Vector-borne Infections

Dengue fever and Malaria

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Objectives:

1. Understand the epidemiology and global burden of dengue fever and malaria
2. Understand the cycle of infection of dengue fever and malaria
3. Define modes of transmission, clinical features, risk factors, and treatment of dengue fever and malaria (Outline how to take history of Malaria patient, and how to give preventive advise)
4. Enlist the factors responsible for antimalarial drug resistance.
5. Enlist the global measures of prevention and elimination for dengue fever and malaria
6. Understand the epidemiology and risk factors related to dengue fever and Malaria in KSA

Vector-borne diseases

- Vector-borne diseases are a serious health problem
- As vectors can **transmit** the disease at a large scale in shorter time than other infectious diseases that necessitate human to human contact.
- **Prevention** of vector-borne diseases is **difficult** and essentially necessitate the elimination of the vector

Vectors:

Are living organisms that can transmit infectious disease between humans or from animals to humans

Eg: Mosquito, tick, sand fly,….

Vector-borne disease:

- Diseases caused by vectors (transmission)
- Often found in tropical regions, where insects prevail and access to drinking water and sanitation is not safe
- Dengue fever, malaria, yellow fever,…

Dengue fever

Dengue Fever

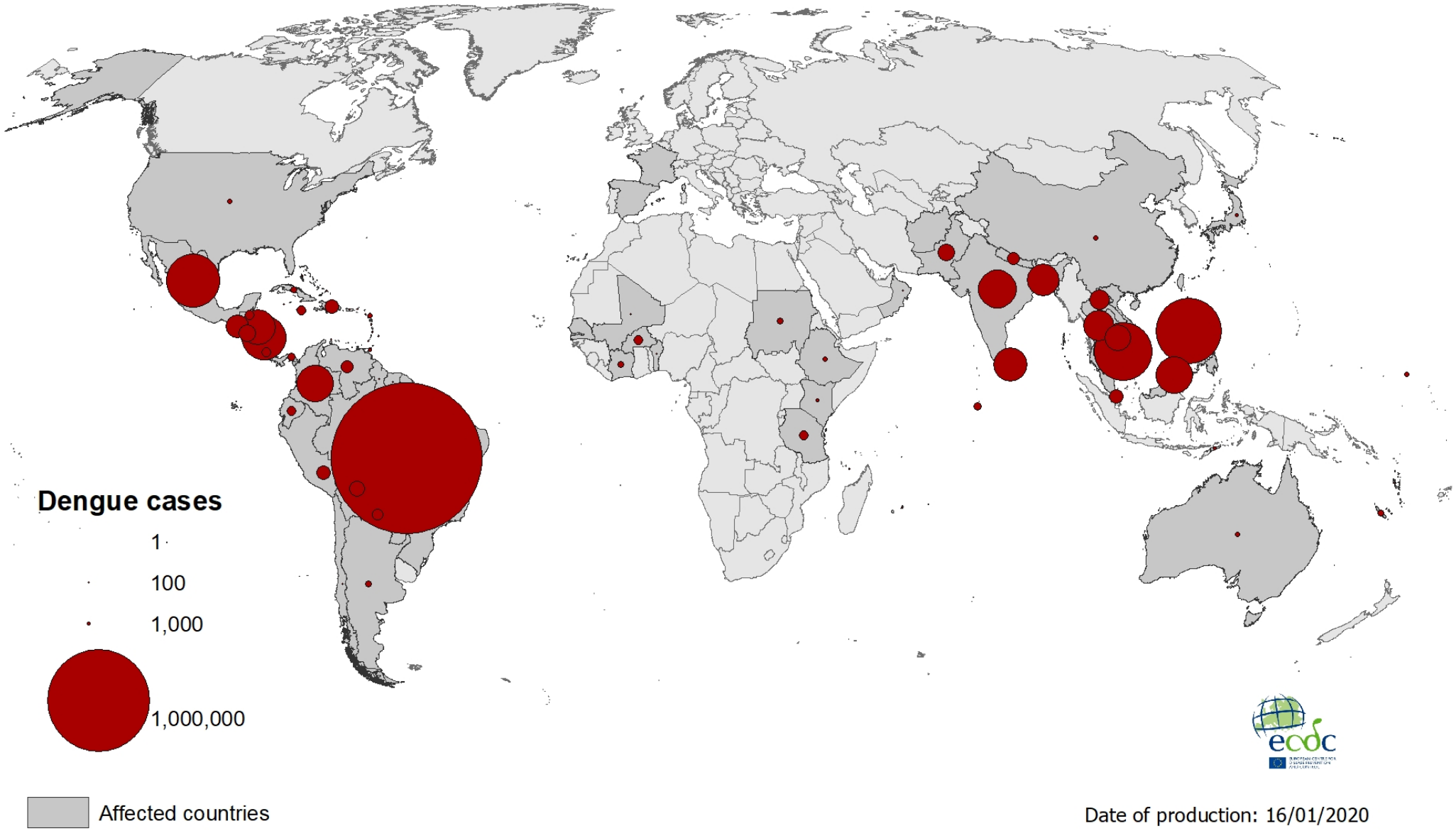
- Vector-borne (mosquito-borne) **viral** disease
- Dengue virus belongs to Flaviviridae family and is **transmitted** by female **mosquitoes** mainly *Aedes aegypti* and, to a lesser extent, *Ae. albopictus*.
- Dengue is widespread throughout the tropics

Global burden

- The number of dengue cases increased over 8 fold over the last two decades
- Reported deaths (between 2000-2015) also increased affecting mostly younger age group.
- About 390 million dengue virus infections per year, of which 96 million manifest clinically (with any severity of disease)
- 90% of infections affecting children under the age of 5 years.
- 2.5% of them die.
- The disease is now endemic in more than 100 countries
- 70% of the actual burden is in Asia

Distribution and outbreaks

- The disease is now endemic in more than 100 countries
- The Americas, South-East Asia and Western Pacific regions are the most seriously affected, with Asia representing ~70% of the global burden of disease.
- The largest number of dengue cases ever reported globally was in 2019. All regions were affected,

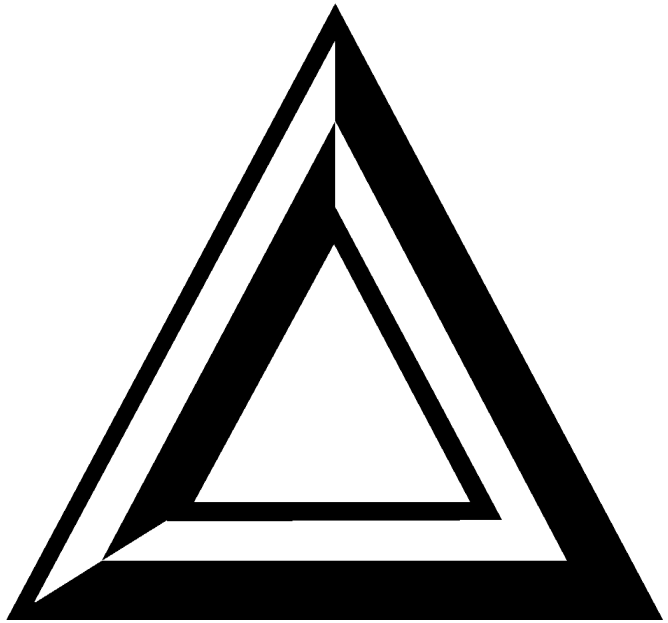

Dengue cases
1
100
1,000
1,000,000
Affected countries
ecdc
Date of production: 16/01/2020

