GNT Microbiology Summary File

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Good Luck!

1- Helicobacter pylori

Associations	**H.Pylori is associated with development of (spectrum of diseases):** ● Asymptomatic carriage ● Chronic active gastritis ● Gastric and duodenal ulcer (Peptic ulcer) ● Gastric adenocarcinoma ● Gastric mucosa-associated lymphoid tissue (MALT) lymphoma.
Transmission	**- Gastric antrum is the most favoured site.** **- Person to person:** **1- oral to oral:** same spoons, forks & toothbrushes & kissing children mouth to mouth **2- fecal-oral:** ingestion of contaminated food or water due poor hygiene.
Prevention	**1- Eradication of infection:** improves symptoms: e.g. (dyspepsia, gastritis, peptic ulcer & cancer) & Potentially reverse progression **2- Dietary methods:** (eating broccoli, cabbage, honey, and drinking green tea) **3- Proper sanitation and clean sources of drinking water.**
Genome	● **H.pylori contains 40kb-long Cag pathogenicity island (PAI) with over 40 pathogenic genes.** ● Asymptomatic patients (over 80%) carry H.pylori strains lacking the Cag pathogenicity island (PAI).
Virulence factors	**1- Flagella which is important for motility.** **2- Adhesins that bind to epithelial cells** **3- Urease enzyme which breaks urea into CO2 and ammonia to neutralize gastric acidity (note that Ammonia is toxic to epithelial tissue)** **4- vacA which damages epithelial tissue** **5- CagA which gives H.pylori the ability to cause cancer, by inducing the release of cytokines(e,g, TNF-alpha and IL-8) ➔ cell mutation ➔Cancer**

Laboratory findings:

Morphology and characteristics	Biochemical findings
● Grows in environments with increased Co2 ● **Fastidious.** ● **Strictly microaerophilic** ● **Blood agar and staining:** - **Small** - **Gram negative spiral rods(bacilli)** - motile by polar flagella.	● **catalase-positive** ● **oxidase- positive** ● **strongly urease-positive** - Urease breaks urea down to Co2+NH3 - Ammonia is a strong base - Urease helps H. pylori survive strongly acidic stomach conditions.

1- Helicobacter pylori cont.

Pathogenesis	**1- Colonization: by surviving the stomach acidity:** ● Using **flagella** it moves through stomach lumen ➔ drill into the mucoid lining of Stomach ➔ Produces adhesions that binds to the epithelial cells. ● Produces large amounts of **urease** enzyme ➔ breaks down urea into co2 + ammonia ➔ neutralizes gastric acid. (**Ammonia** is toxic to epithelial cells along with **proteases**, **VacA protein**, and **phospholipases)** **2- results:** ● Colonization of stomach or duodenum results in chronic gastritis ➔ Inflammation stimulates more production of gastric acid ➔ gastric and duodenal ulcers ➔ atrophy and later cancer.
Peptic ulcer	Mucosal erosions (≥ 0.5cm), **More Peptic ulcers are arise in the duodenum than the stomach.** **Signs & symptoms:** ●Abdominal or Epigastric(burning) **pain** w/severity relating to meal time ○ **Gastric:** shortly after meal ○ **Duodenal:** 2-3 hrs after meal ●**Haematemesis** ●**Melena** ●Rarely, Gastric or duodenal Perforation leading to **acute peritonitis**. **Factors contributing to peptic ulcer:** ● **CagA protein** ● Neutrophil-Activating Protein (**NAP**) ➔ recruitment of neutrophils ➔ inflammation ● **Free radicals , TNF-α** and **Interleukin 8** ➔ Mutations

Diagnosis

Non-invasive method	Invasive method
● **Stool antigen test.** ● **Carbon urea breath test (C14 or C13).** ● **Serology (Blood antibody) tests** → poor accuracy.	● **Histological examination** of biopsy specimens of gastric/duodenal mucosa take at endoscopy. ● **Rapid urease test: High sensitivity and specificity** ● **Culture:** For antibiotics resistance testing. ● **Molecular methods** (e.g. PCR).

Treatment

Clarithromycin Triple therapies (first line):	Second line
PPI (proton pump inhibitor) b.d. (twice a day) + clarithromycin + amoxicillin or metronidazole for 14 days We give metronidazole if patient is allergic to Penicillin (Amoxicillin).	**PPI + bismuth subsalicylate/subcitrate + nitroimidazole + tetracycline (10-14 days) → if primary therapy fails**

2- Normal Flora & intro to infectious diarrhea

Definition	● **microorganisms that are frequently found in various body sites in normal, healthy individuals.** ● **vary according to the age and physiologic status.** ● Can cause disease in immunocompromised patients.	
Site	**Normal flora (low virulence):**	**Potential pathogen (carrier):**
Mouth	- Viridans streptococci - Neisseria spp - Moraxella -Peptostreptococcus	- Candida albicans
Nasopharynx	- Neisseria spp - Viridans streptococci - Moraxella - Peptostreptococcus	- S.pneumoniae - N.meningitidis - H.influenzae - S.pyogenes, - S.aureus
Stomach (empty stomach is sterile)	- Streptococci - Peptostreptococcus + others from mouth	none
Small intestine	scanty, variable	none
Colon of adults	- Bacteroides - Fusobacterium - Eubacterium - Lactobacillus - Enterobacteriaceae - Enterococcus - Clostridium	- B.fragilis - E.coli - Pseudomonas - Candida - Clostridium (C. perfringens, C. difficile)
Rule in diseases	● Many are opportunistic pathogens: 1- perforation of the colon from ruptured diverticulum → feces enter into peritoneal cavity → peritonitis **2- Viridans streptococci of oral cavity → blood → colonize damaged heart valves.** 3- Mouth flora play a role in dental caries ● immunocompromised are at higher risk ● **Salmonella, Shigella and Yersinia are NOT normal flora of the intestinal tract.**	
Intestinal pathogens	● **Invasive and cytotoxic** → dysenteric diarrhea with WBCs and/ or blood in the stool and fever e.g. Shigella, Salmonella, Campylobacter, some E.coli. ● **Enterotoxic**→ watery diarrhea with no fever e.g. Staphylococcus aureus, Vibrio cholera and Clostridium perfringens. ● some causes systemic illnesses	

Diarrhea

Definition	● Stool weight in excess of 200 gm/day due to alteration in normal bowel movement ● less than 14 days duration		
Etiology:	**Viral**	**Bacterial**	**Protozoan**
	70-80% of infectious diarrhea in developed countries.	10-20% of infectious diarrhea but responsible for most cases of severe diarrhea.	less than 10%.
Epidemiology	1.2 - 1.9 episodes per person annually in the general population 2.4 episodes per child <3 years old annually 5 episodes per year for children <3 years old and in daycare Seasonal peak in the winter.		

2- Normal Flora & intro to infectious diarrhea cont.

Diarrhea (cont.)

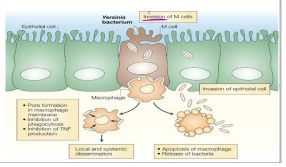
Risk factors	• Food from restaurants. (food poisoning → Staph. Aureus, Clostridium perfringens, Bacillus spp.) • Family member with gastrointestinal symptoms. • Recent travel to developing countries (traveller diarrhea → Enterotoxigenic E.coli (ETEC)) • Antibiotics decrease the normal flora to less than 10^{12} (antibiotic associated → Clostridium difficile). • Patient underlying illness & medication, low stomach acidity, cyst, spores. • Abnormal peristalsis. • Low Immunoglobulin A (IgA). • Median infective dose (ID_{50}).
Lab diagnosis of diarrheal diseases	Stool specimen: - **Microscopy:** ○ presence of polymorphs or blood may help. - **Culture:** ○ On selective media for Salmonella, Shigella & Campylobacter. ○ Culture for Vibrio cholerae, EHEC or Yersinia if suspected. - **Toxin assay:** ○ if C.difficile toxins is suspected.

