



HEMATOPOIETIC & LYMPHATIC SYSTEM

SUBJECT : Microbiology

LEC NO. : 4

DONE BY : Scientific Team

وَقُلْ رَبِّ زِدْنِي عِلْمًا



Salmonella and Brucella



جامعة الهاشمية

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Salmonella Typhi and Enteric Fever

Typhoid

General Characteristics of Salmonella

- Gram-negative
- Coliform bacilli (enteric rods)
 found in most of the all over the site of the cell
 because it starts in the GIT and gets colonized in it.
- Motile by peritrichous flagella
- Facultative anaerobes
 بتفضيل بدون هواء
 needs a little of the oxygen.
- Can ferment glucose but are non-lactose fermenter
 E.Coli is a lactose-fermenter.
- Usually produce H₂S
 Black color colonies
- Resistant to bile salts
 the carriers are found in the gallbladder.
 كى ما بقدر يتحملها
- Contain 3 main antigens O, H and Vi antigens
 Capsule
 ↓
 - Lipooligosaccharide
 - endotoxin
 - outer layer
 ↓
 Flagella
- Important species:
 1. *Salmonella typhi*
 2. *Salmonella paratyphi*
 similar symptoms but they're mild.



Epidemiology

(Developing country) (خا صة بال)

- Typhoid fever is still an important cause of morbidity and mortality worldwide (16–33 million cases of typhoid fever occur annually)
- Typhoid is a **strictly** human disease
- **Transmission:**
- Person to person spread through fecal-oral route by ingestion of contaminated food or water
- If a patient with typhoid has not travelled to an endemic area, the source must be a visitor or someone else who prepared food
- The pathogen can be transmitted in the water supply when sewage from carriers contaminate drinking water
- **Chronic carriers (5%)** are the primary reservoir through chronic infection of the gallbladder and the biliary tract

* some diseases are zoonotic diseases meaning that the life cycle includes animals.

ينتقل من human إلى human

ملوث

→ food or water → intestine

بنسجم مع طبيعة البكتيريا و مكانها

الحياة المائية

has no symptoms

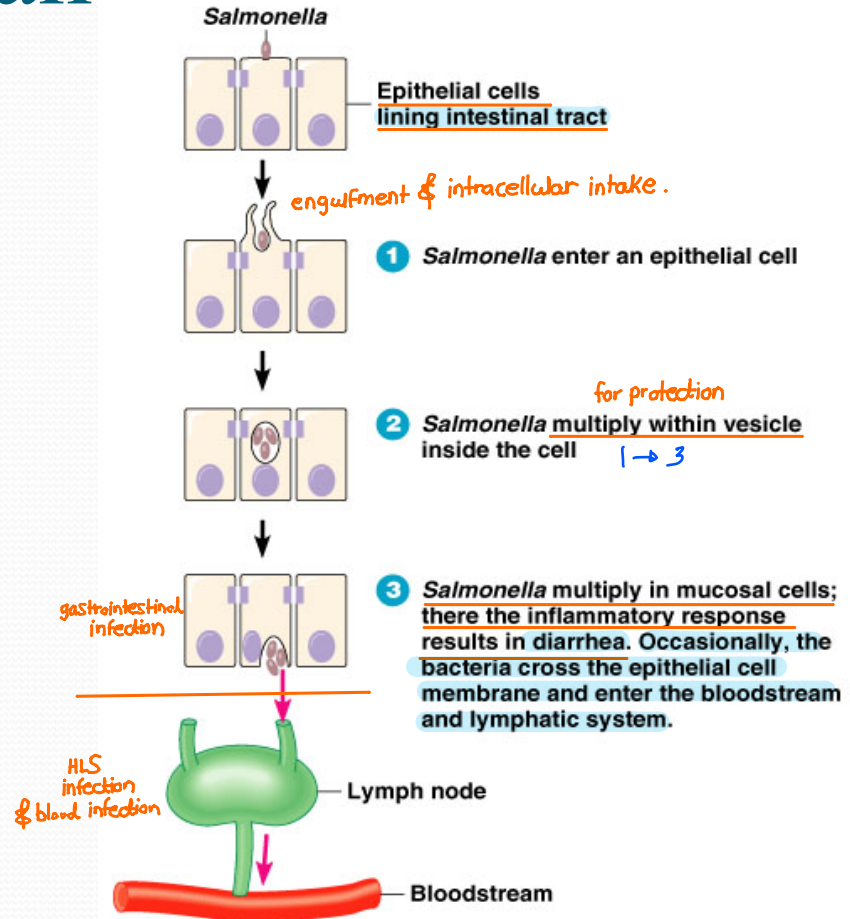
workers should usually go to check if they are carriers or not by doing a stool culture.

