

# Brucellosis

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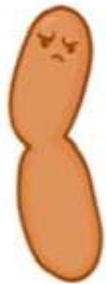
Ahed al quraan

- ***Brucellosis ( undulant fever)*** : is a zoonosis ( a disease of animals that may be transmitted to humans under natural conditions)
- ***Brucellosis is the name of Dz that caused by members of genus Brucella which are primarily pathogens of animals ( domestic and feral)***

## General characteristics

- Gram negative ,unencapsulated coccobacillus arranged singly or in pairs
- Aerobic, Facultative intracellular parasites of epithelial cells and professional phagocytes , LPS is the major virulence factor.
- Environmental persistence extremes in Temperature, pH, humidity, Frozen and aborted materials, dust, soil

*Brucella abortus*



*Brucella melitensis*



*Brucella canis*



*Brucella suis*



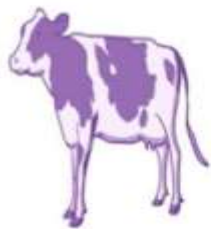
~ ALL CAUSE SYSTEMIC DISEASE - BRUCELLOSIS

~ EACH has a DIFFERENT HOST



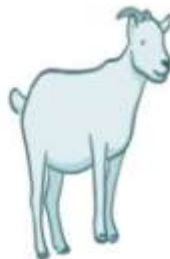
DIFFERENT FORM of DISEASE

~ *B. abortus*



CATTLE

~ *B. melitensis*



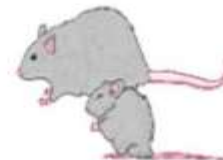
SMALL RUMINANTS

~ *B. canis*



DOGS

~ *B. suis*



SWINE & RODENTS

## ***Brucella in animals***

- ***Brucella is Enzootic disease -in animals –i.e. :is a chronic infection that persists for life in animals, organisms localized in reproductive organs (male , female) and are shed in large numbers in milk , urine ,the placenta and other tissues discharged during delivery or spontaneous abortion .***
- ***is an important cause of abortion, sterility, and decreased milk production in cattle and goats.***

# Mode of transmission

1. Ingestion: Raw milk, unpasteurized dairy products  
Rarely through undercooked meat

2. Mucous membrane or abraded skin contact with infected tissues

3. Aerosol e.g. in Laboratory and slaughter houses.

4. Inoculation with vaccines

5. Person-to-person e.g. conjunctival, blood transfusion, and trans-placental

## ***People at risk***

### ***1. Occupational disease***

- ***Cattle ranchers***
- ***dairy farmers***
- ***Veterinarians***
- ***Abattoir workers***
  - ***Meat inspectors***
- ***Lab workers***

### ***2. Hunters***

### ***3. Travelers***

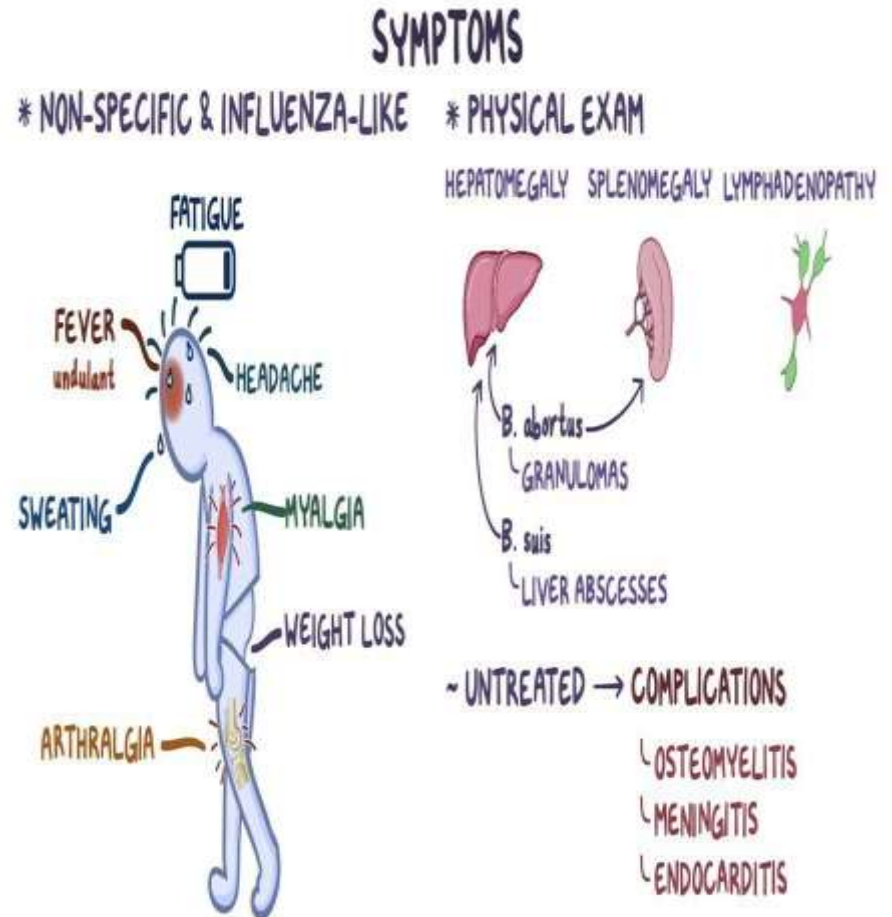
### ***4. Consumers of Unpasteurized dairy product***

- Once it survives in blood & Macrophages it can reach ANYWHERE (multisystem)
- especially RES : spleen, liver and bones
- Form granulomas and cause destructive tissue damage
- Symptoms start to appear 1-3 weeks insidiously after infection , i.e. the incubation period.
- It starts with vague symptoms causing what is called Brucellosis .



