MALARIA: VACCINES AND CHALLENGING CASES

ASTMH UPDATE COURSE IN CLINICAL TROPICAL MEDICINE AND TRAVELER'S HEALTH

SEPTEMBER 28, 2024

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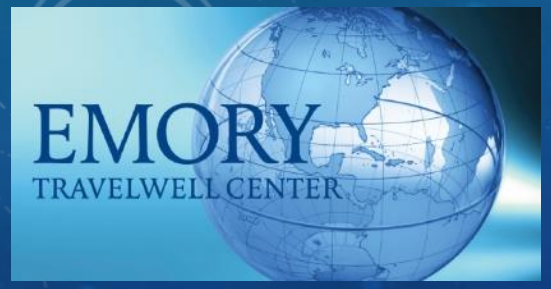
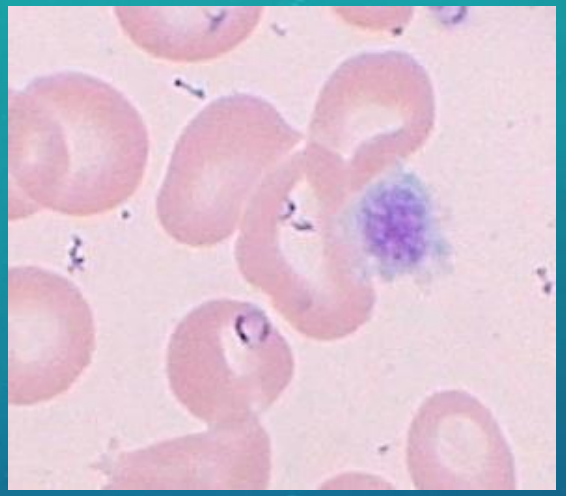
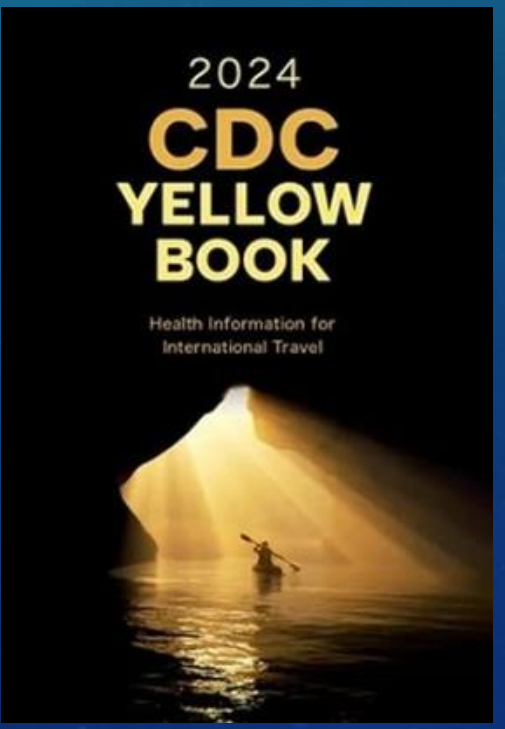


Overview and disclaimer

- Objective: To provide an update on malaria vaccines and present cases that demonstrate some interesting challenges in malaria prevention, diagnosis, and treatment in travelers
- This is a topic with frequent new developments
- Recommendations for prevention, diagnosis and treatment vary worldwide
- See CDC Yellow Book and references for details



CDC, Public health image library



Malaria: Illness and species

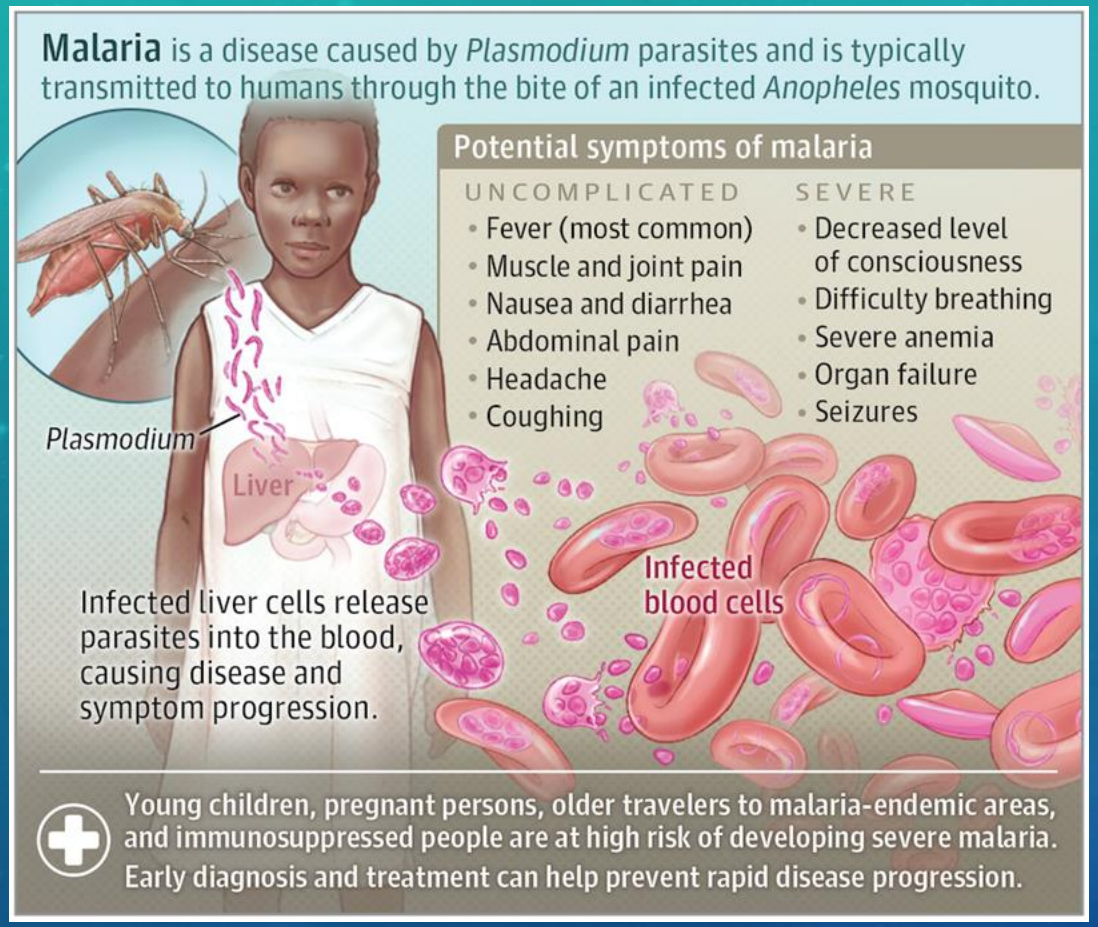


Table 1. Characteristics of Malaria Species Infections

Plasmodium species	Incubation period, d	No. of days between arrival to US and onset of symptoms (%)[a]		Hypnozoite stage	Geographic distribution
		<30 d	≥365 d		
P falciparum	9-14	96.4	0.1	No	Sub-Saharan Africa, South and Southeast Asia, Eastern Mediterranean, Western Pacific, South America
P vivax	12-17 Relapse: 6-12 mo (>2 y in some cases)	59.5	1.4	Yes	Similar to *P falciparum* and also present in the Korean Peninsula
P ovale	16-18 Relapse: 8-45 mo	47.5	7.5	Yes	Sub-Saharan Africa, Southeast Asia, Western Pacific
P malariae	18-40 Persistence for decades	54.8	0	No	South America, Asia, Africa
P knowlesi	9-12	No data	No data	No	Southeast Asia

Daily JP, Minuti A, Khan N. Diagnosis, Treatment, and Prevention of Malaria in the US: A Review. JAMA. 2022;328(5):460–471. doi:10.1001/jama.2022.12366
Walter K, John CC. Malaria. JAMA. 2022;327(6):597. doi:10.1001/jama.2021.21468

Pre-Travel case: Student in East Africa

- A 18 year-old college student seen in travel clinic with his parents in preparation for a summer program trip to Kenya and Tanzania. They come with a list of “required vaccines” they need, which included “yellow fever, typhoid and malaria vaccines.” What do you tell them about the malaria vaccine?

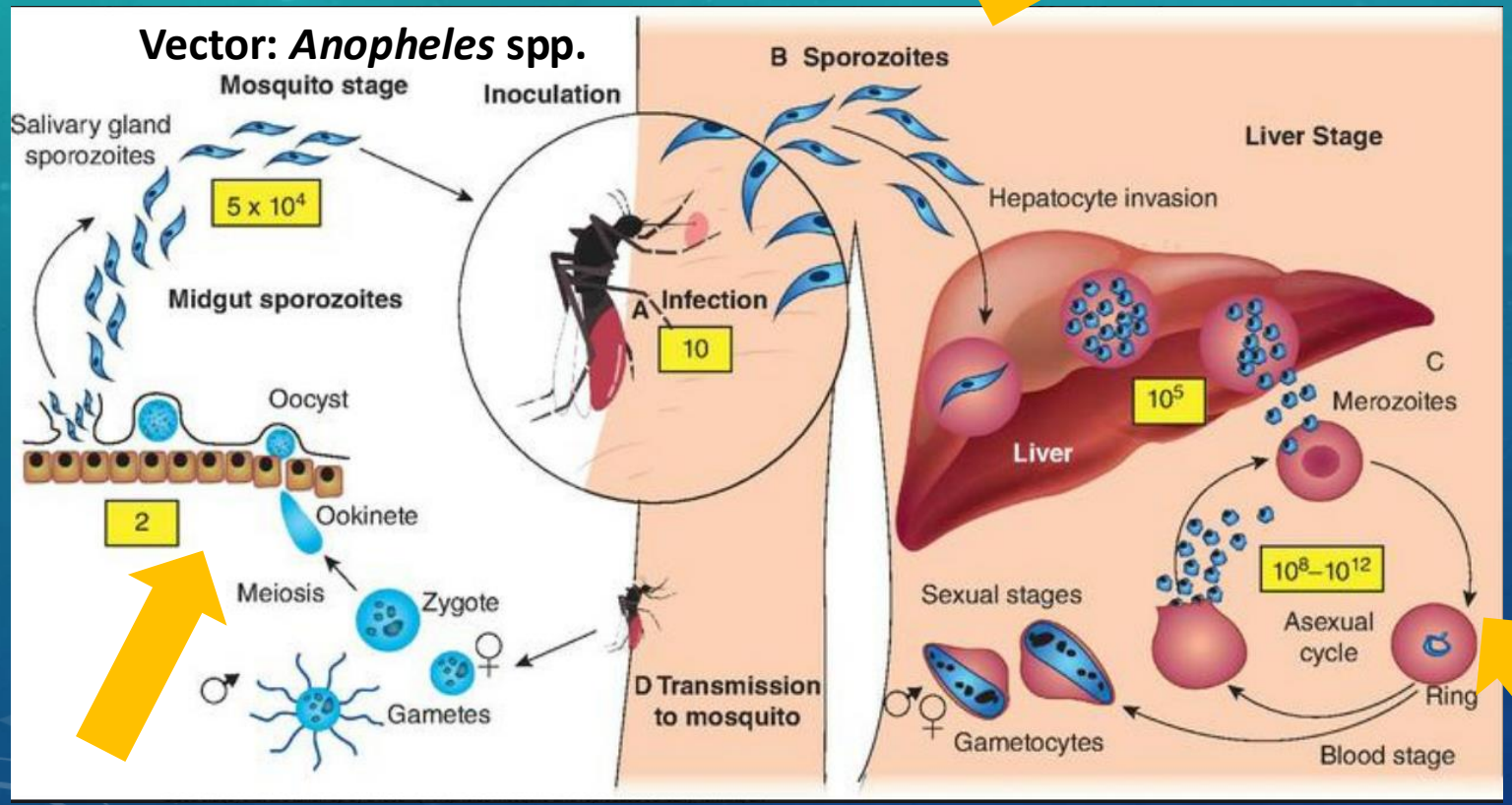
A. There is no effective malaria vaccine

B. There is a malaria vaccine available through an investigational protocol for travelers

C. There is an effective malaria vaccine, but not approved in the US so they should try get it overseas

D. There is an effective malaria vaccine, but not approved in the US, and furthermore it is not recommended for travelers

Malaria life cycle and vaccine considerations



Pre-erythrocytic vaccines

- Life cycle is complex, multiple potential targets
- Pregnancy malaria vaccines
- Vaccination challenges
  - Natural immunity is non-sterile, develops slowly, and requires continued exposure to maintain
  - Antigenic variation within a population
  - Immunity is species specific

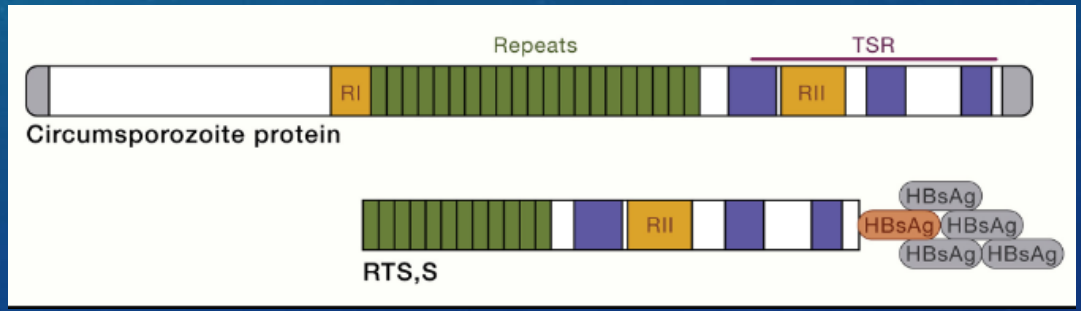
Transmission blocking vaccines

Blood stage vaccines

Schuerman and Christian, Malaria Vaccines from Plotkin's Vaccines (8th Ed), Editor(s): Walter Orenstein, Paul Offit, Kathryn M. Edwards, Stanley Plotkin, Elsevier, 2023, Pages 617-628.

