Common endemic infections in the Middle East

Objectives :

- ★ Common terminology describing Endemicity.
- ★ Common Endemic disease in KSA: especially typhoid, Brucella.
- ★ Viral hemorrhagic fever (Dengue, RVF, KHV).
- ★ Leishmaniasis, MERS-COV, Malaria
- ★ For each endemic diseases: Epidemiology, Pathogenesis, Clinical features, Complications, Diagnostic workup, Differential diagnosis, Treatment & prevention.

MED439

Medicine Team 439

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Introduction

◀ Definitions

Baseline or endemic level	The amount of a particular disease that is usually present in a community is referred to as baseline or endemic level
Sporadic	Is a disease that occurs **infrequently and irregularly.**
Endemic	refers to the **constant presence** and/or usual prevalence of a disease or infectious agent in a population **within a geographic area**.
Hyperendemic	Refers to **persistent, high levels** of disease occurrence
Epidemic	Refers to an **increase**, often sudden, in the number of cases of a disease **above what is normally expected** in that population in that area.[1]
Outbreak	Carries the same definition of epidemic, but is often used for a **more limited geographic area** (e.g. in a hospital or ICU)[2].
Pandemic	Refers to an epidemic that has spread over several countries or continents, usually affecting a large number of people (e.g. Covid-19).

◀ In Saudi Arabia:

Bacterial infections

- Brucellosis
- Enteric Fever (Typhoid fever).

Viral infections

- MERS-COV
- Dengue fever
- COVID-19.

Parasitic infections

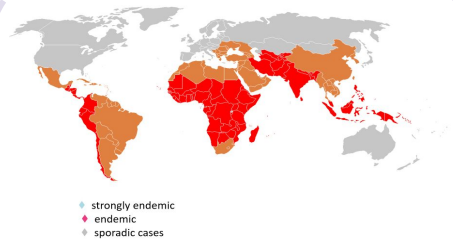
- Visceral Leishmaniasis

1- for example, there are 100 cases of malaria recorded each year, but if there was an increase to 500 in a year it would be called an epidemic
2- for example, outbreak of helicobacter in the ICU of a hospital (it's a very limited area, unlike endemic infections)

Enteric (Typhoid) Fever الحمى التيفية

◀ Introduction

- **Definition:** Enteric fever is characterized by **severe systemic illness** with **fever** and **abdominal pain**.
- It is an acute febrile disease, caused by **Salmonella typhi** and non-**Salmonella. paratyphi A, B or C**
- **Humans** are the only reservoir for **S. Typhi and Infection.**
- Persons with typhoid fever **carry the bacteria in their bloodstream and intestinal tract.**
- **Carriers** recovering from typhoid fever **shed S. Typhi in their feces.**
- It is **transmitted** through direct contact with an infected individual or indirect contact **via contaminated food or water.**
- We are not an endemic area of typhoid fever , most cases we see are immigrants . Citizens get the infection from food contamination by infected restaurant workers.
- Paratyphoid fever is associated with a milder and shorter illness, and complications are uncommon.



Epidemiology of Typhoid fever

- More **common in children and young adults**
- Worldwide, enteric fever is most prevalent in overcrowded areas with poor access to sanitation.
- Incidence More than 100 cases per 100,000 person-years in : **South-central Asia**, **Southeast Asia**, and **southern Africa**.

◀ Pathogenesis

organisms are ingested **and survive exposure to gastric acid** before gaining access to the small bowel, where The organisms penetrate **ileal mucosa** (invade the small bowel wall via peyer's patches)

Reach mesenteric lymph nodes, multiply there and invade blood stream. (disseminate via the lymphatic or haematogenous route)

Infect (reticuloendothelial tissues) : Liver, Gallbladder,, spleen, Kidney, Bone marrow. These **intracellular organisms** are likely sources for **relapsing** infection.

After 7-10 days bacilli pass into bloodstream (secondary bacteremia)

◀ Differential diagnosis

	**Brucellosis**		**Lymphoma**
	**Tuberculosis**		**Adult Still's disease [1]**
	**Infective endocarditis**		**Malaria**

1- Still's disease/juvenile rheumatoid arthritis is an important differential for typhoid fever. Patients will have high grade episodic fever, arthralgia/arthritis and specific skin rash called "salmon-rash' that disappears when the fever settles down. It's not like rose spots which remain in the body for 3-4 days. Patients usually have leukocytosis (around 15,0000), pneumonitis, high serum ferritin.

Enteric (Typhoid) Fever

◄ Clinical presentation

- Incubation period of 5 to 21 days.
- **Diarrhea and constipation** appear to occur with approximately **equal** frequency.
- **Headache** is a frequent symptom.ptn will present with fever/headache/abdominal pain

1st week of illness

- Rising ("stepwise") **fever** reaching **>40°C** and bacteremia develop.
- While **chills are typical,** frank **rigors are rare**.
- **Relative bradycardia**[1] or pulse-temperature dissociation may be observed.

2nd week of illness

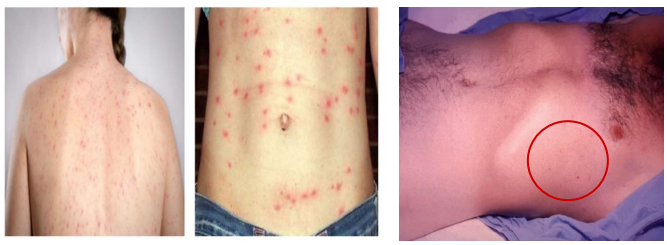
- **Abdominal pain** develops
- **Macular Rash "Rose Spots"** (faint salmon colored macules on the **trunk** and **abdomen**) may be seen, not always present but if a febrile pt presented with rose spots this is highly suggestive of typhoid fever.

3rd week of illness

- **Hepatosplenomegaly**
- **Intestinal bleeding**
- **Perforation** due to ileocecal lymphatic hyperplasia of the **Peyer's patches** may occur
- Together with secondary Bacteremia and peritonitis
- Septic shock or an altered level of consciousness may develop

◄ Rash in typhoid[2]

- **Rose spots**: 2 -4 mm in diameter raised discrete irregular blanching pink(salmon-colored) maculae's found on the chest, trunk and abdomen
- Appear in crops of up to a dozen at a time
- **Fade after 3 – 4 days** so it's acute it will disappear



Rose spots

◄ Carriers

- **Chronic Salmonella carriage**: Excretion of the organism in stool or urine **>12 months** after acute infection.
- 5% (1-6%) of the survivors (Asymptomatic) continue to excrete the organism for months.
- Chronic carriers represent an **infectious risk to others**, particularly in the setting of food preparation.
- Important to keep in mind the food handlers, screening may be done for health check up every 6 months, and there are vaccines for salmonella that can be given.
- In carriers, the bacteria **remain in the gallbladder** and are shed into the intestine (in chronic carriers, there is an increased **risk for gallbladder Cancer and gallstones**).
- In parts of the Middle East and Africa where urinary schistosomiasis is prevalent, chronic carriage of S. typhi in the urinary bladder is also common.
- **Fluoroquinolone therapy** (eg, **ciprofloxacin** 500 to 750 mg orally twice daily for 14 - 28 days eliminated carriage in 90 to 93 percent of cases.)

1- Normally, increase in the temperature will increase the HR (1c° → ↑HR by 10 - 15 beats per minute) , however, if a patient is febrile (39°) and his heart rate is 70-80 and he's not on rate controlling drugs (e.g Beta blockers) then this is called relative bradycardia. This is a sign for enteric fever.

Enteric (Typhoid) Fever

◀ Diagnosis

- The definitive diagnosis of enteric fever requires the culture of S.typhi or S. paratyphi from the patient. Blood culture is positive in most cases in the first 2 weeks. Culture of intestinal secretions, faeces and urine is also used.
- Febrile patient living in, traveling from, or visiting from an endemic area.
- **WBC** (sometimes there is **leukopenia**, if **bone marrow is involved** there will be **pancytopenia**)
- ESR (high)
- **Blood culture: Most important diagnostic tool at disease onset.**
- **Bone marrow culture: the most sensitive culture but is invasive procedure.** patients who have already received antibiotics
- **Stool cultures:** Positive in 30 to 40 % .often positive in the second and third weeks.
- **Widal test (commonly ordered) and is basically USELESS. DO NOT ORDER IT** (serum agglutination test). It has cross reactions– false positives. Also false negatives. Limited clinical utility in endemic areas because **positive results may represent previous infection.** Only ordered in private hospital to waste your money. This test is obsolete.
- In many cases the diagnosis of enteric fever is made presumptively in patients with protracted fever without alternative explanation.

◀ Blood Culture

- Bacteremia occurs early in the disease, Blood Cultures are positive in: (Decrease over time)
  - **1st week in 90%**
  - 2nd week in 75%
  - 3rd week in 60%
  - 4th week in 25% (bone marrow cultures are preferred in this stage)

◀ Treatment and prevention

Treatment	Prevention & control (WHO 2009)
• **Fluoroquinolones (e.g: ciprofloxacin) are the drugs of choice for empiric therapy.** • **3rd** generation **cephalosporins are effective**, like **Ceftriaxone 2gm Twice daily. (2nd choice)** • ESBL (Extended Spectrum Beta-Lactamase) in Pakistan • Fever may continue for several days after starting antibiotics • The majority are cured with antibiotics. • **10% may relapse**. (typically occurs **two to three weeks** after resolution of fever.)	• **Food and water safety:** avoid ingestion of contaminated food or water • Access to fresh water, prioritization of sanitation and hygiene **Control measures:** • Health education • Antibiotic treatment • Excluding disease carriers from food handling. • **A vaccine is available** recommended for travelers to high risk areas. It does not provide full protection • **None are completely effective** against S. Typhi and none have been demonstrated to provide protection against paratyphoid fever caused by S. Paratyphi A.

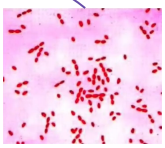
◀ Complications

- **Pneumonia, meningitis, osteomyelitis.**
- Severe **intestinal hemorrhage and intestinal perforation** (necrosis of the Peyer's patches) usually occurs in the ileum during the third week.
- If not treated can be fatal.

