Malaria

(COMM 311)

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Learning objectives

- Understand the epidemiology and global burden of malaria
- Understand the epidemiology and risk factors related to Malaria in KSA
- Understand the cycle of infection of malaria
- Define modes of transmission, clinical features, risk factors, community diagnosis and treatment for malaria
- Enlist the factors responsible for antimalarial drug resistance
- Understand the role and measures taken by WHO to combat the burden of Malaria globally
- Enlist the global measures of prevention and elimination for Malaria

What is malaria?

- “Malaria is a life threatening febrile illness caused by infection with the protozoan parasite, Plasmodium. It is transmitted to humans by the bite of the female **Anopheles mosquito**” (Public Health England 2013).

- There are five protozoan parasites that are known to affect humans:

I. **Plasmodium falciparum**

II. Plasmodium vivax

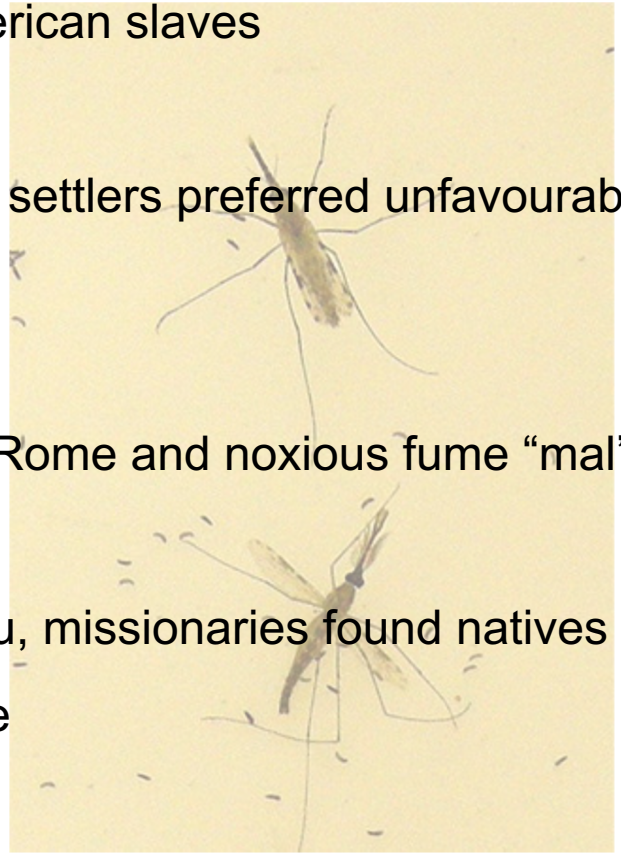
III. Plasmodium ovale

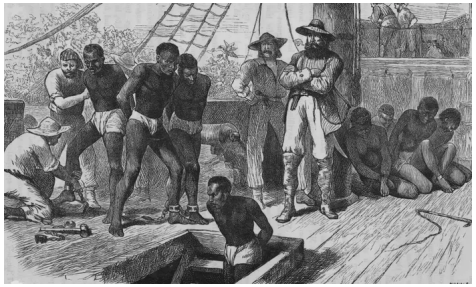
IV. Plasmodium malariae

V. *Plasmodium knowlesi*

How malaria shaped history? (The Economist 2020)

- African v Native American slaves
- In Africa, Europeans settlers preferred unfavourable environment to Anopheles
- The unconquerable Rome and noxious fume “mal’aria”
- Around 1630, in Peru, missionaries found natives ingesting powdered bark of cinchona tree
- Europeans learnt how to extract quinine, grow the cinchona and produce drugs





Epidemiology

- Malaria is globally one of the most important public health issues, predominantly affecting **young children** and **pregnant women**