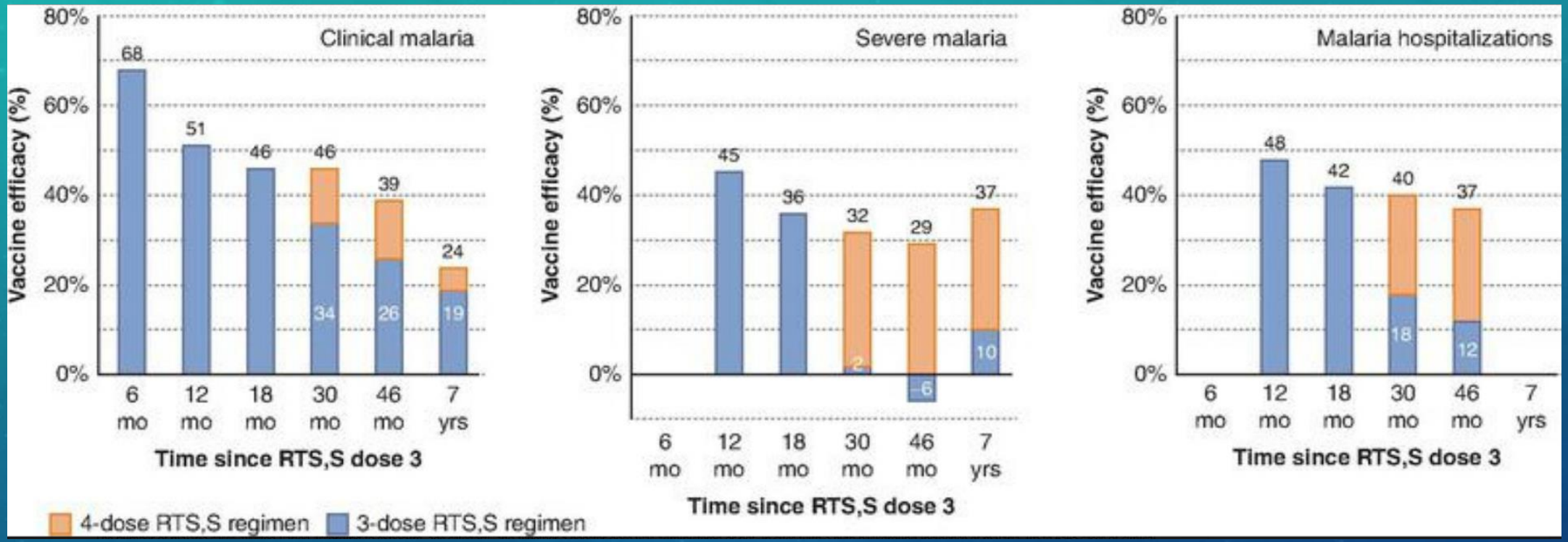
RTS,S/AS01 vaccine (Mosquirix)

- WHO approval in 2021 for children ages 5 mos and older in moderate to high *P. falciparum* areas
- Targets sporozoite CS protein of *P. falciparum*
- Chimeric virus-like particle
  - 19 NANP amino acid repeats, humoral immunity target ("R")
  - C-terminal flanking region with T cell epitopes ("T")
  - Hepatitis B surface antigen ("S"; HbSAg)
- Adjuvanted (AS01)
- 4-dose schedule (0, 1, 2, 20 mos)
- Safety: Small risk of febrile seizures
- Also produces high levels of anti-HbSAg Abs!



Sinnis P et al. Cell 2022, 185:750-4.

RTS,S/AS01 Vaccine efficacy



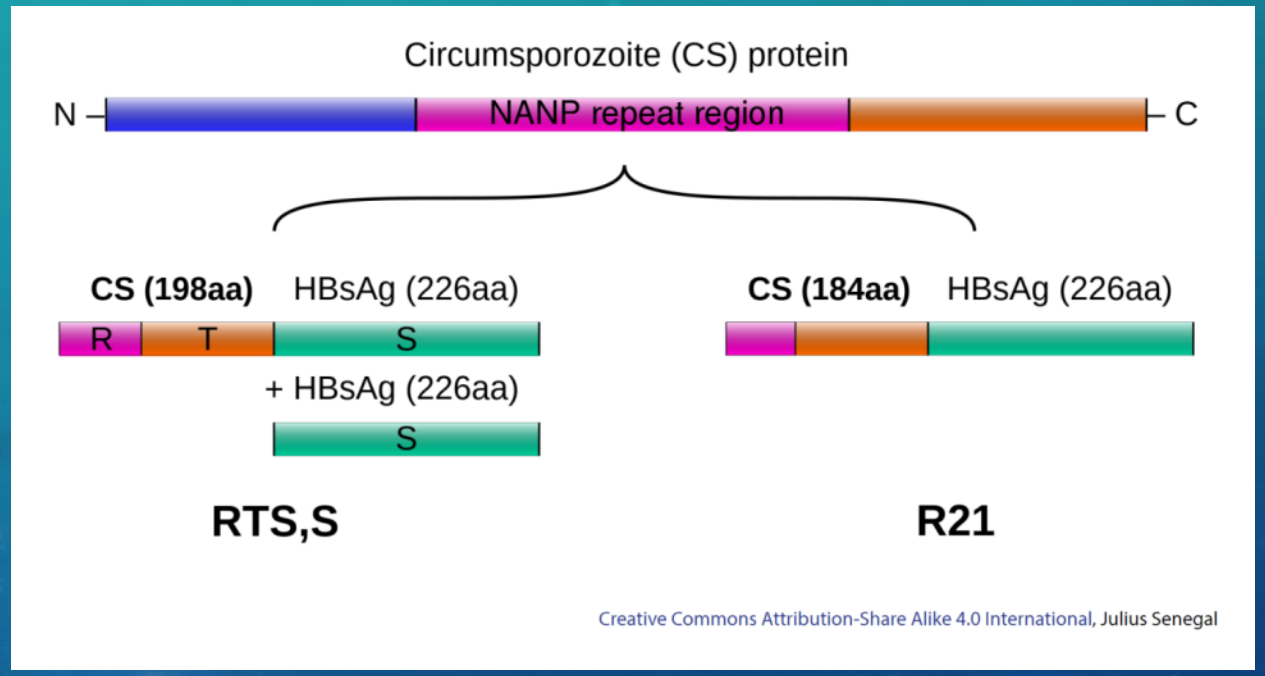
13% reduction in all-cause mortality (non-injury) among vaccinated children in pilot rollout!

Schuerman and Christian, Malaria Vaccines from Plotkin's Vaccines (8th Ed), Editor(s): Walter Orenstein, Paul Offit, Kathryn M. Edwards, Stanley Plotkin, Elsevier, 2023, Pages 617-628.

Osoro CB, et al. BMJ Glob Health 2024;9:e014719. doi:10.1136/bmjgh-2023-014719

The second approved vaccine: R21/Matrix-M

- Phase 3 study vaccine efficacy
  - 67-75% in 12 mos following primary series
- Authorized in Côte d'Ivoire, Nigeria, Ghana, Burkina Faso



Datoo, Mehreen SMahamar, Almahamoudou et al. The Lancet, Volume 403, Issue 10426, 533 - 544

Home 〉 News 〉 Côte d'Ivoire makes history as first nation to deploy R21/Matrix-M™ Malaria Vaccine

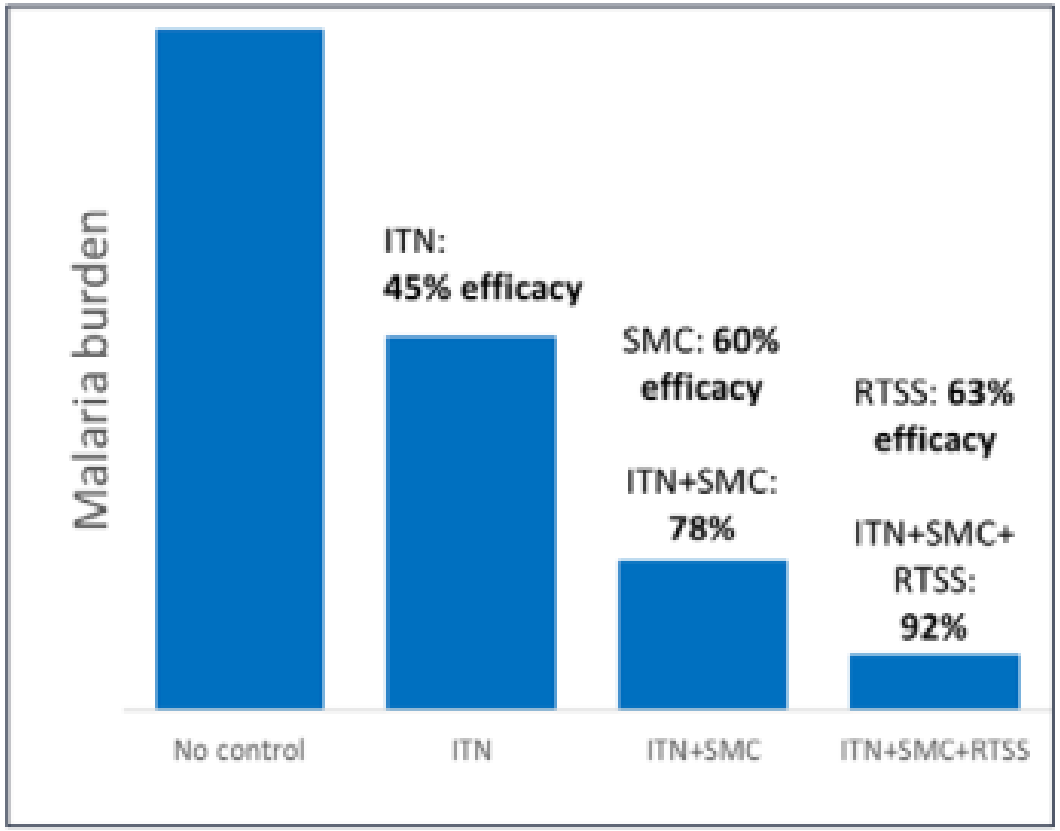
Côte d'Ivoire makes history as first nation to deploy R21/Matrix-M™ Malaria Vaccine

PUBLISHED
15 JUL 2024

https://www.ox.ac.uk/news/2024-07-15-c-te-d-ivoire-makes-history-first-nation-deploy-r21matrix-m-malaria-vaccine

Combination preventative strategies (PATH.org)

Figure. Reduction of malaria burden using preventive tools.



Source: Paul Milligan, London School of Hygiene and Tropical Medicine; 2023.

- ITN: Insecticide treated bednets
- SMC: Seasonal malaria chemoprevention
- RTSS: RTS,S vaccination

https://media.path.org/documents/Product_info_fact_sheet_RTSS-R21_March_2024.pdf

Monoclonal antibodies!

- Targets epitopes CS protein target
- CIS43LS—IV infusion 88% protective against parasitemia over 6 mos in Mali
- Potential for rapid immunity in
  - Infants
  - Pregnant patients
  - Immunocompromised
  - Travelers?

ORIGINAL ARTICLE

Safety and Efficacy of a Monoclonal Antibody against Malaria in Mali

Kassoum Kayentao, M.D., Ph.D., M.P.H., Aissata Ongoiba, M.D., M.P.H., Anne C. Preston, R.N., Sara A. Healy, M.D., M.P.H., Safiatou Doumbo, M.D., Ph.D., Didier Doumtabe, Pharm.D., Abdrahamane Traore, M.D., Hamadi Traore, M.D., Adama Djiguiba, M.D., Shanping Li, M.S., Mary E. Peterson, B.S., Shinyi Telscher, Pharm.D., et al., for the Mali Malaria mAb Trial Team*

Article | Figures/Media | Metrics

24 References | 12 Citing Articles

November 17, 2022
N Engl J Med 2022; 387:1833-1842
DOI: 10.1056/NEJMoa2206966

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 | MAY 2, 2024 | VOL. 390 NO. 17

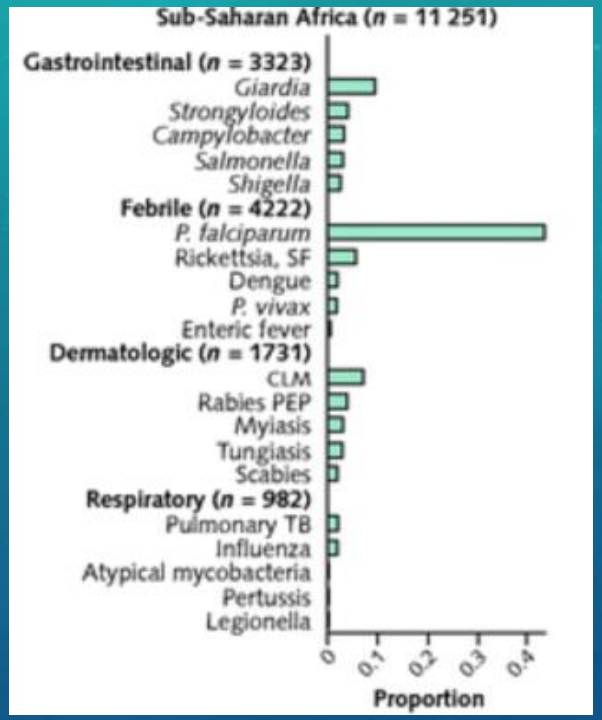
Subcutaneous Administration of a Monoclonal Antibody to Prevent Malaria

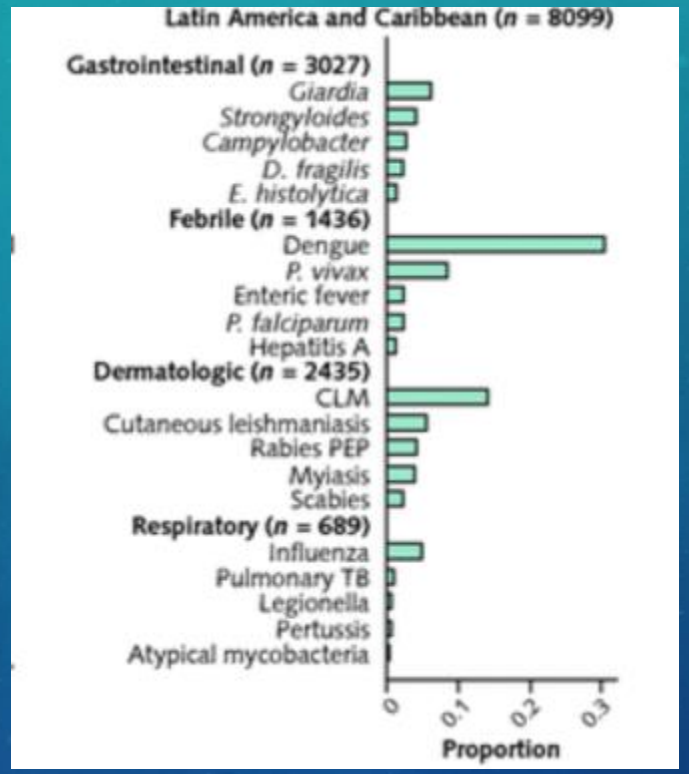
K. Kayentao, A. Ongoiba, A.C. Preston, S.A. Healy, Z. Hu, J. Skinner, S. Doumbo, J. Wang, H. Cisse, D. Doumtabe, A. Traore, H. Traore, A. Djiguiba, S. Li, M.E. Peterson, S. Telscher, A.H. Idris, W.C. Adams, A.B. McDermott, S. Narpala, B.C. Lin, L. Serebryannyy, S.P. Hickman, A.J. McDougal, S. Vazquez, M. Reiber, J.A. Stein, J.G. Gall, K. Carlton, P. Schwabl, S. Traore, M. Keita, A. Zéguimé, A. Ouattara, M'B. Doucoure, A. Dolo, S.C. Murphy, D.E. Neafsey, S. Portugal, A. Djimdé, B. Traore, R.A. Seder, and P.D. Crompton, for the Mali Malaria mAb Trial Team*

