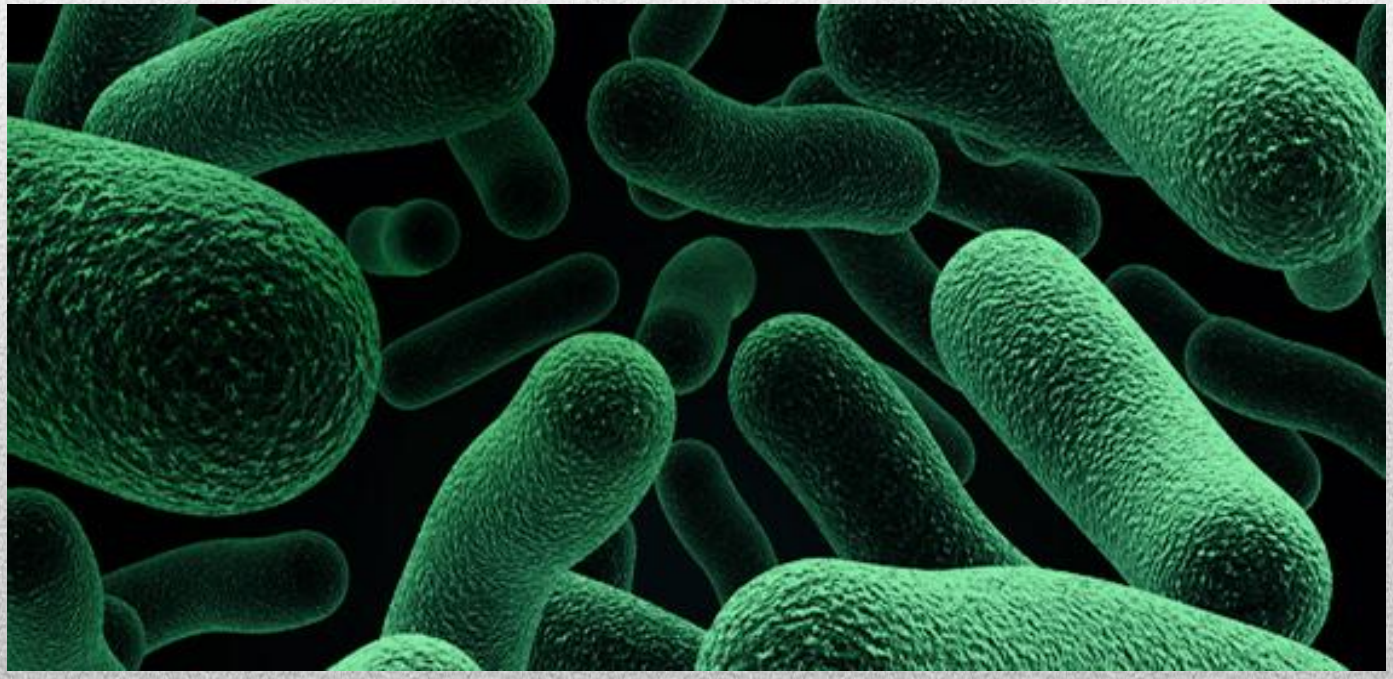
Lecture 1-12

Revision

Microbiology Team - 430



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Role of H.Pylori in Peptic Ulcer and drugs used in Treatment

- When abdominal pain is associate with meals its properly gastric ulcer. If not it most likely to be a case of duodenal ulcer
- Peptic ulcer is characterized by an abdominal pain, Melena, bloating and Haematemesis
- H.Pylori are found closely associated with gastric mucosa and causes chronic active gastritis, gastric and duodenal ulcer (Peptic ulcer) & adenocarcinoma
- H.Pylori is a gram –ve bacteria that can grow on campylobacter selective medium. Small colonies after 3-7 days.
- Diagnosis of infection is usually made by checking for dyspeptic symptoms and some other tests. However, the most reliable method for detecting H. pylori infection is endoscopy followed by histological examination and microbial culture. We can also use Carbon urea breath test (C14 or C13)
- Bacterial strains that have the CagA gene are associated with an ability to cause ulcers .Therefore; patients carry H pylori strains lacking the Cag pathogenicity island (PAI) are Asymptomatic
- H.Pylori enters the stomach and move through it using flagella. Then hide under the gastric mucosa. Produces adhesions that bind to the epithelial cells and produces large amounts of urease enzyme that break down urea into ammonia which is toxic to epithelia therefore it will cause an inflammatory response which lead into ulcer
- Proper sanitation and clean sources of drinking water is the most effective way to prevent H.Pylori infection
- The standard first-line therapy is a one week "triple therapy" consisting of proton pump inhibitors (such as omeprazole, lansoprazole) and antibiotics
- The most effective thereby and the one that it used in KSA is :
- One-week combination of Omeprazole + Amoxicillin + Metronidazole
- Recently, antibiotics (metronidazole, clarithromycin) are becoming resistance to H pylori.