Dengue in KSA

- In 1999 an outbreak was reported for the first time in Jeddah
- From 1994 to 2002, 319 confirmed cases reported in Jeddah
- Then two peaks were reported in 200/2006 and another two in 2008
- Dengue is now **endemic** in **western** and **southern** regions of KSA

Analytical Epidemiology Triad:

HOST



AGENT

ENVIRONMENT

Epidemiological determinants

1- Agent factors:

- Agent: dengue viruses from the genus flavivirus.
- 4 serotypes: DENV-1, DENV-2, DENV-3, DENV-4.
- Vector: mainly of the species *Aedes aegypti* and, to a lesser extent, *Ae. albopictus*

2- Environmental factors:

temperature and humidity

3- Host factors:

Host risk factors

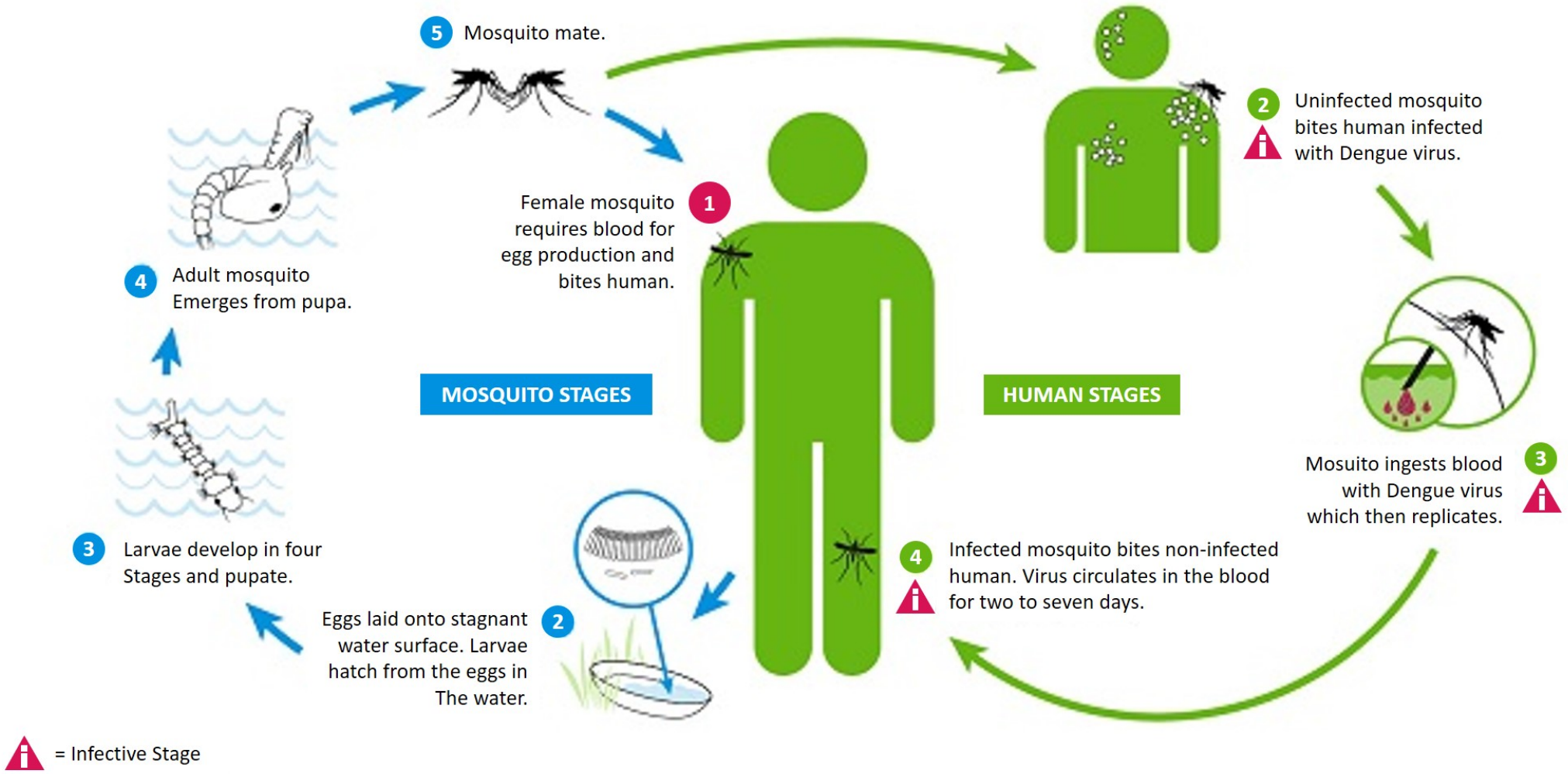
Factors increasing risk of severe disease and complications:

- Infants and elderly
- Obesity
- Pregnancy
- Peptic ulcer disease
- Women who are in menstruation or have abnormal bleeding
- Hemolytic disease such as thalassemia, G6PD, other hemoglobinopathies
- Congenital heart disease
- Chronic diseases such as diabetes, chronic renal failure, liver cirrhosis
- Patients on steroids or NSAID treatment

Transmission

- **Transmission through mosquito bite..** primarily the *Aedes aegypti* mosquito to a lesser extent, *Ae. albopictus*.
- Maternal transmission: babies may suffer from pre-term birth, low birthweight, and fetal distress
- Rare cases of transmission via, blood products, organ donation and transfusions have been recorded.

Infection cycles of Dengue fever



Vector Ecology

- **The *Aedes aegypti*** day-time feeder; eggs can remain viable for several months in dry condition, and will hatch when they are in contact with water.
- ***Aedes albopictus***, (USA, and Europe) tolerance of colder conditions, as an egg and adult. day biter

Signs and symptoms

- Majority are asymptomatic or show mild symptoms, it can manifest as a severe, flu-like illness

- Asymptomatic
- Undifferentiated febrile illness (viral illness)
- Dengue fever (DF)
- Dengue hemorrhagic fever (DHF) (plasma leakage)
- Dengue shock syndrome (DSS)

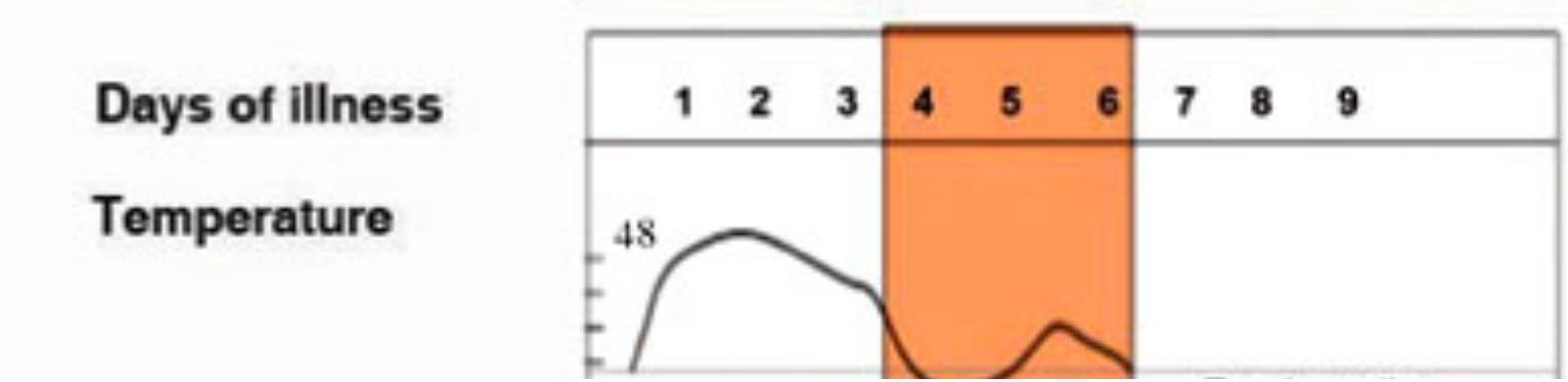
Classica dengue fever symptoms

❖Lasts for 2–7 days,

❖incubation period of 3–10 days

- high fever (39-40°C) **biphasic**
- severe headache
- Retroorbital pain
- muscle and joint pains
- nausea
- vomiting
- swollen glands
- rash.