Acute phase < 8 weeks It starts with flue- like symptoms :

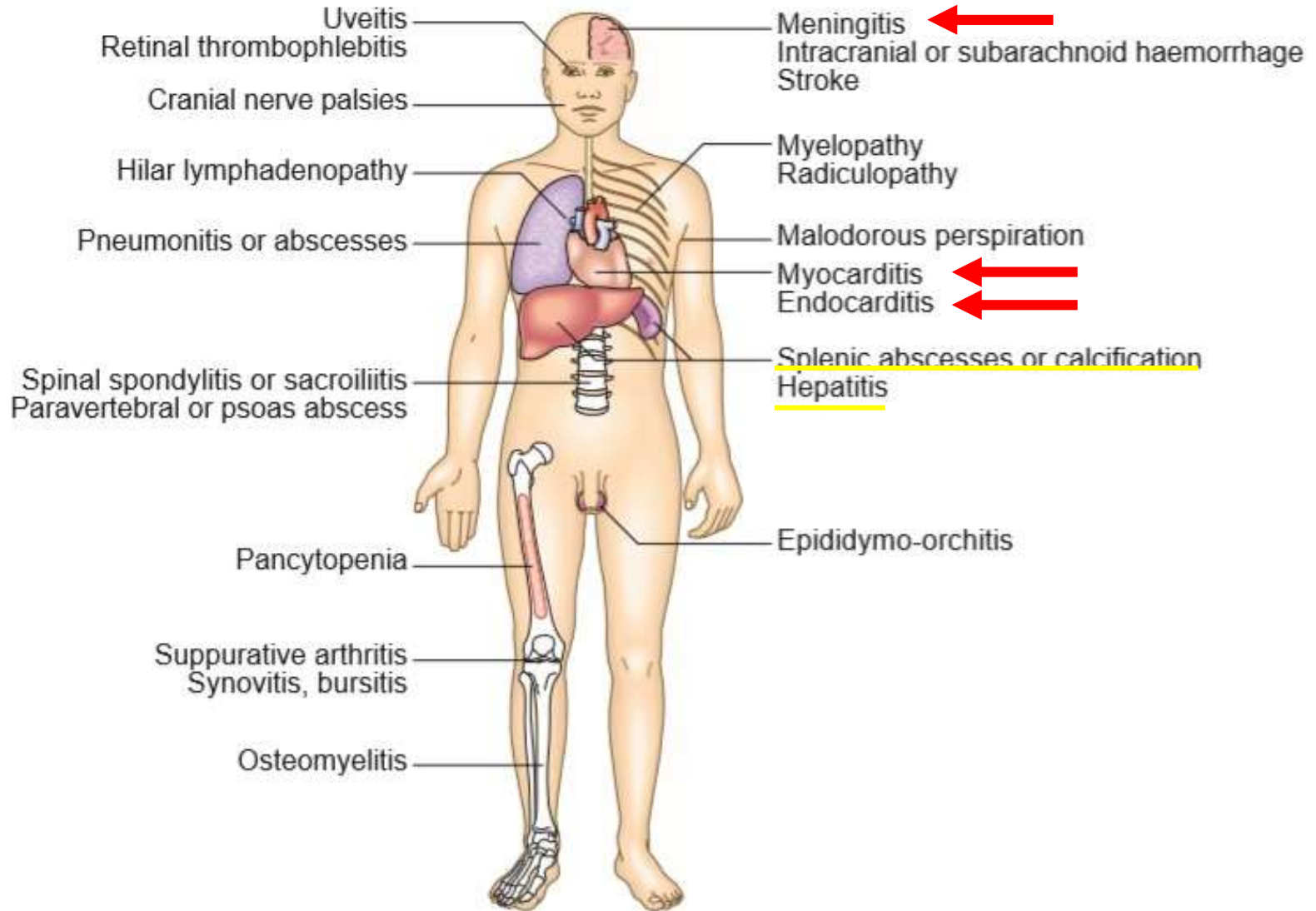
- Headache
- Myalgia
- Anorexia and weight loss up to 20 kg
  - Sweating
  - Undulant fever
  - Arthralgia



## ***Arthralgia Undulant fever***

- ***Fever pattern is classically undulant – alternating btw 37 and 39.5 through morning at night.***
- ***persistent or intermittent patterns could also be seen.***
- ***Fever may stay for a week , months or up to 2 years keeping wax and wane pattern .***

# *Affected multisystem*



- Typically : hepatosplenomegaly and lymphadenopathy

- Other systems:

1. Sacroiliitis & Spondylitis

2. Mono arthritis

3. Osteomyelitis

4. Epididymo-orchitis

5. Meningoencephalitis

6. Endocarditis

## Different forms of disease for each M.O

- B. abortus mild or moderate symptoms, but more likely to become chronic..granuloma
  - B. canis similar to B.abortus but with vomiting & diarrhea.
  - B. suis abscesses.
  - B. melitensis ..severe symptoms ..disability

## Chronic Brucellosis > 8 weeks- 1 year

- If untreated or relapse
- Comes with chronic fatigue
- causes complication in affected organs

Localized infection- in:

Commonly :

1. Nerves..Spondylitis
2. Testicles ..Epididymo-orchitis
3. Joint..Arthritis
4. Liver ..Hepatic abscess and Granuloma .
5. Neurological {only in 5%} ☐ Neurobrucellosis and psychosis

- Others :
- Lungs ..Pneumonia
  - Bones..Osteomyelitis
  - Endocardium..Endocarditis
  - Spleen ..Abscess, granuloma or splenomegaly

