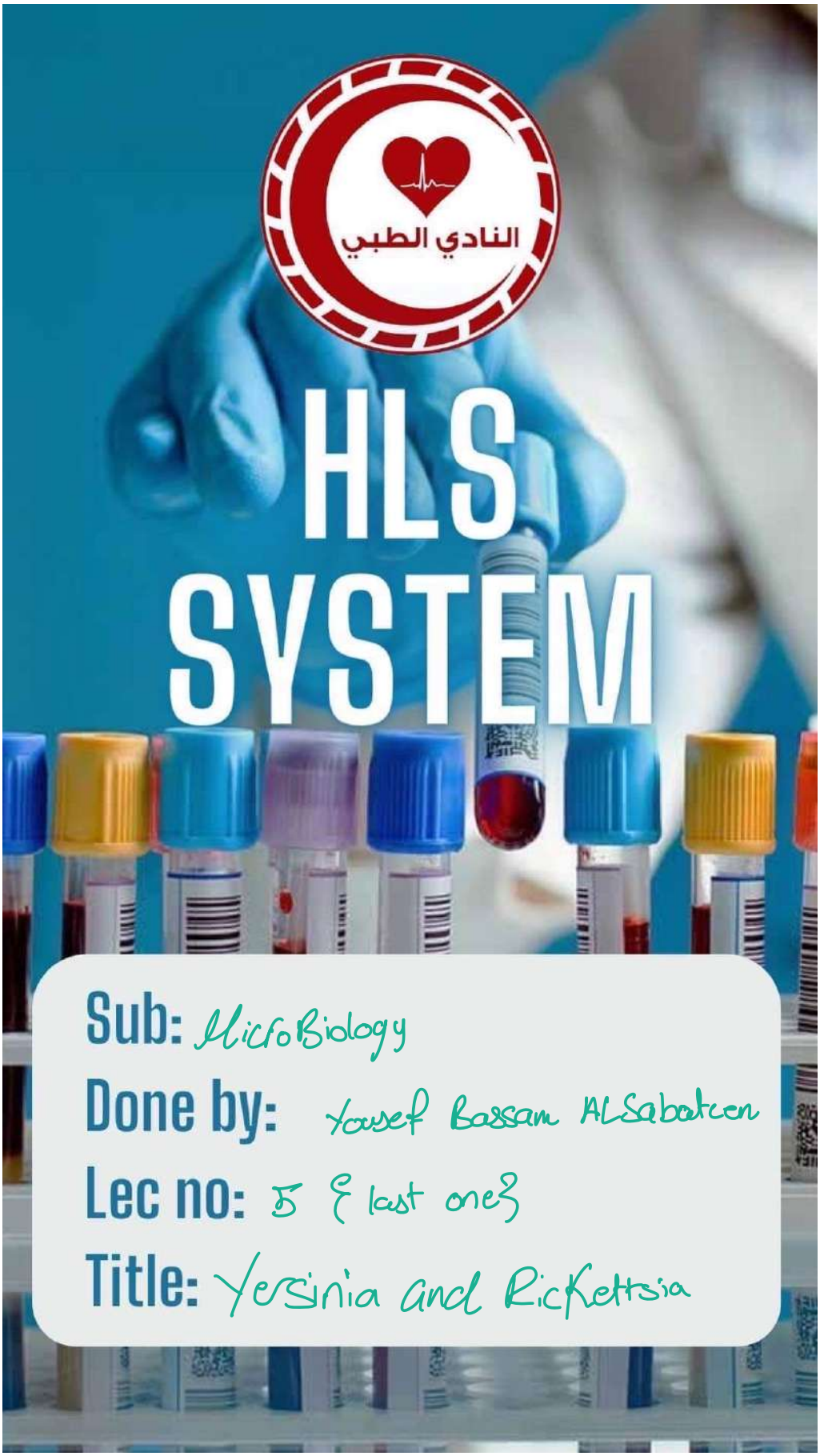


Sub: MicroBiology

Done by: Yousef Bassam ALSabateen

Lec no: 5 & last one3

Title: Yersinia and Rickettsia

Plague (Black Death)

By Prof. Hala Tabl

Introduction

Caused 4 plaque pandemics

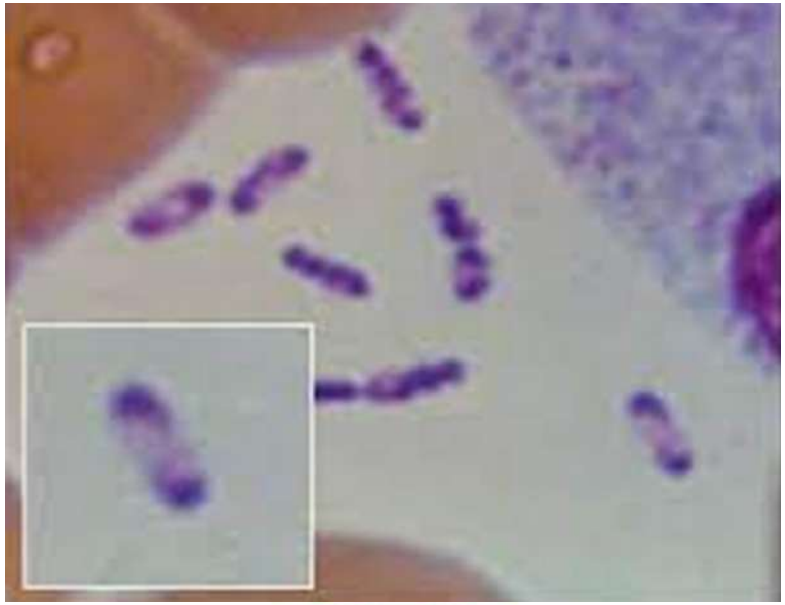
- Plague is an infectious disease caused by short gram –ve bacilli *yersinia pestis*.
- It is enzootic disease of wild rodents, transmitted accidentally to human by the bites of rat fleas.
- It is a serious infection, which in previous centuries produced pandemics of "black death" with millions of fatalities.

