Malaria Investigation and Reporting for Local Public Health Investigators

2.16.2023 (Last updated 8.13.2024)

Irene Ruberto
VBZD & Mycotics Program Manager
vbzd@azdhs.gov

ARIZONA DEPARTMENT OF HEALTH SERVICES

Overview of All Updates added in August 2024

- New Figure Added: Temporal View of Malaria Lifecycle: *P. falciparum* (slide 9)
- New Figure Added: Temporal View of Malaria Lifecycle: *P. vivax* (slide 10)
- Updated Malaria Map & Summary Stats (slide 11)
- Updated Terms for Malaria Transmission in the US (Locally Acquired Malaria) (slide 12)
- Updated Symptoms for Clinical - Severe Malaria (slide 14)
- New Information on Malaria Relapse (slide 15)
- New Information on Other Manifestations of Malaria (slide 16)
- New Information on Initial Clinical Evaluation and Disposition (slide 20)
- Updated Information on Key Diagnostic Tests for Malaria (slide 22)
- New Information on Available Assistance from CDC for Malaria Diagnosis (slide 23-24)
- New Information on Treatment Considerations (slide 25-26)
- Updated Information on Locally Acquired Malaria Cases in 2023 (slide 44)
- New Information on Criteria to Distinguish a New Case from an Existing Case (slide 61)
- New Terms for Classifying Malaria Disease Acquisition (slide 62-63)
- New Guidance on Enhanced Investigations Steps (slide 68-69)
- Updated Resources (CDC Malaria Investigation Best Practices) (slide 82)

What we will cover

- Malaria background
- Lifecycle
- Symptoms
- The vector
- Testing
- *Added in July 2023*- Update on Locally-Acquired Malaria in the US
- Case classification
- Case investigation
- CDC case report form
- Resources

What is Malaria?

DISEASE:

Malaria is a mosquito-borne disease caused by a parasite of the ***Plasmodium*** genus

PARASITE:

Plasmodium is a genus of unicellular eukaryotes that are obligate parasites of vertebrates (reptiles, birds and mammals) and insects **+200** species, **5** infect humans.

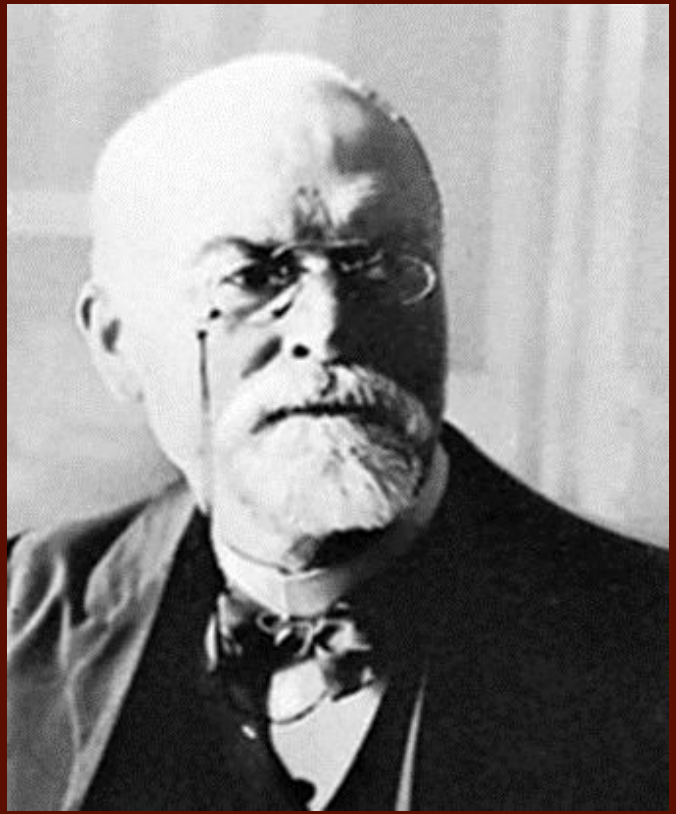
VECTOR:

Female mosquitoes of the genus ***Anopheles***. **+ 400** species, **~30** transmit malaria.

History of Malaria

Dr. Charles Alphonse Laveran (1845-1922)

- French Army doctor working in Algeria
- Described the malaria **parasite** in human blood 1880 (*P. malariae*) disproving the **“mal’aria” (“bad air”)** theory
- Nobel Prize for Medicine 1907



https://www.ncbi.nlm.nih.gov/books/NBK215638/

History of Malaria

Sir Ronald Ross (1857-1932)

- British Army doctor working in India
- Discovered the complete **transmission cycle** of avian malaria in culicine **mosquitoes** & birds in 1897.
- Worked in conjunction with Dr. Patrick Manson who had discovered in 1878 that mosquitoes transmitted filarial parasites in China.
- Nobel Prize for Medicine 1902

https://www.ncbi.nlm.nih.gov/books/NBK215638/

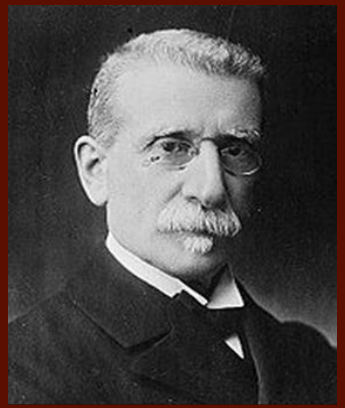
History of Malaria

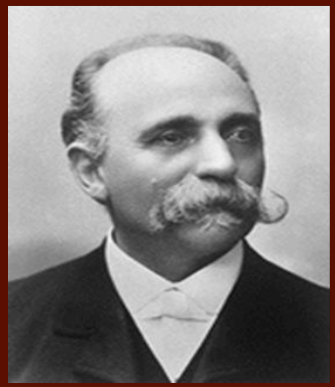
A group of Italian scientists:

Giovanni Battista Grassi (1854-1925), Amico Bignami, Giovanni Bastianelli, Antonio Dionisi, and Angelo Celli

- Confirmed that **human malaria** parasites pass through the same **developmental stages** in the mosquito as the avian parasites observed by Ross
- Grassi and Ross were bitter toward each other for the remainder of their careers, because each claimed credit for discovering malaria's life cycle in the mosquito.

Grassi





https://www.ncbi.nlm.nih.gov/books/NBK215638/

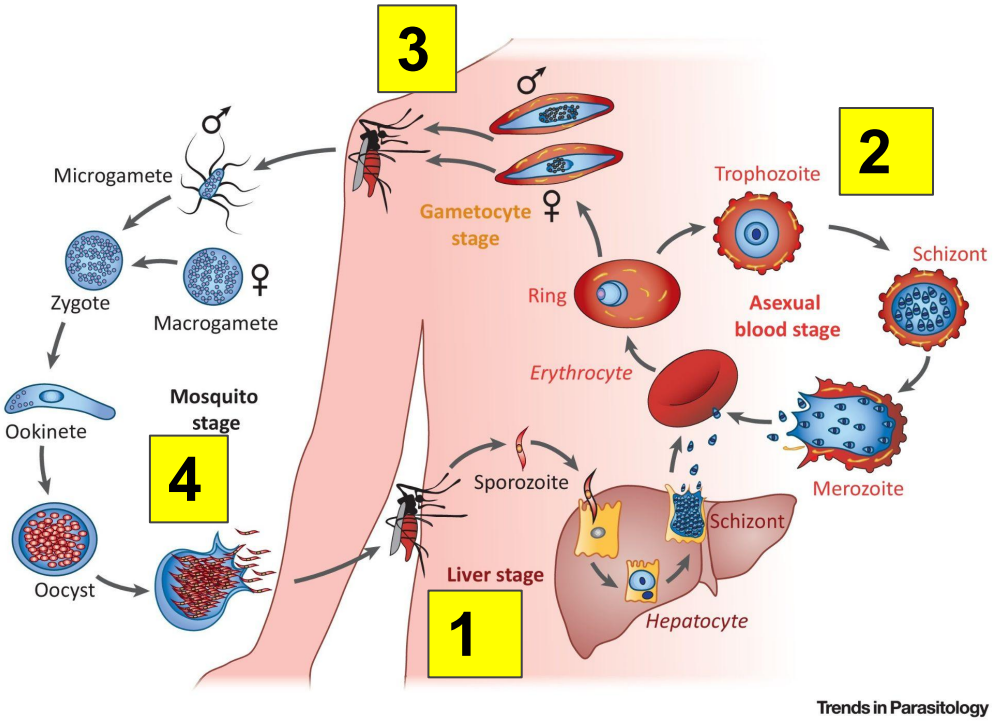
Lifecycle

1. After a mosquito bite, the parasites grow and multiply first in the **human liver cells,** which then rupture releasing merozoites

2. These infected **red blood cells** and grow destroying them, releasing daughter parasites (“merozoites”) that continue the cycle by invading other red cells. The blood stage parasites are those that cause the **symptoms** of malaria.

3. When certain forms of blood stage parasites (gametocytes, which occur in male and female forms) are **ingested during blood feeding by a female *Anopheles* mosquito**, they mate in the gut of the mosquito and begin a cycle of growth and multiplication in the mosquito.

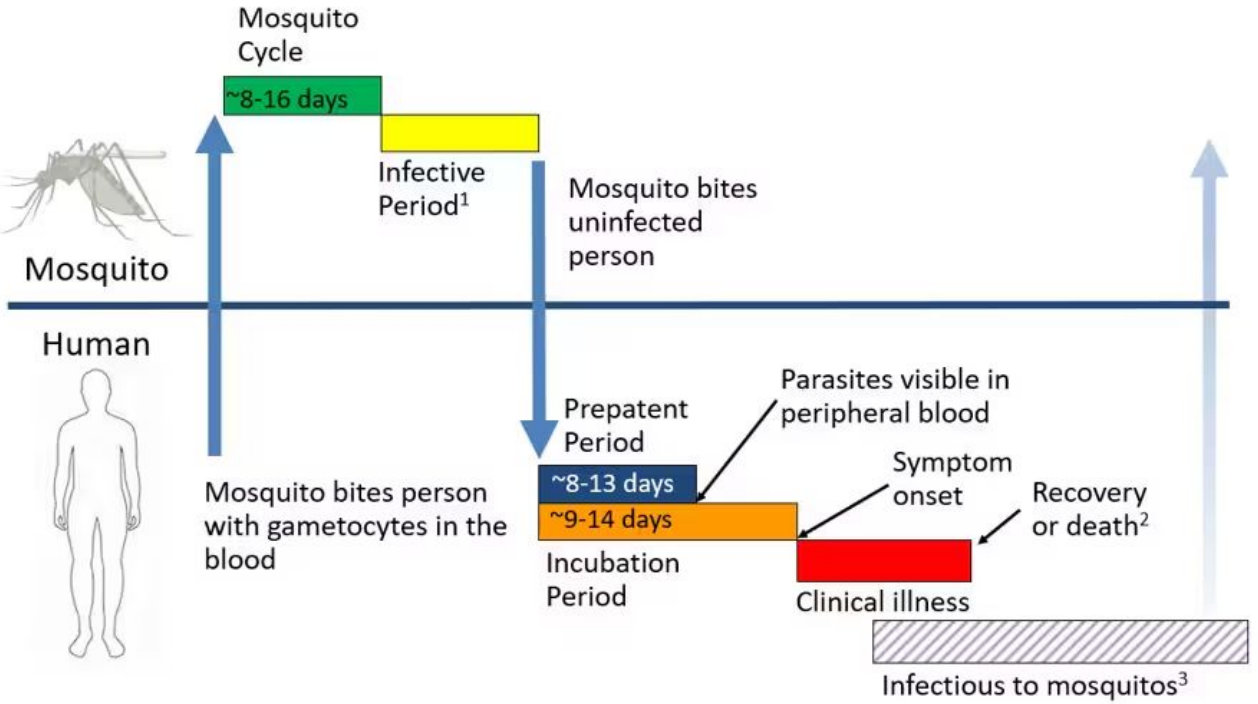
4. After 10-18 days, a form of the parasite called a sporozoite migrates to the **mosquito’s salivary glands**.



https://www.cell.com/trends/parasitology/fulltext/S1471-4922%2818%2930248-4

Temporal View of Malaria Lifecycle: *P. falciparum*

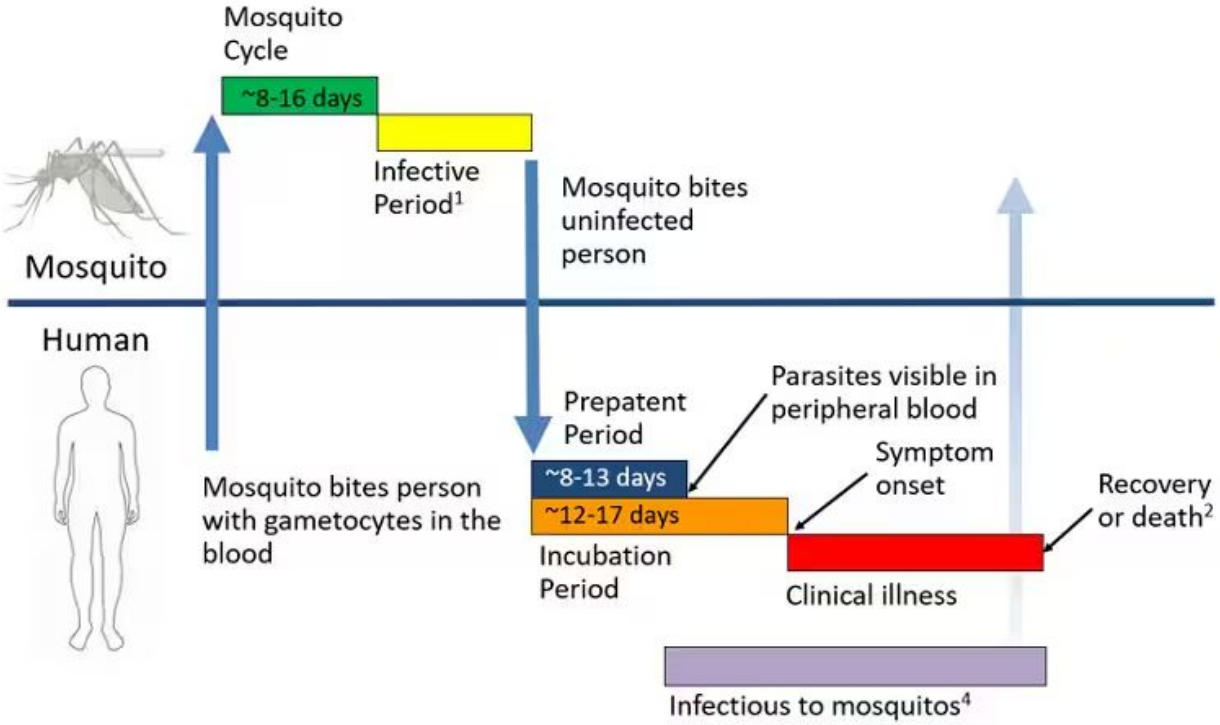
1. *Anopheles* mosquitoes can **live up to 6 weeks after ingesting gametocytes**.
2. Semi-immune individuals (visitors or recent immigrants) **may have prolonged infection** without overt symptoms and may not recover from malaria or die of malaria.
3. ***P. falciparum*** gametocytes usually **appear ~7-10 days** after symptom onset, can **last up to 10-22 days**. Blood stage treatment **does not kill *P. falciparum* mature gametocytes**.



