

Malaria diagnostics, clinical presentation and treatment

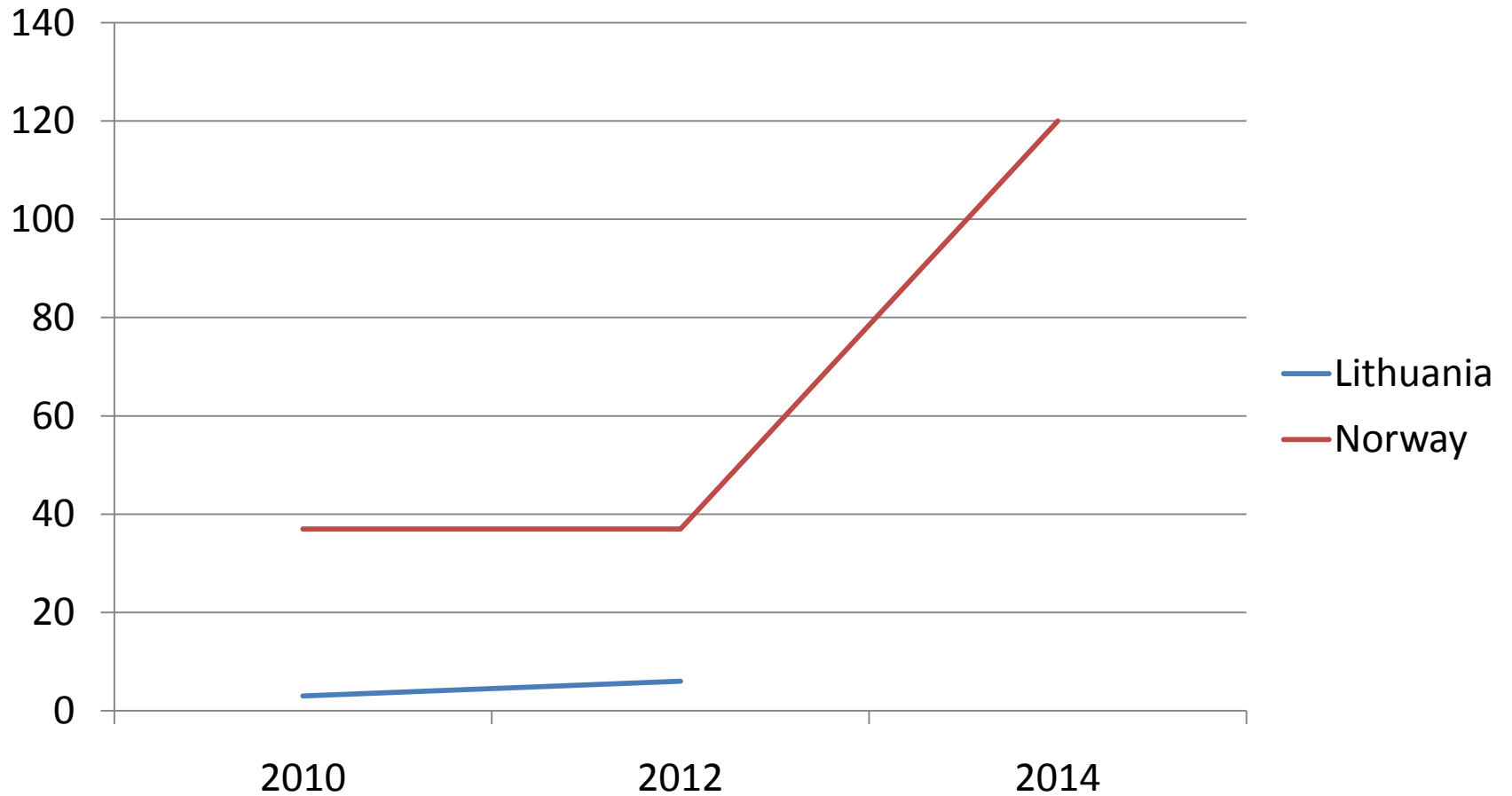


Kristine Mørch, MD, PhD
National centre for tropical infectious diseases
Haukeland university hospital
Bergen, Norway

Malaria epidemiology

- Globally (WHO report 2014):
 - 200 million cases
 - 600 000 deaths
- Europe (ECDC report 2014):
 - 5 161 cases
 - 1/100 000/year
 - Imported cases 99%

