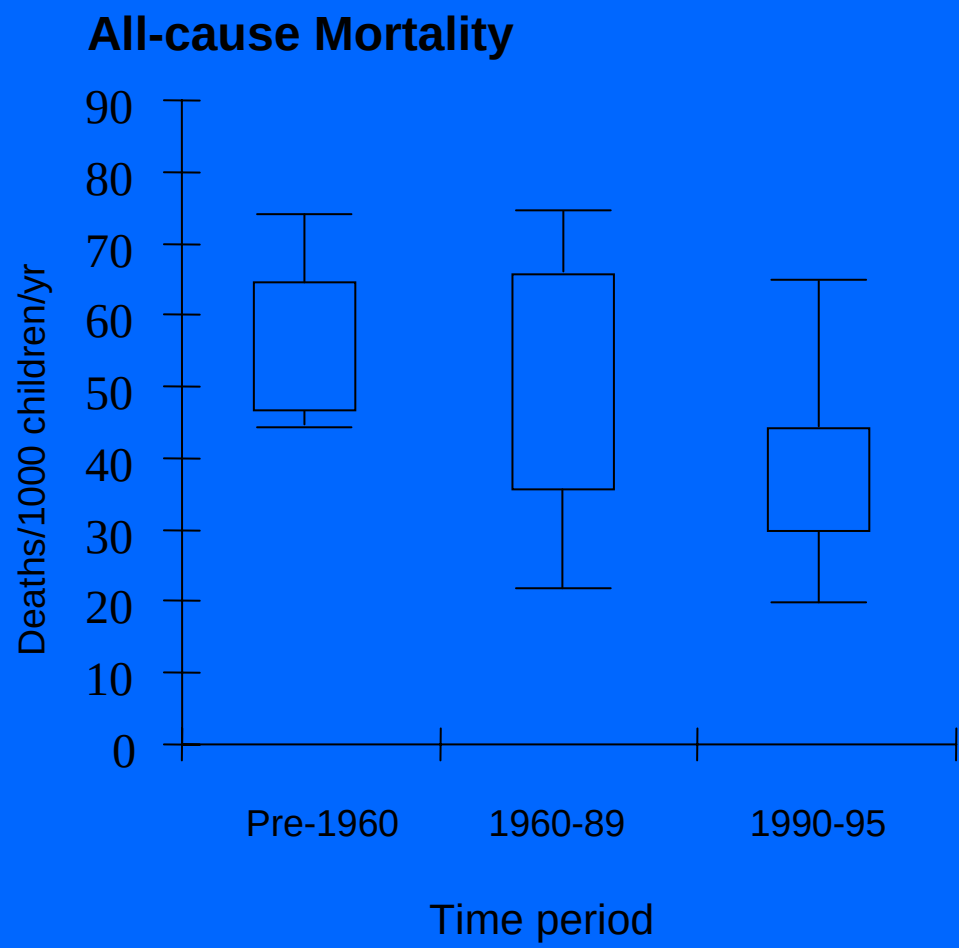
(1946) "…CDC opens in the old Office of Malaria Control in War Areas in downtown Atlanta…CDC has a mission to work with state and local health officials in the fight against malaria, still prevalent in several Southern states…"

Malaria: Worldwide

- 300-500 million new infections annually
- >1 million deaths annually, mostly in children in sub-Saharan Africa
- Responsible >1% loss in African GDP
- ~40% worlds' population at risk & increasing
- ~10,000 travelers from Europe, Japan and NA (~2,000) contract malaria each year
- No vaccine; increasing drug resistant parasites and insecticide resistant vectors limit control

Changing Malaria Mortality, sub-Saharan Africa





(**Source:** RW Snow, et al., *2001*)

Implications of Malaria in Mexico

- Imported cases to US from Mexico
  - 10-30/yr; mostly *P. vivax*; ~2% of imported cases
- ~20 million US travelers to Mexico/yr
- ~2 million visit malarious areas
- 2-week trip→CQ Rx→~$134 million/yr
- Visit malarious area - excluded as blood donor 1 yr
  - ~2 million travelers; ~5% would be blood donors
  - Loss of ~100,000 blood donors/yr

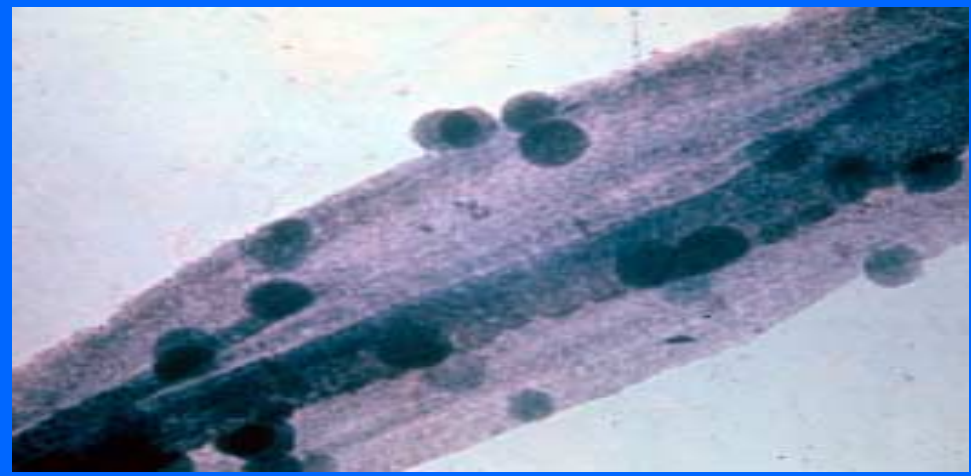
Malaria Vectors Worldwide

- Female anopheline mosquitoes
- Only ~20 of 200 *Anopheles* species are important vectors of human malarias
- How are vectors identified?

Need Replacement for HLC

Human landing collections

Vector Incrimination by Dissection



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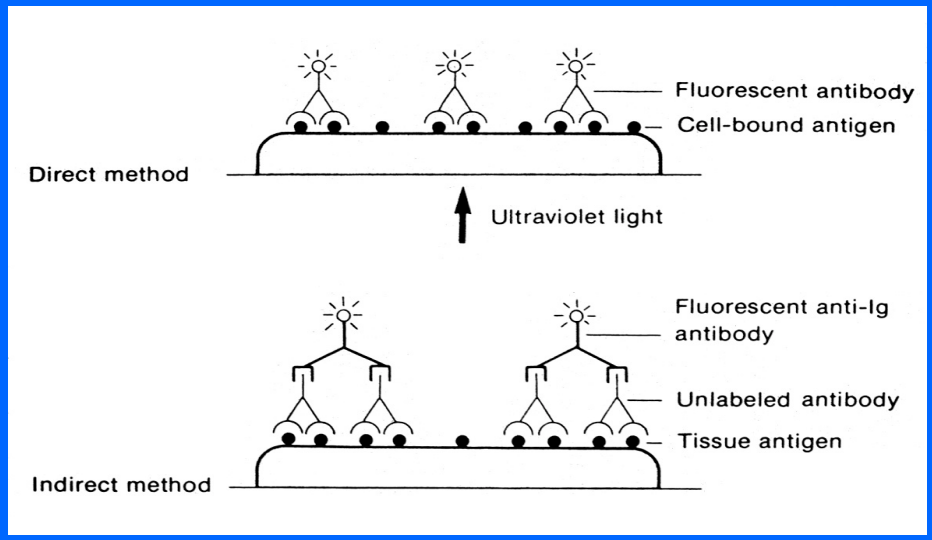
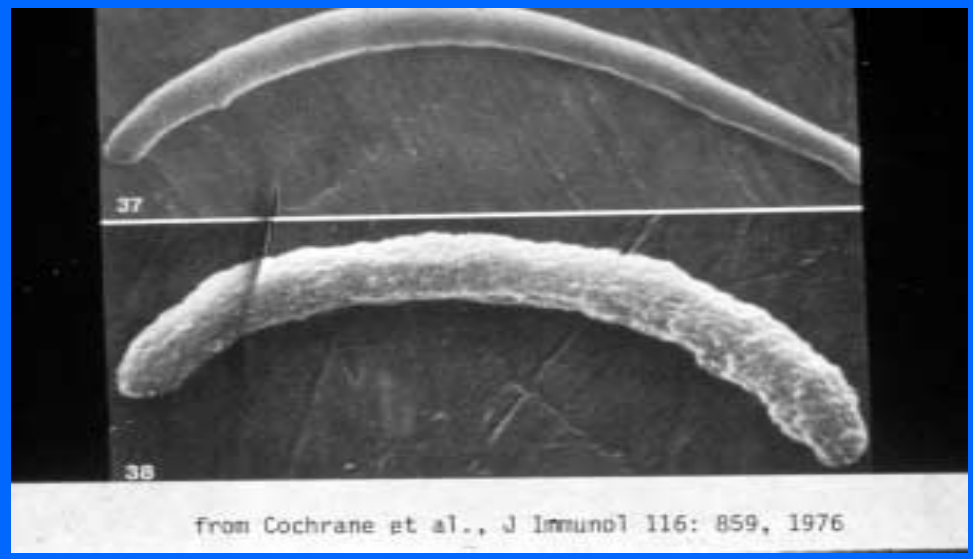
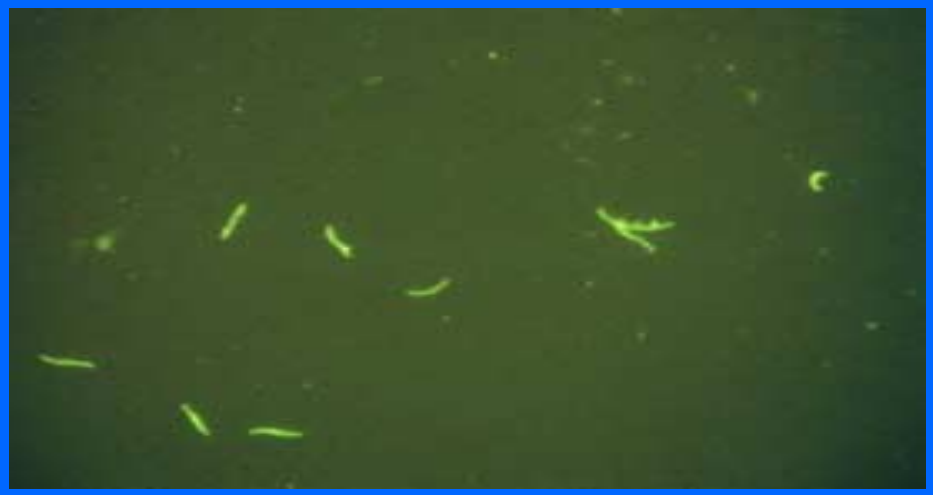
Species ID: IFA & Immunostain



