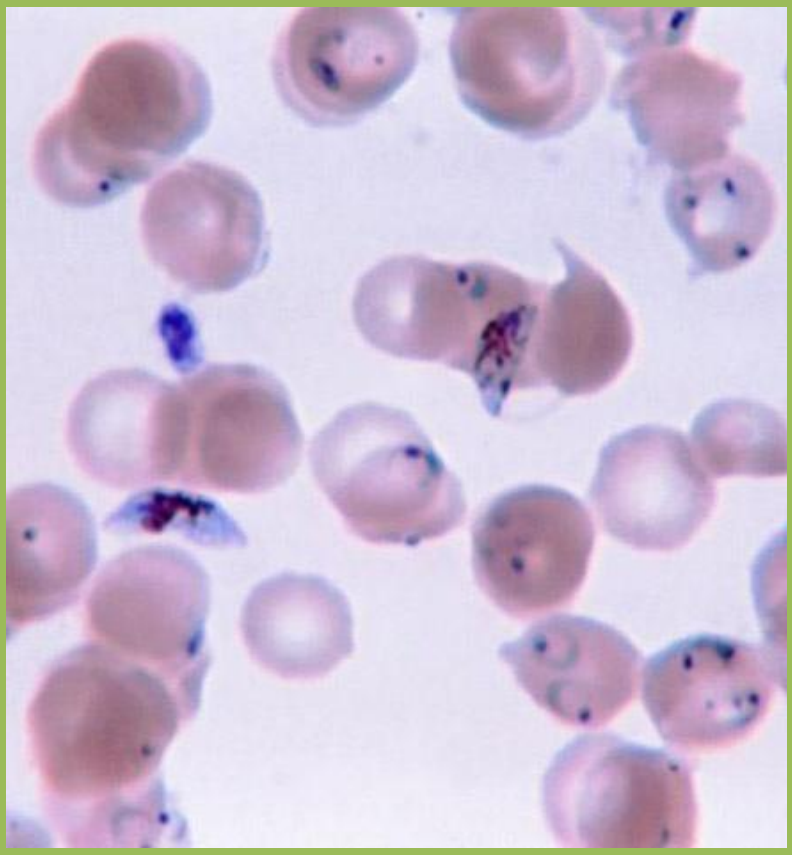
National Malaria Management Guidelines

2nd edition



2013

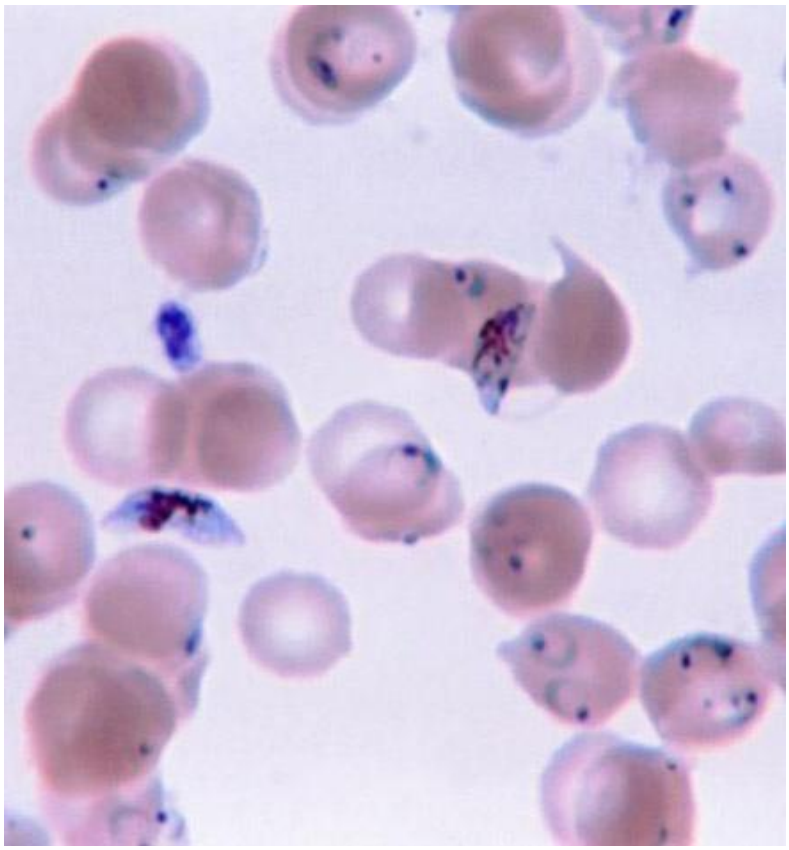
Ministry of Health

National

Malaria Management Guidelines

2nd edition

2013



Ministry of Health

Directorate of Communicable Disease

Malaria Control Program

Telefax: 06/5694080, Amman, Jordan

بسم الله الرحمن الرحيم

يعتبر مرض الملاريا من أهم المشاكل الصحية على مستوى العالم. وهو من الامراض المعدية التي تنتقل بواسطة البعوض ويتوطن في أكثر من ١٠٦ دول حول العالم تقع في افريقيا جنوب الصحراء الكبرى وجنوب شرق اسيا وأمريكا اللاتينية وبعض دول منطقة الشرق الاوسط. وتُقدر منظمة الصحة العالمية عدد السكان المعرضين لخطر الاصابة بالملا ريا بحوالي ٣,٣ مليار نسمة حول العالم, وعدد اصابات الملاريا ب ٢١٦ مليون اصابة سنويا وعدد الوفيات بسبب الملاريا ب ٦٥٥ ألف وفاة سنويا (حسب التقرير السنوي لمنظمة الصحة العالمية للعام ٢٠١١), مما يشكل عبئا صحيا واقتصاديا واجتماعيا كبيرا لكثير من الدول النامية.

كما يعتبر مرض الملاريا من أخطر وأهم الامراض التي كانت مستوطنة في الاردن خلال القرون الماضية, حيث استطاع الاردن بحمد الله من ايقاف نقل العدوى بمرض الملاريا محليا في عام ١٩٧٠ بفضل جهود المكافحة التي قامت بها وزارة الصحة من خلال برنامج مكافحة الملاريا. ولكن بسبب استمرار قدوم حالات ملاريا وافدة من دول أخرى وبسبب تواجد بعوض الانوفليس الناقل وتوفر الظروف البيئية المناسبة لانتقاله محليا ما زال من المهم بذل الجهود اللازمة لمنع عودة انتقال مرض الملاريا محليا.

تقوم وزارة الصحة وبالتعاون مع القطاعات الصحية الاخرى بمكافحة مرض الملاريا من خلال مكافحة البعوض الناقل واكتشاف إصابات الملاريا الوافدة وتقديم العلاج اللازم ومتابعة تلك الحالات حتى الشفاء التام, وذلك بهدف المحافظة على بقاء الاردن خاليا من مرض الملاريا.

