



HEMATOPOIETIC & LYMPHATIC SYSTEM

SUBJECT : _____

LEC NO. : 2

DONE BY : Tabark Aldaboubi



وَقُلْ رَبِّ زِدْنِي عِلْمًا

2- Plasmodium and Malaria

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Hematopoietic and Lymphoid system
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Objectives

- Describe the morphology, life cycle, epidemiology, pathogenesis, immunity, clinical presentations, diagnosis, management and prevention of malaria

Parasitology

هو ال agent المسبب للملاريا

Parasitology مجموعة ال

- The plasmodia are sporozoa in which the sexual and asexual cycles of reproduction are completed in different host species
Sexual and asexual ← 2 part of life cycle
Sporozoa هي العائلة التي
mosquitoes ← host مختلفة
human ←
- The sexual phase occurs within the gut of mosquitoes that subsequently transmit the parasite while feeding on a vertebrate host
الناقل الرئيسي للملاريا
البعض يمرض الإنسان وغيره من ال Vertebrate حتى يتغذى على ال blood تابعه اثناء ذلك ينقل ال parasite لك انسان
- Within the red blood cells (RBCs) of the vertebrate, the plasmodia reproduce asexually; they eventually burst from the erythrocyte and invade other uninvolved RBCs. This event produces periodic fever and anemia in the host, a disease process known as malaria
بروح ال parasite ع RBC وبتبدأ مرحلة ثانية من المرض
ال parasite بصير يتكاثر جوا ال RBC بحطمها بعدها بروح لخلية جديدة
- Of the many species of plasmodia, four are known to infect humans and will be considered here: *Plasmodium vivax*, *P. ovale*, *P. malariae*, and *P. falciparum* الاخطر

Life Cycle

ناقل الملاريا هو البعوض ولكن مش كل انواع البعوض بنقل

1. The sexual cycle

Vector

الملاريا هو نوع واحد الي بنقل واسمه :

1. Begins when a female **Anopheles** mosquito ingests circulating male and female gametocytes while feeding on a malarious human
2. In the gut of the mosquito, the gametocytes mature and effect fertilization. The resulting zygote penetrates the mosquito's gut wall, lodges beneath the basement membrane, and vacuolates to form an oocyst
3. Within this structure, thousands of sporozoites are formed. The enlarging cyst eventually ruptures, releasing the sporozoites into the body cavity of the mosquito
4. Some penetrate the salivary glands, rendering the mosquito infectious for humans

2. The asexual cycle

1. Occurs in the human and begins when the infected Anopheles takes a blood meal from another individual
2. Sporozoites from the mosquito's salivary glands are injected into the human's subcutaneous capillaries and circulate in the peripheral blood
3. Within 1 hour they attach to and invade liver cells (hepatocytes)
4. Each sporozoite producing about 2000 to 40,000 daughter cells, or merozoites *Infection stage transmitted from mosquito to*
5. One to two weeks later, the infected hepatocytes rupture, releasing merozoites into the general circulation

تبدأ ال life cycle بال sexual تتم فيه ال mosquito بتيجي البعوضة بتقرص الانسان عشان يتغذى ع دمه اذا كان الشخص مصاب للملاريا ف ينتقل للبعوضة بروح الملاريا لل gut تاغت البعوضة وبصير mature لل gametocyte يكون بويضة بتفقس ويتكبر وبتنزل لل basement membrane بتتحول من oocystst ل zaygote ببلش يتمون داخلها العديد من ال parasite تسمى sporozoites بتنفجر وبتطلع ال sporozoites ل body cavity تاغ البعوضة وجزء منها بوصل لل salivary gland وهيئ بصير البعوضة ناقلة للملاريا المرحلة الثانية الي هي asexual ينتقل ال parasite للانسان البعوضة الي صار فيها الملاريا بتروح بدها تتغذى مرة ثانية بتروح ع انسان جديد بتقرصوا وبتنقلوا الملاريا (البعوضة بتعمل ingestion لل saliva تاغتها وبتنقل الملاريا