Transferred by rat fleas from rat to rat and accidentally to human

- The chief enzootic areas are Southeast Asia (esp. Vietnam), Africa, and North and South America.
- Plague has been identified by the CDC as a "Category A" agent, meaning it has been given high priority due to its potential threat to national security (could be used as a biological weapon).

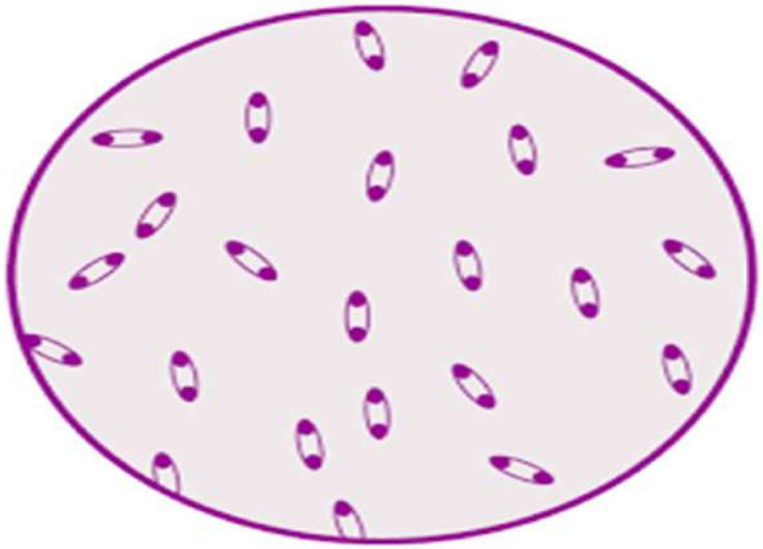
Highest risk

Yersinia Pestis



Morphology:

- It is Gram negative short oval bacillus (coccobacillus), non - motile and capsulated in tissue. Takes up the stain in the ends and less in the middle so it looks like it's a diplococci
- The poles of the bacillus have more affinity for stain (**bipolar staining**) (a safety pin).
- The bipolarity is more marked when the organism is stained with **Leishman's** stain.



Cultural characters:

- The organism is aerobe and facultative anaerobe, optimum temperature **27°C.** But starts adapting to our body temperature
- Can grow on ordinary media, but grows better on blood agar.
- Colonies on blood agar is a very small circular disc, transparent with a slightly granular surface and does not hemolyze blood. Y hemolysis

Biochemical reactions:

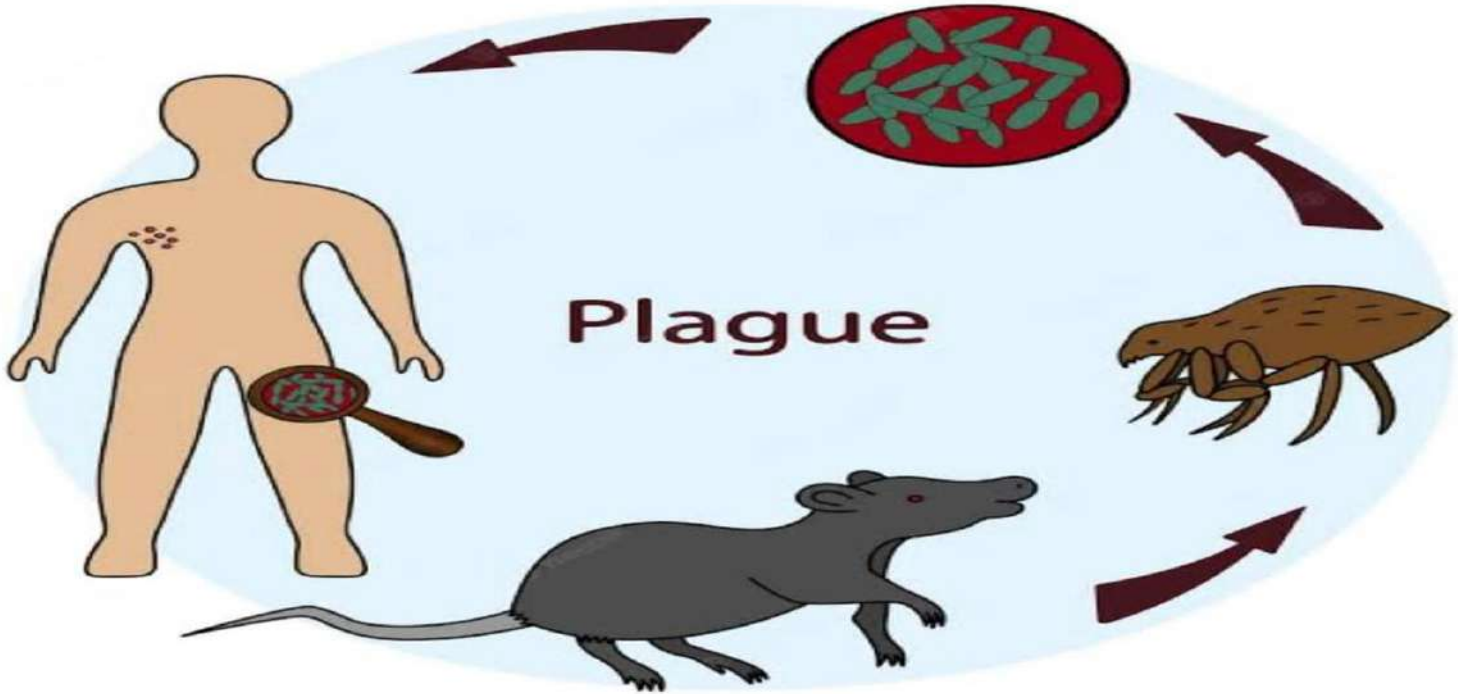
Ferments glucose and mannite with the production of acid only, indole negative and catalase-positive.