لقد تم انجاز هذا الدليل لعلاج حالات الملاريا بالتعاون بين مختلف القطاعات الصحية في المملكة وبعد الرجوع الى المصادر العلمية الحديثة والمعتمدة عالميا وذلك لتسهيل عملية الحصول على المعلومات الضرورية و الحديثة للتعامل مع حالات الملاريا ومعالجتها حسب سياسة علاجية موحدة ومعتمدة وطنيا.

وفي الختام اود أن اتقدم بالشكر الى منظمة الصحة العالمية لتقديمها الدعم اللازم لأعداد هذا الدليل والى جميع الاطباء الذين ساهموا في اعداد هذا الدليل ليكون مرجعا للأطباء والكوادر الصحية في مختلف القطاعات الصحية داخل المملكة.

وزير الصحة

الدكتور علي حياصات

Table of contents

Committee Members of
National Malaria Management Guidelines
2nd edition - 2013

Khalil A. Kanani[1], Mansour F. Karadsheh[2], Mohammad A. Alzubi[3], Waseem T. Hamoudi[4], Faris G. Bakri[5].

1. MD, Department of Parasitic and Zoonotic Diseases, Malaria Control Program, Ministry of Health, Amman, Jordan.
2. MD, Department of Internal Medicine, King Hussein Hospital, the Royal Medical Services, Amman, Jordan.
3. MD, Preventive Medicine Department, The Royal Medical Services, Amman, Jordan
4. MD, Department of Internal Medicine, Al-Bashir Hospital, Amman, Jordan.
5. MD, Division of Infectious Diseases, Jordan University Hospital. Amman, Jordan

Supervised by:

Mohammed M. Al Abdallat: MD, Directorate of Communicable Diseases, Ministry of Health, Amman, Jordan.

List of figures and tables

Abbreviations

ACTs	Artemsinin-based Combination Therapy
Art-Lump	Artemether-Lumefantrine
AS	Artesunate
B. Wt.	Body Weight
CQ	Chloroquine
Clin	Clindamycin
DIC	Disseminated Intravascular Coagulation
DOTs	Direct Observation Treatment Strategy
Dox	Doxycycline
G6PD	Glucose-6- Phosphate Dehydrogenase
IM	Intramuscular
ITNs	Insecticide Treatment Nets
IV	Intravenous
MOH	Ministry of Health
P	Plasmodium
PQ	Primaquine
QN	Quinine
RDT	Rapid Diagnostic Test
SBET	StandBy Emergency Treatment
SFM	Severe Falciparum Malaria
UCFM	Uncomplicated Falciparum Malaria
WHO	World Health Organization

National Malaria Treatment Policy
Jordan-2013

No.	Type and Species of Malaria	First line treatment	Second line Treatment	Pregnancy
1	Uncomplicated *P. falciparum* malaria **(UCFM)**	**Art-Lum** (3 days) followed by: **PQ** (single dose in receptive areas)	**QN** plus **Dox** or **Clin** (7 days)	First trimester **Q**N plus **Clin** (7 days) second and third trimesters **Art-Lum** (3 days)
2	Severe *P. falciparum* malaria **(SFM)** / Severe forms of other species	**QN**. IV infusion followed by: **Art-Lum** (3 days)	**AS.** IV or IM followed by: **Art-Lum** (3 days)	**QN. IV** infusion/ or **AS.** IV or IM followed by: First line oral treatment of **UCFM** according gestational age
3	P. vivax and *P. ovale* malaria	**CQ** (3 days) followed by: **PQ** (14days)	**Art-Lum** (3 days) followed by: **PQ** (14 days)	**CQ** (3 days)
4	*P. malariae* malaria	**CQ** (3 days) followed by: **PQ** (single dose in receptive areas)		**CQ** (3 days)
5	Mixed infection of *P. falciparum* with *P. vivax* or *P. ovale*	**Art-Lum** (3 days) followed by: **PQ** (14 days)	**QN** plus **Dox** or **Clin** (7 days)	First trimester **Q**N plus **Clin** (7 days) Second and third trimester **Art-Lum** (3 days)
6	Mixed infection of *P. falciparum* with *P. malariae*	**Art-Lum** (3 days) **PQ** (one single dose)	**QN** plus **Dox** or **Clin** (7 days)	First trimester **Q**N plus **Clin** (7 days) Second and third trimester **Art-Lum** (3 days)

***** Artesunate injectable is not yet available in Jordan.

Abbreviations:-

- **Art-Lum:** Artemether-Lumefantrine (Coartem).
- **PQ:** Primaquine
- **QN:** Quinine
- **AS:** Artesunate
- **Dox:** Doxycycline
- **Clin:** Clindamycin
- **CQ:** Chloroquine

Unit 1
Introduction

Up to the 1950s, Malaria was endemic throughout the country, except desert. Both *P. vivax* and *P. falciparum* were present, with predominance of the former. Malaria was hyperendemic in the lowlands below the sea level. In other areas it was hypo- to mesoendemic and epidemic-prone, with hyper-endemic pockets.

Malaria eradication program started in 1959. In the course of its implementation, transmission of malaria was interrupted in 1970[1]. Between 1970 and 2012, 9 small isolated local outbreaks took place in different vulnerable sites mainly in the lowlands resulting in 53 introduced cases (figure 1). The major episode of introduced outbreak occurred in 1990 in Al Karak lowlands with 33 introduced vivax malaria cases originating from India, and the last episode of local transmission occurred in 2010 with 2 introduced vivax malaria cases (strain M54 originating from China), which took place in Al-Zarah near the Eastern Dead Sea Coast.

