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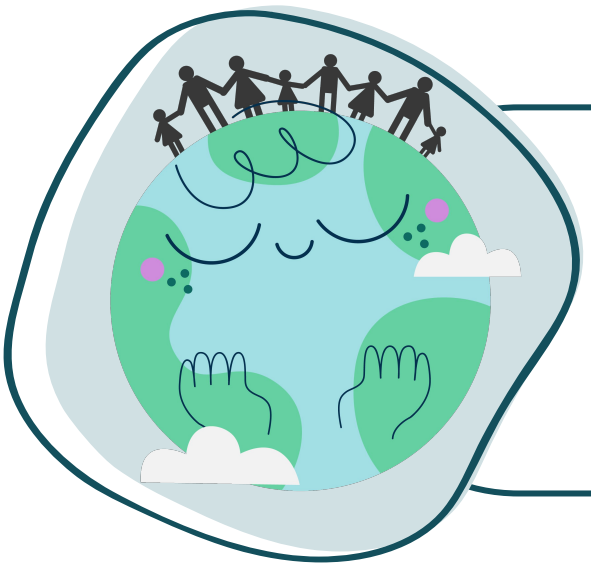

Dengue fever and Malaria

Objectives

- **Understand the epidemiology and global burden of dengue fever and malaria.**
- **Understand the cycle of infection of dengue fever and malaria.**
- **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).**
- **Enlist the factors responsible for antimalarial drug resistance.**
- **Enlist the global measures of prevention and elimination for dengue fever and malaria.**
- **Understand the epidemiology and risk factors related to dengue fever and Malaria in KSA**
- **OSCE**

You can check the references at the end of the lecture if interested

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Editing File

Introduction

Vectors:

Are living organisms that can transmit infectious disease between humans or from animals to humans Eg: Mosquito, tick, sand fly,….

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.

Vector-borne diseases :

- 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[1] and, to a lesser extent, Ae.albopictus.
- Dengue is widespread throughout the tropics.

Dengue in KSA :

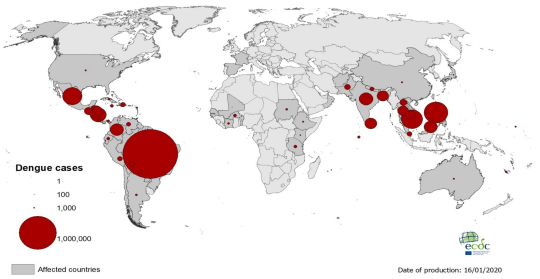
- In 1999 an outbreak was reported for the first time in Jeddah.
- From 1994 to 2002, 319 confirmed cases reported in Jeddah.
- Then two peaks were reported in 200/2006 and another two in 2008.
- Dengue is now endemic in **western** and **southern** regions of KSA.

1. Mnemonic: عابده المصريه
- Vector: Aedes aegypti and, to a lesser extent, Ae.albopictus.
- Causative agent: Dengue virus

Dengue Fever

Global burden :

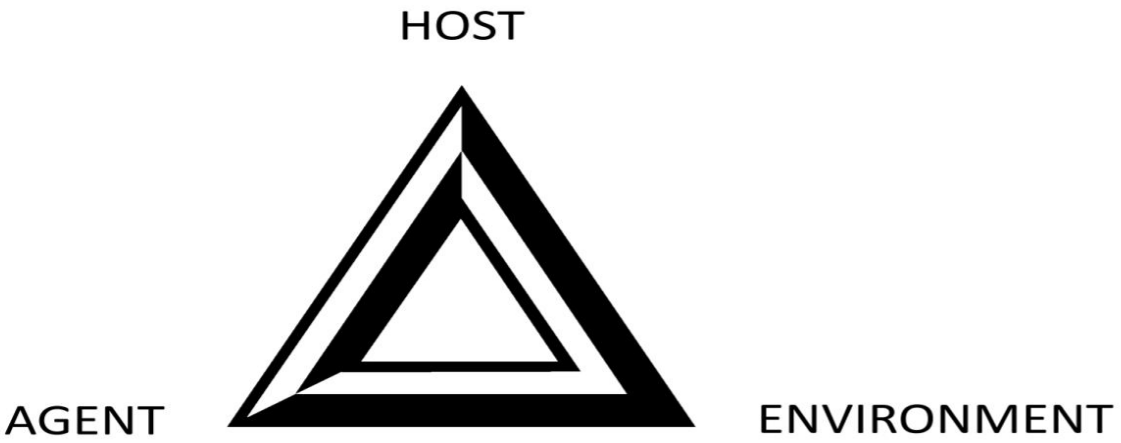
- The number of dengue cases increased over 8 fold over the last two decades.
- Reported deaths (between 2000-2015) also increased affecting mostly younger age group.
- About 390 million dengue virus infections per year, of which 96 million manifest clinically (with any severity of disease).
- 90% of infections affecting children underthe 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,