https://www.cdc.gov/malaria/php/surveillance/appendix-a-malaria-lifecycle.html

Temporal View of Malaria Lifecycle: *P. vivax*

1. *Anopheles* mosquitoes can **live up to 6 weeks after ingesting gametocytes**.
2. Semi-immune individuals (visitors or recent immigrants) **may have prolonged infection** without overt symptoms and may not recover from malaria or die of malaria.
3. ***P. vivax*** gametocytes can **appear before symptom onset**, during the prepatent period, and **are killed with blood stage treatment**.



https://www.cdc.gov/malaria/php/surveillance/appendix-a-malaria-lifecycle.html

Malaria Worldwide

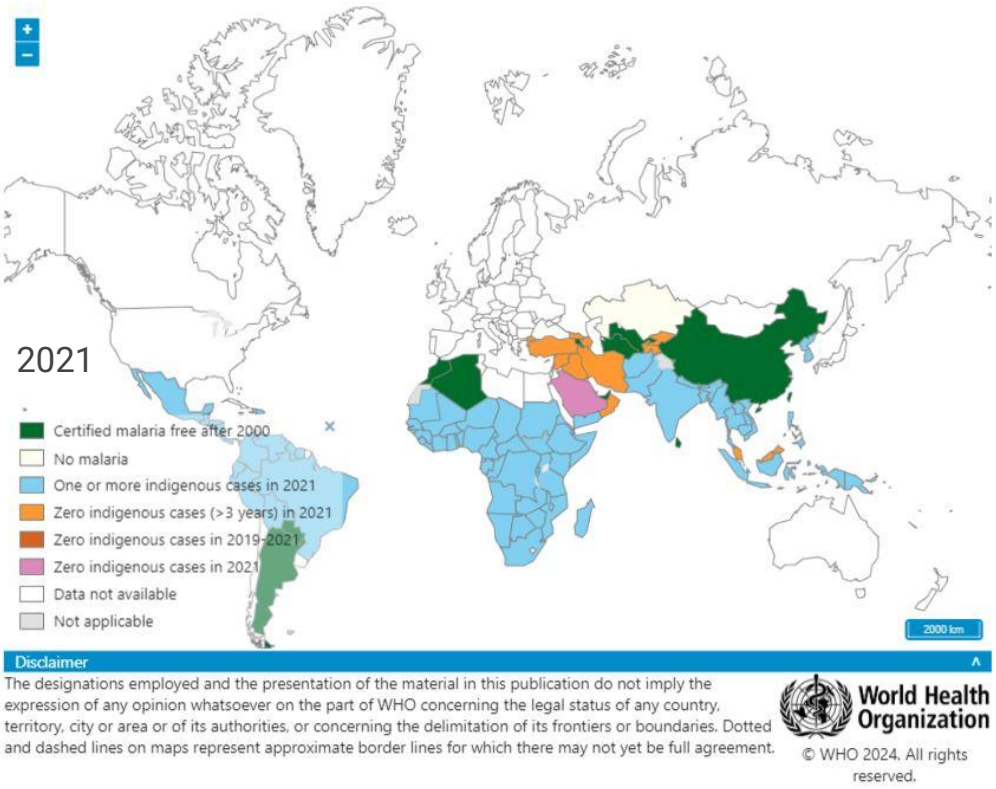
In 2020, malaria caused an estimated 241 million clinical episodes, and 627,000 deaths.

An estimated 95% of deaths in 2020 were in the WHO African Region.

About 2,000 cases of malaria are reported each year in the US

- Between 1957 and 2003, there were 156 cases of locally acquired malaria in the US
- Between 2003 and 2022, there were no reported cases of locally acquired malaria in the US
- In the summer and fall of 2023, there were 10 locally acquired mosquito-transmitted malaria cases in four states

~25 travel-associated cases/year in Arizona

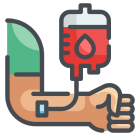


https://www.cdc.gov/malaria/data-research/index.html

Malaria Transmission in the US (Locally Acquired Malaria)

Locally Acquired Malaria:

- In the U.S., a non-endemic setting without indigenous malaria transmission, locally acquired malaria cases are typically classified into the following two categories:
  1. **Induced Malaria**
     - Malaria transmission through a blood transfusion, tissue or organ transplantation, or another parenteral route, not mosquito-borne or congenital transmission. Rare (~1 case/2yrs). No approved tests are available in the US to screen blood donations (prevention is mostly based on screening donors via questionnaire).
  2. **Introduced**
     - Malaria likely acquired by mosquito transmission from an imported case in an area where malaria is not a regular occurrence. Very rare but there is some risk present due to the abundance of competent vectors, especially in the southern states.



Imported Malaria:

- Malaria acquired outside the U.S. The patient must have recent (within ~2 years) travel history to a country or territory with ongoing malaria transmission.

Congenital Malaria:

- Malaria infection transmitted directly from mother to child during pregnancy or childbirth.

https://www.cdc.gov/malaria/php/surveillance/case-definitions.html

Clinical - Uncomplicated Malaria

All symptoms and signs of uncomplicated malaria are **non-specific**.

Classical (but rarely observed) malaria **attacks** consists of:

- A cold stage (sensation of cold, shivering)
- A hot stage (fever, headaches, vomiting; seizures in young children); and
- Finally a sweating stage (sweats, return to normal temperature, tiredness).

More commonly, the patient presents with a combination of the following symptoms:

- Fever
- Chills
- Sweats
- Headaches
- Nausea and vomiting
- Body aches
- General malaise

https://www.cdc.gov/malaria/hcp/clinical-features/index.html

Clinical - Severe Malaria

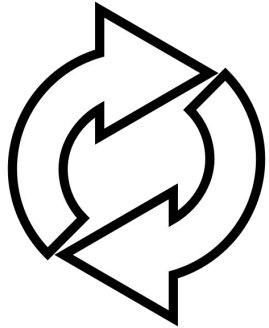
Progression to severe malaria occurs when infections are complicated by **serious organ failures** or abnormalities in the patient's blood or metabolism, usually following delays in diagnosis and treatment. For healthcare providers practicing in the U.S., the criteria for **severe malaria may include any one or more of the following**:

- High percent parasitemia (≥5%)
- Impaired consciousness
- Seizures
- Circulatory collapse/shock
- Pulmonary edema or acute respiratory distress syndrome (ARDS)
- Acidosis
- Acute kidney injury
- Abnormal bleeding or disseminated intravascular coagulation (DIC)
- Jaundice
- Severe anemia (Hb <7 g/dL)

https://www.cdc.gov/malaria/hcp/clinical-features/index.html

Clinical - Malaria Relapse

- In ***P. vivax*** and ***P. ovale*** infections, patients having recovered from the first episode of illness may suffer **additional attacks** (“**relapses**”) after months or event years without symptoms.
- Relapse occurs because *P. vivax* and *P. ovale* have **dormant liver stage parasites** (“hypnozoites”) that may reactivate, infect peripheral erythrocytes, and **begin a new symptomatic episode of malaria**.
- **Treatment** to reduce the chance of such relapses is available and should follow treatment of the first attack.



https://www.cdc.gov/malaria/hcp/clinical-features/index.html

Clinical - Other Manifestations of Malaria

- **Neurological defects** may occasionally persist (sometimes life-long) following cerebral malaria, especially in children. Such defects include trouble with movements (ataxia), palsies, speech difficulties, deafness, neurocognitive deficits, and blindness.
- Recurrent infections with ***P. falciparum*** may result in **severe anemia**. This occurs especially in young children in tropical Africa.
- Malaria during **pregnancy** (especially *P. falciparum*) may cause **severe disease** in the mother and may lead to **premature delivery** or delivery of a **low-birth-weight** baby.
- On rare occasions, ***P. vivax*** malaria can cause **rupture of the spleen**.
- **Nephrotic syndrome** (a chronic, severe kidney disease) can result from chronic or repeated infections with ***P. malariae***.
- **Hyperreactive malarial splenomegaly** (also called “tropical splenomegaly syndrome”) occurs frequently and is attributed to an abnormal immune response to repeated malarial infections. The disease is marked by a very enlarged spleen and liver, abnormal immunologic findings, anemia, and a susceptibility to other infections (such as skin or respiratory infections).

https://www.cdc.gov/malaria/hcp/clinical-features/index.html

Plasmodium Species' Differences

- ***P. falciparum***
  - found worldwide in tropical and subtropical areas, and especially in **Africa**.
  - It can cause **severe malaria** because it multiplies rapidly in the blood causing anemia as well as **cerebral malaria** , that can be fatal.
- ***P. vivax***
  - found mostly in Asia, Latin America, and in some parts of Africa.
  - *P. vivax* (as well as *P. ovale*) has **dormant liver stages** that can activate and invade the blood (**relapse**) several months or years after the infecting mosquito bite. It may cause **severe disease**.
- ***P. ovale***
  - found mostly in Africa (especially West Africa) and the islands of the western Pacific.
  - It is biologically and morphologically very similar to *P. vivax* and can also cause **replases.**
- ***P. malariae***
  - found worldwide, is the only human malaria parasite species that has a **quartan cycle** (three-day cycle). (The three other species have a tertian, two-day cycle.)
  - If untreated, *P. malariae* causes a **long-lasting, chronic infection** that in some cases can last a lifetime.
- ***P. knowlesi***
  - found throughout **Southeast Asia,** particularly in Malaysia, as a natural pathogen of long-tailed and pig-tailed macaques.
  - It can rapidly progress from an uncomplicated to a severe infection; fatal cases have been reported.

Infection and Immunity

- The incubation period in **most cases** varies from **7 to 30 days** (but can be longer).
  - The shorter periods are observed most frequently with *P. falciparum* and
  - The longer ones with *P. malariae*
- **Antimalarial drugs** taken for prophylaxis by travelers can **delay the appearance of symptoms** by weeks or months
- Returned travelers should always remind their health-care providers of any travel in areas where malaria occurs during the **past 12 months**

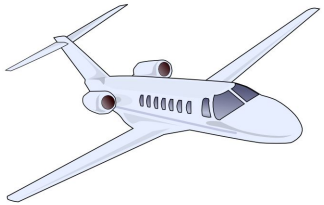
Immunity:

- Following infection with a malaria parasite, there will be some limited **immunity to that species**
- There is **no immunity between malaria species**
- Immunity **declines quickly** after leaving an endemic area

Antimalarial Prophylaxis

- Recommendations for drugs to prevent malaria differ by country of travel and can be found in the CDC web page: Malaria Information by Country.
- **No antimalarial drug is 100% protective and must be combined with the use of personal protective measures**, (i.e., insect repellent, long sleeves, long pants, sleeping in a mosquito-free setting or using an insecticide-treated bednet)
- **Antimalarial drugs**:
  - Atovaquone/Proguanil (Malarone)
  - Chloroquine
  - Doxycycline
  - Mefloquine
  - Primaquine
  - Tafenoquine (ArakodaTM)

Malaria Diagnosis



Initial Clinical Evaluation and Disposition

- **Suspect malaria and perform diagnostic testing** for febrile individuals who:
  - Report recent (weeks to 2 years) travel to a malaria-endemic country.
  - Do not have an alternative diagnosis for fever.
- If concerned about antimalarial drug resistance/treatment failure or if malaria is in a patient with no recent international travel, **save a pre-treatment whole blood sample (purple top, EDTA tube)** for ASPHL (Arizona State PH Lab) to forward to CDC for testing.
- If malaria is suspected in a patient, but malaria testing is not available at your facility, refer or transfer the patient immediately to a facility with malaria testing capacity.

https://www.cdc.gov/malaria/php/surveillance/diagnosis-treatment-quick-reference.html

Malaria Diagnosis

Commercial testing - for fast diagnosis

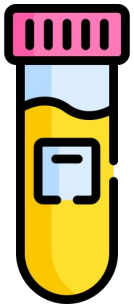
- Ex. Quest Diagnostics: Microscopic Examination with *Giemsa* stain can identify *babesia/plasmodium* (both are parasite that infect red blood cells and can identified in blood smears)
- Ex. Labcorp blood smear parasite examination
- Ex. labcorp *Plasmodium* species PCR

ASPHL submissions - forwarded to the CDC for malaria morphological identification, species confirmation, and evaluation of drug resistance:

- **Thick or thin blood smear** (stained or unstained)
- Stained and unstained blood films may be air-dried or fixed and stored at room temperature (15-25°C) prior to submission.
- **Whole blood** must be collected in unexpired, EDTA-treated vacutainer tubes and refrigerated at 2-8°C prior to shipment.
- Whole blood must be received no more than 3 days post collection to be acceptable for morphologic analysis.
- Symptoms and travel history needed.
- Turnaround time ~ 7 days.