Malaria Lithuania and Norway



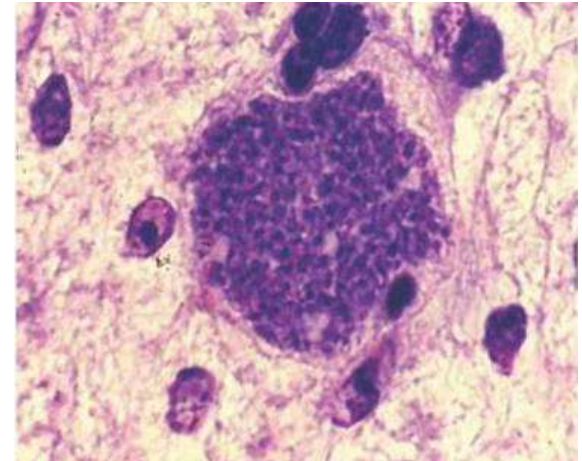
Malaria life cycle



Anopheles



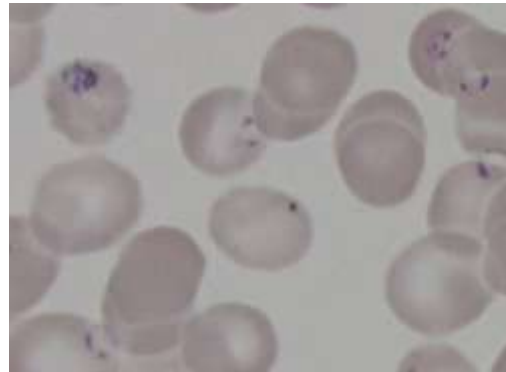
Sporozoites



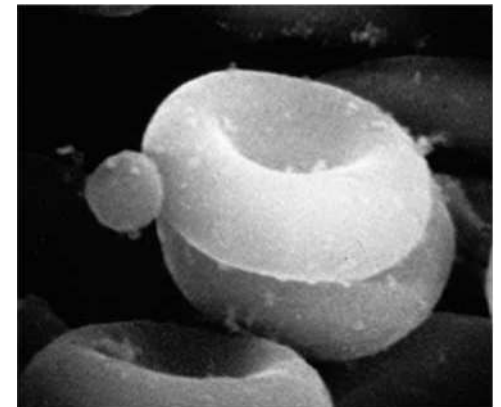
Liver schizont



Gametocytes multiply in mosquito



Parasites multiply in red cells



Merozoite invade red cell

Five species infect humans

Potentially severe malaria:

- *P. falciparum*
- *P. knowlesi*
- (*P. vivax*)

Benign malaria:

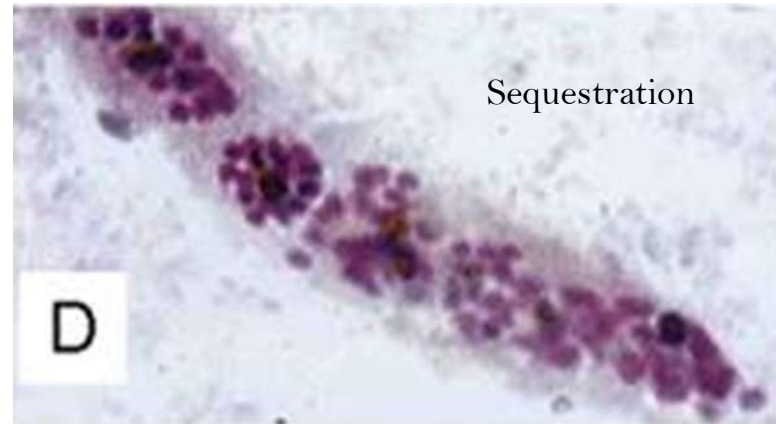
- *P. vivax* (usually)
- *P. ovale curtisi* and *wallikeri*
- *P. malariae*