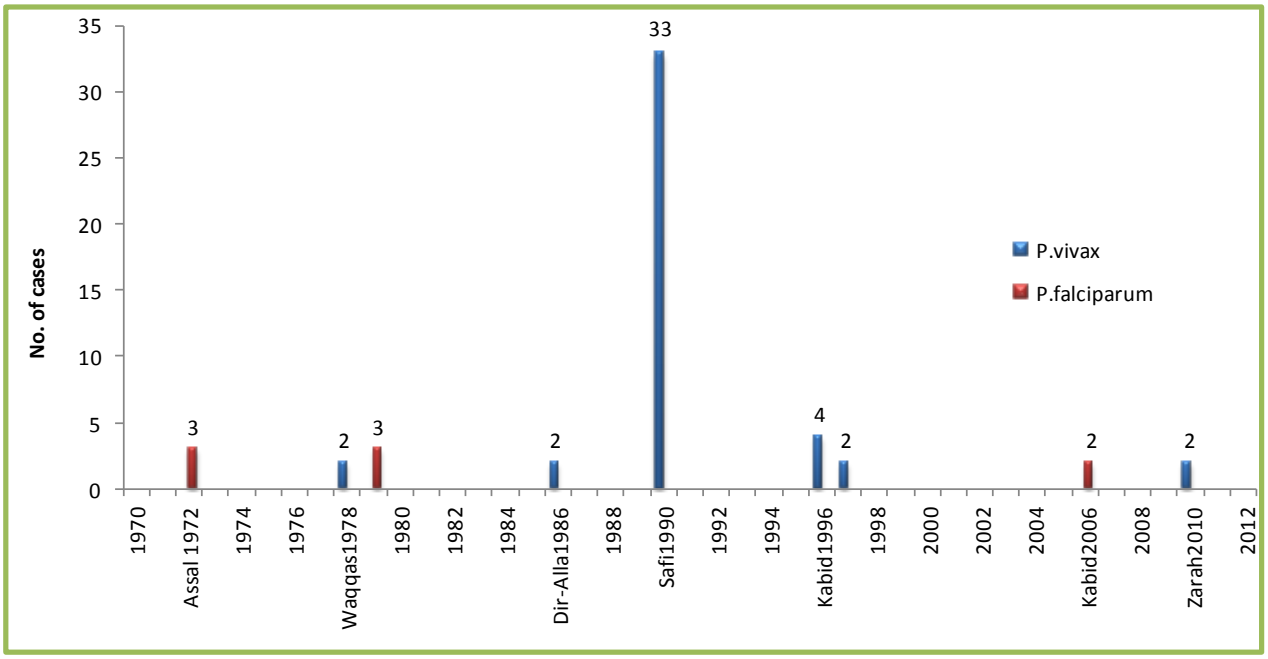


Fig. 1: Local outbreaks of malaria occurred after interruption of malaria transmission in Jordan

The reported number of malaria cases from 2003 to 2012 in Jordan was 903, with an annual average of about 90 cases every year (figure 2). Most of malaria cases (99.5%) were imported; the source countries of malaria infection are mainly countries of sub-Saharan Africa, South-East Asia and some Middle Eastern countries. The majority of reported cases (68%) were Jordanians coming from abroad[2].

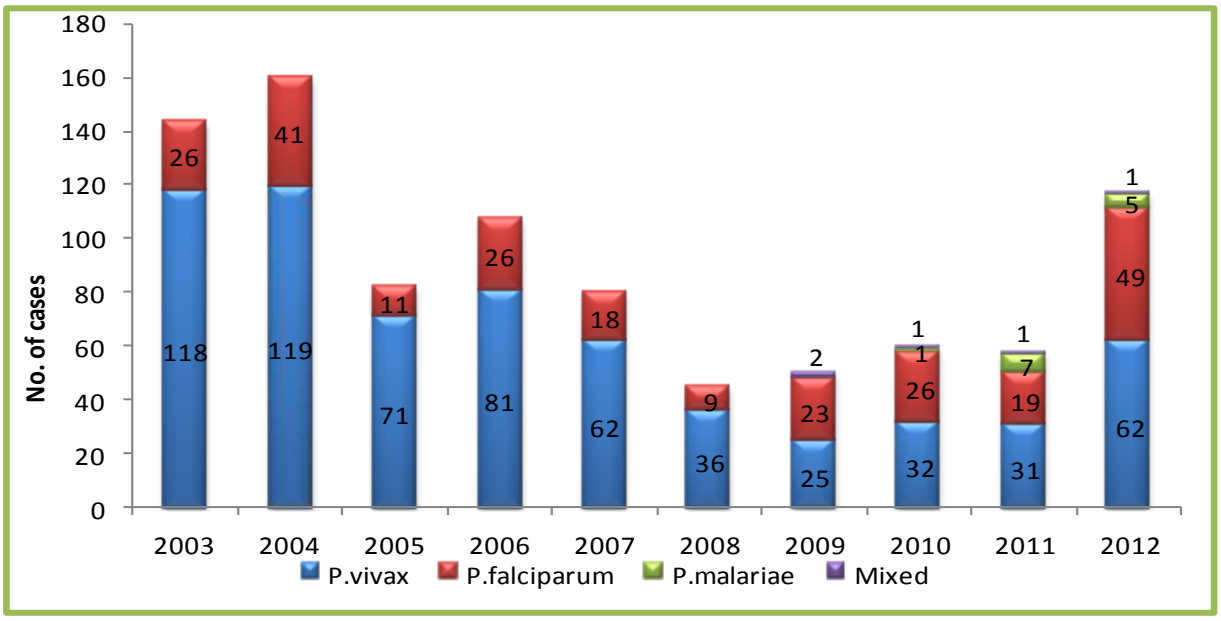


Fig. 2: Reported malaria cases by parasite species in Jordan (2003-2012)

The number and type of reported malaria cases in Jordan reflect the size of travel movements to and from endemic countries (Figure 3).

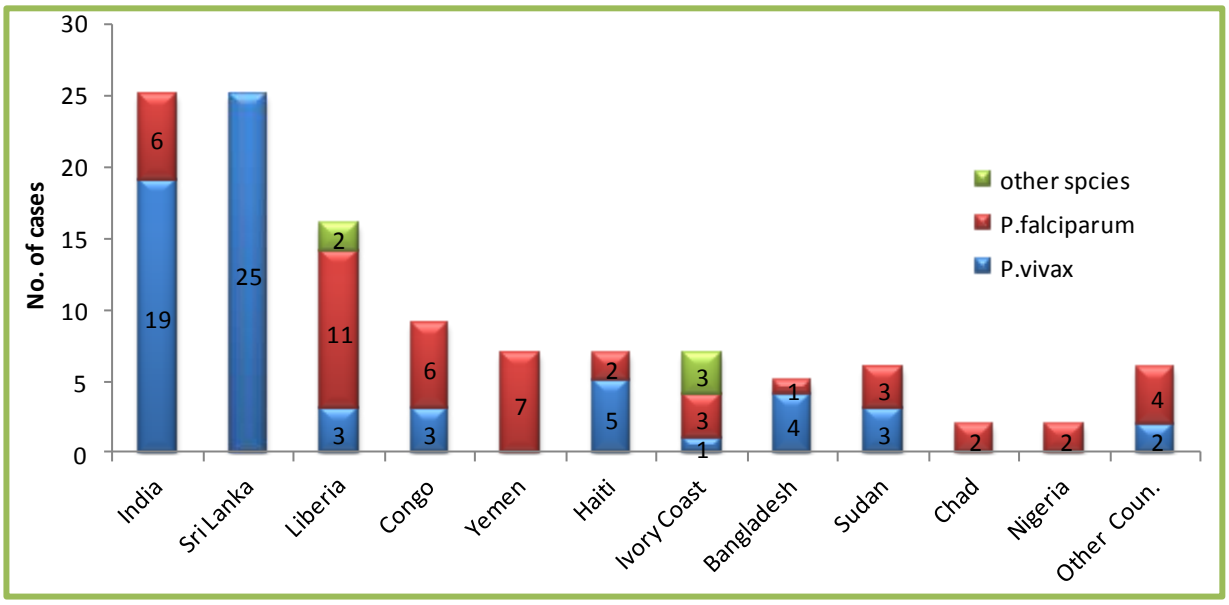


Fig 3: Reported malaria cases in Jordan during 2012 by source countries and parasite species

Malaria receptive areas Jordan are present in both the north-west and middle- west areas adjacent to the Jordan Valley and Dead Sea, where about 17% of the country's population lives. Well- developed surveillance system and anti-vector activities are the main components of malaria control program in the country.