Jordan still has Typhoid fever.

Pathogenesis and Virulence

Virulence attributable to:

- Invasiveness *قدرتها على اختراق الخلايا*
- Intracellular survival & multiplication
- Endotoxin *lipopolysaccharide within the bacteria ما أخبرت شي الجرا*
- Exotoxins: enterotoxins, cytotoxin *responsible for the GIT symptoms. destruction of the cells & tissues.*



1. In the intestinal submucosa, the Vi antigen retards polymorphonuclear neutrophil (PMN) phagocytosis. This may favor uptake by macrophages. The typhoid bacteria remain within a membrane-bound vacuole and replicate, leading to macrophage death (prolonged intracellular survival in macrophages)

2. As the bacteria proliferate in macrophages, they are carried through the lymphatic circulation to the mesenteric nodes, spleen, liver and bone marrow

the immune system will not recognize the bacteria since it's inside the macrophages.

3. Bacteria begin to spill into the bloodstream. This seeding of Gram-negative bacteria and their LPS endotoxin starts the fever, which increases and persists with the continuing of bacteremia

(lipopolysaccharide)

hallmark "high grade"

- ① * Mild Fever & Diarrhea → GIT infection.
- ② * High Grade Fever → HLS infection.

① : enteritis

② : typhoid fever (بالحمى التي يدخل فيها الدم (blood))

أقرب (Lymph nodes) للأعضاء

Clinical Presentations

The main clinical presentation: depending on the virulence of the bacteria

- **Gastroenteritis (enteritis):**

الجموعة
الكبير من
الأعراض

High infectious dose, transmitted by poultry and eggs

دواجن

6-48h incubation period

Nausea, vomiting, diarrhea, fever, cramps, headache

low grade

الحمى

- **Enteric fever**

High grade fever

hall mark
of the disease
meaning that the bacteria
has reached
to the
blood &
lymph nodes.

Typhoid fever caused by *S. typhi* and less severe

paratyphoid fever caused by *S. paratyphi*

(40°-41°)
fever

Septicemia → secondary infection from the blood to other organs.

Particularly *S. typhi*, and *S. paratyphi*

← bacteremia and systemic dissemination to other organs like (spleen/liver/
Kidney/brain...)

- **Asymptomatic carriage** the patient may have all these stages then gets to become a chronic carrier.

Gall bladder is the reservoir for *S. typhi*

(بجوف الكبد)

Enteric or Typhoid Fever

- Enteric fever is a multiorgan systemic infection characterized by prolonged fever, sustained bacteremia, and profound involvement of the RES, particularly the mesenteric lymph nodes, liver, and spleen
- The mean incubation period is 13 days *exposure → first symptom's appearance.*
- The first sign is fever associated with a headache. The fever rises in a stepwise fashion for 72 hours. A relatively slow pulse is normally
↑ fever ↑ pulse rate characteristic. In untreated patients, the elevated temperature persists for weeks. *ببطء
الحرارة
شوي
شوي*
- The fever rises to a high plateau, and the spleen and liver become enlarged. *lymph system involvement.* Rose spots (faint rash) on the skin of the abdomen or chest, are seen briefly in rare cases.
- Diarrhea may occur once or twice but is not a consistent feature
- The chief complications is intestinal hemorrhage and perforation *تقرح اذ (ulcer of intestine) كحل وطلع منه البرصه الثالثه
بحصفر (blood vessels)
له خطيرات جدا قد يوصل الى الوفاة*
- rarely bacteremia may lead to dissemination to other organs



Typhoid Fever Course

- Untreated typhoid fever have 4 stages:
 1. **First week:** the temperature rises slowly with fluctuation, general weakness, and cough
 2. **Second week:** high fever in plateau around 40 °C, possible delirium, tender hepatosplenomegally, and rose spots ← (Second week)
وإذا وصلت الـ Brain بصير للمريض delirium يعني يبطل ←
 3. **Third week:** complication start to appear, death can occur up to 30% if untreated
الأسبوع الثالث
- وصلت لـ (blood) وعملت (complication) في كل مكان
- لو ما عالناهم رح يتوفوا بهذا الأسبوع بس (septicemia) (تسمم الدم)
 4. **Fourth week:** fever might start to subside and the patient become a chronic carrier
الـ (immunity) يتعلم تصممع وبتنتع (B&T cells) عشانه تحضره عن
هذا المرض حتى لو اضطرت تقضي عن الـ (macrophage)

- أعلنة وفاة بالأسبوع الثالث
- لو أعطينا (treatment) بتقطع صاي الـ (circle)

هذا المرض حتى لو اضطرت تقضي عن الـ (macrophage)

عكس الوضع الطبيعي

Laboratory Diagnosis

we have to look for the clinical features & the source of the bacteria, in addition to * proper H1S test. * hepatospleno megal test.