الشخص ما بحس بالقرصة اول ما ينقرص ، البعوضة بتيجي تهدي ع جسم الانسان الها خرطوم بتغرزوا تحت سطح الجلد حتى توصل للدم عندها ال saliva فيها يحتوي ع مجموعة من المواد جزء منها بعمل parastesia بوقف الالم مكان القرصة وجزء anticloting يمنع تجلط الدم خلال ساعة بوصل ع الكبد وبتكاثر هناك وبعدين بطلع ع الدم عشان ما يدخل من اولها قبل ما يتكاثر بمواجهة مع جهاز المناعة ويغلبوا

Life cycle

Habitat: Red Blood Cells (Early after infection the Plasmodium inhabits the liver cells for a certain time).

Vector: Females of *Anopheles* mosquitoes (**definitive host**)
 لئنا هي المصار فيصا ال Sexual

Intermediate host: Humans → Asexual مصار فيصا

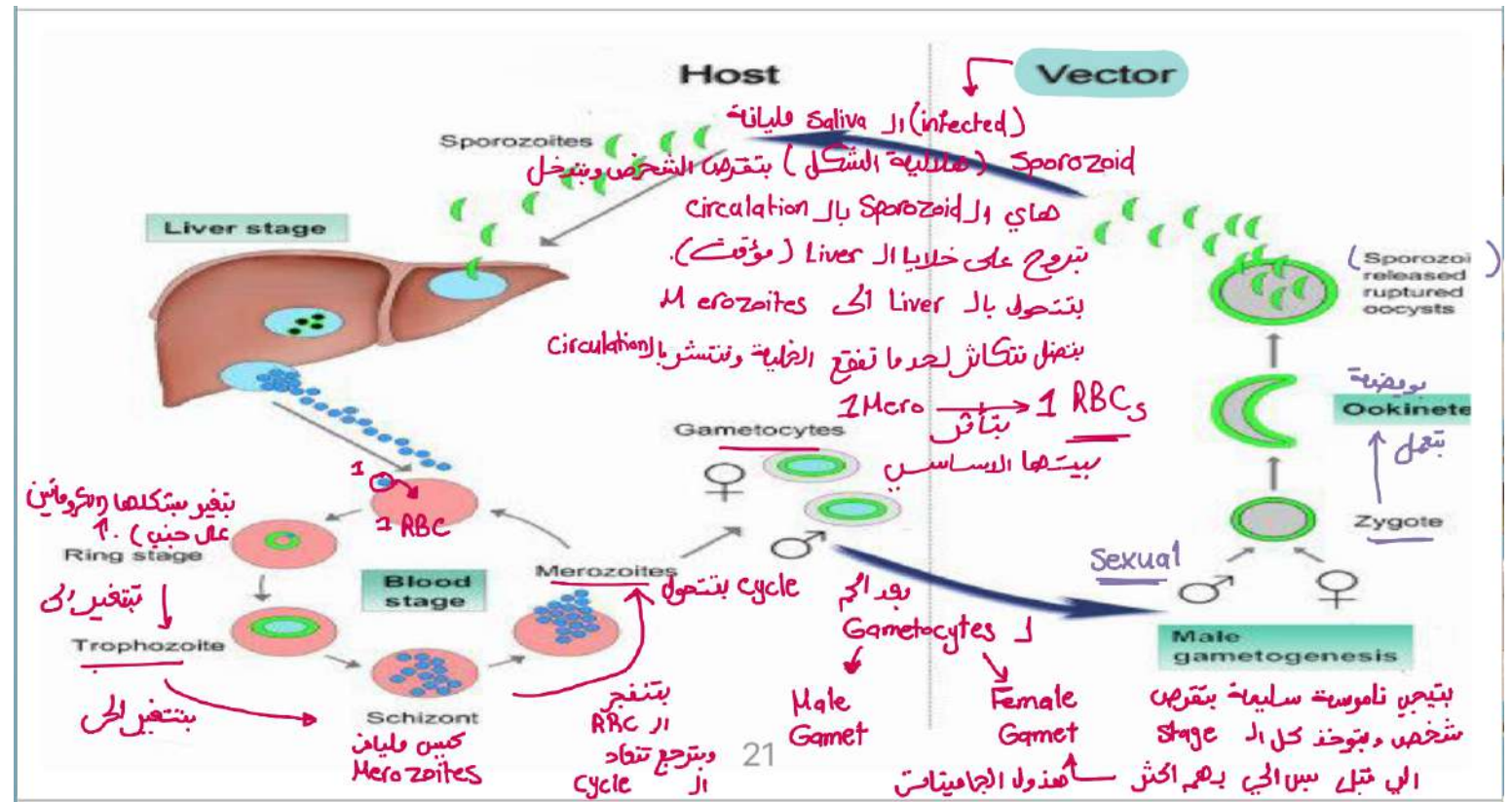
Infective stage: Sporozoites in the saliva of infected female mosquitoes.