Biphasic curve



Dengue Time Frame

Phase	Incubation	Febrile Phase							Critical Phase		Recovery phase
Time frame	3-14 days	3-7 days							1-2 days		3-5 days
Symptoms	None	Fever is present							Fever resolves		
		>Myalgias >Rash >Petechiae >Tourniquet test >Leukopenia >Mild bleeding						Warning signs may occur	>Capillary leak >Shock >Severe hemorrhage >Severe organ involvement		> Fluid Reabsorption >Diuresis
Testing							DENV IGM				
		DENV NS1 DENV PCR									
Day of	0	1	2	3	4	5	6+	7	8	9	10+

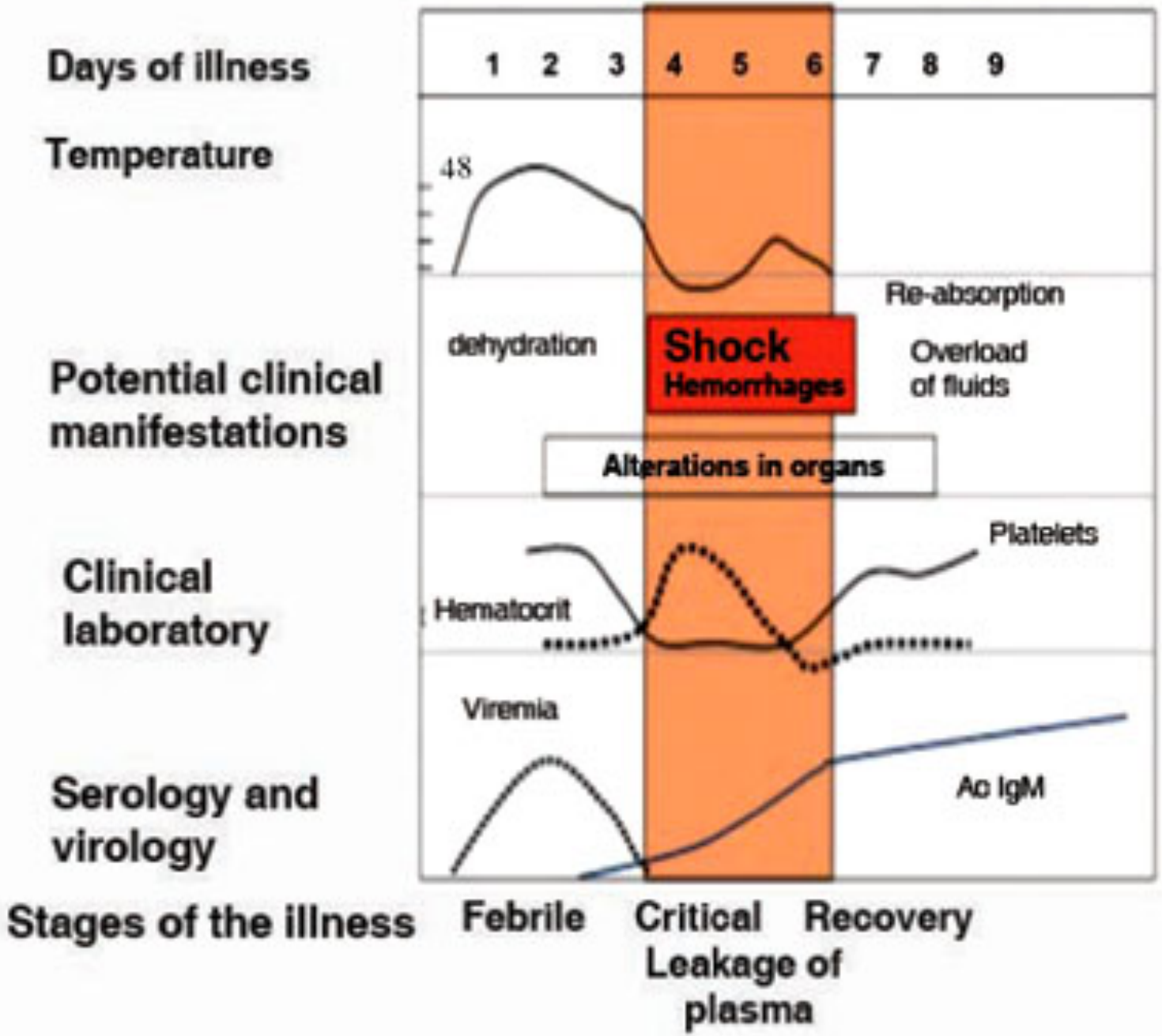
Severe dengue

- During critical phase (3-7 days after illness onset).
- Small portion of patients
- Fever drops (below 38°C/100°F)
- Severe dengue is a potentially fatal complication, due to plasma leaking, fluid accumulation, respiratory distress, severe bleeding, or organ impairment.
- Close observation is essential

