The Brucella

Morphology & I dentification

-Are **gram-negative**, un-encapsulated, **non-motile**, nonsporulating, rods or coccobacilli bacteria that cause **Brucellosis**.

-They are obligate intracellular pathogens, **are Catalase and oxidase positive. and does not ferment carbohydrates**

-Brucellosis, the disease, is known colloquially as **undulant fever** or **Malta fever**, characterized by an acute **bacteremic phase** followed by a chronic stage that may extend over many years and may involve many tissues (Mainly **Reticuloendothelial (RE)** system).

-Brucellosis is a bacterial **zoonosis** transmitted directly or indirectly to humans from infected animals through **occupational** (Farmers, shepherds, goatherds, veterinarians, and employees in slaughterhouses and meat-processing plants in endemic areas) or **domestic exposure** to infected animals or their products (feces, urine, milk, or tissues)

-Brucellosis may be acquired by **ingestion, mucosal or percutaneous exposure** (needlestick, sharp injuries, as well as splashes leading to exposure of the skin or mucosa to blood) or **inhalation** so it could be exploited for **bioterrorism**.

- Although named as species, DNA relatedness studies have shown there is only one species in the genus, B melitensis, with multiple biovars:
  1. **Brucella melitensis** typically infects goats.
  2. **Brucella suis**, swine.
  3. **Brucella abortus**, cattle.
  4. **Brucella canis**, dogs.
  - Other species are found only in animals.

Pathogenesis

-*Brucella* does **not produce a detectable exotoxin**, and the **endotoxin** is **less toxic** than that produced by other gram-negative rods.

-The organisms progress from the portal of entry (ingestion, inhalation, contact skin), Once past the epithelial and innate immune barriers they enter and multiply **in monocytic cells (**macrophages in the liver sinusoids, spleen, bone marrow, and other components of the **reticuloendothelial system)** and eventually form **granulomas** which consist of **epithelioid and giant cells, with central necrosis and peripheral fibrosis.**

-If not controlled locally, and with release of bacteria back into the systemic circulation. These **bacteremic episodes** are largely responsible for the recurrent chills and fever of the clinical illness. These events resemble the pathogenesis of typhoid fever.

Clinically

-The incubation period ranges from 1–4 weeks. Brucellosis almost invariably causes **fever**, **undulant** in nature which may be associated with profuse **sweats**, especially at **night**. **associated with musculoskeletal symptoms.**

-Overall, the presentation of brucellosis often fits a pattern of: **febrile illness that resembles typhoid but is less severe**; **fever and acute monoarthritis**, typically of the **hip or knee**, in a **young child**; and **long-lasting fever, misery, and low-back or hip pain in an older man.**

Diagnosis

-Definitive diagnosis of brucellosis requires **isolation of Brucella** from the blood or from biopsy specimens of the liver, bone marrow, or lymph nodes

- **Blood culture** media readily grow Brucella species bacteria. **Brucella agar**, specifically designed to culture Brucella. All cultures should be incubated in 8–10% CO_2 at 35–37 C and should be observed for 3 weeks before being discarded as being negative results.

-However, culture needs a **prolonged incubation and is hazardous** (Need biosafety level 3 lab BSL-3) therefore the diagnosis is often made **serologically** (usually with **non-agglutinating** assays (ELISA assays) and **agglutination** tests are considered diagnostic if the following result fits the clinical and epidemiologic findings:

- Serum agglutination test, fourfold increase in titer or
- Antibodies against Brucella >1:80 (some books 1: 160) considered positive

-The serology associated with Brucella infection follows the classic antibody response: IgM appears initially, peaks at 3 months, followed by IgG which peaks at 6-8 weeks. IgA levels parallel the IgG levels.

- The point of using IgG is that in the brucella SAT can cross-react with class M immunoglobulins with a variety of other bacteria, such as Francisella tularensis and Vibrio cholerae.

The usual **serologic tests** may **fail** to detect infection with **B canis**.

-If the serum agglutination test result is negative (False negative) in patients with strong clinical evidence of Brucella infection, tests must be made for the presence of “blocking” antibodies.

