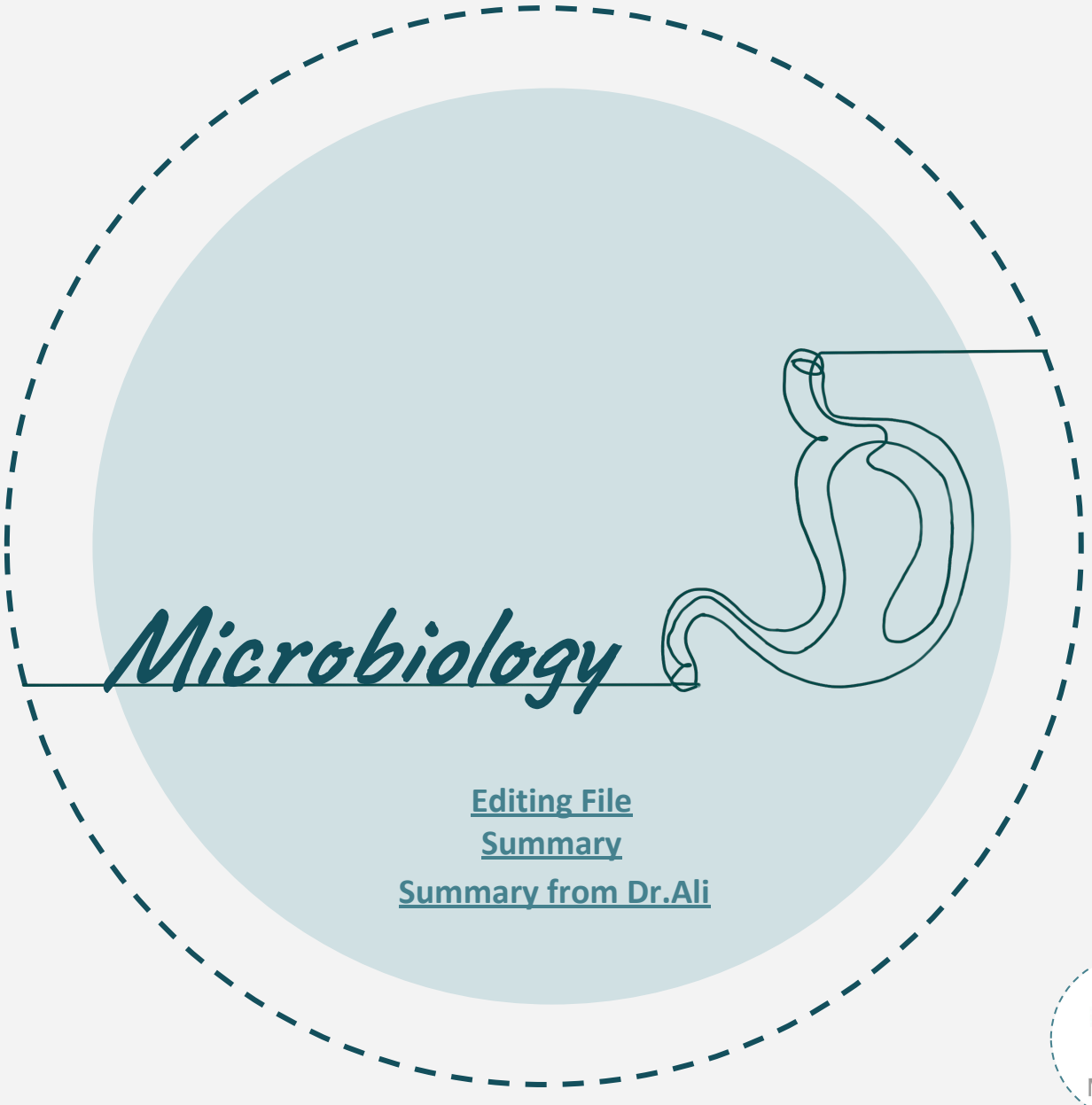
Shigella and Salmonella

PLEASE
Make sure to check the team's summary & memorize it very well.
Distinguishing between salmonella and shigella is extremely important.



Editing File
Summary
Summary from Dr.Ali

MED439
KING SAUD UNIVERSITY

MICROBIOLOGY
Team 439

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Color index

- Girls' slides
- Main content
- Important
- Boys' slides
- Extra
- Drs' notes

Objectives:

- Describe the antigenic structures and virulence factors of Salmonella and Shigella
- Compare the pathogenesis of various species of Salmonella and Shigella
- Describe the clinical features and risk factors for the infection with the two organisms
- Describe the general concepts for the management of gastroenteritis caused by both organisms.