## Clinical features

Often fits one of the three patterns:  
febrile illness resembling typhoid, less severe

fever & acute monoarthritis  
(hip/knee), young child

long lasting fever, LBA, hip pain, older man

- Travel to an endemic area
- Occupation
- Consumption of unpasteurized milk



# Congenital brucellosis

- **Premature delivery**
- **Low birth weight**
- **Fever**
- **Failure to thrive**
- **Jaundice**
- **Hepatomegaly**



# Physical examination

- papulonodular and maculopapular eruption , erythema nodosum .
- **splenomegaly , hepatomegaly , lymphadenopathy**
- **Joint** swelling and pain
- Musculoskeletal pain
- Unexplained **fever**
- right upper quadrant **tenderness and jaundice** if there's hepatic abscess



# Diagnostic

## tests

- **Specimen:** blood , biopsy material from (bone marrow , lymph node , other infected tissues )

### **A. CULTURE :**

grow on commonly used media , including **blood agar , chocolate agar .**

**Brucella agar** it's a high enriched selective media that grow brucella .

All culture should be incubated in 5-10% CO<sub>2</sub> at 35-37°C for **3 weeks.**

so don't discharge culture as negative before 3 weeks.

The observation of tiny gram-negative coccobacilli that are non hemolytic , catalase-positive and oxidase-positive suggests Brucella species.



## B. SEROLOGICAL TEST:

- Includes:

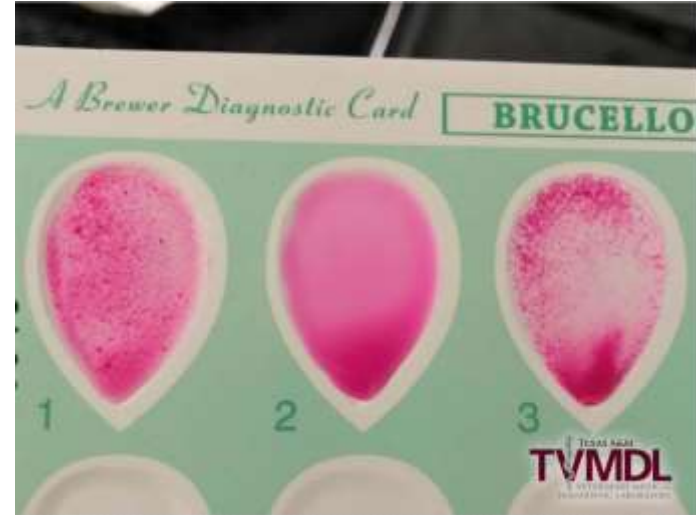
- A. Serum agglutination test**

- Four-fold or greater rise in titer
    - Samples 2 weeks apart

- B. Plate agglutination test ( Brucella ring test)**

1. Drop of serum mixed with drop of Brucella antigen
2. Clumping indicates infection
3. If the mixture remains clear, the result is negative

- c. IMMUNOFLUORESCENCE OR PCR.



# Prognosis

1. **Disease is usually treated successfully with antibiotics.**
2. About 5% of treated cases **relapse**.
  - Most relapses occur within **3 months** after treatment.
  - **Risk factors** for relapse :
    1. Failure to complete treatment.
    2. Male sex.
    3. Bacteremia
  - Most relapses can be treated with repeat course of antibiotics
3. **Death usually caused by endocarditis, meningitis.**

13.44 Treatment of brucellosis	
<b>Adults with non-localised disease</b>	
<ul style="list-style-type: none"> <li>• Doxycycline 100 mg twice daily orally for 6 wks <i>plus</i> gentamicin 5 mg/kg IV once daily for 7 days</li> </ul> <p><i>or</i></p> <ul style="list-style-type: none"> <li>• Doxycycline 100 mg twice daily <i>plus</i> rifampicin 600–900 mg orally once daily for 6 wks</li> </ul>	
<b>Bone disease</b>	
<ul style="list-style-type: none"> <li>• Doxycycline 100 mg twice daily <i>plus</i> rifampicin 600–900 mg once daily orally for 6 wks <i>plus</i> gentamicin 5 mg/kg IV once daily for 7 days</li> </ul> <p><i>or</i></p> <ul style="list-style-type: none"> <li>• Ciprofloxacin 750 mg twice daily orally <i>plus</i> rifampicin 600–900 mg orally once daily for 3 mths</li> </ul>	
<b>Neurobrucellosis</b>	
<ul style="list-style-type: none"> <li>• Doxycycline 100 mg twice daily <i>plus</i> rifampicin 600–900 mg orally once daily for 6 wks <i>plus</i> ceftriaxone 2 g IV twice daily until CSF is clear (though susceptibility should be confirmed because sensitivity to third-generation cephalosporins varies amongst strains)</li> </ul>	
<b>Endocarditis</b>	
<ul style="list-style-type: none"> <li>• Almost always needs surgical intervention</li> </ul> <p><i>plus</i></p> <ul style="list-style-type: none"> <li>• Doxycycline 100 mg twice daily, rifampicin 600–900 mg orally once daily and co-trimoxazole 5 mg/kg of trimethoprim component for 6 mths <i>plus</i> gentamicin 5 mg/kg IV once daily for 2–4 wks</li> </ul>	
<b>Pregnancy</b>	
<ul style="list-style-type: none"> <li>• Rifampicin 600–900 mg orally once daily and co-trimoxazole 5 mg/kg of trimethoprim component for 4 wks, but caution in last week of pregnancy due to displacement of bilirubin from albumin by drugs and risk of kernicterus to the fetus</li> </ul>	

# Treatme

# nt

• 6- 8 weeks of Doxycycline

and Rifampicin for diseased patients

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# Prevention and control

- Education about risk of transmission

Farmers, veterinarians, abattoir workers, consumers, hunters

- Wear protective clothing if dealing with infected animals/tissues

**Gloves, masks.**

- Eradicate infected animals
- Pasteurization of milk

- 
- **Vaccination** of uninfected animals;
    - Young sheep with *B. melitensis Rev-1*
    - Calves with *B.abortus strain 19 and RB51*
  - **NO** human vaccine!