Brucellosis الحمى المالطية

◄ Brucellosis (Mediterranean Fever, Malta Fever, Undulant Fever).

- Systemic febrile illness.
- Caused by the bacterial genus called Brucella
  - Small **aerobic intracellular**[1] **Gram negative coccobacilli**
- **B. melitensis** and **B. abortus** are the most frequent. (there are many types however these are the most common here).
- Localize in the reproductive organs of host animals, causing abortions.
- They are shed in large numbers in the animal's milk, placental fluid, and other fluids.



To date, 8 species have been identified but 4 have moderate to significant human pathogenicity:

Species	Isolated from
Brucella melitensis	sheep and goats, as well as camels
Brucella suis	swine
Brucella abortus	cattle
Brucella canis	dogs

◄ Epidemiology

- It occurs worldwide.
- The heaviest disease burden lies in countries of :
  - The **Mediterranean basin and Arabian Peninsula,**
  - Also common in **India, Mexico, and South and Central America.**
  - 60% of cases of brucellosis occurred in individuals **aged 13-40 years**
- Brucellosis is generally uncommon in infants.
- Very rare in developed countries and if you detect a case , most likely the pt will be an immigrant coming from endemic areas.

◄ Transmission

- Brucellosis is a **zoonotic** infection that are **transmitted** from **animals** :
  - ➢ Contact with **fluids** (vets and people in contact with animals when they give birth) **or meat from infected animals** (**sheep, cattle, goats, pigs, camels or other animals**)
- **The Infection is transmitted to humans through:**

1. **Direct contact with an infected animal, or inhalation of aerosols:**
   Slaughterhouse **workers**, **farmers** and shepherds become inoculated with brucellae through aerosolization of fluids, contamination of skin abrasions, and splashing of mucous membranes.
2. **Consumption of unpasteurized dairy products:**
   can stay viable for 90 days , (especially raw **milk**, soft **cheese**, **butter**, and **ice cream**) is the **most common** means of transmission) **or partially cooked liver كبده مى بوقيه رديه, اوط**
3. **Laboratory workers with exposure to infected specimen** during processing specimens (aerosols) without special precautions.

Need biosafety level 4 for culture (Bioterrorism), In our hospital we don't culture brucella because it **transmit very fast if you try to grow it, it needs very strict infection control measures including negative pressure room and other control measures.**

1-Two facts about intracellular organisms :

- **Spontaneous recovery is the rule**
- **Relapses can happen**

Brucellosis

◄ Pathogenesis

- The organism enters the body → goes to the lymph nodes → to the bloodstream → to the **reticuloendothelial system** → blood → any organ.

Brucella bacteria:

- Is a **systemic disease** and can involve almost **every organ** system.
- Can gain entry into the human body through:
  - ➢ Gastrointestinal (**GI**) tracts (Ingestion).
  - ➢ Break in the **skin**.
  - ➢ **Conjunctival** exposure through eye splash, and inhalation are the most common routes of entry.
- Possess a unique ability to invade both **phagocytic** and **nonphagocytic** cells and to survive in the **intracellular environment**.يعيش داخل خلايا الجسم
- Once within the bloodstream, the organisms quickly become **intracellular pathogens** contained within circulating polymorphonuclear cells (**PMNs**) and **macrophages**.
  - ➢ After ingestion by phagocytes, Brucellae that survive are transported to organs by these cells and may replicate in any organ causing both **localized** and **systemic infection**: **liver, spleen, central nervous system, heart, joints, and genitourinary system.**
- Development of **cell-mediated immunity** is the principal mechanism of recovery.
- **What is the natural history of brucellosis ? Spontaneous recovery**
- The host response to infection with **B abortus** is characterized by the development of **tissue granuloma.**
- In contrast, infection with **B melitensis** and **B suis** (the more virulent species) more commonly results in **visceral micro abscesses.**

◄ Clinical manifestations

- ❖ A careful history is the most helpful tool in the diagnosis of brucellosis.
  - ➢ You should always have a high suspicion because we're living in an endemic area.
  - ➢ Ask about risk factors: **Contact** with animals and **ingesting** unpasteurized milk.
- ❖ The incubation period is 1–4 weeks, occasionally, it maybe take few months.

Symptoms (insidious onset)	Signs (Physical findings)

• **Undulant Fever** (rising and falling like a wave)
• **Night sweats** (drenching)كان احد اجد سطل موبه وكبه عليه
• Fatigue
• Anorexia
• Weight loss like constitutional symptoms
• Arthralgia
• **Low back pain (especially sacroiliac joint)**
• **Depression**
• Headaches & Cough
	• Variable and nonspecific:
	  ○ **Arthritis**
	  ○ hepatomegaly, splenomegaly and/or Painful Lymphadenopathy
	  ○ Hepatosplenomegaly

Brucellosis

◀ Localized brucellosis (Complications)

Osteoarticular disease	Neurobrucellosis [1]	Other
Osteoarticular disease is the most common form of focal brucellosis: **1- Sacroileitis** (usually 2-3 weeks after the onset of symptoms) • **Radiography:** blurring of articular margins and **widening of the sacroiliac spaces.** **2- Vertebral spondylitis: lumbar vertebrae (L4)** are involved more frequently than the thoracic and cervical vertebrae. **3- large joints arthritis.** Can cause abcesses in the back, osteomyelitis and septic arthritis.	- Usually presenting as **meningitis** (acute or chronic), **encephalitis**, radiculopathy. - The **most serious complication** - Occurs in undiagnosed pt for long time, leads to **irreversible brain damage**	**Genitourinary:** especially orchitis and/or epididymitis. **Abscesses:** involving the liver, spleen and abdomen.**psoas muscle** **Cardiovascular**: **Endocarditis** is **the main cause of death** attributable to brucellosis

◀ Differential diagnosis

	**Typhoid fever**		**Lymphoma**
	**Tuberculosis**		**Collagen vascular disease**
	**Infective endocarditis**		

◀ Investigations

Definitive diagnosis of brucellosis is based on **serologic techniques, culture or both**:

- **Blood cultures:**
  - ➢ Gram-negative coccobacilli (usually positive even in relapse).
  - ➢ Slow growth = 2 weeks (notify the lab that you are suspecting Brucellosis so that they don't dispose of the culture after 5 days like they normally do).
  - ➢ Sensitivity depends source of specimen:
    - **Blood (15%-70%)**
    - **Bone marrow (80%-90%).**
- **Serology:**
  - ➢ **Standard Agglutination Test (SAT)** positive in recent infection:
    - Cut off limit 1:640 or 1:320 with symptoms and risk factor (it can be **negative in meningitis**)
    - Titers higher than 1:320 are considered to be diagnostic, especially in endemic areas
    - **Sensitivity 95.6% & Specificity 100.0%.**
- WBC (Pancytopenia is common in brucellosis due to what we call hemophagocytosis; it goes to the bone marrow and cause such kind of complication.
- ESR, CRP (high)
- Radiological assessment if needed especially **for localized joint involvement to rule out osteomyelitis. It affects the 8th cranial nerve(Hearing loss). A pathognomonic feature on MRI is leptomeningeal enhancement of 8th nerve. .**

1- **Could present as acute or chronic meningitis**. in acute meningitis the pt. will present with very bad features of meningitis. the **serology will be negative most of the time** (in acute presentation, only 30% will be positive for CSF samples) so in diagnosing these patients, the history and risk factors are very important. in chronic, it will have chronic features of chronic meningitis (low sugar, high protein and lymphocytes)

Brucellosis

◀ Treatment

General principles of brucellosis treatment include:

- Use of antibiotics with **activity in acidic intracellular environments** (such as doxycycline and rifampin)
- Use of **combination therapy** (given high relapse rates with monotherapy)
- **Prolonged duration** of treatment.

Uncomplicated Brucellosis	Complicated Brucellosis
1st line: Doxycycline (oral) **for 6 weeks + Streptomycin** (Parenteral) **for the first 14 -21 days or** gentamicin (7 Days) + Doxycycline 100 mg BID for 6 weeks **2nd line : Rifampicin + Doxycycline for 6 weeks.** Other drugs that can cover brucellosis: ciprofloxacin, TMP/SMX and **Ceftriaxone (preferable 3rd agent in meningitis) for 1 month .**	- Endocarditis, meningitis, osteomyelitis - No uniform agreement. - Usually **3 anti brucella drugs for 3 or more months** (might extend to 6 months) **For example:** Aminoglycoside, Doxycycline and rifampicin or we add bactrim or ciprofloxacin

Dr notes:

- **Contraindications of streptomycin:**
  - **Patient more than 65 of age, Renal impairment, Diabetic.**
  - So we use Rifampicin and Doxycycline, however, be aware of the drug-drug interactions as it can cause elevated LFT
- **Doxycycline can cause esophagitis**, instruct the patient to sit in upright position for at least 30 mins and drink a lot of water, you can give PPIs as will.
- The lowest relapse rate is with aminoglycoside + doxycycline, second lowest relapse rate is with rifampicin + doxycycline

◀ Relapse vs Re-infection

- About 10% of patients relapse after therapy.
- Most relapses occur within three months following therapy and almost all occur within six months.
- Relapse should prompt **assessment for a focal lesion**, especially **hepatosplenic abscess**
- **Most relapses can be treated successfully with a repeat course of a standard regimen**

Relapse	Failure of therapy	Re-infection
Un-eradicated infection even after receiving the proper treatment	For example: pt has osteomyelitis and you treat for only 6 weeks so they relapse again	**- Because of ongoing risk factor**

◀ Prevention

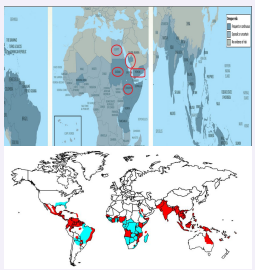
- To avoid contact with possibly infected animals.
- Avoid drinking raw milk (pasteurizing milk / **boiling milk 60 degree for 10 min.**
- Eating processed meat,
- Regular check-up of animals, and their vaccinations.no vaccination for human
- Taking care of health safety when dealing with infected animals,
- Health safety during work in laboratories dealing with Brucella spp.