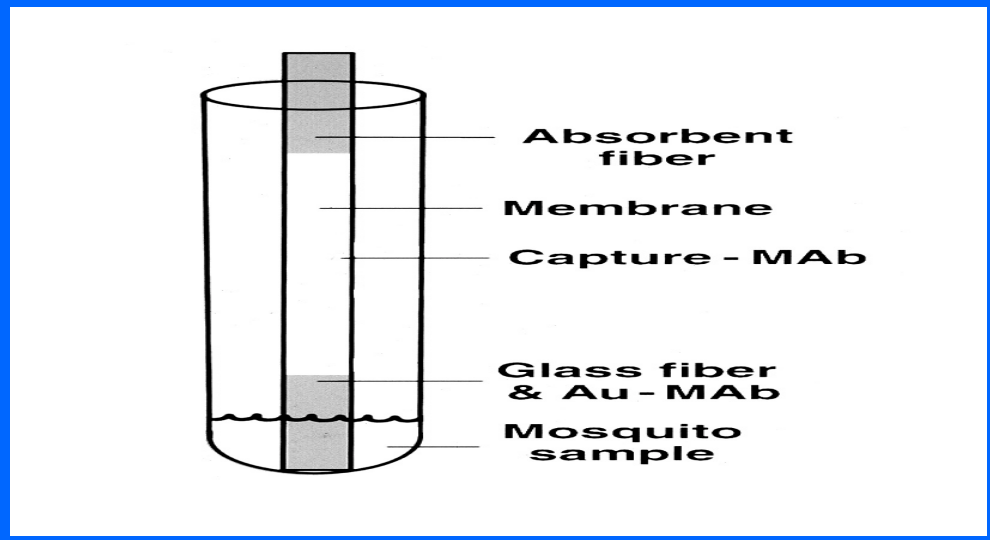


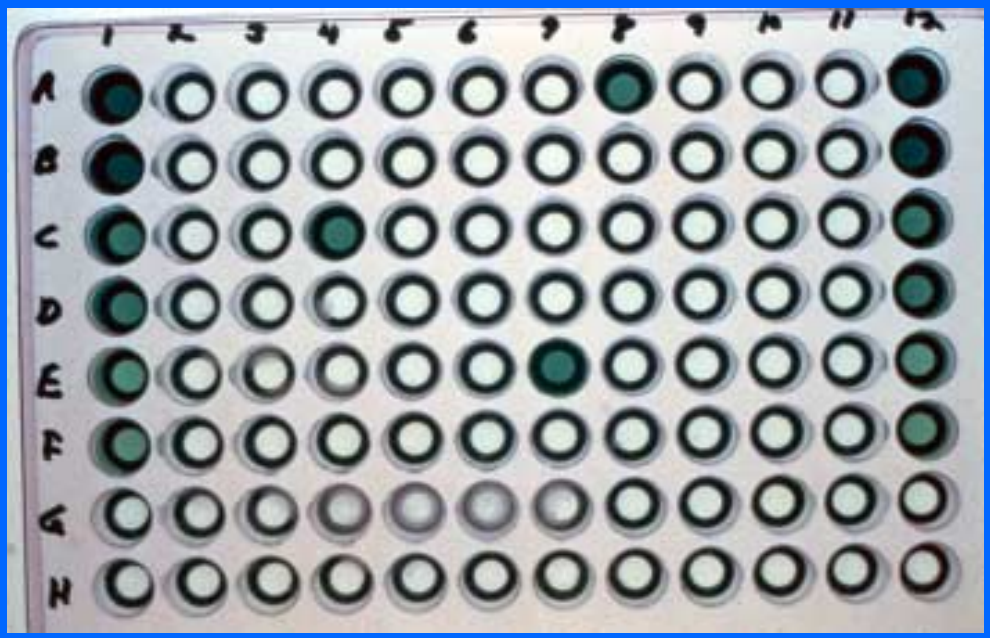
from Cochrane et al., J Immunol 116: 859, 1976