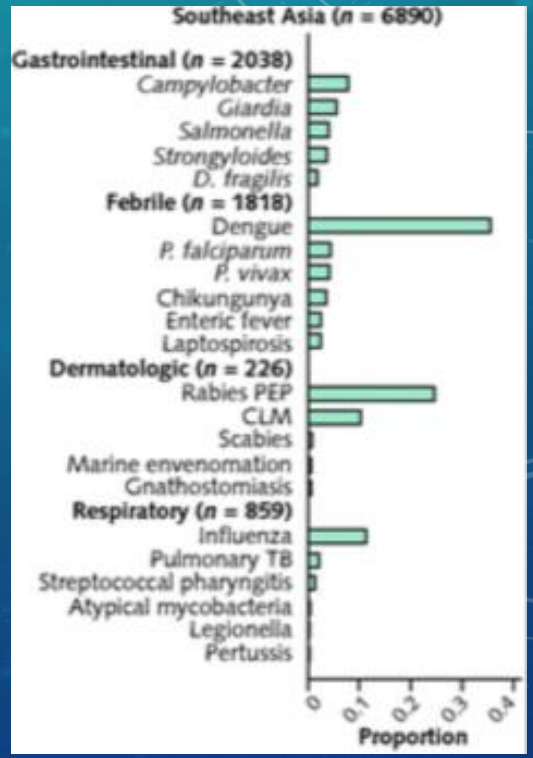
Daily, J. N Engl J Med 2022; 387:460-461

MALARIA IN TRAVELERS

Annals of Internal Medicine
ESTABLISHED IN 1927 BY THE AMERICAN COLLEGE OF PHYSICIANS







From: GeoSentinel Surveillance of Illness in Returned Travelers, 2007–2011

Ann Intern Med. 2013;158(6):456-468. doi:10.7326/0003-4819-158-6-201303190-00005

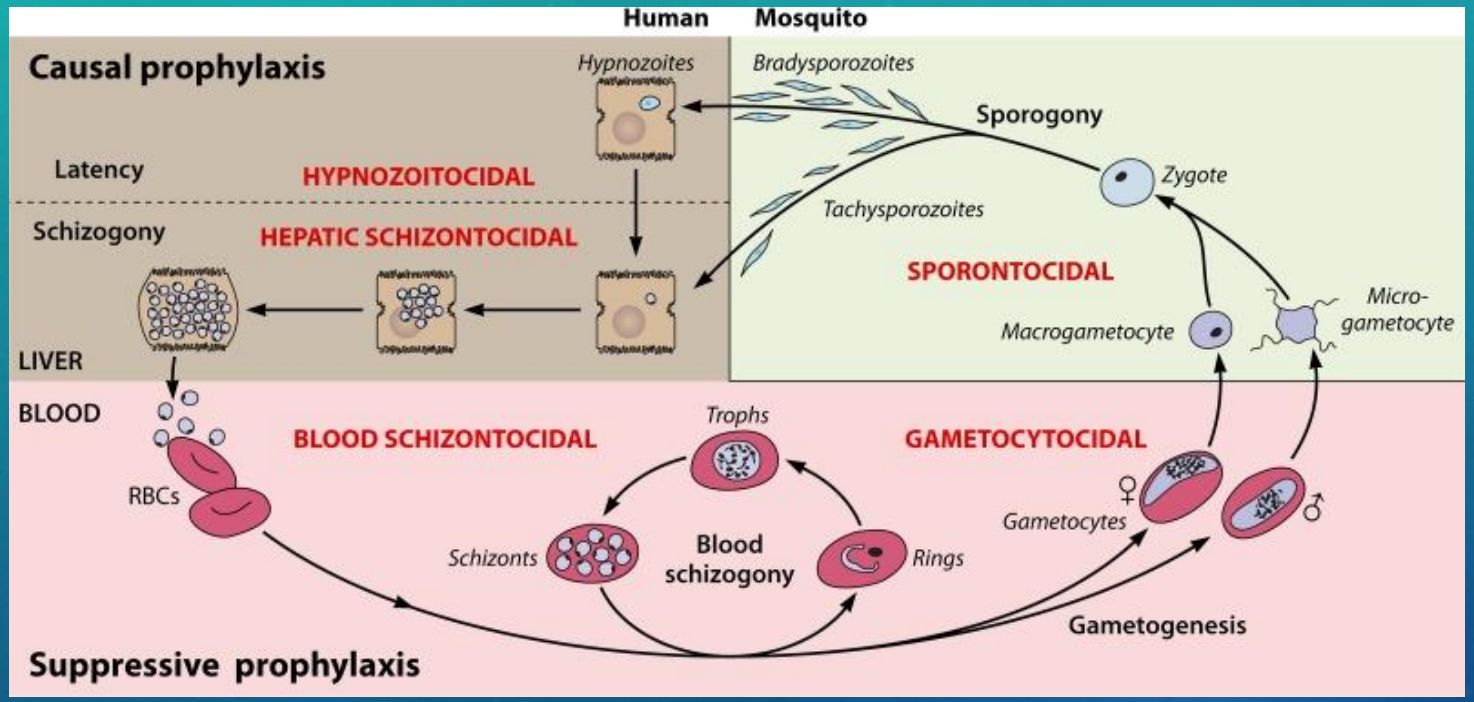
Current state of malaria prevention in travelers

- One of the most common serious infections in travelers
- No malaria vaccine available for travelers
- 3 *layers* of protection
  - Mosquito bite avoidance
  - Prophylaxis
  - Early diagnosis and treatment—Fever after travel to a malarious area demands urgent evaluation *(“THINK MALARIA!”)*

Malaria prophylaxis

- Prevents illness following inoculation
- Schedule
  - Start in advance of exposure risk
  - Continue during travel
  - Continue for a period after travel
- Duration post-travel depends on specific agent
  - Suppressive (blood) agents—4 weeks
  - Causal (hepatic) agents—shorter durations
- Choose regimen based on
  - Local resistance patterns
  - Patient medical considerations (comorbid conditions, drug-drug interactions, G6PD status, etc.)
  - Schedule preference, cost, availability, etc.
- If there is risk of *P vivax/ovale* consider terminal prophylaxis

Causal prophylaxis vs. suppressive prophylaxis vs. terminal prophylaxis



Baird JK. 8-Aminoquinoline Therapy for Latent Malaria. Clin Microbiol Rev. 2019 Jul 31;32(4):e00011-19.

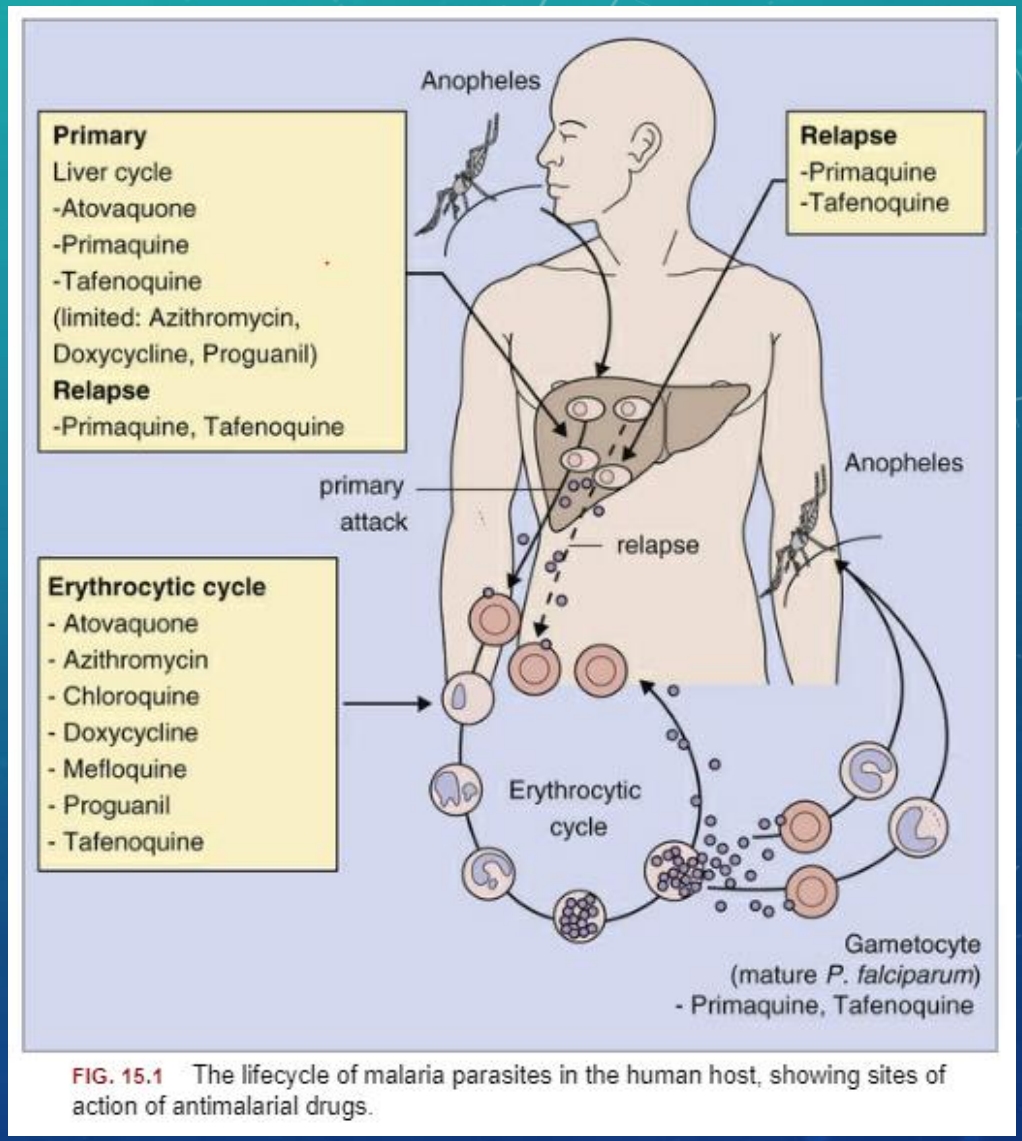


FIG. 15.1 The lifecycle of malaria parasites in the human host, showing sites of action of antimalarial drugs.

Schlagenhauf P, et al. Malaria chemoprophylaxis, Travel Medicine, 4th Ed., 2019.

Commonly recommended prophylaxis regimens*

Drugs	Schedule	Advantages	Disadvantages
Atovaquone-proguanil	Daily, starting days before arrival until 7 days after depart	• High tolerability, shorter duration	• Lots of pills for long-term travelers • Contraindicated w/ CrCl <30
Doxycycline	Daily, starting 1-2 days before arrival until 28 days after depart	• Cheaper (?), widely available	• Common AEs: GI, esophagitis, photosensitivity, yeast infections • Lots of pills for long-term travelers
Mefloquine	Weekly, starting ≥2 weeks before arrival until 4 weeks after depart	• Schedule easier for children • *Considered safe in pregnancy*	• Contraindications: Seizure d/o, neuropsych conditions • AEs: Dizziness, vivid dreams/nightmares, altered mood
Tafenoquine	Loading: Daily x 3 days Continue weekly and take 1 dose during week after return	• Weekly after loading • Shorter post-travel regimen • Also functions as PART	• Need to check G6PD status • Avoid in patients with h/o psychotic disorder
Primaquine	Daily, start 1-2 days before arrival until 7 days after depart	• Also functions as PART	• *Useful only in areas primarily affected by P. vivax* • Need to check G6PD status
Chloroquine, hydroxy-chloroquine	Weekly , start 1-2 weeks before travel until 4 weeks after return	• Less pills • *Considered safe in pregnancy*	• *Only for areas without chloroquine-resistance* • Can exacerbate psoriasis • Eye exams recommended with long-term use

*For details, see CDC Yellow Book 2024 at www.cdc.gov/travel

Pre-Travel Case: Visiting family and relatives….