Virulence factors:

It is one of the most virulent bacteria known (1 to 10 organisms are capable of causing disease).

1. Lipopolysaccharide: which have endotoxic activity.
2. The capsular protein (Fraction 1) confers anti-phagocytic properties. — Ag for protection
3. V&W antigens: have anti–phagocytic activity and prevent intracellular killing.
4. Coagulase: produced only at 28°C but not at 37°C. — Not active in human because of the heat
5. Yops (Yersinia outer proteins) inhibit phagocytosis and cytokine production. — Inhibit immune system
6. Several exotoxins. → much more

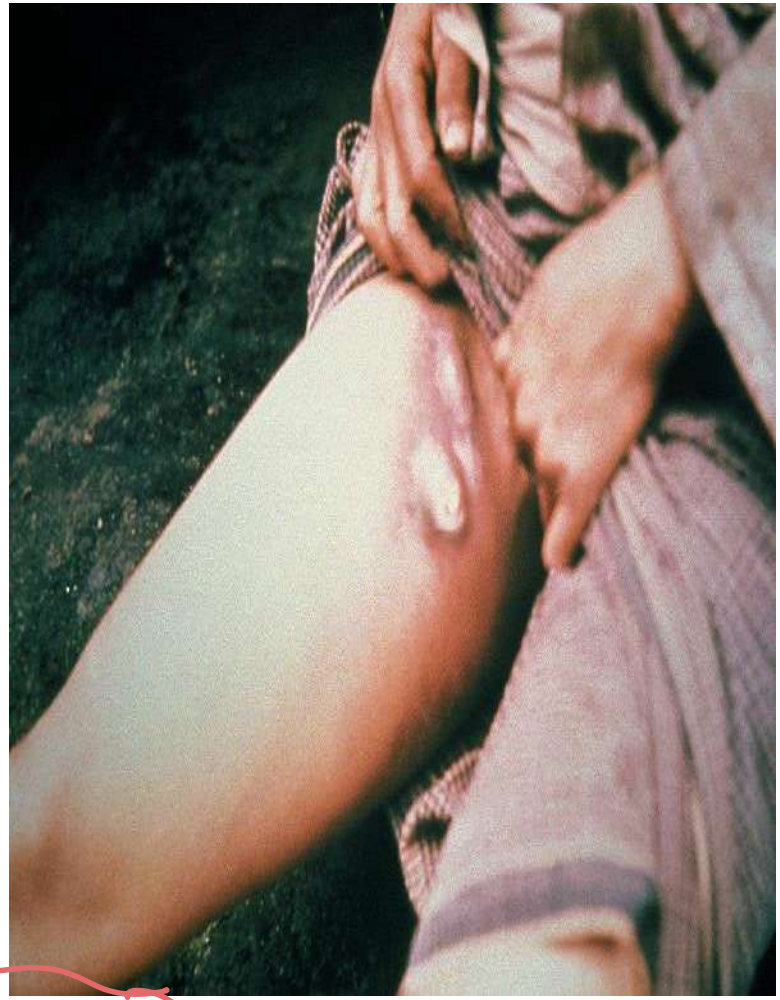
- The reservoir of infection is: the wild **rodents**.
- The enzootic (sylvatic) cycle consists of transmission among rodents by fleas.
- Humans are accidental hosts, the disease is transmitted to man via bite of the **rat-flea Xenopsylla cheopis**.



Pathogenesis & Clinical findings

- From the site of inoculation, *Y. pestis* is carried in lymphatic to nearby lymph glands, usually those in the axilla, groin or neck producing an intense haemorrhagic inflammatory response and become swollen and tender that is called **a bubo** (**Bubonic plague**). These buboes are an early characteristic finding.

usually under the clothes



Can be cured in this stage

2nd stage

- The organisms may enter the blood and disseminate to form abscesses in many organs (**Septicemic plague**). The endotoxin-related symptoms, including DIC, hemorrhages, and gangrene with blackened tissue probably were the genesis of the term **black death**.

ischemia → necrosis → gangrene

- It spreads to the various organs of the body including the lungs to produce (**pneumonic plague**). Secondary pneumonic plague from blood
- **Primary pneumonic plague** results from **inhalation** of infective droplet.
- Pneumonic plague is highly infectious. Before reaching blood
- Both septic shock and pneumonia are the main life-threatening subsequent events. Life threatening

بشكل عام اول ما تدخل البكتيريا على الجسم بتروح على اقرب lymph node عليها ولانها بتنتقل عن طريق fleas فهي عالاغلب هتكون القرصة تحت الاواعي فهتكون اقرب ل axilla/ neck / groin ومن بعدها هيصير في inflammation فيهم يعمل swelling وتصير تشبه الbuboes

من بعدها ممكن ينتقل على الدم ولانه الها endotoxins و exotoxins كثير رح تعمل septicemia وتؤدي الي gangrene و ممكن تنتقل الى الرئة بعدها وتعمل secondary pneumonia

او تبدأ بالرئة وتكون primary pneumonia

Diagnosis:

Specimens:

- Aspirate of enlarged lymph nodes in bubonic plague.
- Blood for blood culture in septicemic plague.
- Sputum in pneumonic plague.

Appear as diplococci

1) Smears: are examined after staining with Leishman's stain to demonstrate bipolarity.

2) Culture: Specimens are cultured on blood agar plates and incubated at 27-30°C for 24hs.

Cultures are identified by colonial morphology, biochemical reactions and animal inoculation. → In rats → high level labs

N.B. All cultures are highly infectious and must be handled with extreme caution.

3) Immunofluorescence.

4) Serology: a rising antibody titer is diagnostic.

