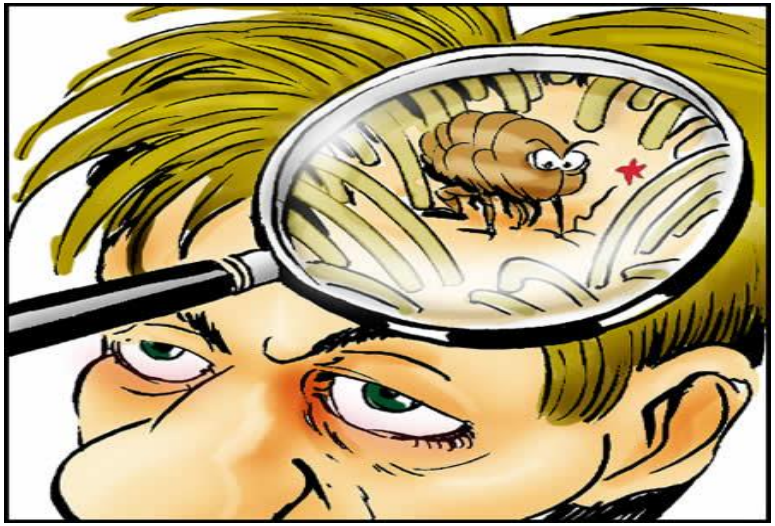
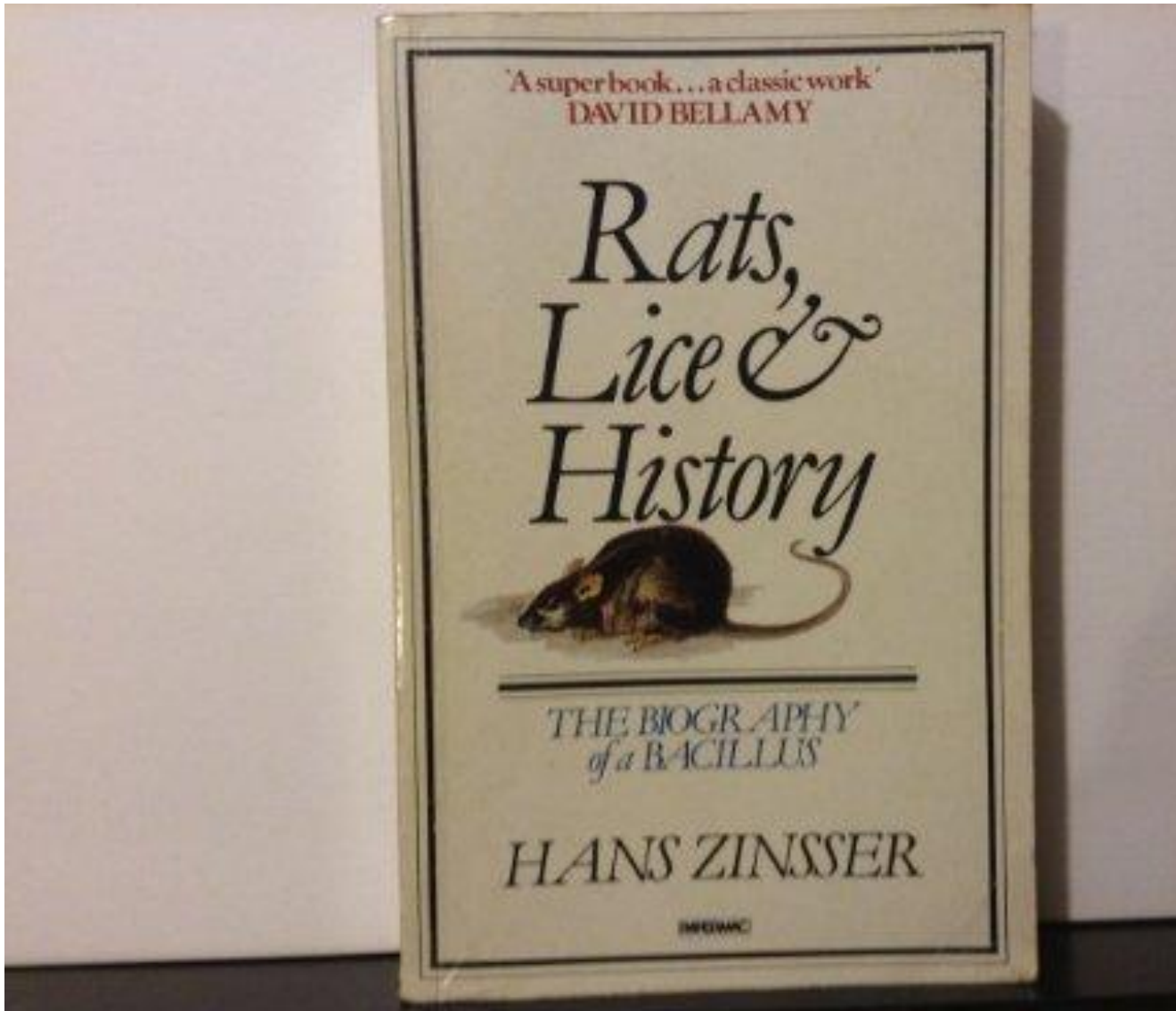
RICKETTSIACEAE