Viral hemorrhagic fevers (dengue fever)حمى الضنك

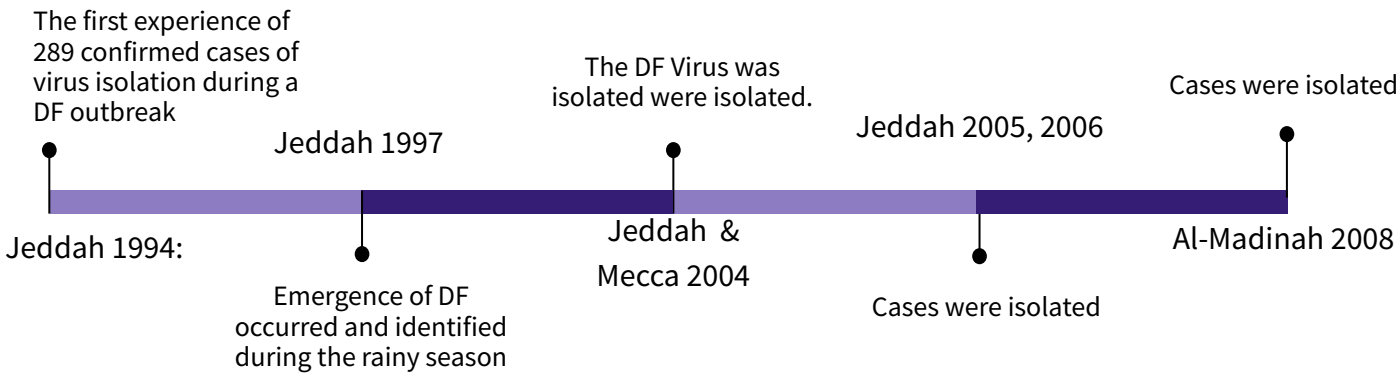
◀ Epidemiology

Press on the picture for extra info

- Aedes aegypti mosquitoes are widely distributed in tropical and subtropical areas from latitude 45°North to 35°South. (high humidity and a hot climate). After rainy seasons
- **Asia:** (incidence of dengue infection is increasing).
  - China , Thailand, Vietnam, Indonesia, India, Pakistan, and SriLanka.
- **Africa and Eastern Mediterranean:** in most of sub Saharan Africa and the Middle East.
- **North America:** present in most areas of Mexico and in the south-eastern United States
- Dengue is also common in more than 100 countries around the world with where 50 million DF occur annually, out of which 22,000 deaths affect mostly children
- **in Saudi, it's present in Makkah, Jeddah, Jizan and najran)**



◀ Dengue fever in Saudi Arabia:



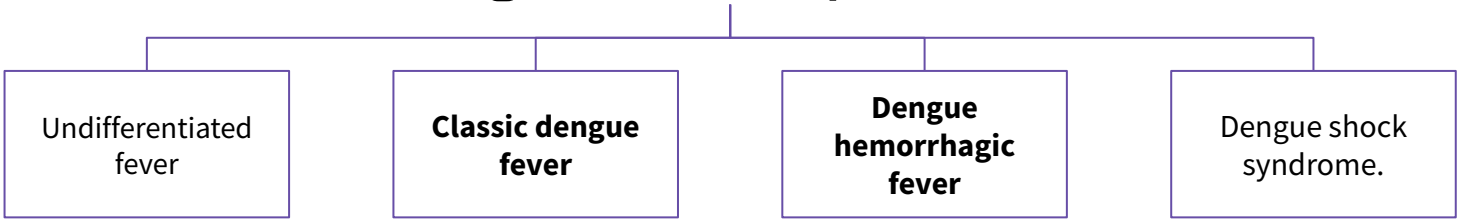
- MOH reported a total of **3350** cases of DF in the Kingdom and estimated the case **fatality rate to be 4.6/1000.**

◀ Dengue Virus

- Causes **dengue** and **dengue hemorrhagic fever**.
- Dengue is a febrile illness caused by infection with one of four dengue viruses
- Has 4 serotypes (DEN-1, 2, 3, 4)
- Is an **arbovirus**. (family Flaviviridae, genus Flavivirus .)
- Composed of **s**ingle-**s**tranded **RNA**.
- Transmitted by : **Aedes Aegypti female mosquitoes.** All dengue viruses are **mosquito-borne human pathogens**
- Infection may be, **Asymptomatic (90%)** or present with a broad range of clinical manifestations including: Mild febrile illness OR Life-threatening shock syndrome.

Most of the time, if you get one of the serotypes, the infection will be mild. You will acquire immunity against this strain. However, if you get infected again with a different serotype you will have a worse presentation. Basically, you wont get cross-immunity to the other serotypes. It's actually a risk factor for disease severity if you get infected by a different serotype.

Dengue Clinical Syndromes



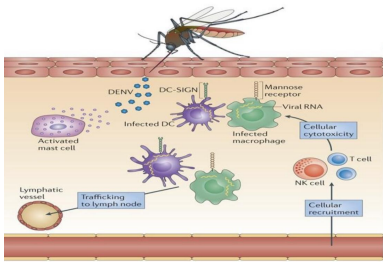
Viral hemorrhagic fevers (dengue fever)حمى الضنك

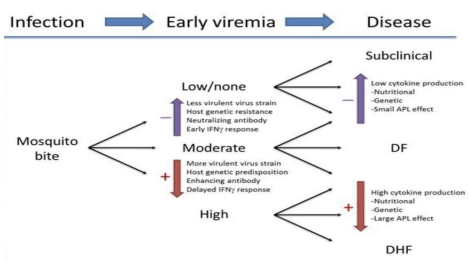
◀ Four Dengue Virus Serotypes (DEN 1,2,3, and 4)

- All can cause severe & fatal infection
- Infection by one serotype gives No cross immunity to other types but life long immunity to the same type, however, more predisposition to DHF/DSS if infected by another serotype.
- 2o immunopathological mechanism triggered by sequential infections with different dengue viral serotypes.
- Complicated pathogenesis – partially attributable to Ab- dependent enhancement.
- Humans are the main reservoir but monkeys may be.

◀ Pathogenesis of Dengue:

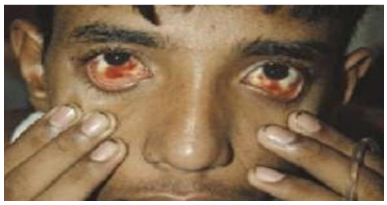
- Dengue virus after entering in the body invades the local macrophages and multiply there.
- Infected local cells then migrate from site of infection to lymph nodes, where monocytes and macrophages are recruited, which become targets of infection.
- Consequently, infection is amplified and virus is disseminated through the lymphatic system. As a result of this primary viremia, several cells of the mononuclear lineage, including blood-derived monocytes
- Viremia develops within 24 hours. During this period, virus travels throughout the body.
- Bone marrow cells have also been shown to be susceptible to infection with DENV
- In severe case, viral load is very high and many vital organs are affected.
- Virus infected macrophages produces a number of signaling proteins such as interferons, cytokines, chemokines, TNF, other mediators which are responsible for many symptoms such as flue like syndrome and pain.
- These mediators affects hemostatic system of body.
- Fluid from blood vessels starts to leak out so that the blood volume decreases resulting in low blood pressure.
- Decrease in blood pressure causes insufficient supply of blood and Oxygen to vital organs such as brains.
- Dengue also infects bone marrow, so that bone marrow cannot produces sufficient platelets.
- Since platelets are needed for blood clotting, dengue infection causes blood clotting defect and increase the risk of bleeding.

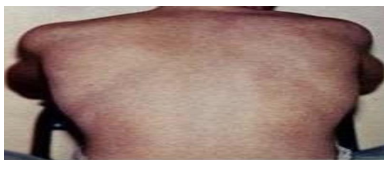




◀ Classic Dengue Fever

- Acute febrile illness
- Severe Hemorrhage mainly **retro-ocular;**
- Myalgia & arthralgia – often severe (breakbone fever);
- Nausea & vomiting > 50%; diarrhea (30%)
- **Rash** (50%) (of variable appearances; maculopapular, petechial, or erythematous.





Viral hemorrhagic fevers (dengue fever)

◀ Clinical characteristics of classic dengue fever

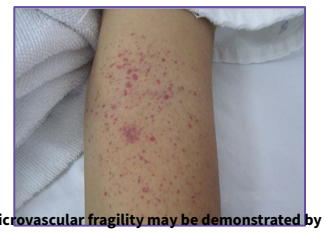
- The incubation period is **3 to 14 days, symptoms typically develop between 4 and 7 days** after the bite of an infected mosquito
- It is an acute febrile illness defined by the presence of **fever and two of the followings:**
  - **Headache & Retro-orbital or ocular pain [1], Myalgia and/or bone pain & Arthralgia Rash and blood test might shows Leukopenia.**

	Fever (abrupt onset) [2]		Generalized Lymphadenopathy
	headache (Mainly retro-orbital that worsens with Eye movements)		**Muscle and joint pain (bone breaking fever)**
	Nausea/Vomiting		Conjunctival suffusion
	Rash (maculopapular, measles-like exanthem)		Severe backache (most prominent symptom)
	**Hemorrhagic manifestations**		

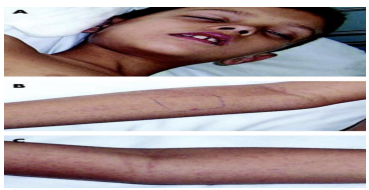
◀ Dengue haemorrhagic fever (DHF)

Hemorrhagic manifestations of Dengue:

- Most serious form of dengue infection
- WHO estimates 500,000 cases /year
- Mortality ≈ 10%; high as 50%
- WHO 4 diagnostic criteria (Fever (2-7 days) – Hemorrhagic manifestations – Low platelet counts (< 100000 /ml) – evidence of leaky capillaries.
- **Skin hemorrhages:** petechiae, purpura, ecchymoses.
- Gingival bleeding (gum bleeding)
- Nasal bleeding (epistaxis)
- **Gastrointestinal bleeding:** hematemesis, melena.
- Hematuria.
- Increased menstrual flow. (vaginal bleeding)
- Plasma leakage due to **increased vascular permeability** leading to ascites and pleural effusion in addition to features of Dengue fever .