1- Campylobacter

Morphology	Gram-negative curved (spiral or S-shaped) Bacilli.
Species	**C.jejuni**, C. coli, C fetus (immunocompromised).
Sources	Dogs, cats, birds, **poultry**, water, milk & meat. Person to person transmission can occur.
Clinical Presentation	• Lower abdominal pain , **watery or dysenteric diarrhea** with pus and blood. fever in some patients . Nausea and vomiting are rare • Self limiting after 2-6 days.
Lab Diagnosis	• Use transport media. • Culture on **CAMPY BAP** media containing antibiotics. • Incubate in **microaerophilic atmosphere** (5%O_2, 10%CO_2, 85%N) at 42°C except C.fetus 37°C
Complications	• **Autoimmune disease (e.g. Guillain-Barrie' syndrome)** • **Extra-intestinal infections (e.g. reactive arthritis**, bacteremia, lung infection and others frequently preceded by C.jejuni infection.)
Treatment	• Erythromycin or Ciprofloxacin (for severe cases only)

2- Yersinia enterocolitica

Epidemiology	○ From: Cats, Dogs & **Swine (chitterlings[1])**. 1: Chitterlings are a prepared food usually made from the small intestines of a pig ○ Survives cold temperatures, associated with transfusion of packed red blood cells.
Clinical Presentation	• Mesenteric lymphadenitis → children. Septicemia → immunocompromised hosts. • **Presents with enteritis, arthritis and erythema nodosum.** • usually mild, but in old children and adult **mimic appendicitis.**
Lab Diagnosis	○ Media(25-30°C): Cefsulodin-Irgasan-Novobiocin **(CIN media)**



2- Normal Flora & intro to infectious diarrhea cont.

3- Escherichia Coli

Enterotoxigenic E.coli (ETEC)	Enteroinvasive E.coli (EIEC)	Enteropathogenic E.coli (EPEC)	Enterohemorrhagic E.coli (EHEC) (MOST COMMON)	Enteroaggregative E.coli (EAEC)
• Produces: 1- **heat-labile toxin (LT)** → accumulation of CGMP → hyper-secretion of fluid. 2- **heat-stable toxin (ST)** • **high infective dose 10^6-10^{10}**	• **Similar to shigella spp (nonmotile, LNF).** ○**Transmission: Fecal-oral route.** • Infective dose 10^6	• **infantile** diarrhea (bottle fed infants). • Outbreak in hospital nurseries and day care centers. • Disrupt microvilli and intestinal absorptive function.	• **Cytotoxin : Shiga-toxin I & II (verotoxin I and verotoxin II)** • **O157:H7** Hemorrhagic diarrhea, colitis and **hemolytic uremic syndrome (HUS) manifested with low platelets, hemolytic anemia and kidney failure. .** • **Most common causes:** **Undercooked hamburgers** ,unpasteurized dairy products, Apple cider, cookie dough	• Pediatric diarrheal • Adhering to the surface of the intestinal mucosa. Producing aggregative stacked brick.
• **Traveler's diarrhea:** Watery diarrhea, abdominal cramps, due to consumption of contaminated food and water. • self-limiting • **No invasion or inflammation.**	• Dysentery especially in children. (Penetration, invasion and destruction).	• Symptoms: Mucus in stool (**no blood**), Low grade fever, malaise, vomiting, watery diarrhea.	• **Symptoms:** **Bloody diarrhea**, low grade fever and stool with no leukocytes • **Diagnosis by:** Culture on SMAC., verotoxin detection by immunological test or nucleic acid testing(NAT). • Management of HUS required. • **Antimicrobial therapy not recommended**	• Symptoms: Mucoid, watery diarrhea, vomiting, dehydration and abdominal pain. • resolve in 2 weeks or more.

4- Clostridium difficile

Cause	**Antibiotic associated diarrhea** (ampicillin, cephalosporins & clindamycin): - Antibiotic used during the last 8 weeks (community acquired) -Or Hospital stay for at least 3 days (hospital acquired).
Pathogenesis	○ Transmitted from person to person via fecal-oral route. ○ Cultured from inanimate hospital surfaces. ○ Disruption of the endogenous bacterial flora of the colon. ○ **Produce toxin A (enterotoxic & cytotoxic effects) and B (cytotoxic)** → bind to surface epithelial cell receptors → inflammation, mucosal injury & diarrhea.
Clinical Presentation	- Patient presents with fever, leukocytosis, abdominal pain and diarrhea. **- Pseudomembranous colitis can result (neutrophils, fibrin, and cellular debris in the colonic mucosa) and toxic megacolon.**
Lab Diagnosis	Direct toxin detection from stool by enzyme immunoassay (EIA), or NAT.
Treatment	Metronidazole ± **oral Vancomycin** (drug of choice) and supportive treatment.

3- Vibrio Cholera

Cholera	• A waterborne life threatening diarrheal disease
	• Caused by **Vibrio cholerae:**
	  ○ **gram-negative, curved or comma-shaped rods with a single polar flagellum**
	  ○ **O1 and O139 serogroup organisms are the causes of epidemic cholera.**
	  ○ **Produce a non-invasive enterotoxin.**
	  ○ **Water-borne (Natural reservoir), infection is mainly through water supply contamination**
	  ○ O1: Classical & El Tor (less severe)
	  ○ O139: in India a & Bangladesh

Transmission	• **Fecal-Oral** route through contaminated food & **water.** • **Children, elderly and people with less gastric acidity are at higher risk.** • Undercooked shellfish. • Blood group O>>B>A>AB • **Has high infectious dose** 10^6 -10^{11} NOT like Shigella, typhoidal Salmonella and Enterohemorrhagic E.coli
Pathogenesis	• Toxin-coregulated pili (TCP) to colonize the human intestine. • **cholera toxin (CT) "enterotoxin" which is an ADP-ribosylating enzyme** on intestinal epithelial cells → binds to GM1 receptor → NAD mediated by CTA1 becomes ADP-ribose→ binds to G protein → increases cAMP → secretion of water, chloride and sodium into intestinal lumen → **secretory diarrhea.**
Clinical features	• Ranges from few hour to 5 days. (depending on gastric acidity and initial Infectious dose) • 75% asymptomatic • 20% mild disease • 2-5% severe • Vomiting, Cramps and **Watery diarrhea** (1L/hour), **flecks of white mucus (rice water stool)** with a fishy odor • Death occurred in 18 hours-several days if not treated due dehydration. • ↓ Ca++ and K can lead to **ileus**, muscle pain and spasm, and even tetany.
Diagnosis	• suspect V.cholera if severe diarrhea with dehydration.(similar to VGE and ETEC) • insert central line IV, collect blood (to measure electrolytes and water loss) and take stool for smear and culture(Not routinely performed).
Lab tests	• Dark field microscopy (shooting stars) • **Gram stain (curve/comma shaped Gram Negative bacilli w/ single polar flagella)** (oxidase positive) • **Culture on thiosulfate citrate bile sucrose (TCBS) agar-yellow colonies (sucrose fermenter)** • Serology & PCR: important to identify virulent serotypes (O1&O139) associated with epidemic disease

Treatment	• **Rehydration**:
	  ○ Oral (if patient is not vomiting)
	  ○ Or IV
	• Antibiotics: to reduce recovery time to 2-3 days & infectivity:
	  ○ **Azithromycin** single-dose (preferred therapy especially in children) or **Ciprofloxacin** or **Tetracycline**, **Doxycycline**.

Prevention	• Clean water sources, water Sanitation, water treatment
	• Vaccination:
	  ○ Killed whole cell vaccine: multiple doses, adults → 50% protection for 6 months. Children → < 25% protection.
	  ○ Live attenuated vaccine: adults → 60% protection for 2 yrs. Children → protection rapidly declines after 6 months. May lead to side effects: mild diarrhea & abdominal cramping.