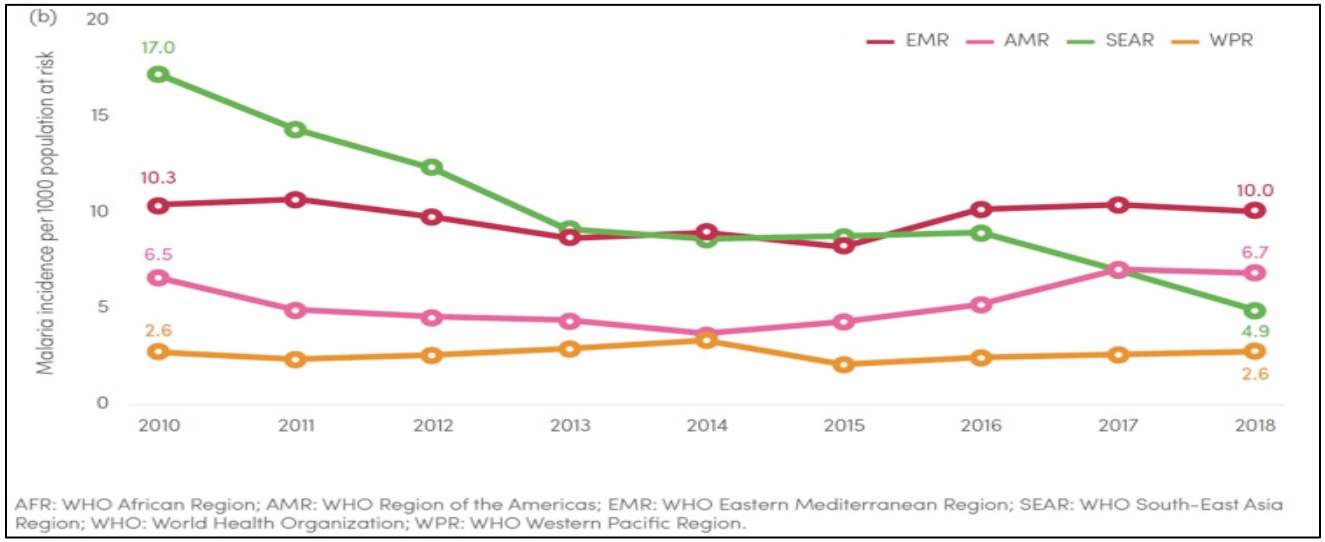
- In 2019, there were 229 million cases and, 409,000 deaths caused by malaria worldwide (WHO 2020)

- 67% of deaths were in children aged less than five years

- 94% of cases and deaths occurred in Africa

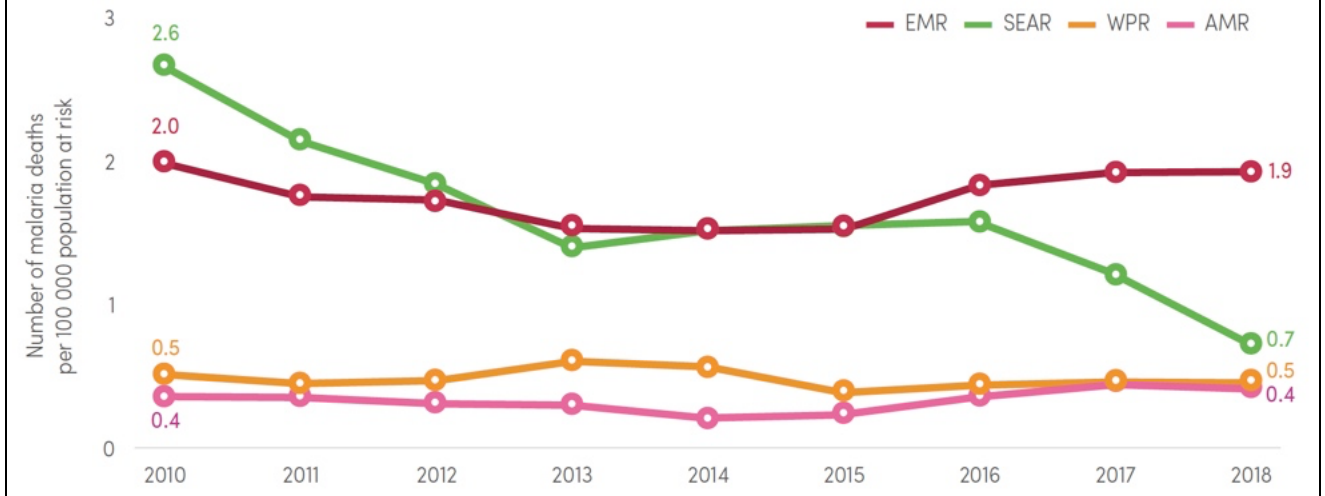
- Multidrug resistance is prevalent in many areas around the world, particularly in South East Asia (Kirwan 2006)

Regional trends and comparisons



AFR: WHO African Region; AMR: WHO Region of the Americas; EMR: WHO Eastern Mediterranean Region; SEAR: WHO South-East Asia Region; WHO: World Health Organization; WPR: WHO Western Pacific Region.

Source: WHO estimates.



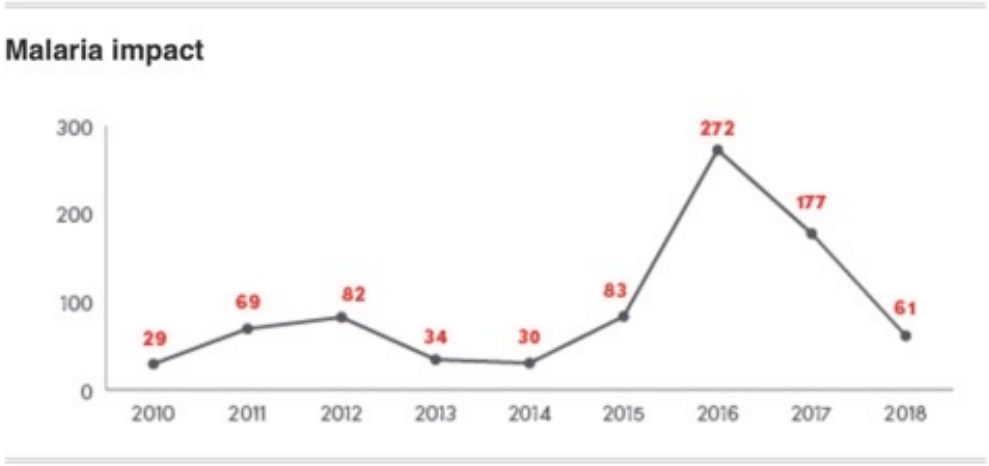
AMR: WHO Region of the Americas; EMR: WHO Eastern Mediterranean Region; SEAR: WHO South-East Asia Region; WHO: World Health Organization; WPR: WHO Western Pacific Region.