Normal Flora & introduction of Infectious Diarrhea:

- Diarrhea is defined as Alteration in normal bowel movement characterized by decreasedconsistency and increased frequency.
- There are two types of strains that cause diarrhea:

  1. Invasive strains = dysentery (due to inflammation) contains WBCs (pus), blood and mucous.

  2. Enterotoxin Strains = watery diarrhea and loss of fluids.
- Causes of infectious diarrhea are: Viral (most common especially rota), bacterial [Campylobcator, Yersinea, Vibrio cholerae, E.coli] or protozoal infections.
- Bacteria that cause Food poisoning are: *Clostridium perfringens*, *S. Aureus* and *Bacillus cereus*.
- Antibiotic associated diarrhea is caused by Clostridium difficile
- The most important risk factors of acute diarrhea are: low stomach acidity, Antibiotics and decreased food and personal hygiene.
- Enterotoxin mediated mechanism is very rapid; IP is 6 – 18 Hrs and takes place in the small intestine and causes watery diarrhea.
- Invasive mechanism is slower; IP is 1 – 3 days, takes place in the colon and causes Dysentery.
- Campylobacter:
- Spiral Gram –ve bacilli.
- Most common species is C.jejuni.
- Most common source is Poultry [Chicken].
- Self-limiting, microaerophilic [requiring oxygen for growth but at lower concentration than is present in the atmosphere]
- Complication: Guillain-Barré syndrome.
- Diagnosis: Gram stain.
- Treatment: Erythromycin " Macrolides"

- **E.coli:**

Pathogen	Infection
Entero-toxigenic E. coli (ETEC).	**Traveler's diarrhea**
Entero-pathogenic E. coli (EPEC).	**Infentile diarrhea**
Entero-invasive E. coli (EIEC).	**Dysentery (blood & mucus)**
Entero-haemorrhagic E. coli (EHEC).	**Bloody diarrhea (very sever)**
Entero-adherent E.coli (EAEC).	**Pediatric diarrheal disease (same as EPEC)**

- **Serotype 0157:H7 of EHEC will cause hemorrhagic diarrhea, colitis, hemolytic uremic syndrome (HUS),hemolytic anemia and kidney failure**
- **EHEC Produces vertoxin1&2, which is similar to (shiga toxin 1&2)**
- **ETEC produces heat labile toxin (LT) and heat stable toxin (ST).**
- **Yersinia enterocolitica: most commonly found in Chitterlings [intestine of pigs], causes: Mesenteric lymphadenitis.**
- **Clostridium difficile: It causes Antibiotic associated diarrhea, Pseudomembranous colitis and treated by Metronidazole.**
- **Listeria monocytogenes has the longest IP (2-6 weeks) and found in cheese (dairy products) and it causes Gastroenteritis and meningitis.**
- **Clostridium botulinum causes paralysis and blurred vision.**

Cholera:

1. Cholera is an infection of the small intestine caused by Vibrio cholera.
2. Vibrio Cholera is a Gram (-) comma shaped bacteria with single flagellum (motile).
3. O-1 is the most common serotype.
4. It's transmitted by fecal-oral route (drinking contaminated water or eating sea food).
5. It's common in developing countries due to poor sanitation and low hygiene.
6. Low acidity in GIT as in using drugs such as anti-acids and PPIs is a risk factor.
7. V.cholera produces an enter toxin that ↑ cAMP and this will lead to ↑ osmolarity of the intestinal lumen and will drag more water with it until it causes dehydration.
8. Communicability is high during acute stage, and remains after recovery for 3 weeks.
9. Symptoms (watery diarrhea, Vomiting and Cramps) appear in 1-3 days.
10. Symptoms will lead to dehydration and it will cause many complications.
11. Patients will show (Sunken eyes and cheeks, decreased skin turgor and dry mucous membranes)
12. Diarrhea consists of fluids and electrolytes with enormous numbers of v.cholera, but there are no RBCs.
13. Confirmation is by isolationof v.cholera from stool by culturing it on TCBS agar and it will appear as yellow colonies.
14. Goal of treatment is fluid rehydration and it will decrease mortality rates to < 1%.
15. Antibiotics such as tetracycline are used as adjacent therapy to decrease duration and Communicability of the disease.