Cholera gravis

• severe form of cholera, due to rapid loss of fluids. 6 L/hr, and rapid loss of bodyweight(>10%)
• Severe **Dehydration and shock** what is the main cause of death in cholera? hypovolemic shock.
• sunken eyes, tenting cold and clammy.
• Hypoglycemia → seizure. or comma.
• Patient is Anuric, has lactic acidosis (Kussmual breathing) → cardiac & renal failure & **aspiration pneumonia.**
• Mortality: 50-60% if untreated (occurs within 2-12 hrs) but <1% if rehydrated.

4- Salmonella and Shigella

Salmonella

General info	• Gram negative ,motile ,facultative anaerobic bacilli Non lactose fermenting colonies. • **Cause disease by invasion**	
Classification	**Two species of Salmonella :** • S.enterica (six subspecies I, II, III, IV, V, VI) • S.bongori (rare) Found in cold blooded animal, birds, rodents, turtles, snakes and fish	
Antigen structures	• **O. Somatic antigen (Heat – stable) is lipopolysaccharide in the outer membrane** • **H. Flagellar antigen H antigen (Heat - labile)** • **K. Capsular antigen (Heat - labile)** • **V_i in Salmonella serotype typhi. (Heat - labile)**	
Clinical diseases	• Acute gastroenteritis & Nontyphoidal bacteremia • Typhoid fever • Carrier state following Salmonella infection	
Source	• Water, food and milk contaminated with human or animal excreta. • **S.typhi and S.paratyphi :** the source is human.	
Clinical manifestation	**Non-typhoid (Salmonella gastroenteritis)**	**Typhoid fever(enteric fever)**
	• Food poisoning through contaminated food • **S. enterica subsp. enterica the common cause** • Source: **poultry**, milk, egg & egg products and handling pets • **High Infective dose** • Fever, chills, watery **diarrhea** and abdominal pain. Self limiting. • **In sickle cell, hemolytic disorders, ulcerative colitis, elderly or very young patients; the infection may be very severe.** • Patients at high risk for dissemination and antimicrobial therapy is indicated.	• Prolonged fever • **Bacteremia** • Dissemination to multiple organs • Ingestion of contaminated food by infected or carrier individual • Caused by Salmonella serotype typhi or S.paratyphi A, B and C (less severe) • **Low infective dose** • **First week:** fever, malaise, anorexia, myalgia and a continuous dull frontal headache then, Patient develops **constipation**, Bacteria released into the bloodstream again and can lead to high fever, Blood culture is positive. • **2nd and 3rd week** Sustained fever & prolonged Bacteremia, It may Invade gallbladder and Peyer's Patches, **Rose spots**(2nd week of fever), can affect Biliary tract, Organism can be isolated from stool + blood
Treatment	• Uncomplicated cases require fluid and electrolyte replacement only.	**CCAATS** • **C**eftriaxone (drug of choice) • **C**iprofloxacin • **A**mpicillin • **A**zithromycin or Ceftriaxone for patients from India and SE Asia due to strains resistant to Ciprofloxacin. Ciprofloxacin can be used for patients from other areas. • **T**rimethoprim – **S**ulfamethoxazole
Complications	• **Necrotizing cholecystitis** • Bowel hemorrhage and perforation • Pneumonia and thrombophlebitis • Meningitis, osteomyelitis, endocarditis and abscesses.	

4- Salmonella and Shigella (CONT.)

Shigella	
General info	• Gram negative **Non-motile**, Non lactose fermenting colonies • Cause **bacillary dysentery** (blood, mucus and pus in the stool) • **Low infective dose** < 200 bacilli • Shigella are non motile, **lack H antigen**
Classification	• **Has 4 species based on O antigen: S. dysenteriae (Causes invasion + Produce shiga toxin thus can lead to HUS)**, S. sonnei, S. flexneri, S. boydii • Shigella has 4 species and 4 major O antigen groups: All have O antigens, some serotypes has K antigen (heat labile removed by boiling)
Pathogenesis	• **Penetrate epithelial cells ,leads to local inflammation, shedding of intestinal lining and ulcer formation.**
Source	• Human is the only reservoir • Person to person through fecal –oral route • Flies, fingers (have a role in spread). • Food and water. • Young children in daycare, people in crowded area and anal oral sex in developed countries.
Clinical manifestation	• High fever, chill, abdominal cramp and pain accompanied by tenesmus, bloody stool with mucus & leukocytes. • **Can lead to rectal prolapse in children** • Complications: **ileus**, obstruction dilatation and **toxic megacolon** • Bacteremia in 4 % of severely ill patient • **Seizures, HUS**
Treatment	**Antibiotics used to reduce duration of illness:** (same as salmonella typhi, paratyphi) Ampicillin, IV ceftriaxone, oral TMP-SMX, Ciprofloxacin or Azithromycin

Laboratory diagnosis of salmonella and Shigella from stool:

- **Both are Gram negative bacilli**
- **MacConkey agar:** Both will appear as Yellow colonies which indicate non-lactose fermenting organism.
- **Culture on selective media (Salmonella produce black colonies due to H2S** Hydrogen sulfide **)**
- Media: SS and XLD, HEA, BS
- Biochemical tests
- Motility test(Non-motile> Shigella, Motile>Salmonella)
- Serology for serotypes.

SS: Salmonella Shigella
XLD: Xylose Lysine Deoxycholate agar
HEA: Hektoen enteric
BS: Bismuth sulfite

5- Viral Gastroenteritis

Definition	inflammation of the gastrointestinal tract which involves both stomach and small intestine leading to acute diarrhea and vomiting.
Epidemiology	- Age: All groups. Mainly infants & young children - Transmit by faecal-oral route. Peaks in winter months. - Endemic infection: group A Rotavirus & Adenovirus 40 & 41. - Epidemic infection: Norovirus (from Caliciviruses)
Clinical Features	- Watery, non-bloody diarrhea with vomiting, fever & abdominal cramps. - Note: dehydration with decreased Na+ is a Life threatening condition caused by diarrhea and vomiting. - Usually children experience diarrhea more than vomiting. But in case the disease was caused by calicivirus(winter vomiting disease), they will experience vomiting more.

Virus	Rotavirus (7 groups (A-G) but GpA is the most common)	Adenoviruses serotype 40&41 (Subgenus F)	Caliciviruses	Astroviruses
Family	Reoviridae	Adenoviridae	Caliciviridae	Astroviridae
Description (All are Non-enveloped)	- 11 segments dsRNA. - RNA-dependent RNA polymerase	- ds-DNA. - the only virus with fiber protruding from capsid vertices: 1- Attachment 2- Hemagglutinin 3- Type-specific Ag	- ss-RNA with +ve polarity. Two morphologic types: - Typical calicivirus (Sapoviruses) - Small round structured virus (Noroviruses)	- ss-RNA with +ve polarity.
Clinical Features (Don't forget to check the pathogenesis in slides)	- Most common cause of GE - Affect all age groups but mainly infants 6-24 months - Infants & young children → GE - Older children & Adults → Asymptomatic - Low immune hosts → Chronic diarrhea - May cause encephalitis as well	Compared to Rotavirus it: - Has longer IP - Less severe - Prolonged illness	- Found in water, shellfish - Outbreaks of GE in schools, camps & cruises - Children: vomiting - Adults: diarrhea. Winter vomiting Disease: Vomiting more than diarrhea	- Mild GE - Outbreak of diarrhea <5 years.