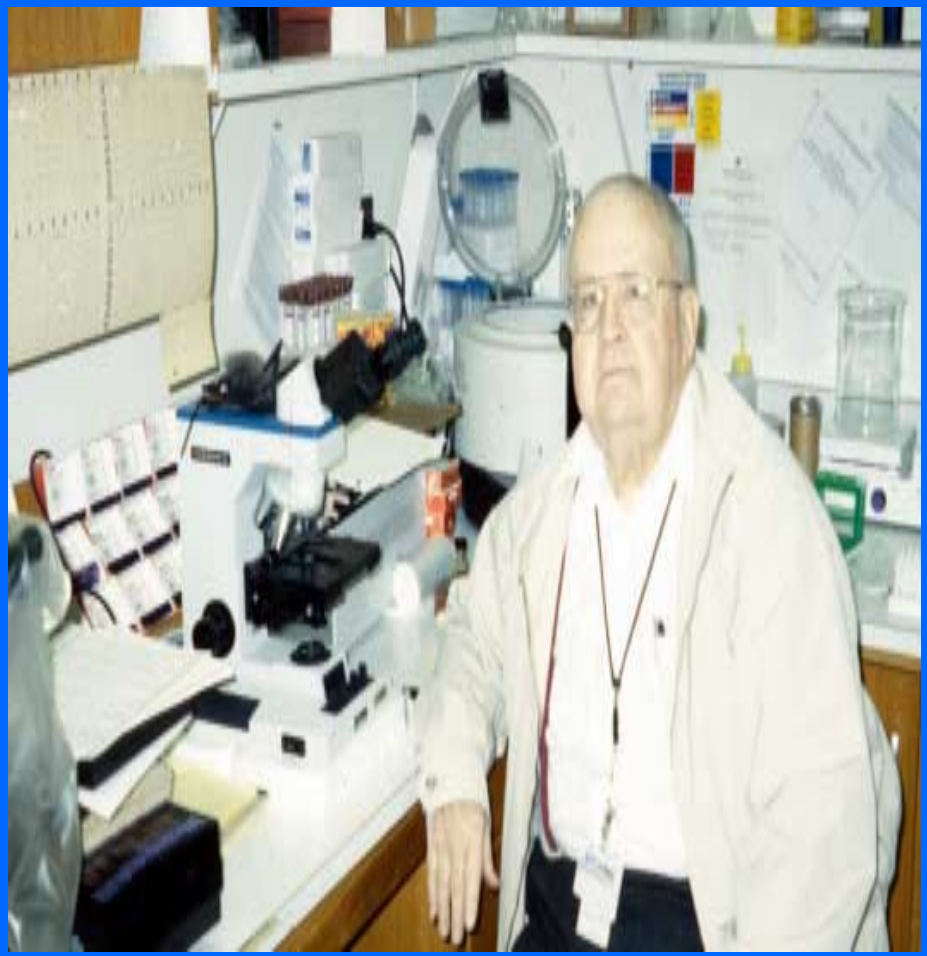
ELISA: >2M

VecTest: >45K



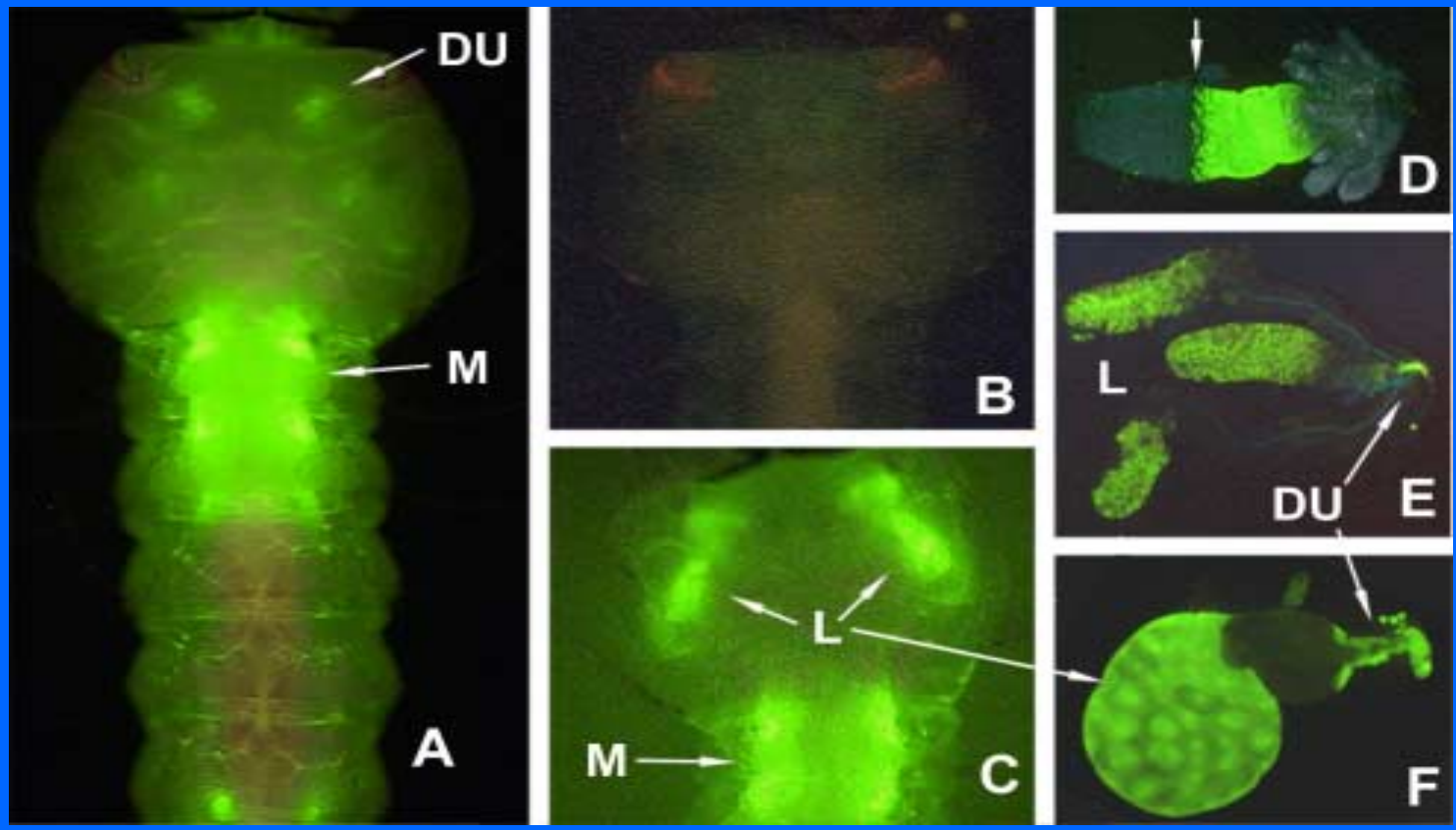


Malaria models: drug and vaccine efficacy testing & sporozoite production



Molecular Studies: Germ line transformation of *A. gambiae* with transposable element expressing GFP

Application: SIT to vector control at the IAEA



Malaria Research and Reference Reagent Resource (MR4) Center

MR4 Vector Reagents

- **Living *Anopheles* stocks (~50 species/strains)**
  - ***A. gambiae*** **(~20 + 2 in acquisition)**
  - ***A. stephensi*** **(2 + 3 in acquisition)**
  - ***A. quadrimaculatus*** **(4)** **- *A. dirus* (1)**
  - ***A. albimanus*** **(3)** **- *A. freeborni* (1)**
  - ***A. atroparvus*** **- *A. farauti* (in acquisition)**
- **Frozen *Anopheles***
  - **Individual specimens and bulk shipments**
  - **Genomic DNA of wild anophelines**

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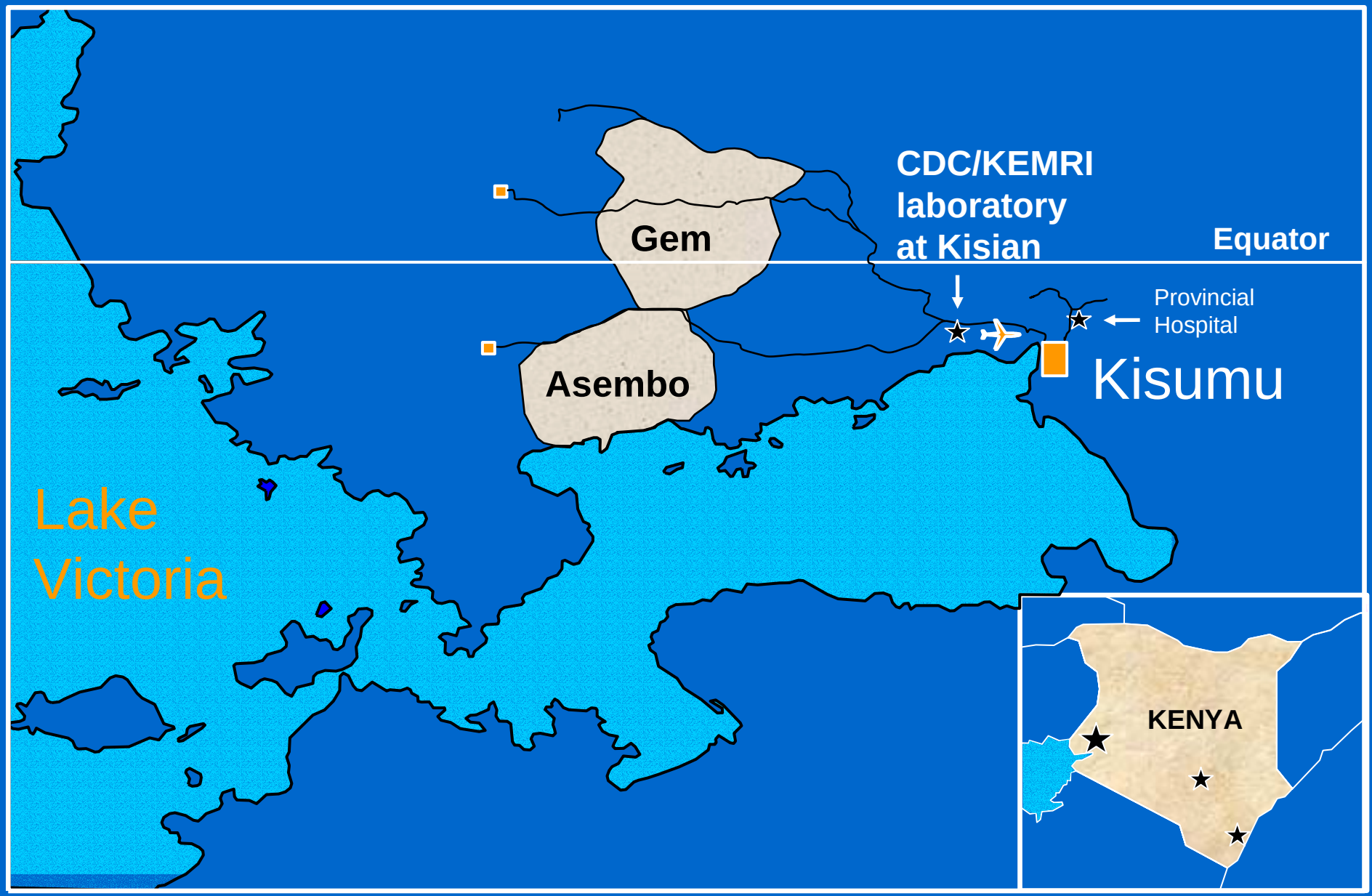
CDC/KEMRI Field Station Western Kenya




21/4/1999

CDC/KEMRI Field Station

Malaria: 4 strategies of Roll Back Malaria

- Vector control
  - Evaluation of treated nets, larval ecology
- Antimalarials/Case management
  - Drug resistance; Response to SP in HIV+
- Epidemics
  - Predictors of highland malaria
- Pregnancy
  - Prevention practices, immunology of placental malaria

ITN Distribution

ITN SUMMARY

38% ↓ Parasitemia
47% ↓ Severe anemia
35% ↓ Placental malaria
28% ↓ Low birth weight

ITNs

Mosquitoes

95% fewer *An gambiae*
90% reduction in transmission

Healthier pregnancies

Healthier children

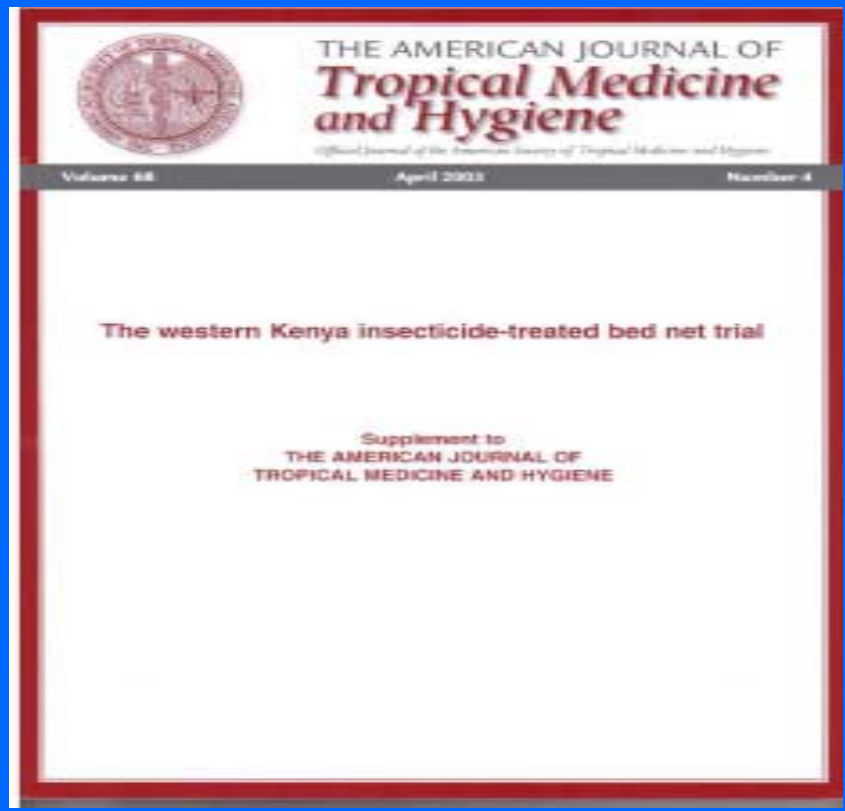
74% ↓ Malaria attack rate
Median time to 1st infection 4.5 →10.7 mo
60% ↓ Incidence of severe anemia
Improved infant and child growth
27% ↓ Sick child visits to the clinic