Send out to CDC

Malaria Diagnosis



Key Diagnostic Tests for Malaria:

- **Microscopy: Thick and Thin Blood Smear**
  - The Gold Standard.
  - Collect both for all suspected cases.
    - Blood smears detect parasites and determine parasite density and *Plasmodium* species. Obtain results rapidly. Should not be a send-out test. It is vital that health-care providers receive results from these tests within hours in order to appropriately treat their patients infected with malaria
    - If the initial test is negative and suspicion for malaria is high, repeat the blood smear every 12-24 hours until positive, or until three tests are negative.
    - CDC can provide malaria diagnostic assistance (see next slide for additional details)

- **Malaria Polymerase Chain Reaction (PCR):**
  - Detection of species specific parasite DNA in a sample of peripheral blood using a Polymerase Chain Reaction (**PCR**)

- **Malaria Rapid Diagnostic Test (RDT):**
  - Detection of circulating malaria-specific *antigens* using rapid diagnostic test (**RDT**)
    - Mostly used in endemic countries
    - Recently available in the U.S. (BinaxNOW)
    - Can shorten the time to treatment but must be collected concurrently with a blood smear

Malaria Diagnosis

CDC can assist with the following (should be coordinated through ADHS):

- **Species confirmation**
  - Send an email for CDC testing approval and submission instructions:
    - Blood smear images for review via telediagnosis (M - F, 9am - 5pm ET): DPDX@cdc.gov
    - Blood smear slides or whole blood for PCR: parasiteslab@cdc.gov
- **Routine molecular surveillance testing**
  - Consider routinely sending whole blood specimens to CDC for molecular surveillance testing: malarialab@cdc.gov
    - Preferred sample type is refrigerated whole blood, treated with EDTA:
      - If whole blood is not available CDC may be able to accept other specimens, please reach out to malarialab@cdc.gov to discuss options.
      - Fo detailed instructions on how to send, please reach out to the malaria laboratory (malarialab@cdc.gov)
- Please copy the malaria hotline in emails regarding lab testing for cases under investigation: malaria@cdc.gov

Malaria Diagnosis

Malaria Molecular Testing (should be coordinated through ADHS):

- CDC has developed a laboratory method to conduct **molecular testing for *P. falciparum* and *P. vivax***. This testing can help **identify markers of resistance, strain relatedness, and geographic origin**.
- State public health laboratories are welcome to submit any malaria specimen to CDC for molecular testing. However, some specific circumstances where CDC is particularly interested in conducting this testing includes the following:
  - Any concern of **drug resistance or recrudescent illness**:
    - If the case-patient was on any type of chemoprophylaxis and developed malaria
    - If the case-patient continued to have positive blood smears after completing treatment
    - If the case-patient continued to have symptoms after completing treatment (if parasite clearance is not documented)
    - Please contact malaria@cdc.gov and malarialab@cdc.gov
  - **Any unusual cases under enhanced investigation**
    - No history of recent travel or other risk factors
    - Concern for transfusion transmitted malaria or other blood-borne transmission
    - Please contact CDC Malaria hotline (770-488-7788 or malaria@cdc.gov) if you would like to submit a specimen for a case with concern of drug resistance or under enhanced investigation.

Treatment Considerations

When a **blood smear or RDT is positive**:

- Start treatment immediately
- Consider hospitalization
- Consult with Infectious Disease specialists
- Find dosing specifics and alternative treatment regimens in CDC's treatment tables
- Contact the **CDC Malaria Hotline** if you have questions (Email malaria@cdc.gov or call M-F, 9am-5pm EST 770-488-7788 or 855-856-4713 (after hours call 770-488-7100)

Treatment Considerations

Treatment of the Blood Stage of Malaria Infections:

- **Treat severe malaria** with IV artesunate. Find information on how to acquire IV artesunate in the United States on CDC's malaria website.
- The **parasite's species and country of origin (a proxy for chloroquine sensitivity)** should guide drug selection (see first column in CDC's treatment tables for further guidance).
- **Treat uncomplicated malaria due to *plasmodium falciparum* (or if species is unknown)** with oral antimalarials for chloroquine-resistant malaria.
    - The preferred treatment is artemether-lumefantrine (Coartem®); atovaquone-proguanil (Malarone®) is the next best option.
- **Treat uncomplicated malaria due to *Plasmodium vivax*** (from most countries*) or *ovale*, with chloroquine or hydroxychloroquine. If chloroquine/hydroxychloroquine is not available, use an antimalarial drug for chloroquine-resistant malaria (e.g., artemether-lumefantrine [Coartem®]).
- **Additional treatment is needed to eliminate the liver hypnozoites of *P. vivax* and *P. ovale*** which cause relapse malaria (see next slide for additional details).

https://www.cdc.gov/malaria/php/surveillance/diagnosis-treatment-quick-reference.html

Treatment Considerations

To prevent **relapse** of confirmed *P. vivax* and *P. ovale* malaria, treat the liver hypnozoites:

- Start **primaquine** or **tafenoquine** as soon as quantitative G6PD result is available, not before.
- **If G6PD is normal:**
  - **Primaquine:** Preferred option (adult dose = 30 mg base per day x 14 days)
    - Give primaquine with food to reduce gastrointestinal side effects.
    - The total dose of primaquine determines effectiveness. When doses are missed, the patient should continue to take the same daily dose for as many days as is needed to complete the course.
    - **For patients > 70 kg, increase the dose** to 6 mg/kg base total, divided into 30 mg/day doses for as many days as needed (e.g., 100 kg patient, 30 mg base for 20 days). Max daily dose 30 mg base.
    - **Contraindications**: pregnant or breastfeeding people, or people with G6PD deficiency (intermediate G6PD deficiency requires dose adjustment, see below)
      - If G6PD is intermediate: Primaquine adjustment = 45 mg base (adult dose) per week for 8 weeks with close monitoring for hemolysis

https://www.cdc.gov/malaria/php/surveillance/diagnosis-treatment-quick-reference.html

Treatment Considerations

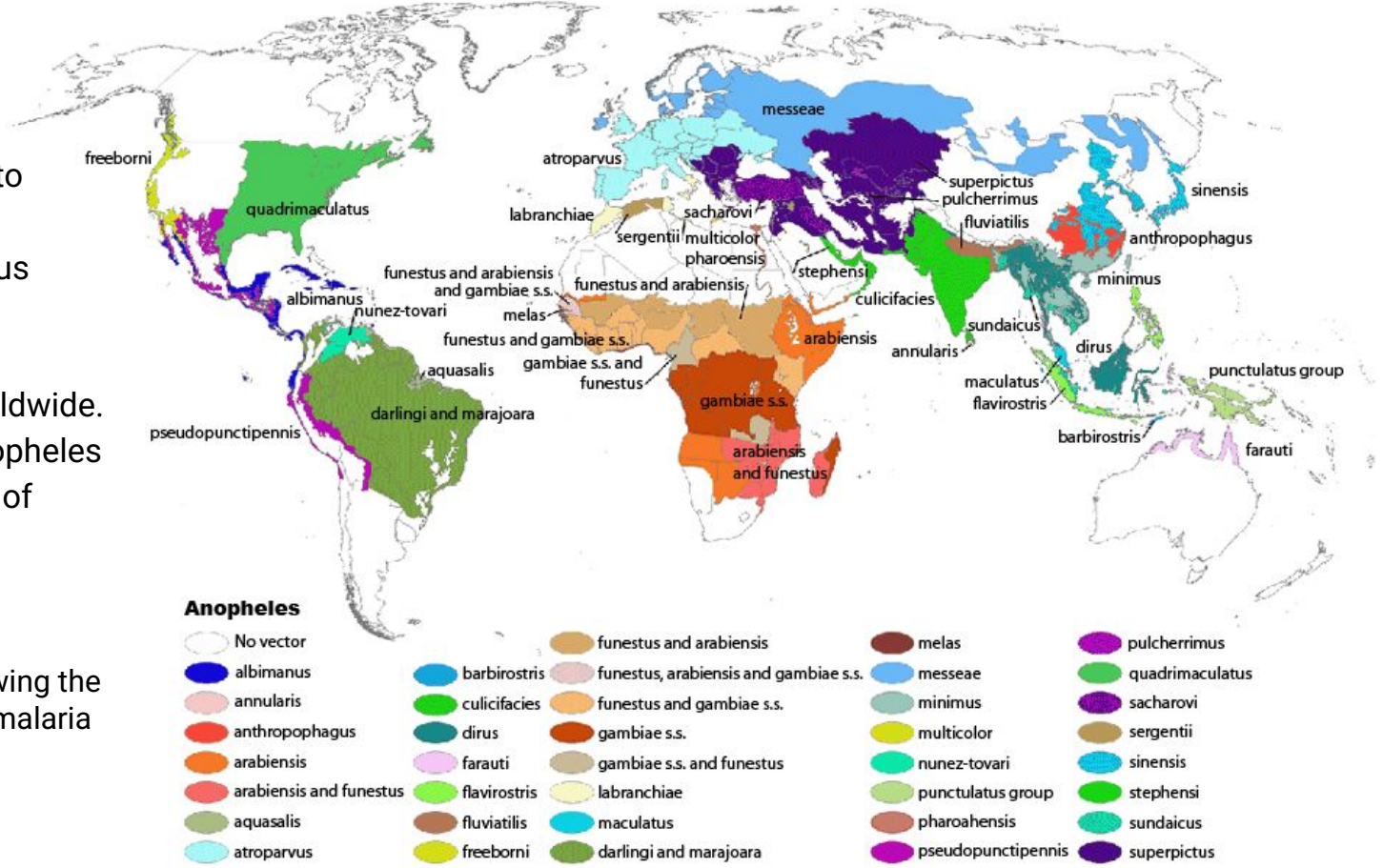
To prevent **relapse** of confirmed *P. vivax* and *P. ovale* malaria, treat the liver hypnozoites:

- Start **primaquine** or **tafenoquine** as soon as quantitative G6PD result is available, not before.
- **If G6PD is normal:**
  - **Tafenoquine:** Tafenoquine 300 mg single dose is an option for adults (only if chloroquine was given for blood stage therapy)
    - Avoid tafenoquine if the patient's weight is over 70 kg
    - **Contraindications:** <16 years of age, pregnant or breastfeeding people, or people with G6PD deficiency of any severity (G6PD activity <70%)
    - **Not recommended:** in patients with psychiatric illness
- **If there is G6PD deficiency:**
  - Chloroquine 300 mg base (adult dose) weekly for 1 year
- Pregnant people can take Chloroquine 300 mg base weekly until delivery

https://www.cdc.gov/malaria/php/surveillance/diagnosis-treatment-quick-reference.html

Vector

- Malaria is transmitted to humans by female mosquitoes of the genus *Anopheles*.
- About 430 recognized *Anopheles* species worldwide.
- But only around 70 *Ano*pheles species capable (16%) of transmitting malaria.



Right- Map of the world showing the distribution of predominant malaria vectors

https://www.cdc.gov/malaria/about/biology/mosquitoes/map.html

Malaria vector in Arizona

Malaria in Arizona

- Arizona once had a large human **malaria reservoir** especially during & after the **American Civil War (1861-1865).**

- Arizona's rivers & streams were once flowing waterways that supported extensive **riparian areas with marshes** or ciénegas(=wetland). These were ideal breeding areas for anopheles mosquitoes.

- Anopheles mosquitoes capable to transmitting malaria are present in AZ.

Co. B, 10th Inf., Crossing the Gila River Near San Carlos, 1885 (courtesy of M. Fink).

Anopheles Mosquitoes

- *Anopheles* will swarm during crepuscular (twilight) periods and prefer to feed at dawn, dusk, and at night.
- It is important to prevent mosquito bites while spending any time outside, especially in the evening and at night.
- Testing of Mosquitoes
  - Testing outside of an area where the locally transmitted malaria cases have been reported will likely not provide positive pools.
  - Given current events, knowing your vectors and being prepared to test and react is important.
- Early detection and treatment of imported human cases is key to lower the risk of further transmission.
- CDC can share testing protocols with programs that conduct enhanced mosquito trapping and control around imported human malaria cases.

Residual Anophelism in Arizona

Anopheles hermsi

- Known competent vector
- Widely distributed in AZ and in the Western US
- Associated with riparian, riverine & natural wetlands, marshes, etc.
- Anthropophilic & endophilic (making it a competent vector species).

https://www.azdhs.gov/documents/preparedness/epidemiology-disease-control/vector-borne-zoonotic-diseases/conferences/2017/frank-ramberg-identification-guide-common-mosquito-species.pdf

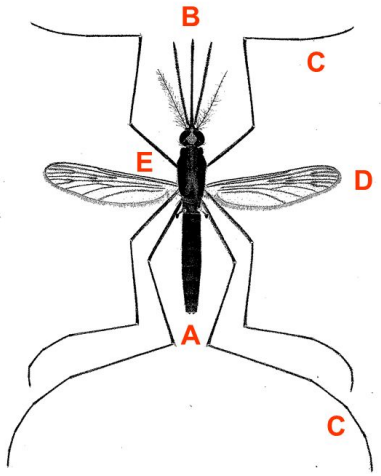
Anopheles Mosquitoes

- *A. hermsi,* and *A. freeborni*
  - Can transmit: Venezuelan equine encephalitis virus (VEEV), Virgin river virus (VRV), *Plasmodium* spp.
  - *A. hermsi* and *A. freeborni* are sibling species and are morphologically indistinguishable. Can be identified with ITS and ETS transcribed spacer regions of the nuclear rDNA.
  - Only *A. hermsi* have been sequenced within Arizona.

Anopheles hermsi
Photo: Frank Ramberg

Anopheles freeborni
Photo: James Gathany

Anopheles hermsi



Characteristics (dark brown in color)

A: Abdomen blunt or rounded & covered w/ dark scales.

B: Proboscis dark scaled w/ no band; palpi as long as proboscis; together they look like a pitch-fork or gig attached to head.

C: Legs dark, no banding but femora & tibiae tipped w/ pale scales.