Lab Diagnosis

(Sample: stool)

- ELISA & Immunochromatography for detection of viral Ag in stool samples (for all the 4 types)
- Latex agglutination, gel electrophoresis, and RT-PCR are secondary tests for Rotavirus

Treatment & Prevention

- Treatment:
Self-limiting, treated by rehydration and supportive treatment.
- Prevention:
No vaccines except for Rotavirus: live attenuated vaccine, oral; Rotarix, RotaTeq

6- Viral Hepatitis B,C,D&G

<table>
<tr><th>Virus</th><th>Hepatitis B</th><th>Hepatitis C</th></tr>
<tr><td>Info</td><td>Hepadnaviridae, dsDNA.
- The serum of infected individual contains three types of hepatitis B particles:
○ Large number of small spherical free HBsAg particles.
○ Some of these HBsAg particles are linked together to form filaments.
○ The complete HBV particles (Dane particles)</td><td>Flaviviridae. ssRNA genome.
6 major genotypes. 4 is the dominant in Saudi patients.</td></tr>
<tr><td>Transmission</td><td colspan="2">Parenterally transmitted hepatitis or blood borne hepatitis. This group includes hepatitis B, C, D & G viruses.
1. Parentally: receiving blood from infected donor, Sharing contaminated needles
2. Sexually: The virus is present in blood and body fluids.
3. Perinatally: during delivery, breastfeeding</td></tr>
<tr><td>Risk Factors</td><td colspan="2">Intravenous drug users, Hemodialysis patients, Health care workers with frequent blood contact, Patients receiving clotting factors, Individuals with multiple sexual partners, Individuals who exposed to tattooing , body piercing or cupping.</td></tr>
<tr><td>Clinical Outcomes</td><td>● 90 % of infected adults will develop acute hepatitis B infection and recover completely.
● < 9 % of the infected adult, 90% of infected infants and 20% of infected children may progress to chronic hepatitis B
● < 1 % may develop fulminant hepatitis B.</td><td>● 20 % acute hepatitis C and recover
● 80 % chronic hepatitis C, about 10%-30% of them can develop cirrhosis within 30 years and liver cancer.
● < 1 % fulminant hepatitis C</td></tr>
<tr><td>markers</td><td>
<table>
<tr><th colspan="2">Acute</th><th>Chronic</th></tr>
<tr><th>Antigen</th><th>Antibody</th><th rowspan="2">the presence of HBsAg or HBV-DNA in the blood for > 6 months. The majority of patients are Asymptomatic. Or symptoms include right upper quadrant abdominal pain, enlarged liver & spleen. Jaundice may or may not developed, fatigue</th></tr>
<tr><td>1. HBV-DNA
2. HBsAg
3. HBeAg</td><td>1. Anti-HBc (IgM)
(The first antibody that appears in the circulation)</td></tr>
</table>
● HBV DNA: Markers of infections, 1st marker that appears in circulation
● HBsAg: Markers of infections, 2nd marker that appears in the blood
● HBeAg: Markers of active virus replications, Highly contiguous, Highly infectious. 3rd maker.
● Anti-HBe: Marker of low infectivity
● Anti-HBs: Marker of immunity. Not Contagious.
- Vaccinated patients: Only Anti-HBs
- patients who recovered from previous HBV infection (Immune patients): Anti-HBs and Anti-HBc</td><td>● hepatitis C virus RNA
○ 1st marker marker of infection.
● hepatitis C core antigen.
○ 2nd marker marker of infection.
● IgG antibody to hepatitis C
○ the last/2nd marker
○ it is not marker of immunity,</td></tr>
<tr><td>Phases</td><td>
<table>
<tr><th>Acute</th><th colspan="3">Chronic</th></tr>
<tr><td rowspan="2">Anicteric: Low grade fever, anorexia, malaise, nausea, vomiting, with raised liver enzymes
Icteric: Jaundice with raised bilirubin,dark bile containing urine and pale stools.
Convalescent: Recovery phase</td><td>replicative</td><td>Inflammatory</td><td>Inactive</td></tr>
<tr><td>DNA: ✔
HBsAg: ✔
HBeAg: ✔
ALT: normal
Biopsy: minimal damage</td><td>DNA: ↓
HBsAg: ✔
HBeAg: ✔
ALT: ↑
Biopsy: damage to hepatocytes</td><td>DNA: ✔
HBeAg: ✘
Anti-e: ✔
ALT: normal</td></tr>
</table>
</td><td><u>Acute hepatitis</u>
jaundice, fatigue & nausea, ↑ ALT, HCV-RNA is +ve, Presence of anti-HCV (-ve in 30-40%) in early stages of disease
<u>Chronic hepatitis</u>
Presence of anti-HCV & ↑ ALT for > 6 months, ALT > AST, Almost all patients with chronic hepatitis C have the genome HC RNA in serum.</td></tr>
<tr><td>Complication</td><td colspan="2">● Cirrhosis
● Hepatocellular carcinoma
○ Alpha-fetoprotein measurement with multiple CT- abdominal scan are the most sensitive method for diagnosis of HCC</td></tr>
<tr><td>Lab diagnosis</td><td>● Hepatitis B infection is diagnosed by detection of HBsAg in the blood.
○ Positive results must be repeated in duplicate.
○ Repeatedly reactive results must be confirmed by neutralization test.
○ Detection of HB-DNA by PCR.</td><td>By detection of both:
● Antibody to HCV in the blood by ELISA, if positive the result must be confirmed by Recombinant ImmunoBlot Assay (RIBA) or PCR.
● HCV-RNA in the blood using RT-PCR.</td></tr>
<tr><td>Treatment</td><td>● Pegylated alpha interferon
● Lamivudine
● Adefovir</td><td>Pegylated alpha interferon & Ribavirin</td></tr>
<tr><td>Vaccine</td><td>
<table>
<tr><th>Pre-Exposure prophylaxis</th><th>Post-Exposure prophylaxis</th></tr>
<tr><td>Active vaccination Contains highly purified preparation of HBsAg particles, produced in yeast</td><td>Who exposed to needle prick or infant born to +ve HBsAg mother should immediately receive both:
- Active vaccine & hepatitis B specific immunoglobulin.</td></tr>
</table>
</td><td>No vaccine</td></tr>
<tr><td>D & G viruses</td><td colspan="2">● Hepatitis D is a defective virus. Composed of small ss-RNA genome. It cannot replicate by its own. The helper virus is HBV.
● It has TWO types of infection:
○ Co-infection: The patient is infected with HBV and HDV at the same time leading to severe acute hepatitis.
○ Super infection: In this case, delta virus infects those who are already have chronic hepatitis B leading to severe chronic hepatitis.
● Hepatitis G virus: Enveloped, ss-RNA with positive polarity. Usually occurs as co-infection with HCV, HBV and HIV.
○ Family: Flaviviridae. Genus: Hepacivirus.</td></tr>
</table>

7- Viral Hepatitis A&E

Hepatitis A	

Characteristics	• Family: Picornaviridae.
	• Genus: Hepatovirus.
	• Non-enveloped virion consisting of
	  ○ Icosahedral capsid.
	  ○ Positive sense ss-RNA.