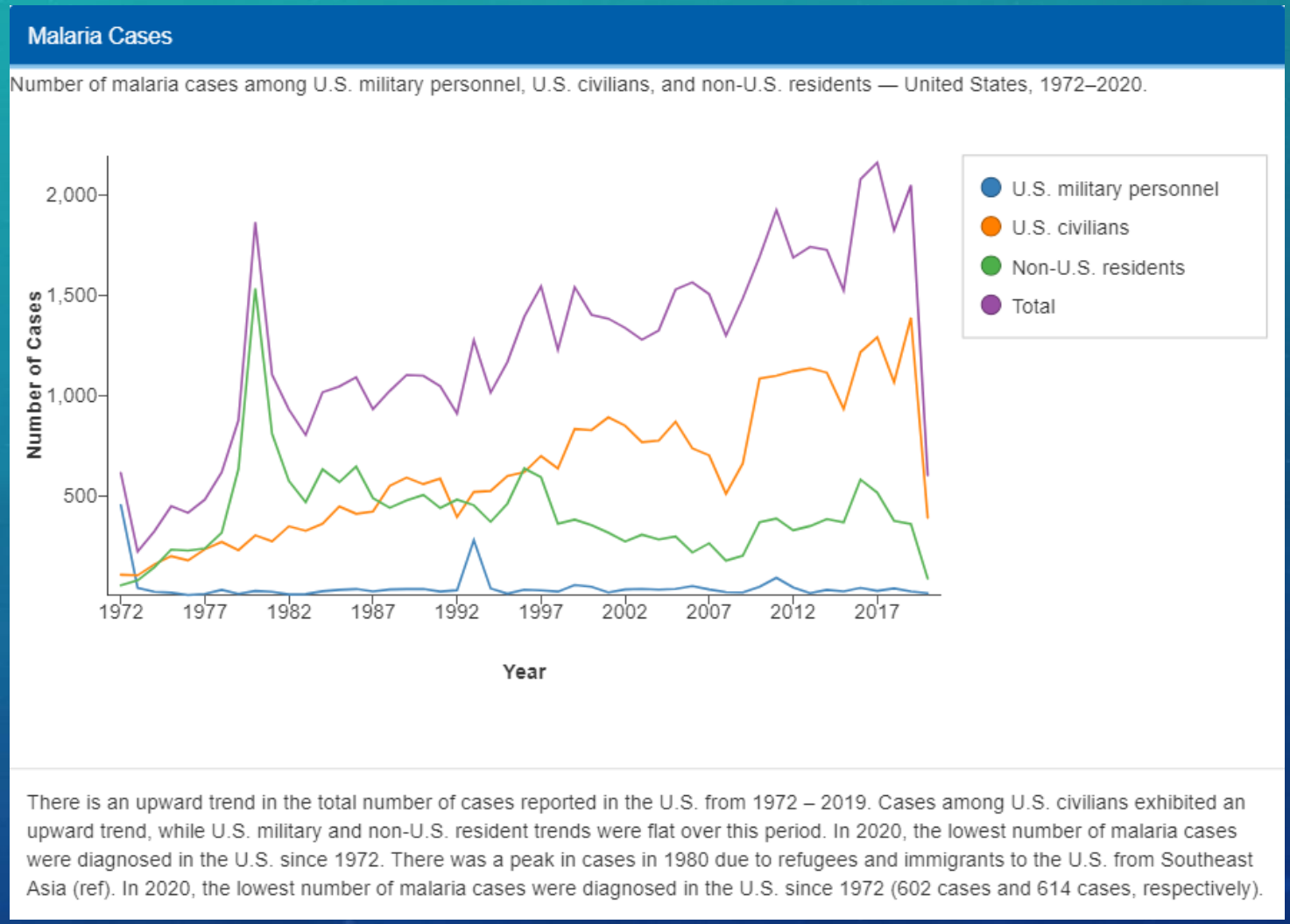
A 56 yo male immigrant from Côte d'Ivoire presents to travel clinic for yellow fever vaccination for an upcoming 30 day trip to his homeland. He immigrated over 30 years ago and has not visited since. He plans to visit family in the capitol and smaller towns. When you review other recommended vaccines and malaria prophylaxis, he says he does not want other vaccines, but he will take a malaria prophylaxis prescription. He asks that you just give him a printed prescription….

"Visiting friends and relatives" (VFR) travelers can present unique challenges in malaria prevention for many reasons including:

A. Misperceptions in personal malaria risk and immunity status
B. Lack of awareness of preventative measures or barriers (socioeconomic, language) to seeking preventative care
C. Higher risk itineraries to lower income areas, villages, rural areas; often staying in homes
D. Longer trip durations or last-minute travel for family emergencies
E. All of the above

US Malaria Surveillance (CDC)

- 2,048 cases in 2019, acquired in:
  - Africa (92%; two-thirds from W. Africa)
  - Asia (4%)
  - S America (1%)
  - Central America/Caribbean (1%)
- VFR travelers account for 60% of US civilian cases



https://www.cdc.gov/malaria/php/surveillance-report/index.html#:~:text=In%202019%2C%202%2C048%20confirmed%20malaria,to%20the%20CDC%20in%202020.

How long does malaria immunity last?

- Repeated exposure required to maintain semi-immunity
  - Antibodies against malaria known to decrease with time; other immune responses may persist longer
  - No robust marker of malaria immunity
- Immigrants and migrants from malaria endemic areas may have various degrees of semi-immunity when living in non-endemic areas
- Observational data
  - Immigrants in France >4 years have less severe *P. falciparum* disease compared to nonimmune European travelers and clear parasites faster
  - Rate of severe malaria in Swedish immigrants increases if in Sweden >10 yrs

Mischlinger J, et al. Clin Microbiol Rev. 2020 Mar 11;33(2):e00104-19. doi: 10.1128/CMR.00104-19. PMID: 32161068; PMCID: PMC7067581.
Färnert A, et al. Clin Microbiol Infect. 2015 May;21(5):494-501. doi: 10.1016/j.cmi.2014.12.011. Epub 2014 Dec 26. PMID: 25656623.

Back to our VFR traveler….

No residual immunity

+

High risk itinerary
- **Longer trip**
- **Higher risk destinations, accommodations**

↓

Chemoprophylaxis and mosquito bite avoidance measures should be strongly recommended for VFR travelers!!

Pre-Travel Case: Long-term traveler

- A 38 yo American woman presents to the travel clinic for pre-travel consultation for a 6 month research trip to Ghana. She has traveled to Ghana before, and is up to date on recommended vaccines. She admits not completing the course malaria prophylaxis that was prescribed for her last trip (atovaquone-proguanil). She will accept a prescription for this trip but mainly “to make my mother happy.”

Which of the following is *least* appropriate?

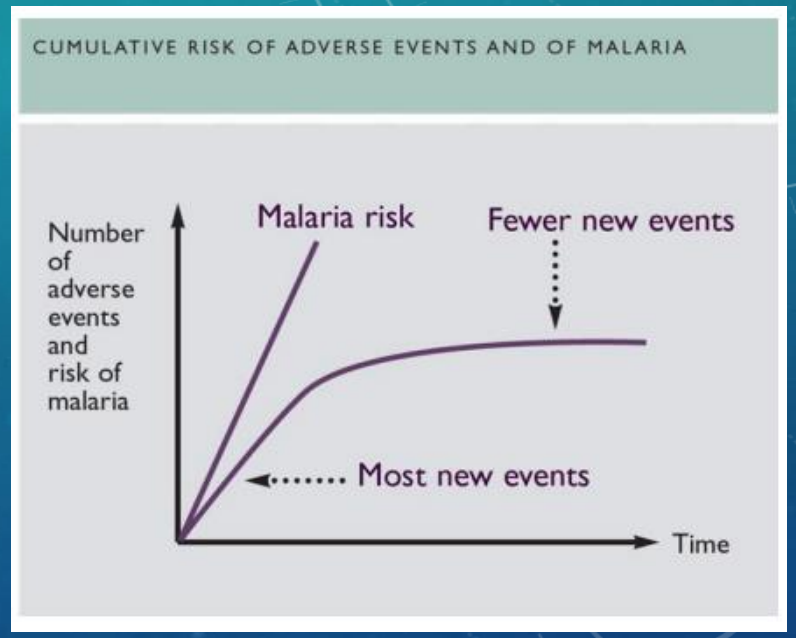
* A. Strongly advise that long-term malaria prophylaxis is safe and strongly recommended for the duration of her trip, in addition to adjunct mosquito avoidance measures such as bed nets and insect repellents
  B. Recommendation A, but discontinuation might be considered after careful assessment of local risk and access to appropriate urgent care for illness
  C. Advise that standby emergency treatment for malaria (SBET) is an option if she is in a lower risk area and prefers not to take prophylaxis
  D. Advise that long-term prophylaxis has significant risk of adverse events, and that she should plan to focus on insect avoidance and accept the risk of malaria working in Ghana

*CDC recommendations

Long-term travelers and malaria

- Long term stays ***increases*** malaria risk
- Long term chemoprophylaxis ***is*** recommended (CDC)
- But travelers often discontinue prophylaxis
  - Study of British expats: 59% report use for 0-3 mos only
- Anecdotal discontinuation reasons:
  - Adverse event concern (e.g. liver inflammation)
  - Local advice
  - Staying in lower risk areas
  - Confidence in local urgent care
  - Presumed failure of prophylaxis when they are diagnosed with “malaria”
  - Assumption of malaria immunity after illness
  - Trouble acquiring medications
- Other considerations
  - Some non-CDC authorities permit “standby emergency treatment” (SBET) for certain itineraries without prophylaxis
  - CDC suggests travelers can carry a “reliable supply” of malaria treatment to be able to take with the advice of a healthcare provider when traveling to areas without adequate treatment

Malaria risk and prophylaxis adverse events and malaria risk over time



Guidelines for malaria prevention in travelers from the UK 2021, Public Health England

Cunningham J, et al. Trav Med Inf Dis 2014;12:341-8.
CDC Yellow Book 2024

Long-term safety and tolerability of malaria prophylaxis

- US CDC does not have time limits for duration of chemoprophylaxis use
- *Some* (non-US) authorities limit duration of certain agents (e.g. atovaquone-proguanil)
- Reported experience supports feasibility
  - Mefloquine: Discontinuation rate due to AEs in Peace Corp volunteers: 0.9% (1989-92 study)
  - Atovaquone-proguanil: Low (1%) discontinuation rate in long-term travelers
  - Doxycycline: Well tolerated IF tolerated in short term
  - Chloroquine: Generally well tolerated (baseline and biannual ophtho exams recommended)

Lobel HO, et al. Lancet 1993;341:848-51
CDC Yellow Book, 2024.

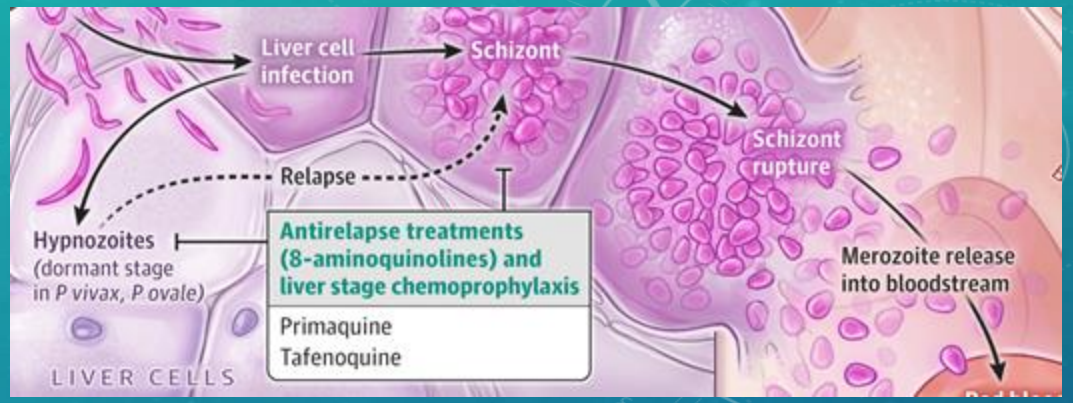
Peace Corp Volunteer to Asia

A 26 year-old healthy man comes to travel clinic for vaccines and advice for a 2 year Peace Corp assignment in South Asia. He will likely be based in rural areas in southern India. He has taken doxycycline chemoprophylaxis before without problem, and would like to take that for this trip. His G6PD level has been screened, and it is normal. What should you recommend?

A. Nothing further, doxycycline alone should be adequate
B. He should consider terminal prophylaxis with primaquine when he returns
C. He should consider terminal prophylaxis with primaquine or tafenoquine when he returns
D. Instead of doxycycline he could take tafenoquine for prophylaxis and eliminate the need for terminal prophylaxis

Primaquine

- 8-aminoquinolines
  - Effective against dormant liver stages of *P vivax (Pv)* and *P ovale (Po)*
  - Can cause hemolysis in G6PD deficiency
- Indications
  - "Radical cure" after treatment of *Pv* or *Po* infection to prevent relapse
  - "Terminal prophylaxis:" An adjunct to primary prophylaxis that is not effective against hypnozoites (presumptive antirelapse therapy, PART)
  - Primary prophylaxis for areas affected mainly by *Pv* (obviates need for PART)
- Also effective against *P falciparum* gametocytes (prevention of transmission)
  - WHO recommendation for adding primaquine when treating *Pf* cases in low-intensity areas



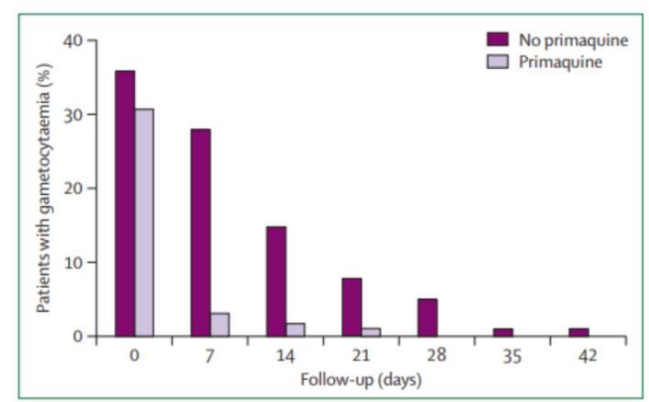


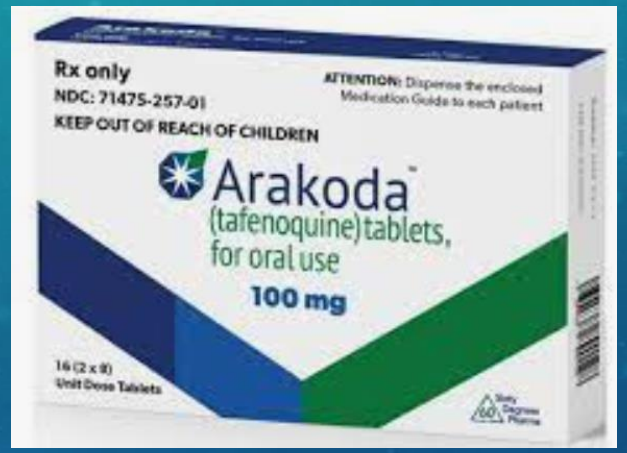
Figure 1: **Comparison of gametocyte carriage in patients with falciparum malaria who did or did not receive primaquine**
In a comparison of different artemisinin-based combination therapies in Myanmar (Burma), 808 patients were randomly assigned one of five different regimens, and half the patients were randomised to receive additional single-dose primaquine 0·75 mg base per kg.[20] Overall 264 patients presented with gametocytaemia assessed by microscopy. Gametocyte clearance accelerated substantially after primaquine.

CDC Yellow Book 2024

White NJ. Primaquine to prevent transmission of falciparum malaria. Lancet Infect Dis. 2013 Feb;13(2):175-81. doi: 10.1016/S1473-3099(12)70198-6. Epub 2012 Nov 23. PMID: 23182932.