Uncomplicated malaria – clinical presentation

- Unspecific fever
- Headache, myalgia, nausea, vomiting, diarrhoea

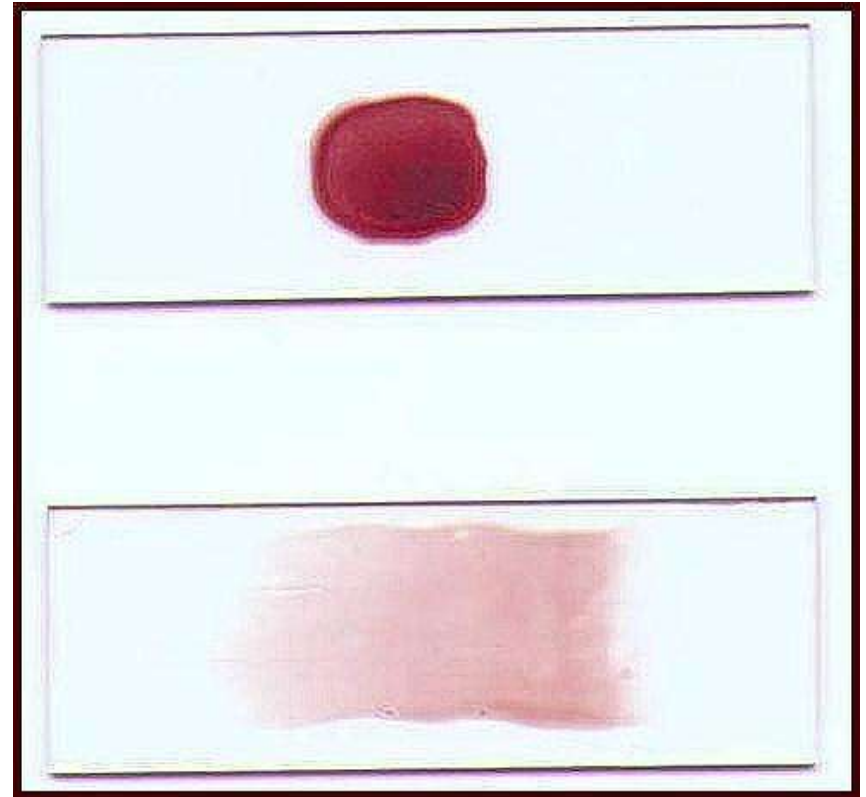
Severe malaria clinical presentation

- Coma (cerebral malaria)
- Severe anaemia
- Kidney failure
- Acidosis
- Pulmonary oedema
- Hypoglycaemia
- Spontaneous bleeding
- Shock
- Haemoglobinuria
- Hyperparasitaemia (>2-4%)