معظم هاي الtests بتكون عشان نعمل diagnosis للحالات الاولى عشان نتاكد انها positive ونمنع انتشارها بس بشكل بنعمل serological tests

Immunofluorecence
بكون عن طريق ab بصبغة fluorescent عشان نقدر نعمللها detection بالمايكرو سكوب

Control

1- Rat and flea control

2- All patients with suspected plague (especially pneumonic plague) should be strictly isolated (quarantine). Special requirements away from community

3- Contacts of patients should receive tetracycline as chemoprophylaxis.

4- Vaccine: there are two kinds of vaccine:

a) Formalin killed vaccine which is available for travellers to hyperendemic areas (Southeast Asia) and for high risk people.

b) Live attenuated vaccine which is recently reported for more protection.

Treatment

The treatment of choice is a combination of streptomycin and a tetracycline, although streptomycin alone can be used.

هسا هون رح احط رسمة سكيتشي للي عاوز
هو شارح فصيليتين من الyersinia بس انا رح اكتب الي داخل
معنا

capsulated

Red colour theme → gram -

1. Rodents are the main Reservoir
2. transmitted to humans by fleas
3. Causes Bubonic plague
4. has a vaccine { Killed }
5. Streptomycin
6. tetracyclin

مش موضح كلشي فيها لانه ركز على الفصيلة
الثانية بس عشان الي بحب ياخذها

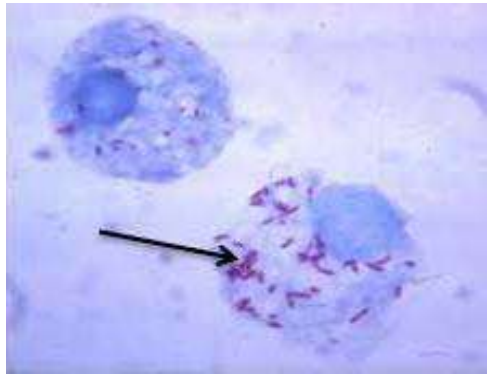
Rickettsia

ح

Important Properties

Micro organism that has the characteristics of both bacteria and viruses

- Rickettsia are very short rods that are barely visible in the light microscope.
- Structurally, their cell wall resembles that of gram –ve rods (peptidoglycan-containing muramic acid).
- They stain poorly with the standard Gram stain, however, can be stained with Giemsa , acridine orange or Macchiavello stain.



- Rickettsiae are **obligate intracellular organisms,** therefore, rickettsiae must be grown in cell culture, embryonated eggs, or experimental animals.
- Rickettsiae divide by binary fission within the host cell.

-

Rickettsial groups

Group	Organism	Disease	Reservoir	Vector
Typhus	*R.Prowazekii*	Epidemic typhus	Man	Body louse
	R.typhi	Endemic typhus	Rodents	Rat flea
	R.Tsutsugamushi	Scrub typhus	Rodents	Mite
Spotted fever	*R. Rickettsii*	Rocky mountain Spotted fever	Dog & Rodents	Tick
	R.Conorii	Boutoneous fever	Rodents	Tick
	R. akari	Rickettsial pox	Mice	Mite
Q Fever	*Coxiella Burnetii*	Q Fever	cattle, sheep, goats	-------

Rickettsial Antigens:

There are three major types of Rickettsial antigens :

a- Antigen shared with certain proteus strains: Same Ag as the one on proteus

Rickettsia share antigens with OX19, OX2 and OXK strains of proteus spp.

This sharing is the basis of Weil - Felix reaction.

b- Group specific antigen: Same For the strains of the same group

A common antigen occurring in each group.

c- Strain - specific antigen:

It is associated with the bodies of rickettsia and specific for each strain.

