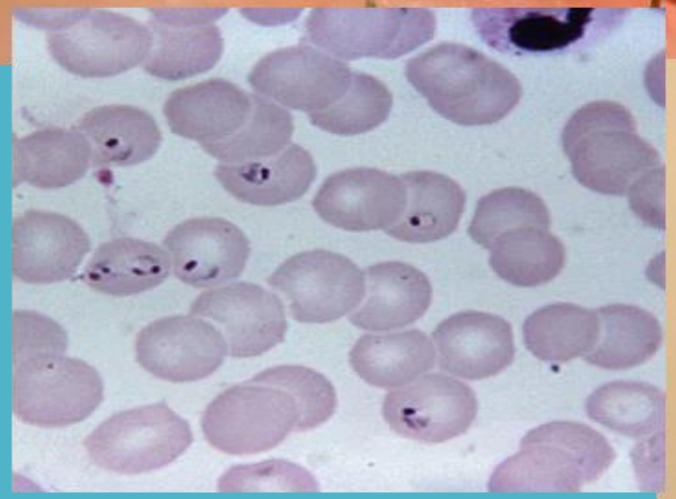
Congenital Malaria



Ishani Ranaweera

Epidemiology of malaria

- Malaria is a major parasitic disease which is endemic in many countries
- Is the most common infection imported to the UK by returning travellers
- 1500-2000 cases are reported annually in the UK, with death occurring in 10-20 of these cases
- Notifiable disease in England, Northern Ireland, and Wales
- Non immune pregnant women are also at high risk – miscarriages, 10% maternal mortality

Symptoms

- High fever, fatigue, vomiting, and headaches.
- In severe cases it can cause yellow skin, seizures, coma, or death

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Pathophysiology

- Transmitted by infected female *Anopheles* mosquito
- Caused by protozoal parasitic genus *Plasmodium*

P. falciparum

- Tropical & subtropical areas, especially in Africa.
- Cause cerebral malaria
- Severe anaemia, thrombocytopenia and TMA due to infected parasites can form micro-thrombi

P. Vivax

- Asia, Latin America
- Has dormant liver stages
- Use Duffy antigen to bind to RBCs

P. malariae

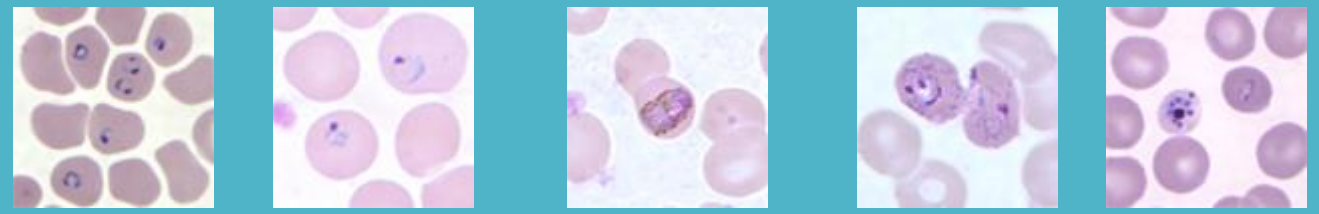
- Worldwide
- 3 day cycle
- Associated with nephrotic syndrome

P. ovale

- mostly in Africa (especially West Africa)

P. Knowlesi

- Southeast Asia



Trophozoites of *Plasmodim* sp.