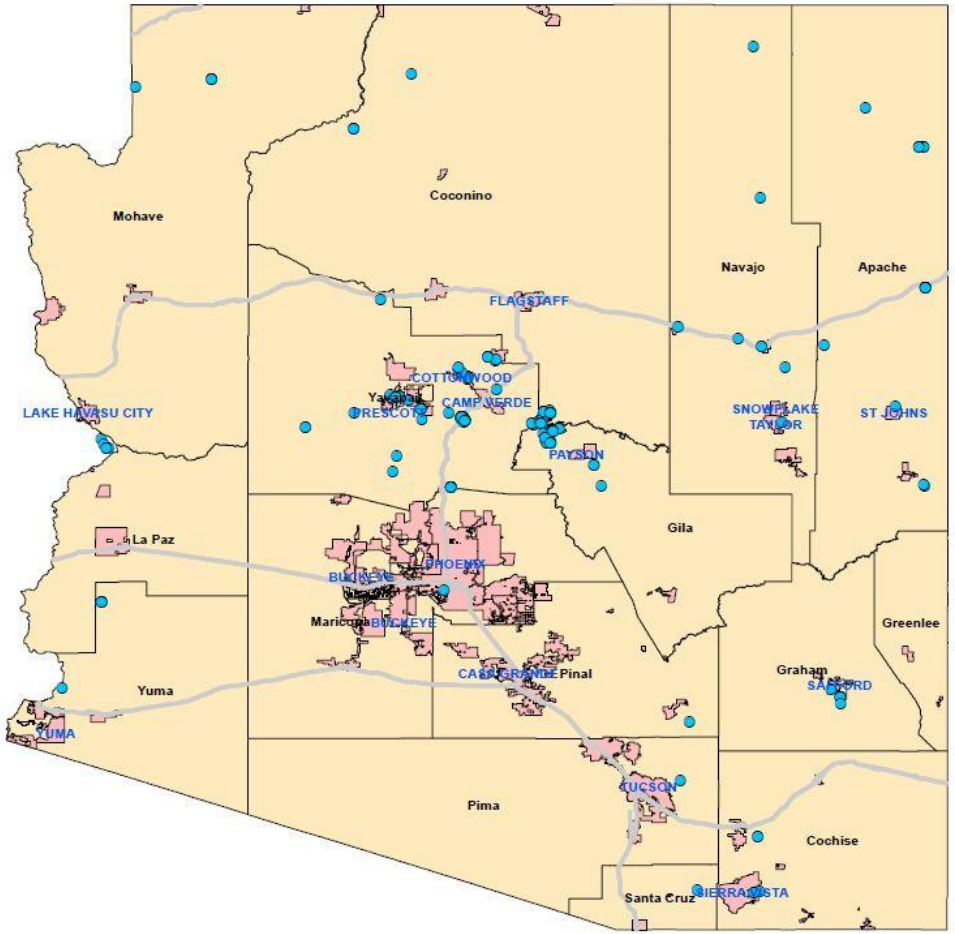
D: Wings have 4 lateral darken spots on outer surface w/ anterior or front edge uniformly dark.

E: Thorax: dark-brown to black; an median, anterior stripe of golden-brown scales that becomes bifurcated at mid-point.

F: Think a 'dark mosquito w/ dark spots on wings & 3-bladed pitch-fork attached to its head.

Read more on the Mosq of Arizona Guide.

Anopheles hermsi
2005 - 2011



Anopheles Mosquitoes

- *A. pseudopunctipennis Group*: 7 species, 7 subspecies
  - Arizona
    - *A pseudopunctipennis*
    - *A. franciscanus*

- *A. pseudopunctipennis*
  - Is anthropophilic (will normally bite humans)
  - Can transmit: Venezuelan equine encephalitis virus (VEEV), *Plasmodium* spp.

- *A. franciscanus*
  - Prefers rabbits/hares and livestock
  - Can transmit: Unknown

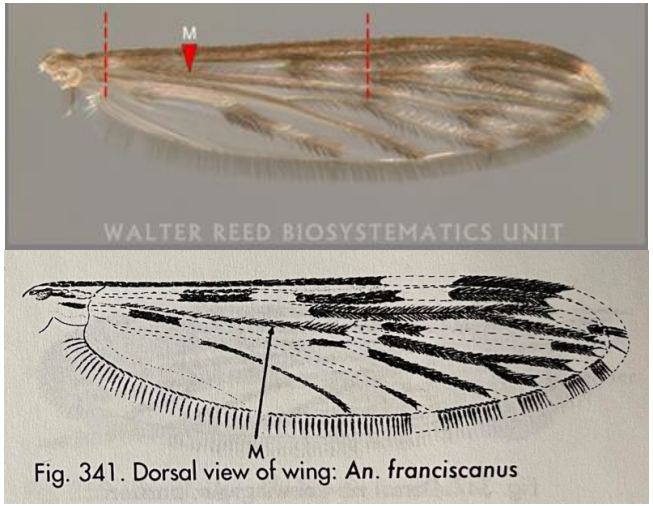
- Two species are very similar morphologically.

Anopheles franciscanus
Photo: Frank Ramberg

Anopheles pseudopunctipennis
Photo: Salvador Vitanza

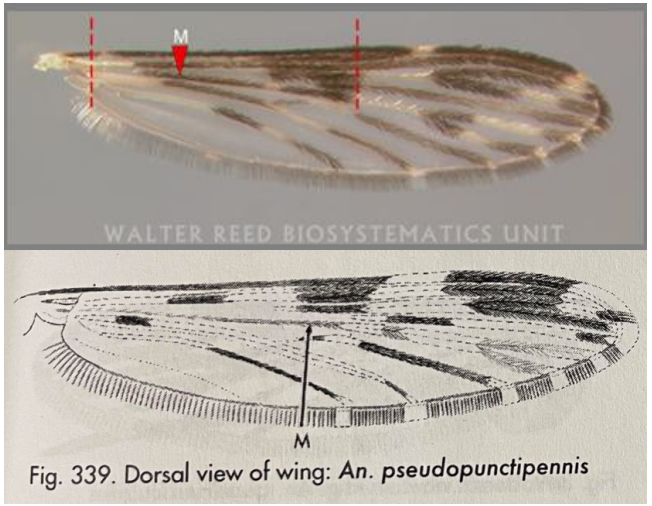
Slide by Daniel Williamson

Wing Differences Between *A. franciscanus* and *A. pseudopunctipennis*



Anopheles franciscanus:

- M vein predominantly dark scaled but is solid color



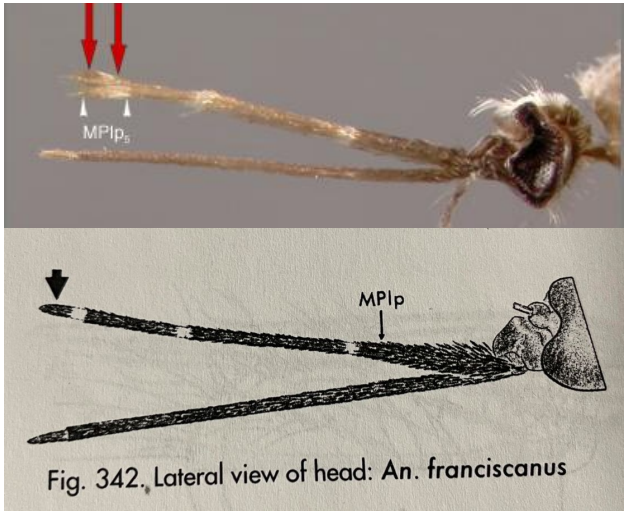
Anopheles pseudopunctipennis:

- M vein predominantly dark scaled but has pale contrasting pale scales

Top Pictures: The Walter Reed Biosystematics Unit
Bottom Pictures: Darsie and Ward

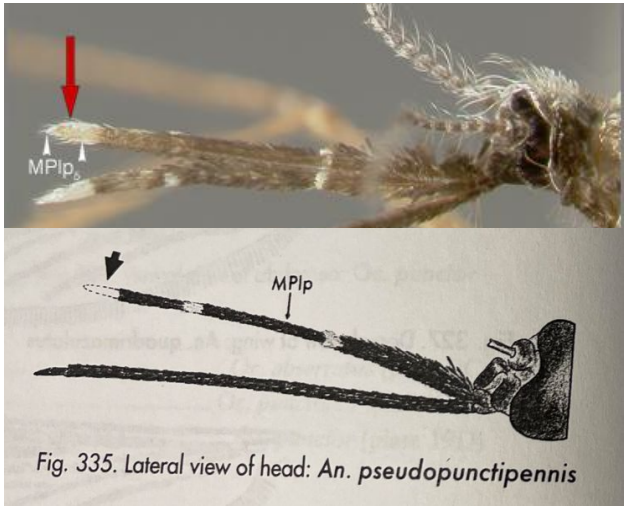
Slide by Daniel Williamson

Palp Differences Between *A. franciscanus* and *A. pseudopunctipennis*



Anopheles franciscanus:

- Final segment of the palps has black scales



Anopheles pseudopunctipennis:

- Final segment of the palps has pale scales

Top Pictures: The Walter Reed Biosystematics Unit
Bottom Pictures: Darsie and Ward

The case of *A. franciscanus*

- *A. franciscanus* feeding habits are primarily zoophilic. Studies have shown that they prefer mostly to feed on rabbits, but will also feed on cattle, horses, and other small mammals. There have been records of *A. franciscanus* biting humans.

  *Note: Many blood analysis studies were conducted in areas with large animal and low human concentrations. In addition, many studies used CO2 baited traps without a light source. Some Anopheles species are not as attracted to CO2 alone.

TABLE 2.—Landing Records

August 10, 1950

Bait and Station	Time 8:00–8:15	8:15–8:30	8:30–8:45	8:45–9:00	Total
2 men—Sta. 1	7	3	2	2	14
2 men—Sta. 2	3	5	3	1	12
2 men—Sta. 3	0	15	7	3	25
2 men—Sta. 4	0	0	0	0	0
2 men—Sta. 5	0	0	0	0	0
2 men—Sta. 6 with birds	5	4	0	0	9
2 men—Sta. 6 with mammals	6	3	1	0	10
Duck and turkey—Sta. 6	4	5	20	3	32
Rabbit and Guinea Pig—Sta. 6	20	5	9	0	34
TOTAL	45	40	42	9	136

TABLE 3.—Biting Records

August 14, 1950—Station 6

Bait	Time 8:00–8:15	8:15–8:30	8:30–8:45	8:45–9:00	Total
10 men	1	0	2	1	4
Horse	1	5	4	1	11
Calf	1	2	1	2	6
Sheep	2	0	0	0	2
Rabbit	0	0	0	0	0
Turkey	0	0	0	0	0
TOTAL	5	7	7	4	23

Belkin, J. N., Ehmann, N., & Heid, G. (1951). Preliminary field observations on the behavior of the adults of Anopheles franciscanus McCracken in southern California. Mosq News, 11, 23-31.

The case of *A. franciscanus*

- *A. franciscanus* was successfully infected with *Plasmodium vivax* in a laboratory setting in 1945.
- Several *Anopheles* species, including *A. franciscanus* were allowed to feed on soldiers suffering from malaria that were returning from the Pacific theater. About 42% of mosquitoes that fed became infected and there was no difference in infectivity between species.
- Infected mosquitoes of all species, besides *A. franciscanus*, were then allowed to feed on people suffering from neurosyphilis. All species were able to transmit malaria to the patients.
- Transmission of malaria to a human host from *A. franciscanus* has not been demonstrated.

Slide by Daniel Williamson

The case of *A. franciscanus* - What does this mean?

- Overall
  - Studies have found evidence that the species will land and feed on human hosts
  - Studies have found evidence that the species can be infected with human *Plasmodium*.

- This suggests that while *A. franciscanus* prefers non-human hosts, transmission is not impossible and if malaria re-establishes, we should not immediately assume *A. fransicanus* is not a participating vector.

- Most research in this field is 50 to 80 years old. Further research on *A. franciscanus* is needed.

If you collect *Anopheles* mosquitoes and do not want to keep them, please send them to us so we can identify them and get a better understanding of the species/subspecies that we may have here in the state.

Slide by Daniel Williamson

Malaria Locally-Acquired Cases Update

July 2023

Locally acquired malaria cases reported in Florida in 2023

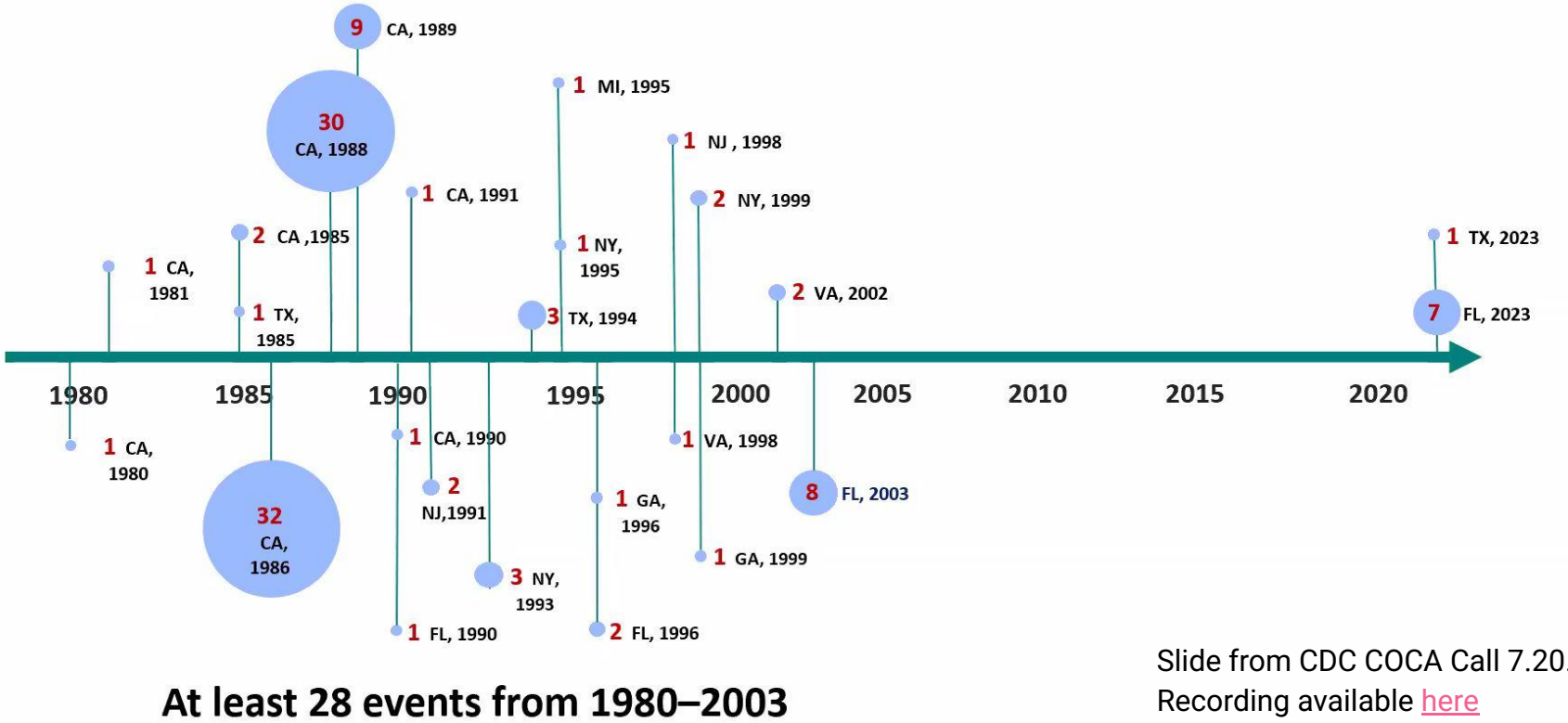
2023 CDC HAN

- FL: 7 cases of locally-acquired malaria reported in June 2023
- TX: 1 case of locally-acquired malaria reported in June 2023
- MD: 1 case of locally-acquired malaria reported in August 2023
- Timeline of locally acquired outbreaks in the US (28)- but the last was in 2003 (see next slide)
- Since 1970s there has been an increase in travel-associated cases (except during COVID)
- **The risk to the public for locally acquired mosquito-transmitted malaria remains very low**.
- However, areas with *Anopheles* mosquitoes and higher numbers of imported malaria cases are at higher risk for local malaria transmission.