Intestinal Helminthes

1- Enterobius Vermicularis, Ascaris Lumberical &Trichuris Trichiura are transmitted by fecal-oral rout.
2- Hook worms transmitted by skin penetration.
3- Diagnosis of Enterobius Vermicularis is done by adhesion tape (scotch tape)& the main clinical presentation is pruritus ani.
4- The diagnosis of Ascaris Luberical is done by seeing eggs in the stool and the main complication is Loeffle's syndrome.
5- Diagnosis of Trichuris Trichiura is done by seeing eggs in the stool and the main complication is rectal prolapsed in children.
6- Trichuris Trichiura usually coexists with Ascaris Lumberical
7- Hook worm is the common cause of anemia.
8- Strongyloides infect Immuno-compromised Pt causing internal autoinfection& it is the most sever one and could lead to death. The diagnosis is done by seeing Rhabditiform larvae in stool&duodenal aspirate.
9- All the nematodes are treated by Albendazole.
10- Taenia saginata&solium are transmitted by ingestion of uncooked beef or pork.
11- Hymenolepis nana transmitted by fecal-oral rout.
12- Echinochoccus granulosus forming Hydatid cyst mainly in the liver.
13- Adult of *Taenia solium causing*taeniasis by ingestion of larvae in uncooked Pork.
14- Larvae of *Taenia solium causing* Cysticercosis by ingestion of egg in uncooked Pork.

Viral Gastroenteritis

1. Viral Gastroenteritis has no antiviral therapy, just a supportive therapy.
2. Clinical presentations -for all viruses- are similar (watery diarrhea, vomiting and fever).
3. Most common virus causing GE is Rotavirus especially group A.
4. No vaccine is availableagainst viruses causing GEexcept for Rotavirus.
5. Rotavirus vaccine is a life attenuated vaccine and it's given orally.
6. All viruses (Rotavirus, Adenovirus, Clicivirus, and Astrovirus) have a RNA genome exceptAdenoviruswhich has DNA genome.
7. Adenovirus type 40 & 41 causes GE.
8. All viruses (Rotavirus, Adenovirus, Clicivirus, andAstrovirus) causing GE are non-enveloped.
9. All viruses that cause GE are transmitted by fecal oral route.
10. Dehydration could happen as a complication of GE due to loss of Na by vomiting & diarrhea.
11. Best sample is stool sample.
12. For lab diagnosis, ELISA test is used to detect antigen in all viruses (Rotavirus, Adenovirus, Clicivirus, and Astrovirus).
13. Immunochromatography is a test that can be used for Rotavirus &Adenovirus.
14. Noroviruses (Clicivirus) infections affect all age groups and occur in closed communities.

Virus	Genome	Important Morphological features	Type of infection
Rotavirus	ds RNA (11 segments)	Double-Shelled With Wheel-Like Structure.	Endemic & epidemic
Adenovirus (40,41 types)	ds DNA	Classical Icosahedron with fibers.	Endemic
Calicivirus (Noroviruses)	ss RNA(+)	Cup-Like depression on its surface.	Epidemic outbreak in school.
Astrovirus	ss RNA(+)	5 or 6-Pointed Star on its surface.	Epidemic →in children

Salmonella and Shegella

	Salmonella	Shigella
Organisms	Non lactose fermenter gram negative bacilli	Non lactose fermenter gram negative bacilli
Motility of the organism	Motile	Non motile
Incubation period	Gastroenteritis →8-36 hrs Typhoid fever →1-2 weeks	24 - 48 hrs (1-2 days)
Infective dose	Low infective dose < 200 bacilli Highly Infectious	10^6 bacteria Low infectious
Source	• Salmonella non typhi → Water, food and milk contaminated with human or animal excreta • Salmonella typhi and S. paratyphi → the source is human	• Person to person through fecal –oral route
Antigenic structure	O. Somatic Antigen (Heat Stable) H. Flagellar Antigen (Heat Labile) VI. Capsular Antigen	O. Somatic Antigen K. Capsular Antigen

- Salmonella Typhi and S. Paratyphi → the source is human
- Shegella cause large intestinal disease
- The best diagnostic ways in salmonella → are blood culture and take specimen from stool but Shegella→ take specimen from stool
- Salmonella cause bacteremia but Shegellararely cause bacteriamia.