Improved infant and child survival

26% ↓ Infant mortality
14% ↓ Child (1-4yr) mortality

ITN Study Summary

- As cost-effective as childhood vaccines
- If ITNs were deployed in malarious Africa, ~400,000 lives would be saved annually

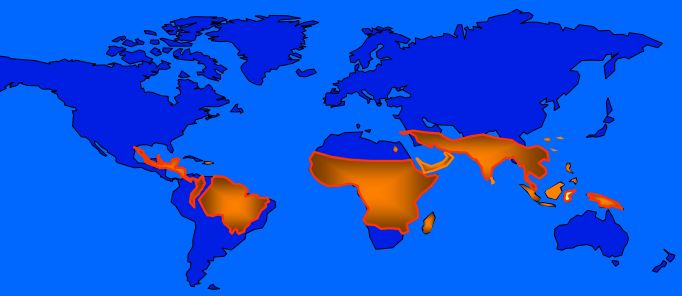


EB Chemistry Activity

- Insecticide treated bed nets (ITNs)
  - Efficacy Evaluations
  - New Treatment Methods
- Anti-malarial drug analysis
  - Resistance vs. compliance
  - Pharmacokinetics
  - QA of pharmaceuticals
  - Counterfeit drug detection

GC Analysis

ITN Bioassay



Analytical Testing Capability for all Available Anti-Malarial Drugs

Quinoline compounds:

- Quinine/ Quinidine
- Chloroquine
- Amodiaquine
- Mefloquine
- Halofantrine
- Primaquine

Antifol combinations:

- Pyrimethamine/ sulfadoxine
- Pyrimethamine/ sulfalene
- Trimethoprim/ sulfamethoxazole

Biguanides and Biguanide/ sulfa combinations:

- Proguanil
- Proguanil/ sulfone

Miscellaneous:

- Tetracyclines
- Clindamycin
- Atovaquone (+ Proguanil)
- Pyronaridine
- Azithromycin
- Artemisinins
- Benflumetol (+ Artemether)

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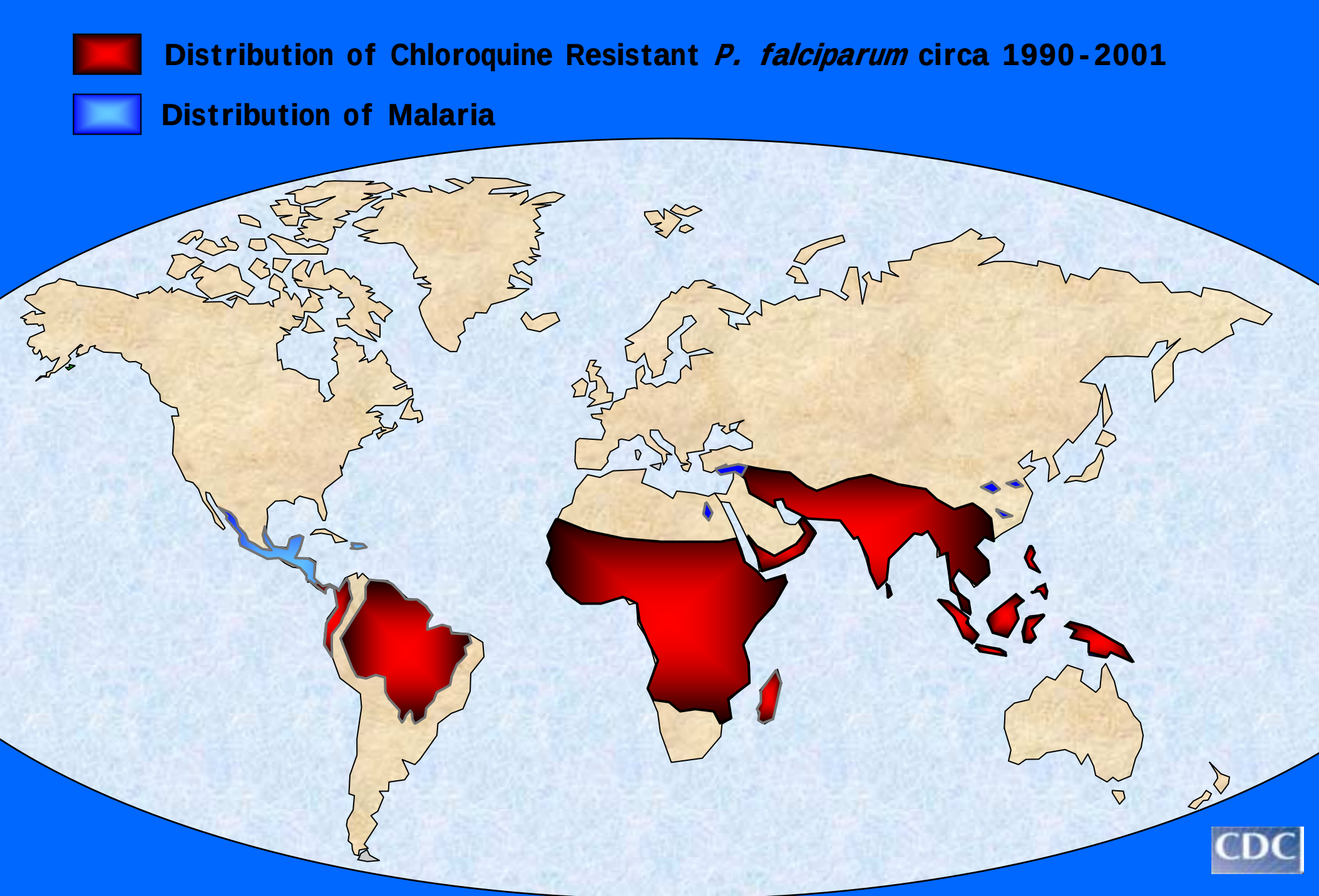
Distribution of Chloroquine Resistant *P. falciparum* circa 1990-2001
Distribution of Malaria
CDC

Malaria Therapy Drug Costs

Chloroquine or SP	**$0.10**
Mefloquine	**$2.84**
Artemisinins	**$3.70**
Malarone	**$35.00**

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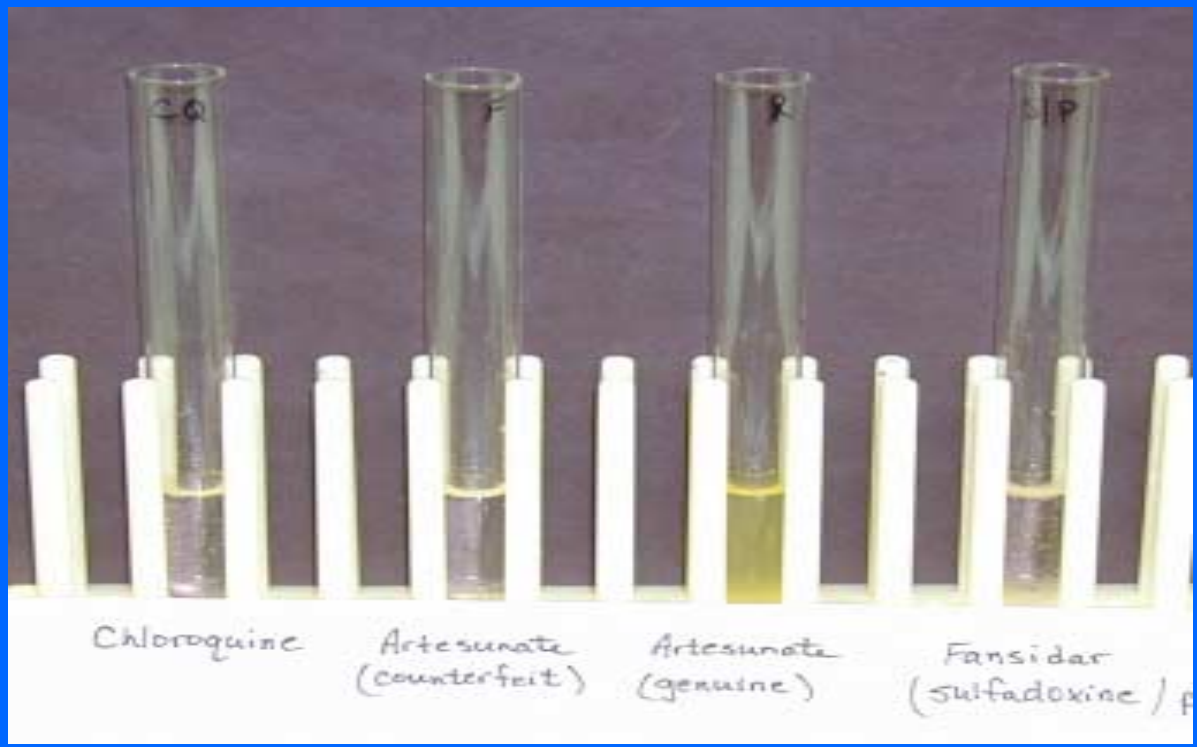