Florida HEALTH Manatee County

From the locally-acquire malaria CDC key messages.

Timeline of Locally Acquired Malaria, U.S.: 1980 - 2023

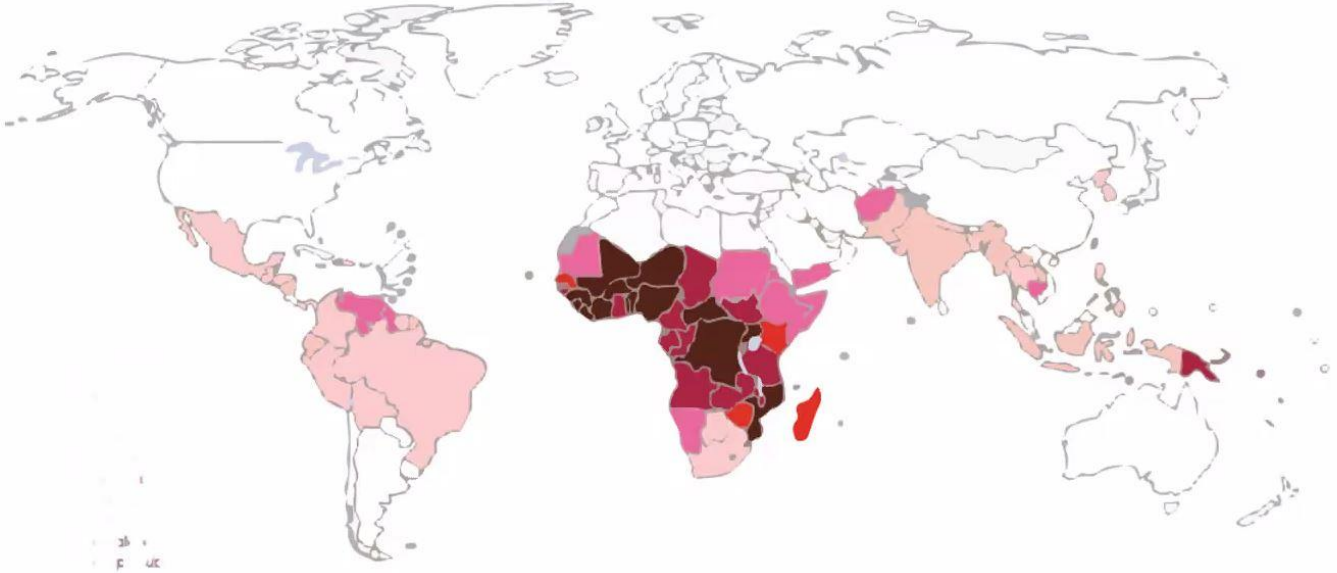


At least 28 events from 1980–2003

Slide from CDC COCA Call 7.20.23
Recording available here

Suspect and Test for malaria when there is fever and travel to a malaria-endemic region

Over 99% of malaria cases in the U.S. are among individuals who reported travel to a malaria-endemic region within 1 year of presentation



Slide from CDC COCA Call 7.20.23 Recording available here

Recommendations for Public Health Officials

Consider the following strategies for rapid identification, prevention, and control:

- How you can support clinicians to identify hospitals that can rapidly diagnose and treat malaria.
- Encourage that all cases of malaria have a **PCR test for species confirmation**, so that patients with relapsing infections (*P. vivax* and *P. ovale*) can receive anti-relapse therapy.
- Educate communities at risk on the importance of precautions for malaria and other diseases **before traveling** internationally to an area where malaria occurs.
- Provide education to communities to prevent mosquito-borne illness including **mosquito breeding site reduction** strategies.
- In areas of higher risk for local malaria transmission or with **higher numbers of imported malaria cases** consider:
  - Assessing capacity of hospitals and laboratories to **rapidly diagnose and treat** malaria. This should include the ability to rapidly acquire and provide treatment.
  - Coordination with mosquito control programs to **enhance mosquito surveillance for *Anopheles*** related to suspect and confirmed cases.

From the locally-acquire malaria CDC key messages.

Recommendations for Clinicians

- Discuss travel plans with patients; prescribe a CDC-recommended **malaria chemoprophylaxis** regimen for those traveling to an area with malaria; and encourage patients to adhere to the regimen before, during, and after travel.
- Routinely obtain a travel history and consider malaria in a sick person who has traveled to an area with malaria in the weeks to months preceding symptom onset.
- Consider the diagnosis of malaria in any person with a **fever of unknown origin regardless** of travel history.
- Follow CDC's Malaria Diagnosis and Treatment Guidelines for U.S. Clinicians.
- Immediately report suspected locally acquired malaria cases to your County Health Department.
- If needed, direct questions regarding suspect malaria cases to the CDC Malaria hotline.
- **CDC Clinician Outreach and Community Activity (COCA) call recordings** here

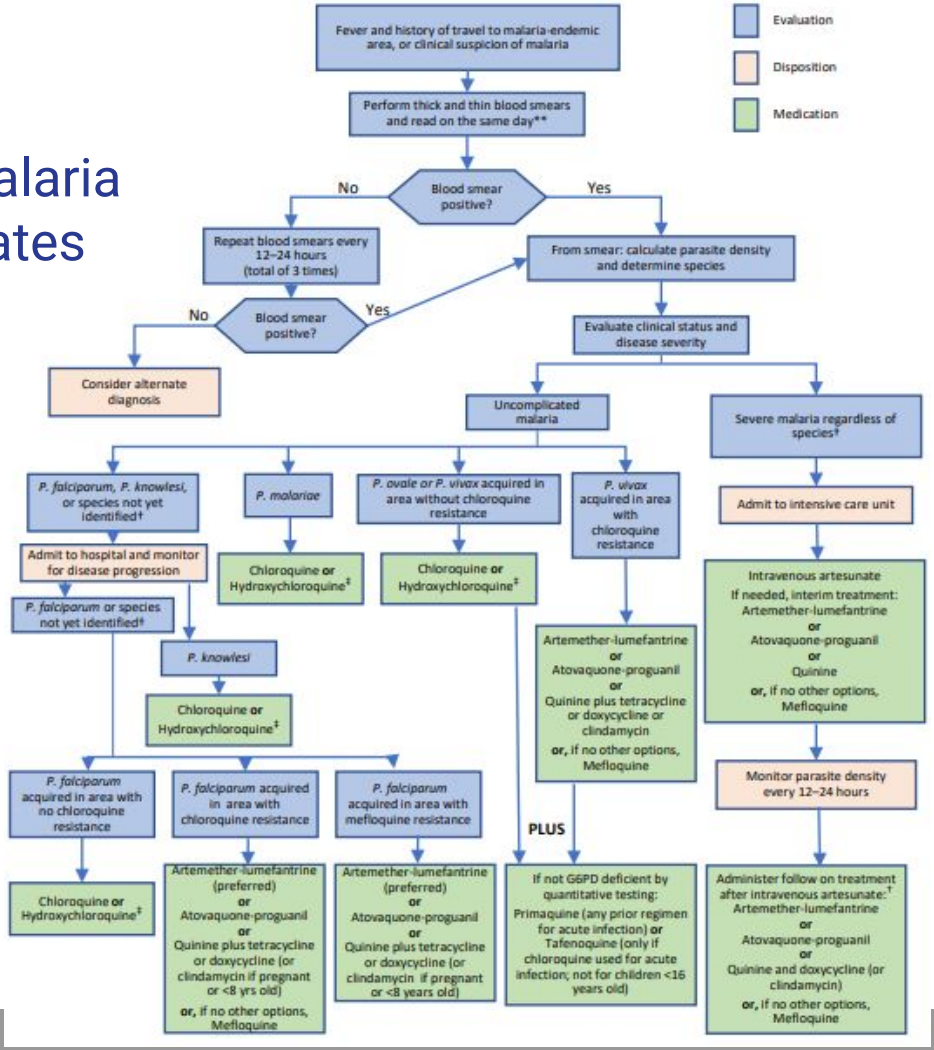
CDC Malaria Hotline
(770) 488-7788 M–F, 9 am to 5 pm EST
(770) 488-7100 after hours, weekends, holidays

CDC Malaria Treatment Table
www.cdc.gov/malaria/resources/pdf/Malaria_Treatment_Table.pdf

Other Notes from the CDC COCA Call

- Most US travel-associated cases have **onset < 3 months** from travel; some longer but < 1 year;
- >1 year are usually relapsed infections
- Without prompt treatment malaria can progress to severe disease (possible with any species but more often with *P. falciparum*)
- The immunity decreases fast when not living in endemic countries
- Presumptive treatment is not recommended in the US, testing should be done first (with a few exceptions)
- **Same day results are needed due to risk of severe disease**:
  - RDT: should be done in addition to the blood smear because it does not give species ID
  - **Blood smear** (gold standard; can speciate and quantify density % cells infected or parasitemia); thick or smear
  - PCR: can have lengthy turnaround time (only available at some labs) - *not recommended*
  - Serology: long and cannot distinguish between prior infection - *not recommended*
- **Traveler returning from malaria endemic areas presenting with fever should be tested.**
- **Species determination is necessary in all cases.**

Algorithm for Diagnosis and Treatment of Malaria in the United States



https://www.cdc.gov/malaria/resources/pdf/Malaria_Managment_Algorithm_20220208.pdf

Other Notes from the CDC COCA Call

- In the US low immunity and available drug regimens

- **Once malaria is diagnosed severity of disease dictates the next steps**:
  - Parasitemia >5% should be treated as having **severe disease**
  - If no severe malaria then direct treatment (oral) should be started and depends on species of malaria and country of travel (see CDC Treatment Table + CDC Malaria Hotline below)

- Severe malaria: required IV treatment (IV artesunate) then need to check parasitemia (every 12-24 hr)
  - if < 1% after 3rd IV then full oral treatment
  - if > 1% IV artesunate should be continued

CDC Malaria Hotline
(770) 488-7788 M–F, 9 am to 5 pm EST
(770) 488-7100 after hours, weekends, holidays

CDC Malaria Treatment Table
www.cdc.gov/malaria/resources/pdf/Malaria_Treatment_Table.pdf

Slide from CDC COCA Call 7.20.23
Recording available here

Recommendations for Hospitals and Laboratories

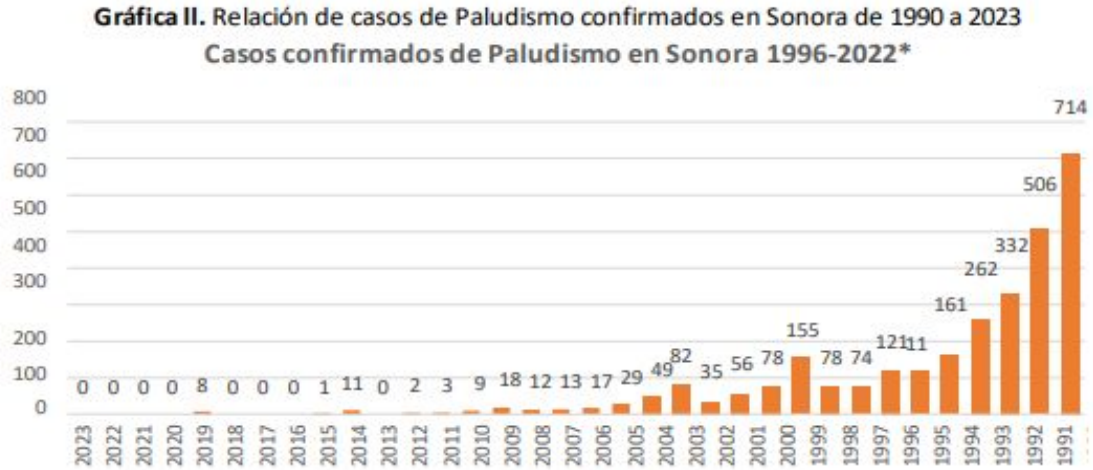
- Have malaria diagnostics available (**blood smear**, or BinaxNow™ rapid diagnostic test [RDT] followed by blood smear) and ensure that there are qualified personnel who can perform these tests.
- If results of malaria testing cannot be obtained in a timely manner, patients in whom malaria is suspected should be referred to a **higher level of care** for prompt evaluation for malaria.
- Stock relevant drugs:
  - **Primaquine** for anti-relapse therapy to prevent *P. vivax* and *P. ovale* relapses.
  - **Artemether-lumefantrine (Coartem®)**, the first-line drug in the United States for most cases of uncomplicated *P. falciparum* or unknown malaria species. **Atovaquone-proguanil (Malarone®)** is another recommended option.
  - **IV artesunate** (Artesunate for InjectionTM) for treatment of **severe malaria** or have a plan in place for emergency procurement. More information on how to acquire IV artesunate in the US can be found here.

From the locally-acquire malaria CDC key messages.

Malaria in Sonora (MX)

Confirmed Malaria cases in Sonora from 1990-2023

- Historically cases of Malaria in Sonora have been found mainly in the towns in the municipalities of Álamos and Navojoa. This is given to their receptive nature ruled by the presence of the vector and its territorial proximity to states of the Republic with active transmission.



- Malaria has had an apparent decline at the state level in the last two decades, due to the intensive actions that were developed by the health systems.
- However, there has been a reduction in antimalarial activities, which leads to an increased risk of becoming a serious public health problem in the state and in the country again.