Microvascular fragility may be demonstrated by a positive "tourniquet test"



- **Positive tourniquet test :** This test is performed by inflating a blood pressure cuff on the upper arm to midway between diastolic and systolic blood pressures for 5 minutes. The results are considered to be positive if more than 20 petechiae per square inch are observed on the skin in the area that was under pressure.

◀ Dengue shock syndrome:

- DHF with marked plasma leakage that leads to circulatory collapse (shock) as evidenced by:

1. **Cold, clammy skin and restlessness.**
2. **Narrowing pulse pressure or hypotension**
3. **Rapid and weak pulse.**

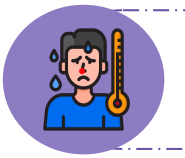
1- **Febrile pt with ocular or retro orbital pain and travel history to endemic area? Dengue should be one of you differentials.**
2- The fever subsides after 3–4 days, the temperature returns to normal for a couple of days and then the fever returns, together with the features already mentioned, but milder. This biphasic or **'saddleback'** pattern is considered characteristic. Severe fatigue, a feeling of being unwell and depression are common for several weeks after the fever has subsided.

Viral hemorrhagic fevers (dengue fever)

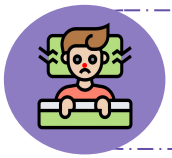
◀ Dangerous signs in Dengue hemorrhagic fever

Abdominal pain - intense and sustained.

Persistent vomiting



Abrupt change from fever to hypothermia, with sweating and prostration.



Restlessness or somnolence

◀ Diagnosis

- Isolation of dengue virus by tissue culture, or detection of viral RNA by PCR in sera obtained during the first few days of illness, is **diagnostic**.

Who to suspect?	Definite tests
Any **febrile** individuals with **typical** clinical manifestations and relevant epidemiologic exposure [residence in or travel within the past two weeks to an area with mosquito-borne transmission of DENV infection] Provisional diagnosis of DENV infection is usually established clinically.	• **RT-PCR** [1]**:** Detection of viral nucleic acid BY reverse-transcriptase polymerase assay, • Detection of viral antigen has **high specificity** but is more labor intensive and costly. • **Serology test:** to detect presence of Immunoglobulin : IgM or IgG. (unreliable in vaccinated patient)

◀ Treatment

- Symptomatic treatment.
- **Hydration**.
- **Avoid NSAIDS or Aspirin** (especially in children to avoid **Reye syndrome**[2]).
- **Only acetaminophen** for fever, headache or arthralgia.
- Platelet transfusion only if platelets <10-20.

◀ Prevention

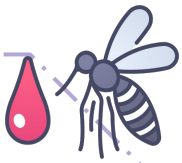
- **Elimination & destruction of mosquitos and larval habitat** (cornerstone of prevention):
  - ➢ Space Spraying of insecticide is not usually effective.
  - ➢ Spraying residual insecticides in-door.
  - ➢ Larval source reduction : **Cover water holding containers.**
- **Personal protection against mosquito biting:**
  - ➢ Screening
  - ➢ Protective clothing
  - ➢ Repellents
- Centralized, vertically-structured programs with military-type organization, strict supervision, high level of discipline.
- A vaccine was recently approved but it is given ONLY to those who have previously gotten Dengue fever. otherwise, you would be increasing their risk for severity.

1- If you have the resources you should go with the highest evidence which is PCR, in poor countries if they suspect a dengue fever case based on the clinical features discussed before they will treat accordingly

2- A rare type of hepatic encephalopathy that is associated with **aspirin** use for **viral** illness in children < 19 years. To memorize the symptoms of Reye syndrome, remember that "It's never Rainy (Reye) in **CHILE**": **C**oma, **H**epatomegaly/**H**ypoglycemia, history of viral **I**nfection, **L**iver failure, **E**ncephalopathy.

Rift valley fever حمى الوادي المتصدِّع

◀ Rift valley fever

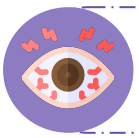


- Rift Valley fever (RVF) is an **acute**, **fever-causing** viral Zoonotic disease that affects domestic (Ruminant) animals (such as cattle, buffalo, sheep, goats, and camels) and humans.
- The disease was first reported among livestock by veterinary officers in Kenya in the early 1900s
- The disease is named after the Rift Valley of East Africa, where the etiologic virus was first isolated **in 1930** among infected sheep on a farm in the **Rift Valley in Kenya**.
- RVF is most commonly associated with **mosquito-borne** epidemics during years of unusually heavy rainfall.
- The disease is caused by the RVF virus, a member of the genus **Phlebovirus** in the family Bunyaviridae.
- Several Outbreaks and epidemics of RVF were limited to the African continent until 11 September 2000, the Ministry of Health (MOH) of the Kingdom of Saudi Arabia (Riyadh) received reports of unexplained severe **hepatitis** in 7 patients (5 died) from the Jizan region at the southwestern border of Saudi Arabia, then Tehama, and Al-Qunfuda.
- A team from the MOH started investigations within 24 h after notification
- Next outbreak was reported in **Yemen**
- Now Rift valley fever is considered to be at a low level of endemicity in Saudi Arabia.
- **Transmission:**
  - ➢ Bites from infected mosquitoes
  - ➢ Close contact with infected mammals, sheeps, goats and camels (more frequently).

◀ Clinical manifestations

	**Low-to-moderate–grade fever (Biphasic)**		**Renal failure**
	**Abdominal pain / Diarrhea**		**muscle pain, back pain, and joint pain**
	**Nausea/Vomiting**		**Malaise and Headache**

◀ Complications Indicative of severe infection



Retinopathy

Meningoencephalitis

Hepatic necrosis : **Elevated liver enzyme levels progressing to liver failure**

Bleeding & disseminated intravascular coagulation (DIC) : RVF is one of the causes of viral hemorrhagic fever, if a pt presented to you with fever and reported bleeding from several sites including gum and nose, you should consider RVF.

◀ Diagnosis and management

Diagnosis	Management
• Polymerase chain reaction **(PCR)** for detection of viral RNA • Enzyme-linked immunosorbent assay (**Elisa**) for detection of IgM antibodies against RVF virus	• Treatment is symptomatic/supportive . • Vaccines for veterinary use are available (for animals).

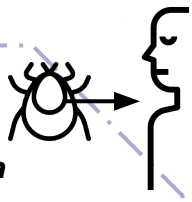
◀ Alkhurma hemorrhagic fever

- Alkhurma hemorrhagic fever (AHF) is caused by **Alkhurma hemorrhagic fever virus (AHFV)**, **a tick-borne virus** of the **Flavivirus family.**
- The virus was initially isolated in 1995 from a patient in Saudi Arabia. Subsequent cases of AHF have been documented in tourists in Egypt, extending the geographic range of the virus and suggesting that geographic distribution of the virus is wide and that infections due to AHFV are underreported.

Epidemiology

AlKhurma is a city in East Taif. it started there, and after that, cases were reported in Jeddah, Makkah, Jizan and Najran. also in the borders of Egypt and Sudan

◀ Transmission



- Transmission is not well understood.
- AHFV is a zoonotic virus
- its described tick hosts (the **soft tick *Ornithodoros savignyi*** and the **hard tick *Hyalomma dromedari)*** are widely distributed.
- People can become infected through a tick bite or when crushing infected ticks. **or dealing with contaminated blood, and this is how it happened in the first cases, butchers were exposed to blood of infected animals.**
- Epidemiologic studies indicate that contact with domestic animals or livestock may increase the risk of human infection.
- **No human-to-human transmission of AHF has been documented.**
- Although livestock animals may provide blood meals for ticks, it is thought that they play a minor role in transmitting AHFV to humans.
- **No transmission through non-pasteurized milk** has been described, although other tick-borne flaviviruses have been transmitted to humans through this route.

Ornithodoros Savignyi

Hyalomma dromedarii

Alkhurma hemorrhagic fever

◀ Signs and symptoms

- after an incubation period that could be as **short as 2-4 days**
- No repeated or chronic symptoms have been reported following recovery.
- Evidence suggests that a milder form may exist, where hospitalization is not required.
- We had an outbreak a couple of years ago but the mortality wasn't high

Initially (first phase)

- non-specific flu-like symptoms, including fever
- anorexia (loss of appetite)
- general malaise
- diarrhea
- vomiting

second phase

- a second phase has appeared **in some patients**
- includes neurologic and hemorrhagic symptoms in severe form.
- Multi-organ failure precedes fatal outcomes.

◀ Risk of exposure

- Contact with livestock with tick exposure are risk factors for humans, as is contact with infected ticks, whether through crushing the infected tick with unprotected fingers or by a bite from an infected tick.
- Slaughtering of animals which may acutely but asymptomatically infected may also be a risk factor, as it is possible that infected animals develop a viremia without obvious clinical signs.