Analytical Epidemiology Triad:



Dengue Fever

Epidemiological determinants :

Agent factors

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

Environmental factors

Temperature and humidity

Host 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 :

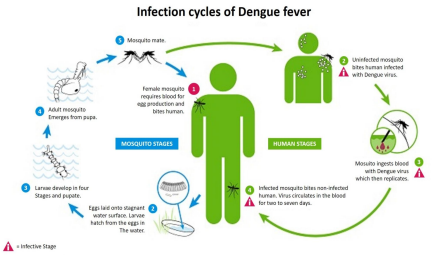
- **Transmission through mosquito bite**.. primarily the Aedes aegypti mosquito to a lesser extent, Ae albopictus.
- Maternal transmission: babies may suffer from pre-term birth, low birthweight, and fetal distress
- Rare cases of transmission via, blood products, organ donation and transfusion have been recorded.
- Aedes usually cause multiple bites. ما بيعض من مريض واحد، بدور على كل الى فى العرفه وبقرصهم
- Time of transmission:
  - Aedes: Day time.
  - Anopheles: Night time

1. Infected individuals develop immunity against 1 serotype only. So they're still susceptible to other serotypes

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.

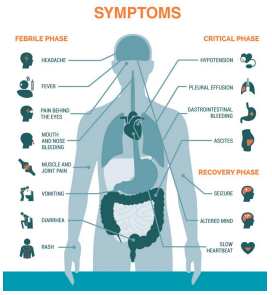


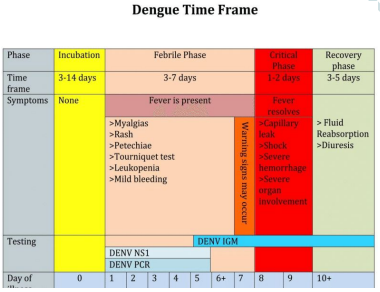
Signs and symptoms :

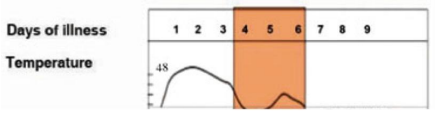
- Majority are asymptomatic or show mild symptoms, it can manifest as a severe, flu-like illness
- Asymptomatic
- Undifferentiated febrile illness (viral illness)
- Dengue fever (DF)
- Dengue hemorrhagic fever (DHF) (plasma leakage)
- Dengue shock syndrome (DSS)

Classical dengue fever symptoms :

- Lasts for 2–7 days,
- incubation period of 3–10 days [1]
  - high fever (39-40°C) biphasic
  - severe headache
  - Retro-orbital pain
  - muscle and joint pains
  - nausea
  - vomiting
  - swollen glands
  - rash.