Tafenoquine

- Long-acting 8-aminoquinoline
- When used for radical cure, tafenoquine should only be used when the patient was treated with CQ (or HCQ)
- No longer recommended for PART/terminal prophylaxis
- Potential weekly chemoprophylaxis drug against all malaria species, for non-pregnant travelers unable to take mefloquine if G6PD normal



https://wwwnc.cdc.gov/travel/news-announcements/tafenoquine-malaria-prophylaxis-and-treatment

Terminal prophylaxis—Under-prescribed??

- *Pv* and *Po*: 15-21% of all US malaria cases (2014-20)*
- Most preventative guidelines do not recommend routine terminal prophylaxis, except for those with “prolonged exposures” to areas with relapsing malaria risk
- Need to confirm normal G6PD before prescribing
- Travel clinics typically do not see travelers after travel

*Cases with confirmed species
CDC Yellow Book 2024
https://www.cdc.gov/malaria/php/surveillance-report/index.html#:~:text=In%202019%2C%202%2C048%20confirmed%20malaria,to%20the%20CDC%20in%202020.

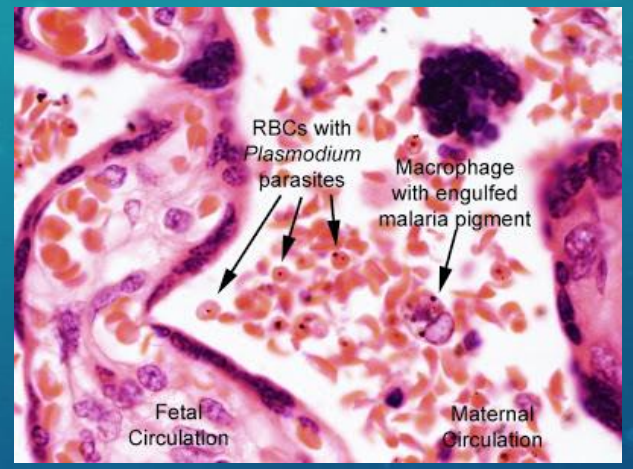
Pre-Travel Case: Pregnant traveler

A 32 year old public health worker will be deploying to Cambodia and Thailand for 4 weeks. She is currently pregnant, in her second trimester. She has no history of neuropsychiatric disorders. She will be staying in the capital cities, but her project might take her to more rural field sites. What should you advise?

A. She should take mefloquine for prophylaxis
B. She should take atovaquone-proguanil for prophylaxis
C. She should not take prophylaxis and focus on mosquito avoidance measures
D. Advise her to postpone her trip until she is no longer pregnant, as there are no pregnancy-approved prophylaxis drugs that are effective in this area.
E. Advise that if she can avoid field site visits to areas that are potentially malarious, she could potentially travel without malaria prophylaxis

Malaria in pregnancy: ↑Susceptibility AND Severity

- Increased malaria prevalence in pregnancy (esp. *P. falciparum*)
- 3-fold higher risk of severe disease vs. non-pregnant
- *P. falciparum* can sequester in intervillous space of placenta, mediated by variant antigen class of PfEMP1 (VAR2CSA)
  - Binds to placental chondroitin sulfate A
  - Lack of previous exposure to VAR2CSA outside pregnancy results in susceptibility during the *first episode of malaria during pregnancy*
  - Potential target for pregnancy malaria vaccine
- Maternal mortality: 0.5-39%
- Birth complications: Miscarriage/stillbirth, low birthweight, pre-term delivery, fetal anemia, congenital malaria, neonatal mortality



http://parasitewonders.blogspot.com/2009_07_01_archive.html

Kimberly L McKinney, MD, Henry M Wu, MD, Kathrine R Tan, MD, Julie R Gutman, MD, Malaria in the pregnant traveler, Journal of Travel Medicine, Volume 27, Issue 4, May 2020, taaa074, https://doi.org/10.1093/jtm/taaa074

Prophylaxis drugs in pregnancy

Table 1. International recommendations for malaria chemoprophylaxis in pregnant travelers

	Canada[84]	Germany[25]	Switzerland[26]	USA[1,58]	UK (Public Health England)[43]	WHO[85]
Atovaquone–Proguanil	N/R[a]	N/R[a]	N/R[a]	N/R[a]	N/R[a]	N/R[a]
Chloroquine[b]	Safe	N/A[c]	N/A[c]	Safe	Safe[d]	Safe
Doxycycline	N/R	N/R	N/R	N/R	N/R[e]	N/R
Mefloquine	Recommended with caution[f]	Safe	Safe	Safe	Recommended with caution[f]	Safe
Primaquine	N/R	N/A[c]	N/A[c]	N/R	N/A[c]	N/A[c]
Tafenoquine	N/A	N/A	N/A	N/R	N/A	N/A

Abbreviations: N/R not recommended or contraindicated; N/A not applicable or not available.

[a]Not recommended during pregnancy. However some authorities allow use of atovaquone–proguanil during pregnancy if no other options are available and after careful risk–benefit assessment. Recommendations from Canada and the UK specify that atovaquone–proguanil can only be considered after the first trimester.

[b]For travel to areas with chloroquine sensitive malaria.

[c]Regimen not included in prophylaxis recommendations for non-pregnant travelers.

[d]Use with proguanil and folic acid supplementation recommended.

[e]Contraindicated in pregnancy but might be considered under special circumstances before 15 weeks of gestation if no other options are available. The doxycycline course, including 4 weeks after travel, must be completed before 15 weeks of gestation.

[f]Can be used in all trimesters, but caution in first trimester is advised.

Kimberly L McKinney, MD, Henry M Wu, MD, Kathrine R Tan, MD, Julie R Gutman, MD, Malaria in the pregnant traveler, Journal of Travel Medicine, Volume 27, Issue 4, May 2020, taaa074, https://doi.org/10.1093/jtm/taaa074

Risk assessment and rec's for this traveler

- Malaria exists in rural border regions of Thailand and most areas of Cambodia outside of Phnom Penh
- MQ and CQ are the only drugs considered safe in pregnancy, BUT
- CQ resistance present in Asia, and MQ resistance is present in SE Asia (Myanmar, Thailand, Laos, Vietnam)
- Recommendation
  - Modify trip to avoid malarious areas, or postpone travel
  - Mosquito avoidance (always!)
  - (I did not offer atovaquone-proguanil)

www.fitfortravel.nhs.uk

Delayed *P. falciparum* malaria?

HPI: A pregnant woman (3rd trimester) in presents to an emergency department in Portland, Oregon (US) in the month of September, complaining of 2 weeks of loose stools and abdominal pain, chills and night sweats without fevers. She is found to be anemic and thrombocytopenic, and a rapid malaria test was positive. A blood film demonstrated 0.2% parasitemia with *P. falciparum*.

PMH: Sickle cell trait, pre-eclampsia, malaria during childhood

SH: Immigrated from Sub-Saharan Africa 11 years ago *with no international travel since*

Drummond W, et al. Emerg Infect Dis. 2024;30(1):151-154. https://doi.org/10.3201/eid3001.231231

Emerg Infect Dis. 2024 Jan; 30(1): 151–154.
doi: 10.3201/eid3001.231231
PMCID: PMC10756375
PMID: 38147068

Delayed *Plasmodium falciparum* Malaria in Pregnant Patient with Sickle Cell Trait 11 Years after Exposure, Oregon, USA

Wendi Drummond, Kathleen Rees, Stephen Ladd-Wilson, Kimberly E. Mace, Douglas Blackall, and Melissa Sutton

A thorough public health investigation found no evidence supporting local malaria transmission. A diagnosis of *Pf* malaria with a delayed (11 yr) presentation of made.

Although rarely reported, delayed presentations of *Pf* malaria (3 months to years) are reported in immigrants in nonendemic areas. Which of these might medical risk factors might contribute to a delayed presentation?

A. Waning immunity in chronically infected persons living in nonendemic areas

B. HIV infection

C. Sickle cell disease and trait

D. Splenectomy

E. Pregnancy

F. All of the above

Post-Travel Case: Traveler back from Costa Rica

54 yo healthy male, 10 days ago returned from a 14 day trip to Costa Rica presents to clinic with fevers and body aches. He spent his time in rainforests in the Osa Peninsula, staying in tent camps. He did not take malaria prophylaxis (not recommended in 2018). He swam in freshwater streams. Got mosquito and tick bites.

Headache onset 8 days after return followed by aches in calves, ankles, thighs, and arms. Developed fever to 38.6 C, fatigue and malaise.

Malaria seemed very unlikely compared to other febrile illnesses (dengue, leptospirosis, etc.)

- No reported recent transmission in the country
- Recent reports of migrant travelers through Central America did raise some concern for reintroduction

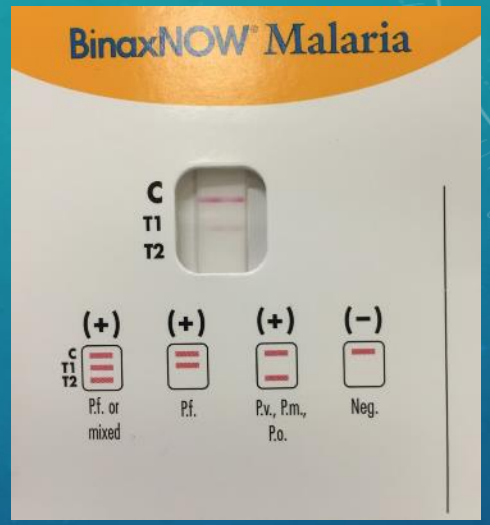
Post-Travel Case: Traveler from Costa Rica

Malaria RDT (Binax NOW) is POSITIVE for *P. falciparum*.

The patient was started on atovaquone-proguanil. The next day, the thick and thin films are read as NEGATIVE.

What should we do?

A. Repeat the tests
B. Continue the patient on malaria treatment
C. Stop the A/P, this is a false-positive RDT result
D. Send the specimen for PCR testing



- BinaxNOW Malaria (Abbot)
  - Antigen T1 (HRP-2; falciparum specific)
  - Antigen T2 (aldolase; pan-plasmodium)
- Performance (package insert)
  - Sens: *Pf* (99.7%), *Pv* (93.5%)
  - Spec: *Pf* (94.2%), *Pv* (99.8%)
- Performance (reported from centers in non-endemic areas)
  - Sens (*Pf*): 93-97%
  - Spec 99.8%

Dimaio MA, et al. Performance of BinaxNOW for diagnosis of malaria in a U.S. hospital. J Clin Microbiol. 2012 Sep;50(9):2877-80.

CDC: May 10, 2018

Malaria in U.S. Traveler to Costa Rica

On May 4, 2018, a case of *P. falciparum* malaria in a U.S. traveler who returned from Costa Rica was reported to CDC. The 54-year-old man was traveling in the Osa Peninsula in Puntarenas Province in Costa Rica April 7–20, 2018, for ecotourism. Seven days after returning, he developed fever, body aches, and gastrointestinal symptoms, and was admitted to the hospital. Thick and thin blood smears for malaria were negative, but a malaria rapid diagnostic test was positive. Further testing with polymerase chain reaction confirmed *P. falciparum* malaria. This patient was treated with atovaquone-proguanil and fully recovered. Costa Rica had no local transmission of malaria from 2013 through most of 2016. Then, at the end of 2016, 4 cases of locally transmitted *P. vivax* were reported, and again in 2017 9 cases of *P. vivax* were reported, all in the northern part of the country. The Osa Peninsula is at the southern part of Costa Rica bordering a part of Panama that has had rare *P. falciparum* cases, but none in the previous two years. Because of the very limited transmission, travelers to this area had been previously advised to practice only mosquito avoidance measures to prevent malaria.

CDC recommends that travelers to the Osa Peninsula in Costa Rica take medications to prevent malaria. Effective antimalarial options include atovaquone-proguanil, chloroquine, doxycycline, and mefloquine.

https://www.cdc.gov/malaria/new_info/2018/Costa_Rica_5_2018.html#:~:text=On%20May%204%2C%202018%2C%20a,20%2C%202018%2C%20for%20ecotourism.

May 22, 2018

Rescind: Malaria in U.S. Traveler to Costa Rica

CDC is rescinding its malaria notice posted on May 10, 2018 regarding a case of *P. falciparum* malaria in a U.S. traveler who returned from Costa Rica. The 54-year-old man was traveling in the Osa Peninsula in Puntarenas Province in Costa Rica April 7–20, 2018 for ecotourism. Seven days after returning, he developed fever, body aches, and gastrointestinal symptoms, and was admitted to the hospital. Thick and thin blood smears for malaria were negative, but a malaria rapid diagnostic test (RDT) at the hospital was positive, and testing at a state health department laboratory with polymerase chain reaction (PCR) was positive for *P. falciparum* malaria. However, further testing at CDC's laboratory with two methods of PCR, antigen detection, and serology were all negative. The conclusion is the previous RDT and PCR were false positives, and that there is no evidence of malaria in this patient.

Costa Rica had no local transmission of malaria from 2013 through most of 2016. Then, at the end of 2016, 4 cases of locally-transmitted *P. vivax* were reported, and again in 2017 9 cases of *P. vivax* were reported, all in the northern part of the country.

https://www.cdc.gov/malaria/new_info/2018/Costa_Rica_5_22_2018.html

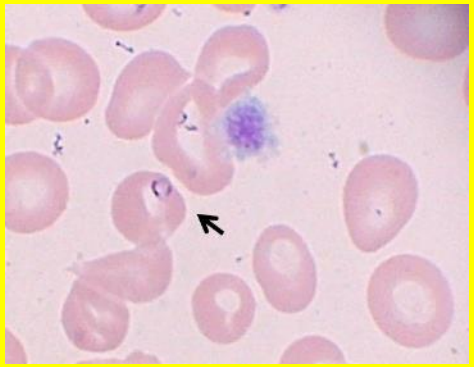
Malaria diagnostics

Test	Sens	Spec	Comments
Microscopic examination (thick and thin blood smears)	High	High	• "Gold standard" • Multiple tests may be necessary to confirm infections in previously naïve patients who are symptomatic at very low parasite densities • Advantages: Technically simple. When read by competent technicians, smears provide species identification and quantification of parasites. • Disadvantages: Proficiency in reading can be limited, especially in non-endemic areas where malaria is not routinely diagnosed.