◀ Diagnosis

- Clinical diagnosis could be difficult due to similarities between AVHF, Crimean-Congo Hemorrhagic fever (CCHF), and Rift Valley fever (RVF) , which occur in similar geographic areas . Laboratory diagnosis of AHF can be made in the early stage of the illness by **molecular detection by PCR or virus isolation from blood**. Later, **serologic testing using enzyme-linked immunosorbent serologic assay (ELISA) can be performed**

Treatment	Prevention
- There is no standard specific treatment for the disease. - **Patients receive supportive therapy,** which consists of balancing the patient's fluid and electrolytes, maintaining oxygen status and blood pressure, and treatment for any complications. - Mortality in hospitalized patients ranges from 1-20%	- Given that **no treatment or specific prophylaxis is presently available**,prevention and increased awareness of AHFV are the only recommended measures. Complete control of ticks and interruption of the virus life cycle is impractical; in endemic regions, **it is important to avoid tick-infested areas and to limit contact with livestock and domestic animals**. - **Individuals should use tick repellants on skin and clothes** and check skin for attached ticks, **removing them as soon as possible.** Tick collars are available for domestic animals, and dipping in acaricides is effective in killing ticks on livestock. - **People working with animals or animal products in farms or slaughterhouses should avoid unprotected contact with the blood, fluids, or tissues of any potentially infected or viremic animals.**

Leishmaniasis

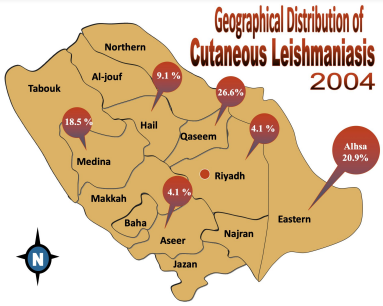
◀ Introduction

- leishmaniasis is a **protozoal** disease caused by Leishmania parasite
- Transmitted by the bite of infected female **phlebotomine sand fly (Phlebotomus Papatasi)**
- Relapse is seen in Patients who become immunocompromised.
- **Leishmaniasis is of three types:**

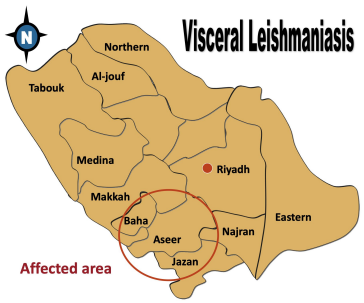
Cutaneous Leishmaniasis (most common)	Muco-cutaneous leishmaniasis	Visceral leishmaniasis (kala-azar) (most serious)

◀ Epidemiology of Leishmaniasis in Saudi Arabia

Cutaneous Leishmaniasis

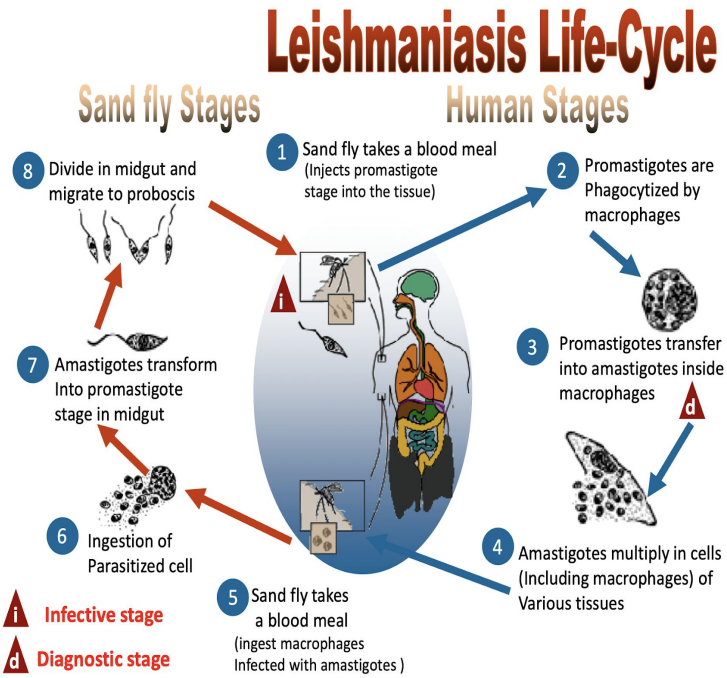


Visceral Leishmaniasis



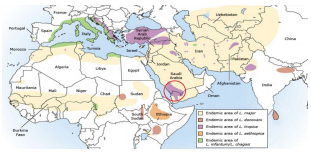
◀ Leishmaniasis Life Cycle:

1. The parasites are found as oval **amastigotes** (Leishman- Donovan bodies).
2. These bodies multiply inside the macrophages and cells of the reticuloendothelial system and are then released into the circulation as the cells rupture.
3. Parasites are taken by sandfly where they can be inoculated into a new host.



Cutaneous Leishmaniasis

◀ Cutaneous Leishmaniasis



- Cutaneous lesions tend to occur on **exposed areas of the skin**, **face is the most commonly affected site**, and ulcerative pattern accounts for 90% of lesions.
- begins as a **pink-colored papule** that enlarges and develops into a nodule (often with central softening), leading to a **painless ulceration** with an **indurated** border.
- Multiple lesions may be present.
- **The main causative species are:**
    - **Leishmania major (L. major) infection.**
    - **Leishmania tropica (L. tropica) infection.**

◀ Cutaneous Leishmaniasis in Saudi Arabia

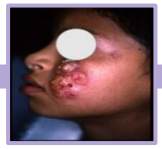
- The disease is endemic in many parts of KSA, with the majority of cases concentrated in six regions, including **Al-Qaseem, Riyadh, Al-Hassa, Aseer, Ha'il, and Al-Madinah.**
- Leishmania major (L. major) and Leishmania tropica (L. tropica) are the main dermotropic species, and **Phlebotomus papatasi** (vector of L. major) and **Phlebotomus sergenti** (vector of L. tropica) are the **proved vectors** of the disease.
- **Psammomys obesus** and **Meriones libycus** have been defined as the **principal reservoir** hosts of zoonotic Cutaneous Leishmaniasis in Al-Hassa oasis, Al-Madinah, and Al-Qaseem provinces.
- **Clinically**, males are affected more than females, and there is no variation between the Saudis and expatriates in terms of number of reported cases, but the disease tends to run a more severe course among non-Saudis.

Phlebotomus papatasi

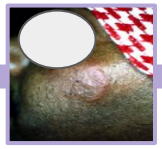
Psammomys obesus

Meriones libycus

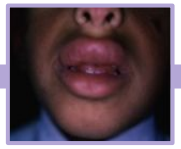
◀ Types of Cutaneous leishmaniasis



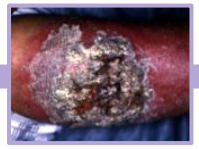
Hyperkeratotic



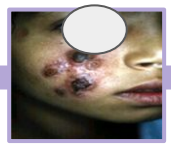
Recidivans



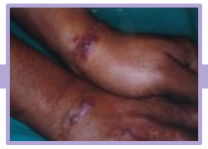
Mucosal



Erysipeloid



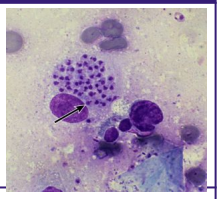
Plaque



Can transmit to other skin areas through **lymphatic chain**

Cutaneous Leishmaniasis

◀ Diagnosis of Cutaneous leishmaniasis

Definitive diagnosis requires demonstration of the parasite in a clinical specimen (usually skin) by:	
Histopathology	• Giemsa staining is typically used, the **Leishmania amastigote** is an **oval to round organism** • The cytoplasm is blue, the nucleus violet-blue, and the kinetoplast red to violet **(diagnostic characteristic)** 
Culture	Typical liquid media consists of **Schneider's drosophila media** supplemented with calf serum, or Novy, MacNeal, Nicolle **(NNN) media.**
Molecular techniques	**Polymerase chain reaction** is one of the most sensitive diagnostic tests for CL.

◀ Differential Diagnosis of Cutaneous leishmaniasis

01	02	03	04
Sporotrichosis	Mycobacterial infection	Leprosy	Skin cancer

◀ Treatment & Prevention of Cutaneous leishmaniasis

Treatment:

- **Cutaneous leishmaniasis** (CL) is **not life-threatening** but it can have disfiguring lesions and devastating effects on local communities
- Small lesions usually require no treatment
- Many CL infections eventually **resolve with spontaneous healing** occurring over months to years. Most patients will not wait for spontaneous resolution because the ulcer is usually on an exposed area
- **CL** due to **L. major** may **heal spontaneously** within **4–6 months** in 50– 75% of cases and almost in all patients at 8 months,
- While in **L. tropica** spontaneous **healing** occurs within **1 year** or longer

Therapeutics for CL consist of local/topical:

- **Cryotherapy** immediately followed by intralesional pentavalent antimony.
- **Topical paromomycin ointment** (may be used for treatment of ulcerative lesions due to L. major.), imidazole ointment.
- **Local infiltration of lesion with antimonials** (sodium antimony gluconate; Pentostam).
- **Parenteral sodium stibogluconate** (SSG)

Prevention:

- NO pre or post exposure prophylaxis.
- Effective prevention requires health education regarding risk of infection and epidemiology of transmission.
- Covering skin with clothing is helpful as sand fly mouthparts do not penetrate clothing (in contrast, mosquito mouthparts do penetrate clothing).
- Clothing can be impregnated with an insecticide such as **permethrin**.
- An insect repellent such as DEET (NN-diethyl-3-methylbenzamide) can be applied to exposed skin areas.
- Use of fine mesh insecticide-treated bednets may also be helpful.

Visceral Leishmaniasis

◀ Visceral Leishmaniasis

- Visceral leishmaniasis (VL), also known as **kala-azar** , is a disease caused by: **Leishmania donovani & L. infantum** that is transmitted by **phlebotomine sandflies.**
- The most important clinical manifestation of VL is the syndrome known as **kala-azar** (Hindi for **"black fever"**).
- The incubation period is usually **two to six months** but can range from a few weeks to several years. Most cases are detected in the south, the pt will mention that s/he traveled to **Jizan** a few months ago.
- Onset of symptoms is usually **insidious** or **subacute**
- Parasites replicate in the **reticuloendothelial system**, very high parasite loads accumulate in the spleen, liver (Causing hepatosplenomegaly) , and bone marrow.
- **Hemophagocytic lymphohistiocytosis** (HLH) is a systemic disorder of excess immune activation that can be triggered by certain infections it is an uncommon complication of VL

◀ Clinical Features

Symptoms

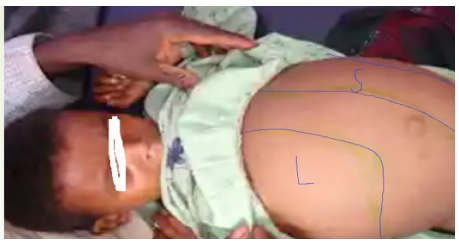
- Asymptomatic infection or slow progression of malaise, fever, weight loss

Laboratory Findings

- Severe **anemia** , **Leukopenia**, **Thrombocytopenia**,
- **Hypergammaglobulinemia**
- **Hypoalbuminemia**, and **edema**.