Epidemiology in Saudi Arabia

- Dominant species in indigenous cases: **P. Falciparum** (93%) — mainly transmitted by Anopheles Arabiensis (MOH 2019; WHO 2019)

- In 2018, number of confirmed cases was 2711, of which, 2650 (97.7%) were either **imported** or *introduced* and, only 61 cases were indigenous

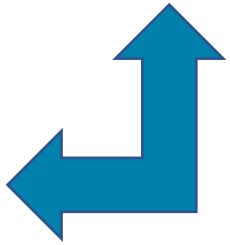
- Zero indigenous deaths from 2010 to 2018



Source: *World malaria report 2019*

High-risk populations in KSA (MOH 2019)

- Migrants (e.g., undocumented workers from Yemen and its neighbouring countries)



Imported cases which represent (97%) of all cases (WHO 2019)

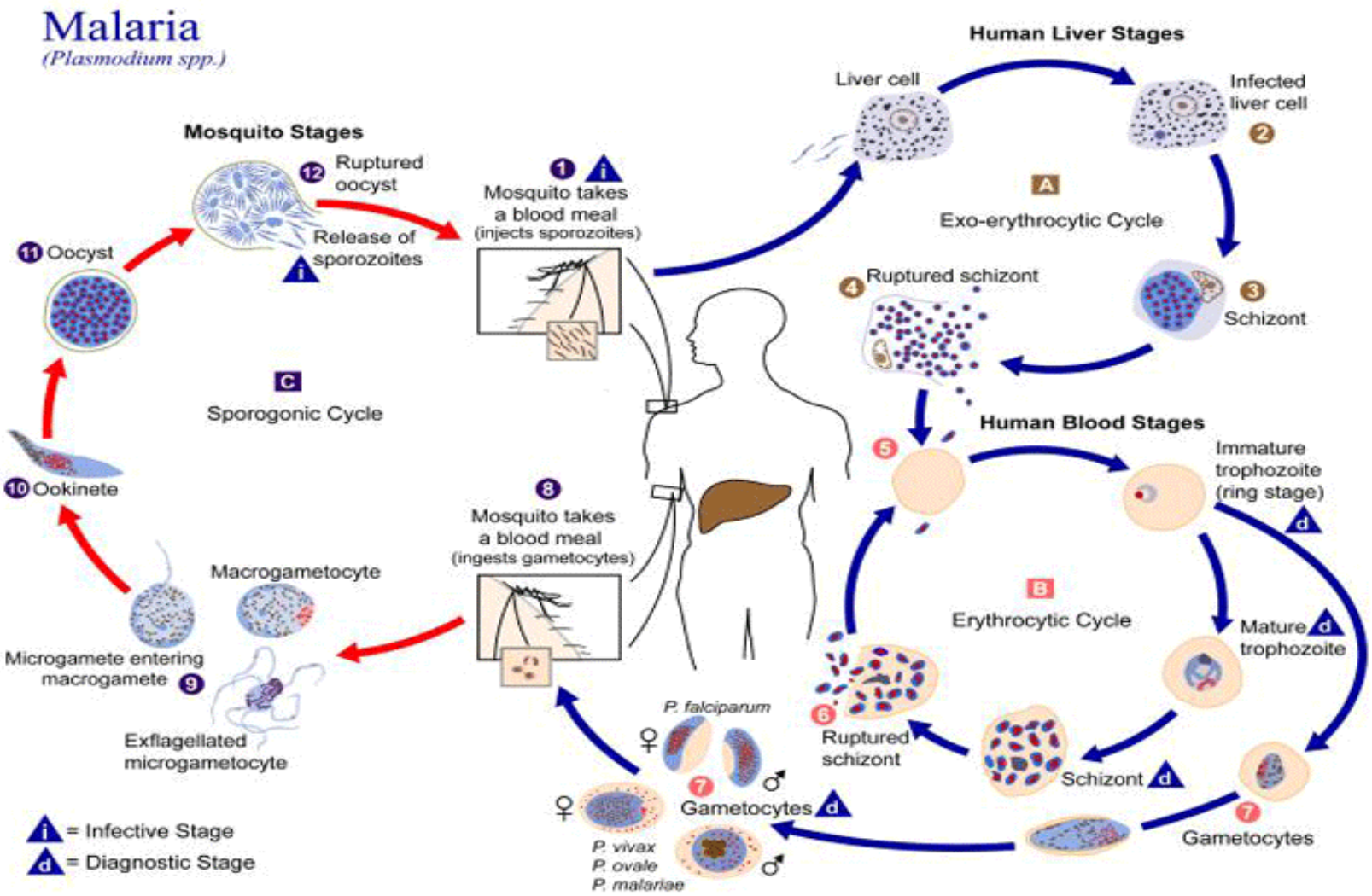
- Pilgrims from endemic countries

- Southern and South-Western populations (Jazan and Aseer) in coastal areas, low lands and mountains due to seasonal anomalies (i.e., unusual high annual rainfall)

Mode of transmission

- Vector (female Anopheles mosquitoes)
- Blood (injection/transfusion of contaminated blood)
- Congenital (rare)

Life-cycle of a Plasmodium (BMJ 2020)



Incubation period (Kirwan 2006)

Incubation period

	Prepatent period (Time between infective bite and detection of the parasites in a blood smear)	Incubation period (Time between infective bite and the onset of clinical symptoms)
P. falciparum	6-12 days	9-14 days
P. vivax	8-12 days	12-18 days
P. ovlale	8-12 days	12-18 days
P. malariae	12-16 days	18-40 days

Some strains of *P. vivax*, may have an incubation period of 8-10 months or longer[1].

Transfusion associated malaria (rare) has a shorter incubation period[2].

Period of Communicability

Humans may infect mosquitoes as long as infective gametocytes are present in the blood.

Anopheles mosquitoes remain infective for life.

History and clinical features (BMJ 2020)