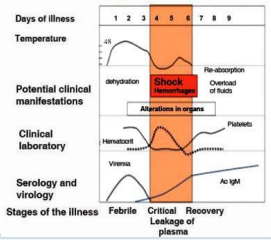






Severe dengue :

- 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



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**

1. The induration of the bite have already disappeared.

Dengue Fever

Diagnosis :

Probable case definition:

Fever with two or more of the following:	At least one of the following:	Laboratory diagnosis:
• Headache • Retroorbital pain • Myalgia • Arthralgia • Rash • Hemorrhagic manifestations • Leukopenia • Thrombocytopenia • Rising hematocrit (5-10%)	• Supportive serology • Occurrence at the same time and location of confirmed cases	• 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

Dengue Fever

Prevention and control :

1

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

2

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;

3

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;

4

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 bite of the female infected Anopheles mosquito**[1]

A typical attack comprises **three** distinct stages: cold stage, hot stage and sweating stage

- **COLD STAGE:** The onset is with **lassitude**, **headache**, **nausea** and **chilly sensation** followed in an hour or so by **rigors**. The temperature **rises rapidly to 39-41°C.** Headache is often severe and commonly there is **vomiting**. In early part of this stage, skin feels cold; later it becomes hot. Parasites are usually demonstrable in the blood. The pulse is rapid and may be weak. This stage lasts for 15 mins -1 hour.
- **HOT STAGE:** The patient feels **burning hot and casts off his clothes.** The skin is **hot and dry to touch**. **Headache is intense** but **nausea commonly diminishes.** The pulse is full and respiration rapid. This stage lasts for 2 to 6 hours.
- **SWEATING STAGE:** Fever comes down with profuse sweating. The **temperature drops rapidly** to normal and **skin is cool and moist.** The pulse rate becomes **slower**, patient feels relieved and often falls asleep. This stage lasts for 2-4 hours

Epidemiology

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

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 outbreak in 1998.
- Since then, only a few cases were reported
- In 2012, only 82 casesof 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.

1: Life threatening if not treated properly
2: There's always a risk of reintroduction to other countries
3: Like Saudi is chloroquine resistant
4: Why are the cases increasing ? Usually it's political reasons (like wars) more than health reasons. Poverty, war, etc can increase the chance of disease incidence and this will also cause the death percentages to increase

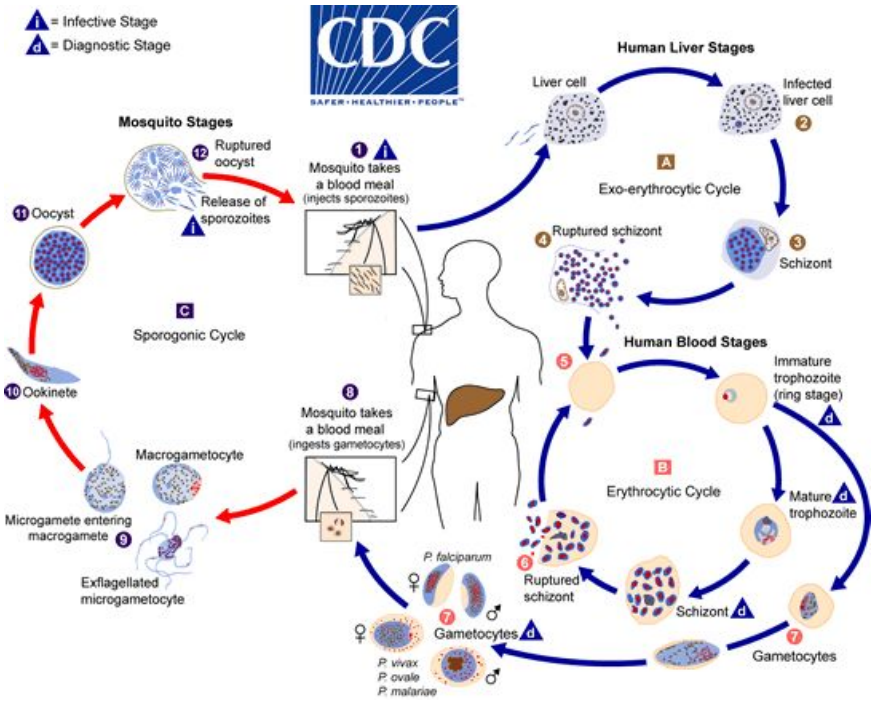
Plasmodium Parasites

Five protozoan parasites that are known to affect humans:

Plasmodium falciparum | **P. vivax**[1] | **P. ovale** | **P. malariae** | **P. knowlesi**[2]

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

Mode of transmission and lifecycle:



- **Transmitted :**
  - **Vector** (through the bites of infected female Anopheles mosquitoes)
- **Other modes of transmission:**
  - Blood (injection/transfusion of contaminated blood)
  - From mother to unborn child

Recall from Microbiology
Explanation for the picture:
1. Malaria is mainly carried by **female anopheles mosquito.**
2. The infected mosquito will **bite and inject sporozoites** from it salivary gland into the bloodstream of human
3. Which then will travel through blood until it reaches the liver and enter the hepatocytes where it will multiply asexually to form **merozoites inside the schizont (Exoerythrocytic schizont).**
4. When the **hepatic schizont rupture (clinical symptoms appear)** the merozoites will be released into blood, then it will enter the erythrocytes forming **immature trophozoites (ring stage)** which will have 2 pathways:
a. **First pathway:** It goes through the **erythrocytic cycle** starting from ring stage then into Mature trophozoites, then the merozoites will multiply inside the RBCs forming **schizont (Erythrocytic schizont**), which will rupture (hemolysis) and release the merozoites into the bloodstream (Clinical attack of malaria is due to this stage) and the cycle will repeat over and over again.
b. **Second pathway:** Some immature trophozoites will become **gametocytes (male and female)** those gametocytes will be ingested by another mosquito; in the mosquito:
i. There are Micro(Male) and Macro(Female) gametocytes, the microgametocytes will enter into the macrogametocytes in which they will form Ookinete then it will develop into Oocyst which will rupture releasing **sporozoites** in mosquito, then the cycle will go over and over again.

1- India, Afghanistan
2- Documented in South east Asia.

History and Clinical features OSCE

Symptoms are not specific

- Chills
- Fever
- Headache

Early symptoms

Severe symptoms

If not treated early might progress to:

- severe anemia
- Respiratory distress
- Cerebral malaria
- Multiorgan failure

Paroxysmal fever : 

1. Cold stage: lassitude, headache, nausea, chills. (¼ -1 h) skin cold then hot
2. Hot stage: skin hot and dry (2 -6 h)
3. Sweating stage: fever subsides, sweating (2 -4 h)

History and 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

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

Investigations

OSCE

Diagnosis;

1. **Rapid diagnostic test (RDT)**[1]
2. **Light Microscopy:**[2]
   Giemsa-stained blood smear; Thin film, thick film.
3. **Serology:**
   two weeks after infection, past infection in epidemiological studies.

Community diagnosis

Pre-eradication[4]

- **spleen rate,**
- **parasite rate**

Areas with advanced malaria control

-Universal access to diagnostic tests/ capabilities.

- **Surveillance**/mapping.

- Focused **screening** (e.g., those who present with danger signs) and treatment (e.g., active case strategy in Oman).

Eradication

microscopic diagnosis

- **Parasite incidence**
- **Blood examination rat**

Areas where malaria has been eliminated

- Prevent re-introduction.

- Considerable resources are still needed.

- Different strategies (e.g., border control, active case management).

- Maintain high-quality diagnosis

Vector indices

- Human blood index
- Sporozite rate
- Mosquito density
- Man biting rate
- Inoculation rate

- Vigilance (e.g., investigations of unusual increase in cases with fever)

- **Field surveys with RDTs**

Which of the following preventive measures is included in the malaria control program ? Case Management

1: Anyone can do it, but not specific and you can't tell the type of Protozoa. It is used in community diagnosis (because it is rapid) where you scan a lot of people.
2: It's specific. It tells you the type of Protozoa but someone has to be very skilled in order to count on it as diagnostic (picture it as an Ultrasound where it's operator dependent)
3: New diagnostic tool it's still under development but promising because it's cheap and specific
4: Saudi is in this stage

Management

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

Treatment will depend 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)

I just want you to know that malaria treatment is never a single medication it's always a combination therapy for at least 3 days.