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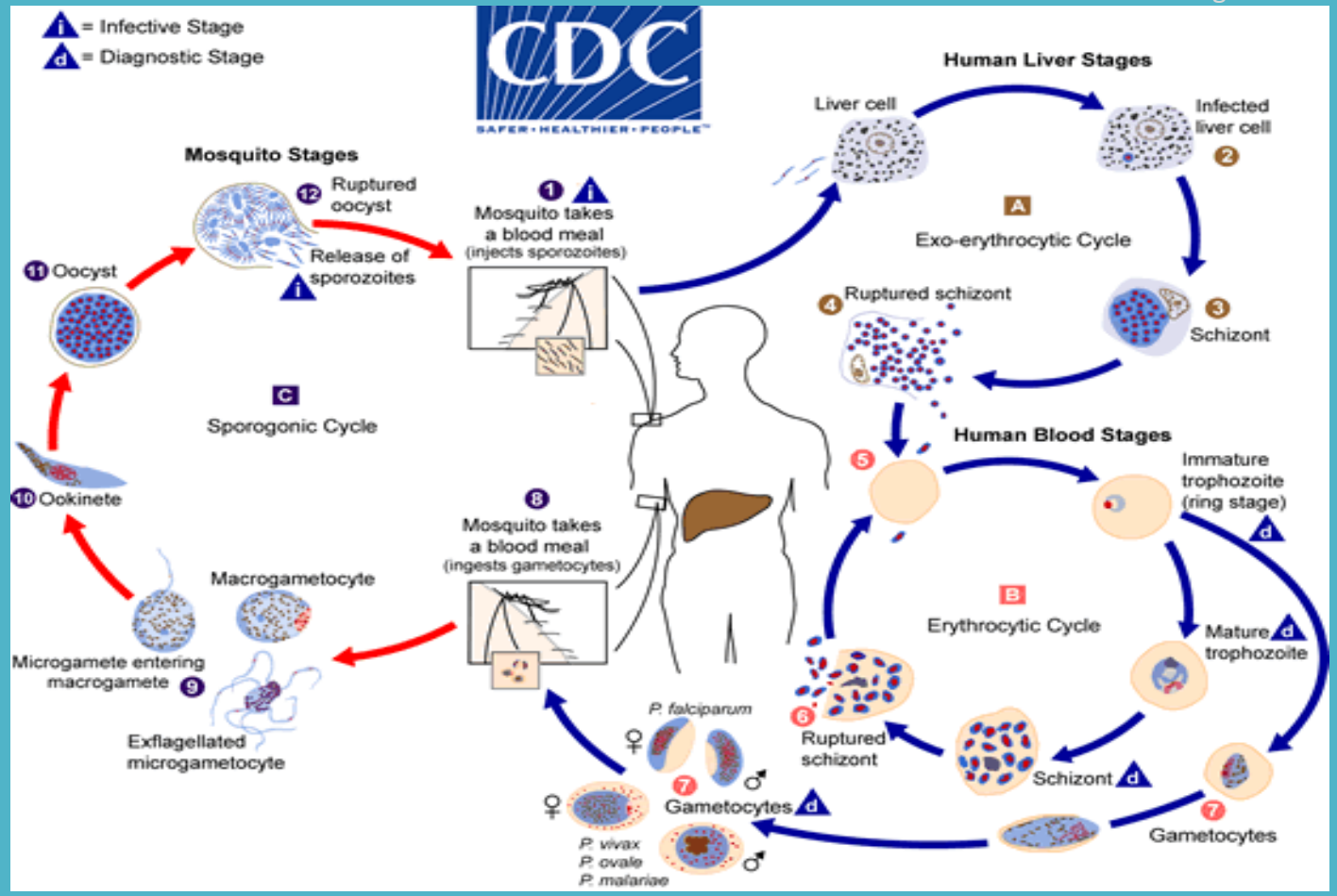

Life cycle of Malaria parasite

- Two hosts, Sporogonic cycle in *Anopheles* mosquito; and
- Exoerythrocytic cycle: Maturation into schizont, dormant hepatic hypnozoites
- Erythrocytic cycle: asexual multiplication in the erythrocytes, maturation to trophozites & gametocytes

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Diagnosis

- Thin and Thick films stained with Giemsa at pH 7.2 or Field stain
- Examined by two trained BMSs
- Parasitaemia for *P. falciparum* and *P. Knowlesi*
- Antigen-based rapid diagnostic tests as supplementary test
- Real-time PCR and LAMP nucleic-acid detection - 10-fold more sensitive than microscopy

Treatments

- Artemisinin combination therapy or Oral quinine or atovaquone with proguanil hydrochloride for uncomplicated *P. falciparum* malaria.
- Intravenous artesunate in severe or complicated *P. falciparum* malaria
- Exchange blood transfusion in severe *P. falciparum* malaria with parasitaemia above 10%
- For a radical cure, primaquine with chloroquine treatment: dormant hepatic forms of *P. vivax* and *P. ovale*
- Primaquine may cause haemolysis in G6PD deficient individuals
- Drug resistance - Chloroquine-resistant *P. vivax* & *P. falciparum*