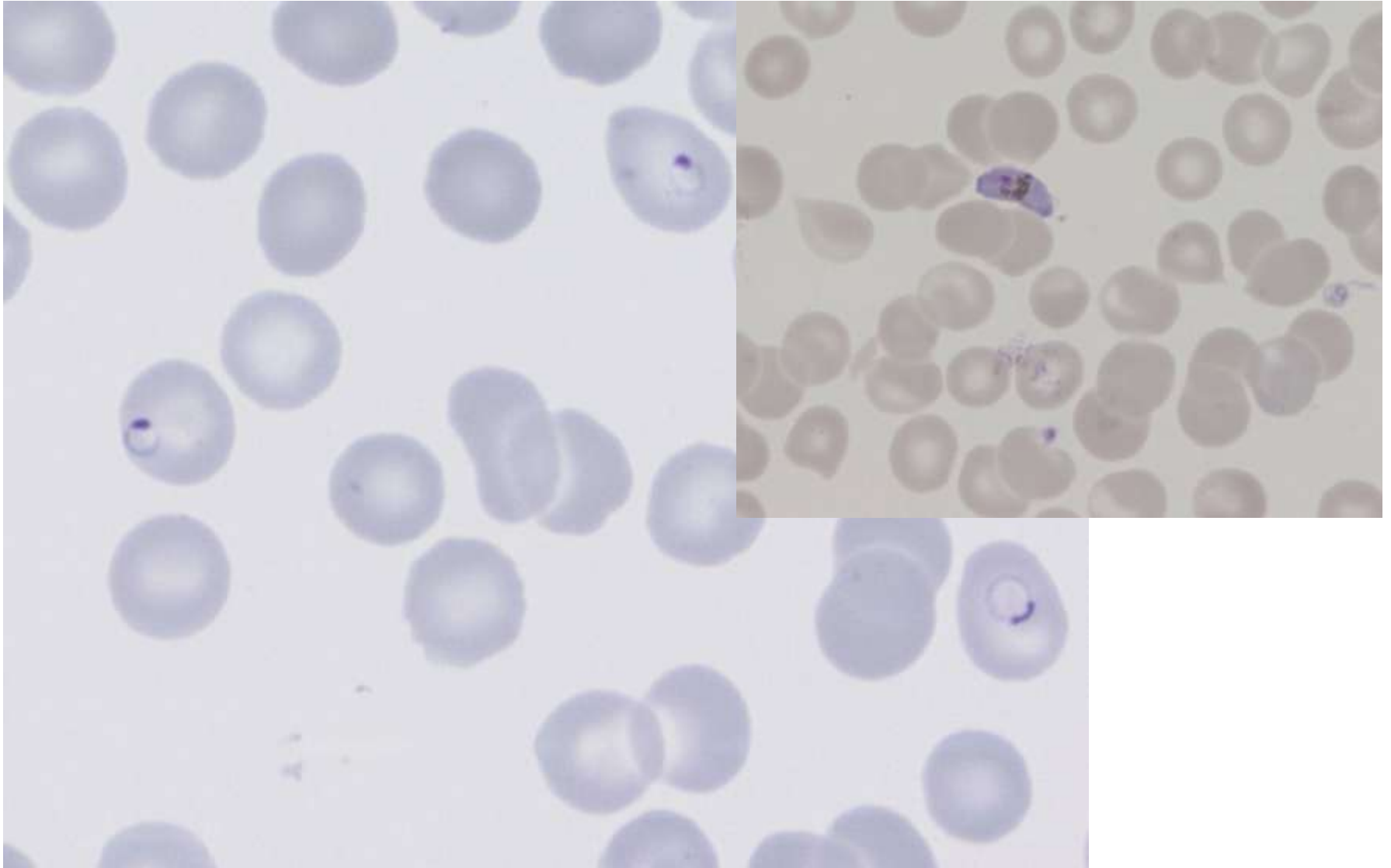


Diagnostics

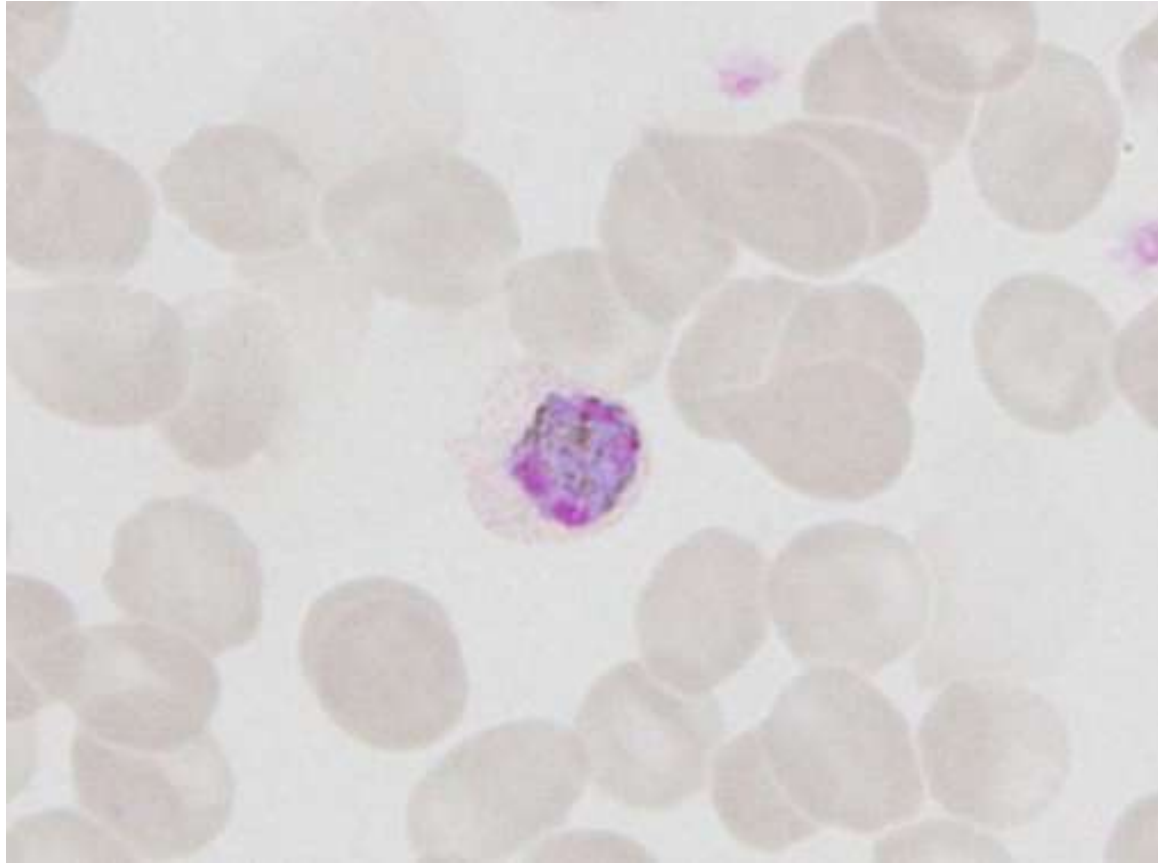
- Giemsa stained blood slides
- Rapid diagnostic tests
- PCR