- ↑ suspicion index (e.g., **travel history**); the presentation within 3 months of exposure (P. falciparum) or up to 1 year (P. vivax & ovale).

Symptoms are non-specific:

- Common→ paroxysms of chills/rigors followed by fever and sweats. A pattern *might* develop (i.e., fever occur every 2-3 days). Also, headache, weakness, muscle and joint pain.
- Less common→ anorexia, nausea, vomiting, diarrhoea and abdominal pain.
- In children→ influenza-like respiratory symptoms.

History and risk factors (BMJ 2020)

- **Travel history** is key in patients presenting in non-endemic countries. If positive, history of prophylaxis must be obtained.
- Settled migrants
- Low host immunity
- Pregnancy
- Children aged less than five years
- Elderly

Case history (BMJ 2020)

Exercise: identify key risk factors and common clinical features

A 42-year-old Nigerian woman presents to her primary care physician with a 2-day history of fever, chills, and sweats with associated headache and myalgia. She is febrile (38.6°C [101.4°F]) and tachycardic, but examination is otherwise unremarkable. A presumptive diagnosis of influenza is made, and she is advised to return if she does not improve. Two days later she presents to the emergency department with similar symptoms and frequent vomiting. On examination she appears ill, with a temperature of 38.8°C (101.8°F), pulse rate 120 beats per minute, blood pressure 105/60 mmHg, and mild jaundice. Further history reveals that she recently visited family in Nigeria for 2 months, returning 1 week before presentation. She did not take malaria prophylaxis.

Physical examination (BMJ 2020)

Bedside examination *might* reveal the following signs:

- *Hepato-splenomegaly*
- *Anaemia signs (e.g., pallor)*

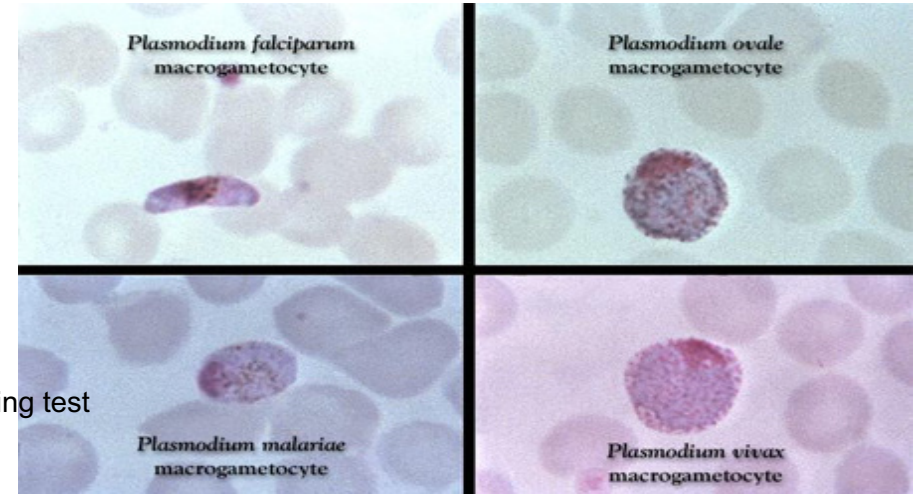
It is important to pick up the complications of severe malaria such as:

- *Confusion/altered level of consciousness*
- *Seizures*
- *Hypotension*
- *Oliguria/anuria*
- *Jaundice*
- *Respiratory distress*

Investigations (BMJ 2020)

Laboratory

- Light microscopy (Giemsa-stained blood smear; thin v thick film)
- Rapid diagnostic test (RDT)
- Polymerase Chain Reaction (PCR)
- Loop-mediated Isothermal Amplification (LAMP) – an emerging test



Other baseline tests

- Full blood count (FBC)/clotting profile and, serum electrolytes, urea and creatinine (U&E), liver function tests (LFTs) and blood glucose. Urinalysis and arterial blood gas (ABG).

Community diagnosis (WHO 2013)

Areas with advanced malaria control (pre-elimination)

- 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)

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

Epidemic-prone areas

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

Community diagnosis: case study

(WHO 2013)

Case study 1:

A child aged 3 years is brought in for fever over the past 24 h. The father reports no cough or diarrhoea.

Physical examination shows a temperature of 38.6 °C but no other major sign.

RDT is negative.

(1) What is your diagnosis?

(2) What advice do you give to the father, and what treatment do you prescribe?

Case study 1: non-specific fever (without danger signs)

1) Diagnosis: non-specific fever or non-malaria fever or flu-like syndrome

2) Reassure the father that his child does not have malaria. Tell him to bring the child again if the fever persists or if a new problem appears. Treat the child with an antipyretic only.

Take home message: RDT is negative → no malaria → no antimalarial treatment

Community diagnosis: case study

(WHO 2013)

Case study 2:

An infant aged 11 months is brought to a dispensary for fever over the past 48 h. The mother reports difficulty in breastfeeding since the previous day and one episode of convulsion.

Physical examination shows a temperature of 38.6 °C and slight drowsiness but no other major sign.

Explain the actions you would take, one by one.

Case study 2: severe febrile illness at dispensary level

- Difficulty to suck, convulsion, drowsiness = Danger signs
- Do not lose time by asking for malaria tests; they will be done at the hospital.
- Immediately prescribe an antimalarial and an antibiotic treatment (and antipyretic)
- Refer the infant urgently to hospital

Take home message: Danger signs antimalarial + antibiotic + immediate referral

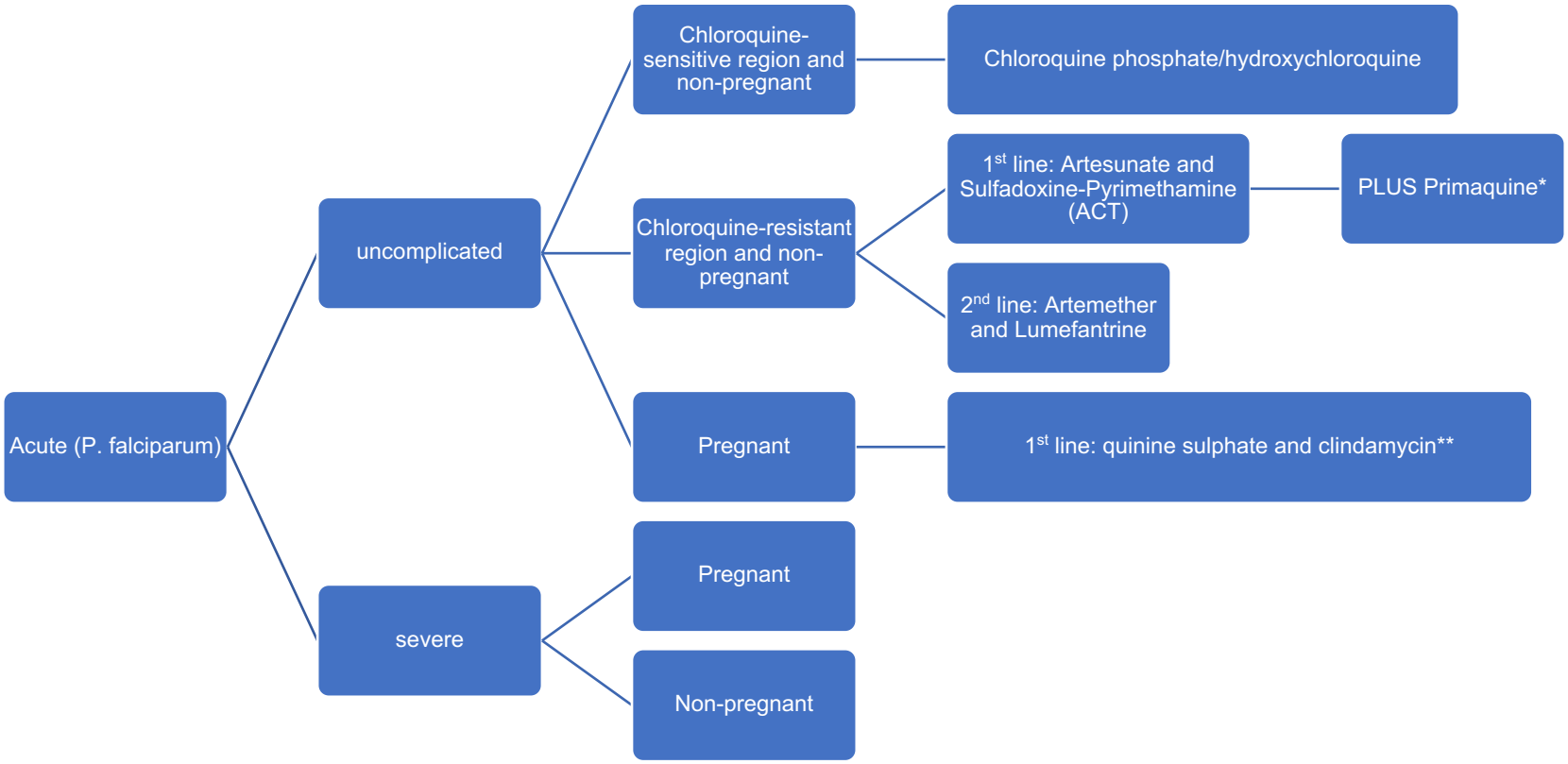
Management (BMJ 2020)