Mode of infection:

- Bite of Females of *Anopheles* mosquitoes.
- Blood transfusion. - Transplacental transmission (congenital malaria).

Diagnostic stages: All stages (Ring, trophozoites, schizonts and gametocytes).

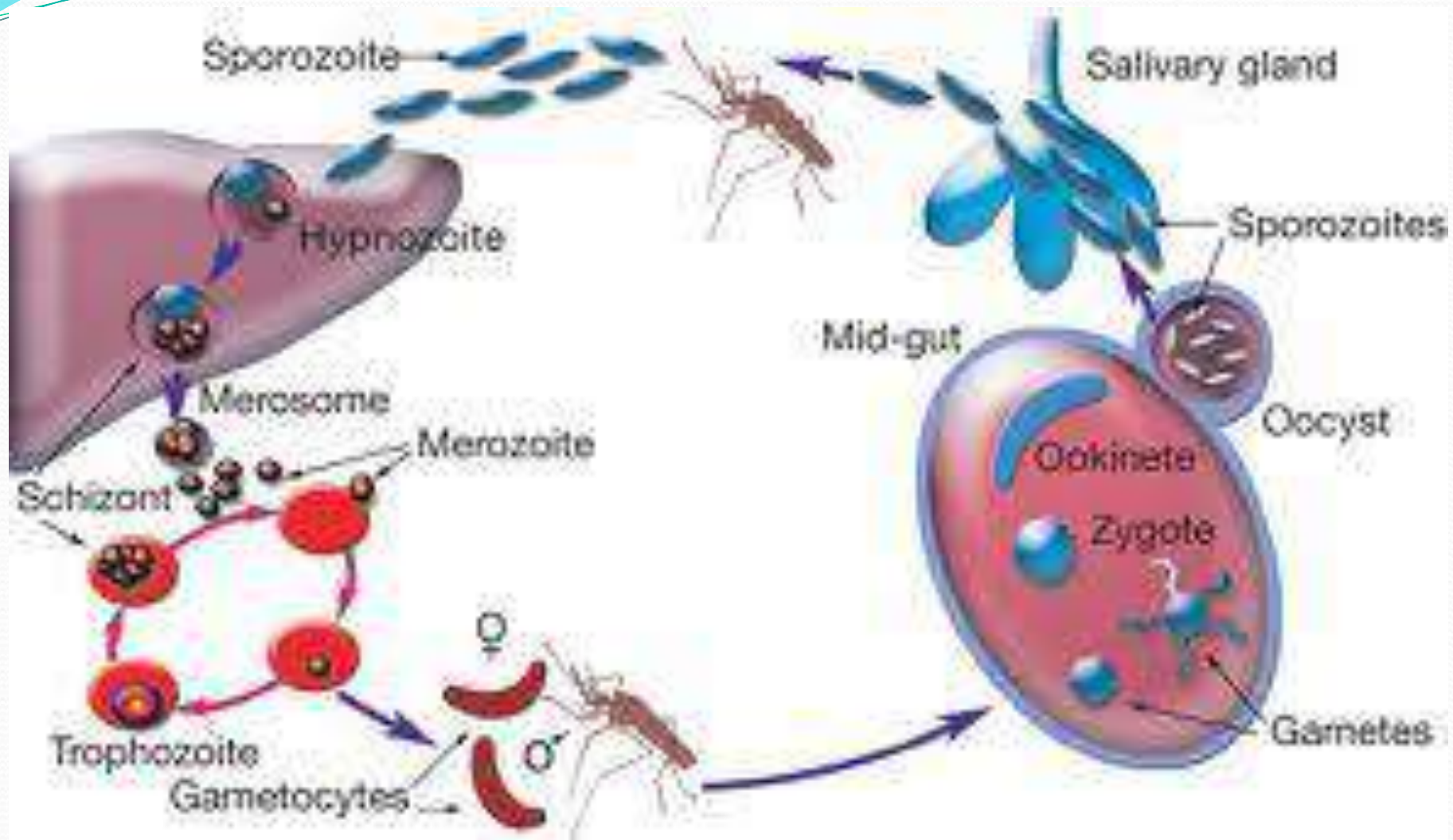
ربط مع مايكرو الجينيرال



3. The erythrocytic phase

target cell in malaria: RBC (mature)
B 19: premature RBC

1. Starts with the attachment of merozoite to a specific receptor on the RBC surface
2. After attachment, the merozoite invaginates the cell membrane and is slowly endocytosed. The intracellular parasite initially appears as a ring-shaped trophozoite, which enlarges and becomes more active and irregular
3. Within a few hours, nuclear division occurs, producing the multinucleated schizont
4. Cytoplasm eventually condenses around each nucleus of the schizont to form an intraerythrocytic cluster of merozoite daughter cells
5. Infected erythrocytes rupture, releasing the merozoites and producing the first clinical manifestations of disease