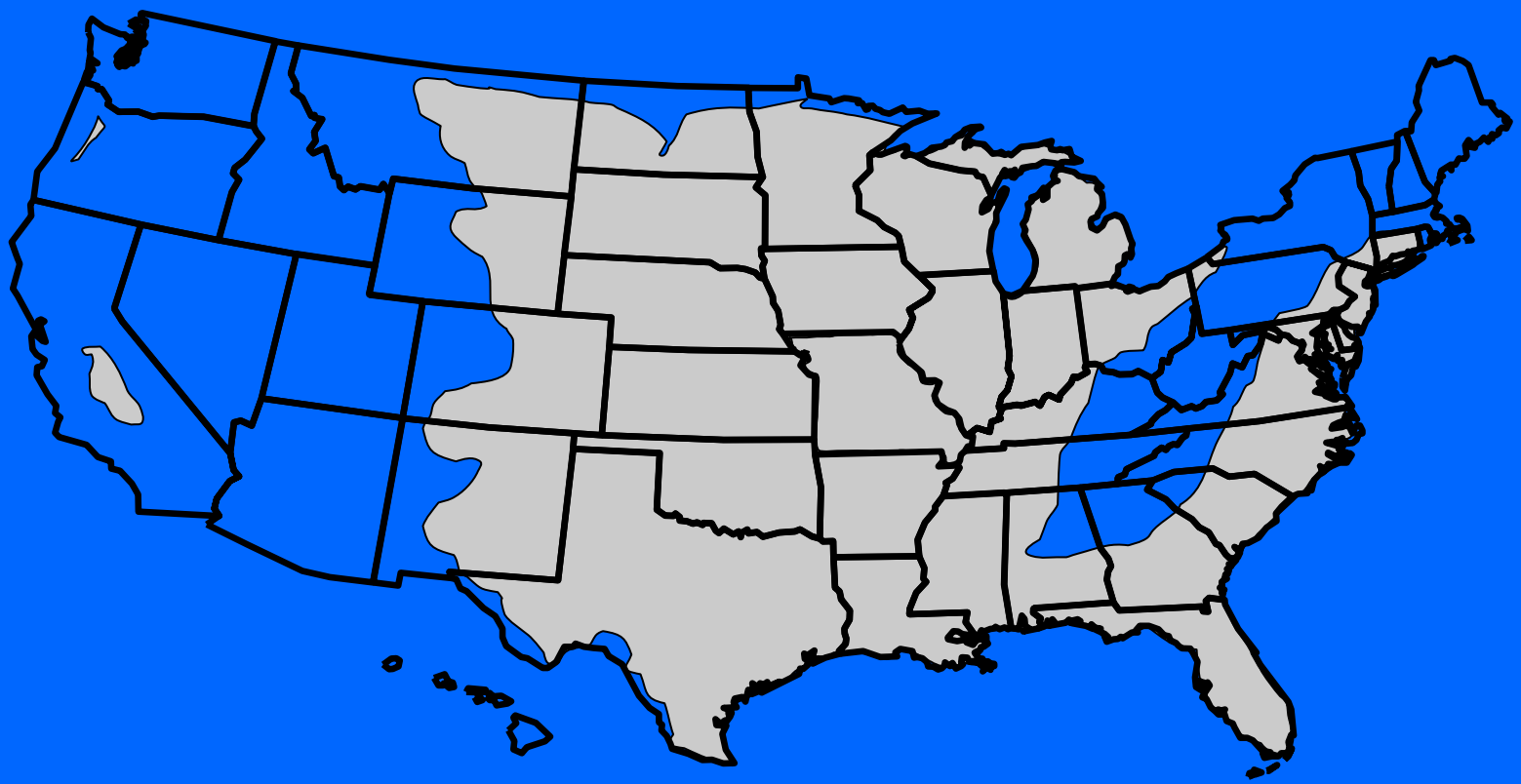
Assay uses two stable, inexpensive solutions
<10 minutes; >99% of tablet available for use

2000-01 Survey: No artesunate in 38% OTC tablets in Vietnam, Cambodia, Laos, and Myanmar (Burma)

Malaria in the US

- Most likely brought to the “New World”
  - *P. vivax* and *P. malariae* by European settlers
  - *P. falciparum* by African slaves
- Spread with migration of settlers
- By 1850, well established except
  - New England
  - Mountainous highlands
  - Inland deserts

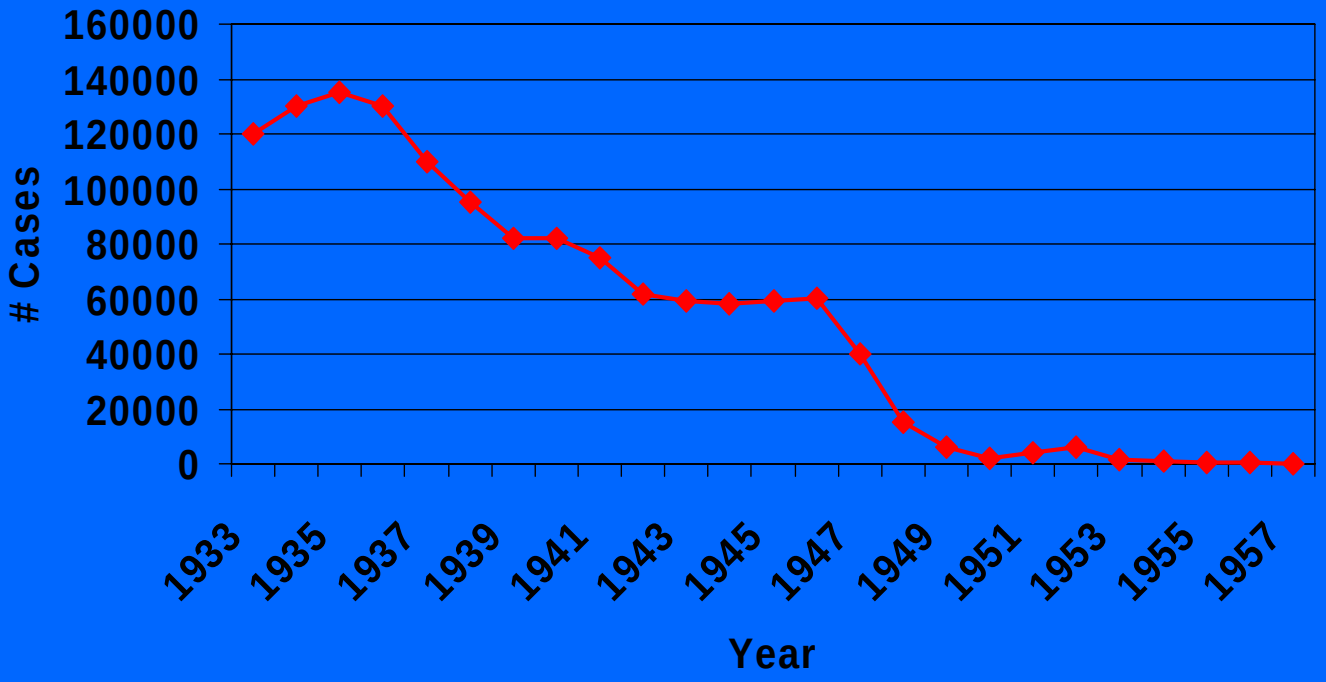
Endemic Malaria, circa 1882



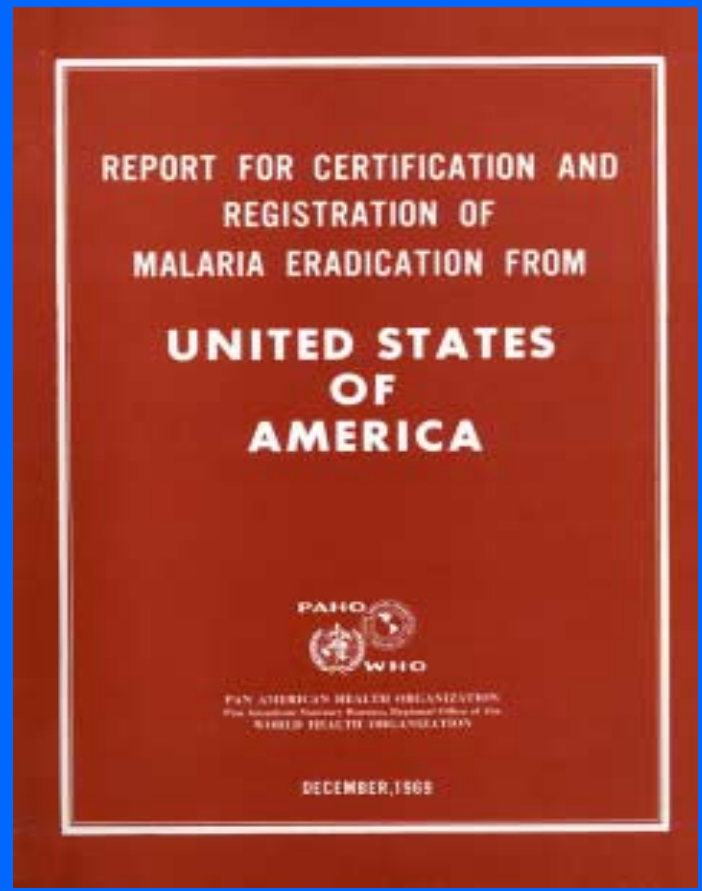
General Regression of Malaria

- Industrialization, rural to urban shift esp. North
- Drainage for agriculture & suburban development
- Access to health care; inexpensive drugs & DDT
- Socio-economic conditions, housing, nutrition