Prevention, early diagnosis, and prompt treatment of malaria are mandatory to reduce morbidity and mortality and to prevent reintroduction of malaria.

These guidelines will be periodically updated according to newly added WHO qualified anti-malaria drugs.

Unit 2
Clinical and epidemiological aspects of malaria

2-1. Clinical presentation:

Typical manifestations of malaria include fever, chills, rigors, headaches and body pains. Others are malaise, nausea, vomiting and general weakness. Physical examination may reveal pallor and hepato-splenomegaly.

The typical presentation as mentioned above may not manifest. Hence, any patient with fever without obvious cause, especially in patients with a history of possible natural exposure to malaria infection by the bite of *Anopheles mosquito* or by other unnatural modes of transmission, should be suspected as a case of malaria until proven otherwise.

2-2. Case definition

- **Suspected malaria:** Malaria is suspected when a patient presents with fever (or history of fever) and other symptoms and signs suggestive of malaria[3,4]. History of possible exposure to infection by natural or unnatural modes of transmission and absence of obvious cause of fever, all strengthen malaria suspicion.

- **Confirmed malaria:** A malaria case is confirmed by demonstration of malaria parasites in thick or thin blood film or by rapid diagnostic tests (RDTs)[3,4].

2-3. General steps of malaria management

- Step 1: Clinical suspicion of malaria on the basis of signs and symptoms, and taking in consideration the following points:
  - History of travel to endemic areas.
  - Blood transfusion or organ-transplantation from infected donor.
  - History of malaria.
  - Possibility of introduced transmission by imported case.
- Step 2:Contact MOH (Malaria Control Program) for
  - Confirmation of malaria by laboratory diagnosis.
  - Dispensing the correct drugs (first dose given preferably by DOTs).
- Step 3: Referral to secondary/tertiary level care, if necessary.
- Step 4: Education of patient or family on:
  - Administration of drugs (adherence).
  - Danger symptoms of malaria.
  - Prevention of malaria transmission.

Unit 3
Laboratory diagnosis of malaria

Laboratory diagnosis and identification of malaria type (parasite species) by malaria microscopy or by rapid diagnostic tests (RDTs) is recommended in all suspected malaria cases before treatment is started.

Laboratory diagnosis of malaria can be made through microscopic examination of thick and thin blood smears. Thick blood smears are more sensitive in detecting malaria parasites because the blood is more concentrated allowing for a greater volume of blood to be examined; however, thick smears are more difficult to read. Thin smears aid in parasite species identification. Blood films need to be read immediately.

A negative blood smear makes the diagnosis of malaria unlikely. However, because non-immune individuals may be symptomatic at very low parasite densities that initially may be undetectable by blood smear, blood smears should be repeated every 12-24 hours for a total of 3 sets. If all 3 are negative, the diagnosis of malaria has been essentially ruled out.

In addition to microscopy, other laboratory diagnostic tests are available. Several antigen detection tests (RDTs) using a "dipstick" or cassette format exist. Laboratories that do not provide in-house on-the-spot microscopy services should maintain a stock of malaria RDTs so that they will be able to perform malaria diagnostic testing when urgently needed.

Parasite nucleic acid detection using polymerase chain reaction (PCR) is more sensitive and specific than microscopy but can be performed only in reference laboratories and should be reserved for specific instances (e.g., back-up or confirmation of microscopy). Serologic tests, also performed in reference laboratories, can be used to assess past malaria experience but not current infection by malaria parasites.

3-1. Microscopical diagnosis of malaria: - Malaria microscopy is the gold standard test for malaria diagnosis using both thick and thin blood films. Good laboratory setup is essential in addition to trained microscopist. A skilled microscopist is able to detect asexual parasites at densities of fewer than 10 per µl of blood, but under typical field conditions the limit of sensitivity is approximately 100 parasites per μl^3.

Giemsa stain is recommended by WHO to be used for malaria microscopy. The following information can be stated clearly by microscopical examination of a blood film:

- Presence or absence of infection (positive or negative result for malaria parasites)
- Type of malaria (species of malaria parasite).
- Stages of malaria parasite life cycle.
- Parasite count (density of infection means the number of parasites per µl of blood).

Methods of parasite count (infection density):

- Number of parasites per micro liter of blood; which reflects the number of malaria parasite corresponding to 8000 leucocytes in tested thick blood film.
- The "plus" system: It is a semi-quantitative method developed for epidemiological purposes rather than disease management. Table (1) below shows the correlation between the two systems.

Table 1: The Correlation between two systems used to determine infection density of malaria parasites

Plus system	No. Parasite per micro-liter of blood
+ 1-10 parasite per 100 field	4-40 parasites per µl
++ 11-100 parasites per 100 field	40-400 parasites per µl
+++ 1-10 parasites per one field	400-4000 parasites per µl
++++ 11>100 parasites per one field	4000>40000 parasites per µl

3-2. Rapid diagnostic tests (RDTs):

Rapid diagnostic tests are relatively simple to perform and to interpret, and they do not require electricity or special equipment. WHO recommends that such tests should have a sensitivity of > 95% in detecting plasmodia at densities of more than 100 parasites per µl of blood[3]. WHO evaluates performance of commercially available tests, and it maintains a list of RDT manufacturers with ISO 13485:2003 certification as evidence of quality of manufacture.

RDTs are very useful in some specific situations such as epidemics, remote areas and lack of skilled microscopist, to avoid unnecessary use of malaria drugs and when quality malaria microscopy for any reason is not available.

Unit 4
Treatment of uncomplicated falciparum malaria (UCFM)

UCFM is symptomatic *p. falciparum* infection with parasitemia but without evidence of vital organs dysfunction.

4-1- Treatment of UCFM

(*Artemether –lumefantrine*) is the first line treatment for UCFM. It is one of the Artemisnin-based combination therapy (ACTs). Each tablet contains a synthetic derivative of artemisinin (artemether, 20mg); and lumefantrine (120mg). It has a high clinical and parasitological cure rate and rapid gametocyte clearance. There are as yet no serious adverse reactions documented, and studies have shown no indications of cardio toxicity.

The treatment protocol of the *artemether-lumefantrine* combination is six doses, twice per day for three days (table 2).

It is recommended that each dose of the drug be taken with **fatty meal**, to optimize absorption. Milk has been shown to improve the absorption of Lumefantrine component of the combination. **The dose should be repeated if the drug is vomited within 1 hour**.