6. Other daughter cells are transformed into sexual forms or gametocytes, continue to circulate in the peripheral vasculature until ingested by an appropriate mosquito



من تغريغ زفحة امل

هون بغوت ال parasite نجوا خلايا الدم عن طريق receptor معين يتصل فيه وبصير لها endocytoses لجوا الخلية

وال Merozoites بتصير Trophozoite يكون ring-shape **دشكرا الخاتم**

هسا يتقسم جوا خلايا الدم كل وحدة بتعطي 20-30 وحدة تقريبا وخلال ساعات بتصير على شكل multinucleated schizont اللي خليا نقول عبارة عن كمتة trophozoites بتجمعات مع بعض

بعدين بتجمع ال Cytoplasm حوالي كل نواه من الأنوية الموجودة بال schizont وبتنج merozoite جداد جوا ال RBC

بعد فترة معينة هاني ال RBC يزيد فيها الحمل وبتفجر وبتطلع كل ال merozoite اللي جواتها لبرا (وهون ينشوف اول clinical picture للملاريا= اللي هي ال fever)

Stage transmitted between RBC : merozoites

وهطول ال merozoites يرجعو بروحو على خلايا دم ثلثة، وهكذا، وبتستمر الدائرة

بعض هطول ال merozoites يكون gametocytes، وهسا بالحالة هاني اذا اجت بعوضة وقرصت هاط الشخص بعدين قرصت واحد تاني، رجعا عالدارة من اولها بشخص تاني

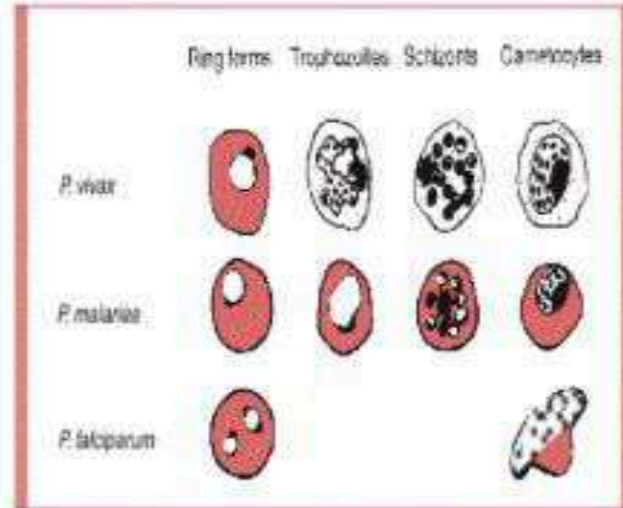
Sexual reproduction
↓
بتؤخذ منه ال gametocyte وبصير