Transmission	• Faecal-oral route [major route] • Sexual contact (homosexual men) • Blood transfusion (very rarely)
Pathogenesis	Enters the body by ingestion of contaminated food → replicates in the intestine (epithelium) → spreads to the liver where it multiplies in the hepatocytes → Cell mediated immunity → Damage of virus-infected hepatocytes → increase ALT, AST & Bilirubin
Manifestations	• Short Incubation Period: 2-6 weeks. • Pre-icteric phase: Fever, Fatigue, Nausea, Vomiting, & Right upper quadrant pain • Icteric phase: Dark urine, Pale stool & Jaundice.
Lab Diagnosis	Serology: • Detection of anti-HAV IgM: Indicates Current infection • Detection of Anti-HAV IgG: Previous infection, Immunity(vaccinated)

Prevention	• Hig (human immunoglobulin) for:
	  ○ travellers, unvaccinated, exposed patients.
	  ○ Given before or within 2 weeks of exposure (shorter immunity)
	• Combination vaccine (HAV & HBV, inactivated) for:
	  ○ Patients at high risk of infection and severe disease

Prognosis	• Self-limited disease • Fulminant hepatitis (rare) • No chronicity or malignancy changes
Hepatitis E	
Characteristics	• Family: Hepeviridae • Genus: Hepevirus. • Non-enveloped virion consisting of: Icosahedral capsid, Positive sense ss-RNA.
Transmission	• Water-borne • Zoonotic food-borne(undercooked beef or pork) • Perinatal • Blood-borne
Clinical Features	Similar to HAV infection with exceptions: • Longer IP =4-8 Ws • Chronic hepatitis, cirrhosis, but not HCC • Fulminant disease • Mortality rate ~10 times higher than HAV (20% in pregnancy)
Lab Diagnosis	Serology: • Detection of anti-HEV IgM by ELISA
Prevention	• Sanitation & Hygiene measures • No Immunoglobulin • No vaccine

7- Viral Hepatitis A&E

Epstein – Barr Virus (EBV)

Characteristics	• dsDNA , Icosahedral & Enveloped Viruses • It's lymphotropic • it has oncogenic properties: Burkitt's lymphoma	**Transmission**	• Saliva (kissing disease) • Blood (rare)
Epidemiology	Age: Depends on socio-economic status: • Low SE : early childhood • High SE : adolescence	**Treatment and vaccines**	• Treatment : Antiviral drug is not effective in Infectious mononucleosis • No Vaccine
Clinical Features	**Immunocompetent host:** • Asymptomatic (usually) • Chronic EBV infection • Infectious mononucleosis (or glandular fever). ○ Mainly in teenagers & young adults, IP= 4-7 weeks ○ Fever, pharyngitis, malaise, lymphadenopathy hepatosplenomegaly, abnormal LFT & hepatitis. ○ Complications (rare but serious): ■ acute airway obstruction, splenic rupture, CNS eddinfection		**Immunocompromised host:** • Lymphoproliferative disease (LD) • Oral hairy leukoplakia (OHL)
Diagnosis	**Hematology:** • Increased WBC: ○ Lymphocytosis (atypical lymphocytes)		**Serology:** • Non-specific AB test via Paul-Bunnell or Monospot test: ○ Heterophile Abs +ve • EBV-specific AB test: ○ IgM Abs to EBV capsid antigen

Cytomegalovirus (CMV)

Characteristics	• dsDNA , Icosahedral & Enveloped Viruses • Its replication cycle is longer • Infected cell enlarged and multinucleated		• Resistant to acyclovir • Latent in monocyte, lymphocyte & other
Transmission	**Early in life:** • Transplacental, Breast milk, Birth canal	**Young children:** • Saliva	**Later in life:** • Sexual contact, Organ transplant, Blood transfusion
Clinical Features (Acquired infections)	**Immunocompetent host:** • Asymptomatic and Self-limited illness ○ Hepatitis ○ Infectious mononucleosis-like syndrome [Heterophile AB is –ve]		**Immunocompromised host:** • Encephalitis • Pneumonia • Esophagitis • Colitis • Retinitis • Hepatitis
Diagnosis	**Histology:** • Intranuclear inclusion bodies [Owl's eye]	**Culture:** • In human fibroblast: 1-4 weeks: CPE • Shell Vial Assay: 1-3 days	**Serology:** • Antibodies: ○ IgM: current infection ○ IgG: previous exposure • Antigen: CMV pp65 Ag by IFA
Treatment	• Ganciclovir: treatment of severe CMV infection • Foscarnet: the 2nd drug of choice	**Prevention**	• Screening: Organ donors, Organ recipients & Blood donors. • Leukocyte-depleted blood. • Prophylaxis: Ganciclovir, CMV IG, No vaccine

Arthropod –borne Viruses (Yellow Fever virus)

Characteristics	• Family: Flaviviridae, enveloped, ssRNA +ve polarity. • Asymptomatic to Jaundice (hepatitis) + Fever ± hemorrhage ± renal failure	**Lab Diagnosis**	• Isolation (Gold standard) • IgM-Ab - ELISA, IF: (most used) • Arbovirus RNA by RT-PCR
Epidemiology	jungle yellow fever: • Vector: Aedes mosquito • Reservoir: monkeys (It is a disease of monkeys) • Accidental host: humans		Urban Yellow Fever: • Vector: Aedes mosquito • Reservoir: human (It is a disease of humans)
Prevention	• Vector Control: Elimination of vector breeding sites, using insecticides, avoidance contact with vectors. • Vaccine: Yellow fever vaccine (Live attenuated vaccine, one dose /10 yrs) for travelers.		

8- intestinal helminths

Enterobius vermicularis: (pin, seat, thread worm)

Affect	**Children** in nursery	**Location**	**Adult worms:** **Large intestine** (lumen of cecum) **Female worm:** **migrate to the rectum to deposit her eggs on perianal skin**
Diagnosis	look for eggs around the anus by **swap** or using **cellulose adhesive tape before defecation and bathing**	**Transmission**	1-Direct human to human (swallowing of eggs) 2- Autoinfection by contamination of the fingers.
Diagnostic stage	**Unembryonated egg**	**Infectious stage**	**Embryonated egg**
Clinically	• Most are asymptomatic if in small amounts • **Nocturnal Perianal itching (pruritus ani)** • Ectopic enterobiasis cause appendicitis, valvo-vagintis, salpingitis		

Ascaris lumbricoides (roundworm)

Location	**Small intestine (Jejunum and upper ileum)**	**Life cycle**	Ingestion of Embryonated egg then pass to the duodenum to become a Larva→Enter the bloodstream→enter the pulmonary circulation and stay in the alveoli for 3 weeks → The larva coughed up ,swallowed ,returned back to the small intestine where it become adult (Feed on semi digested food)→pass in stool as Fertilized eggs or unfertilized eggs
Mode of transmission	**Fecal-oral route (Food contaminated)**		
Infectious stage	**Embryonated egg**	**Diagnostic stage**	**1- Fertilized & unfertilized eggs in stool** **2- Adult in stool** **3- Larva in sputum**
Pathogenicity	**1- Adult worm (small intestine):** - Light infection: Asymptomatic - Heavy infection: Intestinal obstruction - Migrating adult: to bile duct-jaundice		**2- Larvae in the lung: Loeffler's syndrome** - Pneumonitis and bronchospasm, cough with bloody sputum **- Eosinophilia** **- Urticaria**

Trichuris trichiura (Whipworm)

- it coexists with Ascaris because of similar requirement. **Diagnosis: Eggs in stool characterized by its barrel shape**
- **Rectal prolapse** in children is a common complication
- **Light infection**: Asymptomatic
- **Heavy infection**: Abdominal pain, bloody diarrhea. Whole length of the large intestine is affected

Location(adult)	**large intestine** especially caecum and appendix	**Diagnostic stage**	**Unembryonated (Fertilized) egg**	**Infectious stage**	**Embryonated egg**

Hookworms

- Its buccal capsule (mouth) lined with hard hooks, **Triangular cutting plates, anticoagulant glands. Diagnosis:** eggs in stool
- Filariform larval invade the skin and cause **cutaneous larva migrans**, commonly caused by **walking barefoot.**
- **Clinical pictures:**
- **Larvae:**
- **At the site of entry**: Ground itching and dermatitis
- **Migration phase:** pneumonia and bloody sputum, eosinophilia urticaria. (Less severe than ascaris)
- **Adult worm**

1- Epigastric pain, vomiting, hemorrhagic enteritis
2- Hypoproteinemia (edema)
3- Sever Anemia (microcytic hypochromic anemia) due to blood withdrawal by the parasite

Diagnostic stage	Eggs in feces	**Route of infection**	Penetration of the skin when walking with **barefoot (not fecal-oral)!**	**Clinically**	- **Iron deficiency anemia (microcytic-hypochromic)** - Protein deficiency - Intestinal inflammation
Infectious stage	Filariform larva				

8- intestinal helminths (Cont.)