- **Blood:** CBC (Leucopenia), LFT (elevated transaminases)
- **Specimens:** Blood, stool, duodenal drainage
- **Gram stain:** gram-negative rods
- **Culture:**

من المرحلة المتوسطة من المرض

من المرحلة الأولى والأخيرة من المرض

meaning that the bacteria has arrived to the liver.

if the same family has more than one person infected, then it will have a chronic carrier within it.

1. Differential media: MacConkey agar for rapid detection of lactose non-fermenting enterobacteria with inhibition of gram-positive bacteria

non-lactose

2. Selective media: Salmonella-shigella agar (SS agar) which favor growth of Salmonella and Shigella over other enterbacteriaceae

* mortality test } tests for differentiation.
* antibody test

هذا المرض يسببه تكثير البكتيريا (overpopulation) يحصل تشخيص الالتهاب (leucocytosis) (Leucocytosis) ولبس

3. Enrichment culture: enriched broth media that allow growth of Salmonella and inhibit normal intestinal flora

to increase the positive outcome.

Incubation for 24 hours in ambient air at 35-37 °C, produce colorless colony

يمكنه نطلب (Antibody test) بغيرنا بس مع تطور

- **Biochemical test:**
 - Oxidase-negative
 - Catalase-positive
 - Glucose fermentation positive while lactose fermentation is negative
 - Reduce nitrates to nitrites

- يتميز هذا المرض بظلاله :

- Relatively slow pulse

- Leukopenia NOT Leukocytosis

The gold standard
is stool & blood culture of the
bacteria for short period.

• Serological tests:

1. Agglutination test: Known sera (Salmonella specific antibodies) and unknown culture are mixed on a slide and observed for clumping
2. The dilution agglutination test (Widal test):
 - To detect formation of specific anti-Salmonella antibodies in patients serum
 - Serial dilutions of serum are tested against known salmonella antigens (O and H antigens)
 - Positive with titer with O antigen $>1:320$, titer with H antigen $>1:640$, or rise in antibody titer in 2 specimens obtains with 7-10 days interval
إنا كما نرى بخلي المريض يرجع كان
حزنة قبل الفحص.
 - The test is usually positive after 1-2 weeks of infection, and false-positive and false-negative results occur.
 - The test is not useful in diagnosis of enteric fevers caused by salmonella other than Salmonella Typhi.
* patient becomes +ve after the 2nd week.
* high rate of false positive & positive false results.
أو احنا قلنا أنه أخطر شيء آخر الـ Widal test الثاني واول نتائج فالتا ليعتد المريض (Widal test) صديق أو بعرضه حماه للخطر

Treatment

Enteritis: only GI symptoms
with negative blood culture

- Fluid and electrolyte replacement
- Control of nausea and vomiting
- Antibiotics not recommended for enteritis because it prolong disease duration

Enteric fever:

*clinical symptoms
*positive blood culture

aplastic anemia.

bone marrow suppression.

drug of choice

isn't used anymore
لا نستخدمه!

- Antibiotics (chloramphenicol, ceftriaxone, ciprofloxacin)
↳ giving IV & for inpatients
- With proper antimicrobial therapy, patients feel better in 24 to 48 hours, their temperature returns to normal in 3 to 5 days, and they are generally well in 10 to 14 days

Prevention

- Control by proper preparation of food "**Boil it, cook it, peel it, or forget it**"
- The provision of clean water supplies
- Hygiene and sanitation with emphasis on proper hand washing
- Vaccination can reduce risk of disease for travelers in endemic areas (vaccination is available and is 50-70% effective) covering for only 2 years before going to the endemic areas * people who haven't ever been exposed to the bacteria will develop the complications.
- Identify & treat carriers of *S. typhi* & *S. paratyphi*