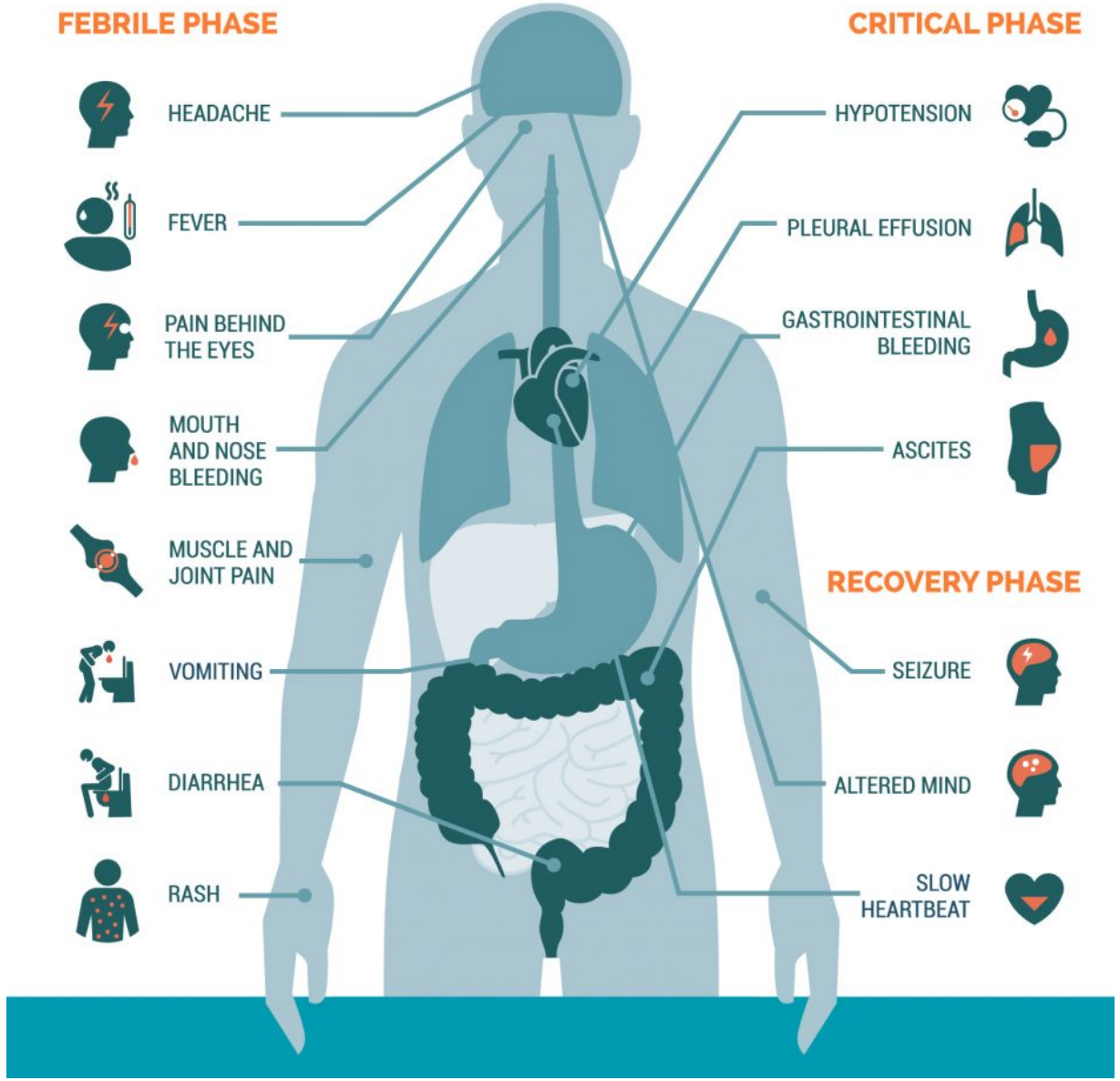
Severe dengue

- **Warning signs**
- severe abdominal pain
- persistent vomiting
- rapid breathing
- bleeding gums or nose
- fatigue
- restlessness
- liver enlargement
- blood in vomit or stool.

Plasma leakage
Thrombocytopenia


Days of illness
1 2 3 4 5 6 7 8 9
Temperature
48
Potential clinical manifestations
dehydration
Shock
Hemorrhages
Re-absorption
Overload of fluids
Alterations in organs
Clinical laboratory
Hematocrit
Platelets
Serology and virology
Viremia
Ac IgM
Stages of the illness
Febrile
Critical
Leakage of plasma
Recovery

SYMPTOMS


FEBRILE PHASE
HEADACHE
FEVER
PAIN BEHIND THE EYES
MOUTH AND NOSE BLEEDING
MUSCLE AND JOINT PAIN
VOMITING
DIARRHEA
RASH
CRITICAL PHASE
HYPOTENSION
PLEURAL EFFUSION
GASTROINTESTINAL BLEEDING
ASCITES
RECOVERY PHASE
SEIZURE
ALTERED MIND
SLOW HEARTBEAT

Diagnosis

Probable case definition:

Fever with two or more of the following:

- Headache
- Retroorbital pain
- Myalgia
- Arthralgia
- Rash
- Hemorrhagic manifestations
- Leukopenia
- Thrombocytopenia
- Rising hematocrit (5-10%)

At least one of the following:

- Supportive serology
- Occurrence at the same time and location of confirmed cases

Laboratory diagnosis

- **Virus isolation methods**
- (RT–PCR) the gold standard.
- testing for a virus-produced protein, called NS1. (rapid does not require specialized laboratory techniques or equipment)
- **Serological methods**
- Serology (ELISA), recent or past infection (antibodies).

Treatment

- There is no specific treatment (Supportive care)
- pain killers (acetaminophen)
- Avoid NSAIDs (non-steroidal anti-inflammatory drugs), and aspirin to reduce the risk of more bleeding and Reye's syndrome

- Monitoring for warning signs
- IV fluids, oxygen, transfusion for severe and shock cases

Vaccination against dengue

- The first dengue vaccine, Dengvaxia® (CYD-TDV)
- licensed in December 2015 approved in ~20 countries.
- Limited use to **prisoners** in endemic areas

Notification

- In dengue-endemic countries,
- Probable, suspected and confirmed cases have to be notified to authorities
- In Saudi Arabia, immediate notification to MOH

Prevention and control

- **Prevention of mosquito breeding:**
  - Preventing mosquitoes from accessing egg-laying habitats by environmental management and modification;
  - Disposing of solid waste properly and removing artificial man-made habitats that can hold water;
  - Covering, emptying and cleaning of domestic water storage containers on a weekly basis;
  - Applying appropriate insecticides to water storage outdoor containers;
- **Personal protection from mosquito bites:**
  - Using of personal household protection measures, such as window screens, repellents, coils and vaporizers. (mosquito vectors bites throughout the day)
  - Wearing clothing that minimizes skin exposure to mosquitoes is advised;

Prevention and control

- **Community engagement:**
  - Educating the community on the risks of mosquito-borne diseases;
  - Engaging with the community to improve participation and mobilization for sustained vector control;
- **Active mosquito and virus surveillance:**
  - Active monitoring and surveillance of vector abundance and species composition should be carried out to determine effectiveness of control interventions;
  - Prospectively monitor prevalence of virus in the mosquito population, with active screening of sentinel mosquito collections;
  - Vector surveillance can be combined with clinical and environment surveillance.

WHO responds to dengue

- supports countries in the confirmation of outbreaks through its collaborating network of laboratories;
- provides technical support and guidance to countries for the effective management of dengue outbreaks;
- supports countries to improve their reporting systems and capture the true burden of the disease;
- provides training on clinical management, diagnosis and vector control at the country and regional level with some of its collaborating centres;
- formulates evidence-based strategies and policies;
- support countries in the development of dengue prevention and control strategies and adopting the Global Vector Control Response (2017-2030)
- reviews the development of new tools, including insecticide products and application technologies;
- gathers official records of dengue and severe dengue from over 100 Member States; and
- publishes guidelines and handbooks for surveillance, case management, diagnosis, dengue prevention and control for Member States.