Slide by Giselle Quintana

Confirmed Malaria cases in Sonora (continued)

- From the years **1996** to **2022**, **2,682** cases of malaria have been confirmed in Sonora.
- It is noteworthy that the highest percentage of confirmed cases are found to the South of the State.
- The last confirmed case of Malaria in Sonora occurred in **epi week 45** of the year **2019**.
- These cases were found in the the towns of Mochibampo, Bavícora and El Salitral, belonging to the municipality of Álamos in the south of the state,accumulating a total of **8** cases.

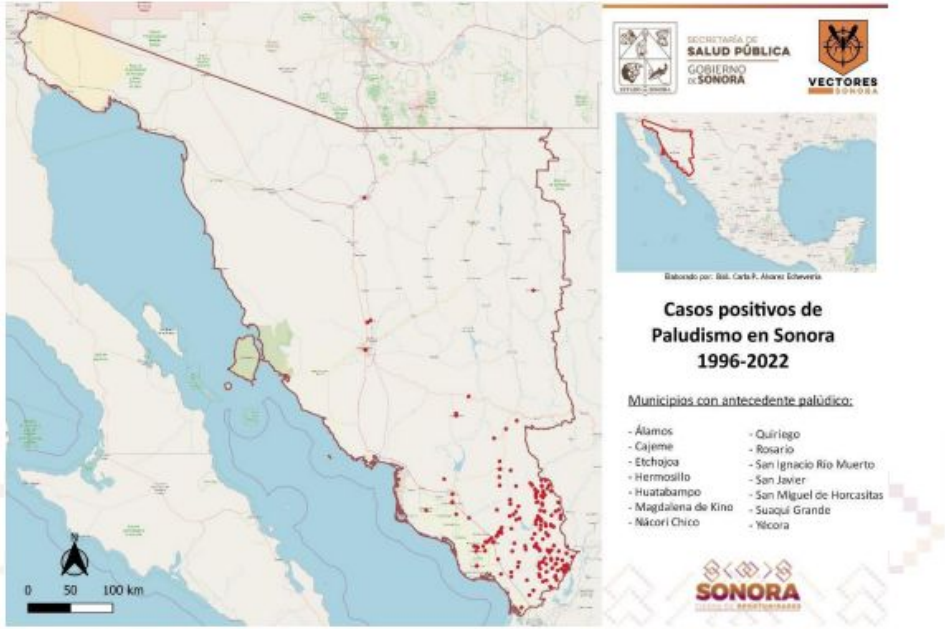


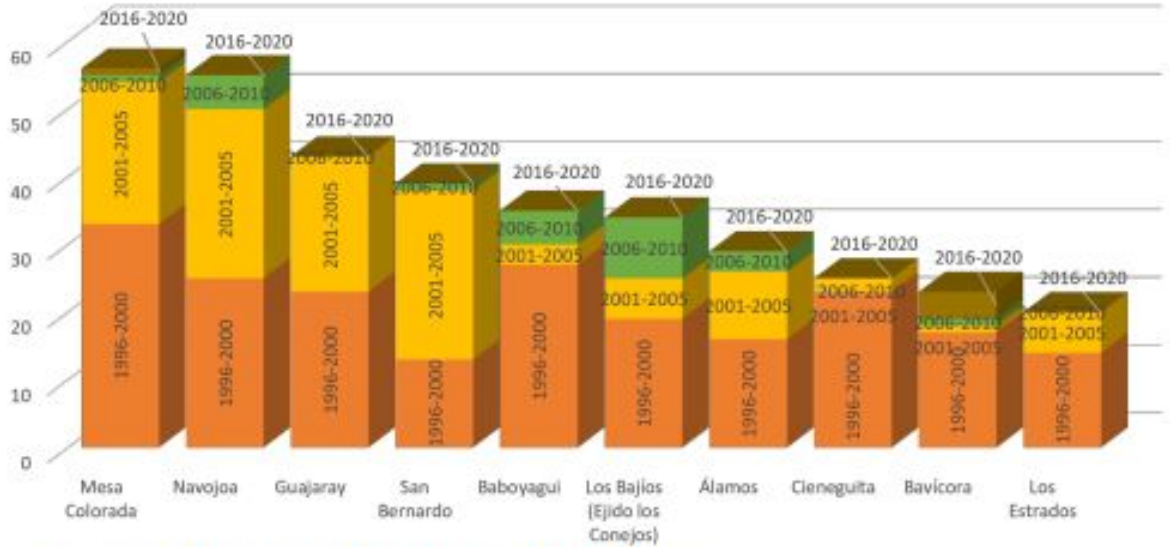
Figura 2. Distribución de casos positivos de Paludismo en Sonora acumulado de 1996 al 2022.

- All confirmed positive cases in the past have correspond to *P. vivax*, except **1** case in **2009** caused by *P. falciparum*.

Slide by Giselle Quintana

Confirmed Malaria cases in Sonora from 1996- 2020 by location

Gráfico 3. Casos confirmados de Paludismo en Sonora de 1996-2020 por localidad.



Fuente: Secretaria de Salud/Sistema Nacional de Vigilancia Epidemiológica

Slide by Giselle Quintana

Mexico -CDC Yellow Book

https://wwwnc.cdc.gov/travel/yellowbook/2024/itineraries/mexico

Plasmodium vivax malaria prophylaxis is currently recommended only for travelers going to Chiapas and the southern part of Chihuahua

Malaria

Dramatic decreases in malaria incidence in recent decades mean risk for infection among travelers to Mexico is low. Major resorts are free of the disease, as is the US–Mexico border region. *Plasmodium vivax* malaria prophylaxis is currently recommended only for travelers going to Chiapas and the southern part of Chihuahua (see Sec. 2, Ch. 5, Yellow Fever Vaccine and Malaria Prevention Information, by Country). Mosquito avoidance (but not chemoprophylaxis) is recommended for travelers visiting Campeche, Durango, Nayarit, Quintana Roo, Sinaloa, Sonora, and Tabasco.

Map 2-10 Malaria prevention in Mexico

Malaria Case Investigation

Case Classification

(Malaria is reportable by providers and labs within 5 working days)

Confirmed

• **Detection and specific identification** of malaria parasite species by **microscopy on blood films** in a laboratory with appropriate expertise in any person (symptomatic or asymptomatic) diagnosed in the United States, regardless of whether the person experienced previous episodes of malaria while outside the country; OR

• **Detection of *Plasmodium* species by nucleic acid test*** in any person (symptomatic or asymptomatic) diagnosed in the United States, regardless of whether the person experienced previous episodes of malaria while outside the country; OR

• Detection of **unspeciated malaria parasite by microscopy on blood films** in a laboratory with appropriate expertise in any person (symptomatic or asymptomatic) diagnosed in the United States, regardless of whether the person experienced previous episodes of malaria while outside the country.

* *Laboratory-developed malaria PCR tests must fulfill CLIA requirements, including validation studies*

https://www.azdhs.gov/documents/preparedness/epidemiology-disease-control/disease-investigation-resources/casedefinitions/case-definitions.pdf

Case Classification

Suspect

Detection of *Plasmodium* species by **rapid diagnostic antigen testing** *without confirmation by microscopy or nucleic acid testing* in any person (symptomatic or asymptomatic) diagnosed in the United States, regardless of whether the person experienced previous episodes of malaria while outside the country.

Criteria to Distinguish a New Case from an Existing Case

- A subsequent attack experienced by the same person but caused by a **different *Plasmodium* species** is counted as an **additional case**.
- A subsequent attack experienced by the same person and caused by the **same species** in the United States may indicate a **relapsing infection or treatment failure** caused by drug resistance or a separate attack (= **same case**).

https://www.azdhs.gov/documents/preparedness/epidemiology-disease-control/disease-investigation-resources/casedefinitions/case-definitions.pdf

Criteria to Distinguish a New Case from an Existing Case

- **NEW Effective in 2025** - A **relapse** (only in *P. vivax* or *P. ovale* species) or a subsequent episode of malaria in a person who previously had malaria should be counted as an **additional case** (requiring a separate case report form) unless the case is indicated as a treatment failure within 4 weeks of initial presentation (recrudescence of original infection).
    - The infecting species should be determined, and potentially relapsing cases should be carefully investigated to assess if the person had traveled since their previous illness.
    - CDC classifies cases according to where the person acquired the infection. If the initial infection was acquired internationally, then the relapse case is classified as imported. If the initial infection was acquired through a local exposure, for example by locally acquired mosquito transmission, then those relapse cases will also be classified as introduced.

https://www.azdhs.gov/documents/preparedness/epidemiology-disease-control/disease-investigation-resources/casedefinitions/case-definitions.pdf

Classifying Disease Acquisition

Based on the case investigation, CDC classifies each malaria case according to the following definitions (**to be added to the ADHS Case Definition in 2025**):

- **Congenital malaria:** Malaria infection transmitted directly from mother to child during pregnancy or childbirth.
- **Cryptic malaria**: An isolated case of malaria that cannot be epidemiologically linked to additional cases, and for which epidemiologic investigation does not identify the mode of acquisition.
- **Imported malaria**: Malaria acquired outside the U.S. The patient must have a recent (within ~2 years) travel history to a country or territory with ongoing malaria transmission.
- **Locally acquired malaria**: In the U.S., a non-endemic setting without indigenous malaria transmission, locally acquired malaria cases are typically classified in two categories:
  1. **Induced malaria**: Malaria transmission through a blood transfusion, tissue or organ transplantation, or another parenteral route, not mosquito-borne or congenital transmission.
  2. **Introduced**: Malaria likely acquired by mosquito transmission from an imported case in an area where malaria is not a regular occurrence.

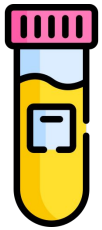
Classifying Disease Acquisition Continued

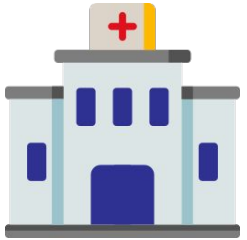
- **Recrudescent malaria**: A repeat attack of malaria due to the survival of malaria parasites in red blood cells can occur for any *Plasmodium* species and typically occurs in the first four weeks after an initial illness due to failure of the antimalarial treatment to clear all parasites. Some explanations for recrudescence include: (i) incomplete adherence to an appropriate antimalarial regimen, (ii) inappropriate use of oral antimalarials for severe illness (especially if there is hyperparasitemia, where ≥5% of red blood cells are infected), and (iii) antimalarial drug resistance.
- **Relapsing malaria**: *P. vivax* and *p. ovale* species can reactivate dormant liver-stage parasites (hypnozoites), resulting in a malaria **relapse**, typically 3 months to 3 years after the initial infection. *P. falciparum* and *P. malariae* species do not have liver hypnozoites that can be reactivated, so illnesses caused by these species do not result in relapses.

More detailed malaria case definitions and classifications are available at https://ndc.services.cdc.gov/case-definitions/malaria-2014/

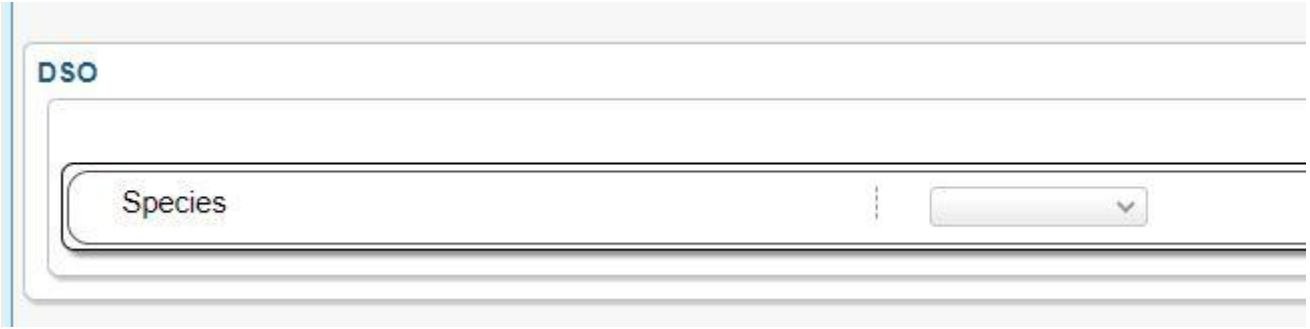
Case Investigation Steps - 1

1. Confirm the diagnosis:
    a. Review available **test results**
    b. If **species** is available enter it in the DSO (see next slide)
    c. If possible, arrange for a **blood smear** to come to the State Lab so we can send it to the **CDC for species confirmation and evaluation of drug resistance**
    d. Request **medical records** and obtain **clinical information** including symptoms, **date of onset**, hospitalization, outcome (enter all this info in the MEDSIS case)
    e. **Classify** the case (only test results needed)





The only ‘DSO’ field in a malaria case is the species (options include unspecified and unknown)



Case Investigation Steps - 2

2. Conduct case investigation:

a. **Interview the case** to confirm symptoms and onset
b. Can use the CDC Case Report Form (**CRF**) to guide the interview (since there is no full DSO)
c. Obtain **detailed travel history** (fill **Travel Table** in MEDSIS and **CRF**)
d. Provide **education** (on practicing mosquito avoidance while ill and how to prevent future infections)- *see slides 38 and 39*

The Travel Table in the MEDSIS case is under Case Management

Enhanced Investigation Steps

Enhanced Investigation is warranted if the initial case investigation does not yield:

- A recent travel history (in the past two years) OR
- Prior malaria illness (within 2 - 3 years)

Enhanced investigation is used to assess the patient's classification as possibly cryptic or locally acquired.