US Malaria Morbidity: 1933-57



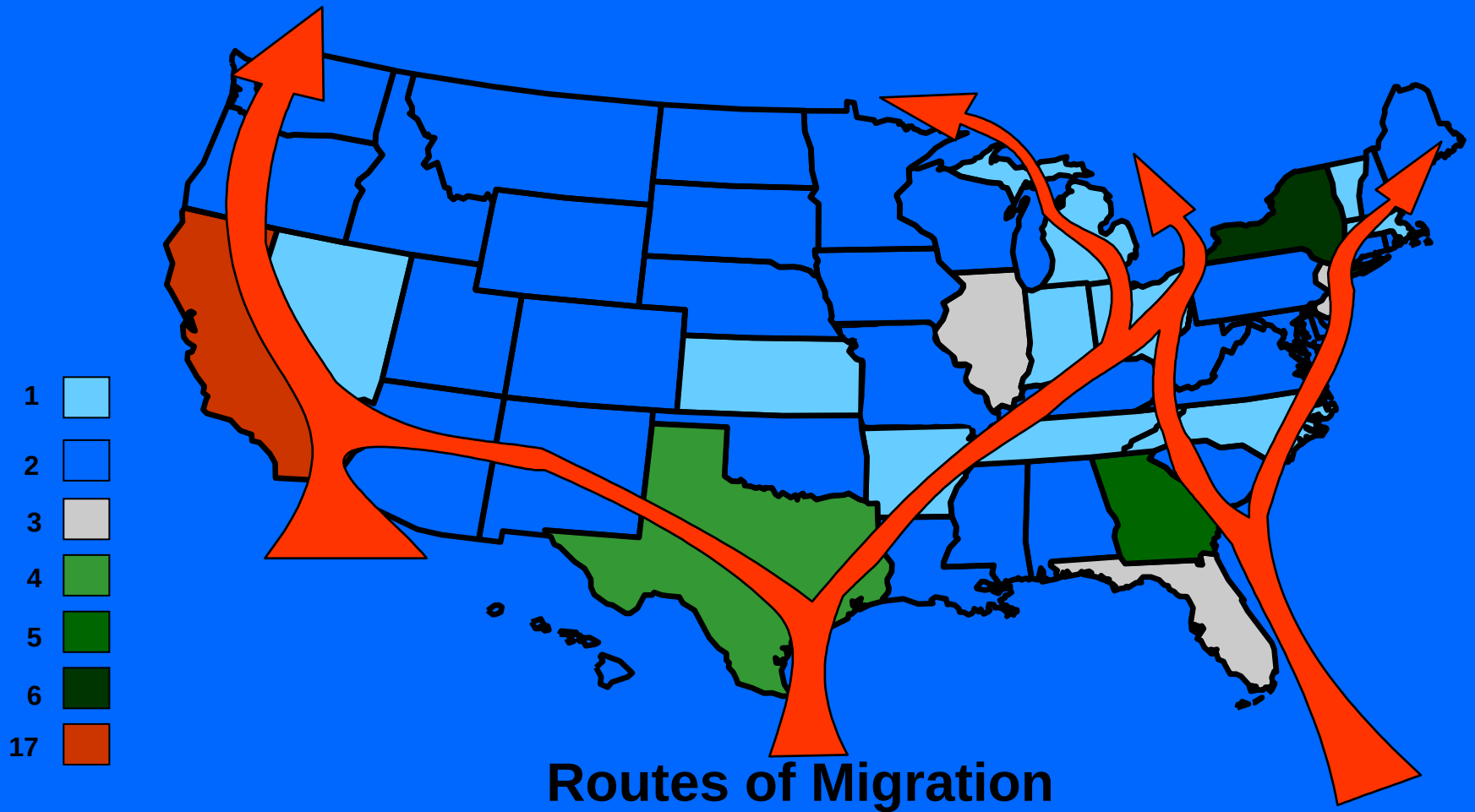
US Eradication: Dec. 1969



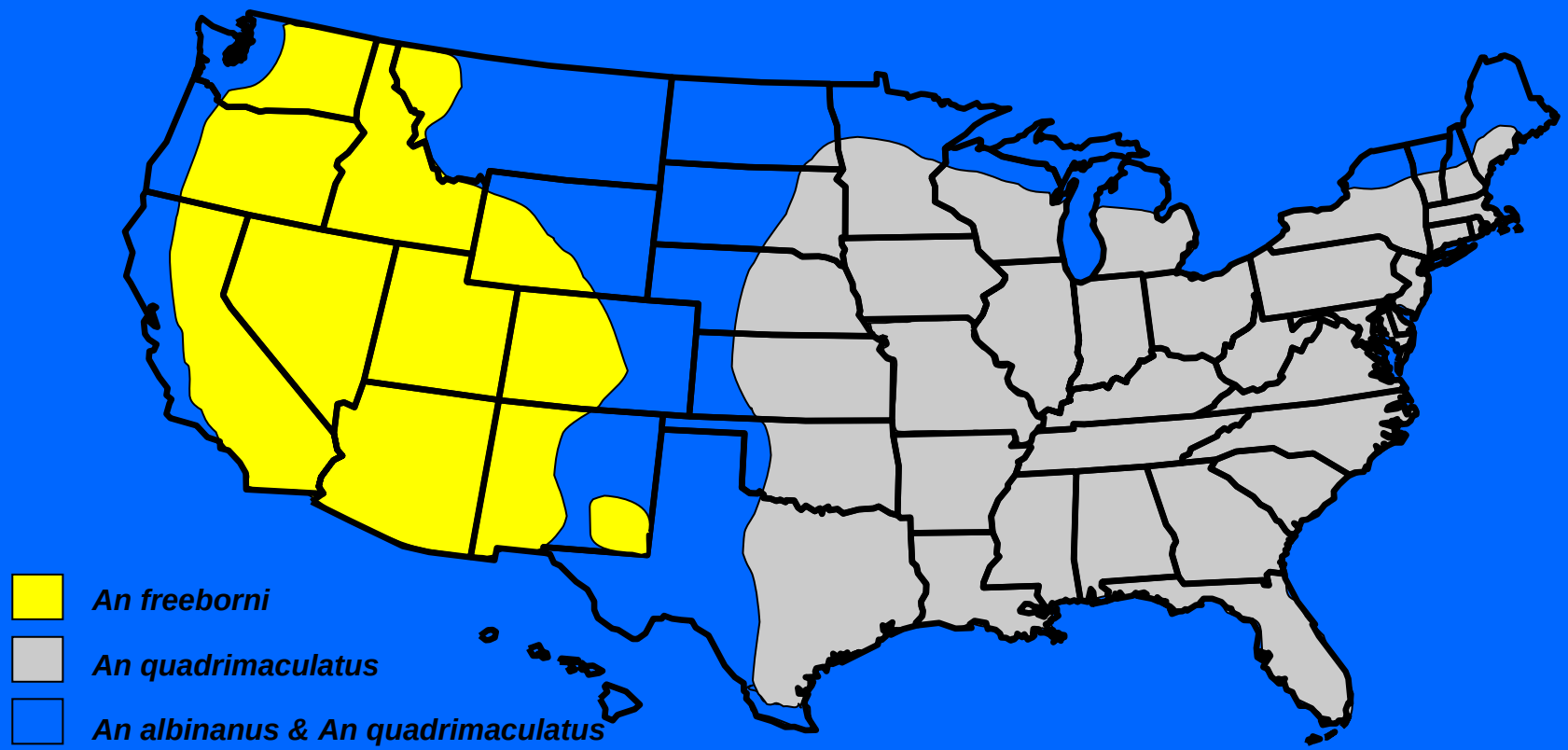
Continued mosquito transmitted malaria in the US because:

- Increased migration of peoples from endemic areas providing parasitic reservoirs.
- Continued presence of competent vectors.
- Conducive weather patterns.