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.
- Saudi Arabia is **considered as a chloroquine-resistant** area as the first case of resistance was reported in the late 1980s, therefore, Artemisinin Combination Therapy (ACT) is recommended (MOH 2019).
- Treatment of malaria in pregnancy must be discussed with an infectious diseases specialist.

★ **Primaquine is contraindicated in:**

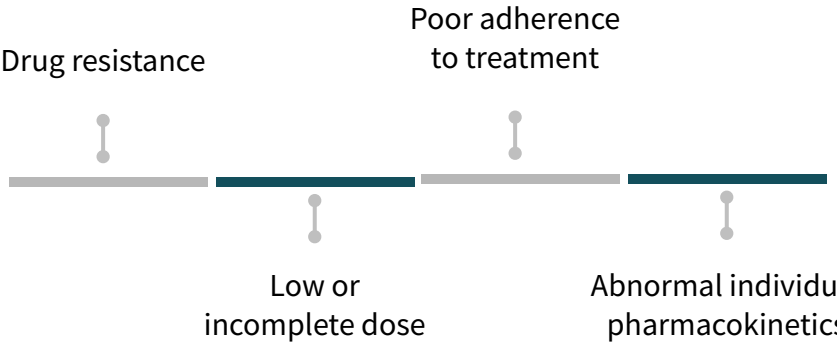
G6PG deficiency[1] ↕ Infants <6m ↕ Pregnancy ↕ Hypersensitivity ↕ lactating mothers for babies <6m

1- The evidence is still uncertain if patients with P. Falciparum infection and glucose-6-phosphate dehydrogenase deficiency (G6PD) should not be given primaquine (BMJ 2020).

Management

Treatment failure :

- Failure to resolve or recurrence of fever or parasitemia:
  - Early (1-3 days of treatment)
  - Late: (4 days – 6 weeks after treatment)
- Causes:



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 "GTS" (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

Malaria Control

WHO efforts in malaria control cont.

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

1.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.

2. 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.

3. Environmental control

- **Source reduction :** Environmental sanitation, water management, drainage
- **Social participation :** Health education , community participation

4. Destruction of larvae

- Larviciding of water surfaces, intermittent irrigation, biological control

5. Chemoprophylaxis

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

6. Vaccination

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

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 healthcare facilities.

Summary

	Malaria	Dengue
Causative Agent	Plasmodium parasite	Dengue virus
Vector	Female Anopheles	Female Aedes aegypti & Ae.albopictus to a lesser extent.
Time of transmission	Night time	Day time
Fever	Paroxysmal fever	Biphasic fever
Treatment	Combination of Antimalarial drugs for at least 3 days	No specific treatment (Supportive care)

Quiz

MCQ

1- Sporozoites when injected into the human skin it migrates to?

A- Hepatocytes. B- Intestinal wall. C- Macrophages. D- Lymphocytes.

2- What is the main organ affected in malaria infection?

A- Liver. B- kidney. C- RBCs. D- intestine.

3- which one of the following has immunity against malaria:

A- sickle cell trait B- microcytic anemia C- G6PG deficiency D- children less than 6

4- the main way to reduce malaria transmission at a community is

A- human control B- vector control C- environmental control

5- You work in prevention of malaria in west Africa, what is the best prevention?

A- Mass vaccination B- Use insecticides in beds and crops C- use spray nets D- Drinking a lot of orange juice

6- What is the main mode of transmission in malaria?

A- Blood Transfusion B- Animal bite C- TransPlacental D- Vector borne

Answers

Q1	Q2	Q3	Q4	Q5	Q6
A	C	A	B	C	D

Thank You and Good Luck

Community Medicine
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Wish you all the best!