Treatment will depend on:

- Geographical area (sensitivity v resistance)
- The infecting species (falciparum v the rest)
- Blood smear appearance (parasite load; stage)
- Clinical status (acute v ongoing; uncomplicated v severe; pregnancy)

Treatment algorithm: an example

(BMJ 2020; MOH 2019)



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).

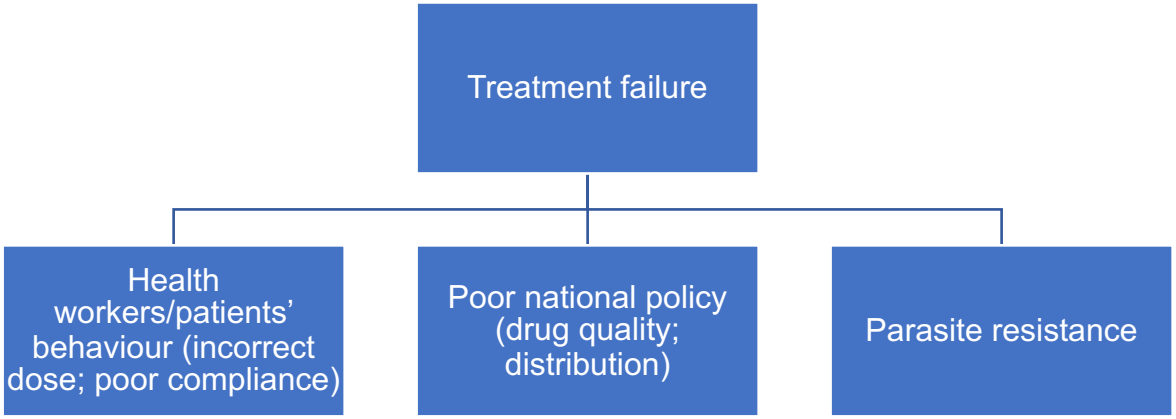
*Primaquine is contraindicated in: pregnant women, infants aged <6 months, and women breastfeeding infants aged <6 months. The evidence is still uncertain if patients with P. Falciparum infection and glucose-6-phosphate dehydrogenase deficiency (G6PD) should not be given primaquine (BMJ 2020).

**Treatment of malaria in pregnancy must be discussed with an infectious diseases specialist.

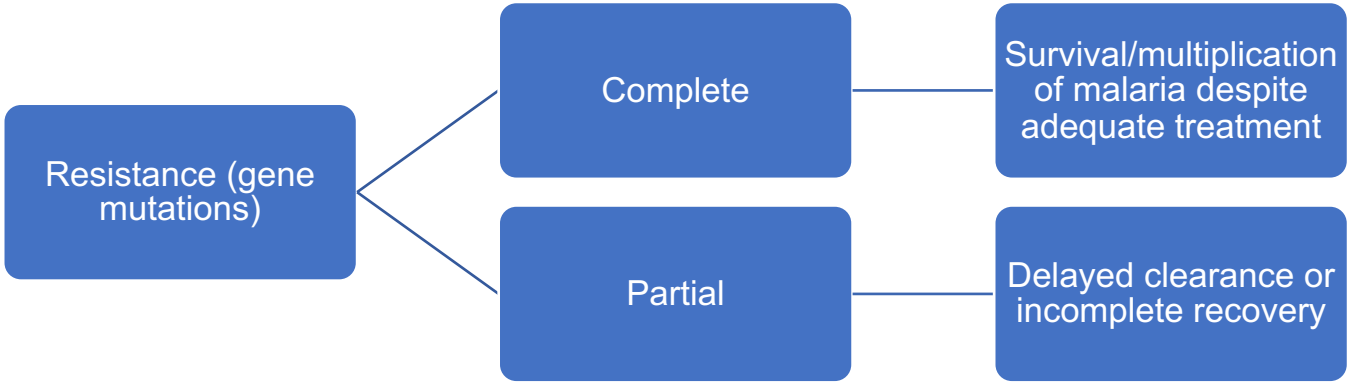
Treatment failure and resistance

(WHO 2018; WHO 2019)