Table 2: Dosage schedule of (*Artemether* 20 mg +*Lumefantrine* 120 mg)[3]

Weight in Kg* (age in years)	Day 1		Day 2		Day 3		Total number of tablets
	Initially	After 8 hours	Morning	Evening	Morning	Evening	
5-14 (<3)	1	1	1	1	1	1	6
15-24 (3-8)	2	2	2	2	2	2	12
25-34 (9-14)	3	3	3	3	3	3	18
35+ (>14)	4	4	4	4	4	4	24

*In case of discrepancies between the weight and age follow the weight for the proper dosage**.**

Art-Lum should be followed by PQ 0.75mg base /kg in one single dose in receptive areas if there are no any contraindications (as gametocidal therapy).

4-2- Second line treatment

QN and Dox or Clin can be used simultaneously as a second line treatment of UCFM in case of Art-Lum treatment failure that is defined as fever or parasitemia failing to resolve or recur within 2 weeks. The oral dose of QN for UCFM is 10mg QN salt/kg B. Wt. /8hourly, for 7 days (Table 3).

- Dox100mg once daily for 7days is given simultaneously with QN (Dox is contraindicated in pregnancy and young children, where Clin7- 13mg/kg up to 450mg is a good alternative to Dox)[5].
- PQ: in one single dose as gametocidal has to be given following QN to patients

to prevent possible local transmission. The total dose in adult patient is 45mg (or 0.75mg base/kg body weight). PQ is contraindicated in pregnant and lactating woman, infants, and G6PD severe deficiency cases.

Table 3: Dosage schedule of QN sulphate 300mg/tablet

Age (year)	B. Wt. (kg)	Number of tablets/dose
<1	<10	1/4
1-4	10-18	1/2
5-7	19-24	1
8-10	25-35	1 1/4
11-15	36-50	1 1/2
Above 15	>50	2

4-3. Treatment of UCFM in Pregnancy:

Pregnant women are at risk of developing severe complicated malaria. So, any pregnant woman with *P. falciparum* infection should be admitted when it is possible. Assess the severity of the condition by general examination and laboratory investigation. If the condition is classified as UCFM, then treat according the gestational age.

- In the first trimester: give oral QN and Clin both for 7 days. The QN dose is 10mg/kg body weight/8 hourly and the Clin dose 450mg/8 hourly.
- In second and third trimesters give Art-Lum using the standard dose for 3 days as mentioned in table 2.

Unit 5
Management of severe falciparum malaria (SFM)*

(*For further information on management of SFM see reference no. 8.)

Severe malaria is most commonly caused by infection with *P. falciparum*, although *P. vivax* and *P. knowlesi* can also cause severe disease[6]. Nearly all deaths due to severe malaria result from infections with *P. falciparum*.

5-1. Case definition of SFM:

A patient is defined as SFM case if there are asexual forms of *P. falciparum* in a blood film and the patient shows any of the clinical and laboratory features of SFM. SFM is a severe, life threatening acute *P. falciparum* infection with evidence of vital organs dysfunction. The condition requires immediate hospitalization, proper and specific treatment.

5-2. Clinical features of severe malaria:

• Impaired consciousness (including deep coma).
• Prostration.
• Repeated convulsions: more than two episodes within 24h.
• Deep breathing and respiratory distress (acidotic breathing).
• Acute pulmonary edema and acute respiratory distress syndrome.
• Circulatory collapse or shock, systolic blood pressure < 80mm Hg in adults and < 50mm Hg in children.
• Acute kidney injury.
• Abnormal bleeding /DIC.

5-3: Laboratory and other findings:

• Hypoglycemia (< 2.2mmol/l or < 40mg/dl);
• Metabolic acidosis (plasma bicarbonate < 15mmol/l);
• Severe normocytic anemia (hemoglobin < 5g/dl, packed cell volume < 15% in children; <7g/dl, packed cell volume < 20% in adults);
• Hemoglobinuria;
• Hyperlactatemia (lactate > 5mmol/l);
• Renal impairment (serum creatinine > 265μmol/l more than 3 mg/dl); and
• Pulmonary edema (radiological).

5-4: Complications and their management:

Hematological findings in severe malaria
Anemia is normocytic and may be ‘severe’ (as mentioned in 5-3). Thrombocytopenia

(< 100 000 platelets/μl) is usual in malaria, and in some cases the platelet count may be extremely low (< 20 000/μl). Polymorph nuclear leukocytosis is found in some patients with the most severe disease.

Management

- Anemia
  If the hematocrit falls below 20% or the hemoglobin concentration falls below 7g/dl, give blood transfusion.
- Bleeding disorders and DIC
  Transfuse fresh blood, clotting factors or platelets as required.
  Give vitamin K, 10mg, by slow intravenous injection.
  Start gastric protection with a parenteral histamine2-receptor blocker or a proton- pump inhibitor.
- Thrombocytopenia
  It is almost always present in falciparum malaria, usually with no other coagulation abnormalities. In most cases, it is not accompanied by bleeding and requires no treatment. The platelet count usually returns to normal after successful treatment of the malaria.

Cerebral malaria

- Patients with cerebral malaria are comatosed.
- Convulsions and retinal changes are common but papilledema is rare.
- Motor abnormalities such as decerebrate rigidity and decorticate rigidity (arms flexed and legs stretched) occur.
- The abdominal reflexes are absent.

Management

- Treat convulsions if they arise with a slow intravenous injection of benzodiazepine (e.g. diazepam at 0.15mg/kg B. Wt.).
- Treat status epilepticus by giving phenytoin (18mg/kg loading dose then a maintenance dose of 5mg/kg per day for 48h).
- Phenobarbitone may be used (15mg/kg intramuscularly or a slow intravenous loading dose, then a maintenance dose of 5mg/kg per day for 48h).

Acute kidney injury

Renal injury in malaria is caused by acute tubular necrosis and is always reversible in survivors

Management

- Exclude dehydration (hypovolemia) by clinical examination; including measurement of jugular venous pressure and the decrease in blood pressure between that taken when the patient is laying supine and that when he or she is propped up to 45°.

- If the patient is dehydrated, carefully infuse isotonic saline to correct hypovolemia, monitoring the jugular venous pressure clinically with the patient propped up to 45°.
- If the patient remains oliguric after adequate rehydration and blood urea and creatinine continue to rise, consider renal hemodialysis.

Hypoglycemia

Hypoglycemia (blood glucose < 2.2mmol/l , 40mg/dl) is an important manifestation of falciparum malaria and is associated with an increased risk of mortality. It occurs in three groups of patients, which may overlap:

• Patients with severe disease, especially young children.
• Patients treated with quinine as a result of a quinine-induced hyperinsulinemia.
• Pregnant women, either on admission or after quinine treatment.

Management:

• If hypoglycemia (threshold for intervention, 3mmol/l) is detected, give 25g of dextrose (preferably as 10% dextrose) over a few minutes.

The usual dosage is 50ml of 50% dextrose (25 g) diluted with 100ml of any infusion fluid and infused over 3–5min.

• Follow with an intravenous infusion of 200– 500mg/kg per hour of 5% or 10% dextrose.