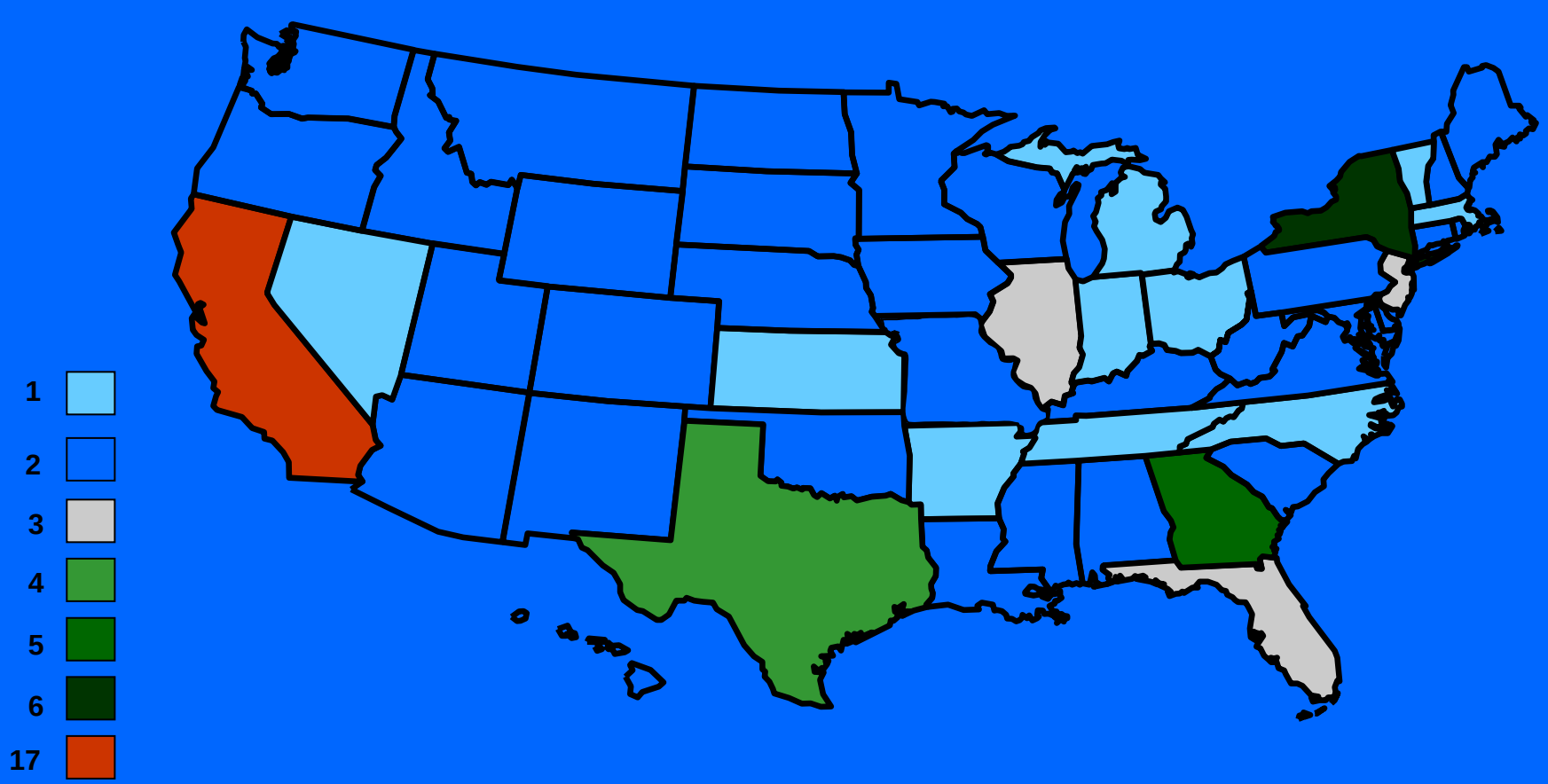
Mosquito-borne Malaria Episodes, 1957-2003



Potential Malaria Vectors in the US



156 cases in 63 separate outbreaks in 56 years



Palm Beach County 2003 Outbreak

- *Plasmodium vivax;* 8 cases
- Active transmission ~ 2 months
- Onset dates of July 12 – Sept 14
- All male, homeless to banker
- Age = 17-45 years (median = 37 years)

PALM BEACH COUNTY
Malaria Events

PALM BEACH COUNTY HEALTH DEPARTMENT
Environmental Health and Engineering

FLORIDA DEPARTMENT OF HEALTH

7th case Residence
Date of Onset 12/19

1st & 2nd case Residence
Date of Onset 7/2017/18

5th case Residence
Date of Onset 5/14

4th case Homeless camp
Date of Onset 12/12

3rd case Residence
Date of Onset 7/12

5th case Residence
Date of Onset 12/12

6th case Residence
Date of Onset 12/17

PURDY
CRESTHAVEN
HAVERHILL
MILITARY
KIRK
CONGRESS
FLORIDA MANGO
10TH
FEDERAL
LAKE WORTH
MELALEUCA
12TH
LANTANA
HYPOLUXO
KNOLLWOOD
MINER
BEACREST
GATEWAY
22ND
LAWRENCE
LE CHALET
OLD BOYNTON

Legend
- Malaria Events
- pbc_major_roads
- PBC_water
- pbc_natural_areas

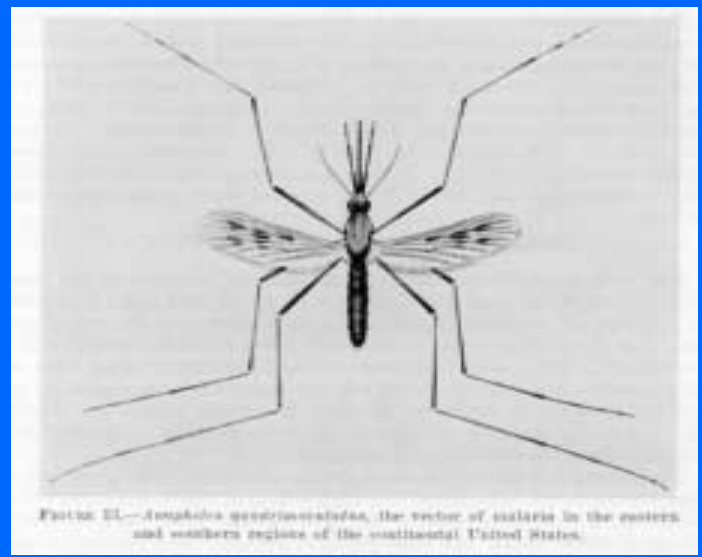
0 0.25 0.5 1 1.5 2 Miles

Malaria vectors in the Eastern US

- ***Primary Vector***
  - *Anopheles quadrimaculatus* Group (Faust, 1949)
- **Secondary Vectors**
  - *Anopheles punctipennis* - vector of *P. vivax* in California (Gladney and Turner, 1969)
  - *Anopheles crucians*
- Note: not all species of *Anopheles* are vectors of malaria

An. quadrimaculatus Group

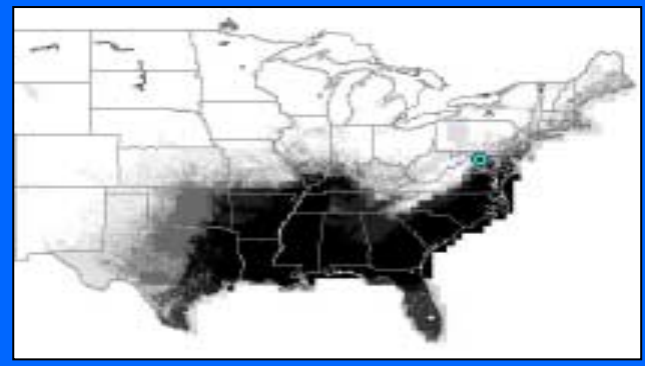
- *Anopheles quadrimaculatus* Say 1824
- *Anopheles smaragdinus* Reinert 1997
- *Anopheles diluvialis* Reinert 1997
- *Anopheles inundatus* Reinert 1997
- *Anopheles maverlius* Reinert 1997