For cases under **enhanced investigation,** a more detailed patient interview should **review the risk factors for acquiring malaria**, including detailed travel history, sick contacts (e.g., household members), occupation, outdoor activities:

- **Ask about lifetime and recent travel to a malaria-endemic country**:
  - Identify specific dates the patient was in a malaria-endemic country and the areas visited.
  - If the person previously lived in a malaria-endemic country, when did they immigrate to the U.S. or to another non-endemic country?
- **Ask about blood exposures** such as blood transfusions, organ transplants, needlestick injuries, unsafe needle sharing, or home tattoos.
- **Prior to illness, were there any visitors, household members, co-workers who were sick with malaria or another febrile illness?**

https://www.cdc.gov/malaria/php/surveillance/case-investigation.html

Enhanced Investigation Steps Continued

Additional questions for cases under **enhanced investigation:**

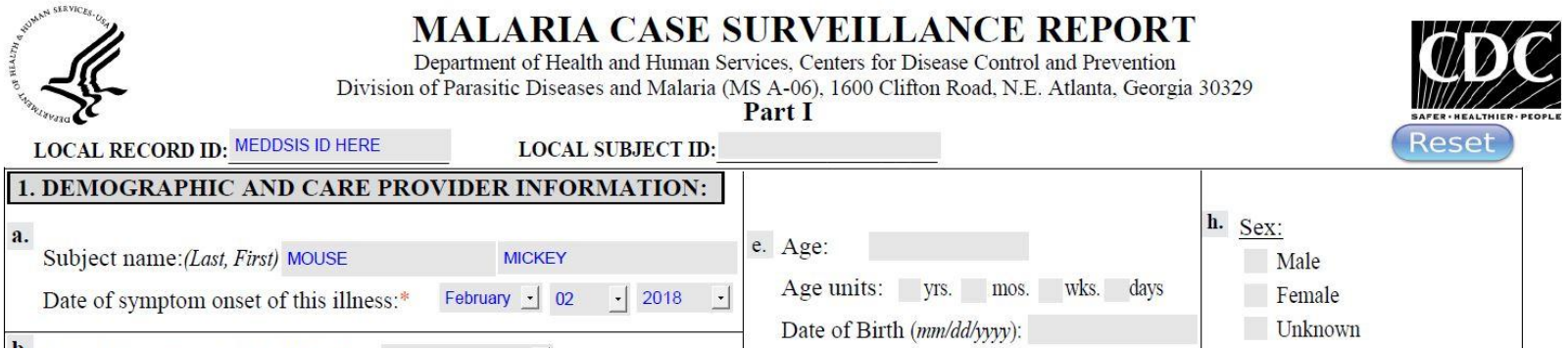
- **Ask about prior diagnoses of malaria (in lifetime), or previous unexplained febrile illness after international travel:**
  - If yes, specific dates and if (and what) treatment received?
  - If diagnosed with a relapsing species (*P. vivax* or *P. ovale*), did they receive antirelapse therapy (primaquine for 14 days, or a single dose of tafenoquine)?
- **Has the patient been in an area where Babesia parasites are transmitted? Has the patient had a recent tick bite?**
- **Has the patient recently slept outdoors? Are they currently or have they recently experienced unstable housing or homelessness?**

Obtain additional details from the medical record including past medical history (especially immunocompromising conditions, asplenia, and pregnancy status), recent hospitalizations and medical procedures.

Please contact ADHS for malaria diagnosed in a newborn without travel (congenital malaria). Congenital cases occurring in non-endemic settings have been reported weeks or up to two months after birth. ADHS will connect with CDC malaria surveillance epidemiologist or the CDC Hotline malaria@cdc.gov.

CDC Case Report Form

- Available under Malaria here
- Fill **electronically** (fillable PDF, words/date should appear blue, don't print and write)
- Can be completed ~ 1-2 months after the report (to collect Part II info)
- Attach to the MEDSIS case (ADHS will fax it to CDC)



MALARIA CASE SURVEILLANCE REPORT

Department of Health and Human Services, Centers for Disease Control and Prevention
Division of Parasitic Diseases and Malaria (MS A-06), 1600 Clifton Road, N.E. Atlanta, Georgia 30329

Part I

CDC SAFER · HEALTHIER · PEOPLE

Reset

LOCAL RECORD ID: MEDDSIS ID HERE LOCAL SUBJECT ID:

1. DEMOGRAPHIC AND CARE PROVIDER INFORMATION:

a. Subject name: *(Last, First)* MOUSE MICKEY

Date of symptom onset of this illness:* February 02 2018

e. Age:

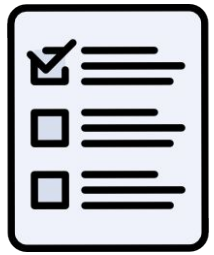
Age units: yrs. mos. wks. days

Date of Birth *(mm/dd/yyyy)*:

h. Sex:

Male
Female
Unknown

CDC Case Report Form



Part I

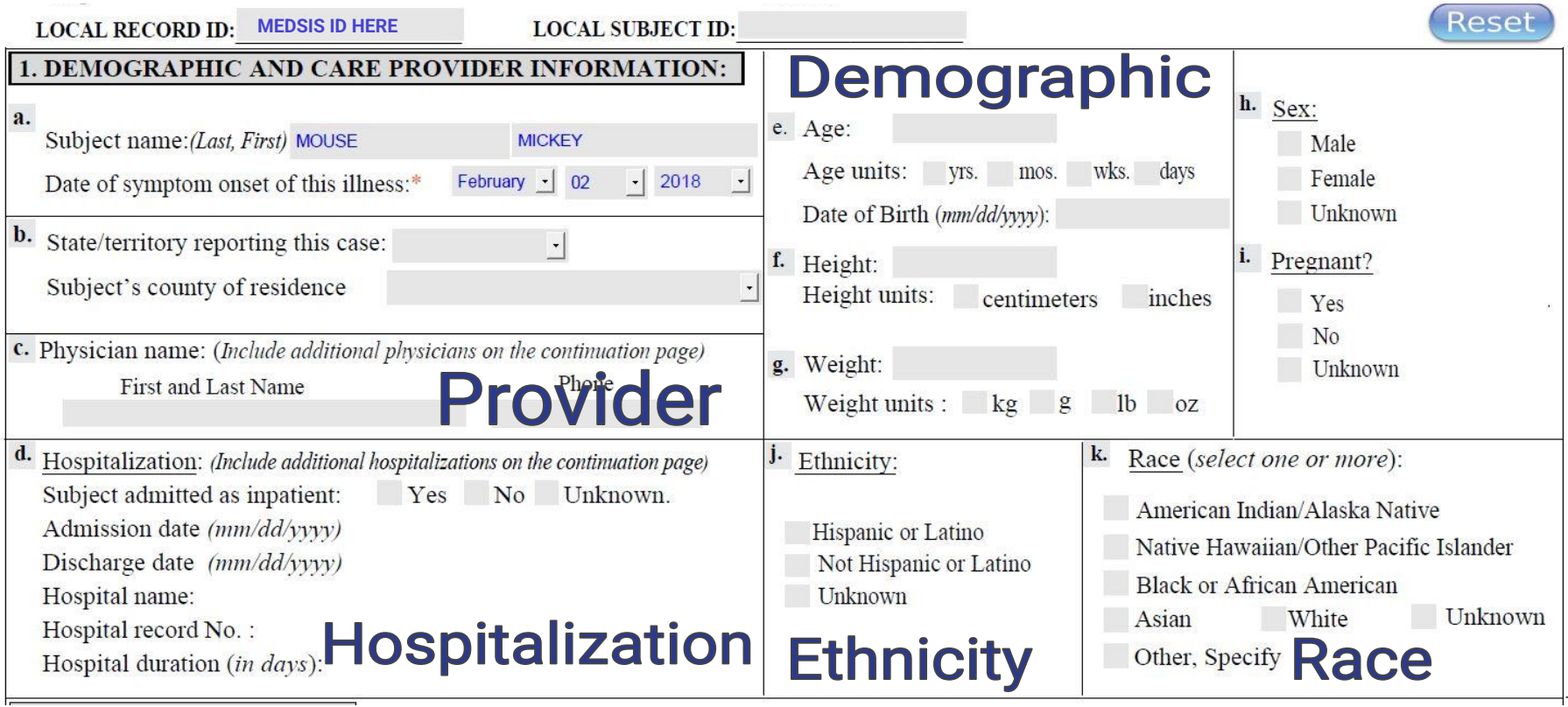
1. Demographic and Care Provider Information
2. Laboratory Results
3. Travel History
4. Specimen
5. Clinical and Treatment Information
6. Submitter Information

To avoid doing a double interview, the individual can be contacted ~1-2 month after the report, so likely ~ 4 weeks after treatment

Part II

7. Treatment Follow-up (to be completed **4 weeks after treatment**)
8. Continuation page (for extra Part I space)
9. INSTRUCTIONS

1. Demographic and Provider Information



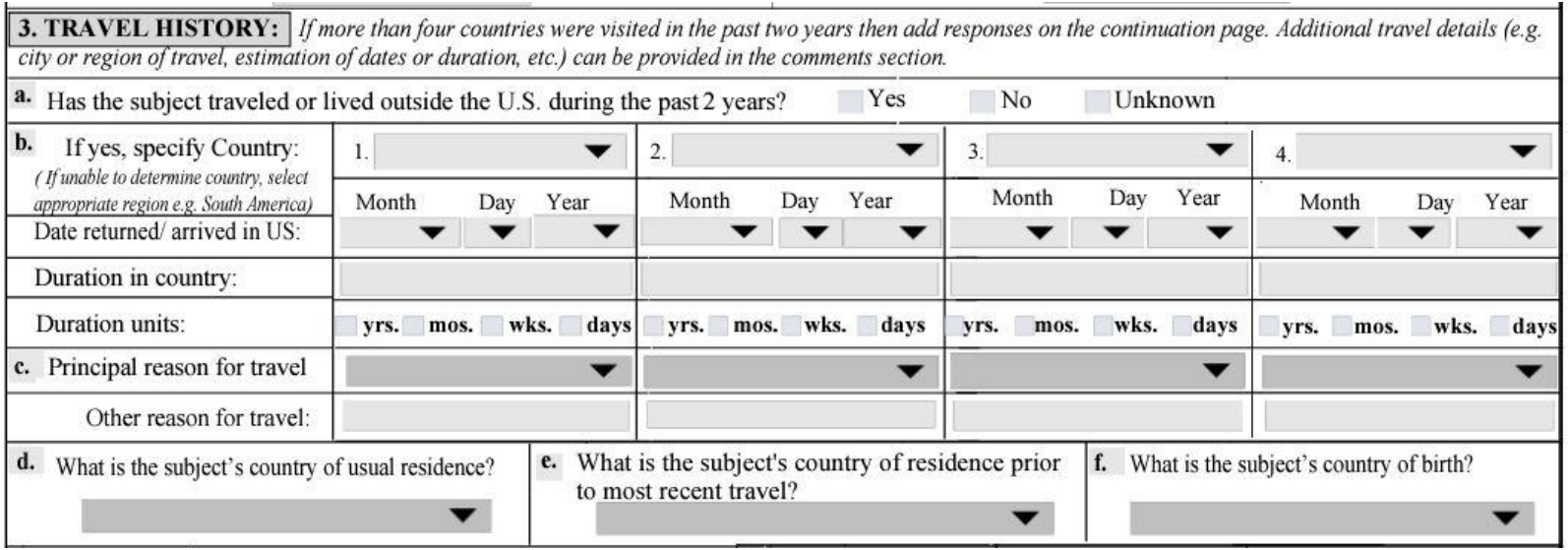
2. Laboratory Results

2. LABORATORY RESULTS: *Complete a minimum of one positive malaria diagnostic test. If more than two tests were done then additional results may be included on the continuation page. It is preferable to include the following tests: (i) blood smear with the highest percentage parasitemia, (ii) the test that indicates the Plasmodium species, and (iii) a confirmatory PCR (if applicable). For conflicting lab results for the species identification, include only the test with the final result. For a lab result that identifies more than one species, multiple species can be selected for that one test. If the species determination is inconclusive, then select "Not determined"; if there is a suspicion towards a particular species (e.g. "non-falciparum" select "Not determined" and "Other" and write the suspected species in the "Other species, specify" section.*

I. Diagnostic lab test:	II. Diagnostic lab test:
a. Type: ☐ Blood Smear ☐ PCR ☐ RDT ☐ Other ☐ No test done/ unknown	a. Type: ☐ Blood Smear ☐ PCR ☐ RDT ☐ Other ☐ No test done/ unknown
Specimen collection date *(mm/dd/yyyy)*:	Specimen collection date *(mm/dd/yyyy)*:
Lab result date *(mm/dd/yyyy)*:	Lab result date *(mm/dd/yyyy)*:
b. Result: ☐ Pos ☐ Neg ☐ Unknown ☐ Not done	b. Result: ☐ Pos ☐ Neg ☐ Unknown ☐ Not done
c. Species: ☐ Vivax ☐ Falciparum ☐ Malariae ☐ Ovale	c. Species: ☐ Vivax ☐ Falciparum ☐ Malariae ☐ Ovale
☐ Not Determined ☐ Other species (specify):	☐ Not Determined ☐ Other species (specify):
d. Parasitemia (%):	d. Parasitemia (%):
Lab name :	Lab name :
Lab phone :	Lab phone :

- **At least one** positive test (if multiple tests, use continuation page)
- Preferably include test with **highest parasitemia**, with **specific species identified**, smear and PCR
- Multiple species can be selected, if needed
- If the species determination is inconclusive select “Not determined”
- If there is a suspicion towards a certain species select “Not determined” and “Other” and write the species.

3. Travel History - very important



3. TRAVEL HISTORY: *If more than four countries were visited in the past two years then add responses on the continuation page. Additional travel details (e.g. city or region of travel, estimation of dates or duration, etc.) can be provided in the comments section.*

a. Has the subject traveled or lived outside the U.S. during the past 2 years? ☐ Yes ☐ No ☐ Unknown

b. If yes, specify Country: *(If unable to determine country, select appropriate region e.g. South America)*	1.	2.	3.	4.
Date returned/ arrived in US:	Month Day Year	Month Day Year	Month Day Year	Month Day Year
Duration in country:				
Duration units:	☐ yrs. ☐ mos. ☐ wks. ☐ days	☐ yrs. ☐ mos. ☐ wks. ☐ days	☐ yrs. ☐ mos. ☐ wks. ☐ days	☐ yrs. ☐ mos. ☐ wks. ☐ days
c. Principal reason for travel				
Other reason for travel:				

d. What is the subject's country of usual residence?

e. What is the subject's country of residence prior to most recent travel?

f. What is the subject's country of birth?