- Treatment Failure ⊃ Antimalarial Drug Resistance



- There are three species known for resistance: P. falciparum, vivax and malariae.
- Resistance to one drug confers resistance to others (cross-resistance) which leads to multidrug resistance



WHO vision 2030 (WHO 2016)

VISION – A WORLD FREE OF MALARIA

GOALS	MILESTONES		TARGETS
	2020	2025	2030
1. Reduce malaria mortality rates globally compared with 2015	At least 40%	At least 75%	At least 90%
2. Reduce malaria case incidence globally compared with 2015	At least 40%	At least 75%	At least 90%
3. Eliminate malaria from countries in which malaria was transmitted in 2015	At least 10 countries	At least 20 countries	At least 35 countries
4. Prevent re-establishment of malaria in all countries that are malaria-free	Re-establishment prevented	Re-establishment prevented	Re-establishment prevented

World Health Organisation role

(WHO 2016)

- Global technical strategy “GTS” (2016-2030)

STRATEGIC FRAMEWORK

– comprising three major pillars, with two supporting elements: (1) innovation and research and (2) a strong enabling environment

Maximize impact of today’s life-saving tools

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

Supporting element 1. Harnessing innovation and expanding research

- Basic research to foster innovation and the development of new and improved tools
- Implementation research to optimize impact and cost–effectiveness of existing tools and strategies
- Action to facilitate rapid uptake of new tools, interventions and strategies

Supporting element 2. Strengthening the enabling environment

- Strong political and financial commitments
- Multisectoral approaches, and cross-border and regional collaborations
- Stewardship of entire heath system including the private sector, with strong regulatory support
- Capacity development for both effective programme management and research

Global measures to combat malaria (WHO 2016)

- Pillar 1: ensure universal access to malaria prevention, diagnosis and treatment

Vector control

- Maximise the impact of vector control
- Maintain adequate entomological surveillance and monitoring
- Manage insecticide resistance and residual transmission
- Strengthen capacity for evidence-driven vector control
- Implement malaria vector control in the context of integrated vector management

Global measures to combat malaria (WHO 2016)

- Pillar 1: ensure universal access to malaria prevention, diagnosis and treatment

Chemo-prevention

Expand preventive treatment to prevent disease in the most vulnerable groups

Protect all non-immune travellers and migrants

An example:
Someone plans travelling to an endemic chloroquine-resistant country? → doxycycline (before/during/after travel)

Global measures to combat malaria (WHO 2016)

- Pillar 1: ensure universal access to malaria prevention, diagnosis and treatment

Diagnostic testing and treatment

- Ensure universal diagnostic testing of all suspected malaria cases
- Provide quality assured treatment to all patients
- Monitor safety and efficacy of antimalarial medicines and manage antimalarial drug resistance
- Contain antimalarial drug resistance
- Eliminate falciparum malaria from the Greater Mekong subregion
- Remove all inappropriate antimalarial medicines from markets
- All countries should aim to eliminate malaria
- Scale up community - based diagnostic testing and treatment

Global measures to combat malaria (WHO 2016)

- Pillar 2: accelerate efforts towards elimination and attainment of malaria-free status

- Refocus programmes
- Enact legislation
- Renew political commitment and deepen regional collaboration
- Reduce the number of undetected infections
- Implement targeted malaria vector control
- Prevent re-establishment of local malaria transmission

Global measures to combat malaria (WHO 2016)

- Pillar 2: accelerate efforts towards elimination and attainment of malaria-free status

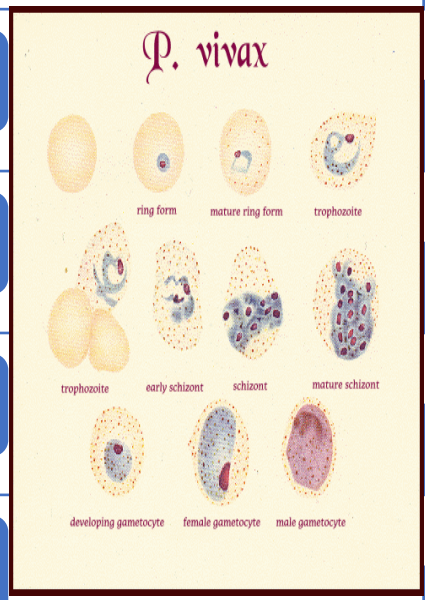
Implement transmission-blocking chemotherapy