Strongyloides stercoralis

The parasite shows 3 modes of development:

1) **Autoinfection (very important criteria):**
   - **Internal:** when the rhabditiform larva become a filariform larva in the intestine and penetrate the intestine
   - **External:** fecal contamination of skin –Rh larva > **filariform penetrates the skin**
1) **Direct development:** The rhabditiform larva pass from stool and become directly a Filariform larva if the environment of the soil is suitable.
2) **Indirect development:** In external environment Rh. Larva becomes free living adults, produce eggs, rhabditiform larvae and Filariform larva

Pathology & picture	• **Cutaneous:** little reaction on penetration. severe dermatitis at perianal region in case of external autoinfection • **Migration:** pneumonitis during larval migration. • **Intestinal**: inflammation of upper intestinal mucosa, diarrhea, upper abdominal pain in the epigastric colicky in nature. • **Disseminated strongyloidiasis:** in **Immunocompromised patients**, uncontrolled diarrhea, granulomatous changes, necrosis, perforation, peritonitis, death.	**Infective stage**	**Filariform larvae**
		Diagnostic stage	**Rhabditiform larva**

Tape worms

	DISEASE	TRANSMISSION	LOCATION OF ADULT	LOCATION OF LARVA	CLINICAL PICTURE	LAB. DIAGNOSIS
Taenia saginata	**taeniasis**	ingestion of larva in **undercooked beef**	Small Intestine	not present	vague digestive disturbances	eggs or proglottids in stools
Taenia solium-ADULT	**taeniasis**	ingestion of larva in **undercooked pork**	Small Intestine	not present	vague digestive disturbances	eggs or proglottids in stools
Taenia solium-LARVA	Cysticercosis	ingestion of egg	not present (except in Autoinfection, small intestine)	Subcutaneous, muscles, brain, eyes	depending on locality: from none to epilepsy	X-ray, CT, MRI Serology
Hymenolepis nana	hymenolepiasis	ingestion of egg	Small Intestine	Intestinal Villi	Enteritis diarrhoea	eggs in stools
Echinochoccus granulosus	**hydatid disease**	ingestion of egg contaminate with dog feces.	not present	**Hydatid cyst in Liver**, lungs, Bones etc	depending on locality	X-ray, CT, US Serology Hydatid sand

Taenia saginata

- CATTLE become infected by ingesting grass contaminated with **eggs or gravid segments** which passed from human faeces.
- **In the cattle the onchosphere** hatches out go to circulation and transformed to cysticercus stage **in the muscle** known as **CYSTICERCUS BOVIS**
- Man become infected by eating **undercooked or improperly cooked beef**, the adult worm lives in **small intestine** of man passing eggs and gravid proglottids to the environment.
- Infective stage: **Eating Undercooked beef contains cysticercus**
- Diagnostic stage: **Eggs or gravid segments**

Echinococcus granulosus

Definitive host	**Dogs**	**Intermediate host**	**sheep, cattle, pigs, goats, and camels and also Humans**	**Clinically**	Onchosphere reach various organs **mainly the liver causing hydatid cyst. if ruptured it can lead to anaphylactic shock**,

Treatment

Strongyloides stercoralis, Hookworms, Ascaris lumbricoides, Enterobius vermicularis: Albendazole, Mebendazole

Trichuris trichiura: Albendazole

Tapeworms:

- **Intestinal stages:** Praziquantel.
- **Tissue stages (Hydatid, cysticersosis):** Depends on clinical condition: Surgical and/or Albendazole

9- Intestinal Protozoa

Giardia Lamblia

(Water is a major source of transmission & could be transmitted by food as well)

Life Cycle (cyst: infective and diagnostic stage) (trophozoites: replicative and diagnostic stage)	Cyst ingestion (resist acidity) → excystation occurs in the small intestine → with release of trophozoites(pear-shaped) → replicate by binary fission→Trophozoites are then localized in the small intestine, they attach to the mucosal surface of the duodenum and jejunum. However, the trophozoite does not invade the mucosal epithelium → excretion in the stool as cyst or trophozoite.
Clinical Picture (Mainly asymptomatic)	• Diarrhea • Malaise • Weight loss • Persistent infection → Malabsorption • Abdominal cramps • Vomiting

Laboratory Diagnosis	• Stool examination
	  ○ Microscopy for cysts & trophozoites
	  ○ Antigen detection assays: Detection of Cysts/trophozoites antigens in stools
	• Examination of duodenal contents for trophozoites

Treatment	• Metronidazole (Drug of choice)

Entamoeba Histolytica

(Transmitted through fecal-oral route and homosexuals)

Life Cycle	cysts (cyst is Infective and diagnostic stage) pass through the stomach → to the small intestine, where they excyst to form trophozoites (trophozoites is vegetative and diagnostic stage) → trophozoites can invade and penetrate the mucous barrier of the colon (large intestine) → causing tissue destruction colitis and increased intestinal secretion and can thereby ultimately lead to bloody diarrhea . (It cause flask shaped ulcer)	
Clinical manifestation	Majority are asymptomatic , Some have amebic dysentery (Abdominal pain, bloody diarrhea, and mucus in stools) & Fulminant amebic colitis with bowel necrosis leading to perforation and peritonitis. NOTE: It has a very little infective dose(!cyst)	
	Intestinal Amoebiasis	**Extra-Intestinal Amoebiasis**
Pathology Low infective dose (very virulent)	They produce enzymes that lyses host tissues, Lesions are mainly in the colon, They may heal or it may cause complications: • Perforation of the colon, Amoeboma, Blood invasion; Amoebic liver abscess, lung , brain.	• Direct extension: To liver (progress to abscesses) →Subdiaphragmatic abscess → To lung (as pleuro-pulmonary abscess). • Haematogenous spread: Through liver (progress to abscesses) → To ectopic sites (Brain and Lung).

Treatment	• Asymptomatic (cystic only):
	  ○ Diloxanide furoate (Furamide)
	• Symptomatic (cysts & trophozoites):
	  ○ Metronidazole
		• Metronidazole

Laboratory Diagnosis	• Serology: IHA , ELISA (Mainly for invasive infections)
	• Molecular: Detection of DNA or RNA in feces
	• Stools examination (Microscopy):
	  ○ Wet mount (cysts and trophozoites)
	  ○ Concentration methods (only cysts)
		• For Extra-intestinal infections:
		  ○ Serology: IHA , ELISA
		  ○ Surgical aspirate (not used)
		  ○ Sigmoidoscopy and/or colonoscopy and taking biopsy: Trophozoite.

Cryptosporidium Parvum

(Oocyte is the infective and diagnostic stage) (Fecal-oral route)

Route Of Transmission	• Self-limited diarrhea in normal immunocompetent hosts. • Severe debilitating diarrhea with weight loss and malabsorption in HIV-infected patients.
Treatment	Self-limiting but In AIDS patients we give paromomycin.
Laboratory Diagnosis	• Oocysts in feces by modified acid-fast stain (ZN) or safranin stain & by Antigen detection or enzyme immunoassays ELIZA & IF. • From duodenal aspirates, bile secretions & biopsy from affected gastrointestinal tissue also we can do (PCR) or enzyme immunoassays(ELIZA) & IF.