Morphology

- The morphology of the stained intraerythrocytic parasites shows three characteristic features:
 1. red nuclear chromatin
 2. blue cytoplasm
 3. brownish-black malarial pigment, or hemozoin
- The change in the shape of the cytoplasm and the division of the chromatin at different stages of parasite development are obvious
- Gametocytes can be differentiated from the asexual forms by their large size and lack of nuclear division

division

النوع Gametocytes ما يعملو nuclear division ويكونو كبار ويكونو banana shape



إحنا بنعرف انه ال RBC ما فيها نواه ولا organelles

فالأصل ما نشوف اشي جواتها زي النقط الحمراء اللي بالرسمات، هاي الشغلات اللي جوا عبارة عن ال parasite و ال nuclear material تبعته

شوي شوي يتبلش تكبير تا نعمللنا ring-shape اللي حكيئا عنه فوق

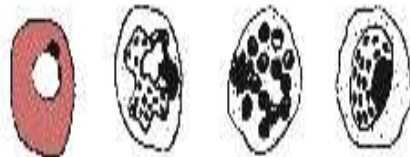
وبعديها بتعمل ال clusters اللي قلنا عنهم هي الرسمات واضحات

قارتوهم باللي حكيناه عن ال erythrocytic phase

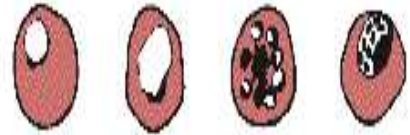
لاحظو اشي من الرسمة انه ال p.falciparum فيها 2 rings مش واحد بس وهذا اشي مميز الها بخليئا
تميزها أكثر بالمجهر، واحنا قلنا اصلا انها اسوء واحظرو وحدة