# Quick CASES



# #

# 1

- A 30 year old **veterinarian** on a **cattle ranch** presents with a 1-to-2 month history **malaise** , **chills** ,drenching malodorous **sweats** , **fatigue** and **weakness** . He has **anorexia** and has lost 15 pounds . He has **intermittent fevers** that range up to 39.6 C . A physical examination reveals mild **lymphadenopathy** , petechiae and **cardiac murmur** consistent with aortic insufficiency . What is the most likely etiology agent ?

# #

# 2

- a 30 year old man presents with 5 weeks history of fever , anorexia , arthralgia and weight loss . He emigrated from turkey 2 months ago . He has no significant past medical history . On admission to the hospital he is febrile and tachycardic , his abdomen is soft and non tender with enlarged liver and enlarged spleen . On review of his history had worked extensively with animals in turkey and been exposed to their products .

# #3

- A 66 year old Mexican farmer presents with a 2 year history of lower back pain and intermittent fever . He keeps goats and frequently drinks unpasteurized goat's milk . On physical examination his temperature is slightly elevated and there is mild tenderness over the lower lumbar vertebrae , with no association deformity or neurologic abnormality .

THANK

YOU



# Typhoid fever

done by : mohammad nuseir

- ► Typhoid fever (or Enteric fever) is a systemic infection, the origin and focus of which is the gastrointestinal tract, caused by **Salmonella typhi**
- Salmonella typhi is from Enterobacteriaceae family, encapsulated, flagellated, Gram- negative Rods, facultative intracellular pathogens, facultative anaerobes, , bile-resistant and acid liable.

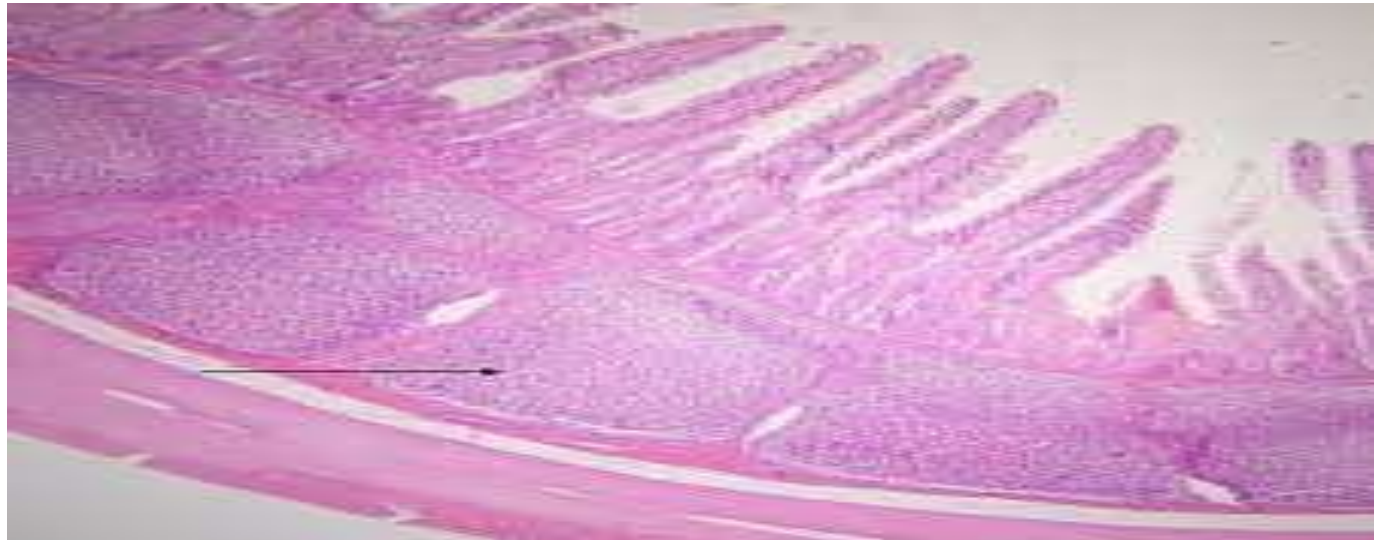


- only infect humans, who are also the only known reservoir; and its route of transmission is fecal to oral - even if the feces come from a currently asymptomatic host.
- endemic to Asia, Africa, Latin America, and the Caribbean.

*S. typhi* is sensitive to gastric acids, so half of the time, it takes a large inoculum, of around 100,000 microorganisms, to cause an infection