10- Malaria

Malaria

Overview

- Human to human transmission can occur by blood transfusion or vertical transmission across the placenta.
- The main symptoms and signs are periodic fever, headache ,anorexia and anemia.
- Symptoms are due to:
  - Hemolysis of Red Blood Cells
  - Plugging of capillaries by parasitized erythrocytes

Species of malaria

- Plasmodium falciparum
- Plasmodium vivax
- Plasmodium ovale
- Plasmodium malaria
- Plasmodium knowlesi

Life Cycle

Malaria is mainly carried by female anopheles mosquito → The infected mosquito will bite and inject sporozoites from it salivary gland into the bloodstream of human →Which then will travel through blood until it reaches the liver and enter the hepatocytes where it will multiply asexually to form merozoites inside the schizont (Exoerythrocytic schizont) →When the hepatic schizont rupture the merozoites will be released into blood, then it will enter the erythrocytes forming immature trophozoites (ring stage) which will have 2 pathways:

- First pathway: It goes through the erythrocytic cycle starting from ring stage then into Mature trophozoites, then the merozoites will multiply inside the RBCs forming schizont (Erythrocytic schizont), which will rupture (hemolysis) and release the merozoites into the bloodstream (Clinical attack of malaria is due to this stage) and the cycle will repeat over and over again.
- Second pathway: Some immature trophozoites will become gametocytes (male and female) those gametocytes will be ingested by another mosquito
  - In the mosquito: There are Micro(Male) and Macro(Female) gametocytes, the microgametocytes will enter into the macrogametocytes in which they will form Ookinete then it will develop into Oocyst which will rupture releasing sporozoites in mosquito, then the cycle will go over and over again.

Pattern of fever in different species

Occurs every 48hrs - tertian:
- plasmodium Vivax
- plasmodium Ovale

Occurs every 72hrs - quartan:
- Plasmodium Malariae

quotidian, tertian, irregular:
- Plasmodium Falciparum

Malarial Paroxysm

Cold stage:
- feeling of intense cold
- vigorous shivering
- lasts 15-60 minutes

Hot stage:
- due to rupture blood schizonts.
- intense heat
- dry burning skin
- throbbing headache
- lasts 2-6 hours

sweating stage:
- profuse sweating
- declining temperature
- exhausted and weak and sleep
- lasts 2-4 hours
- Then the cycle starts again

Clinical picture

Acute:
- Non-severe Acute Febrile disease → Severe malaria e.g.Cerebral Malaria → Death

Chronic:
- Chronic Asymptomatic Infection → Anemia → Developmental Disorders, Transfusions & Death.

Chronic:
- Infection During Pregnancy → Placental Malaria → Low Birth weight → Increased Infant Mortality

Complication of severe Malaria

Severe malaria is defined as: symptomatic malaria in a patient with P. falciparum with one or more of the following complications:
- Cerebral malaria (unrousable coma not attributable to other causes).
- Hypoglycemia and pulmonary edema in pregnancy can lead to abortion and stillbirth,seen in Tropical contrary.
- Acute renal failure (blackwater fever)
- Hemoglobinuria associated with malaria (blackwater fever)

Diagnosis

- Light microscopy:
  - The gold standard (Thin film & thick film)
- Rapid diagnostic tests (RDTs):
  - detect malaria antigens

Treatment

Sporontocides:
- Primaquine
- Pyrimethamine
- Proguanil

Gametocide:
- Primaquine

Tissue Schizonticides:
- Primaquine
- Pyrimethamine
- Tetracycline
- Proguanil

Blood Schizonticides:
- Chloroquine
- Sulfadoxine/ Pyrimethamine
- Quinine
- Artemisinins

Anti-relapse (P.vivax):
- Primaquine

11- Leishmaniasis

Leishmaniasis

Introduction

- A parasitic disease **caused by the Leishmania parasite**. This parasite typically lives in infected **Sand flies**.
- **Infective stage : promastigote**
- **Diagnostic stage : Amastigote**
- The disease can present in three main ways : Cutaneous, Mucocutaneous and Visceral leishmaniasis

Leishmania species

- **Cutaneous: 1) Leishmania tropica 2) Leishmania major** 3) Leishmania aethiopica 4) Leishmania mexicana
- **Mucocutaneous: Leishmania braziliensis**
- **Visceral: 1) Leishmania donovani 2) Leishmania infantum** 3) Leishmania chagasi

Cutaneous

- The most common form of leishmaniasis. **Oriental sore (most common) classical self-limited ulcer**
- This starts as a **painless papule** on exposed parts of the body, generally the **face**
- The lesion ulcerates after a few months producing an ulcer with an **indurated margin**
- **It has two types:** Leishmania Major & Leishmania Tropica

Leishmania Major	Leishmania Tropica
• **Zoonotic** leishmaniasis • **Wet type** lesions with severe reaction • the ulcer may spread with an inflammatory zone around **which heal slowly**	• **Anthroponotic (human to human)** leishmaniasis • **Dry type** lesions with minimal ulceration • In some cases the ulcer remains dry and **heals readily**

Muco-cutaneous

- starts as a pustular swelling in the **mouth or on the nostrils**
- Secondary infection is very common with destruction of the nasal **cartilage** and the **facial bone**
- may become ulcerative after many months and then extend into the naso-pharyngeal mucous membrane

Visceral

- The most serious form. The diseases is called **kala-azar**. If Untreated, the diseases can be fatal
- **Leishmania infantum mainly affect children Leishmania donovani mainly affects adult**
- The early symptoms are generally low-grade fever, malaise, sweating and anemia
- In later stages, the **fever becomes intermittent and then liver enlargement, spleen enlargement or hepatosplenomegaly because of the hyperplasia of the lymphoid-macrophage system and bone marrow.**
- **Clinical Presentation: Fever, Splenomegaly, or Hepatomegaly or Hepatosplenomegaly, Epistaxis**, Weight loss, Anaemia, Cough, Diarrhoea
- After recovery it might produce a condition called post kala-azar dermal leishmaniasis (PKDL)

Lab diagnosis

Cutaneous & Mucocutaneous	Visceral
• The parasite can be isolated from the **margin** of the ulcer. A diagnostic skin test, known as Leishmanin test (Montenegro test), is useful • Smear: **Giemsa stain - microscopy for LD bodies (Leishman-Donovan bodies, amastigotes) in tissue macrophages** • Skin Biopsy: microscopy from LD bodies or culture in **NNN medium for promastigotes** • Polymerase chain reaction (PCR) tests are available for the detection of Leishmania DNA	• **Parasitological diagnosis:** **Bone marrow aspirate**, splenic aspirate, lymph node, liver biopsy using: 1) microscopy (LD bodies) (amastigotes) 2) culture in NNN medium (promastigotes) • **Immunological diagnosis:** - Specific serologic tests: Direct Agglutination Test (DAT), ELISA, IFAT - Skin test (leishmanin test) for survey of populations and follow-up after treatment. - Polymerase chain reaction (PCR) tests are available for the detection of Leishmania DNA **NOTE: bone marrow aspirate is the most common and number #1 in diagnosing visceral leishmaniasis, so if they asked you a question about the diagnosis and the answers were : bone marrow aspirate , splenic aspirate, lymph nodes, liver biopsy choose bone marrow aspirate**

Treatment (NOT IMP)

- No treatment - self-healing lesions - Medical: - Pentavalent antimony (Pentostam) - Antifungal drugs - +/- Antibiotics for secondary bacterial infection. - Surgical: - Cryosurgery - Excision - Curettage - Cutaneous Leishmaniasis: cutaneous ulcers often heal without treatment. However, treatment can speed healing, reduce scarring, and decrease risk of further disease. Any skin ulcers that cause disfigurement may require plastic surgery. - Mucocutaneous Leishmaniasis: These lesions don't heal naturally. They always require treatment. Liposomal amphotericin B and paramomycin can treat this.	**Visceral disease always requires treatment. Recommended treatment varies in different endemic areas: - Pentavalent antimony - sodium stibogluconate (Pentostam) - Amphotericin B - Paromomycin - Miltefosine (Impavido)**

12- Trypanosomiasis

Trypanosomiasis

Introduction

- There are 4 stages of hemoflagellates : **Trypomastigote**, Epimastigote, Promastigote and **Amastigote.**
- **There are two types of trypanosomiasis:** African & American trypanosomiasis

African Trypanosomiasis

Introduction

- **African trypanosomiasis (Known as African sleeping sickness).** is a parasitic disease Caused by **Trypanosoma brucei** parasites in Africa **transmitted by the bite of tsetse fly (intermediate host).**
- Humans, domestic cattle and wild animals are the main reservoir host for Trypanosoma (definitive host).
- **T. gambiense** causes a chronic illness. **T. rhodesiense** causes a more acute illness & more rapid in developing the disease.