Detect all infections to attain elimination and prevent reestablishment

Use of medicines to reduce the parasite pool

Devise P. vivax-specific strategies

Use surveillance as an intervention in elimination programmes



Global measures to combat malaria (WHO 2016)

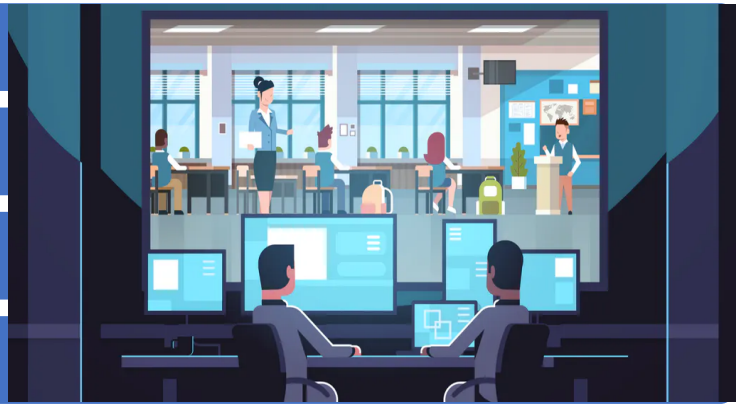
- Pillar 3: transform malaria surveillance into a core intervention

Surveillance in areas of high transmission

Surveillance in areas of low transmission

Surveillance in areas targeted for elimination of malaria

Invest in routine information systems



Collect necessary data for understanding disease trends and overall programme performance

Develop national strategic plans that take into account the epidemiology and heterogeneity of malaria in a country

Monitor the implementation of national malaria strategic plans at regular intervals

Ensure the surveillance system is monitored

Global measures to combat malaria (WHO 2016)

- Supporting element 1: harnessing innovation and expanding research

Vector control

Diagnostic testing and treatment

Malaria vaccines

Surveillance

Elimination

Global measures to combat malaria (WHO 2016)

- Supporting element 2: strengthening the enabling environment

Increase international and domestic financing

Ensure robust health sector response

Strengthen health workforce and malaria expert base

Ensure the sustainability of malaria responses

Improve government stewardship

Strengthen multisectoral collaboration

Encourage private sector participation

Empower communities and engage with non-governmental organisation

References

- British Medical Journal 2020, *Malaria Infection*, British Medical Journal, viewed 30 December 2020, <https://bestpractice.bmj.com/topics/en-gb/161/aetiology>.
- The Economist 2020, *Bloodsuckers – how malaria has shaped humanity?*, The Economist, viewed 5 January 2021, <https://www.economist.com/christmas-specials/2020/12/19/how-malaria-has-shaped-humanity>.
- Maria Kirwan 2006, *Malaria*, Health Knowledge, viewed 28 December 2020, <https://www.healthknowledge.org.uk/public-health-textbook/disease-causation-diagnostic/2b-epidemiology-diseases-phs/infectious-diseases/malaria#ref%205>.
- Ministry of Health 2019, *Progress towards Malaria Elimination in the Kingdom of Saudi Arabia: A Success Story*, Ministry of Health, viewed 29 December 2020, <https://www.moh.gov.sa/Ministry/MediaCenter/Publications/Documents/Malaria.pdf>.
- Public Health England 2013, *Malaria factsheet*, Public Health England, viewed 28 December 2020, <https://www.gov.uk/government/publications/malaria-prevention-transmission-symptoms/malaria-transmission-incubation-period-symptoms >.
- World Health Organisation 2013, *Universal access to malaria diagnostic testing: an operational manual*, World Health Organisation, viewed 3 January 2021, <https://apps.who.int/iris/bitstream/handle/10665/44657/9789241502092_eng.pdf;jsessionid=D894F7F40DE110523967FFC5A0E56534?sequence=1>.
- World Health Organisation 2016, *Global technical strategy for Malaria 2016-2030*, ISBN: 978-92-4-156499-1, World Health Organisation, viewed 5 January 2021, <https://www.who.int/malaria/areas/global_technical_strategy/en/>.
- World Health Organisation 2018, *Antimalarial drug efficacy and drug resistance*, World Health Organisation, viewed on 14 January 2021, <https://www.who.int/malaria/areas/treatment/drug_efficacy/en/>.
- World Health Organisation 2019, *World Malaria Report 2019*, ISBN: 978-92-4-156572-1, World Health Organisation, viewed 29 December 2020, <https://apps.who.int/iris/rest/bitstreams/1262394/retrieve>.
- World Health Organisation 2020, *Malaria*, World Health Organisation, viewed 28 December 2020, <https://www.who.int/news-room/fact-sheets/detail/malaria>.