- In 1935, Harvard Medical School physician and researcher



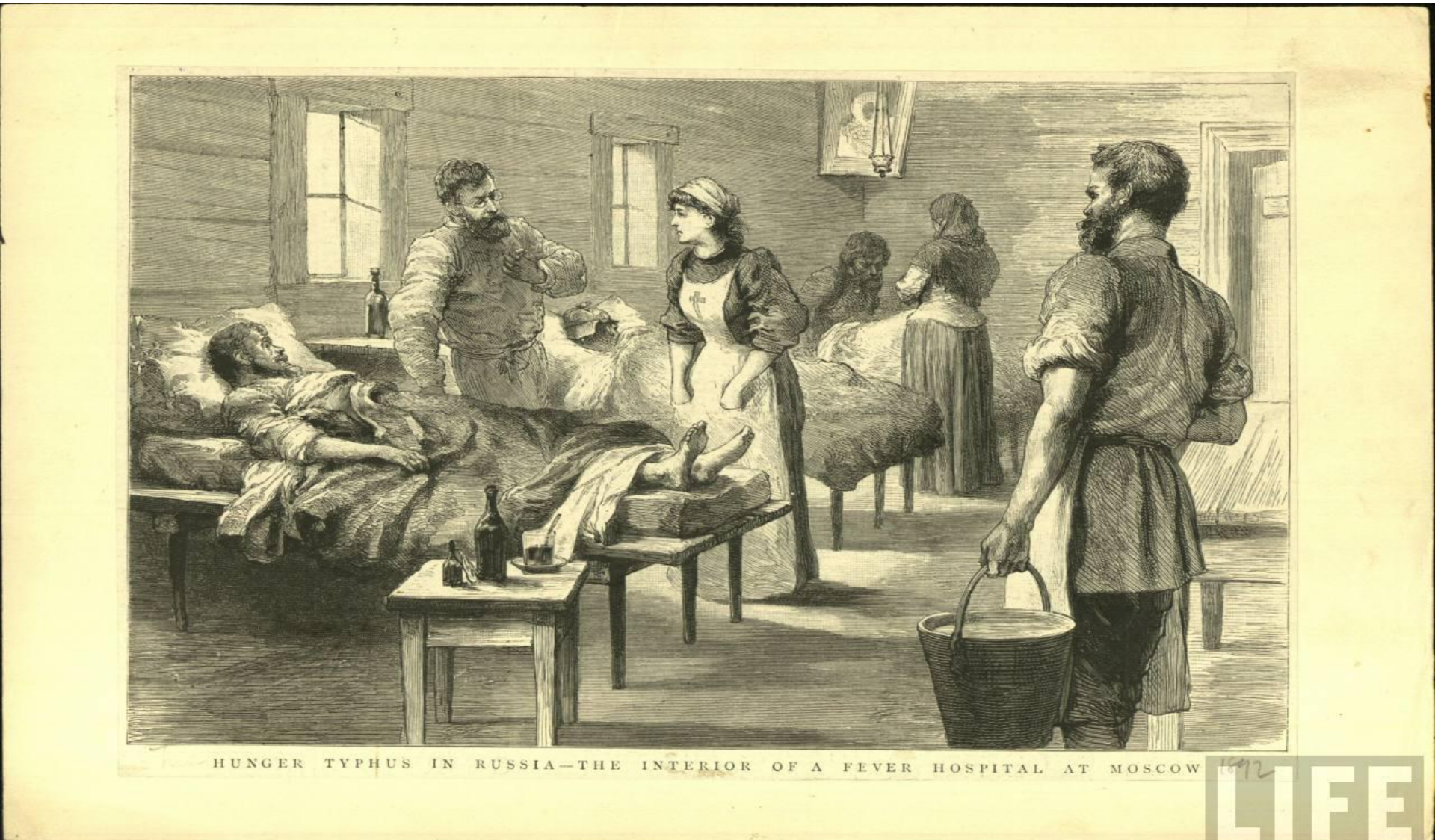
Zinsser, Lice And History

Charles Nicolle (left), to whom Hans Zinsser (right) dedicated *Rats, Lice and History*