P. falciparum



P. vivax



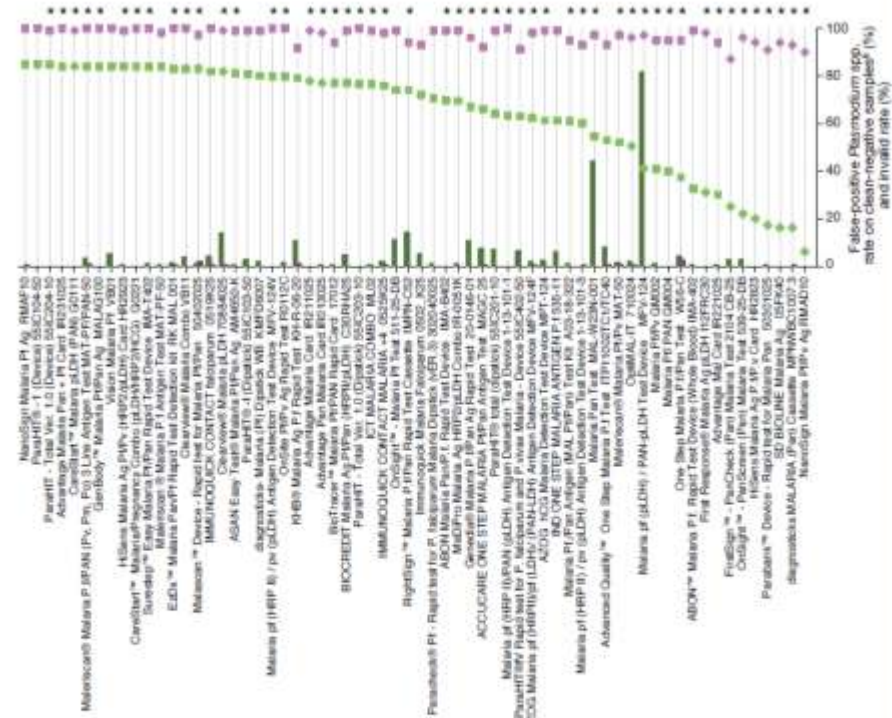
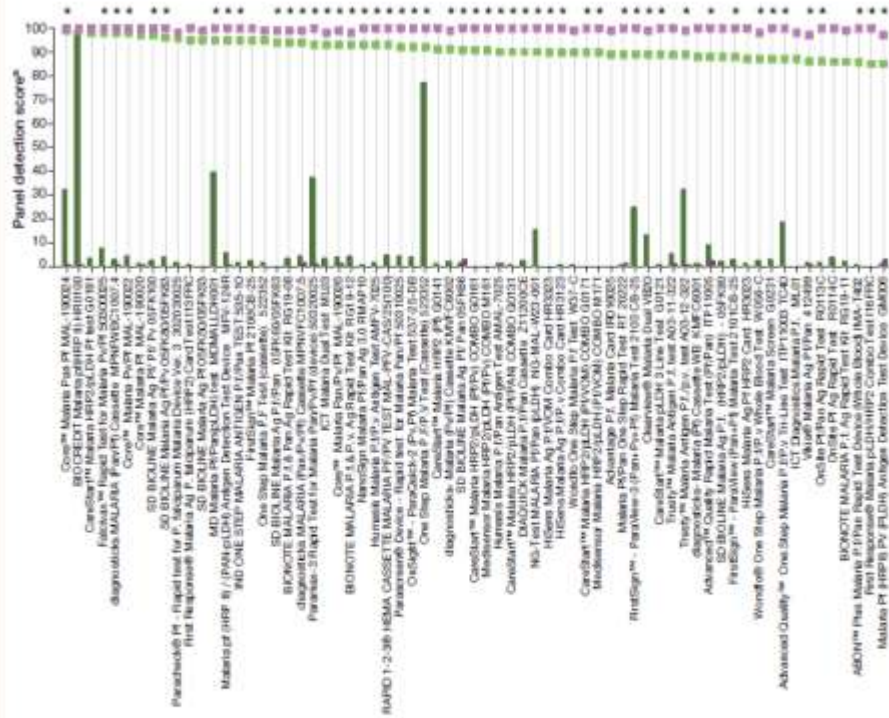
Rapid diagnostic tests

- Detects
 - Histidine rich protein-2 (*P.falciparum* specific)
 - *Plasmodium* specific aldolase (pan-malaria)
 - *Plasmodium* associated LDH (pan-malaria)



WHO quality assurance reports

Figure S1: Malaria RDT performance in phase 2 of rounds 2-5 against wild-type (clinical) samples containing *P. falciparum* at low (200) and high (2000-5000) parasite density (parasites/ μ L) and clean-negative samples



* Panel detection score: A sample is considered detected only if all RDTs from both kits read by the first technician, at the maximum specified reading time, are positive.

* Clean-negative, blood samples from healthy volunteers with no known current illness or blood abnormality.

* Indicates tests that also detect other non-*P. falciparum* parasites

PCR

- Detects parasite DNA
- Most sensitive method
- Not available in routine diagnostics

PCR versus microscopy

Bergen – Norway

Table 2 Genus-specific results from a cohort of 132 fever patients with potential imported malaria

Samples (n = 135)	New single-round amplification mitochondrial (PCR _{PgMt19 F3 & B3} [21])	Modified single-round amplification 18S PCR (<i>rPLU 6 & 5</i> [9])	Genus-specific nested 18S PCR [10]	Microscopy
Positive	28	27	27	26
Negative	107	108	108	109

PCR versus microscopy globally

- Meta analysis:
 - 70 paired microscopy and PCR estimates from endemic areas (Africa, Asia, Americas)
- Microscopy detected 50.8% of malaria cases detected by PCR

Artesunate compared to quinine -efficacy

- Artesunate reduces mortality in endemic areas:
 - Relative risk 0.61 in adults
 - Relative risk 0.75 in children

Treatment

- **Severe**
 - Artesunate i.v.
 - Quinine i.v.
 - Change from i.v. to a full course of oral drug when condition allows
- **Uncomplicated *P. falciparum***
 - Artemether-lumefantrine
 - Atovaquone-proguanil
 - Mefloquine
- ***P. vivax* , *P. ovale***
 - Chloroquine + primaquine
- ***P. malariae***
 - Chloroquine



Table 2 Dosage of recommended medication for adult patients with malaria (Table 1) [5, 7]