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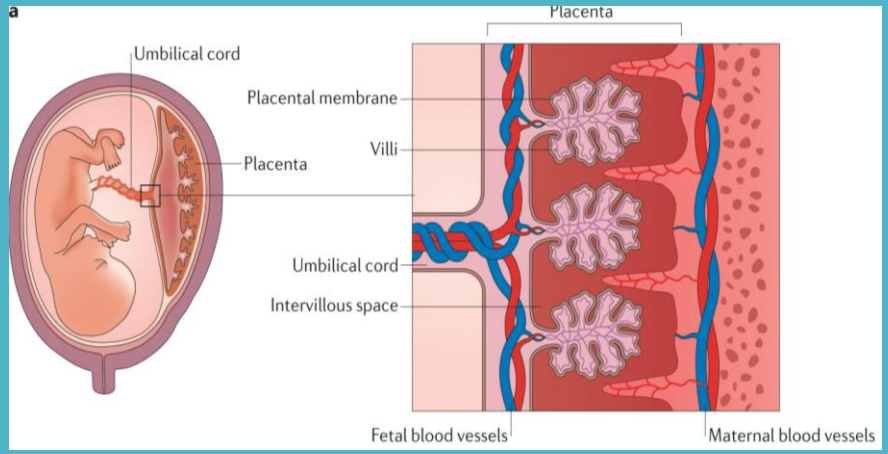
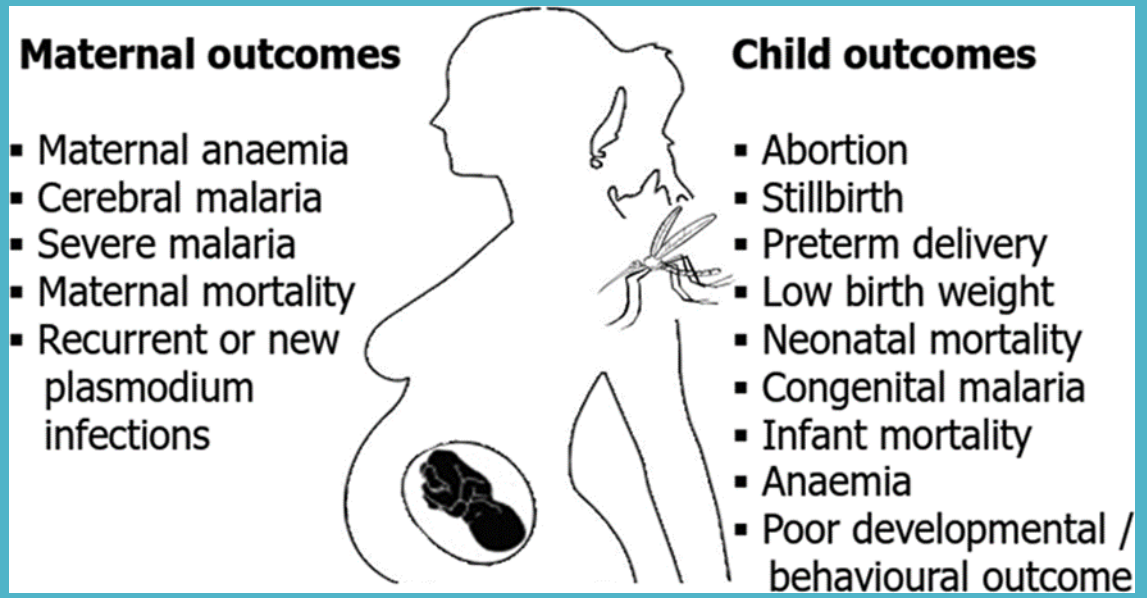
Congenital malaria

- Potentially life-threatening infection of neonates
- Cause due to vertical transmission of malaria during pregnancy or at birth.
- Postulated mechanisms
  - Transmission include maternal transfusion into the foetal circulation either at the time of delivery or during pregnancy,
  - Direct penetration through the chorionic villi
  - Penetration through premature separation of the placenta
- Presence of asexual stages of the parasite cord blood or in the peripheral smear of the neonates in the early stage of life



- Infected RBCs lodge in intervillous space
- Placental sequestration cause impaired utero-placental blood flow
- Increase in monocyte infiltrates in placental intervillous space and cytokines affect nutrient transport mechanisms.

Neonatal deaths, stillbirths, low birth weight, preterm delivery spontaneous abortions, intrauterine growth retardation and anaemia.