History

- 17th-19th century
  - Epidemics in Europe as a result of war, disaster, or in prisoners
- 1909: Transmission by lice
- 1917-1925: Russia
  - Estimated 25 million cases
- End of WWII
  - DDT used for control
  - Vaccine developed

Historical Photograph on Typhus



HUNGER TYPHUS IN RUSSIA—THE INTERIOR OF A FEVER HOSPITAL AT MOSCOW

Napolean's retreat from Moscow

- Either socialism will defeat the louse or the louse will defeat socialism

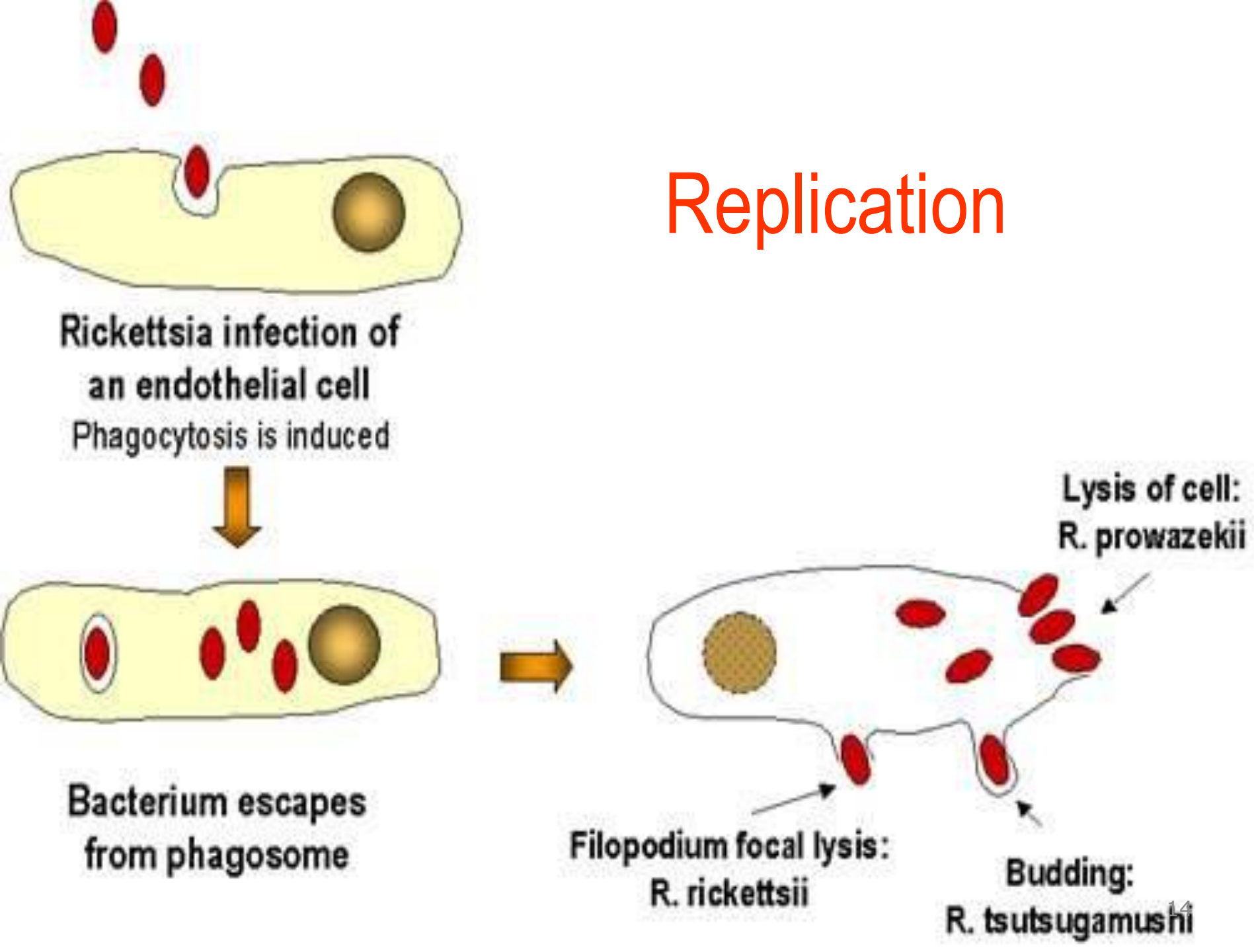
General Characteristics

- Small obligate intracellular coccobacilli
- Gram negative (poorly), better stained with Giemsa (Blue), Gimenez & Macchiavello
- Have cell wall, bigger than virus but smaller than bacteria
- Have DNA and RNA
- Hematophagus arthropod vectors (*e.g.*, ticks, mites, lice or fleas)
- Sensitive to antibiotics
- Multiply by binary fission
- Large enough to be seen under light microscope