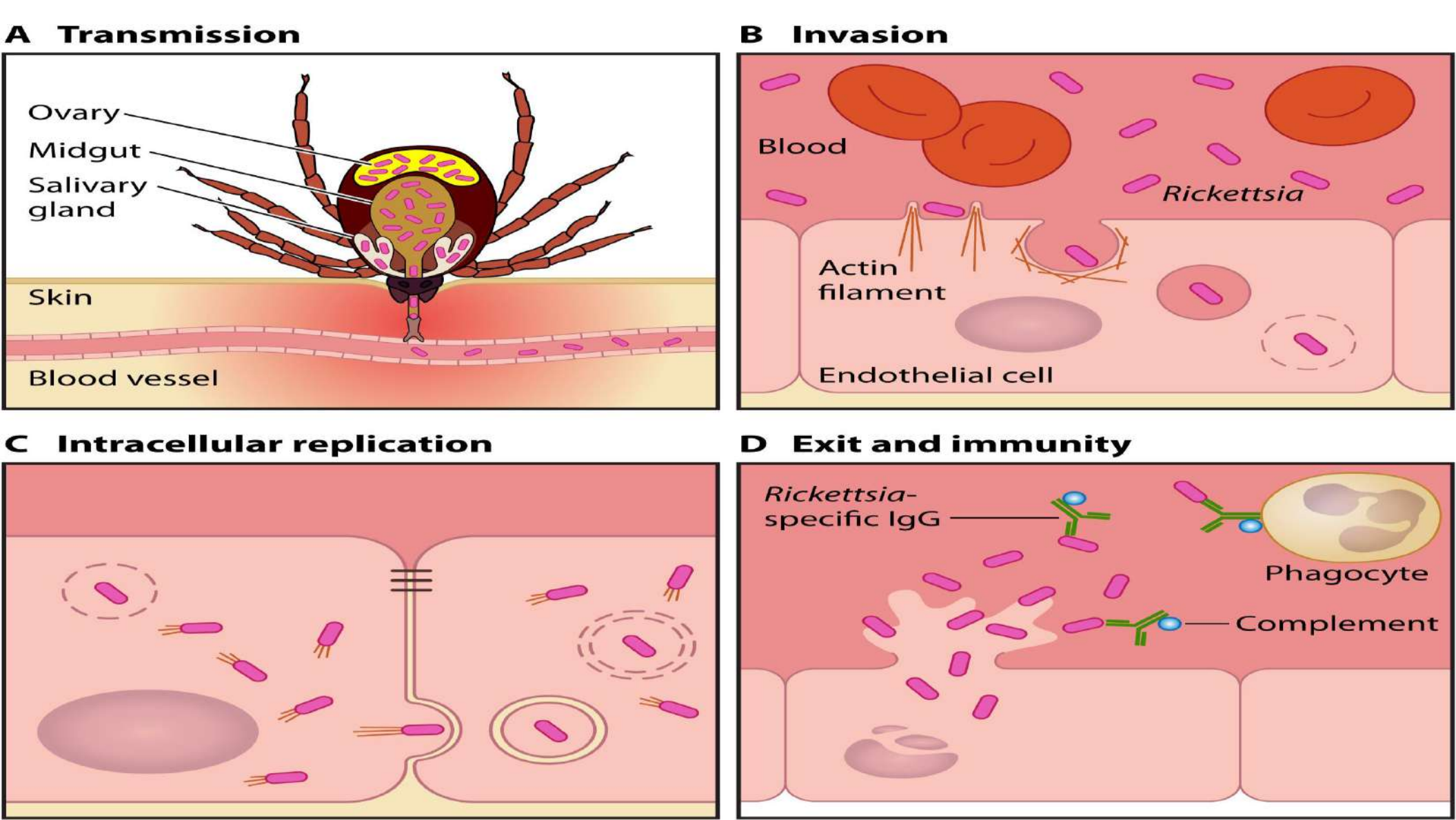
Transmission

We have 4 rules

- All rickettsiae are transmitted to humans by the **bite of the arthropod** such as ticks, lice, fleas, and mites **EXCEPT *C. burnetii***, the cause of Q fever, which is transmitted by aerosol inhalation. 1st rule
- Virtually all rickettsial diseases are zoonoses (i.e., they have an animal reservoir), **EXCEPT *R. prowazekii,*** the cause of epidemic typhus, which occurs only in humans. It occurs only in humans because the causative organism, is transmitted by the **human** body louse. 2nd rule

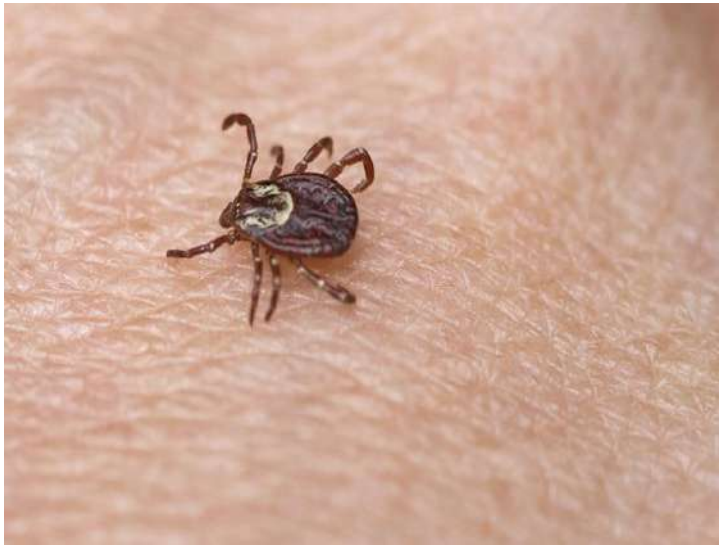
Pathogenesis 3rd rule

- Rickettsiae, (**except** for *C. burnetii),* circulate in the blood stream during the first week. All cause vasculitis except. C burnetii
- They invade and multiply in endothelial cells of small blood vessels→ destruction of these cells→ local and systemic vasculitis→ thrombosis of the vessel→ rupture and necrosis.
- Vascular lesions are prominent in the skin, but can occurs in many organs specially brain and heart.
- DIC and vascular occlusion may develop.


A Transmission
Ovary
Midgut
Salivary gland
Skin
Blood vessel
B Invasion
Blood
Rickettsia
Actin filament
Endothelial cell
C Intracellular replication
D Exit and immunity
Rickettsia-specific IgG
Phagocyte
Complement

Rocky Mountain Spotted Fever → Disease

تعليم الاحرف من الدكتورة
عشان التسهيل علينا



- **Caused by *R. Rickettsi***
- The **tick** is an important reservoir as well as the vector of *R. rickettsi,* the organism is passed by the transovarian route from tick to tick, and a lifetime infection results. Complete life cycle between ticks
- Certain animals, such as dogs and rodents, are also reservoirs of the organism.
- Humans are accidental hosts and are not required for the perpetuation of the organism in nature; there is **No person-to-person** transmission.
- The name is derived from the region in which the disease was first found.

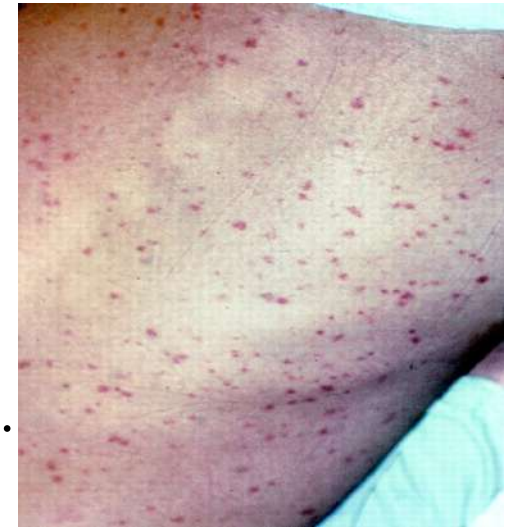
Clinical findings:

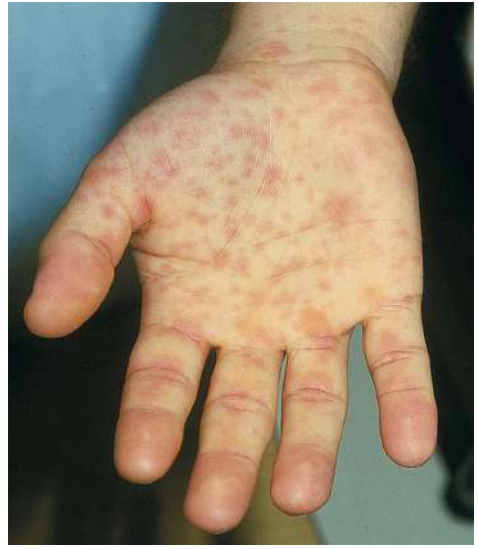
- Acute onset of nonspecific symptoms (FAHM).
- The typical rash appears 2 to 6 days later:
  - Begins with macules that frequently progress to petechiae.
  - Appears first on the extremities, moves centripetally, and involves the palms and soles.