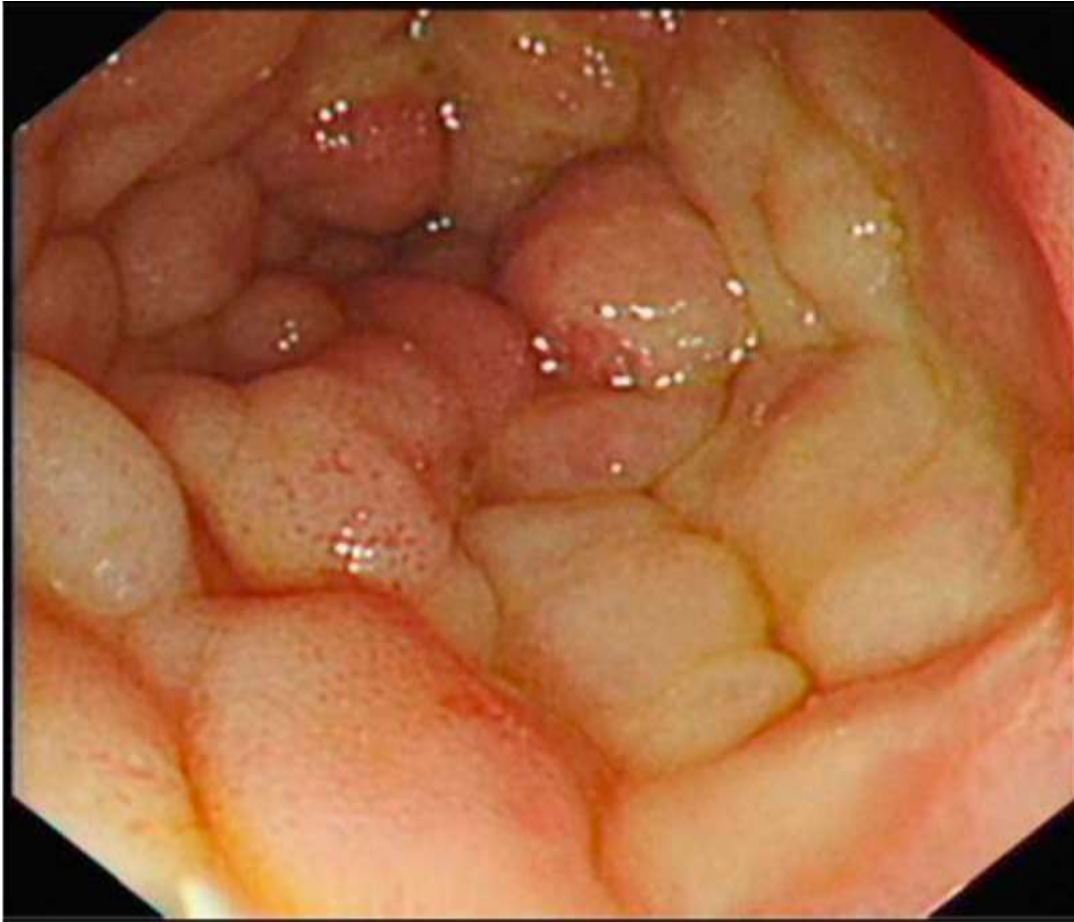


- Once Salmonella is ingested and reaches the distal ileum of the small intestine, it targets the epithelial layer of the mucosal lining. Here, it uses surface appendages to adhere to microfold cells, or **M-cells**. And these M-cells eat, or phagocytose, the bacteria from the intestinal lumen and spit it out into the underlying **Peyer's patches** - a type of mucosal immune tissue that extends into the submucosa.



- And, well, *S. typhi* has a virulence factor, which helps protect the bacteria from being tagged with antibodies that signal leukocytes like neutrophils. Moreover, neutrophil recruitment is also suppressed. (leukopenia)
- ► On the other hand, the recruitment of monocytes and macrophages is induced, making them the primary cells that respond to the infection.

- ► And as they are recruited to the infection site, they cause hypertrophy (could cause constipation) and necrosis of the surrounding tissues; which can damage the epithelial lining, and potentially lead to ileal perforation, consequently, a secondary infection of the peritoneum.

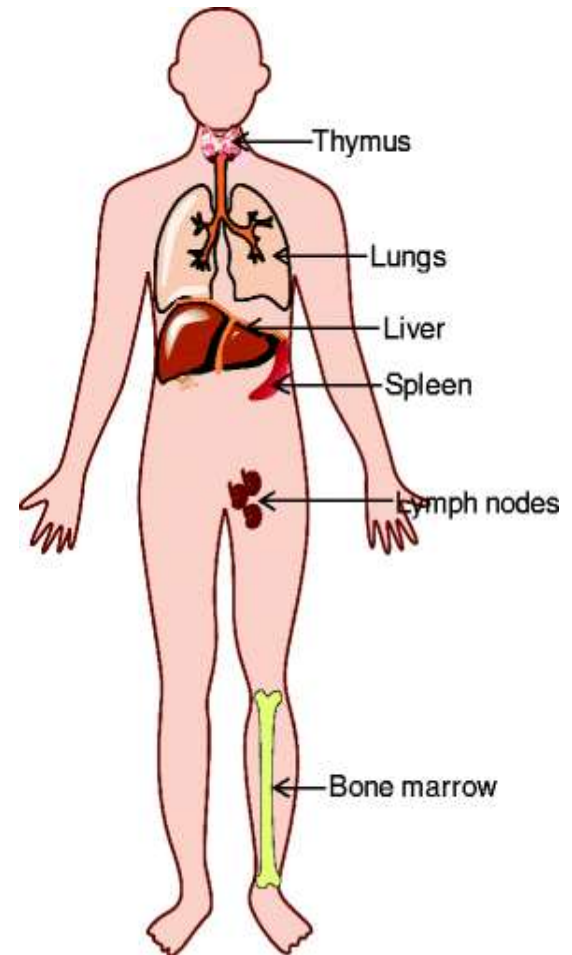


Colonoscopic  
image of  
hypertrophic  
Peyer's patches in  
the terminal  
ileum.



Source: J.L. Jameson, A.S. Fauci, D.L. Kasper, S.L. Hauser, D.L. Longo, J. Loscalzo: Harrison's Principles of Internal Medicine, 20th Edition Copyright © McGraw-Hill Education. All rights reserved.