Parasite density: Quantifying parasites (asexual)

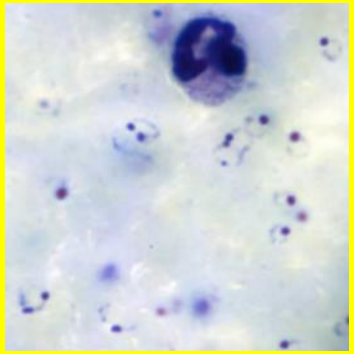
Measuring asexual parasites against RBC on a *thin smear*

% parasitemia = (parasitized RBCs/total RBCs) × 100



Measuring parasites per µl blood (WBC method, on a *thick smear*)

Parasites / µl blood = (#parasites/#WBC) × WBC count[a] / µl



[a]8,000 WBC / µl may be used if actual WBC count is unknown

Image: cdc.gov/dpdx

High parasite density (e.g. "hyperparasitemia") => a poor prognostic indicator

- **In *low transmission* areas, mortality from *Pf* increases with parasitemia >2.5%**
- **In *high* transmission areas, higher parasitemias can be tolerated**

https://www.cdc.gov/dpdx/diagnosticprocedures/blood/microexam.html

Management of severe malaria – a practical handbook. https://www.who.int/publications/i/item/9789241548526

Malaria diagnostics

Test	Sens	Spec	Comments
Rapid diagnostic test (RDT)	Varies	Varies	• Should be performed in conjunction with microscopy • Different assays based on different Ag targets • Advantages: Rapid results, performed with limited training. • Disadvantages: Generally less sensitive and specific compared to microscopy. Least sensitive w/ *P. ovale* and *malariae,* or low parasitemias. No parasite density quantification. Numerous RDT kits with varying accuracy and lot-to-lot variation.
PCR	High	High	• Advantages: Increasingly available, fast if locally performed, multi-pathogen multiplexed assays • Disadvantages: Current assays do not determine parasite density, $$$

MULTIPLEX PCR IS HERE….

BioFire® Global Fever Panel GF
1 Test, 6 Targets, in 50 Minutes

BioFire® Global Fever Special Pathogens Panel SP
1 Test, 16 Targets, in 50 Minutes

GF	SP	
		Bacterial
	■	*Bacillus anthracis*
	■	*Francisella tularensis*
■	■	*Leptospira* spp.
	■	*Yersinia pestis*
		Viral
■	■	Chikungunya virus
	■	Crimean-Congo hemorrhagic fever virus
■	■	Dengue virus (serotypes 1, 2, 3 and 4)
	■	*Ebolavirus* spp. (Bundibugyo, Reston, Sudan, Taï Forest, Zaire)
	■	Lassa virus
	■	*Marburgvirus*
	■	West Nile virus
	■	Yellow fever virus
		Protozoan
	■	*Leishmania* spp.
■	■	*Plasmodium* spp.
■	■	*Plasmodium falciparum*
■	■	*Plasmodium vivax/ovale*

JOURNAL ARTICLE EDITOR'S CHOICE

Clinical evaluation of BioFire® multiplex-PCR panel for acute undifferentiated febrile illnesses in travellers: a prospective multicentre study FREE

Daniel Camprubí-Ferrer, MD ✉, Ludovico Cobuccio, MD, Steven Van Den Broucke, MD, Leire Balerdi-Sarasola, MD, Blaise Genton, PhD, Emmanuel Bottieau, PhD, Jessica Navero-Castillejos, BSc, Miguel J Martinez, PhD, Corinne Jay, MSc, Anne Grange, DSc … Show more

Journal of Travel Medicine, Volume 30, Issue 3, April 2023, taad041,
https://doi.org/10.1093/jtm/taad041
Published: 29 March 2023

ELSEVIER
The Lancet Infectious Diseases
Volume 22, Issue 9, September 2022, Pages 1356-1364

Articles

Clinical evaluation of the BioFire Global Fever Panel for the identification of malaria, leptospirosis, chikungunya, and dengue from whole blood: a prospective, multicentre, cross-sectional diagnostic accuracy study

Prof Yukari C Manabe MD [a q] ✉, Joshua Betz MS [b], Olivia Jackson BS [c], Victor Asoala PhD [d], Isabel Bazan MD [e], Paul W Blair MD MHS [a], Aileen Chang MD [f], Sarunyou Chusri MD [h], Prof John A Crump MD [i j], Kimberly A Edgel PhD [k], Dennis J Faix MD MPH [k], Stefan Fernandez PhD [l], Anne T Fox MD [m], Jose A Garcia PhD [k], Max Grogl PhD [e], Erin A Hansen BS [n], Vireak Heang MBA [k], Stacey L House MD PhD [o], Krisada Jongsakul MD [p], Michael B Kaburise MBChB [d]… Brian W Jones PhD [c]

https://www.biofiredefense.com

Case: Failed chemoprophylaxis?

Two weeks after returning from a month long VFR Ghana trip, a 46 yo male presents with a severe HA and fever to 39 C. He was prescribed atovaquone-proguanil (A/P) prophylaxis, but took it intermittently and stopped completely on the way home due to "diarrhea and stomach cramps."

A malaria RDT is positive for *P. falciparum,* and a quick review of a thin smear demonstrates a parasitemia of <1%. He has no laboratory or clinical evidence of severe malaria.

For treatment, he asks if he can just take the leftover pills, which he has brought to clinic. Is this reasonable?

A. Yes, A/P at high dose (4 tablets daily x 3 days) is a CDC recommended treatment

B. No, artemether-lumefantrine (Coartem®) or another treatment would be more appropriate given his A/P use for prophylaxis

https://www.cdc.gov/malaria/hcp/clinical-guidance/malaria-treatment-tables.html

Treatment of uncomplicated *P. falciparum* malaria

Uncomplicated	
Preferred: Artemisinin combination therapy (ACT)	
• Artemether-lumefantrine* • Artesunate amodiaquine • Artesunate-mefloquine	• Artesunate-sulfadoxine-pyramethamine • Dihydroartemisinin-piperaquine • Artesunate pyronaridine
Alternatives • Atovaquone-proguanil**, quinine plus doxycycline (or tetracycline or clindamycin), mefloquine. • Chloroquine (or hydroxychloroquine) *only* if chloroquine-sensitive	
For details see: • https://www.who.int/publications/i/item/guidelines-for-malaria • https://www.cdc.gov/malaria/hcp/clinical-guidance/malaria-treatment-tables.html	
NOTE: ****Only ACT available in US*** *****Patients should not be treated with the same medication used for prophylaxis in a breakthrough infection.***	

Post-Travel Case: Severe malaria

Previously healthy 38 yo woman returned from a 2 week tourism trip to a major coastal city in West Africa. She had grown up in the US and had never been to a malaria endemic area previously. She did not take malaria prophylaxis. 4 days after return she had fevers, sore throat, and malaise. She was seen at an urgent care clinic, and tested for influenza (negative). Fevers persisted, and 5 days later her family noted that she was confused, and then found her unresponsive and bleeding.

Post-Travel Case: Severe malaria

Upon arrival to the ED

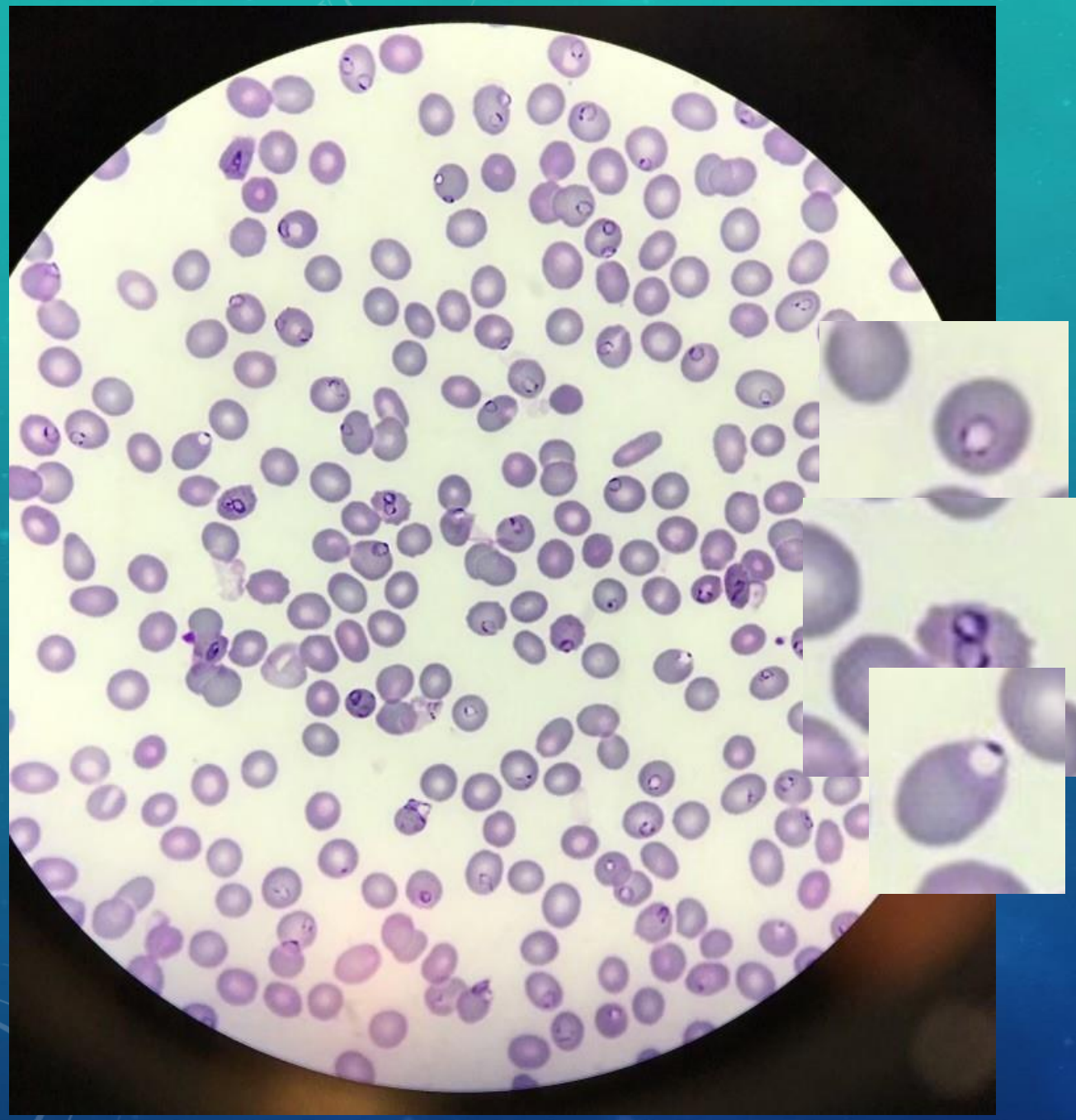
T = 40.1 C
BP 108/67, P 123
RR 24 (95% on RA)
Neuro AxO x 1 (“mumbling”), moves extremities, no nuchal rigidity
CV tachycardic
Chest nl sounds
Abd soft, no HSM

CBC:
WBC 5.5
Hgb 9.7 →7.0 gm/dL
HCT 28.9 →20%
PLT 49

CXR: NAD

CT HEAD: NAD
CT Chest: Bibasilar atelectasis
CT ABD/pelvis: NAD

CMP:
Na 132 →126 mmol/L
K 4.3
Cl 90
CO2 21 →18 mmol/L
Glucose 66
BUN 38
Cr 0.9
Prot 4.2 gm/dL
Alb 2.1 gm/dL
ALT 105 u/L
AST 138 u/L
Tbil 3.8 mg/dL



Thin smear

- High parasitemia (>35%)
- RBC of all ages (sizes) infected
  - Old (senescent)
  - Young (reticulocyte)
- Trophozoites: Rings with delicate cytoplasm with 1 or 2 chromatin dots (“headphones”)
- Multiply infected RBCs
- Appliqué (attache) forms

- →→*Plasmodium falciparum*

Table 2. Diagnostic Criteria for Severe Disease[a]

Plasmodium species	Criteria	
	Signs and symptoms	Laboratory and radiology
P falciparum	Impaired consciousness: Glasgow Coma Scale score <11	Acidosis: base deficit of >8 mEq/L or plasma bicarbonate <15 mEq/L or venous plasma lactate ≥5 mmol/L
	Multiple convulsions: >2 seizures within 24 h	Anemia: hemoglobin concentration <7 g/dL or hematocrit <20% with a parasite count >10 000/μL
	Prostration: unable to sit, stand, or walk without assistance	Hypoglycemia: blood or plasma glucose <40 mg/dl
	Significant bleeding: recurrent or prolonged bleeding from the nose, gums, or venipuncture sites; hematemesis or melena	Parasitemia: ≥5% **WHO criteria: ≥10% (*P. falciparum*)**
	Shock: circulatory collapse/shock	Jaundice: plasma or serum bilirubin >3 mg/dL and parasite count >100 000/μL
		Kidney impairment: plasma or serum creatinine >3 mg/dL or blood urea nitrogen >56 mg/dL
		Pulmonary edema: radiologically confirmed or oxygen saturation <92% on room air with a respiratory rate >30/min
P vivax	Defined as for falciparum malaria but with no parasite density thresholds	
P knowlesi	Defined as for falciparum malaria except as below	
	P knowlesi parasite density >100 000/μL	
	Jaundice and parasite density >20 000/μL	

Severe malaria CFR:

- **Untreated: >90%**
- **Treated**
  - **8.5% (children)**
  - **15% (adults)**
  - **2.8% (US, 2018)**

SI conversion factors: To convert plasma glucose to mmol/L, multiply by 0.0555; plasma or serum bilirubin to μmol/L, multiply by 17.104; plasma or serum creatinine to μmol/L, multiply by 88.4; and urea nitrogen to mmol/L, multiply by 0.357.

[a] Severe malaria can rarely occur in *P ovale* and *P malariae*, with no parasite density thresholds.