Very imp for differentiating between different strains

- Enlargement of the spleen and liver.
- CNS manifestations like headache, delirium and coma.
- DIC and circulatory collapse may ensue in severe cases.

Difference between the rash and petechia if you press on a rash spot it will disappear but comes back instantly/ petechia will not disappear

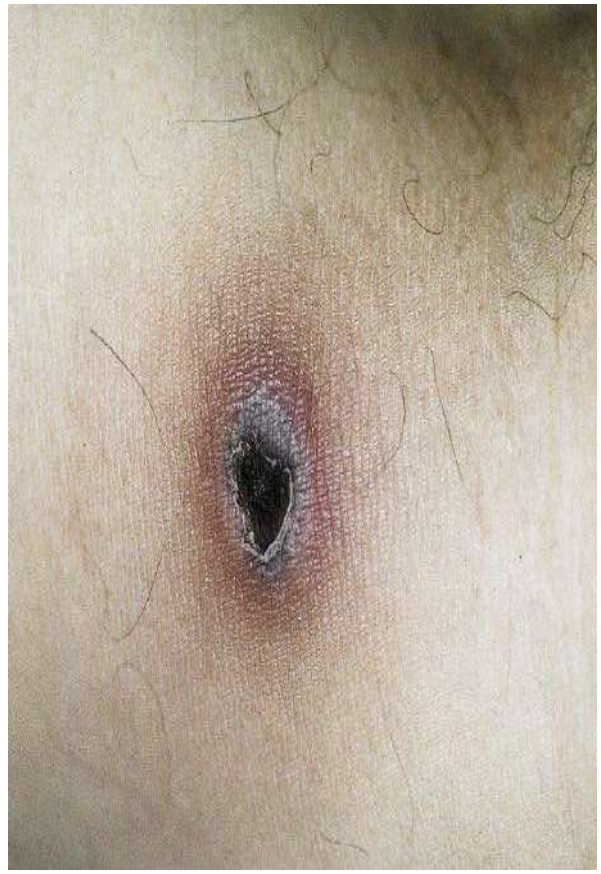




Eschar-Associated Rickettsial Diseases

Eschar is a dark scab from dead cells

- Rickettsial eschars are necrotic lesions that occur at the site of tick or mite bites.
- Eschars are hallmarks of less severe spotted fever diseases, *R. conorii*, and *R. akari*.
- Eschars generally do not occur with Rocky Mountain spotted fever (RMSF).
- The presence of eschars can help differentiate less severe spotted fever rickettsioses from RMSF.



Epidemic Typhus

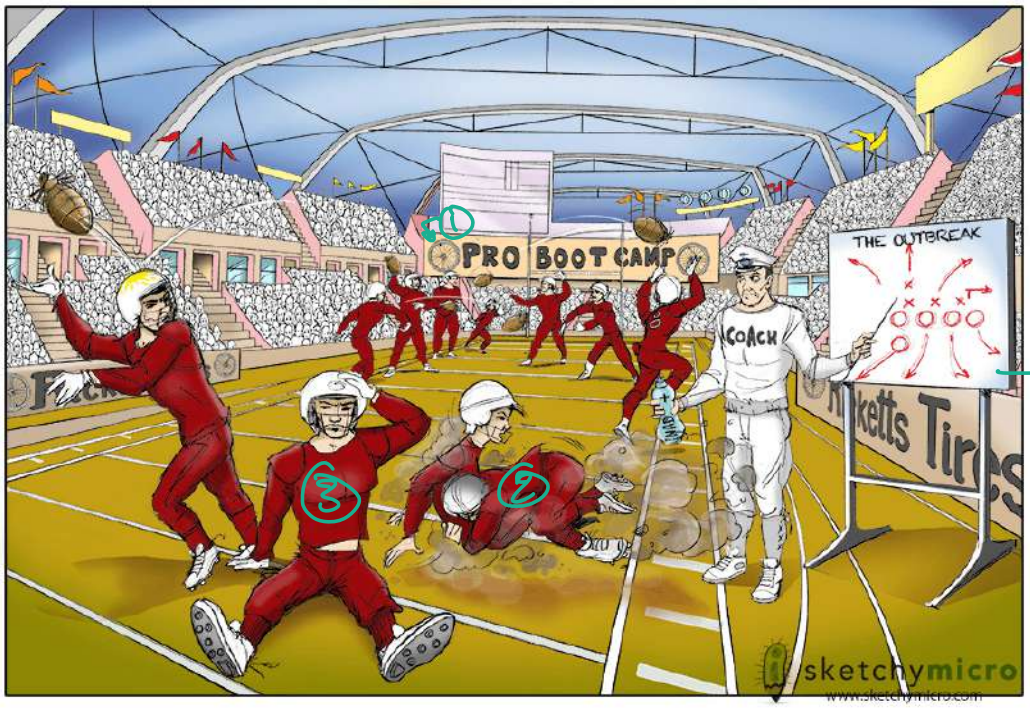
- **Caused by *R. Prowazekii.***
- Epidemic typhus is transmitted **from person to person** by the **human body louse,** *Pediculus*.
- The infected louse dies after a few weeks, and there is no louse-to-louse transmission; therefore, human infection is an obligatory stage in the cycle.
- It occurs only in humans with **No animal reservoirs**.