Treatment & Prevention

- Generally, the antibiotics doxycycline and rifampin are recommended in combination for a minimum of **6-8 weeks**

-The mainstay of veterinary prevention is a national commitment to testing and slaughter of infected herds/flocks (with compensation for owners),

-Pasteurize milk, especially goat milk.

-Active **immunization of humans** against Brucella infection is still **experimental**

Leptospira

Morphology & Identification

-The genus Leptospira (is divided into **2 species**, the **human pathogenic L.interrogans** and the **saprophytic biflexa**) is a tightly coiled, thin, flexible spirochetes ;a **spirally** shaped (Question mark appearance)

-Leptospirae are,Too thin to visualize, but gram-negative cell envelope With hooked ends and two periplasmic flagella, best can be seen **microscopically** by **dark-field** examination and after **silver impregnation** staining of tissues.

-They are motile, grow best under aerobic conditions

-**Leptospirosis** is a **zoonosis** of worldwide distribution characterized by a broad spectrum of clinical manifestations, varying from **asymptomatic** infection **to fulminant, fatal disease** (**Weil's syndrome).**

-**Kidney involvement** in many animal species is chronic, many animal species are **shedding** a large number of leptospirae in the **urine** and this is probably the **main source of environmental contamination resulting in infection of humans**.

-Exposure to water or other materials contaminated with animal urine (Rats, mice, wild rodents, dogs, swine, and cattle) are the principal sources of human infection (sewer workers). **Human urine** also may contain spirochetes in the **second and third weeks of disease**.

-**Skin exposure is the most common route**, followed by mucosal and rarely ingestion.

Pathogenesis

- Mechanisms of pathogenesis of Leptospira are largely unknown.

-After **entry**, and an incubation period of 1–2 weeks, it **cross tissue barriers**, and disseminate **hematogenously** to all organs **-leptospiremic phase-**

-They then **establish** themselves in the **parenchymatous organs** (particularly **liver and kidneys**), producing **hemorrhage and necrosis** of tissue and resulting in **dysfunction** of those **organs** followed by -**immune phase**- the appearance of antibodies coincides with the disappearance of leptospires from the blood

Clinically

-Although leptospirosis is a potentially fatal disease with bleeding and multi-organ failure as its clinical hallmarks, the **majority of cases** are thought to be relatively **mild**, presenting as the sudden onset of a febrile illness.

-Mild **symptomatic** leptospirosis usually presents as a **flu-like illness** of sudden onset, with **fever, chills**, headache, **nausea, vomiting, abdominal pain**, conjunctival suffusion (redness without exudate), and myalgia.

- **Weil's syndrome, encompasses the triad of hemorrhage, jaundice, and acute kidney injury).**

Diagnosis

- For microscopic examination, specimens consist of blood, CSF, or urine and tissues are examined by Dark-field examination or thick smears stained by the Giemsa technique.
-For **Culture**, Leptospires grow best in semisolid medium (eg, Ellinghausen-McCullough-Johnson- Harris **EMJH)**. Growth is slow, and cultures should be kept for at least **8 weeks.**
-The diagnosis of leptospirosis in most cases is **confirmed serologically** with microscopic agglutination test (MAT) and ELISA.
-Agglutinating antibodies first appear 5–7 days after infection and develop slowly, reaching a peak at 5–8 weeks. Very high titers may be attained (>1:10,000)

Treatment & Prevention

-Leptospira are highly susceptible to a broad range of antibiotics-mild to moderate disease – tetracyclins and for sever one IV penicillin is recommended.
-Early intervention may prevent the development of major organ system failure.
-**Avoidance** of exposure to **urine and tissues** from infected animals through proper eyewear, footwear, and other protective equipment.
-Targeted rodent control strategies could be considered. (reservoir)
-**Vaccines** for agricultural and companion **animals** are generally available, and their use should be encouraged.