Drug	Dosage
Artesunate	2.4 mg/kg intravenously immediately and after 12 and 24 hours, then once daily, normally for up to 3 days Change to peroral drug as with uncomplicated falciparum malaria when the patient can swallow tablets and parasitaemia < 1 %
Quinine	1 200 mg (20 mg/kg) infused over 2–4 hours as saturation dose, then 600 mg (10 mg/kg) at 8-hour intervals. The total dose per day should not exceed 1 800 mg Change to peroral medication as for uncomplicated falciparum malaria when the patient can swallow tablets and parasitaemia < 1 %
Artemether–lumefantrine (artemether 25 mg, lumefantrine 120 mg)	4 tablets at 0, 8, 24, 36, 48 and 60 hours Should be taken with fatty food
Dihydroartemisinin–piperazine (dihydroartemisinin 40 mg, piperazine tetraphosphate 320 mg) [14]	36–75 kg: 3 tablets once a day for three days 75–100 kg: 4 tablets once a day for three days To be taken between meals
Mefloquine	Initially 750 mg (3 tab.), after 6–8 hours 500 mg (2 tab.) and for patients > 60 kg after a further 6–8 hours 250 mg (1 tab.) To be taken with food
Proguanil–atovaquone (proguanil 100 mg, atovaquone 250 mg)	4 tablets once a day for three days Should be taken with fatty food
Hydroxychloroquine	Initially 600 mg (4 tab.), after 6 hours 300 mg (2 tab.). Then 300 mg daily for 2 days To be taken with food
Primaquine	15 mg per day for 14 days If acquired in areas with primaquine resistance (see text) or in areas where relapses have been recorded after normal dosage: 22.5 mg or 30 mg or 0.5 mg/kg per day for 14 days Primaquine is contra-indicated during pregnancy or in cases of G6PD deficiency ¹

- Mørch, Myrvang: Treatment of malaria in Norway. Tidsskr nor legeforen 2012.

Side effects

- Artesunate: Post treatment haemolysis
 - May require repeated blood transfusions
 - Hgb should be monitored 2-4 weeks after treatment
- Quinine: Arrhythmia, hypoglycaemia, cinchonism
 - Infusion slow (2-4 hours)
 - Cardiac monitoring during infusion

Preparedness for severe malaria in a non-endemic country

- Among all hospitals in Norway
 - 40% (19/48) not artesunate or quinine available
 - 6% no diagnostic methods available
- In Lithuania?

Malaria patient

- Previously healthy doctor
- Did not turn up at work as usual
- Colleagues alarmed the police who found him in his home; confused
- Admitted to department of neurology with tentative diagnosis cerebral stroke

Findings

- Dysphasia
- Awake but confused
- RF 40, puls 120, temperature 39
- Sent for MRI

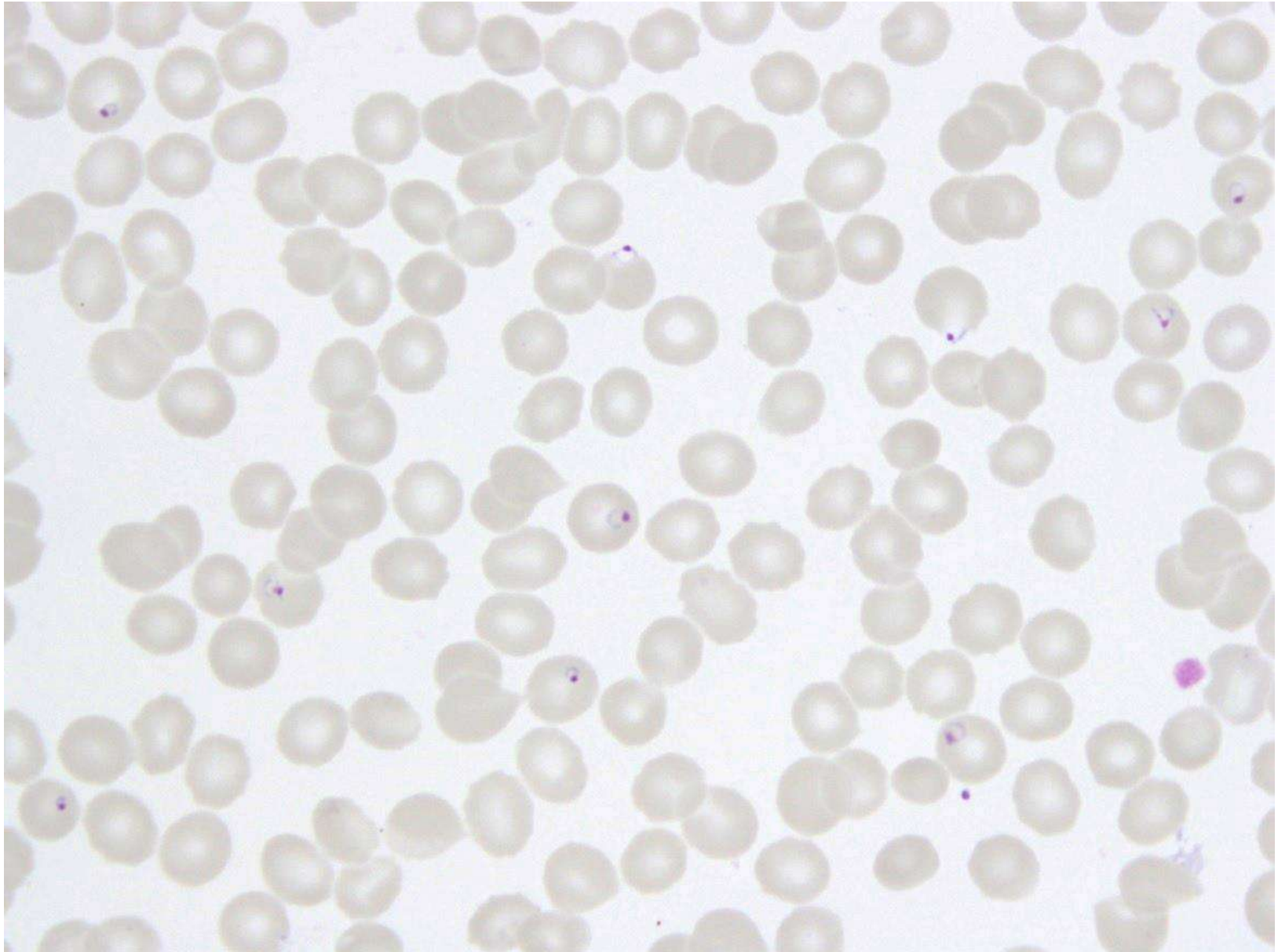
The nurse received information saving
the patient