Ring forms Trophozoites Schizonts Gametocytes

P. vivax



P. malariae



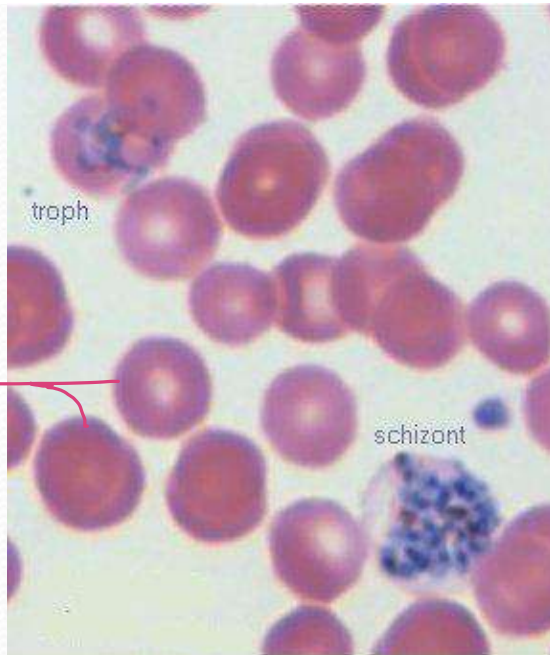
P. falciparum



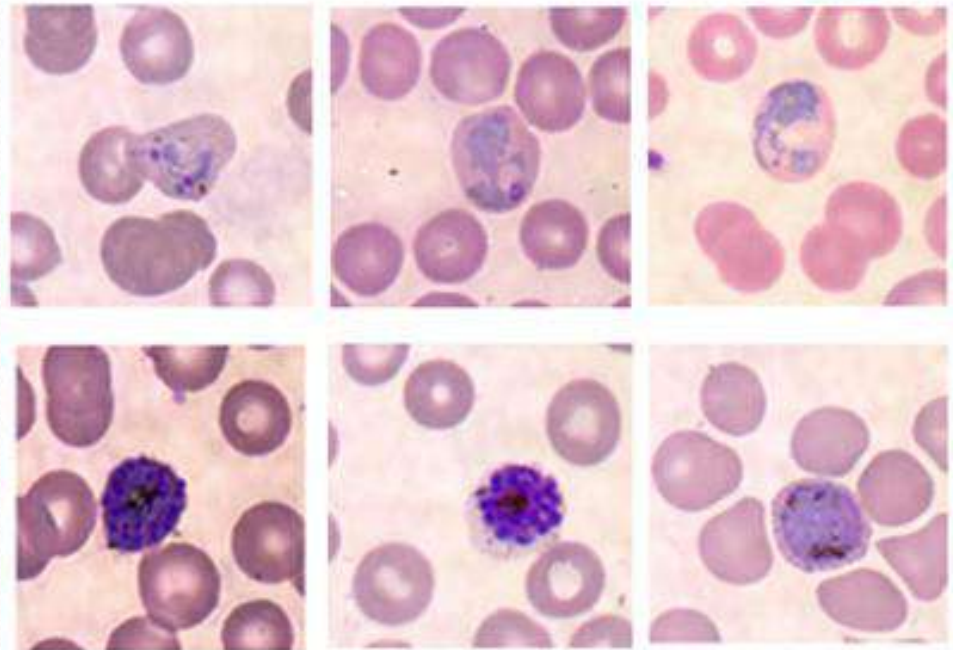
double ring form



Examples of erythrocytic stages of malarial parasites. Note: Trophozoite and schizont forms of *Plasmodium falciparum* occur in visceral capillaries rather than in blood. Male and female gametophytes show distinctive morphologic differences.



Plasmodium vivax



Normal

لونها احمر طبيعي
وجود الهيموجلوبين

بتغير لونها مع دخول
الParasite لئذ يتقلص
الصيغ.

Epidemiology

البعض يحب المناطق الحارة والرطبة تكون فيها الملاريا endemic مثل أفريقيا، العراق، مصر، السودان، اليمن

- Malaria has a worldwide distribution . *P. vivax* is the most widely distributed of the four species, and together with the uncommon *P. malariae*, is found primarily in temperate and subtropical areas. *P. falciparum* is the dominant organism of the tropics. *P. ovale* is rare and found principally in Africa
- In hyperendemic areas transmission is usually constant, and disease manifestations are moderated by the development of immunity
- Mortality is largely restricted to infants and to nonimmune adults who migrate into the region

* بالمنطقة الـ endemic اول ما يتولد الطفيل بتقرصها البعوضات

يدخل الـ Parasite بجل infection ويقل كل الـ Symptom بعد ان يرجع يتقرصوا ثمان

مرة بصير infection ولكن صعد جهاز المناعة بيش تتعرف عليها رصكنا لحد ما يصير عنده مناعة كاملة.

Pathogenesis

* بصير الحرارة أثناء الـ WBC بتفرز Cytokines بتروح على الـ brain
وتتفع درجة الحرارة وهو نوع من انواع الحماية للجسم .

1. Fever

- The hallmark of malaria, appears to be initiated by the process of RBC rupture that leads to the liberation of a new generation of merozoites (sporulation)
- The resulting fever is irregular and periodic. Because temperatures in excess of 40° C destroy mature parasites, a single population eventually emerges, sporulation is synchronized, and fever occurs in distinct paroxysms at 48hour or, in the case of *P. malariae*, 72-hour intervals

Pathogenesis

1. Fever

- The **hallmark** of malaria, appears to be initiated by the process of RBC rupture that leads to the liberation of a new generation of merozoites (**sporulation**)
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ليش ال fever بتكون متقطعه؟

بكل بساطة لانه الهدف من ارتفاع درجة الحرارة نقتل ال merozoites اللي موجودة بالدم برا ال RBCs , فبترتفع الحرارة بتقتلهم بس بضل اللي جوا ال RBC, بترجع تنخفض الحرارة, بعد 48 ساعة او 72 ساعة بترجع تنفجر كمان RBCs فبرجع بصير في عنا ارتفاع بدرجة الحرارة

وهكذا..... (paroxysms)

2. Anemia

يعني بالعقل, عنا parasite وقاعد بتكاثر جوا ال RBCs أكيد بده يصير عنا أنيميا , أكثر من سبب, يلا نحكي الأسباب