Mycobacterium

Morphology & Identification

-The **genus Mycobacterium** is mainly known for its **two major pathogenic species M.Leprae & M.Tuberculosis (Mtb).**
-Mtb is the principal pathogen responsible for most cases of Tuberculosis mainly the pulmonary. However, TB is a communicable infectious disease that be caused by any member of the family Mycobacterium tuberculosis complex (MTC)
-M.Bovis was responsible for 6 % of tuberculosis cases before the introduction of **milk pasturization and development of BCG vaccine**.
- Mycobacteriumis a slow growing, obligate aerobe, **facultative intra- cellular bacterium.**
-**Non-spore** forming, **non-motile**
-**Very weakly** "**Gram-positive** but **Acid fast** with **Ziehl Neelsen ZN stain:** it could **retain** red **basic** fuchsin **dye** after **rinsing** with **acid alcohol** (lipid rich cell wall)
-M. tuberculosis divides every 18–24 h which is extremely slow compared with other bacteria.

Pathogenesis

-Not everyone infected with TB bacteria becomes ill. Consequently, **Two TB-related conditions exist**: **Latent Tuberculosis (LTBI)** People who have latent TB infection-**do not have any symptoms**, and **cannot spread TB to others** (Bacteria is dormant intracellularly) and **Active TB disease** which can be **acute primary post infection or secondary post reactivation**.

-About one third of the world's population is infected with TB bacteria (TB latency). People with weakend immune system have much greater risk of falling ill.
-TB bacteria can attack any part of the body yielding **pulmonary TB** in **80-90 %** of cases and **extra-pulmonary 10-20%** such as Lymph Node TB (Tuberculous Lymphadenitis), Pleural TB, Skeletal TB, Genitourinary TB and **Gastrointestinal TB.**

- **Gastrointestinal TB is uncommon, making up 5% of extra-pulmonary TB**:
The tubercle bacilli may enter the intestinal tract **through 3 pathways: the ingestion of infected milk or sputum**. The **second pathway is hematogenous &lymphatic spread** from tubercular **focus** from elsewhere in the body to abdominal solid organs, kidneys, lymph nodes and peritoneum. **The third pathway includes direct spread to the peritoneum from infected adjacent foci**, including the fallopian tubes or adnexa, or psoas abscess, secondary to tuberculous spondylitis.
- The **formation of granuloma** in the lymphoid tissue **is the pathology hallmark- caseous necrosis & ulceration of the overlying mucosa which can later spread into the deeper layers.**

Clinically
-Abdominal TB presents with general complaints of Fever, weight loss, anorexia, and night sweats. plus, local symptoms depending on the site involved
-Gastrointestinal TB tend to be non -specific but abdominal pain and swelling and a palpable mass are common presentations.

Diagnosis
-To Diagnose abdominal TB, High index of suspicion is necessary and include Smear microscopy with **ZN** or Auramine immunefluorescence **staining**.
-Mtb can be further identified through **culture** of recovered specimens in Both **liquid and solid** mycobacterial **cultures** that include **Lowenstein-Jensen** or **Middlebrook 7H10 agar** plates.
Tuberculin skin tests **(TSTs)**, Interferon-gamma release assays **(IGRAs)** are commonly used especially in the developed world to Identify **TB exposure**.

Treatment & Prevention
-TB treatment depends on whether the individual is in the latent or active stage, and on his or her probability of risk:
-For **active TB** an **intensive** initial **2-month phase** of: isoniazid (INH), rifampin (RIF), pyrazinamide (PZA), and either ethambutol (EMB) or streptomycin (SM).
followed by a slower **4- to 6**-month **continuation phase**: isoniazid (INH), rifampin (RIF),
-While for **latent TB** isoniazid is the drug of choice for 9 months
-Mycobacterium bovis Bacillus Calmette–Guérin (BCG), an attenuated vaccine derived from M. bovis, is the only licensed vaccine against tuberculosis (TB)
-Despite its protection against **TB in children** especially TB **meningitis** and the disseminated TB form (**Miliary TB**), its protective value in adults against pulmonary TB is questionable, with efficacies ranging between 0 to 80 %