Daily JP, Minuti A, Khan N. Diagnosis, Treatment, and Prevention of Malaria in the US: A Review. JAMA. 2022;328(5):460–471. doi:10.1001/jama.2022.12366

Post-Travel Case: Severe malaria

The positive thin film for *P. falciparum* confirmed severe malaria. The patient was intubated for worsening mental status associated with cerebral malaria and admitted to the ICU. In addition to supportive care and close monitoring (including blood glucose, HCT, lactate, etc.), initial treatment for this patient should include:

A. Artemisinin-based combination therapy (ACT)
B. IV treatment with artesunate
C. Exchange transfusion
D. B and C

Initial treatment of severe malaria (all species)

Parenteral therapy (at least 24 hr and until PO treatment tolerated)
Artesunate (IV/IM) Alternatives: IM artemether, IV quinine/quinidine
• Follow parenteral therapy with a full oral course of treatment (ACT preferred) after 24 hrs of IV treatment, if parasitemia <1%, and tolerating oral meds. • Exchange transfusion is NOT recommended
For details see: https://www.who.int/publications/i/item/guidelines-for-malaria https://www.cdc.gov/malaria/diagnosis_treatment/clinicians1.html#severe

Severe malaria: Case conclusion

- The patient was initially treated with IV quinidine/doxycycline*
- Developed AKI requiring CRRT, subsequently recovered
- Encephalopathy, respiratory failure gradually recovered
  - Prolonged intubation required tracheostomy
- Acquired nosocomial ventilator-associated pneumonia and UTI
- Did NOT develop delayed onset anemia (associated with artesunate)
- Discharged to acute rehab on day 34 of hospitalization

Parasitemia
Day 1: 35%
Day 2: 5.8%
Day 3: 1.25%
Day 4: <1%
Day 9: Negative

*Artesunate was not immediately available

Prevention and timely treatment: Our most effective interventions

- Missed opportunities: Travelers often present to a travel clinic for vaccinations, including YFV (often required in W Africa)
- In 2018, *all* malaria deaths in US had a delayed diagnosis, delayed treatment, or inappropriate treatment for severe malaria
- Advise travelers on
  - Symptoms of malaria and potential for long incubation periods
  - Need for emergent evaluation if malaria is possible
  - Telling their physicians where they have traveled to when sick

Mousa A, et al. The impact of delayed treatment of uncomplicated P. falciparum malaria on progression to severe malaria: A systematic review and a pooled multicentre individual-patient meta-analysis. PLoS Med. 2020 Oct 19;17(10):e1003359.
Mace KE, Lucchi NW, Tan KR. Malaria Surveillance — United States, 2018. MMWR Surveill Summ 2022;71(No. SS-8):1–29.

EMERGING ISSUES

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Urgent action needed as malaria resists key drug

18 July 2024

James Gallagher
Health and science correspondent • @JamesTGallagher

The New York Times

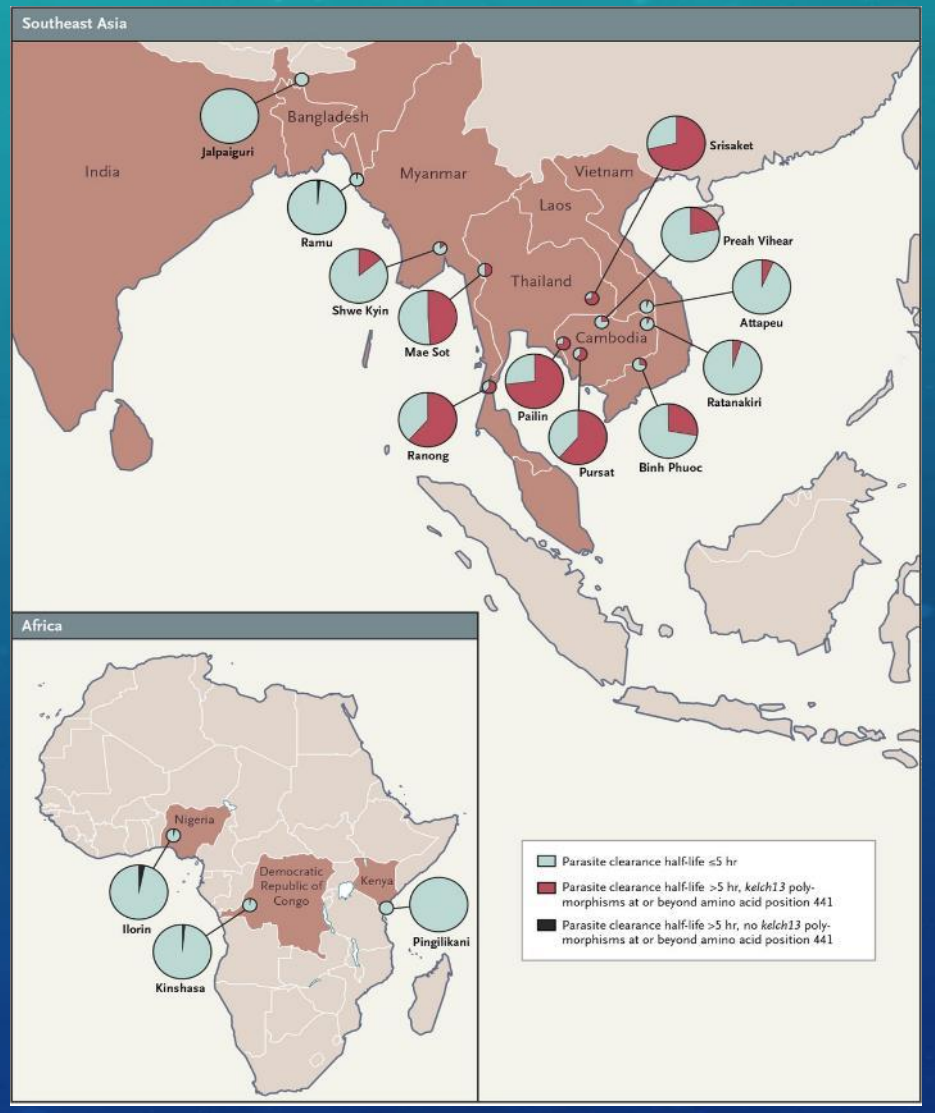
U.S. Sees First Cases of Local Malaria Transmission in Two Decades

Five people, four in Florida and one in Texas, have acquired malaria in the United States in recent months.

By Emily Anthes
Published June 27, 2023 Updated July 3, 2023

Artemisinin resistance in *P. falciparum*

- Mediated mainly by mutations in *kelch*13 (PfK13) protein
- Initially emerged in SE Asia (Greater Mekong Region) with reports of prolonged parasitemia or treatment failures with some ACTs
- Prolonged ACT courses (6 days) or triple ACT (TACT) regimens are considered
- Recent reports of emergence emerging resistance in Rwanda, Uganda, S. America (Amazon)



Ashley EA et al. N Engl J Med 2014;371:411-423.

Rosenthal PJ. Has artemisinin resistance emerged in Africa? Lancet Inf Dis 2021;21:1056-7.
Balikagala B, et al. Evidence of Artemisnin-Resistant Malaria in Africa. NEJM 2021;385:1163-71.

Science

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HOME > SCIENCE > VOL. 385, NO. 6706 > ARTEMISININ-RESISTANT MALARIA IN AFRICA DEMANDS URGENT ACTION

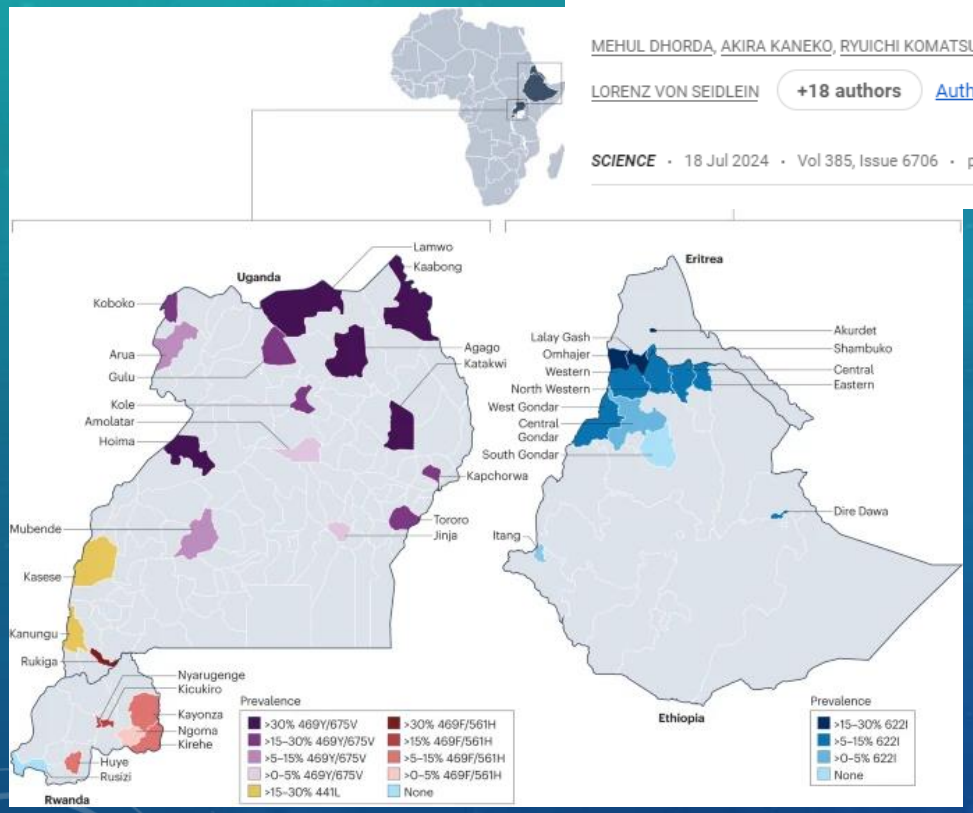
POLICY FORUM | GLOBAL HEALTH

Artemisinin-resistant malaria in Africa demands urgent action

Investment in community health workers is essential

MEHUL DHORDA, AKIRA KANEKO, RYUICHI KOMATSU, ACHYUT KC, SALUM MSHAMU, SAMWEL GESASE, NTULI KAPOLOGWE, ASHENAFI ASSEFA, JIMMY OPIGO, [...], AND LORENZ VON SEIDLEIN +18 authors Authors Info & Affiliations

SCIENCE · 18 Jul 2024 · Vol 385, Issue 6706 · pp. 252-254 · DOI: 10.1126/science.adp5137



A multipronged approach

Policy changes and other action needed now to limit the impact of artemisinin-resistant malaria in East Africa

Drug therapy

- Change from ACTs to TACTs now.
- Add single low-dose primaquine to antimalarial regimens for *P. falciparum*.
- Accelerate the development and roll-out of additional TACTs and new classes of antimalarials.

Vector control

- Expand the coverage of ITNs and IRS.
- Improve the quality of distributed ITNs in terms of bioefficiency and durability alongside initiatives to increase their use.
- Validate and implement effective new vector control tools.
- Explore innovative approaches for combining vector control interventions for outdoor and indoor biting mosquitoes.

CHW

- Adapt and implement sustainable CHW networks in every village to ensure access to early diagnosis and treatment of uncomplicated malaria episodes and pre-referral management of patients with severe malaria with rectal artesunate suppositories.

Vaccines

- Include malaria vaccines in childhood vaccination programs.
- Implement vaccination campaigns of entire populations.

Monitoring

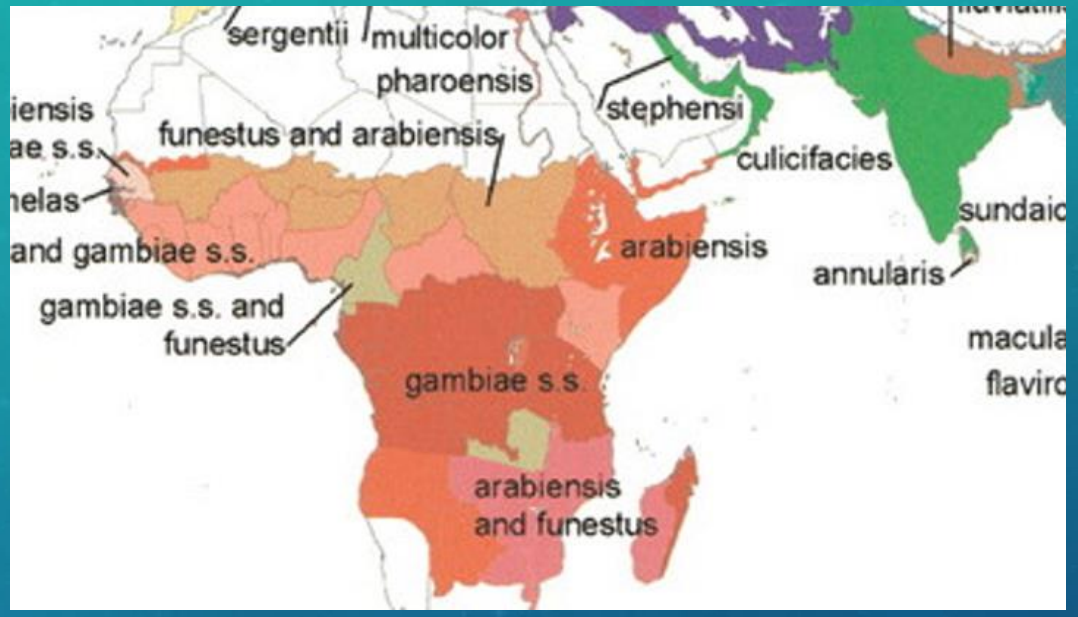
- Monitor the containment of ART-R.
- Extend and validate molecular surveillance.
- Conduct appropriate therapeutic efficacy studies.
- Monitor the efficacy of SMC and PMC in East Africa

ACT, artemisinin combination therapy; ART-R, artemisinin resistance; CHW, community health worker; IRS, indoor residual spraying; ITN, insecticide-treated bed net; PMC, perennial malarial chemoprevention; SMC, seasonal malaria chemoprevention; TACT, artemisinin combination therapy including two partner drugs (i.e., triple therapy).