- macrophages also phagocytose *S. typhi* within vacuole (sac). *S. typhi* survives and replicates within the vacuole inside the macrophages. All the while, *S. typhi* is using the host macrophage to ride to the nearby lymphatic vessels that drain into local mesenteric lymph nodes. Once there, the macrophage can continue to flow through the thoracic duct and into systemic lymphatic circulation where they can enter reticuloendothelial tissues in the liver, spleen, bone marrow, gall bladder and additional lymph nodes.



- ► At about this point, *S. typhi* can induce macrophage apoptosis, or cell death, so the bacteria is released into the bloodstream, called **bacteremia**. Bacteremia can progress to **sepsis**, an acutely life-threatening condition characterized by systemic vasodilation and hypoperfusion of vital organs - which means the organs aren't getting enough nutrient and oxygen-rich blood (septic shock))

- Another complication can arise in individuals with spleen issues, because the spleen plays an important role in immunity against encapsulated bacteria. This includes people who have undergone a splenectomy, or spleen removal
- In these individuals, *S. typhi* can cause **osteomyelitis**,
- which is an acute infection of the bones.



- ▶ On the other hand, some people can become **chronically** infected with *S. typhi*, and that means they are carriers for the bacteria for decades or a lifetime, even after symptoms have resolved. In these cases, *S. typhi* typically remains in the gallbladder, and is periodically swept along with bile through the bile duct to the intestines, where it can be excreted in feces.

# symptoms

- Now, symptoms of typhoid fever first appear about 1-2 weeks after initial infection, and can take 4-6 weeks to resolve
- there's a high, sustained fever, abdominal pain, constipation followed by diarrhea children diarrhea and vomiting may be prominent early, and rose or salmon-colored spots on the body especially chest and abdomen



- Hepatomegaly and splenomegaly may also occur as the infection spreads.
- Dehydration, weakness, headaches, and an overall cloudy or confused mental state can occur, especially in advanced cases.

**i****11.42 Clinical features of typhoid fever****First week**

- Fever
- Headache
- Myalgia
- Relative bradycardia
- Constipation
- Diarrhoea and vomiting in children

**End of first week**

- Rose spots on trunk
- Splenomegaly
- Cough
- Abdominal distension
- Diarrhoea

**End of second week**

- Delirium, complications, then coma and death (if untreated)

**i****11.43 Complications of typhoid fever****Bowel**

- Perforation
- Haemorrhage

**Septic foci**

- Bone and joint infection
- Cholecystitis
- Meningitis

**Toxic phenomena**

- Myocarditis
- Nephritis

**Chronic carriage**

- Persistent gallbladder carriage

# Investigation

- ▶ Cultures from blood; intestinal secretions, like vomit or a duodenal aspirate; or stool cultures, which can identify *S. typhi*, particularly in the first week of infection
- ▶ For asymptomatic carriers, bile cultures are the most effective diagnostic tool because the bacteria can be absent from stool.

# Treatment

- Treatment involves managing symptoms, particularly fluid and electrolyte replenishment for diarrhea and non-steroidal anti-inflammatory drugs for pain and fever.
- ▶ Commonly, broad-spectrum antibiotics are used, like fluoroquinolones or cephalosporins, like ceftriaxone.
- For carriers, a combination of antibiotic therapy with fluoroquinolones and surgical removal of the gallbladder is the most effective form of treatment.



# Prevention

- ▶ Hygiene
- ▶ Prophylaxis is available in the form of an intramuscular vaccine (containing Vi capsular polysaccharide) or oral vaccine, (live attenuated vaccine)
- ▶ Usually given to travellers to countries where enteric infections are endemic