- Shegella are non-motile organism → lack H antigen (flagella antigen)
- Typhoid fever may be complicated to necrosis of the gall bladder or Bowel hemorrhage and perforation
- Shegella cause bacillary dysentery (blood, mucus and pus in the stool)
- The main symptoms of patient with Shegella are High fever, chill, abdominal cramp and pain accompanied by tenesmus of bloody stool with mucus

Human is the only reservoir in case of Shegella

- Shegella may be lead to rectal prolapsed in children
- No treatment in case of gastroenteritis expect in special situation.
- The treatment ismust in all cases of Shegella expect s.sonnieS. dysenteries type 1 associated with morbidity and mortality.

Trematodes (Schistosoma & Fasciola Hepatica)

1. Schistosomiasis is caused by infection of S. Haematobium, S. Mansoni,S. japonicum

2. Eggs hatch in water and Cercariadevelop in snails (intermediate host).

3. Infective stage of Schistosomiasis is penetrating human skin by Cercaria
And this will cause Schistosoma dermatitis (swimming itch).

	S. Haematobium	S. Mansoni
Route	veins draining the urinary bladder	veins draining large intestine
Complications	- Haematuria - Inflammation of bladder	- Dysentery - Hepatomegaly and splenomegaly
Diagnosis	Eggs in urine	Eggs in stool

5. Adult grows in liver and produces eggs which cause:
Deposition of eggs in liver tissue→cellular reaction (delayed hypersensitivity)
→Granuloma→fibrosis→long-term complications which are:
- Hepatosplenomegaly

- Periportal fibrosis (portal hypertension)

- Esophageal varices→Haematemesis
6. Eggs are responsible for the pathological condition not adults

7. Praziquantel is the drug of choice for Schistosomiasis.

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1. Fascioliasis is caused by Fasciola hepatica

2. Eggs hatch in water, Cercariadevelop in snails (intermediate host), and Metacercaria develop in aquatic plants
3. Infective stage of Fascioliasis is by eating contaminated water plants (Metacercaria)

4. Metacercariaexists in the duodenum then migrates to liver to become adults

5. Adults are responsible for the true infection which causes biliary obstruction and liver damage

6. False infection is by eating animals liver containing Fasciola eggs and disease does not occur, But eggs pass in stool (diagnostically there is an infection, but it is a false infection)
7. Diagnosis of Fasciola hepatica is done by finding eggs in stool or duodenal aspirate.

8. Triclabendazole is the drug of choice for Fascioliasis

Intestinal Protozoa

- Giardia lamblia are found in Cyst form in the external environment (which is diagnostic & infective stages), and in Trophozoites form in the duodenum (diagnostic stage)
- We can diagnose Giardia lamblia infection by Stools examination where we can find both cyct and trophozoites or we can do examination of duodenal contents looking for trophozoites. Then treat it with Metronidazole
- There are 6 species of intestinal Entamoeba. The invasive form and the one that cause amoebiasis is E.histolytica where is E. dispar specie is harmless and non-invasive.
- Entamoeba histolytica: goes into two forms :
  - Trophozoite: which is the active form and it only found in the small intestine and the large intestine (where it multiply). it goes under Vegetative stage " in large intestine " and the diagnostic phase
  - Cyst: is the form that is necessary to survive the environment. It goes under Infective stage and Diagnostic stage
- E.Histolytica is a water-borne infection with Fecal – oral rout & found only in humans
- As Giardia lamblia, E.Histolytica infection starts from contaminated food or water as mature cysts. And become Trophozoites at the small intestine. When it reach the mucosa of large intestine as Trophozoites it multiply and hydrolyze host tissues and cause flask -like ulcers lesions
- Lesions which are caused by E.Histolytica infection can be found in the cecum , colon ,or appendix (intestinal) and cause Amoebic dysenteryor invade & reach to blood vessels and then by portal circulation go to liver or to other organs such as brain or lungs (extra – intestinal).
- In order to diagnose E.Histolytica infection we use Stools examination for intestinal one and Serology "IHA , ELISA" for both intestinal (if its invasive) and extra intestinal
- Symptomatic patients with Amoebiasis are treated with Metronidazole as for the Asymptomatic (cysts only): Diloxanidefuroate (Furamide)
- Cryptosporidium Parvum can be ingested from swimming pools then excystation occurs in epithelial cells of the GIT or others tissues then it undergoes asexual multiplication
- Cryptosporidium Parvum, usually occurs in immune suppressed patients, infants, children and the elderly ones.
- We can diagnose C.parvum by using certain stains (acid-fast stain, safranin) or Serology (IFAT)
- C.parvum is Self-limited in immunocompetent patients but in immune suppressed patients (AIDs) we use paromomycin