If the louse doesn't effect the human and dies there will be no disease in any other living organism

Clinical findings:

- Nearly similar to those of Rocky mountain Spotted fever except in that skin rash begins on the trunk and spreads peripherally but **spares** the face, palms, and soles.
- Diseases are usually severe, with high mortality rate if untreated.
- A recurrent form of epidemic typhus is called **Brill-Zinsser disease** which is similar to epidemic typhus but less severe, of shorter duration, and rarely fatal.
- Recurrences can appear as long as 50 years later and can be precipitated by another intercurrent disease.

Incomplete eradication → causes Recurrence with immune deficiency → called brill zinsser disease



* the game plan → start from the middle and spread wide → {the rash}

* rash is the red suit → spares the face / feet / hands

* Tetracyclin is the Drug of choice

* the ball shape → Body louse

(2) Causes pneumonia and muscle pain {the dirt and tackling}

(3) headache / encephelopathy

Endemic Typhus

0

- **Caused by *Rickettsia typhi.***
- The clinical picture of endemic typhus has many features in common with that of epidemic typhus, but the disease is milder and is rarely fatal except in elderly patients.

ImmunoCompromised

Q Fever

- **Caused by *Coxiella burnetii.***
- The "Q" comes from "query" fever, the name of the disease until its true cause was discovered in the 1930s.
- Q fever is a zoonosis. The important reservoirs and sources of infections are cattle, sheep, and goats.
- *C. burnetii* infections are mainly transmitted by: No vector

  1. Airborne: via inhalation of animal aerosols (especially from urine, feces, placental tissue, and amniotic fluid of the animals).

  2. Ingestion: of milk from infected animals.
- Q fever is usually an occupational hazard. People at high risk include farmers, abattoir workers and veterinarians as well as laboratory personnel.