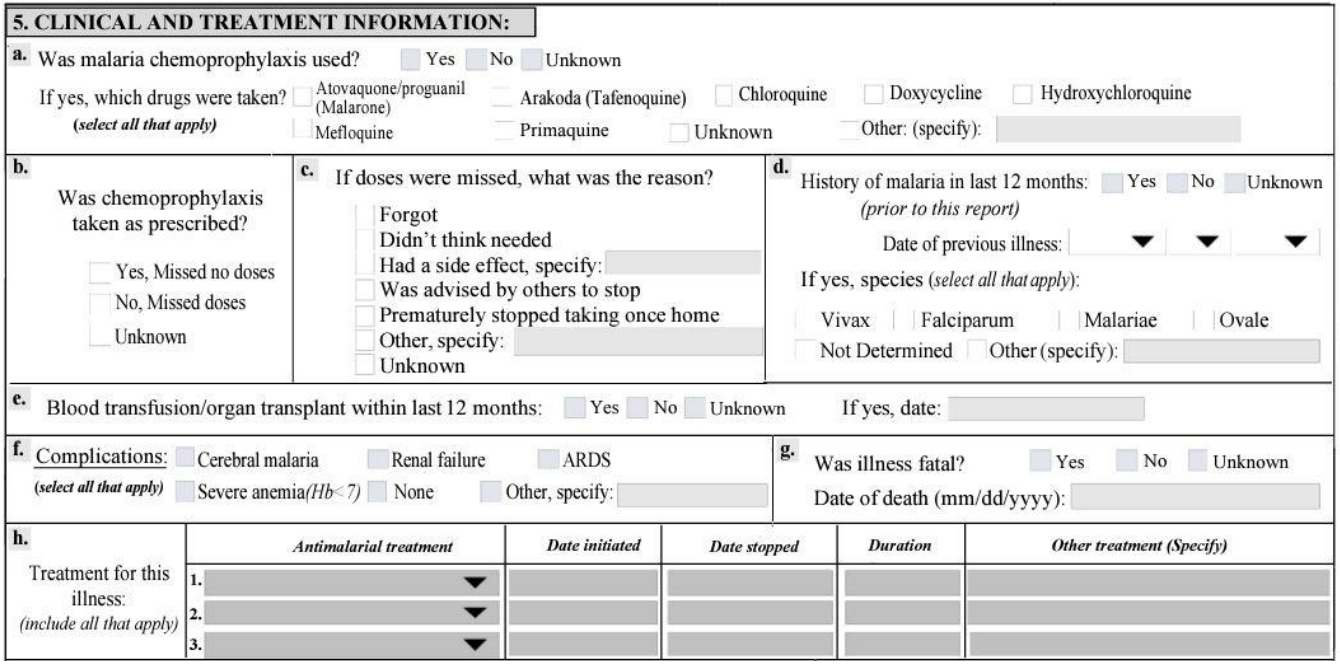
- **Try and obtain of these details as possible**
- International travel in the **past 2 years**
- **Country**, return **date, duration**, duration units, **reason for travel** (tourism, military, business, peace corps, visiting friends and relatives, refugee/immigrant, etc.)
- Country of residence, residence prior to most recent travel
- Country of birth

4. Specimen

4. SPECIMEN:	b. Specimen Type	Other specimen(specify)	CDC ID (from 50.34 submission)
Was a specimen(s) sent to CDC ? a. ☐ Yes ☐ No ☐ Unknown If yes, type of specimen sent to CDC *(For each specimen, enter the CDC ID)*	1.		
	2.		
	3.		
	4.		
	5.		

- If the local investigator has not arranged for a sample to be sent to CDC via ASPHL, then mark **No**
- If you have requested one and can check that it has reached ASPHL, then mark **Yes**

5. Clinical and Treatment Information - important



5. CLINICAL AND TREATMENT INFORMATION:

a. Was malaria chemoprophylaxis used? ☐ Yes ☐ No ☐ Unknown

If yes, which drugs were taken? *(select all that apply)*
☐ Atovaquone/proguanil (Malarone) ☐ Arakoda (Tafenoquine) ☐ Chloroquine ☐ Doxycycline ☐ Hydroxychloroquine
☐ Mefloquine ☐ Primaquine ☐ Unknown ☐ Other: (specify):

b. Was chemoprophylaxis taken as prescribed?
☐ Yes, Missed no doses
☐ No, Missed doses
☐ Unknown

c. If doses were missed, what was the reason?
☐ Forgot
☐ Didn't think needed
☐ Had a side effect, specify:
☐ Was advised by others to stop
☐ Prematurely stopped taking once home
☐ Other, specify:
☐ Unknown

d. History of malaria in last 12 months: ☐ Yes ☐ No ☐ Unknown *(prior to this report)*
Date of previous illness:
If yes, species *(select all that apply)*:
☐ Vivax ☐ Falciparum ☐ Malariae ☐ Ovale
☐ Not Determined ☐ Other (specify):

e. Blood transfusion/organ transplant within last 12 months: ☐ Yes ☐ No ☐ Unknown If yes, date:

f. Complications: *(select all that apply)*
☐ Cerebral malaria ☐ Renal failure ☐ ARDS
☐ Severe anemia *(Hb< 7)* ☐ None ☐ Other, specify:

g. Was illness fatal? ☐ Yes ☐ No ☐ Unknown
Date of death (mm/dd/yyyy):

h. Treatment for this illness: *(include all that apply)*

	Antimalarial treatment	*Date initiated*	*Date stopped*	*Duration*	*Other treatment (Specify)*
1.					
2.					
3.					

PEP

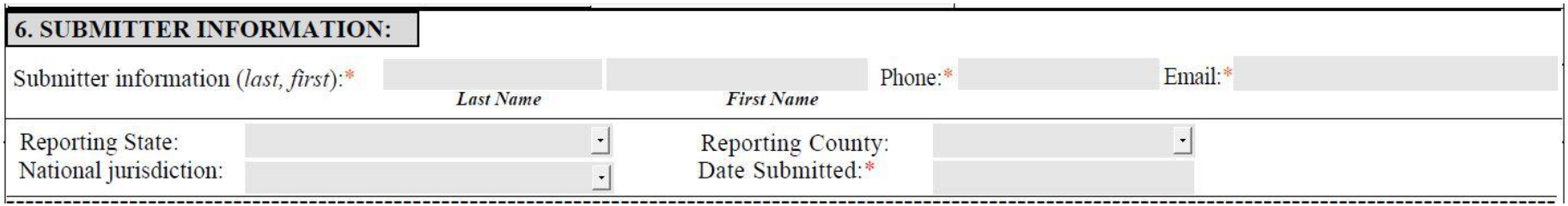
Treatment

- Malaria Pre-Exposure Prophylaxis (started before the illness, not for treatment)- refer to https://www.cdc.gov/malaria/hcp/drug-malaria/?CDC_AAref_Val=https://www.cdc.gov/malaria/travelers/drugs.html
- Was that taken as prescribed (some require to be taken from before to after traveling for a period of time)
- If doses missed, indicate the reason
- Indicate if the case had been diagnosed with malaria before (in the US or abroad) and date of onset for that illness
- Indicate any blood transfusion, complications, outcome and **treatment** (drug, start and stop date, duration in days)

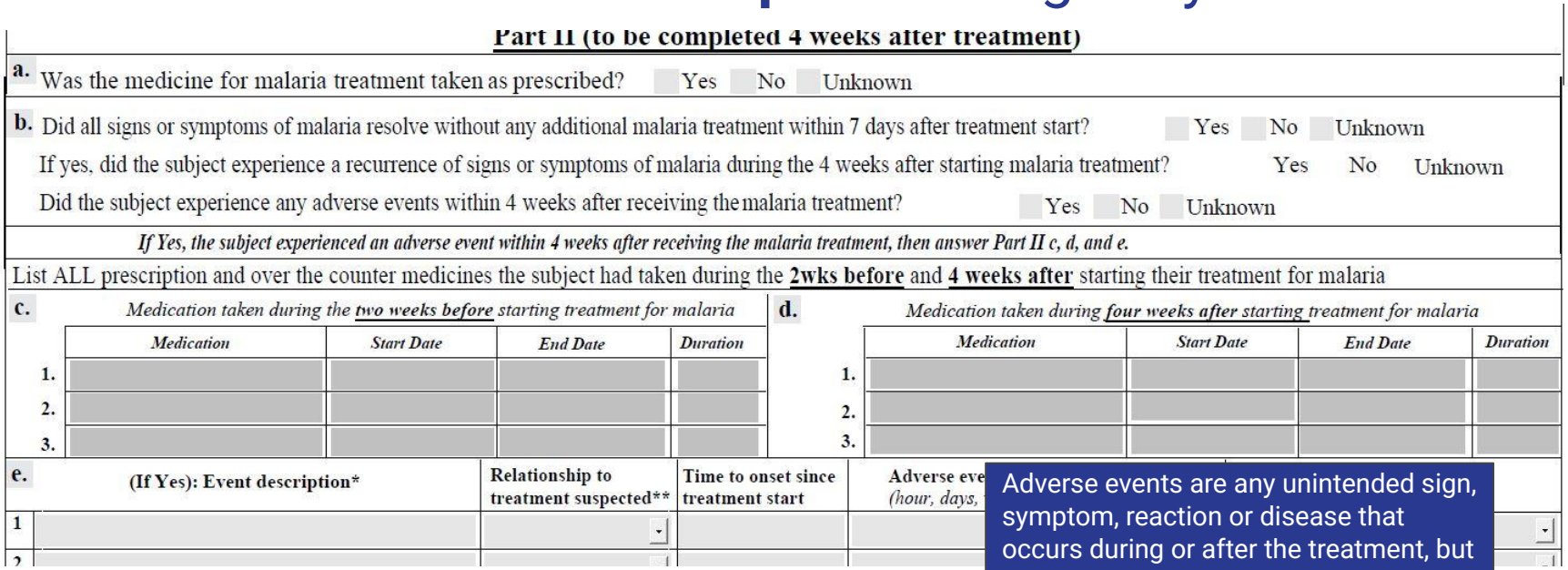
6. Submitter Information

In theory, this is the person reporting to CDC and that CDC can contact with any additional questions.

In practice it is often the **local investigator completing the form**, since CDC does have ADHS/Vector team contact information, may they need more information or clarification.



7. Part II Treatment Follow-up - not obligatory



Part II (to be completed 4 weeks after treatment)

a. Was the medicine for malaria treatment taken as prescribed? Yes No Unknown

b. Did all signs or symptoms of malaria resolve without any additional malaria treatment within 7 days after treatment start? Yes No Unknown

If yes, did the subject experience a recurrence of signs or symptoms of malaria during the 4 weeks after starting malaria treatment? Yes No Unknown

Did the subject experience any adverse events within 4 weeks after receiving the malaria treatment? Yes No Unknown

If Yes, the subject experienced an adverse event within 4 weeks after receiving the malaria treatment, then answer Part II c, d, and e.

List ALL prescription and over the counter medicines the subject had taken during the **2wks before** and **4 weeks after** starting their treatment for malaria

c. *Medication taken during the two weeks before starting treatment for malaria*

	Medication	Start Date	End Date	Duration
1.				
2.				
3.				

d. *Medication taken during four weeks after starting treatment for malaria*

	Medication	Start Date	End Date	Duration
1.				
2.				
3.				

e.

	(If Yes): Event description*	Relationship to treatment suspected**	Time to onset since treatment start	Adverse eve (hour, days,
1				
2				

Adverse events are any unintended sign, symptom, reaction or disease that occurs during or after the treatment, but it is not necessarily caused by it.

- Indicate if the case **adhered to the treatment** prescribed
- Indicate **if the treatment worked** (no symptoms after 7 days) and whether there were any **re-occurence** or **adverse event** (within 4 weeks after starting treatment)
- If adverse event occured, then fill table c (medication 2 weeks before treatment), d (medication 4 weeks after treatment) and e (adverse event occured)

DONE!

Just attach the form to the case in MEDSIS

Thank you!

Malaria Prevention

Anti-malaria **chemoprophylaxis** for travelers

- An individual risk assessment should be conducted for every traveler, taking into account not only the **destination** country but also the detailed itinerary, including specific cities, **types of accommodation**, season, and style of travel.
- Travelers going to rural areas or staying in accommodations without screens or air conditioning will also be at higher risk.
- The highest risk for malaria is associated with first- and second-generation immigrants living in non-endemic countries who return to their countries of origin to **visit friends and relatives** (VFRs).

Mosquito avoidance measures (during travel and <u>afterwards if ill</u>):

- Remaining in well-screened areas, sleeping under mosquito nets (preferably insecticide-treated nets),
- Use an effective insecticide spray in living and sleeping areas during evening and nighttime hours, and
- Wearing clothes that cover most of the body.

https://wwwnc.cdc.gov/travel/yellowbook/2020/travel-related-infectious-diseases/malaria

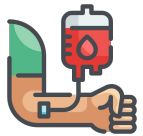
Malaria Awareness

Know the symptoms of malaria:

- Travelers who become ill with a fever or flu-like illness either while traveling in a malaria-risk area or after returning home (**for up to 1 year**) should seek immediate medical attention and should tell the physician their travel history.
- Travelers who are assessed at being at high risk of developing malaria while traveling should consider carrying a full treatment course of malaria medicines with them.

Be aware of blood donation eligibility*:

- Most travelers to an area with malaria are deferred from donating blood for **3 months** after their return (previously one year).
- Former residents of areas where malaria is present will be deferred for **3 years**.
- People diagnosed with malaria cannot donate blood for **3 years after treatment**, during which time they must have remained free of symptoms of malaria.

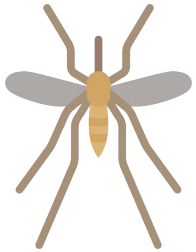


*During April 2020, in light of the COVID-19 public health emergency, FDA updated guidance on blood donor screening to ensure a sufficient and safe blood supply. This revised guidance is intended to remain in effect for the duration of the public health emergency.

https://www.cdc.gov/malaria/symptoms/index.html

Resources

- NEW in 2024- CDC Malaria Investigation Best Practices
- ADHS Malaria Investigation Protocol https://www.azdhs.gov/documents/preparedness/epidemiology-disease-control/investigation-manual/vectorborne/malaria-protocol.pdf
- CDC Malaria website https://www.cdc.gov/malaria
- CDC Yellow Book https://wwwnc.cdc.gov/travel/yellowbook/2020/travel-related-infectious-diseases/malaria
- CDC Malaria Case Report Form (CRF) https://www.azdhs.gov/documents/preparedness/epidemiology-disease-control/disease-investigation-resources/malaria-form.pdf
- For clinical questions, CDC malaria hotline 24 hours a day: Monday – Friday 9 am – 5 pm at 770-488-7788, or afterhours at 770-488-7100.



Questions?

vbzd@azdhs.gov

All icons used in this presentations are from https://www.flaticon.com.