- Parasitized erythrocytes are phagocytosed by a stimulated reticuloendothelial system or are destroyed at the time of sporulation

تکسیر ال RBC بعلل انیمیا

2. Anemia

- Parasitized erythrocytes are phagocytosed by a stimulated reticuloendothelial system or are destroyed at the time of sporulation
- Depression of marrow function, sequestration of erythrocytes within the enlarging spleen, and accelerated clearance of nonparasitized cells all appear to contribute to the anemia بکبر حجمه فبمبیر
یوکل RBC اکثر
- Intravascular hemolysis, although uncommon, may occur, particularly in falciparum malaria. When hemolysis is massive, hemoglobinuria develops, resulting in the production of dark urine. This process in conjunction with malaria is known as blackwater fever

hypotension ← vasodilation توسع

3. Circulatory Changes

- The high fever results in significant vasodilatation. In falciparum malaria, vasodilatation leads to a decrease in the effective circulating blood volume and hypotension
- The intense parasitemias *P. falciparum* is capable of producing adhesion of infected RBCs to the endothelium of visceral capillaries can impair the microcirculation and precipitate tissue hypoxia, lactic acidosis, and hypoglycemia. Although all deep tissues are involved, the brain is the most intensely affected

↓ الـ bone marrow نخان ، الـ RBC انقصر عليه بقل الـ Platelet وبصير

4. Thrombocytopenia

- Is common in malaria and appears to be related to both splenic pooling and a shortened platelet lifespan

5. **Acute transient glomerulonephritis** in *falciparum* malaria and progressive renal disease in chronic *P. malariae* malaria. These phenomena probably result from the host immune response, with deposition of immune complexes in the glomeruli

Immunity

فيه مناعة بس slow ان تكمن الاصابة مرة واحدة
حتى تصير Immune

- Once infected, the host quickly mounts a species- and strain-specific immunologic response that typically limits parasite multiplication and moderates the clinical manifestations of disease
- Without eliminating the infection. A prolonged recovery period marked by recurrent exacerbations in both symptoms and number of erythrocytic parasites follows
- With time, these recrudescences become less severe and less frequent, eventually stopping altogether

Clinical Manifestations

- The incubation period between the bite of the mosquito and the onset of disease is approximately 2 weeks
- The clinical manifestations vary with the species but typically include chills, fever, splenomegaly, and anemia
- The hallmark of disease is the malarial paroxysm. This manifestation begins with a cold stage, which persists for 20 to 60 minutes. During this time, the patient experiences continuous rigors and feels cold. With the consequent increase in body temperature, the rigors cease and vasodilatation commences, ushering in a hot stage. The temperature continues to rise for 3 to 8 hours, reaching a maximum of 40 to 41.7° C before it begins to fall. The wet stage consists of a decrease in fever and profuse sweating. It leaves the patient exhausted but otherwise well until the onset of the next paroxysm

الحمى ← Symptom Fever (كل ٤٨ ساعة)

المرحلة Stage

١. تبدأ بـ Cold stage (٣٧,٥ - ٣٨) ر ٣ دقائق
في حرارة بس المريض يكون مقشعر

٢. Hot stage (٣٨ - ٣٩) ر ٣ - ٨ ساعات

٣. Wet stage (٤٠ - ٤١)

بتكسر الـ RBC بتفسير تتجمع حوالين بعض ولسير
الـ blood vessel

malignant

- In falciparum malaria, capillary blockage can lead to several serious complications
- When the central nervous system is involved (cerebral malaria), the patient may develop delirium, convulsions, paralysis, coma, and rapid death
- When splanchnic capillaries are involved, the patient may experience vomiting, abdominal pain, and diarrhea with or without bloody stools
- Jaundice and acute renal failure are also common in severe illness
- Most deaths occur within 3 days