Splenomegaly

- **Splenomegaly** with or without hepatomegaly [The spleen is usually firm] over a period of weeks to months



The spleen is enlarged reaching up to the Suprapubic area. **Interestingly, visceral leishmaniasis is one of the causes of huge splenomegaly crossing the midline**

Kala-azar

- Kala-azar ("black fever") refers to darkening of the skin, which is a common symptom in South Asia but not elsewhere.
- Kala-azar is nearly always fatal without treatment.

Immunosuppression

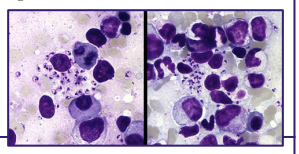
- Immunosuppression **increases risk** for secondary bacterial infections.

◀ Visceral Leishmaniasis in Saudi Arabia

- Visceral Leishmaniasis in KSA caused by **L.Donovani and the Rattus rattus** is the reservoir.

Visceral Leishmaniasis

◀ Diagnosis of Visceral leishmaniasis

Diagnostic tools of Visceral leishmaniasis	
Histopathology (bone marrow or spleen aspirations)	**Bone marrow aspirates are generally safer than splenic aspirates.** Diagnosis requires visualization of **amastigotes** [**spherical** or **ovoid** bodies that measure 1- 5 microns long by 1 - 2 microns wide within macrophage] under microscope. 
Culture	Typical liquid media consists of Schneider's drosophila media supplemented with calf serum, or Novy, MacNeal, Nicolle (NNN) media.
Molecular techniques	**P**olymerase **c**hain **r**eaction is one of the **most sensitive** diagnostic tests for VL

◀ Treatment

- **Liposomal amphotericin B is the drug with the highest therapeutic efficacy** and the most favorable safety profile monotherapy (total dose 20 to 21 mg/kg
- The pentavalent antimonial drugs **sodium stibogluconate (SSG)** and meglumine antimoniate, are still widely used; however, monotherapy with antimonial agents is no longer a first-line treatment for VL.
- Two new drugs have been added **paromomycin** and **miltefosine**.
- Nutritional support.
- Response to treatment is generally assessed clinically, based on resolution of fever, decrease in spleen size, and weight gain.
- **Pregnancy:** VL infection in the setting of pregnancy has been associated with congenital infection and fetal death.

Liposomal amphotericin B is the drug of choice for treatment of VL in pregnancy.

◀ HIV co-infection

Visceral leishmaniasis is strongly associated with HIV-related immunosuppression, and the two infections may be passed on together through injecting **drug use.**

An area for your notes

Mucocutaneous leishmaniasis

◀ Mucocutaneous leishmaniasis

- Mucocutaneous leishmaniasis occurs in 3–10% of infections with **L. b. braziliensis** and is most common in Bolivia and Peru
- Relapses are common following treatment. Patients may die because of secondary bacterial infection or, occasionally, laryngeal obstruction.

◀ Clinical features

- The cutaneous sores are followed months or years later by indurated or ulcerating lesions affecting mucosa or cartilage, typically on the lips or nose ('espundia').
- The condition can remain static, or there may be progression over months or years affecting the nasopharynx, uvula, palate and upper airways.

◀ Diagnosis & Management

Diagnosis	Management
• Biopsies usually show only very scanty organisms, although parasites can be detected by PCR; serological tests are frequently positive.	• Amphotericin B is the treatment of choice

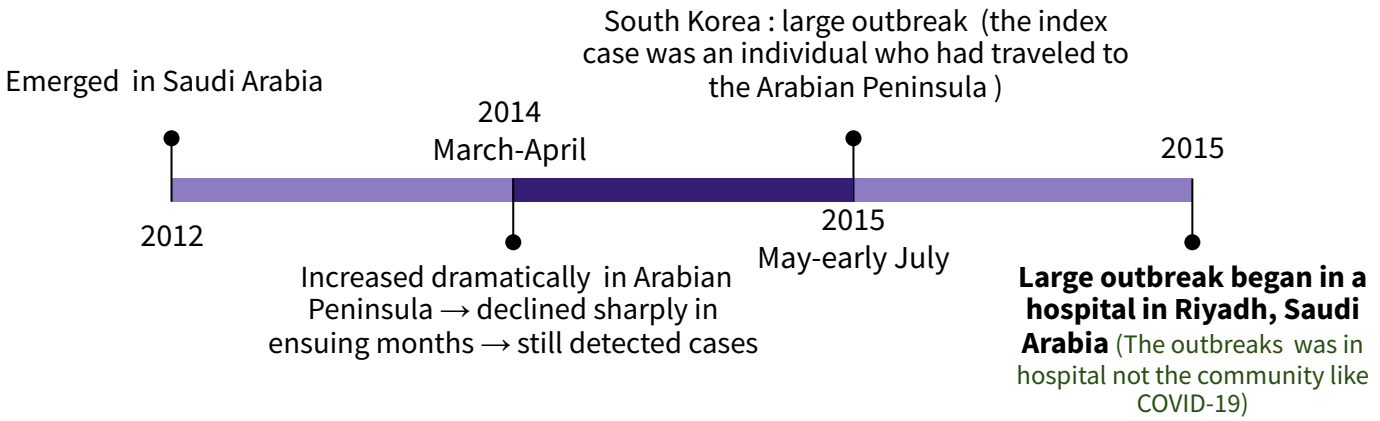
◀ Prevention

Prevention of leishmaniasis relies on control of vectors and/or reservoirs of infection :

- Insecticide spraying, control of host animals and treatment of infected humans may all be helpful.
- Personal protection against sandfly bites is also necessary, especially in travellers visiting endemic areas.
- Sandflies are poor fliers and sleeping off the ground helps prevent bites.

An area for your notes

◄ Middle East Respiratory Syndrome Coronavirus (MERS-CoV)



- September 2012, a case of novel coronavirus infection was reported in Saudi Arabia involving a man who was admitted to a hospital with **pneumonia and acute kidney injury** in June 2012.
- Subsequent cases and clusters of infections have been reported
- **Mortality rate is high (34%),** whereas for SARS it is 10% , for COVID-19 it will reach 3% maximally.
- r0 was <1 (this means that one person infects less than one person). COVID r0 is around 7.

	March and April 2014	May 2015	Feb –Aug 2015	Early 2019
Countries	• **Saudi Arabia** • United Arab of emirate	• South Korea.	• Saudi Arabia	• Oman
No. of cases	• More than 500 cases	• Large outbreak	• Outbreak: 153 cases	• 13 cases

◄ Where does the virus come from?

- MERS-COV is a **betacoronavirus** found in humans and **camels** that is different from the other human beta coronaviruses (severe acute respiratory syndrome coronavirus)
- Partial sequence found in **bat** in Saudi Arabia near location of human case.
- Growing evidence that **camels play an important role in transmission across the region**.
- Virus has been detected in dromedary camels (especially young camels <2 years) in:
  - Saudi Arabia, Egypt and Qatar.
- Exposure to the **mucous membrane of young camels** is the most common mood of transmission between camels and humans
- Antibodies have been found in camels in: (? Cross reactivity !!)
  - Jordan, Tunisia, Ethiopia, Nigeria, Egypt, Saudi Arabia, Canary Islands, UAE.
- MERS-CoV likely widespread in camels throughout region.
- Transmission likely occurring from camel to human. **However, human to human transmission is common and it is the cause of most cases of MERS-CoV.**

MERS-CoV

◀ Possible sources and transmission

Human-to-human transmission

- Case clusters in the United Kingdom, Tunisia, and Italy and in healthcare facilities in Saudi Arabia.
- In South Korea, a total of 186 cases were reported as a result of a single imported case.

Camels

- Appear to be the primary animal host for MERS-CoV
- Study has shown that 55% of infected patients had direct contact with camels in the 14 days preceding their illness.

◀ Case Definition and surveillance guidance

Suspect case (patients who should be tested for MERS-CoV) -any of the following-:

I

A person with fever and community-acquired pneumonia or acute respiratory distress syndrome based on clinical or radiological evidence.

II

A hospitalized patient with healthcare associated pneumonia based on clinical and radiological evidence.

III

A person with 1) acute febrile (>38oC) illness, **AND** 2) body aches, headache diarrhea or nausea/vomiting, with or without respiratory symptoms, **AND** 3) unexplained leucopenia (WBC<3.5x109/L) and thrombocytopenia (platelets <150x109/L)

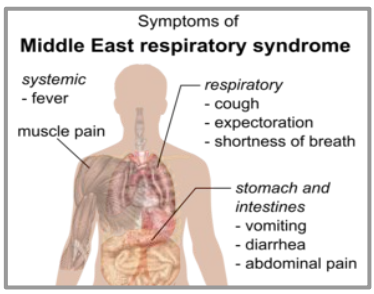
IV

A person (including healthcare workers) who had protected or unprotected exposure to a confirmed or probable case of MERS-CoV infection and who present with upper or lower respiratory illness within 2 weeks after exposure.