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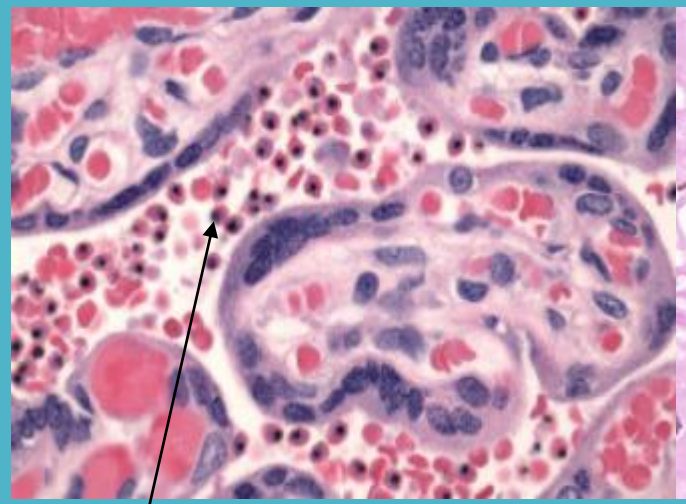
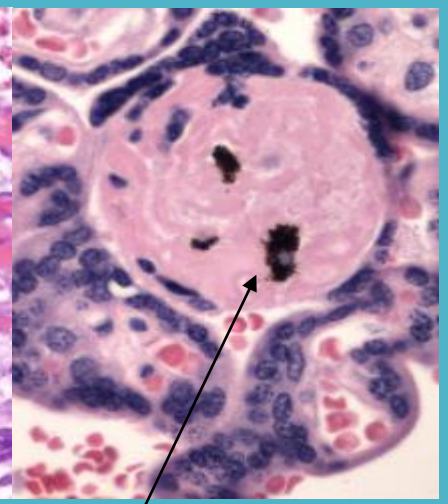
Diagnosis of Congenital malaria

In case of suspected congenital malaria, neonates should be screened for malaria with gold standard thick and thin blood films at birth and weekly for 28 days

- Cord blood sample, placenta blood sample, fresh placental tissue sample required for PCR
- Placental smear /histological sections of placenta to detect malarial pigment (haemozoin)





Parasitized erythrocytes sequester in the intervillous space

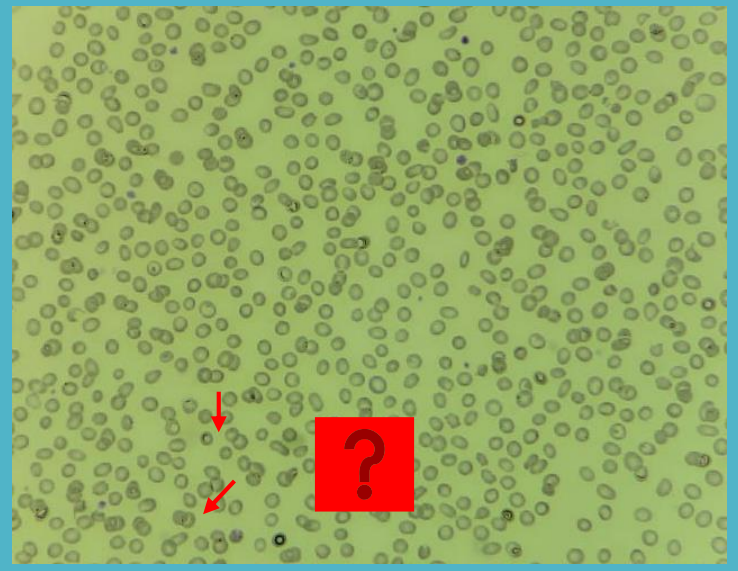
Haemozoin deposition in fibrin mesh

Clinical case

37 year old pregnant woman, 36 weeks gestation, feeling unwell with generalised body pains, headache, vomiting with lower abdominal pain. No PV bleed. Recently arrived from Nigeria. Last prenatal done in Nigeria.

Blood results showed elevated inflammatory markers, and mild thrombocytopenia. Patient received an emergency C-section.

FBC					
WBC	7.4	Mono	0.6	NA	141
RBC	4.02	Eos	0.0	K	3.9
HB	- 94	Baso	0.0	AKI Stage	0
HCT	- 0.29	Coag		D	
MCV	- 71.2	PT	12.0	HCRP	
MCH	- 23.3	INR	1.1	HCRP	+ 115.7
MCHC	327	Fib Derive	+ 6.5	Liv.Profil	
RDW	14.9	APT	29.4	ALB	- 29
PLT	- 81	APTR	1.0	TBIL	11
Neuts	5.9	EC		ALP	105
Lymph	- 0.8	EGFR	>90	ALT	10
		CREAT	- 36		



Samples from delivery suite : platelets dropped further, blood film (pH 6.8) shows thrombocytopenia and ring form trophozoites in RBCs.

Ward informed of possible Malaria infection and sample was processed for MP - Positive for *P. falciparum*, parasitaemia of 1.75%. Patient was treated with Artesunate.