- Giardis lamblia a Oral– fecal rout transmission where is C.parvum & E.Histolytica have an Fecal-oral rout
- C.parvum, Parasitize occurs in epithelial cells of the GIT or other tissues such "respiratory tract" where it undergoes asexual multiplication.
- Entamoeba histolytica affected large intestine and may cause Amoebic dysentery that may complicated to Amoeboma:Granulomatous mass obstructing the bowel

Viral hepatitis

Virus	Type of virus	Mode of infection	IP	Other comments
Primary infection (affecting liver)				
Hepatitis A (HAV)	ssRNA	Fecal oral	2-4 weeks	No carrier state, common in tropical countries.
Hepatitis B (HBV)	dsDNA	Blood borne, sexual	6 weeks - 6months	Carriage associated with liver cancer
Hepatitis C (HCV)	ssRNA	Blood borne	2 months	Carriage associated with liver cancer
Hepatitis D (HDV)	ssRNA	From blood	2-12 weeks	Needs concurrent hepatitis B virus infection
Hepatitis E (HEV)	ssRNA	Fecal oral (waterborn)	6-8 weeks (shortest)	Common in far east, no carrier state, outbreak of water born, zoonatic.
Generalized infection (systemic including hepatitis)				
Yellow fever	ssRNA	Mosquito	3-6 days	Common in Tropical Africa and south America
Epstein - Barr Virus (EBV)	dsDNA	Saliva & blood		Worldwide distribution
Cytomegalovirus (CMV)	dsDNA	Saliva	Replication cycle is longer.	Worldwide distribution

Diagnosis & management:

Virus	Diagnosis (detection of :)	preventation	Treatment
Primary infection (affecting liver)			
Hepatitis A (HAV)	Anti-HAV IgM	Vaccine (killed) HIG	Supportive
Hepatitis B (HBV)	Hepatitis B surface antigen (HBsAg)	Vaccine (recombinant, 6 doses) Specific HIG	α –interferon
Hepatitis C (HCV)	Antibody to HCV	No vaccine	pegylated alpha interferon and ribavirin
Hepatitis D (HDV)	Anti-HDV antibodies		
Hepatitis E (HEV)	Anti-HEV IgM.	NO vaccine	Supportive
Generalized infection (systemic including hepatitis)			
Yellow fever	IgM -AB	Vaccine (Life attenuated vaccine)	supportive
Epstein – Barr Virus (EBV)	↑ WBC, lymphocytosis IgM Abs positive Heterophile Abs	No vaccine	supportive
Cytomegalovirus (CMV)	Intranuclear inclusion bodies [Owl's eye]. IgM Ab IFA →CMV pp65 Ag Heterophile AB is –ve	No vaccine	Ganciclovir Foscarnet

- HAVcausescell mediated Immunity (CMI)result in(↑ ALT, AST & bilirubin).
- There is acombination vaccinefor(HAV & HBV).
- HEVissimilartoHAV except: HEVhaslonger IP4-8 weeks, higher mortality rates, causesfulminant diseaseand there'sno vaccine.
- Epstein – Barr Virus (EBV)is alymphotropic, has anoncogenic properties (can result in Burkitt's lymphoma or Nasopharyngeal carcinoma)
- EBVcan causeInfectious mononucleosis [glandular fever] in immunocompetent Pts, whileCMVcausesInfectious mononucleosis like syndrome

Markers of hepatitis B:

Types	Description
HBV DNA	Marker of infection.
(HBsAg) Hepatitis B surfaceantigen	Marker of infection.
(HBeAg) Hepatitis B e antigen	Marker of active virus replication, the patient is highly infectious; the virus is present in all body fluids.
(Anti-HBe) Antibody to hepatitis B e antigen	Marker of low infectivity, the patient is less infectious.
(Anti-HBc) Antibody to hepatitis B core	Marker of exposure to hepatitis B infection.
(Anti-HBs) Antibody to hepatitis B surface antigen	Marker of immunity.