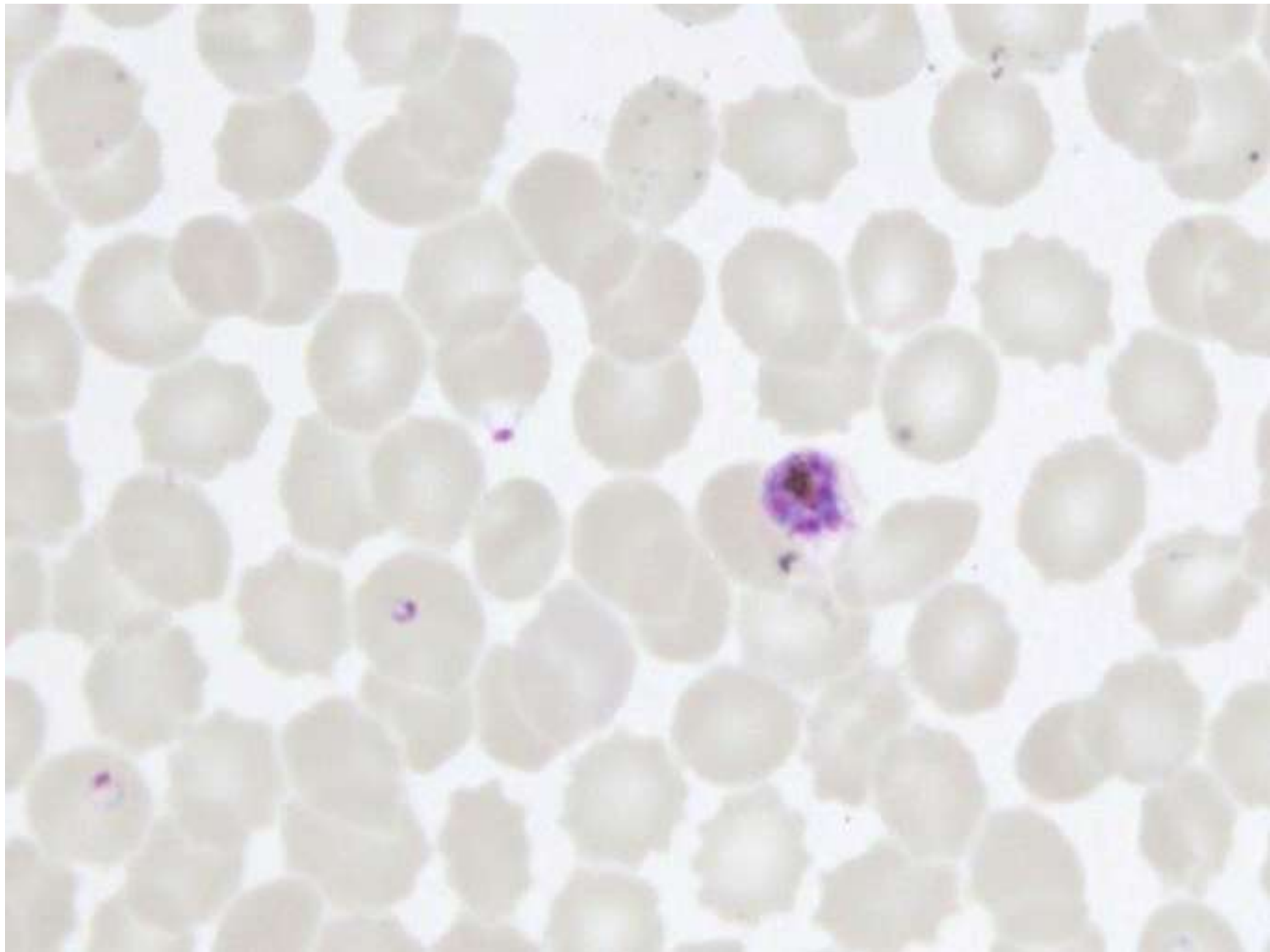


Test results

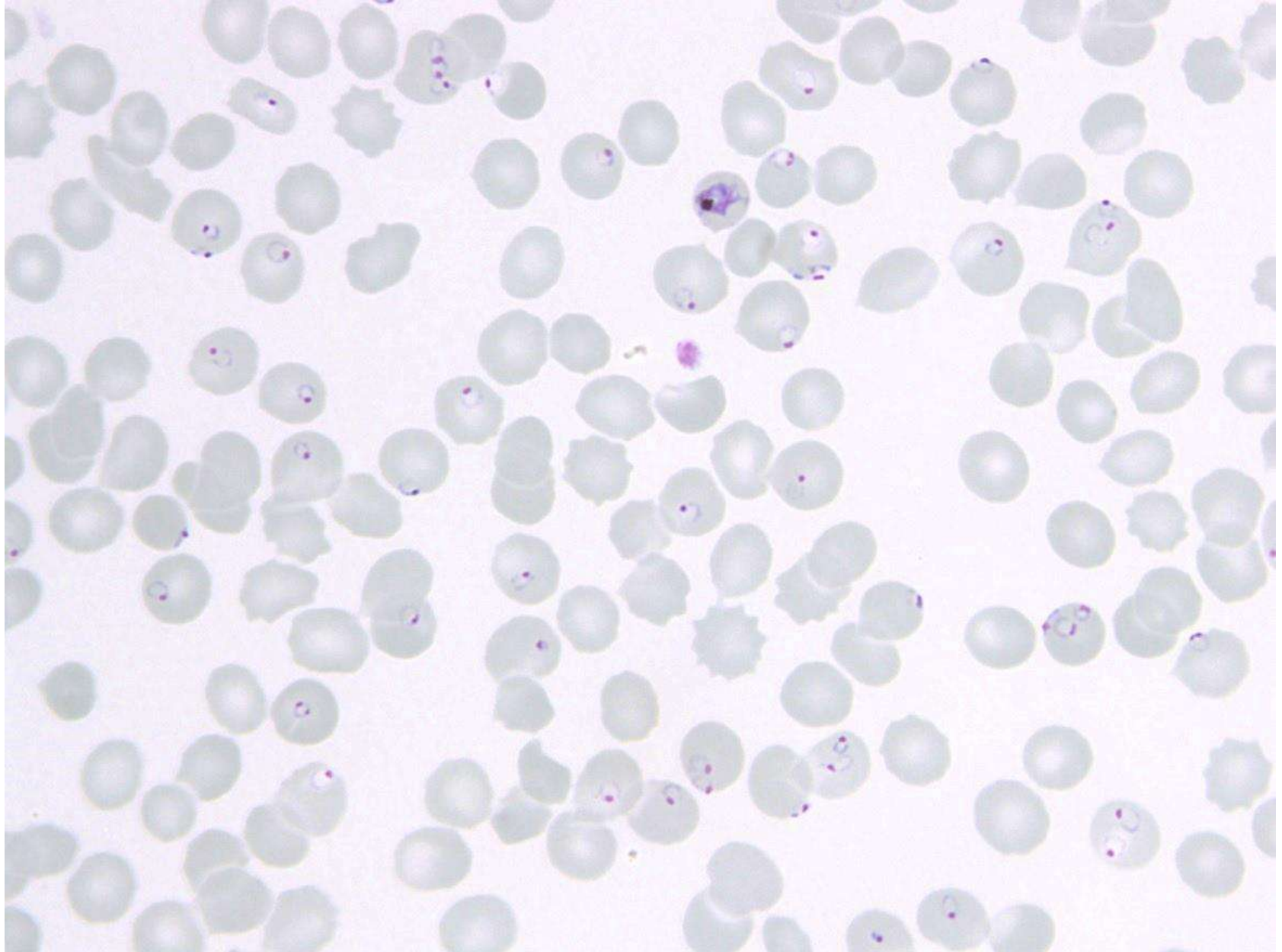
- Malaria rapid test: *P. falciparum* positive
- Lactate: 10
- Platelets: 11
- Creatinine: 120
- Bilirubin: 121
- LD: 522
- INR 1.4, APTT 46, D-dimer > 20 (DIC)

Blood smear





Blood smear two hours later



Treatment

- **Artesunate**



- **Exchange transfusion**



A close-up photograph of several pink cherry blossoms in full bloom. The petals are a soft, light pink color, and the centers show delicate stamens. The background is a soft-focus mix of green leaves and dark branches, suggesting a tree in bloom. The lighting is bright, creating a warm and pleasant atmosphere.

Thank you for your attention

A wide river at sunset with stone steps leading into the water and a small boat in the distance.

Klausimai?