Diagnosis

blood smear

CBC → فحیة هیموجلوبولین
ولالک

↑↑ Bilirubin
↑ LDH

ممکنه تدورعی ال ال Antigen

- Malarial parasites can be demonstrated in stained smears of the peripheral blood in virtually all symptomatic patients. Blood are stained with Wright or Giemsa stain and examined for the presence of erythrocytic parasites. Thick smears, where erythrocytes are lysed with water concentrate the parasites and allow detection of mild parasitemia
- Simple, specific card antigen detection procedures are now available. The most widely used test, ParaSight F, detects a protein (HRP2) excreted by *P. falciparum* within minutes. The test can be performed under field conditions and has a sensitivity more than 95%. A second rapid test, OptiMAL, detects parasite lactate dehydrogenase, and, unlike ParaSight F, can distinguish between *P. falciparum* and *P. vivax*
- Serologic tests are offered at large reference laboratories but are used primarily for epidemiologic purposes

Treatment

Antimalaria

- The indications for treatment rest on two factors:
 1. The first is the infecting species of Plasmodium
 2. The second is the immune status of the afflicted patient
- Falciparum malaria is potentially lethal in nonimmune individuals such as new immigrants or travelers to a malarious area and immunosuppressed indigenous individuals such as pregnant women. These individuals must be treated emergently
- The complete treatment of malaria requires the destruction of the erythrocytic schizont, the hepatic schizont, and the erythrocytic gametocyte

• Termination of Acute Attack

1. Several agents can destroy asexual erythrocytic parasites. Chloroquine, has been the most commonly used *drug of choice*
2. Chloroquine-resistant strains of *P. falciparum* are now widespread in Africa and Southeast Asia
3. Other agents include quinine/quinidin

• Radical Cure

In *P. vivax* and *P. ovale* infections, hepatic schizonts persist and must be destroyed to prevent reseedling of circulating erythrocytes with consequent relapse. Primaquine, is used for this purpose

بعض
هنا
الدوا

Liver بتحنو بال

Prevention

1. Personal Protection

In endemic areas, mosquito contact can be minimized with the use of house screens, insecticide within rooms, and/ or insecticide-impregnated mosquito netting around beds. Those who must be outside from dusk to dawn, the period of mosquito feeding, should apply insect repellent and wear clothing with long sleeves and pants. In addition, it is possible to suppress clinical manifestations of infection with a weekly dose of chloroquine



2. General

Malaria control measures have been directed toward reducing the infected human and mosquito populations to below the critical level necessary for sustained transmission of disease. The techniques employed include those mentioned previously, treatment of febrile patients with effective antimalarial agents, chemical or physical disruption of mosquito breeding areas, and use of residual insecticide sprays

3. **Chemoprophylaxis:** anti-malaria prophylaxis before travelling to endemic area

4. Vaccines

Advances in the last decade have produced the hope that an effective malaria vaccine might be within reach of medical science for the first time

Prevention

اللي يعرف حدا بسافر على مناطق فيها ملاريا زي قوات حفظ السلام بالجيش ودكاترة أطباء بلا حدود يعرف انه في اجراءات وقائية يتبعوها عشان ما يتعرضو للأصابة خلال فترة وجودهم بهاي البلد

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يعني بتحاول قدر الامكان تقلل من احتمال انه تقرصك ناموسة

وبكون في عنا كل اسبوع dose مع ال chloroquine

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3. Chemoprophylaxis: anti-malaria prophylaxis before travelling to endemic area

بالعادة ال tetracycline and doxycycline مفيدين كثير بالوقاية, واحيانا يستخدمو ال chloroquine كمان

فبتلاقي الشخص طول فترة وجوده بهاي الدولة قاعد بوخذ العلاج as a prophylaxis treatment وبضل يستخدمه لبعده ما يرجع من السفر بأسبوع اسبوعين, خوفا من انه يكون صابه بأخر فترة ولسا الاعراض ما طلعت

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⊕ vaccine ما في اي

مع انه الملاريا قضت على حياة كثير ناس ولكن للحظة هاي ما حدا قدر يعمل لقاح مضاد لها

وبشكل عام اصلا ال parasitic infections ما الهم لقاحات عكس ال viral

لا يأس أعدو
المُحاولة مُجدداً

واستعن بالله

ستفجح

بالتأيد

esraaartstudio