Metabolic acidosis

Metabolic acidosis is common in severe malaria and is an important cause of death. It is associated with hyperlactatemia. Low plasma bicarbonate is the single best prognostic indicator in severe malaria. In adults and older children, acidosis may result from acute renal failure. Acidosis commonly accompanies hypoglycemia.

Management

If there is evidence of dehydration:

• Give only isotonic fluid (0.9% saline) by slow intravenous infusion to restore the circulating volume, but avoid circulatory overload, which may rapidly precipitate pulmonary edema.
• Monitor blood pressure, urine volume (hourly) and jugular venous pressure.
• Improve oxygenation by clearing the airway, increasing the concentration of inspired oxygen and supporting ventilation artificially, if necessary.

Pulmonary edema management

• Keep the patient upright; raise the head of the bed or lower the foot of the bed.
• Give a high concentration of oxygen, even mechanical ventilation if needed.
• Give the patient a diuretic, such as furosemide at 0.6mg/kg (adult dose, 40mg), by intravenous injection. If there is no response, increase the dose progressively to a maximum of 200mg.
• In well-equipped intensive care units, mechanical ventilation with positive end-expiratory pressure may be needed.

• If there is pulmonary edema due to over hydration in addition to the above:
    - Stop all intravenous fluids and give furosemide.
    - If there is no improvement, withdraw 250ml of blood by venesection into a blood transfusion donor bag so that it can be given back to the patient later.
    - If there is renal impairment and no response to diuretics, use hemodialysis.

Shock management

• Correct hypovolemia with an appropriate plasma expander (fresh blood, plasma, or colloids). If these are not available, give isotonic saline.

• Take blood for culture, and immediately start the patient on broad-spectrum antibiotics.

• Once the results of blood culture and sensitivity testing are available, reassess the antibiotic treatment.

5-5. Specific treatment of SFM:

SFM is a medical emergency. Effective parenteral anti-malarial treatment should be given as soon as possible after admission, general assessment and confirmation of diagnosis[7].

- **Treatment with Quinine Hydrochloride injection:**
    - Parenteral Quinine (QN) is an effective treatment of SFM.
    - QN. IV infusion must be diluted in 5% glucose or 5% glucose in normal saline
    - Rapid administration of QN IV is unsafe. It may precipitate hypotension and fatal cardiovascular toxicity.
    - The loading dose is 20mg/kg of QN salt infused over 4 hours.
    - Then after 8 hours from the start of the loading dose, give a maintenance dose of 10mg/kg of QN salt (infused over 4 hours) every 8 hours.
    - Treatment with QN IV should continue for at least 24 hours or until the patient become able to take and tolerate oral medication.
    - Then give complete first line treatment course of UCFM (Art-Lum for 3 days).

- **Treatment with Artesunate (AS0 injection:**
    - Artesunate (AS) injection is an effective alternative treatment of SFM.
    - The dose of AS is 2.4mg/kg B.Wt. given slowly IV or IM.
    - First dose of AS has to be given as soon as possible (0 time) and repeated after 12hours, 24hours, and then once every 24hours.
    - Treatment with AS should continue for at least 24hours or until the patient become able to take and retain oral medication.
    - Then give complete first line treatment course of UCFM (Art-Lum for 3 days).

**Once AS injection becomes available in Jordan; it will be used for the treatment of SFM replacing (QN) injection.*

Unit 6
Treatment of Malaria caused by *P. vivax, P. ovale* or *P. malariae*[7,8]

6-1. Treatment of malaria caused by *P. vivax* or *P. ovale*:

- CQ 25mg base/kg B. Wt. divided over 3 days up to a total dose of 1500mg, the dosage schedule by age can be estimated (Table 4).
- PQ 0.25mg base/kg B. Wt. taken with **food** once daily for 14days as radical treatment following the 3days of CQ **(**Table 5). For *P. vivax* infections originating from Oceania and South East Asia, the dose of PQ should be increased to 0.5 mg base/kg body weight for 14 days.

Table 4: Dosage schedule of CQ base in (mg) by age groups for the treatment of *P. vivax*, *P. ovale* or *P. malaria*e sensitive strains. (Each 250mg tablet contains 150mg CQ base)

Age group	Day 1		Day 2/Dose	Day 3/Dose
	First dose	Second dose*		
<2 week	37.5	18.5	18.5	18.5
2-12weeks	75	37.5	37.5	37.5
4-12months	120	60	60	60
1-2years	150	75	75	75
3-6years	200	100	100	100
7-11years	300	150	150	150
12-14years	450	225	225	225
≥15years	600	300	300	300

* The second dose should be given 6 hours after the first dose

Table 5: Dosage schedule of PQ by age group as radical treatment for *P. vivax* or *P. ovale* (Each tablet contains 15mg PQ base)

Age group (years)	Dose in mg PQ base/day	Dose in tablets/day
1-2	3.75	1/4
3-6	5	1/3
7-11	7.5	1/2
12-14	11.25	3/4
≥15	15	1

Notes

- The duration of radical treatment with PQ is 14 days.
- PQ is contraindicated in pregnant, lactating women; infants; G6PD deficiency and any condition predisposing to granulocytopenia.
- Consider performing G6PD assay before starting PQ if the test is available.
- Patients should be warned to stop PQ and report immediately to a doctor if they have abdominal pain, and become weak, pale, jaundiced or notice darkening of the urine.
- PQ as gametocidal in *P. falciparum* or *P. malariae* is given in one single dose of 0.75mg/kg B. Wt.

6-2. Treatment of malaria caused by resistant strains of *P. vivax*

- Art-Lum for 3 days as shown in (table 2), followed by PQ.
- PQ has to be given as mentioned in 6-1.

6-3. Treatment of severe malaria due to *P. vivax*

- *P. vivax* malaria can occasionally result in severe disease, as in *P. falciparum* malaria; in addition splenic rupture may occur.
- Treatment and case management of severe *P. vivax* malaria is the same as for severe and complicated *falciparum* malaria.

6-4. Treatment of malaria caused by *P. malariae*

- CQ 25mg base/kg B. Wt. divided over 3 days (table 4).
- PQ 0.75mg base/kg B. Wt. in one single dose as gametocidal therapy following CQ.

Unit 7
Treatment of mixed infections[7,8]

- Mixed malaria infections are simultaneous co-infection with two various species of malaria parasites, the most common mixed malaria infections are *P. falciparum* and *P. vivax*; *P. falciparum* and *P. ovale* or *P. falciparum* and *P. malariae*.
- Art-Lum is the treatment of choice; it is effective against all malaria species. The dose and duration of treatment is the same as for UCFM.
- A second line treatment could be QN sulphate combined with Dox. Or Clin. orally in case of Art-Lum treatment failure. The dose and duration of treatment is the same as for UCFM.
- PQ 0.25mg base/kg B. Wt. for 14 days (as radical or anti-relapse treatment) should be given to mixed infections with *p. vivax* or *P. ovale*.
- PQ 0.75mg base/kg B. Wt. single dose (as gametocidal) is given in cases of mixed infection with *P. malariae*.