Brucella and Brucellosis

Introduction

البحر الأبيض المتوسط

- Brucellosis = Malta fever = Mediterranean Fever = Undulant fever
ups & downs
بتنقلها تطلع وتيجي
- David Bruce (1855-1931) sent to Malta to provide medical care to the troops. 1887 isolated “micrococcus” from spleens of 4 soldiers died of the disease
↓
small bacteria that reaches the spleen.
- Zoonotic disease
transported through animals
- Six species
 - 1. *B. abortus* - mainly cattle
 - 2. *B. melitensis* - sheeps & goats
 - 3. *B. suis* - pigs
 - 4. *B. canis* - dogs (تنتقل من الكلاب فقط لو شربت حليبها او اكلت لحومها 🐶. وهيك)
 - 5. *B. ovis* - sheep (not human pathogen)
 - 6. *B. neotomae* - desert wood rat (not human pathogen)

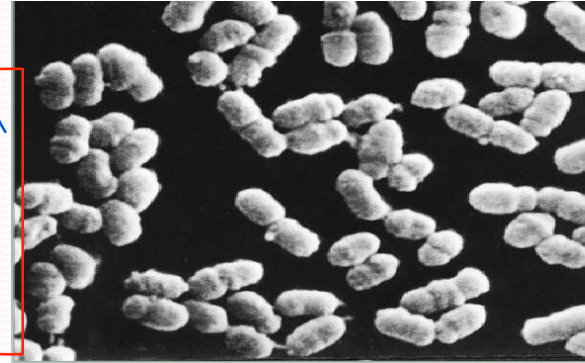
ينتقل هذا المرض من تناول لحوم الحيوانات أو شرب حليبها

we care mostly about them

General Characteristics

- Gram - ve cocci, **coccobacilli**, bacilli
- Very small
- Non fermenters
- Strict aerobic
- Non motile ^{has no flagella}
- Non spore forming ^{both are non spore forming.}
- Grow in regular media -prolonged incubation > 4 weeks
- Two major antigenic variants (A and M)
- True pathogens: isolation always associated with disease, always clinically significant

- bacilli : (salmonella) ك
- glucose fermenter
- facultative anaerobe
- flagella (motile)
- No spore forming
- يو صا بالكتير اسودع بالذراعة



مايزيل تصير (Normal flora)

Epidemiology

- 500,000 human cases per year worldwide
- The disease is common in Mediterranean and Arabic area
- Animals are natural reservoir mainly domestic animals
- Brucellosis is a genitourinary infection of sheep, cattle, pigs, and other animals
mainly through milk
- Concentrated in animal milk, urine, genital organs
- Rout of transmission:
 - 1. Oral : unpasteurised milk & products of raw milk or meet
عروضي
 - 2. Skin: accidental penetration or abrasion; at risk farmers & veterinarians
(genitourinary tract) (ممكنه يكونه مجروح من ايده وصفه ايده على منطقه الإماية للحيوانه خاصة ال (genitourinary tract))
 - 3. Other routes: conjunctival, blood transfusion, and transplacental
أو كما انه يعمل (Manual milking) بحلب بالحيوانه فبدرج المرض بال (blood) ويقلد بعضا بالشفط لكهاليدته الطرية الدنية

- People at risk:
 1. Farmers
 2. ^{العام} Abattoir employees, government meat inspectors, and others who handle livestock or meat products
 3. Veterinarians
 4. Laboratory workers
- An outbreak of *B. melitensis* in Texas was traced to unpasteurized goat cheese brought in from Mexico

unpasteurised milk

infected animals



life cycle



Pathology and Virulence

- Facultative intracellular pathogens of mononuclear-phagocyte system
 1. Bacteria are phagocytosed by macrophage or polymorphonuclear leukocyte
 2. Survive intracellularly by inhibiting killing *like Salmonella*
 3. Carried to spleen, liver, bone marrow, lymph nodes
 4. Form **granulomas** (mass of granulation tissue produced in response to chronic infections, inflammation, or foreign bodies) and cause destructive tissue damage *with no treatment.*
 - hallmark*
 - العلامة المميزة*
 - consolidation around the macrophages & not effectively trying to kill the bacteria.*
 5. Release of bacteria from granuloma into the systemic circulation responsible for the recurrent chills and fever of the clinical illness
 - كل ما تطلع البكتيريا على الـ (blood) بترفع الحرارة بتجمعها (granulomas)*
 - بعضها بالـ (spleen) بتفتقير الحرارة. وبعدها، بعد المريض (on and off)*

Clinical Presentation

• اللأسف لا يمكن علاجها بشكل كامل بعد بنخفة الأخرافه
ميكروبيا يتكونه بال (granuloma) محاطه بال (macrophage)
ومتصلبه توصل اليها الـ (Antibiotics) حتى لو أعطيت