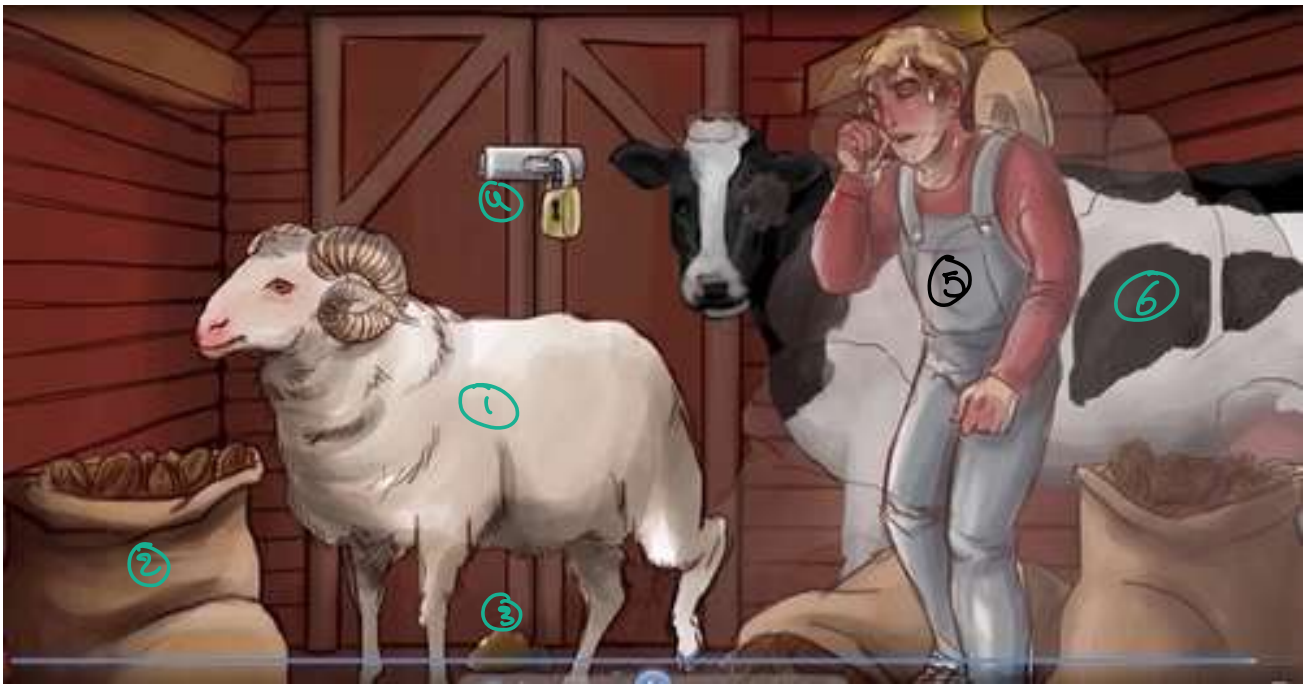
Clinical findings

No vasculitis → different pathogenesis

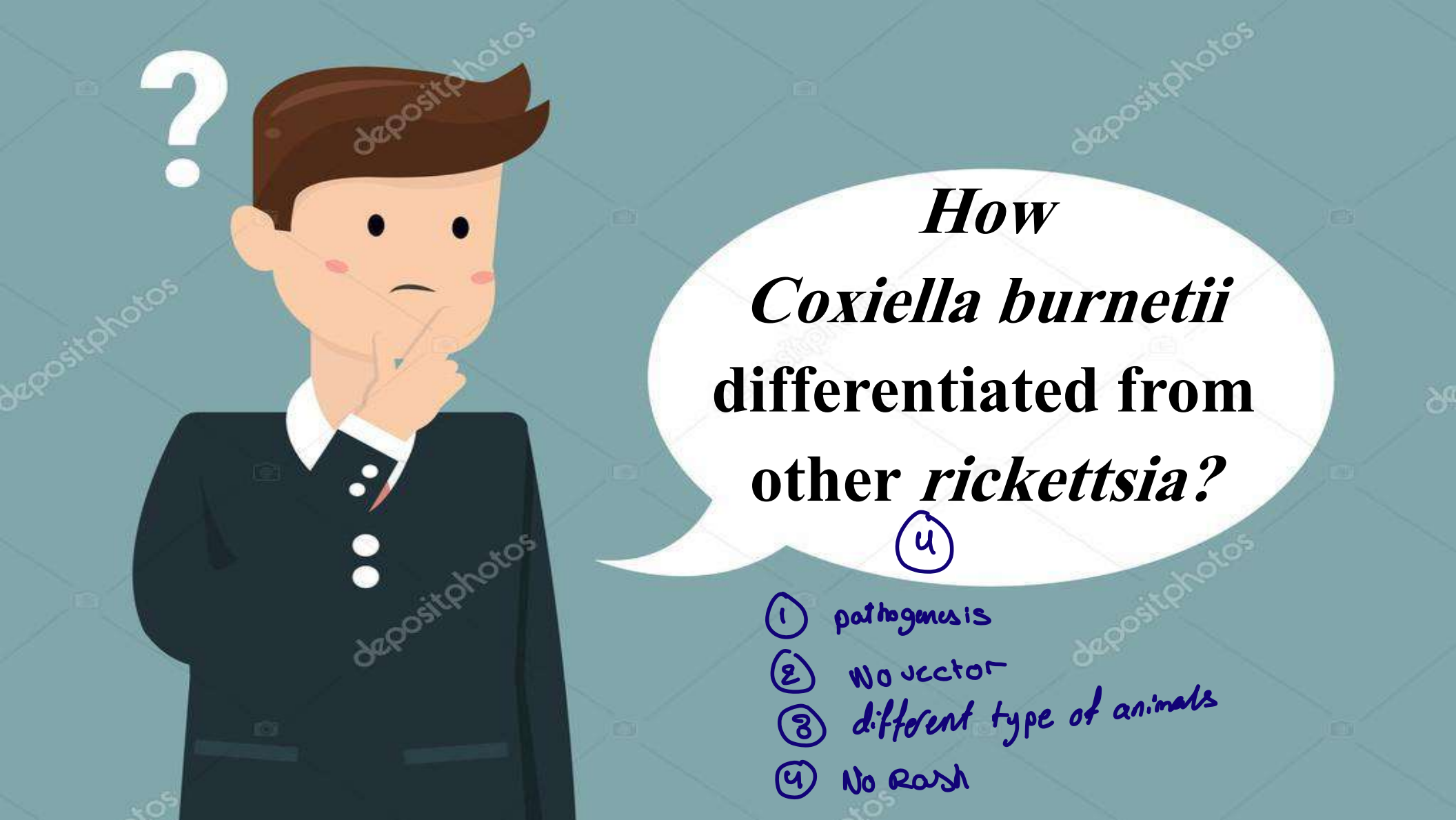
- Unlike other rickettsial diseases, the main organ involved in Q fever is the lungs and liver.
- The alveolar macrophages are the primary cells infected via the respiratory route. Kupffer cells in the liver are also susceptible and may be infected via the blood stream or from the digestive route.
- In the majority of cases, infection remains **asymptomatic**.
- **Acute Q fever:**
  - It begins suddenly with FAHM
  - Atypical pneumonia.

  → atypical→caused by an organism that is hard to find → intracellular →hard to detects
  - Hepatitis (combination of pneumonia and hepatitis should suggest Q fever).
  - Unlike in the other rickettsial diseases, **No rash.** 4th rule
- **Chronic Q fever** rarely, characterized by life-threatening endocarditis.

P



1. white colour with no rash
2. spore forming
3. transmitted by feces
4. locked door → obligate intracellular
5. fever / headache / pneumonia
6. Hepatitis


How
Coxiella burnetii
differentiated from
other rickettsia?
4
1 pathogenesis
2 No vector
3 different type of animals
4 No Rash

Laboratory Diagnosis

A) During 1st week:

1- Isolation of the organism:

Isolation is carried on by inoculating the patient's whole blood sample into either yolk sac of embryonated egg or Intraperitoneal in mice or guinea pig as ricketssia are obligate intracellular parasites. Not practical → hard to find

2- Immunofluorescence to detect ricketssia in tissues or petechial rash.

3- PCR.

N.B. Isolation of rickettsiae is of only limited usefulness in diagnosis as it is technically difficult and hazardous (needs specialized laboratories).

B) From 2nd week (Serology):

- It is the most applicable in diagnosis.
- A fourfold or greater rise in titer between the acute and convalescent serum samples (2 weeks) is the most common way of the laboratory diagnosis.
- If the clinical picture is typical, a single acute-phase titer of 1:128 or greater is accepted as presumptive evidence.
- Of the serologic tests, the indirect immunofluorescence and ELISA tests are most often used.
- **Weil-Felix Reaction: (non specific)**

Test that finds the shared ab (mostly used) because it's cheap

It is a tube agglutination test based on the cross - reactions between antibodies produced in acute R. infections and the OX19, OX2 and OXK strains of proteus.

Treatment

- The treatment of choice for all rickettsial diseases is tetracycline, with chloramphenicol as the second choice.
- The diagnosis must be made on clinical grounds and therapy started promptly, because the laboratory diagnosis is delayed until a rise in antibody titer can be observed.

Prevention

- Prevention of Q fever based on Proper pasteurization of milk and vaccination for occupationally exposed (**killed vaccine**). Q fever has a vaccine
- Prevention of typhus is based on personal hygiene and "delousing" with insecticide.
- Prevention of Rocky Mountain spotted fever based on personal prophylaxis in the form of protective clothing, tick repellents; and frequent removal of attached ticks (the tick must be attached for several hours to transmit the disease). Ticks must remain attached to the body for 20 hrs for an infection to happen

Thank you