1

Salmonella

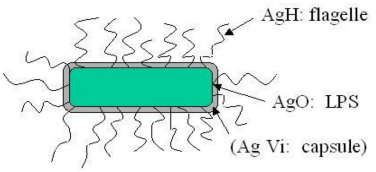
Overview

- Gram negative, **motile**, facultative anaerobic bacilli
- Non-lactose fermenting colonies so it appears as white on MacConkey agar (unlike E.coli which appears pink)
- Highest during the rainy season in tropical climates and during the warmer months in temperate climates.(1)

Sources

- Water, food and milk contaminated (like Shawarma) with human or animal excreta. From cold blooded animals.
- Source is human in : **S.typhi** and **S.paratyphi** It can be transmitted from humans , and it stays in gallbladder . (If a gallbladder stone was developed, it will be carried forever. Cholecystectomy might be indicated in such a case).

Antigenic Structure



1	O. Somatic antigen
2	H. Flagellar antigen
3	K. Capsular antigen (in salmonella typhi we call it Vi antigen)
4	O-Antigen (Heat – stable)(2) is lipopolysaccharide in the outer membrane A,**B**,C1,C2,**D**,E you don't need to remember it
5	H-Antigen (Heat labile) Not important
6	**VI in *Salmonella* serotype *typhi*** (virulence heat-labile capsular homopolymer of N-acetyl- galactosamino-uronic acid) vs phagocytosis

1) We can see Salmonella All the time of the year, but it can be noticed in certain time in certain areas
2) Sometimes it is hard to detect the capsule, so we have to heat the organism (get rid of H antigen to test for O antigen). However, this is a diagnostic technique and no need to memorize it

Salmonella

Classification

Two species [1] of Salmonella :

- S.enterica (six subspecies I, II, III, IV, V, VI)[2]
- S.borgori (rare) Found in cold blooded animals (birds, rodents, turtles, snakes and fish)

Dr. Somily: don't worry about this table. We just want to show you that enterica is the most common.

Salmonella species and subtypes		NO. Of stereotypes within species	Usual habitat
S. Enterica	S. enterica subsp. enterica (I)	1504	◦ Warm-blooded animals
	S. enterica subsp. salmae(II) S. enterica subsp. arizonae (IIIa) S. enterica subsp. diarizonae (IIIb) S. enterica subsp. houtenae (IV) S. enterica subsp. indica(VI)	502 95 333 72 13	◦ Cold-blooded animals ◦ The environment
S. Bongori(V)		22	◦ Cold-blooded animals ◦ The environment

Virulence factors

1. Fimbria - Adherence
2. Endocytosis
3. Enterotoxin
4. Replication in macrophage

◦ SPI 1 (Salmonella pathogenicity island 1)
◦ T3SS(type 3 secretory system) : **Virulence** (invasion & enteritis)

◦ TLR (Toll like receptor) : IC survival ,growth & systemic infection) , helps with attachment

1) You just know there are two species of salmonella if any on ask you.
2) There are more than 2000 serotypes within subspecies.

Salmonella

Clinical Diseases

Typhoid Fever
It is a systemic disease and can go to small intestine to cause very severe disease.
Caused by salmonella typhi

Acute Gastroenteritis
Very simple mild disease
Caused by other types of salmonella

Nontyphoidal Bacteremia
It infect elderly and neonate(especially in immunocompromised)

Carrier state
(following Salmonella infection)

Enteric (Typhoid) Fever

Etiology	Caused by ***Salmonella*** serotype ***S.typhi*** or ***S.paratyphi*** A, B and C (less severe)
Source	Ingestion of contaminated food by infected or carrier individual
Prevalence	Common in tropical, subtropical countries, and travelers (sewage, poor sanitation).
Pathogenesis	- **Prolonged fever**, **Bacteremia** → Involvement of the reticuloendothelial system (liver, spleen, intestines and mesentery) → **Dissemination to multiple organs** -Incubation period (IP) : 9-14 days (long) You can travel and come back then develop fever (if you read travelers in the case think about it).