Malaria

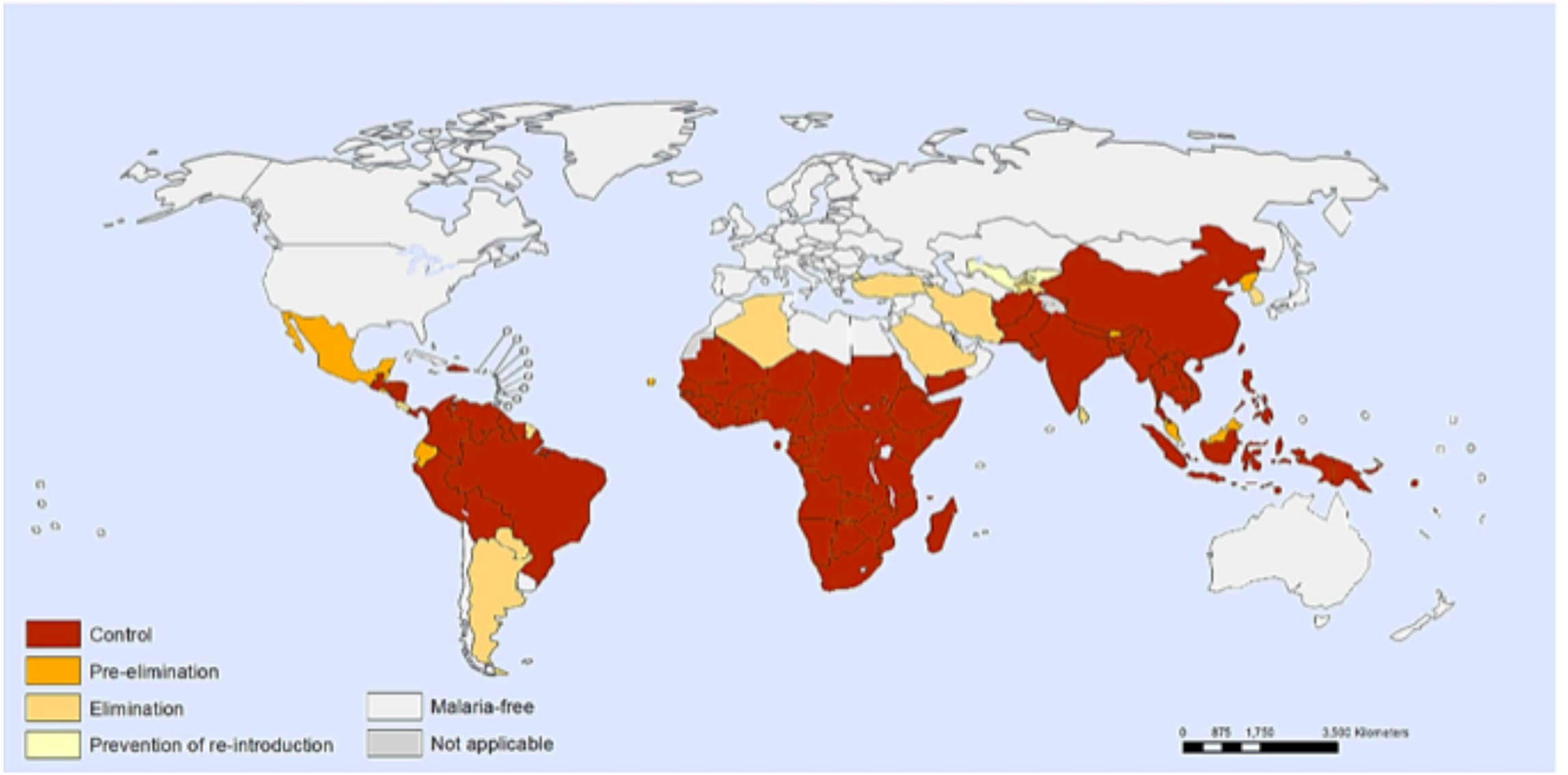
Malaria is a life-threatening disease caused by **Plasmodium parasites** that are transmitted to people through the **bites of infected mosquitoes.**

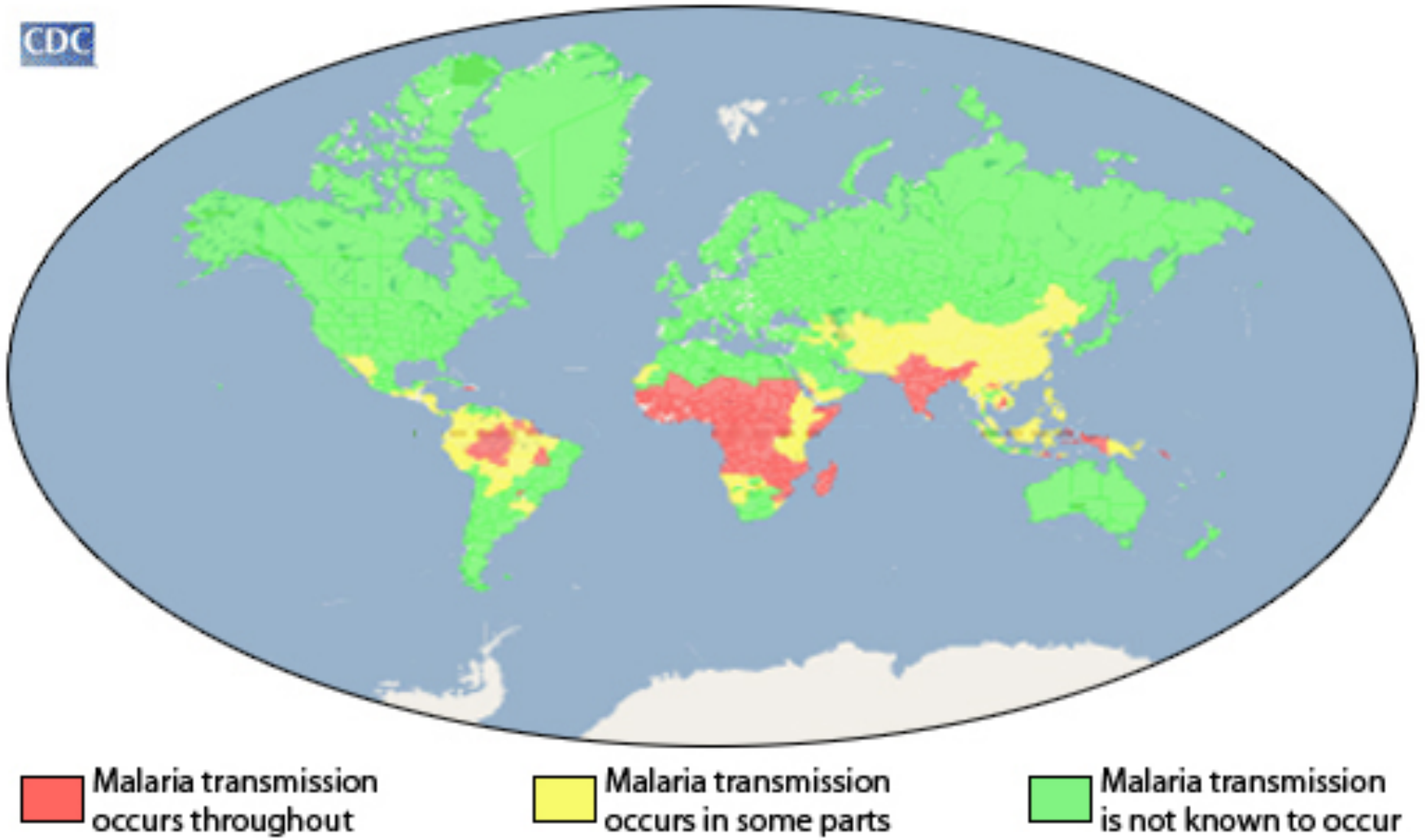
Malaria is responsible for approximately 1-3 million deaths per year

Epidemiology

- In 2016, there were 216 million cases and 445,000 deaths caused by malaria worldwide.
- Between 2000 and 2015, malaria **incidence** fell by 37% globally.
- During the same period, malaria **mortality** rates decreased worldwide by 60% among all age groups, and by 65% among children under 5.
- In 2014, 13 countries reported zero cases of the disease and 6 countries reported fewer than 10 cases.

Classification of countries by stage of malaria elimination, as of December 2014





An approximation of the parts of the world where malaria transmission occurs.

Malaria in Saudi Arabia

- Areas at the **southern region** are at risk of malaria transmission, specifically Asir and Jizan. The Dominant Malaria Species in Saudi Arabia is **P. Falciparum** .
- Saudi Arabia achieved a decrease in malaria cases and case incidence rates of ≥75%.