- Hepatitis B viruses transmitted mainly parentally and prenatally , where is Hepatitis C virusestransmitted mainly parentally.
- Chronic hepatitis is limited to hepatitis B, C, D and may be G viruses.
- The majority of patients with chronic hepatitis B and C are asymptomatic or has mild fatigue only.
- HCV is extremely HETEROGENOUS, and has a high mutation rate.
- Hepatitis D viruses are a defective virus that cannot replicates by its own. So they need helper virus like HBV to replicate.
- Chronic cases of HBV and HCV may complicate to cirrhosis and hepatocellular carcinoma.
- The chronic hepatitis C patients may present as "Carrier state" with normal liver enzymes or typical chronic active hepatitis.

Haemoflagellates
(Leishmaniasis & Trypanosomiasis)

1. **there are 2 main types of leishmaniasis cutaneous and visceral**

leishmaniasis	*cutaneous*	*visceral*
Pathogen	*L.Tropica and L.Major*	*L.Donovani and L.Infantum*
Vector	*Sand fly*	
Occur in	*skin*	*the reticuloendothelial system (spleen, liver and bone marrow)*
Clinical presentation	- *Skin sore*	- *Hepatosplenomegaly* - *Fever, Anemia, weight loss, diarrhea*
Diagnosis	- *Skin biopsy or smear:* • *Microscopy → LD bodies* • *Culture in NNN media → promastigotes*	- *Bone marrow aspiration:* • *Microscopy → LD bodies* • *Culture in NNN media → promastigotes*

2. **Amastigotes inside humans and promastigotes inside sand flies (vector of disease)**
3. **Trypanosomiases cause 2 diseases sleeping sickness in Africa, and Chagasdisease in Latin America**

Trypanosomiases	*Sleeping sickness*	*Chagas disease*
Pathogen	*Trypanosoma brucei:* *T.rhodesiense and T.gambiense*	*Trypanosoma cruzi*
Vector	*Tsetse fly*	*Reduviid (Triatomine) bugs*
Clinical presentation	*Chancre(skin stage)* *Lymphadenopathy (Winterbottom's stage)* *Deep coma(CNS stage)*	*Chagoma* *Ocular lesion ''Romana's sign''* *Heart damage*
Diagnosis	*lymph node aspiration* *CSF aspiration*	*Blood film* *Serology*

Malaria

1- The infective stage of malaria is when Sporozoites enter the human body. Then, it divides & multiplies in the liver in a cycle called Exo-erythrocytic cycle.
2- TheMalarial Paroxysm occurs after the rupture of Schizont releasing Merozoites and other substances in the infected RBC which cause mediate the clinical picture.
3- Malarial Paroxysm is presented with chills and vigorous shivering at first (Cold stage). Then the patient feels an intense heat accompanied by severe headache (Hot stage). Next a period of profuse sweating & the fever will start to decline. The patient is exhausted and weak and will usually fall asleep (Sweating stage)
4- Hypnozoites in P.Vivax&P.Ovale causing relapse.
5- Complications of malaria are mostly caused due to P.falciparum because it causes impairment of microcirculation (main pathogensis)&anemia leading to tissue hypoxia.
6- The main complications of malaria are cerebral malaria (causing Opisthotons which is an unrousable coma), severe anemia, pulmonary edema, hypoglycemia, renal failure, shock, dysentery & Jaundice
7- The pattern of fever in P.falciparum is usually quotidian (at the start). However, in P.Vivax & P.Ovale the fever appears every 48 hrs& in P.Malaria, it appears every 72hr
8- Haemoglobinuria associated with malaria causes black-water fever and it is uncommon.
9- Haemoglobinuria associated with malaria may present in adults as sever disease with anemia & renal failure, it could be precipated by drugs. People with G6PD deficiency treated with primaquine may suffer from acute hemolysis.
10- Light microscopy is the gold standard for diagnoses of malaria. But using Rapid diagnostic tests RDTs is also an option.