Clinical Features

First week	2nd and 3rd Week
- **fever**, malaise, anorexia, myalgia and a continuous dull frontal headache Thumping pulsating headache - Patient develops **constipation** - Mesenteric lymph node → bloodstream, liver, spleen and bone marrow - Engulfment of Salmonella by mononuclear phagocytes . - Bacteria is released into the bloodstream again and can lead to high fever . - **Blood culture is positive.**	- **Sustained fever and prolonged bacteremia.** - **Invade gallbladder** (favorite place) - **Peyer's patches** - **Rose spots** 2nd week of fever - Biliary tract → GIT - Organism isolated from stool. - Also, they will have some sort of bradycardia

Treatment (1)

- we treat every one if they get infected. (2)
- **Ceftriaxone** Best (3)
- Ciprofloxacin (4) Not for pregnant or children.
- Trimelhoprim – Sulfamethoxazole
- Ampicillin If the bacteria is sensitive we shift to Ampicillin.
- Azithromycin (drug of choice in pediatrics) or Ceftriaxone for patients from India and SE Asia due to strains resistant to Ciprofloxacin. Ciprofloxacin can be used for patients from other areas.

1) Treatment is empirical: start with ceftriaxone and check susceptibility. if it was sensitive, we shift to ampicillin.
2) Salmonella typhi: antibiotics treatment is mandatory. Salmonella non-typhi: treatment is only for pediatrics, elderly, with sickle cell disease, or immunocompromised patients.
3) Best because it is secreted through biliary tree (which is the favorite site of salmonella typhi)
4) Ciprofloxacin salmonella resistance is emerging nowadays.

Salmonella

Salmonella Gastroenteritis	
Etiology	S. enterica subsp. is the most common cause **EXTREMELY IMPORTANT** ★ Infective dose: 10^6 bacteria [1] **(less than cholera & more than shigella)** ◦ Incubation period : 8 – 36 hrs.
Source	◦ food poisoning through contaminated food , Poultry seen in all raw chicken (that is why it needs to be cooked very well), milk, egg and egg products ◦ Handling pets
Symptoms	- Fever, chills, **watery diarrhea** and abdominal pain, **Self limiting**. ★ **The infection may be very severe in patients with:** they will have severe infection , and they will come complaining of severe pain in joints and bones. 1. sickle cell, and hemolytic disorders (blood diseases) 2. Ulcerative colitis 3. Elderly or very young patients 4. Patients at high risk for dissemination and antimicrobial therapy is indicated
Treatment	Uncomplicated cases require fluid and electrolyte replacement **only**. We don't treat adult.We just treat neonates and elderly.

Complications [2]

- Necrotizing cholecystitis
- Meningitis, osteomyelitis, endocarditis and abscesses.
- Bowel hemorrhage and perforation
- Pneumonia and Thrombophlebitis [3]

Typhoid mary : **Read** a story of asymptotic carrier (mary mallen)

Watch documentary :

1) high infective dose means that the bacteria is less virulent
2) complications of both disease
3) Salmonella loves blood vessels and endothelial cells.

Shigella

Overview

- Gram negative bacilli **non-motile.**
- Non-lactose fermenting
- Cause : **bacillary dysentery** (blood, mucus and **pus** in the stool)

Clinical infection (1)

1) S.sonnei in west (group D1) : most predominant in USA (fever, watery diarrhea)
2) S.flexneri (group B15) : 2nd most common, Young adults (man who have sex with man).
3) **S. dysenteriae** in our region (group A6) and S. boydii (group C 20) : are most common isolates in developing countries.
4) S. dysenteriae type 1 : associated with **morbidity** and **mortality**
5) Human is the only reservoir. It is a serious infection with low infectious dose.

Antigenic Structure

- Shigella has **4 species** and 4 major O antigen groups :

1	All have **O** antigens
2	Some serotypes has **K** antigen(heat labile removed by boiling)
3	lack **H** antigen; no flagella (Shigella are non motile)

1) No need to remember the species

Shigella

Transmission	◦ Person to person transmission through **fecal –oral route** . ◦ Spread by Flies and fingers (have a role in spread) ◦ **Food and water.**
Risk factors	◦ Young children in **daycare** ◦ People in crowded area ◦ Anal oral sex in developed countries.
Pathogenesis	- Penetrate (invade) epithelial cells → local inflammation → shedding of intestinal lining and ulcer formation. (They cause desyntry, pus, mucosal damage) ★ **Low infective dose < 200 bacilli** - Incubation period : 24 - 48 hrs [1] Shorter than salmonella
Treatment	- Antibiotics are used to reduce duration of illness: - Ampicillin, IV ceftriaxone, oral TMP-SMX, **Ciprofloxacin** or Doxycycline. Same as salmonella typhi but duration is less

Symptoms

High fever and chill

Abdominal cramp and pain accompanied by tenesmus [2]

Bloody stool with mucus and leukocytes.