- **Acute disease** often develops with initial nonspecific symptoms of malaise, chills, fatigue, weakness, myalgias (muscles), weight loss, arthralgias, and cough
بتشيل الميكروبيا الموجوده بالدم بعد مستطيله تقدر تصير اليه
محاطه بال (macrophage)
للأسف 😞
- **Chronic disease** and recurrence are common because it can survive in phagocytic cells and multiply to high concentrations
- 1. Fever with sweating in the evening (periodic fever)
- 2. Headache, anorexia, body aches and weight loss
- 3. Lymphadenopathy, hepatomegaly, and splenomegaly
found in the blood
- **Complications:** arthritis, epididymoorchitis, spondylitis, neurobrucellosis, liver abscess, and **endocarditis** (the latter potentially fatal)

Hallmark

- Brucellosis starts with malaise, chills, and fever 7 to 21 days after infection. Drenching sweats in the late afternoon or evening are common, as are temperatures in the range of 39.4 to 40° C. The pattern of periodic nocturnal fever (undulant fever) typically continues for weeks, months, or even 1 to 2 years
- Patients become chronically ill with associated body aches, headache, and anorexia. Weight loss of up to 20 kg may occur during prolonged illness
- Less than 25% of patients show detectable enlargement of the reticuloendothelial organs, the primary site of infection. Of such findings, splenomegaly is most common, followed by lymphadenopathy and hepatomegaly

Laboratory Diagnosis

1. **Specimen**: blood, biopsy tissue from lymph nodes, bone marrow
2. **Gram stain**: small gram-negative coccobacilli
3. **Culture**:
 - Grow on commonly used media, including chocolate and blood agar
 - **Brucella agar medium** is highly enriched selective media that grow *Brucella* species bacteria very well
 - All cultures should be incubated in 8–10% CO₂ at 35–37°C and should be observed for 3 weeks before being discarded as negative
 - Colonies: small, convex, smooth colonies appear on enriched media in 2–5 days

4. Biochemical tests:

Catalase positive

Glucose: Negative

Oxidase positive

Urease positive

5. Serology: *more useful because the disease is chronic.*

- 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
- Antibodies that agglutinate suspensions of heat-killed organisms typically reach titers of 1: 640 or more in acute disease

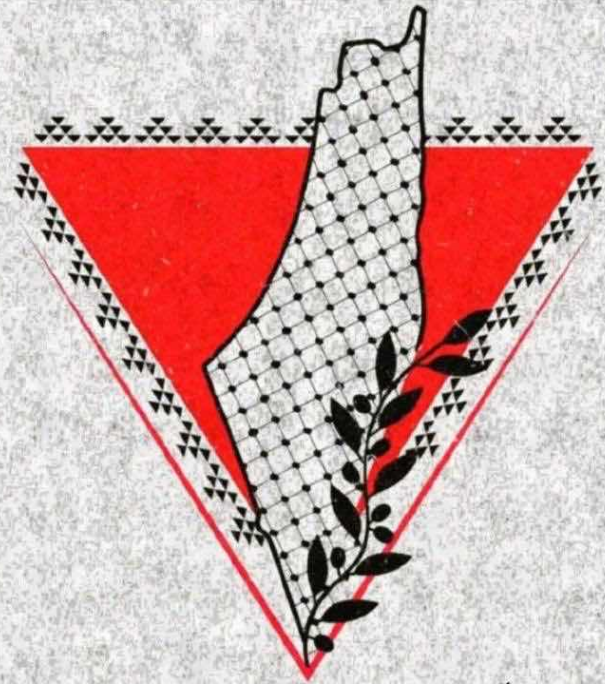
6. ELISA: detects specific IgG and IgM antibodies

previous or prolonged term infection *acute infection*

Treatment and Prevention

- Treated with combination of tetracycline and doxycycline ^{Drug of choice} treatment isn't found for the granuloma.
- Prevention: ^{(Chemo prophylaxis of Malaria) له كانه}
_{but not drug of choice of M}
- 1. Serology & confirmatory bacterial culture to identify infected animals
- 2. Positive animals are destroyed
- 3. Vaccination is available but is not a 100% effective and is costly to cattle ranchers ^{ل (vaccine) للحيوانه مشه للإنسانه}
- 4. Milk, milk products and meat need to be boiled or cooked properly

Thank you..



اللهم بدل حال فلسطين
من الخوف إلى الأمان، ومن
العسر إلى اليسر، ومن الظلم
إلى العدل يا أرحم الراحمين

INSTA: TAAMOL_92