# **PARATYPHOID**

**AHED MA'AROF IRSHIED**

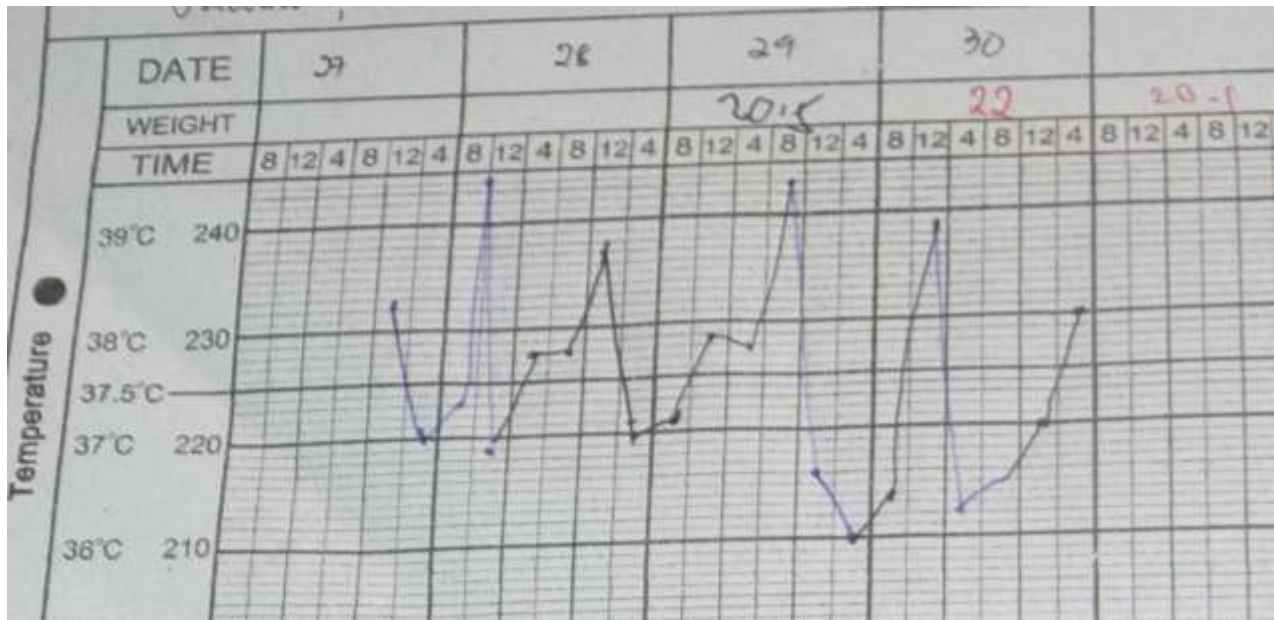
**MOHAMMAD OLIMAT**

# INTRODUCTION

- **Paratyphoid fever**, also known simply as **paratyphoid**,
- is a **bacterial infection** caused by one of the three types of *Salmonella enterica*.
- Symptoms usually begin 6–30 days after exposure and are the same as those of typhoid fever.
- Often, a **gradual onset** of a high fever occurs over several days.
- Weakness, loss of appetite, and headaches also commonly occur. Some people develop a **skin rash with rose-colored spots**.
- Without treatment, symptoms may last weeks or months.
- Other people may carry the bacteria without being affected; however, they are still able to spread the disease to others.

# INTRODUCTION

- Paratyphoid is caused by the bacterium *Salmonella enterica* of the serotypes Paratyphi A, Paratyphi B, or Paratyphi C growing in the intestines and blood.
- **Diagnosis** may be based on symptoms and confirmed by either culturing the bacteria or detecting the **bacterial DNA** in the blood, stool, or bone marrow. Culturing the bacteria can be difficult. Bone-marrow testing is the most accurate
- Typhoid and paratyphoid are of similar severity.
- Paratyphoid and typhoid fever are types of enteric fever.



- This is **stepwise pattern of fever**, characterized by a rising temperature over the course of each day that drops by the subsequent morning. The peaks and troughs rise progressively over time. The stepladder fever pattern that was once the hallmark of typhoid fever now occurs in as few as 12% of cases

# introduction

- While **no vaccine is available** specifically for paratyphoid
- the typhoid vaccine may provide some benefit.
- Prevention includes drinking clean water, better sanitation, and better handwashing.
- Treatment of the disease is with antibiotics such as **azithromycin**.
  - Resistance to a number of other previously effective antibiotics is common.

# Epidemiology

- Factors outside the household, such as unclean food from street vendors and flooding, help distribute the disease from person to person. Because of poverty and poor hygiene
- the disease is more common in [undeveloped countries](#), principally owing to the problem of unsafe drinking water, inadequate sewage disposal, and flooding.
- Occasionally causing [epidemics](#),
- paratyphoid fever is found in large parts of Asia, Africa, and Central and South America. Many of those infected get the disease in Asian countries.
- About [16 million cases](#) occur a year, which result in about [25,000 deaths](#) worldwide

# Cause

- Paratyphoid fever is caused by any of three serovars of *Salmonella enterica*
- subsp. *enterica*:
- S. Paratyphi A
- S. Paratyphi B
- S. Paratyphi C



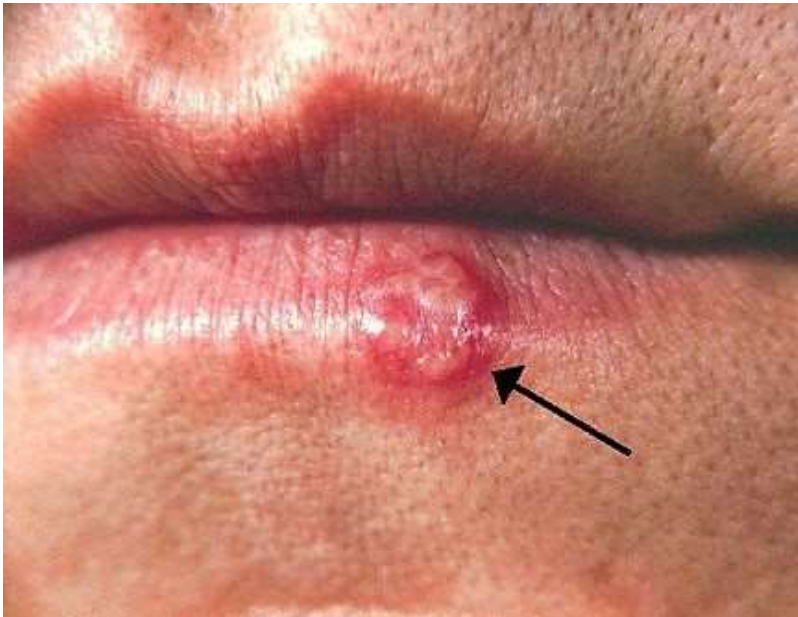
# Transmission

- They are usually spread **by** eating or drinking food or water contaminated with the feces of an infected person.
- They may occur when a person who prepares food is infected.
- Risk factors include **poor sanitation** as is found among poor crowded populations.
- Occasionally, they may be **transmitted by sex**.
- Humans are the **only** animals infected.

# Paratyphoid B

- Paratyphoid B is more frequent in Europe. It can present as a typhoid-like illness, as a severe gastroenteritis.
- Herpes labialis, rare in true typhoid fever, is frequently seen in paratyphoid B.
- Rarely a subdural empyema can occur.
- Diagnosis is with isolation of the agent in blood or stool and demonstration of antibodies antiBH in the Widal test.
- The disease responds well to chloramphenicol or cotrimoxazole

# Herpes labialis



- rare in true typhoid fever, is frequently seen in paratyphoid B.