References

1. Malaria Country Profiles for Jordan, 2011. World Health Organization; 2013. Available from: emro.who.int/malaria/publications/malaria-country-profiles.htm
2. Annual Malaria Report for 2012. Amman-Jordan: Ministry of Health, Malaria Control Program. 2013.
3. Guidelines for the treatment of malaria. 2nd edition. Geneva. World Health Organization. 2010.
4. Parasitological confirmation of malaria diagnosis: WHO technical consultation. Geneva: 6-8 October 2009.
5. Guideline for Treatment of Malaria in the United States: (Updated September 23, 2011) USA. CDC. 2011.
6. Management of Severe Malaria, third edition. Third Edition. Italy: World Health Organization; 2012. Available from: http://www.who.int/malaria/publications/atoz/9789241548526/en/idex.html
7. Malaria case management (Operational Manual). Geneva. World Health Organization, Global Malaria Program; 2009.
8. Malaria case management (Training module for program managers and experts on malaria control and elimination). Geneva. World Health Organization, Global Malaria Program; 2009.
9. Paul M. Arguin, Stefanie F. Steele. The Pre-Travel Consultation, Malaria. In: Travelers' Health- Yellow Book, Centers for Disease Control and Prevention (CDC).

Annex I

Malaria Prevention and Chemoprophylaxis

Malaria prevention consists of a combination of mosquito avoidance measures and chemoprophylaxis.

Depending on level of risk, it may be appropriate to recommend no specific interventions, mosquito avoidance measures only, or mosquito avoidance measures plus chemoprophylaxis. For areas of intense transmission, such as West Africa, exposure for even short periods of time can result in transmission[9].

- Mosquito avoidance measures, these are mostly standard personal protective measures and include.
    a. Insecticide treated nets (ITNs).
    b. Insect repellents.
    c. Screening of houses.
    d. Air conditioning and fan.
    e. Special clothing that covers exposed areas of body like wearing long sleeves long pants and socks.

- **Chemoprophylaxis**: is recommended as a short term measure for international travelers to endemic areas. All recommended primary chemoprophylaxis regimens involve taking a medicine before, during, and after travel to an area with malaria. Beginning the drug before travel allows the antimalarial agent to be in the blood before the traveler is exposed to malaria parasites. In choosing an appropriate chemoprophylactic regimen before travel, the traveler and the travel health provider should seek advice from the national malaria control program (tel. 06 5694080).

  Recommended drugs for malaria prophylaxis are shown in table (6) and include:

  - CQ: a weekly dose of 5mg base/kg/B.Wt. (up to 300mg base/week in adult) is used in areas where malaria is due to *P. vivax* or CQ sensitive *P. falciparum*.
  - Mefloquine: weekly dose 5mg/kg/ body weight (up to 250mg/week in adult) is used in areas where malaria can be caused by non-chloroquine sensitive *P. falciparum*.

- Dox: daily dose of 100mg can be used as alternative to Mefloquine, starting one to two days before entering the endemic area and lasting for 28 days after leaving the endemic area.
- PQ: can be given as terminal prophylaxis (or radical presumptive treatment) after leaving the endemic area at the dose of 0.25mg base/kg for 14 days, and in combination with any one of the above schizontocidal prophylactic drugs[11].

Chemoprophylaxis with Mefloquine and CQ has to be started one to two weeks before entering the endemic area and last until 4 weeks after leaving it.

Table (6): Drugs for malaria chemoprophylaxis by parasite species.

Countries endemic for	**1st choice**	**2nd choice**
P. falciparum malaria	**Mefloquine** 5mg base/kg/week (up to 250mg/week)	**Doxycycline** 100mg/daily (except in pregnancy and children less than 8 years)
P. vivax, p. ovale or P. malariae	**Chloroquine** 5mg base/kg (up to 300mg base)/week	—

- Mefloquine: is contraindicated in pregnant women, children <15kg B. Wt. and in patients on B-blockers, Calcium channel Antagonists or antidepressants.
- Dox: is contraindicated in pregnant women and children less than 8 years of age.
- Areas endemic for both falciparum and other species should be given prophylactic treatment against falciparum malaria.
- Chemoprophylaxis with Mefloquine or CQ has to be started one-two weeks before entering the endemic area and last until 4 weeks after leaving the areas.
- Chemoprophylaxis with Dox. has to be started one-two days before entering the endemic area and lasting for 28 days after leaving it.

Annex II
Standby emergency treatment (SBET) of malaria

- Travellers to remote malaria endemic areas are advised to carry anti-malarial drugs for self-administration as stand-by emergency treatment[9].
- They should take SBET, if they experience fever one week or more after entering the endemic area and no prompt medical help is available.
- SBET combined with protection against mosquito bites, may be indicated in remote rural areas like Thailand, South-East Asia and the Amazon basin, where there is multidrug resistant malaria with very low risk of infection, and the risk of side effects of chemoprophylaxis outweigh that of contracting malaria[9].
- The choice of SBET will depend on the same principles as for the treatment of uncomplicated *falciparum* malaria.

Annex III

معلومات وارشادات حول مرض الملاريا

<u>وبائية مرض الملاريا في الاردن:</u>

- ينتقل طفيل الملاريا بشكل اساسي عن طريق بعوض الانوفيليس الناقل ولا ينتقل من شخص لأخر عن طريق الاختلاط او اللمس او الاتصال المباشر.
- كانت الملاريا متوطنة في الاردن قديما وتم إستئصال المرض محليا عام ١٩٧٠.
- انواع الملاريا التي تصيب البشر هي: الملاريا النشطة، الملاريا المنجلية، الملاريا البيضاوية والملاريا الوبالية، اما المتصورة من نوع نوليزي فهي قد تنتقل الى الانسان وتسبب الملاريا في بعض مناطق جنوب شرق اسيا.
- تعتبر الملاريا المنجلية من أخطر انواع الملاريا لأنها قد تؤدي الى حدوث مضاعفات وخيمة والوفاة أكثر من انواع الملاريا الاخرى.
- اصابات الملاريا المكتشفة في الاردن معظمها حالات وافدة من دول يتوطن فيها المرض وهي معظم دول افريقيا جنوب الصحراء الكبرى وجنوب شرق آسيا وبعض مناطق الشرق الاوسط
- المعدل السنوي لعدد حالات الملاريا المسجلة سنويا حوالي ٩٠ اصابة ملاريا معظمها وافدة بين الاردنيين و الاجانب القادمين من مناطق موبؤة بالملاريا

<u>اعراض الملاريا:</u>

- نوبات من الحمى تبدأ على شكل قشعريرة ثم حمى وتنتهي بالتعرق الشديد
- صداع
- آلام مفصلية وعامة
- غثيان وقيء واحيانا اسهال
- حدوث مضاعفات أخرى مثل فقر الدم، اليرقان، فشل كلوي، فشل الكبد، تشنجات، غيبوبة في مرحلة متقدمة وفي حال تأخر التشخيص والعلاج