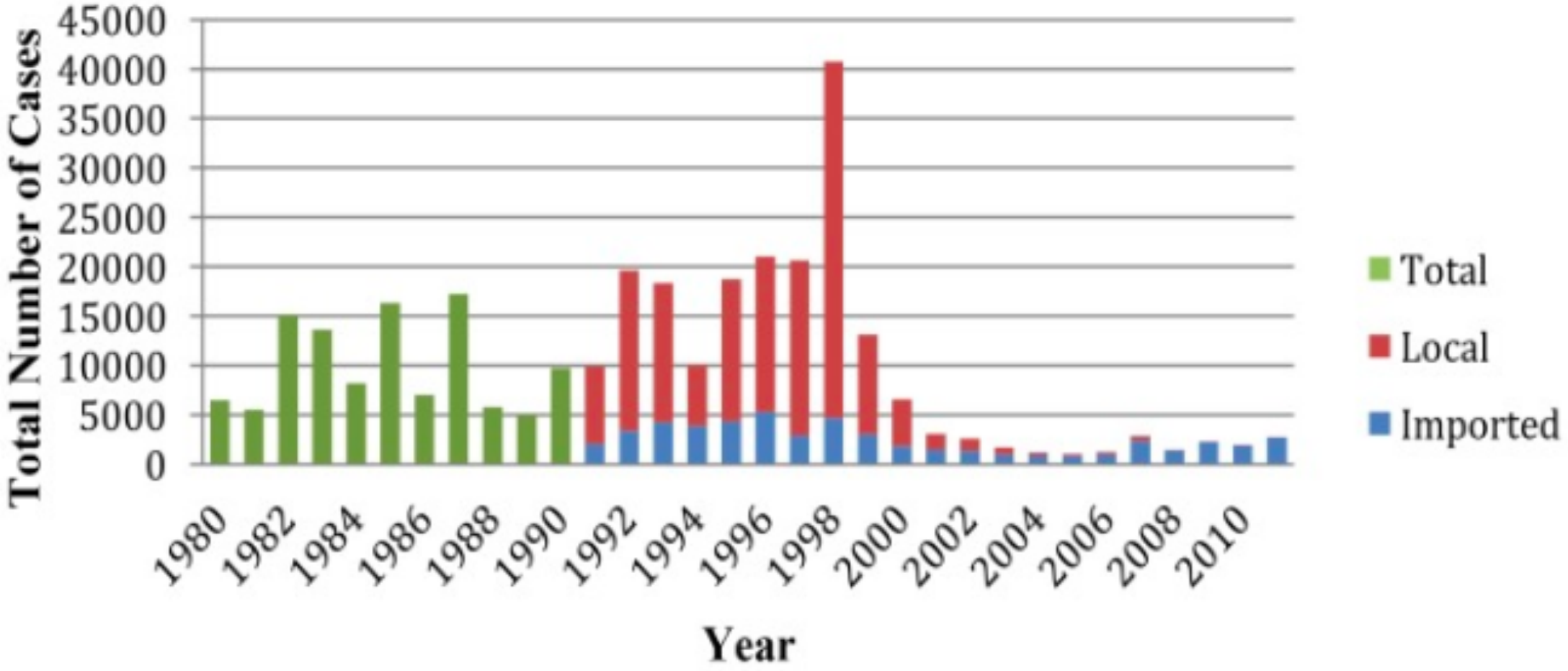
Malaria in Saudi Arabia

- Malaria outbreak in 1998.
- Since then, only a few cases were reported
- In 2012 , only 82 cases of malaria were reported..
- The proportion of imported malaria has increased from 23% to 99% of total detected cases.

- **Imported malaria:** via asymptomatic travelers from malaria endemic areas, sustains a threat for possible resurgence of local transmission:

  Workers, immigrants, pilgrims.

Indigenous cases of malaria Saudi Arabia 2014 :



Imported malaria in Saudi Arabia 1999-2010 :

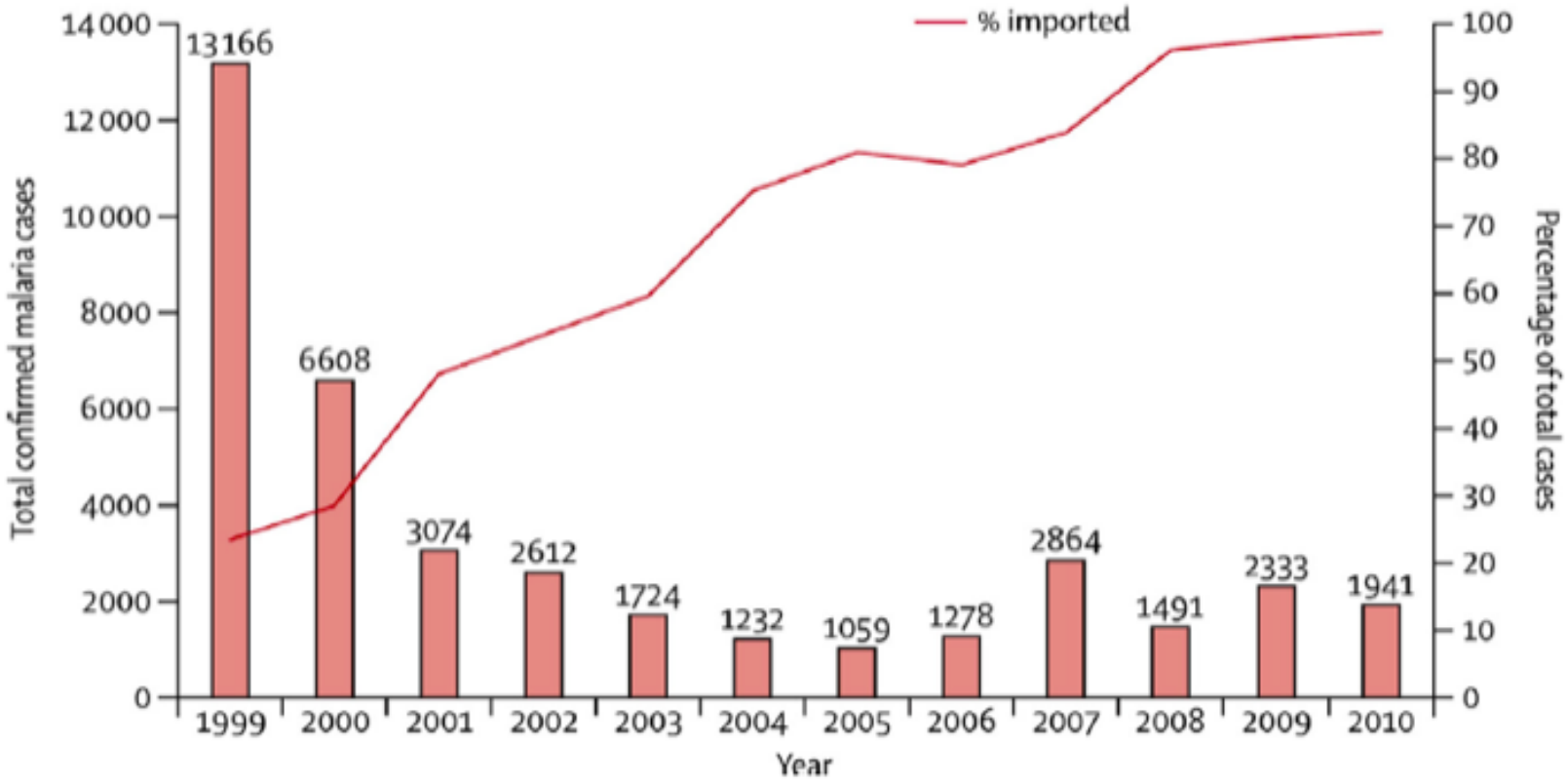
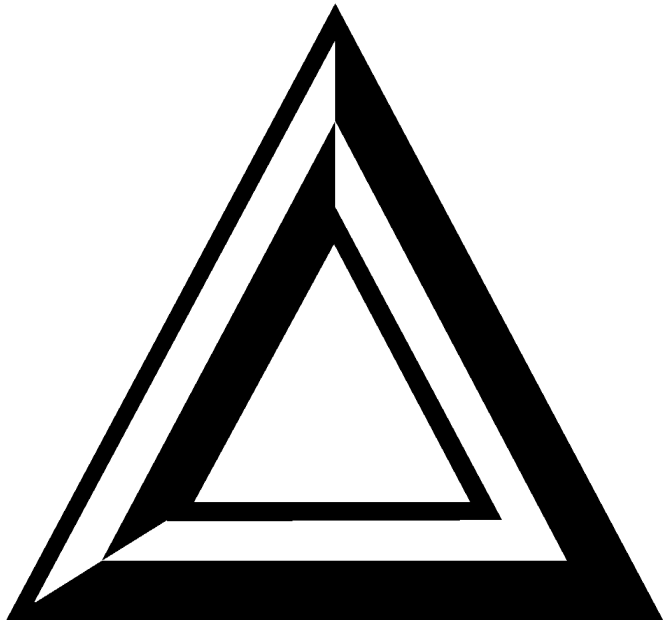