# Paratyphoid C

- Paratyphoid C is a rare infection, generally seen in the Far East.
- It present as a **septicemia** with **metastatic abscesses**.
- **Cholecystitis** is possible in the course of the disease.
- Antibodies to paratyphoid C are not usually tested and the diagnosis is made with blood cultures.
- **Chloramphenicol** therapy is generally effective
- Paratyphoid fever C **may be manifested by typhoid fever, acute gastroenteritis, and septicemia**

# Carriers

- **Humans** and, occasionally, **domestic animals** are the carriers of paratyphoid fever.
- Members of the same family can be transient or permanent carriers.
- In most parts of the world, **short-term fecal carriers** are more common than **urinary carriers**.
- The chronic urinary carrier state occurs in those who have schistosomiasis (parasitic blood fluke).
- Continuing to shed *Salmonella* Paratyphi is possible for **up to one year**, and during this phase, a person is **considered to be a carrier**.
- The chronic carrier state may follow **acute illness**, or **mild** or **even subclinical infections**. Chronic carriers are most often women who were infected in their middle age.

# Pathophysiology

- **After ingestion**, Eventually the bacteria passes down to bowel, then penetrating the intestinal mucosa (lining) to the underlying tissue.
- If the immune system **is unable to stop the infection** here, bacteria multiplies and spread to the bloodstream, after which the first signs of disease are observed in the form of fever.
- Bacteria can penetrate **further to the bone marrow**, liver and bile ducts, and are excreted into the bowel contents.
- In the second phase of the disease, bacteria **penetrates the immune tissue** of the small intestine, and the initial symptoms of small-bowel movements begin.

# Signs and symptoms

- Paratyphoid fever resembles typhoid fever.
- Infection is characterized by a **sustained fever**, **headache**, **abdominal pain**, **anorexia**, a **nonproductive cough** (in early stage of illness), a **relative bradycardia** (slow heart rate), and **hepatosplenomegaly** (an enlargement of the liver and spleen).
- About 30% of patients develop **rosy spots on the central body**.
- In adults, constipation is more common than diarrhea



- small, speckled, and rose-colored exanthem on the lower chest and abdomen.



# Signs and symptoms

Only 20 to 40% of people initially have abdominal pain.

Nonspecific symptoms such as

- chills
- sweating,
- headache,
- loss of appetite,
- cough, weakness
- , sore throat,
- dizziness, and
- muscle pains

are frequently present before the onset of fever

Some very rare symptoms are psychosis (mental disorder), confusion, and seizures.

# Prognosis

- Because paratyphoid fever is **milder than typhoid fever** ,The intestinal hemorrhage and intestinal perforation are less common.
- However, **paratyphoid fever C** can cause osteomyelitis and multiple abscesses in the body cavity or tissue, which should be cautious.
- Those diagnosed **with Type A** of the bacterial strain rarely die from it except in rare cases of severe intestinal complications
- the mortality rate **falls to less than 1%**
- Antibiotics such as **azithromycin** are particularly effective in treating the disease
- **So, the prognosis is better**

# Prevention

- Providing basic sanitation and safe drinking water and food
- careful handwashing after defecation and sexual contact, before preparing or eating food
- Food handlers should be educated in personal hygiene prior to handling food
- Those who travel to countries with poor sanitation should receive [a live attenuated typhoid vaccine—Ty21a \(Vivotif\)](#), which, in addition to the protection against typhoid fever, may provide some protection against paratyphoid fever caused by the *S. enterica* serotypes A and B.
- This [cross-protection by a typhoid vaccine](#) is most likely due to [O antigens](#) shared between different *S. enterica* serotypes.
- Exclusion from work and social activities should be considered for symptomatic patients

# TREATMENT

- If appropriate treatment is initiated within the first few days of full-blown illness, the disease begins to remit after about 2 days, and the patient's condition markedly improves within 4-5 days. **Any delay in treatment** increases the likelihood of complications and recovery time.
- **The genes for antibiotic resistance** in *S typhi* and *S paratyphi* are acquired from *Escherichia coli* and other gram-negative bacteria **via plasmids**.
- This explains the sudden appearance of MDR strains of *S typhi* and *S paratyphi*, often without intermediate strains that **have less-extensive resistance**.

MDR : Multidrug-Resistant

# CONTD.

- **Chloramphenicol** was used universally to treat typhoid fever from 1948 until the 1970s, when widespread resistance occurred . **Ampicillin** and **trimethoprim-sulfamethoxazole (TMP-SMZ)** then became treatments of choice . However , in the late 1980s, some S typhi and S paratyphi strains (multidrug resistant [MDR] S typhi or S paratyphi) developed simultaneous plasmid-mediated resistance to all three of these agents.
- **Fluoroquinolones** are highly effective against susceptible organisms, yielding a better cure rate than **cephalosporins**. Unfortunately, resistance to first-generation fluoroquinolones is widespread in many parts of Asia.

# CONTD.

- In recent years, **third-generation cephalosporins** have been used in regions with high fluoroquinolone resistance rates, particularly in south Asia and Vietnam . Unfortunately, sporadic resistance has been reported , so it is expected that these will become less useful over time.
- <https://www.microbiologyresearch.org/content/journal/jmm/10.1099/jmm.0.47170-0#tab2>

# CONTD.

- if the **origin of the infection is unknown**,
- **the combination of a first-generation fluoroquinolone and a third-generation cephalosporin should be used**. This allows for most effective clearance if the organism is fluoroquinolone-susceptible but still covers strains that are not.
- <https://emedicine.medscape.com/article/231135-medication#showall>

THANK YOU