<u>الفئات الأكثر تعرضا للاصابة بالملاريا:</u>

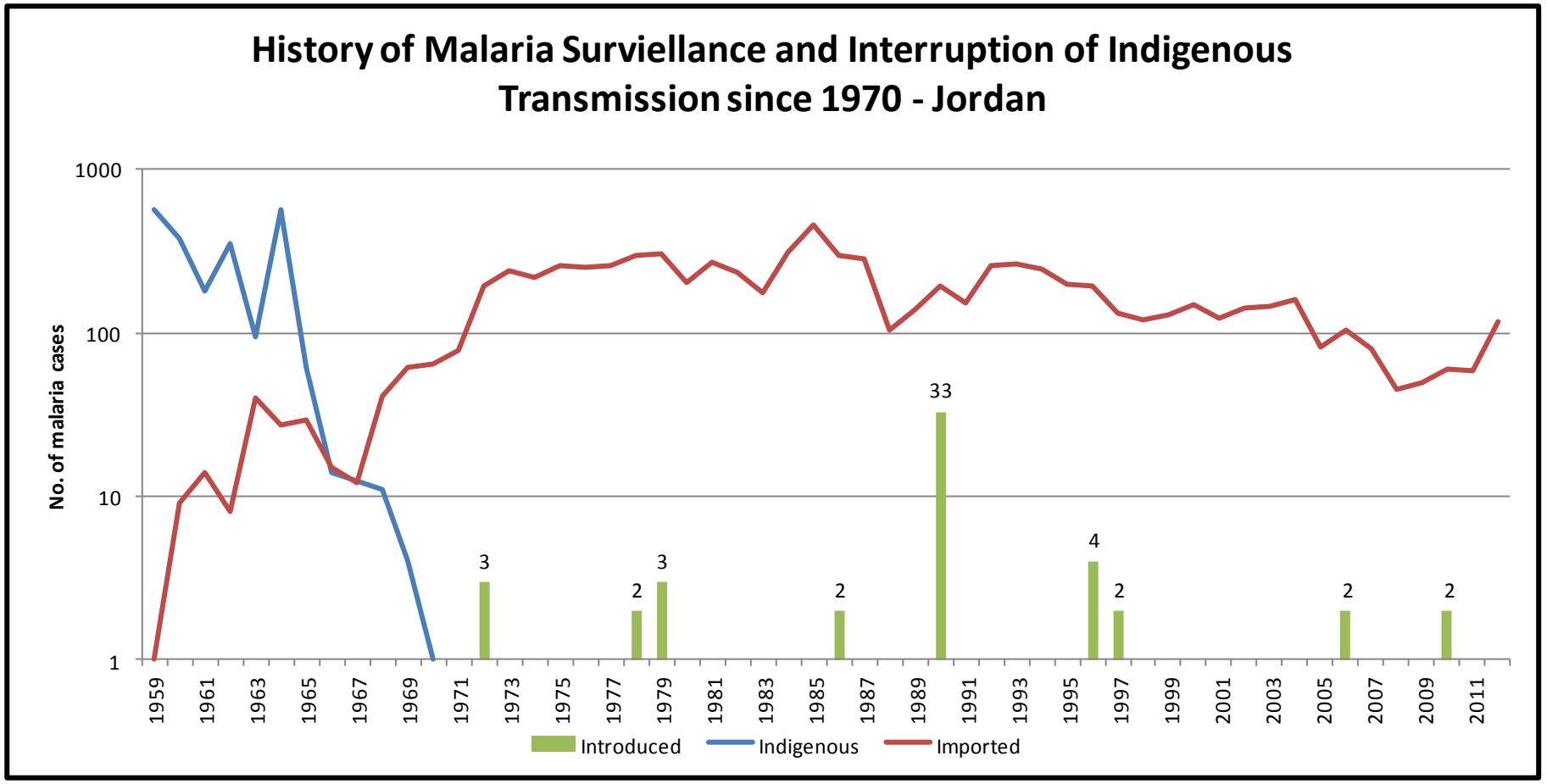
- المشاركون في قوات حفظ السلام الدولية في دول يتوطن فيها مرض الملاريا
- الطلاب او المسافرون العائدون من الدول الموبؤة بالملاريا
- الزوّار والمرضى العرب القادمون من السودان واليمن ودول اخرى تتوطن فيها الملاريا
- العمال الاجانب القادمون من مناطق موبؤة بالملاريا (الباكستان ،الهند، سيريلانكا .....)
- الخادمات القادمات من دول جنوب شرق آسيا

<u>التشخيص والعلاج:</u> يرجى التنسيق أو مراجعة المختبرات التابعة لبرنامج مكافحة الملاريا/ وزارة الصحة المتواجدة في المواقع التالية وعلى ارقام الهاتف المبينة:

- قسم الامراض الطفيلية والمشتركة – عمان – جبل الحسين – ميدان الشهيد فراس العجلوني (٠٦/٥٦٦٧١٥٥/٥٦٩٤٠٨٠)
- مكتب الملاريا والبلهارسيا–اربد (٠٢-٧٢٧٢٤٥١)
- مكتب الملاريا والبلهارسيا–المشارع – الاغوار الشمالية (٠٢-٦٥٦٣٢٤٥)
- مكتب الملاريا والبلهارسيا– ديرعلا (٠٥-٣٥٧٣٠٥٣)
- مكتب الملاريا والبلهارسيا–الشونة الجنوبية (٠٥-٣٥٨١٢٢٠)
- مكتب الملاريا والبلهارسيا–الكرك (٠٣-٢٣٥١٠٩٥)
- مكتب الملاريا والبلهارسيا–غور الصافي (٠٣-٢٣٠٢٤٥٦)

ارشادات حول التبرع بالدم:

- ينتقل مرض الملاريا عن طريق التبرع بالدم أو الاعضاءعندما يكون المتبرع يحمل طفيل الملاريا في جسمه أو عن طريق الادوات الجراحية الملوثة بدم مصاب.
- ينصح الاشخاص الذين سافروا الى مناطق تتوطن فيها الملاريا عدم التبرع بالدم لمدة عام من تاريخ العودة من المنطقة الموبؤة.
- ينصح جميع الاشخاص الذين اصيبوا بالملاريا عدم التبرع بالدم لمدة خمسة أعوام من تاريخ اخر اصابة بالمرض.


History of Malaria Surviellance and Interruption of Indigenous Transmission since 1970 - Jordan
No. of malaria cases
1000
100
10
1
3
2
3
2
33
4
2
2
2
1959
1961
1963
1965
1967
1969
1971
1973
1975
1977
1979
1981
1983
1985
1987
1989
1991
1993
1995
1997
1999
2001
2003
2005
2007
2009
2011
Introduced
Indigenous
Imported