Baby was already delivered; Thus cord/placenta samples were not taken

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Blood samples were processed from new-born, blood cultures were negative, MP negative
Received Benzylpenicillin & Gentamycin
Discharged with weekly follow-up appointments

FBC				EC			
WBC		18.4		CREAT		40	
RBC	-	4.50		NA		140	
HB		151		K		4.4	
HCT		0.48		D			
MCV		105.5		HCRP			
MCH	+	33.5		HCRP		0.3	
MCHC		318		SLIDE			
RDW	+	16.3					
PLT		234					
Neuts		13.3					
Lymph		2.5					
Mono	+	2.1					
Eos	+	0.5					
Baso		0.1					

Date\Time	RDW	PLT
0803231128	16.3	234
1003231652	16.4	225
2203230333	16.0	133
2403231129	16.2	19
2403231711	15.9	32

Week 2 appointment - DNA
Week 3 appointment
22/3/23 – Admitted with fever, B/C-, CSF – no growth, No diagnosis

24.03.23	K,23.1453682.X	WILL	D,EC,F,HCRP,LB,MC,SLIDE,UR
22.03.23	K,23.1452632.X	WILL	CFPR
22.03.23	K,23.1452119.M	AE	EC,F,HCRP,LB,UR
22.03.23	K,23.1452631.B	WILL	CFGL
16.03.23	K,23.1444880.Q	ASP	HCRP
10.03.23	K,23.1446677.N	DS	F,MC,MP,SLIDE
09.03.23	K,23.1445800.P	ASP	HCRP
08.03.23	K,23.1445271.P	DS	D,EC,F,HCRP,SLIDE

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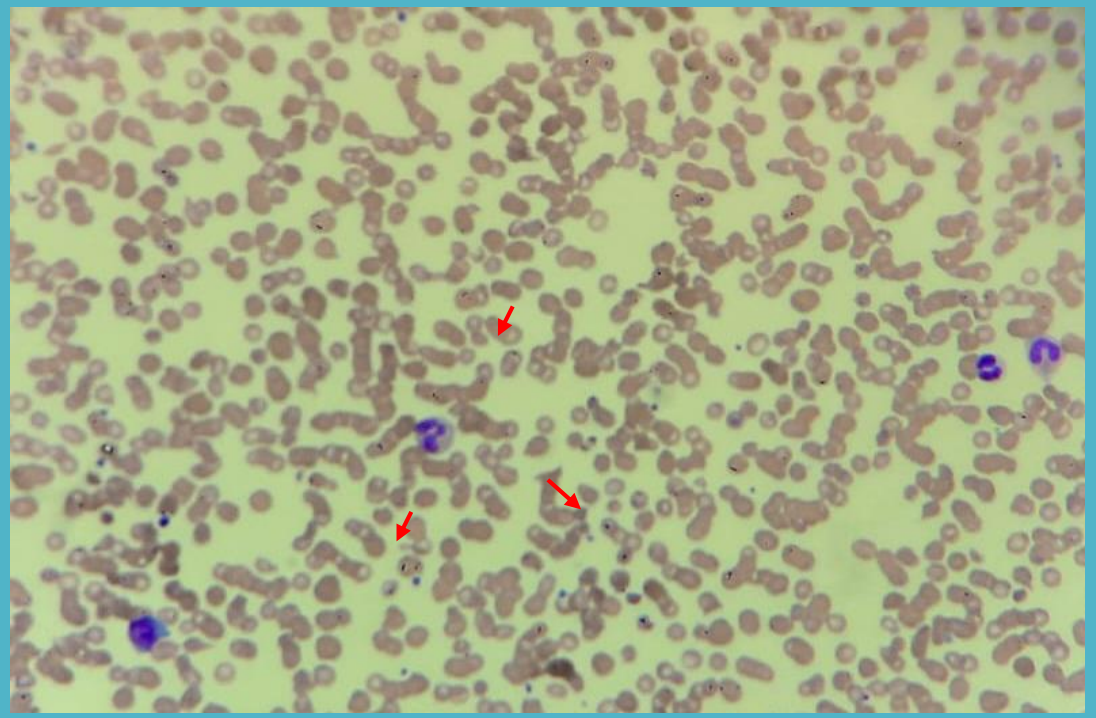
Department: Haematology