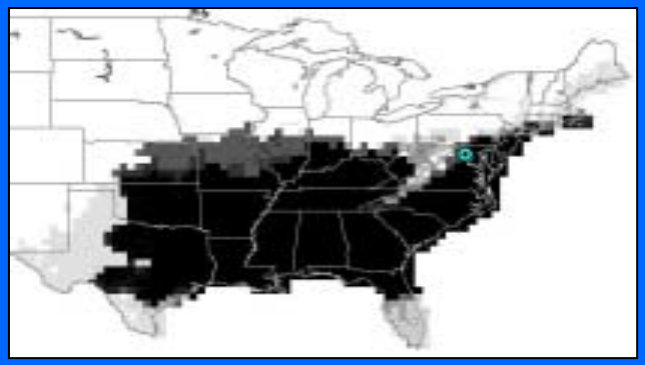
Predicted Distributions

An. diluvialis

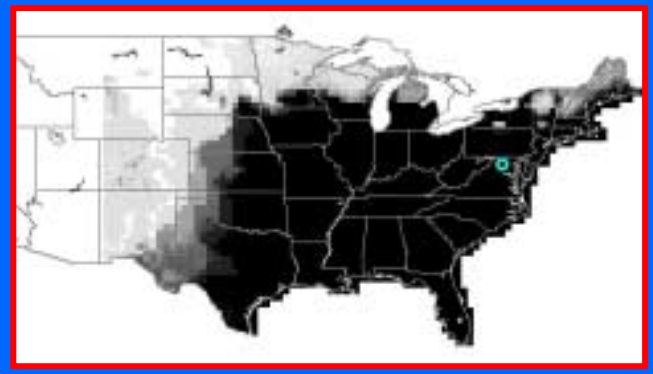
An. inundatus



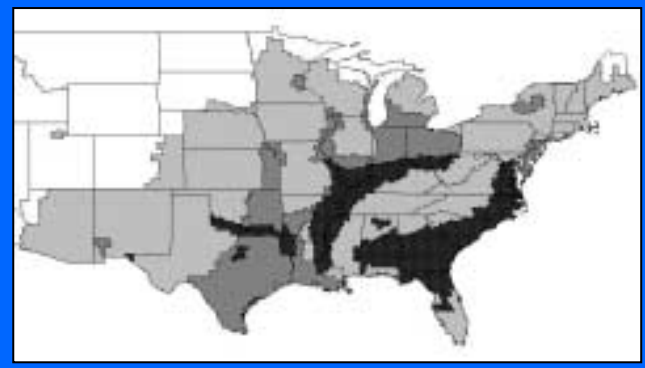
An. maverlius



An. smaragdinus



An. quad. sensu strictu



1850 malaria

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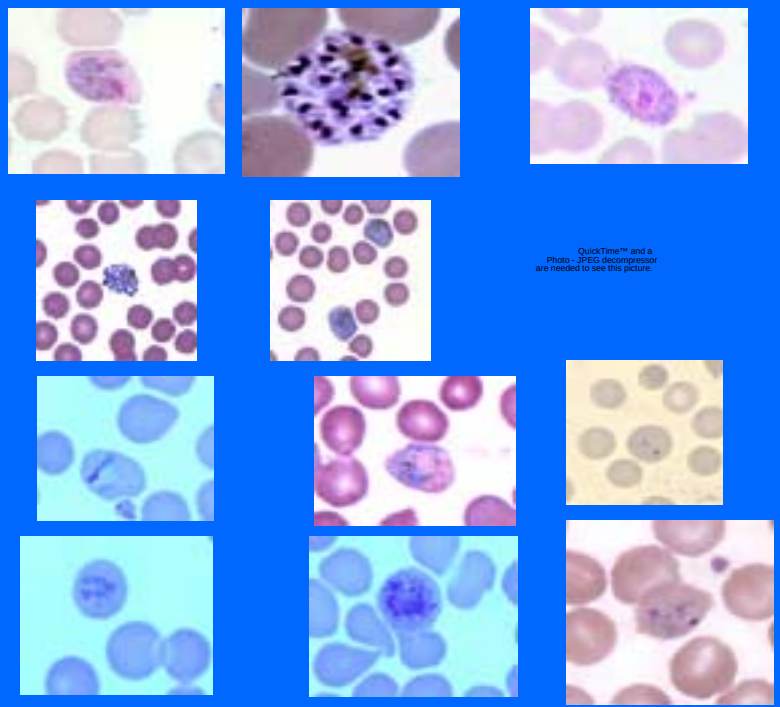
Laboratory Diagnosis of Malaria

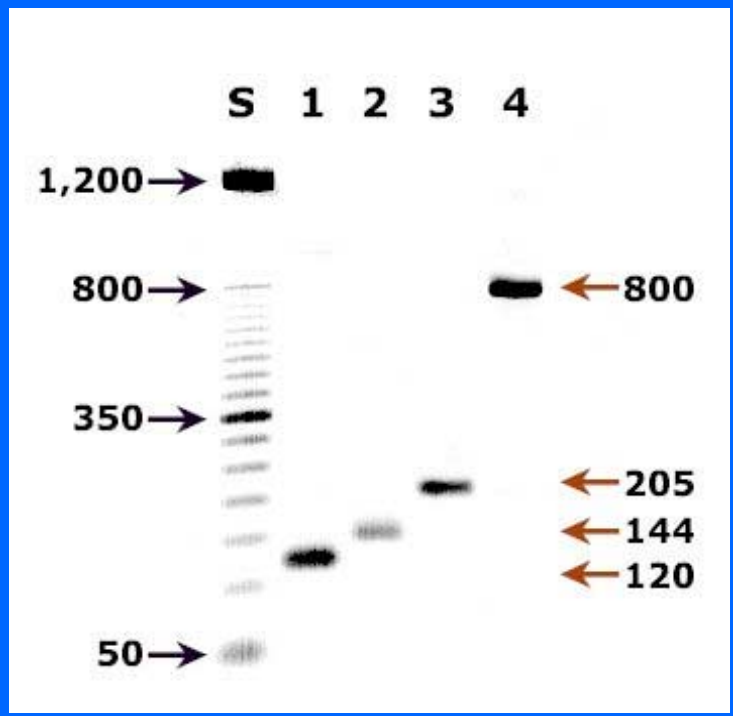
Microscopic Based Diagnosis

Giemsa Stained Morphology



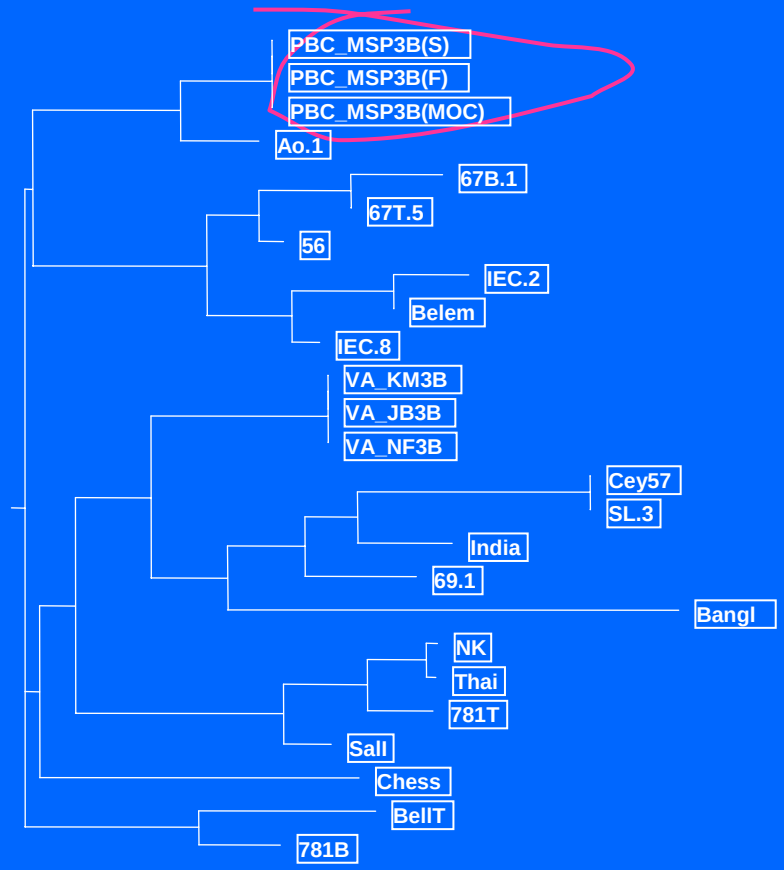
PCR based Diagnosis

rRNA Genes



Multi-locus Genetic Analysis of PBC *P. vivax*

- The MSP-3α and MSP-3β genes were 100% identical by sequence or RFLP.
- The CSP gene in all eight isolates contained type I (VK210) repeats and were identical.
- Conclusion: All eight *P. vivax* infections most likely originated from a single source of infection.



MSP-3β Phenogram

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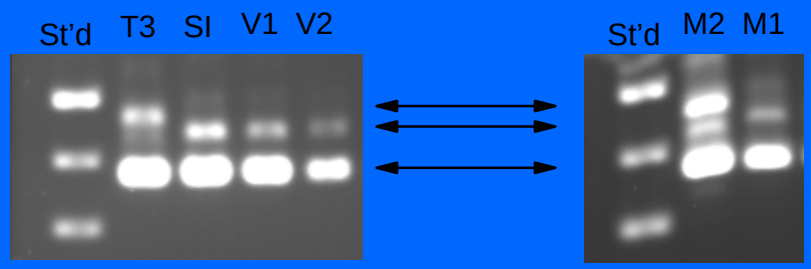
Origin of the PB County *P. vivax* Infections

- *P. vivax* S-type rRNA genes of New World type isolates have a deletion mutation.
- *P. vivax* ORF 470 gene has a nonsynonymous mutation that changes an isoleucine residue to a valine in New World isolates.

A- & S-type rRNA genes



ORF 470

Virginia_B ORF470	Q	F	E	R	T	L	L	I	V	N	E	H	S	Y	V	V	Y	L	E	G	C	T
Virginia_K ORF470	Q	F	E	R	T	L	L	I	V	N	E	H	S	Y	V	V	Y	L	E	G	C	T
Miami I ORF470	Q	F	E	R	T	L	L	I	V	N	E	H	S	Y	V	V	Y	L	E	G	C	T
Miami II ORF470	Q	F	E	R	T	L	L	I	V	N	E	H	S	Y	I	V	Y	L	E	G	C	T
New World ORF470	Q	F	E	R	T	L	L	I	V	N	E	H	S	Y	V	V	Y	L	E	G	C	T
Old World ORF470	Q	F	E	R	T	L	L	I	V	N	E	H	S	Y	I	V	Y	L	E	G	C	T

*Li J, Collins WE, Wirtz RA, Rathore D, Lal A, McCutchan TF. Geographic subdivision of the range of the malaria parasite *Plasmodium vivax*. Emerg Infect Dis. 2001 7:35-42.

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Will the US continue to have malaria transmission?

- Increased imported cases providing parasitic reservoirs?
- Increased migration of people from endemic areas providing parasitic reservoirs?
- Continued presence of competent vectors?
- Conducive weather patterns?

YES

The best way to prevent infection:

Acknowledgements

Entomology & Malaria Branches

- John MacArthur
- Monica Parise
- Scott Filler
- John Barnwell
- Alexandre Dasilva
- Louise Causer

The Mosquito Net – by John Singer Sargent

Mosquito Dissection Training