◀ Clinical features

- Like any other infection the symptoms are nonspecific but you should remember that the majority of patients are febrile.
- **The median incubation period was 5 days, symptoms included:**

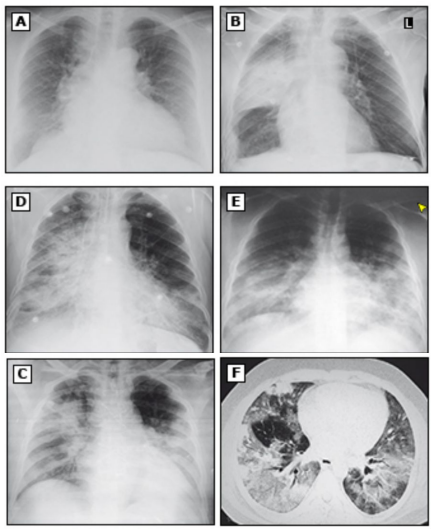
1	asymptomatic infection	2	Fever (>38°C) 98%	3	Shortness of breath
4	Cough – 83%	5	Abdominal pain	6	Myalgia
7	Sore throat	8	Vomiting & Diarrhea		



MERS-CoV

◀ Laboratory and imaging findings

CBC	• Leukopenia, lymphopenia, lymphocytosis, thrombocytopenia.
LFT	• **Elevated enzymes and LDH.** (very serious)
Renal function	• **Rising blood urea nitrogen and creatinine (some patients).** (very serious)
Imaging findings	• Ground-glass opacity in a peripheral location (most common). • Airspace opacities, **patchy infiltrates or consolidation.**



◀ Diagnosis

- Real-time reverse-transcriptase polymerase chain reaction **(rRT-PCR)** for respiratory secretions.
- **Nasopharyngeal swab** specimen *but* **Lower respiratory tract specimens**: Sputum, endotracheal aspirate, or Broncho-alveolar lavage) **are more sensitive**.

◀ Treatment

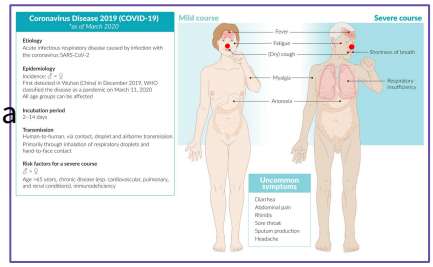
- Treatment is mainly **supportive.**
- **No effective antiviral therapy is available**

- **Experimental Treatment:**
  - Convalescent plasma
  - Corticosteroids
  - Combination therapy
  - Nitazoxanide
  - IVIG
  - IFN
  - Ribavirin
  - Cyclosporin A
  - Protease Inhibitor used in HIV infection
    - Lopinavir / Ritonavir (Kaletra) and Ribavirin have shown to be promising in a recent study.
    - Convalescent plasma is used with a variable response.

◀ Prevention

- **No vaccine available yet,** although KAIMRC are in phase 2 or 3 for a MERS-CoV Vaccine study.
- Use of standard, contact, and airborne precautions for the management of hospitalized patients with known or suspected MERS-CoV infection.
- Avoiding camels.

◀ Introduction

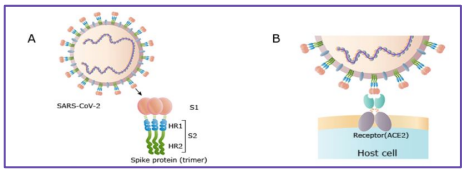


- Coronaviruses are important human and animal pathogens.
- At the end of 2019, a novel coronavirus was identified as the cause of a cluster of pneumonia cases in **Wuhan, a city in China.**
- It rapidly spread, resulting in an epidemic throughout China, followed by a **global pandemic.**
- In February 2020, the World Health Organization designated the disease COVID-19.
- The virus that causes COVID-19 is designated (SARS-CoV-2).

Coronavirus virology: Coronaviruses are enveloped positive-stranded RNA viruses.

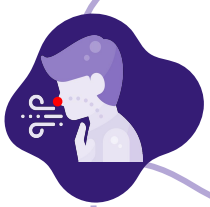
EPIDEMIOLOGY: Globally, over 100 million confirmed cases of COVID-19 have been reported.

◀ Genome sequencing and analysis



- Full-genome sequencing and analysis indicated that SARS-CoV-2 is a **betacoronavirus** in the same subgenus as:
  - ➢ Severe acute respiratory syndrome (SARS) virus
  - ➢ Several bat coronaviruses.
- The closest **RNA sequence similarity** is **to two bat coronaviruses,** and it appears likely that **bats are the primary source. But intermediate host is unknown.**
- The host receptor for SARS-CoV-2 cell entry is the **angiotensin-converting enzyme 2 (ACE2).**
- SARS-CoV-2 binds to ACE2 through the receptor-binding gene region of its spike protein.

◀ Transmission



1. **Person-to-person:** respiratory transmission occur mainly through close-range contact (**within approximately six feet or two meters) via respiratory particles**;

   When infected patient coughs, sneezes, or talks, the virus is released in the respiratory secretions which might infect another person if it is inhaled or makes direct contact with the mucous membranes.

2. **A person's hands are contaminated** by secretions from contaminated surfaces.

3. **Airborne transmission:** inhalation of particles that remain in the air over time and distance). still in doubt .

★ **What is the most likely mode of transmission of COVID-19 ?**
Respiratory particles "air droplets" directly from an infected person.

◀ Clinical Manifestations of COVID-19

The incubation period is within **14 days following exposure (most cases 4 -5 days).**
The spectrum of illness associated with COVID-19 is wide, ranging from asymptomatic infection to life-threatening respiratory failure:

- **Asymptomatic infection**, the majority and most dangerous because they will spread the infection.

- **Symptomatic infection:**

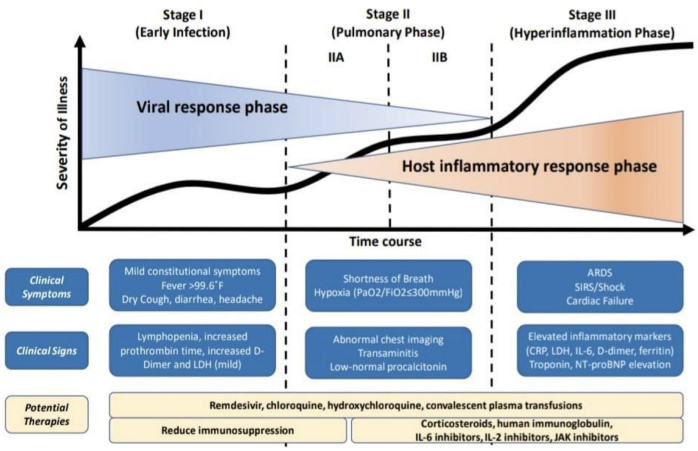
  - **Mild cases** (80% of Patients):
    - Fever, fatigue, and dry cough.
    - Headache, rhinorrhea, and sore throat are less common.
    - **Smell and taste disorders have also been reported.**
    - Gastrointestinal symptoms are not frequently reported but may be the presenting feature. (abdominal pain, vomiting, diarrhoea)

  - **Severe cases** (20 to 30% of patients -five to eight days after symptoms-:
    - They will develop pneumonia and a minority around 1-2% of the whole infected people will need ICU admission and ventilator.
    - **Respiratory failure:** Dyspnoea which might Progress to acute respiratory distress syndrome (ARDS) rapidly requiring mechanical ventilation (10 – 20%). **Thus, the onset of dyspnoea is generally an indication for hospital evaluation and management.** **The majority on ventilators will recover**
    - **Cardiac complications**: arrhythmias, acute cardiac injury.
    - **Neurologic complication**s: **Encephalopathy** is a common esp. among critically ill patients. A few cases presented primarily with encephalopathy and then turned to be covid19 positive, a rare manifestation.
    - **Thromboembolic complications**: pulmonary embolism and acute stroke

Dr notes:

It has different stages of infection:

1. **Viral response phase**, high viral replication.
2. **Pulmonary phase** where there will be a decrease in viral replication and an increase in the host's immune reaction.
3. **Hyperinflammation phase** where the immune reaction is high and is associated with ARDS, shock and complications from the chemokine storm.



COVID-19

◀ Diagnostics

Laboratory Evaluation

- **Lymphopenia** (up to 90%).
- **Elevated AST & ALT.**
- **Elevated LDH.**
- **Elevated inflammatory markers** (eg, ferritin,, C-reactive protein, and erythrocyte sedimentation rate).

Chest Imaging

- **Chest x-ray**: Consolidation and ground-glass opacities, with bilateral, peripheral, and lower lung zone distributions.
- **CT- SCAN**: (**more sensitive** than chest radiograph)

Diagnostic Testing

- **RT-PCR for SARS-CoV-2 is the primary test used to diagnose active COVID-19.**
- The test is performed primarily on upper respiratory specimens: **(Nasopharyngeal swabs, nasal swabs, and saliva).**
- Lower respiratory tract samples can also be taken using a bronchoscope.
- The optimal time to test for COVID-19 following exposure is uncertain; **five to seven days following exposure.**
- **Serology**: Measure antibodies to SARS-CoV-2 (indicate past infection).

◀ Treatment

- **Supportive**.
- No specific and effective medication
- Many medications have been tried, however none showed to be effective **except for steroids, which are now the standard of care**.
- **Low dose dexamethasone:** we use it now , it is thought to decrease the transfer for ICU.
- As for Remdesivir, it showed no difference in the WHO study, although in some reports it showed to be effective in around 30%.
- None of the used drugs has been proven to decrease mortality. They only decrease the duration of febrile illness.