Rosenthal, P.J., Asua, V. & Conrad, M.D. Emergence, transmission dynamics and mechanisms of artemisinin partial resistance in malaria parasites in Africa. Nat Rev Microbiol 22, 373–384 (2024). https://doi-org.proxy.library.emory.edu/10.1038/s41579-024-01008-2

Anopheles stephensi

- Native to S. Asia and parts of Arabian Peninsula
  - Primary vector of urban malaria in India
- Can transmit *P falciparum* and *P vivax*
- More adapted to urban and man-made breeding sites than usual Africa vectors *An. gambiae, An. funestus*
- Prefers to bite earlier in the evening
- Often insecticide-resistant
- Expanding range to East and West Africa

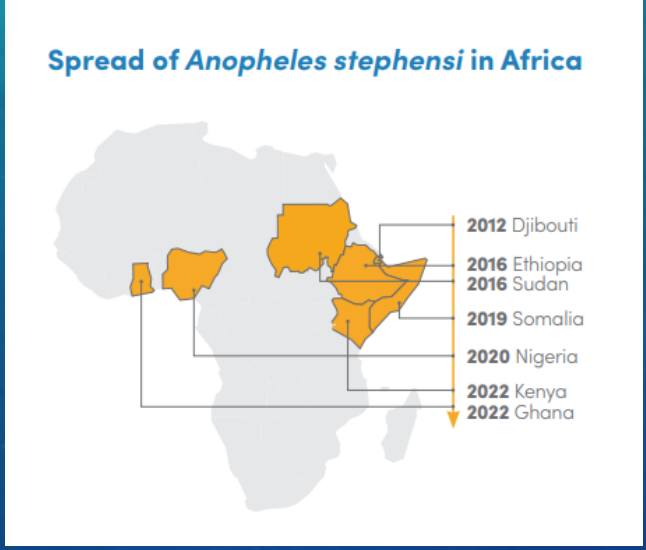


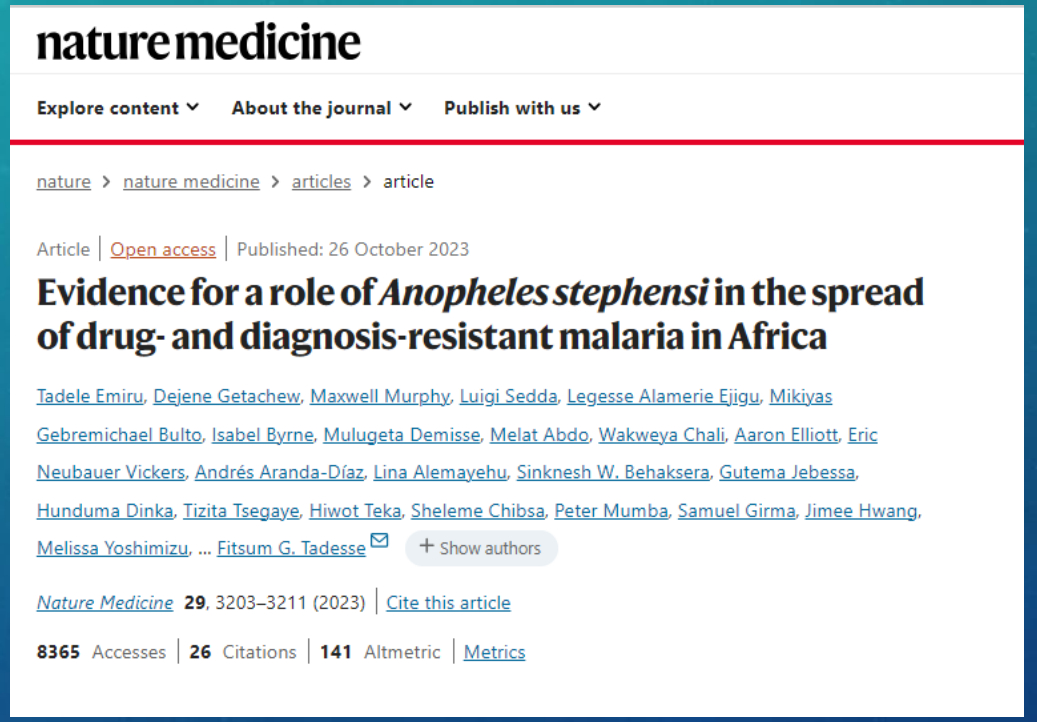
A. stephensi CDC Public health image library

Kiszewski A, et al. Am J Trop Med Hyg. 2004 May;70(5):486-98. PMID: 15155980.
Sinka ME, et al. Proc Natl Acad Sci U S A. 2020 Oct 6;117(40):24900-24908. doi: 10.1073/pnas.2003976117. Epub 2020 Sep 14. PMID: 32929020; PMCID: PMC7547157.

Anopheles stephensi: Potential impact

- Increased number of Africans at malaria risk (126 million)
- Increased malaria cases in Ethiopia by 50%

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Evidence for a role of *Anopheles stephensi* in the spread of drug- and diagnosis-resistant malaria in Africa

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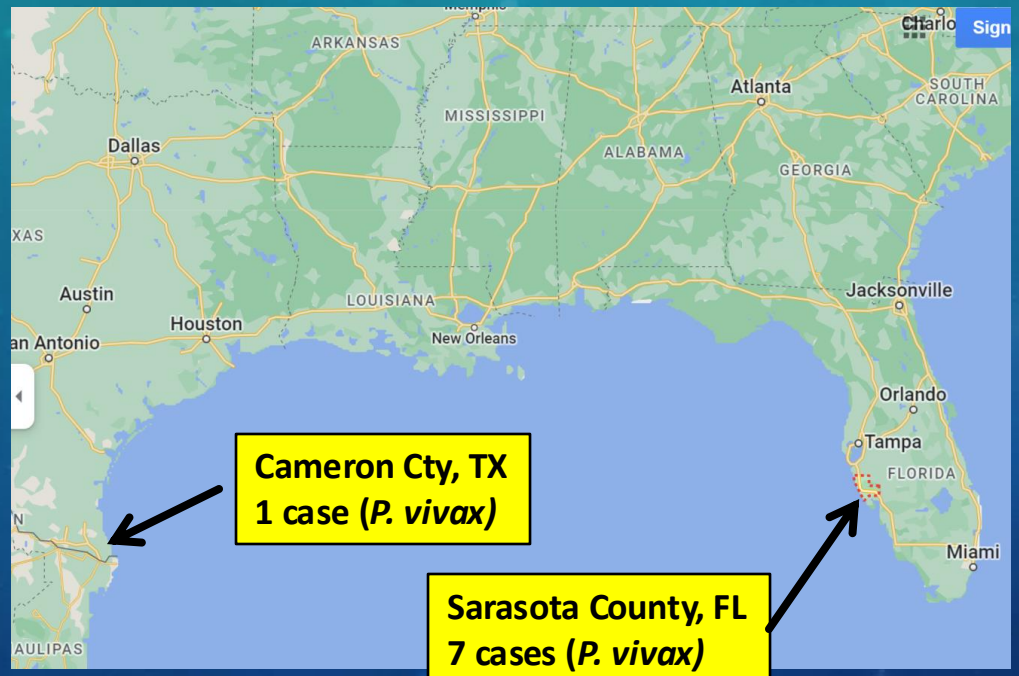
https://www.who.int/publications/i/item/WHO-UCN-GMP-2022.06

Sinka ME, et al. A new malaria vector in Africa: Predicting the expansion range of Anopheles stephensi and identifying the urban populations at risk. Proc Natl Acad Sci U S A. 2020 Oct 6;117(40):24900-24908. doi: 10.1073/pnas.2003976117. Epub 2020 Sep 14. PMID: 32929020; PMCID: PMC7547157.

2023: First reported autochthonous malaria cases in US since 2003

Centers for Disease Control and Prevention
MMWR
Morbidity and Mortality Weekly Report
Weekly / Vol. 72 / No. 36
September 8, 2023

Outbreak of Locally Acquired Mosquito-Transmitted (Autochthonous) Malaria — Florida and Texas, May–July 2023



Notes from the Field

Locally Acquired Mosquito-Transmitted (Autochthonous) *Plasmodium falciparum* Malaria — National Capital Region, Maryland, August 2023

Monique Duwell, MD[1]; Timothy DeVita, MD[2]; David Torpey, PhD[3]; Jenny Chen[3]; Robert A. Myers, PhD[3]; Kimberly Mace, PhD[2]; Alison D. Ridpath, MD[2]; Wycliffe Odongo[2]; Brian H. Raphael, PhD[2]; Audrey Lenhart, PhD[2]; Jon Eric Tongren, PhD[2]; Stephen Stanley, MPH[1]; David Blythe, MD[1]

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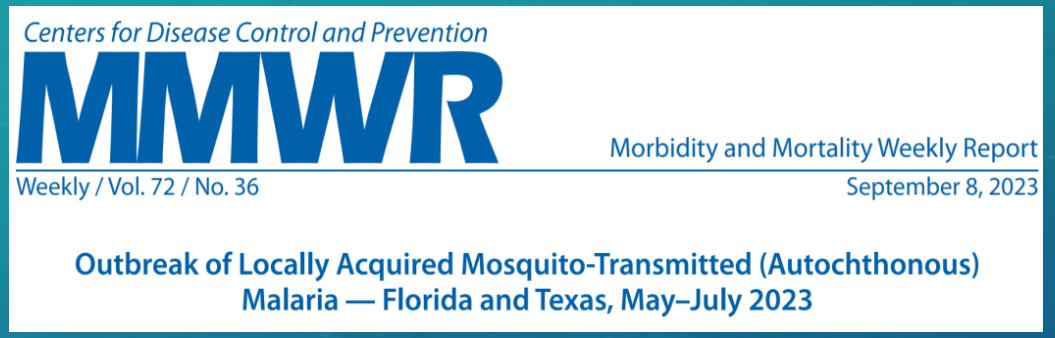
Malaria transmission in US

- Likely due to gametocytemic persons in areas with *Anopheles* vector activity
  - Also possible: “Airport” (“suitcase,” “Odyssean”) malaria
- Recent US surge—why now?
  - Increased travel and human migration?
  - Climate change, increased mosquito vectors?
- Clinicians: Consider malaria for fever of unknown origin
- Patients treated for malaria should still practice mosquito avoidance measures!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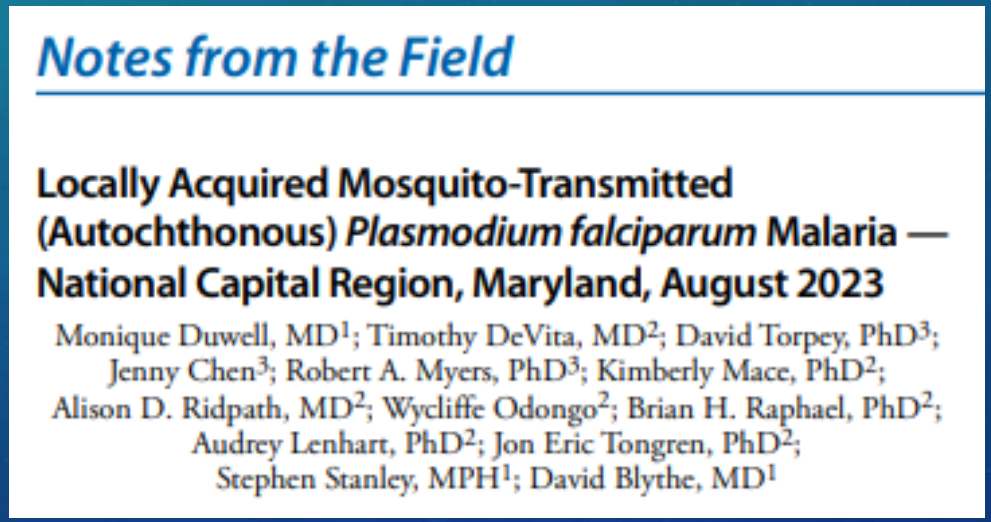
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Thank you! Questions?

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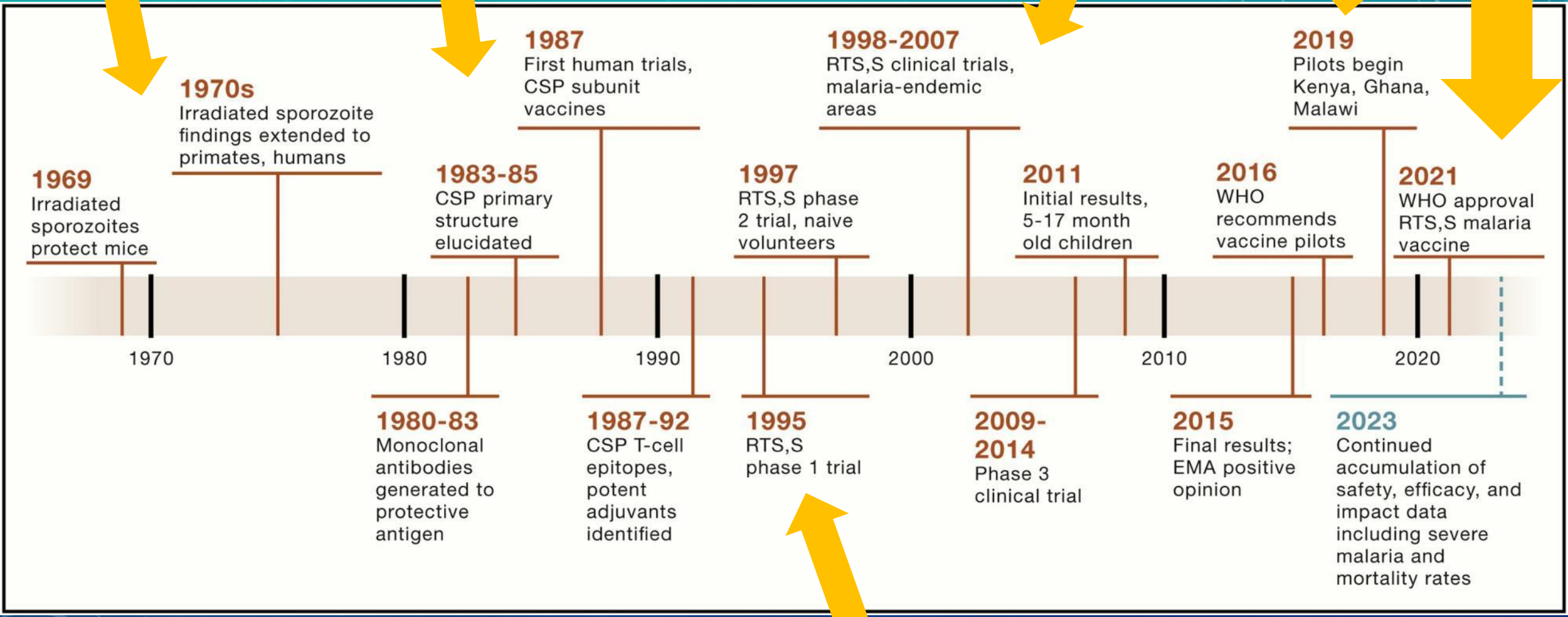
RTS,S/AS01 VACCINE: DECADES IN THE MAKING

Malaria Vaccine Implementation Project (MVIP)



Sinnis P et al. Cell 2022, 185:750-4.