Can lead to rectal prolapse in children

Complications [3]

★ **Dr: I want you to remember the complications**

Ileus , obstruction dilatation and toxic megacolon

Seizures

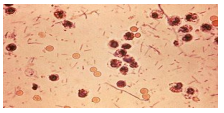
Bacteremia in 4 % of severely ill patient (Very rare)

Hemolytic Uremic Syndrome **(HUS)**
Just as EHEC 0157:H7

1) Most enteropathogens have IP about three days except S.typhi it has one week as IP.
2) is the feeling that you need to pass stools, even though your bowels are already empty.
3) majority of complications are localized unlike salmonella which was disseminated

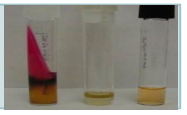
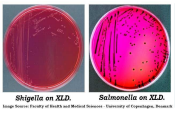
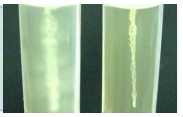
Shigella

Laboratory diagnosis



Dysentery stool
Shigella you can see WBC and RBC in the stool (dysentery stool) unlike salmonella which is only watery diarrhea .

- Of Salmonella and Shigella [1] from stool :

1:	**Gram stain**	Both are Gram negative bacilli
3:	**Biochemical tests**	
3:	**Culture**	★ on **selective media (XLD)** (Salmonella produce black colonies due to H2S)[2] 
6:	**Motility test** [3]	
5:	**Serology** [4]	in Salmonella, Shigella & E.coli the final detection is by serotyping using agglutination Ag+Ab test.

Diagnosis

Stool culture on : No need to remember

- Selective Selenite Enrichment Broth Media.
- XLD
- MAC (MacConkey agar).
- SS (Salmonella Shigella).
- HEA (Heckton enteric agar).
- BS (bile salt agar).

Sero-grouping based on O and H antigen.

Sereny test [5] 

1) diagnosis of shigella is very difficult because it is fastidious and dies quickly before culturing it.
2) Salmonella is motile and has H2S while Shigella is non-motile and has no H2S.
3) Positive: Diffuse, hazy growths. Negative: Growth that is confined to the stab-line.
4) For differentiation.
5) inject the bacteria into animal's eye to measure bacterial invasiveness.

Drs' notes

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Make sure to check the team's summary & memorize it very well. Distinguishing between salmonella and shigella is extremely important.

Prof. Somily

- Both salmonella and shigella are enterobacteriaceae and facultative anaerobes. However, salmonella is motile (has flagella) whereas shigella is non-motile.
- Salmonella has three important antigens, (1) O. somatic which is the body antigen of the bacteria, (2) H. Flagellar antigen, (3) K. Capsular antigen. These antigens are detected in all salmonella except *salmonella typhi* (which has a capsule antigen but we call it **Vi** because it is very virulent and has to be given a specific name).
- *S.paratyphi* cause Less severe symptoms than *Salmonella* serotype typhi.
- Source of *S.typhi* and *S.paratyphi* is human. (you need to remember this). After transmission, it goes and stays in gallbladder. (if a gallbladder stone was developed, it will be carried forever unless cholecystectomy is done). Furthermore, *salmonella typhi* has the ability to go inside macrophages and disseminate to various parts of body. (Favorite site to stay? GALLBLADDER).
- There are two possible clinical presentations of salmonella. (1) Typhoid fever which is a severe invasive disease that can invade lymph nodes, cause bacteremia, cause bradycardia, and it loves to stay in gallbladder. caused by *salmonella typhi* and *paratyphi*, and its treatment is mandatory. (2) Gastroenteritis which a mild disease is caused by other *salmonella* serotypes (non-typhoid), and it is only treated in special case e.g. immunosuppressed, elderly, and pediatrics with severe symptoms. Why? Because if *salmonella* gastroenteritis was treated, the carriage rate will increase and patient might carry the organism for longer time (mechanism is unknown).
- In typhoid fever infection the Incubation period (IP) : 9-14 days (so patient might have traveled and came back before symptoms start) Dr: you should think about it when you see travel history in the case.
- Treatment of *S.typhi* is empirical (start with ceftriaxone (best because it gets excreted from gallbladder which is favorite site of salmonella typhi) and check susceptibility. If it was sensitive, we shift to ampicillin).
- *Salmonella* can still be carried and present in stool after recovery from symptoms (this is a public health concern as it can spread if carriers have poor hygiene practices).
- Mostly, the incubation period enteropathogenic bacteria in general ranges from 12 hrs - 3 days. Except *salmonella typhi* as it can take up to one week before developing symptoms.
- Incubation period:-
  - Rapid/short incubation period (~1hr) = food poisoning with *staph. aureus.*
  - Middle incubation period (1-3 days) = *Salmonella*, *Shigella*, and other enteropathogenic enterobacteriaceae.
  - Long incubation period (weeks) = *Salmonella typhi/paratyphi, entameba histolytica*, and *listeria.*
- *Shigella* always has to be treated (unlike *salmonella* where we only treat *S.typhi*).
- Infectious dose in *shigella* is very low (200 organisms can cause infection).
- Both are invasive however salmonella disseminate while shigella almost never enters the blood