◀ Prognosis

- **The overall case fatality rate is estimated to be between 2 and 3%.**
- **Risk factors for poor outcome:**
  - **Increased age.**
  - **Presence of chronic illnesses : CVS, Pulmonary, diabetes mellitus, kidney disease, and cancer.**
- Recovery and long-term sequelae — The time to recovery from COVID-19 is highly variable:
  - Mild infection: recover relatively quickly (within 2 weeks).
  - Severe disease: have a longer time to recovery (2 - 3 months).
- **The most common persistent symptoms include**
  - **fatigue, dyspnea, chest pain, cough, and cognitive deficits..**

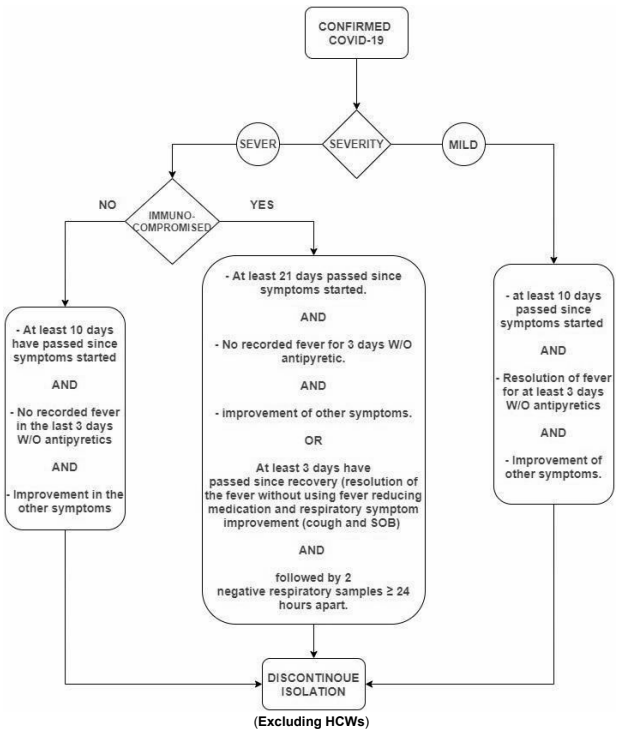
◀ Definition of COVID-19 Suspected Cases

Clinical Presentation	Criteria
• Patient with acute respiratory illness (sudden onset of at least one of the following: fever (measured or by history), cough, or shortness of breath.	• Not required
• Patient with sudden onset of at least one of the following: headache, sore throat, rhinorrhea, nausea, diarrhea or loss of smell or taste. • • **AND** in the 14 days prior to symptom onset, met at least one of the following criteria.	• Had contact with a confirmed COVID-19 case. • OR Working in or attended a healthcare facility where patients with confirmed COVID-19 were admitted.
• Any admitted Adult patient with unexplained severe acute respiratory infection(SARI), either Community Acquired Pneumonia (CAP) or Hospital Acquired Pneumonia (HAP).	• Not required

◀ Definition of COVID-19 Confirmed Cases

Patient status	Description	Instructions
Severe infection	Patients who are hospitalized at noncritical wards with laboratory confirmed COVID-19.	Isolation should last until all of the following criteria are fulfilled: - At least 10 days have passed since the onset of symptoms AND recorded fever in the last 3 days without the use of antipyretics AND improvement of other symptoms (Cough, SOB and GI symptoms). - Patients can be discharged before recovery based on clinical criteria, per evaluation of the treating physician, home isolation should be continued until fulfilled the recovery criteria.
	Immunocompromised and critical cases (ICU admitted patients).	Isolation should last until one of the following criteria fulfilled: - At least 21 days after symptoms onset AND resolution of fever at least 3 days. AND clinical improvement of symptoms other than fever (Cough, SOB and GI symptoms). **OR** - At least 3 days have passed since recovery (resolution of the fever without using fever reducing medication and symptoms improvement (Cough, SOB and GI symptoms) AND followed by 2 negative respiratory samples in 24 hours apart.
Mild confirmed cases	Confirmed COVID-19 patients never hospitalized due to mild symptoms or asymptomatic presentation.	These patients can end self-isolation 10 days after the onset of symptoms AND resolution of fever for at least 3 days AND clinical improvement of other symptoms. For asymptomatic lab-confirmed cases 10 days have passed since the date of collection of the respiratory sample with the first positive PCR result.

◀ Discontinuation of Isolation algorithm & Triage checklist



(Excluding HCWs)

This is the latest isolation algorithm, recovery and cessation of isolation is after 10 of the onset of symptoms, provided the patient had at least 3 days without symptoms.

Respiratory Triage Checklist

Date: Time

Name: Hospital:

Circle the number reflecting the patient's condition (exposure and clinical picture) and calculate the final score:

Risks for Acute Respiratory Illnesses	**Score**	
A. Exposure Risks	***Any Patient (Adult or Pediatric)***	
A history of travel abroad during the 14 days prior to symptom onset. **OR** Visiting or being a resident of a high-risk area for COVID-19 in the kingdom during the 14 days prior to symptom onset*. **OR** A close physical contact with a confirmed case of COVID-19 or MERS-CoV in the past 14 days. **OR** An exposure to camel or camel's products (direct or indirect**) in the past 14 days. **OR** Working in a healthcare facility.	**3**	
B. Clinical Signs and Symptoms and Medical History	***Pediatric***	***Adult***
1. Fever or recent history of fever.	**1**	**2**
2. Cough (new or worsening).	**1**	**2**
3. Shortness of breath (new or worsening).	**1**	**2**
4. Nausea, vomiting, and/or diarrhea.	**-**	**1**
5. Chronic renal failure, CAD/heart failure, Immunocompromised patient.	**-**	**1**
Total Score		

* As determined and announced by the Ministry of Interior or Ministry of Health. Updated regularly on: www.covid19.cdc.gov.sa

** Patient or household

A score ≥ 4, ask the patient to perform hand hygiene, wear a surgical mask, direct the patient through the respiratory pathway and inform MD for assessment.
MRSE-CoV OR COVID-19 testing should be only done according to case definitions.

Staff name: _____ Signature: _____

skipped by the doctor

An area for your notes

Summary

Enteric (Typhoid) fever	Clinical features	fever,Malaise, headache, abdominal pain, constipation or diarrhoea (Bloody), rose-colored spots on the chest (skin rash), enlarged spleen and liver.
	Diagnosis	The best initial test is for blood and/or fecal leukocytes
	Treatment	Fluoroquinolones, like ciprofloxacin are also effective (treatment of choice)
brucellosis	Clinical features	Fever, Night sweats, Fatigue, Anorexia, Weight loss, Arthralgia, Low back pain, Depression
	Diagnosis	Diagnose with culture of blood, CSF, urine, marrow
	Treatment	Streptomycin (10 days) + Doxycycline for 6 weeks.
Dengue fever	Clinical features	Fever (abrupt onset), headache, Nausea/Vomiting, Rash, Hemorrhagic manifestations
	Diagnosis	PCR, ELISA
	Treatment	Symptomatic treatment.
Rift valley fever	Clinical features	low-to-moderate–grade fever, Abdominal pain, Vomiting, Diarrheaelevated liver enzyme levels progressing to liver failure, encephalopathy or encephalitis, (DIC), renal failure
	Diagnosis	-
	Treatment	Treatment is symptomatic.
Visceral Leishmaniasis	Clinical features	Fever is common (first sign of infection) The liver and especially the spleen become enlarged The skin becomes rough and pigmented. profound pancytopenia develops
	Diagnosis	Specific diagnosis is made by demonstrating the parasite in stained smears of aspirates of bone marrow, lymph node, spleen or liver.
	Treatment	pentavalent antimony salts (e.g. sodium stibogluconate and meglumine antimoniate).
Cutaneous Leishmaniasis	Clinical features	Single or multiple painless nodules
	Diagnosis	The diagnosis can often be made clinically in a patient who has been in an endemic area.
	Treatment	Large lesionss can be treated locally by curettage or topical antiparasitic agents.
MERS-coV	Clinical features	pneumonia or acute febrile illness
	Diagnosis	(rRT-PCR
	Treatment	Supportive
COVID-19	Clinical features	Fever & upper respiratory Sx
	Diagnosis	RT-PCR
	Treatment	Mainly Supportive, Steroids

Lecture Quiz

Q1: A 14-year-old girl is brought to the physician by her father because of fever, chills, abdominal pain, and profuse non-bloody diarrhea. Her symptoms began one week ago, when she had several days of low-grade fever and constipation. Her temperature is 39.3°C (102.8°F). Examination shows diffuse abdominal tenderness and mild hepatosplenomegaly. There is a faint salmon-colored maculopapular rash on her trunk and abdomen. Which of the following is the most likely causal organism?

A. Shigella
B. Salmonella Typhi
C. Complicated Brucellosis
D. Viral hemorrhagic Fever

Q2: A 51-year-old man presents to accident and emergency with a lesion on his forearm. He mentions that he has spent the past three months travelling around South America and only returned home 3 days ago. While his lesion has been present for a few weeks he was reluctant to see a doctor in South America. On examination, there is a 3 × 3 cm erythematous ulcer on the left forearm with a raised edge. What is the most likely diagnosis?

A. Leishmaniasis
B. African trypanosomiasis
C. Herpes zoster
D. Schistosomiasis

Q3: A 40 year old man from Turkey presents with a history of chronic back pain and fever. On examination an MRI scan shows sacroiliitis. He has a long history of consuming unpasteurised milk and the initial work-up includes testing with a serum agglutination test, which comes back positive at high titre. What would be an appropriate initial antimicrobial regimen?

A- Streptomycin and Doxycycline
B- Rifampicin and isoniazid
C- Chloramphenicol
D- Metronidazole

Q4: A previously healthy 32-year-old man comes to the emergency department because of a high-grade fever and malaise for 3 days. He has severe generalized joint and body pains refractory to acetaminophen. He also has a severe stabbing pain behind his eyes. He returned from a trip to Taiwan 1 week ago. He is sexually active and uses condoms inconsistently. His temperature is 38.7°C (101.7°F), pulse is 102/min, and blood pressure is 100/70 mm Hg. Examination shows nontender inguinal lymphadenopathy. There is a maculopapular rash over the trunk and extremities with some sparing of the skin over his back and groin. Abdominal examination shows no abnormalities. Urinalysis is normal. Which of the following measures is most likely to have prevented this patient's condition?

A- Vaccination
B- pasteurizing the milk before drinking it
C- Mosquito repellent
D- prophylaxis with doxycycline

Q5: A 24 year old female student presents with fever and diffuse abdominal pain. She has not had diarrhoea. On examination, pulse is 56 beats/min, BP 97/54 mmHg and temperature 39.4°C. She has a tender right iliac fossa and small faint spots on her abdomen but no other skin lesions. What is the likeliest diagnosis?

A. Brucellosis
B. Dengue
C. Scrub typhus
D. Typhoid

Answers: Q1:B | Q2:A | Q3:A | Q4:C | Q5:D

Answers Explanation File!

GOOD LUCK !

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