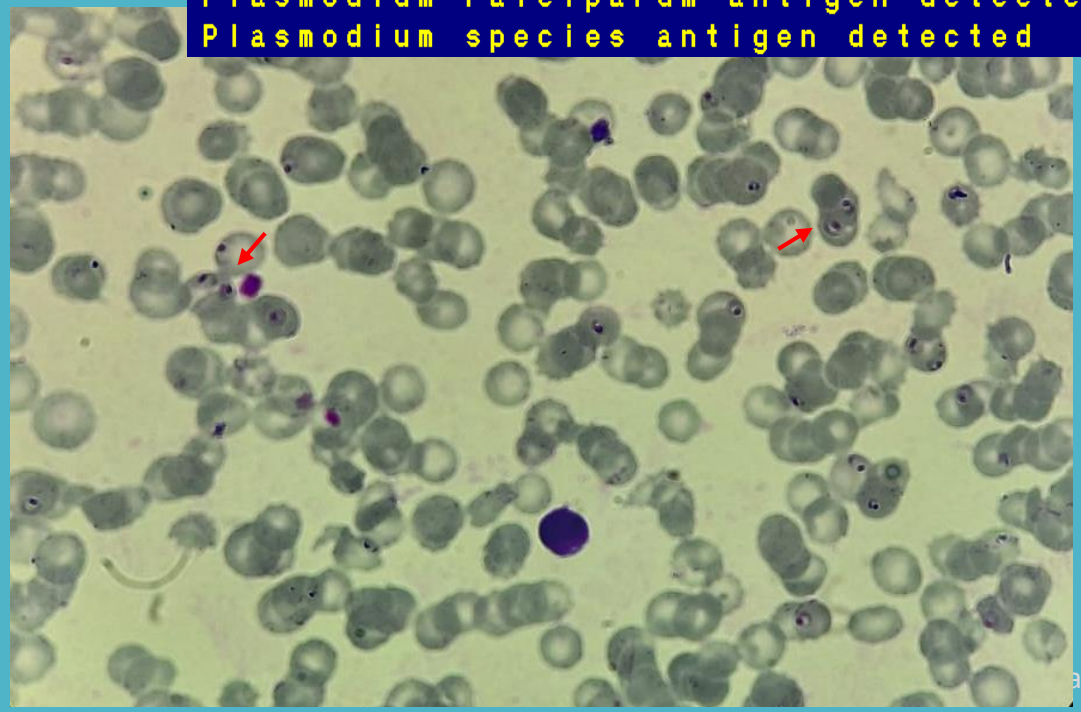
Talk title: Congenital Malaria

FBC					
WBC	6.9	Mono	0.6		
RBC	3.60	Eos	0.0	Liv/Bone p..	
HB	118	Baso	0.0	ALB	33
HCT	0.35	EC		TBIL	+ 79
MCV	97.2	CREAT	28	ALP	183
MCH	32.7	NA	142	CA	2.27
MCHC	336	K	5.1	PO4	1.76
RDW	+ 16.2	AKI Stage	0	Adj. Ca	2.41
PLT	- 19	D		ALT	28
Neuts	- 0.4	HCRP			
Lymph	5.8	HCRP	+ 34.7		
D	Platelet numbers appear markedly reduced on blood film				

Results from samples collected on 24/3/23



Early and late Trophozoites of P.Falciparum
Parasitaemia 9.5%
Plasmodium Falciparum antigen detected
Plasmodium species antigen detected



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- Treated with Artesunate, Cefotaxime and Amoxixillin
- Monitored VBG, ECG, risk of haemolysis, urine out-put, Potassium, glucose levels and renal function, parasitaemia levels and inflammatory markers
- Paediatric team liaised with South Thame Retrieval service

Date\Time	Specimen	MP
100323 1652	K,23.1446677.N	N
240323 1711	K,23.1453867.Q	P
250323 0026	K,23.1455090.H	P
260323 1219	K,23.1455799.V	N
290323 1040	K,23.1454451.J	N
060423 1045	K,23.1460990.Y	N
170423 1524	K,23.1465669.G	N

Plasmodium falciparum parasitaemia = 0.8%

Follow-up MP screening with negative results

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Conclusion

- Congenital malaria is rare, but can occur
- Pregnant women are the most vulnerable group of malaria-associated morbidity and mortality
- Congenital malaria has devastating effects on the developing foetus and new-born resulting in various outcomes
- Diagnosis of congenital malaria can be very challenging
- Guidelines on laboratory diagnosis, treatment and management of congenital malaria under discussion
- Open-up the discussion of MTD approach, importance of communication and updating the procedures and guidelines

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