Prof. Hanan

- *Salmonella* survives in macrophages due to the effect of TLR (toll like receptor).
- ★ **It is important to know that gastroenteritis is way more severe in patients with sickle cell anemia and hemolytic disorders.**
- Enteric fever/typhoid fever is systemic (symptoms all over the body) whereas gastroenteritis is considered to be local (restricted to GIT),
- *Shigella dysenteriae* is associated with high mortality because it produces shiga-toxin I-II (like E.coli).
- Diarrhea in salmonella is watery whereas in shigella it is bloody with pus cells.

Quiz

MCQ

Q1: Q5: a 36-year-old male who traveled recently is presented with prolonged fever and rose spots, which of the following is most likely diagnosis?

A- Salmonella Gastroenteritis
B- Shigella Gastroenteritis
C- carrier state following salmonella infection
D- Typhoid fever

Q2: a 17-year-old female presented to ER with abdominal pain, watery diarrhea and fever for 3 days. Upon taking history, the patient mentioned that she has hemophilia. stool sample was collected which showed a gram negative bacilli on gram stain. Culture on XLD media showed black colonies. And on MacConkey agar showed non-lactose fermenting colonies. What is most likely diagnosis?

A- Salmonella Gastroenteritis
B- Enteric fever
C- Shigella Gastroenteritis
D- Nontyphoidal Bacteremia

Q3: which one of the following gastroenteritis circumstances does not need to be treated by antibiotics?

A- Sickle cell anemia with mild symptoms
B- Pregnancy
C- A neonate
D- Patient with AIDS

Q4: Serology tests of a stool sample showed Vi antigen in a certain bacteria. What is the most likely organism?
A- Salamonella Enterica
B- Salmonella Arizonae
C- Salmonella. Typhi
D- Shigella

Q5: a 2-years-old boy is presented to the ER, His mother reported that the daycare called when they noticed bloody stool with mucus. Upon examination the child had a seizure. blood and stool samples were collected, Blood culture was negative. The stool sample showed gram negative bacilli and XLD media showed growth without black colonies. What is the most likely causative organism?

A- Salmonella Bongori
B- Shigella dysenteriae
C- E.Coli
D- Salmonella Enterica

Q6: Q5: a 58-year-old female from India presented with Constipation, fever and abdominal pain. Blood sample revealed Bacteremia and blood culture was positive. Which of the following course of treatments you would not choose for her?

A- Azithromycin
B- Trimethoprim – Sulfamethoxazole
C- Ampicillin
D- Ciprofloxacin

Answers: Q1:D | Q2:A | Q3:B | Q4:C | Q5:B| Q6:D

SAQ

Case: A 4 year old child presented with fever, diarrhea and skin rash her mother said that she has a fever, constipation and malaise last week. The doctor took stool and blood samples for culture ,gram stain and motility tests. The gram stain showed gram negative bacilli , the motility test was positive and the culture on XLD media showed the growth of black colonies.

Q1: What is the most likely diagnosis?
A:Typhoid fever

Q2: What is the most likely causative agent?
A: S.Typhi

Q3: What do you expect the blood culture to show?
A: positive for salmonella typhi

Q4: what caused the growth of black colonies on XLD media?
A: H2S production by salmonella

Q5: name 2 complication of this disease?
A: Meningitis , bowl hemorrhage, necrotizing polycystitis , Pneumonia

Q6: How would you treat this patients?
A: ceftriaxone:

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