Transmission

- **Trypanosoma are transmitted from human to human through the bite of the tsetse fly which is only found in rural parts of Africa.**
- Transmitted from mother to child as the parasite can cross the placenta in the blood and infect the baby while it is still in the womb (uterus)
- Contaminated needles can also contribute to the spread of trypanosomes, but this is rare.

Life cycle

- The trypanosome parasite is first introduced into the mammalian host as **trypomastigotes (Infective stage** & Diagnostic stage) when a tsetse fly takes a blood meal and secretes parasite-filled saliva into the host's skin.
- Once in the bloodstream the **trypomastigotes multiply in the blood , lymph or spinal fluid**

Clinical picture (3 stages)

- **Skin stage:** A primary reaction occurs at the site of inoculation of trypomastigotes, **chancre** which resolve in 2-3 weeks.
- **Haemato-lymphatic stage: intermittent fever**, headache & generalized lymphadenopathy mainly in the **cervical & sub-occipital region (Winterbottom' sign)** , anemia.
- **(CNS) stage:** This stage begins when the trypanosome parasites cross from the BBB into the spinal fluid, infecting the CNS including the brain, result in change in behavior, confusion, poor coordination difficulties with speech and **disturbance of sleep** (sleeping during day and insomnia at night.) & (Meningoencephalitis) In a typical case, there is daytime sleeping, psychological changes, tremors, convulsions and finally coma. without treatment, the disease is invariably fatal.

Diagnosis

- Recognition of the **trypomastigote in peripheral blood** & CSF during fever, sternal bone marrow,lymph node aspirates and CSF. Motile organisms may be visible in the buffy coat
- Serological testing is also common as IF and ELIZA.

American Trypanosomiasis

Introduction

- **Known as Chaga's disease. Caused by Trypanosoma cruzi. Transmitted by the 'kissing' bugs (Reduviid (Triatomine) Bug)**
- **Parasite when free in bloodstream in form (Trypomastigote), but in the tissue (muscle) it become in form of (Amastigote).**
- **Infective & Diagnostic stages: Trypomastigotes**

Pathogenesis

1) The parasites produce focal lymphangitis and oedema at the site of parasites entry **(chagoma)**
2) After that parasites (trypomastigote) enter the bloodstream and find their way, mainly on the **face near the eyelids**, it produces a **swelling of the eye** and temporal region with conjunctivitis **(Romana's sign)**
3) and also find their way mainly the cardiac muscles cells . The most constant feature of the cardiac disease is **cardiomyopathy**, in severe cases can lead to partial or complete heart block which may lead to cardiac failure.

Clinical features

Acute phase

- T.cruzi causes Acute illness in children, which is followed by chronic manifestations later in life. In the early stage, symptoms are typically either not present or mild, and may include fever, swollen lymph nodes, headaches, or local swelling at the site of the bite **(chagoma).**
- The most recognized marker of acute Chagas disease is called **Romaña's sign**, which includes swelling of the eyelids on the side of the face near the bite wound or where the bug feces were deposited or accidentally rubbed into the eye.

Chronic phase

- **T. cruzi causes a chronic illness with progressive myocardial damage → to cardiac arrhythmias and cardiac dilatation and may result in sudden death.**
- Gastrointestinal involvement leading to **megaesophagus and megacolon.**
- Intracellular amastigotes destroy the intramural neurons of the **autonomic nervous system in the intestine and heart, leading to mega intestine and heart aneurysms**, If left untreated, Chagas disease can be fatal, in most cases due to heart muscle damage

Diagnosis

- **Microscopical examination of Giemsa – stained blood film**
- **Serology: IFAT** (immunofluorescence antibody test)
- **Xenodiagnosis:** feeding bugs on a suspected cases.
- **PCR:** used to detect Trypomastigotes

13- Trematodes

Trematodes

Life cycle

- **Cercaria (THE INFECTIVE STAGE)** emerge from **snail** in the water and penetrate the skin of the human. The cercaria is transformed into a schistosomula inside the host tissues.
- The schistosomula first enters the systemic circulation and then
  - S. mansoni & S. japonicum worms go to portal circulation & mature in the mesenteric veins of the portal circulation
  - S. haematobium worms generally remain in the systemic circulation and mature in the blood vessels of the vesical plexus.
- **The eggs (DIAGNOSTIC STAGE)**
  - S. mansoni & S. japonicum are passed mainly in stool and
  - S. haematobium passed mainly in the urine

Pathology

- **The EGGs is the main cause of pathology.** Many eggs become stranded in the tissues or carried by the blood stream to other organs mainly the LIVER. The host reaction to the eggs may vary from small granulomas to extensive fibrosis
- The extent of damage is generally related to the number of eggs present in the tissues.
- Schistosome dermatitis, or "swimmers itch" occurs when skin is penetrated by a free-swimming, fork-tailed **infective cercaria.**

Developing Schistosoma in liver:

- **S. mansoni & S. japonicum located mainly in mesenteric vein** and its branches, the worm discharges EGGS, the eggs travel in 2 directions:
  1. Some eggs find their way into the lumen of the bowel and appear in the faeces,
  2. Other flow with blood stream in the portal circulation and enter the LIVER. Most of these eggs are trapped in the liver and give rise to pathology, again some of these eggs find their way through the liver tissue and enter the systemic circulation to another organ as brain, fibrosis of the liver caused from eggs settled in the liver may produce **portal hypertension, which may lead to hepatomegaly, splenomegaly esophageal varices and ascites.**

S. haematobium:

- The worm is located in the vesical venous plexus surrounding the **urinary bladder(Leads to hematuria) .**
- Many eggs are trapped in the wall of the bladder where they may give rise to calcification and granuloma formation
- Constriction of the orifice of the ureter may produce kidney damage, Hydronephrosis and cancer of the bladder.

Schistosoma haematobium (Egg has Terminal spine)	Schistosoma mansoni (Egg Has lateral spine)
Causes urinary schistosomiasis **1. PREPATENT PERIOD 10-12 wks** **2. EGG DEPOSITION AND EXTRUSION:** a. painless hematuria b. Inflammation of bladder and burning micturition c. CNS involvement (rare) **3. TISSUE PROLIFERATION AND REPAIR:** a. Fibrosis, papillomata in the bladder and lower ureter leading to obstructive uropathy b. Periportal fibrosis c. Lung and CNS involvement	**Causes intestinal schistosomiasis** **1. PREPATENT PERIOD 5-7 wks.** **2. EGG DEPOSITION AND EXTRUSION:** a. dysentery (blood and mucus in stools) b. hepatomegaly splenomegaly c. CNS involvement (rare) **3. TISSUE PROLIFERATION AND REPAIR:** a. Fibrosis, Papillomata in intestine b. Periportal fibrosis, hematemesis c. Lung and CNS involvement

Diagnosis

Parasitological: Examination of **urine** **Immunological:** Serological tests **Indirect:** Radiological & Cystoscopy	**Parasitological:** Examination of **stools** **Immunological:** Serological tests **Indirect:** Radiological & Endoscopy

Treatment

Drug of choice for schistosomiasis is **Praziquantel**

Fasciola hepatica

Info

- **True infection:**
  - occur when man accidentally ingests water plant (watercress) contaminated with METACERCARIA, the adult worm can causes mainly biliary colic with **biliary obstruction, jaundice**, generalized abdominal pain, cholecystitis.
- **False infection:**
  - is when eggs are eaten in infected animal liver and passed in stools.
- Snail is the intermediate host of Fasciola hepatica
- **Diagnosis:** eggs in stools or duodenal aspirate.
- **Treatment: Triclabendazole.**