Fig. 1. Indigenous and imported malaria in Saudi Arabia, 1999–2010 (Cotter et al., 2013).

Analytical Epidemiology Triad:

HOST



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Plasmodium Parasites

- **Five** species cause malaria in humans:

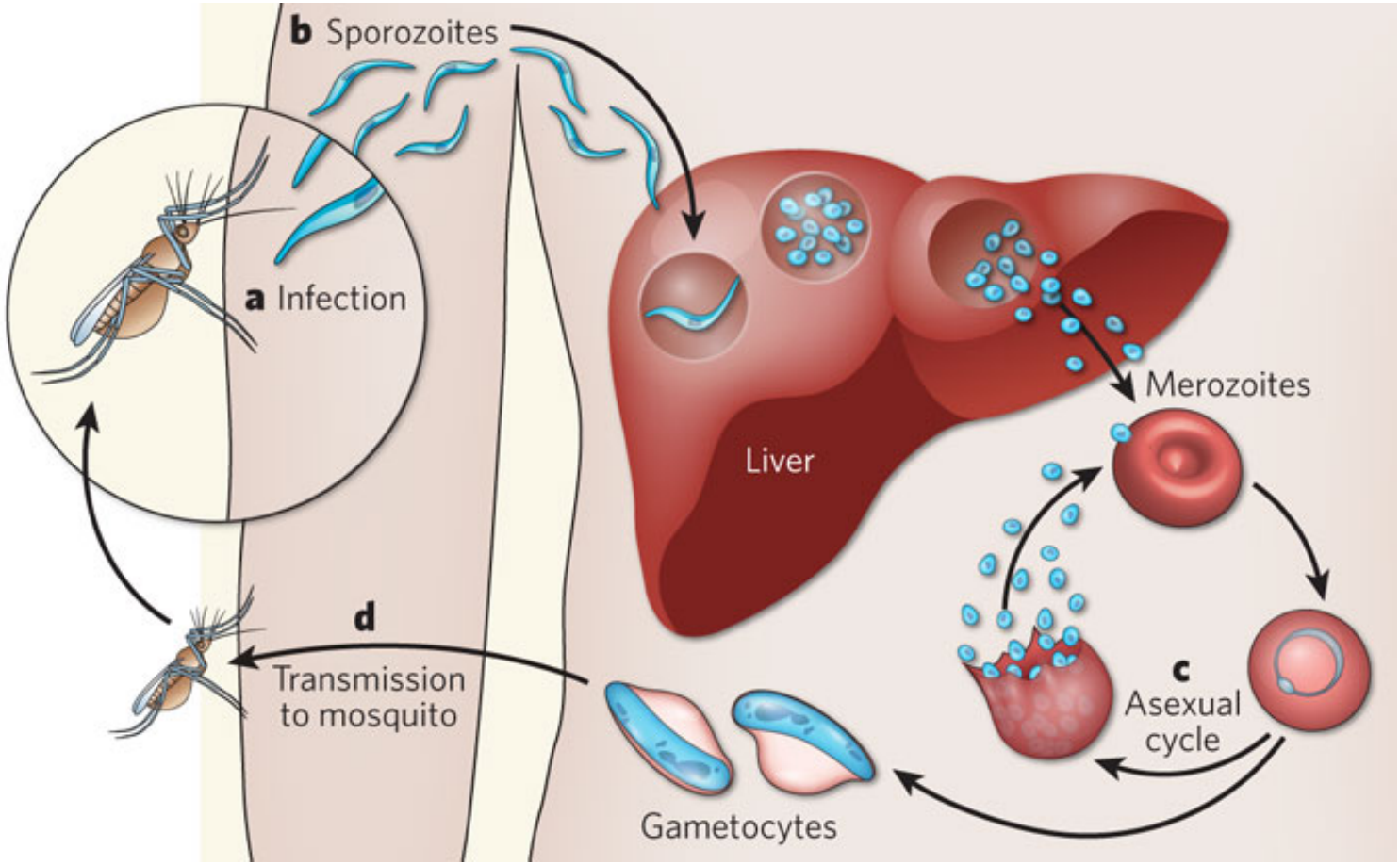
Plasmodium falciparum, P. vivax, P. ovale, P. malariae and P. knowlesi

- **P. falciparum and P. vivax** pose the greatest threat.

Plasmodium Parasites

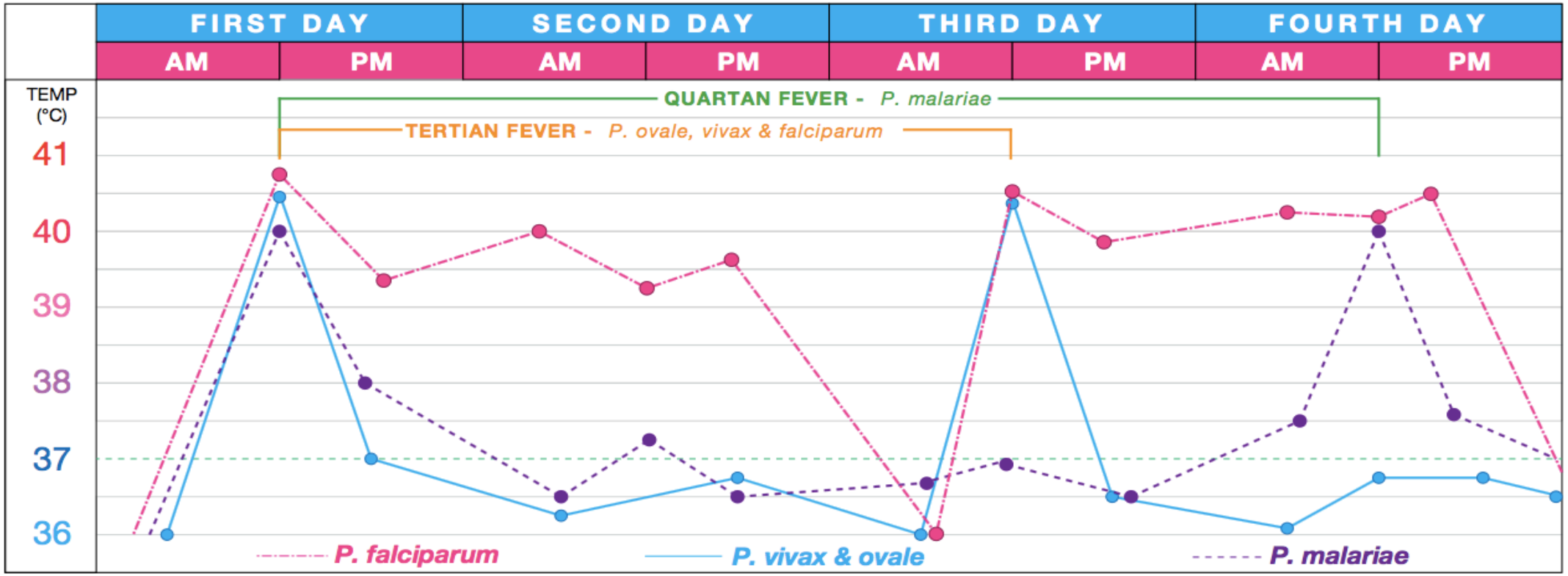
- **Transmitted** through **the bites of infected female Anopheles mosquitoes (vector)**.
- **Other modes of transmission:**
- From mother to unborn child
- Blood transfusion

Plasmodium Parasites transmission and lifecycle:



Clinical features

Paroxysmal fever



Cold stage: lassitude, headache, nausea, chills. (¼ -1 h) skin cold then hot

Hot stage: skin hot and dry (2 -6 h)

Sweating stage: fever subsides, sweating (2 -4 h)

Symptoms

Early symptoms

Fever

Headache

Chills

If not treated early might progress to

Severe illness

Severe anemia

Respiratory distress

Cerebral malaria

Multiorgan failure

Risk factors

No or little immunity against the disease in areas with high transmission

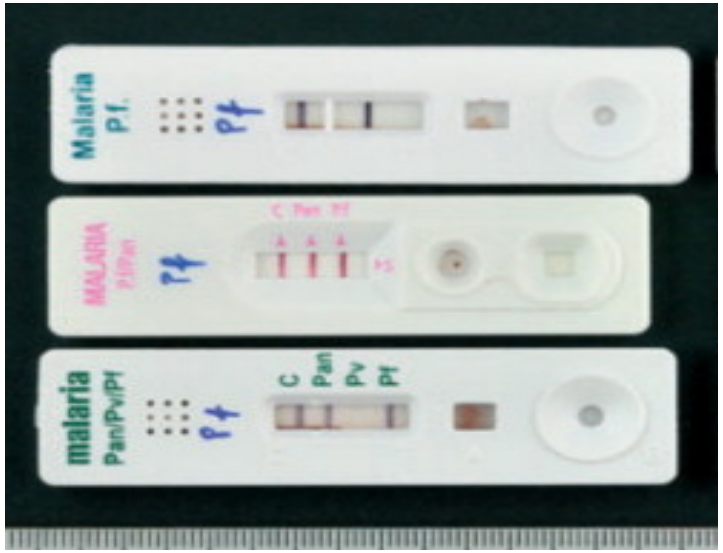
- **Young children**, who have not yet developed partial immunity to malaria
- **Pregnant women**, whose immunity is decreased by pregnancy.
- **Travelers or migrants** coming from areas with little or no malaria transmission, who lack immunity.
- People with low immunity such as HIV patients
- Poverty
- **Environmental**: rain seasons

Immunity against malaria (protection)

- **Genetic Factors:** Biologic characteristics present from birth can protect against certain types of malaria: (having the **sickle cell trait**)
- **Acquired Immunity:** newborns in endemic areas will be protected during the first few months by maternal antibodies.
- **Repeated attacks of malaria**

Diagnosis

- Microscopy: thin film, thick film
- Serology: two weeks after infection, past infection in epidemiological studies.
- Rapid diagnostic test (RDT):



Community diagnosis

- Pre-eradication: spleen rate, parasite rate,…..
- Eradication: microscopic diagnosis
  - Parasite incidence
  - Blood examination rate
- Vector indices
  - Human blood index
  - Sporozite rate
  - Mosquito density
  - Man biting rate
  - Inoculation rate

Treatment

Choice of treatment line depends on:

- Type of plasmodium species and stages of malaria parasites.
- Clinical status of patient: Uncomplicated or Severe, or pregnancy.
- Drug sensitivity of the infected parasite (area)
- Previous exposure to anti-malarial drugs.

Artemisinin combination therapy (ACT): (3days)

- Monotherapy is not recommended for malaria treatment to prevent drug resistance

For uncomplicated malaria:
First line: (ARTESUNATE + SP); alternative (ARTESUNATE + MEFLOQUINE)
Second Line: (ARTEMETHER + LUMEFANTRINE)
Third Line : (oral QUININE + DOXYCYCLINE)

A single dose of Primaquine is added to the first day as a gametocidal medication.

- Primaquine is contraindicated in:
  - G6PG deficiency,
  - pregnancy,
  - children < 6m,
  - lactating mothers for babies <6m or
  - hypersensitivity

Treatment failure

Failure to resolve or recurrence of fever or parasitemia:

- Early (1-3 days of treatment)
- Late: (4days – 6 weeks after treatment)

Causes:

- Poor adherence to treatment
- Low or incomplete dose
- Abnormal individual pharmaokinetics
- Drug resistance

Antimalarial drug resistance

- The ability of the parasite to survive and/or multiply despite the administration and absorption of medication.

- **Reason:**
- Exposure of the parasite to insufficient amount of the drug.
    - Low dose prescribed
    - Lesser amount dispensed
    - Incomplete treatment
    - Vomiting
    - Low absorption

WHO efforts in malaria control

- **Global Technical Strategy for Malaria 2016–2030**

1. Ensure universal access to malaria prevention, diagnosis and treatment
2. Accelerate efforts towards elimination and attainment of malaria-free status
3. Transform malaria surveillance into a core intervention

Control:

The main way to reduce malaria transmission at a community is **vector control**

- Decrease human-mosquito contact
- Destruction of adult mosquitoes
- Destruction of larvae
- Environmental control
- Chemoprophylaxis
- Vaccination

Decrease human-mosquito contact

- Insecticide-treated mosquito nets (ITNs)
- For **all at-risk persons**
- Provision of **free LLINs**
- **Everyone sleeps under a LLIN every night.**

Destruction of adult mosquitoes

- Indoor spraying with residual insecticides
- **At least 80%** of houses in targeted areas are sprayed
- Protection depends on type of insecticide.

Destruction of mosquito larvae

- Larviciding of water surfaces, intermittent irrigation, biological control

Source reduction

- Environmental sanitation, water management, drainage

Social participation

- Health education , community participation

Chemoprophylaxis

- To travelers
- Pregnant women
- Infants in endemic areas
- Seasonal chemoprevention

Vaccination

- Since 2021, RTS,S/AS01 malaria vaccine
- Recommended for children in endemic regions
- Significantly reduce malaria, and deadly severe malaria, among young children.

Risk factors in Saudi Arabia

- Heavy rainfall season
- Army personnel and employees working at the Southern borders
- Travelers to countries with active malaria transmission
- Pilgrimage from regions with active malaria transmission

Prevention and control of malaria in KSA

The current elimination strategy in Saudi Arabia focuses mainly on:

1. Targeting **high risk areas** for sustained preventative measures such as (Long lasting insecticide treated nets, Indoor residual spraying)
2. **Management of infection** through rapid confirmed diagnosis and treatment.
3. Individual case follow up and reactive **surveillance** with appropriate treatment and vector control.
4. Active case detection **at borders** with screening and treatment.

Malaria and Hajj season

Measures applied before inlet of Pilgrims:

- Spray health care facilities pilgrims camps with residual insecticides.
- Surveillance at Hajj Entry ports (suspected cases/ necessary measures).

Measures applied during Hajj season:

- Epidemiology investigation malaria cases (proper diagnosis/treatment).
- Secure malaria drugs and treatment policy for all health care facilities.

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