Family Rickettsiaceae

GENUS	SPECIES
RICKETTSIA	R.Prowazekii
	R. Typhi
	R. Rickettsii
	R. Conorii
	R.Australis
	R. Siberica
	R.Akari
ORIENTIA	O. tsutsugamushi

Replication



Cultivation

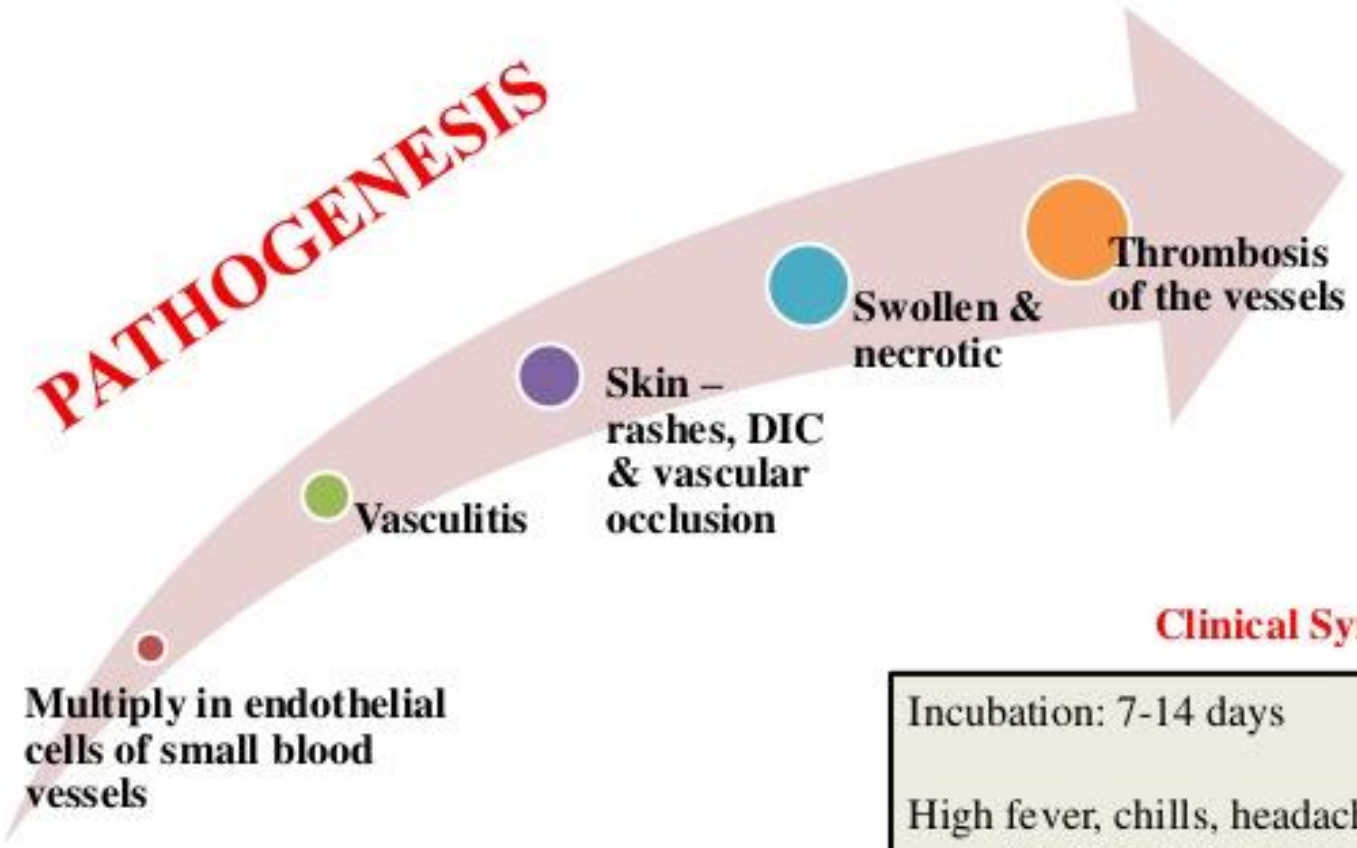
- Grows in the cell cytoplasm
- Grows at 33 to 35^0 c
- Grows in yolk sac of developing chick embryo
- Grows in mouse fibroblasts, Hela,Hep2, Detroit 6
- Guinea pig, Mice are lab animals

Susceptibility

- Inactivated by hypochlorite, 1% Lysol, 2% formaldehyde, 5%H_2O_2, 70% ethanol.
- Easily inactivated by heat
- Survive in dried feces of infected lice for months

Antigenic structure

- Group specific soluble antigens
- Alkali stable polysaccharide- Sharing of antigens between Rickettsia and Proteus basis of Weil – Felix Heterophile agglutination Test.
- Used Proteus strains 0X 19, OX2 OXK

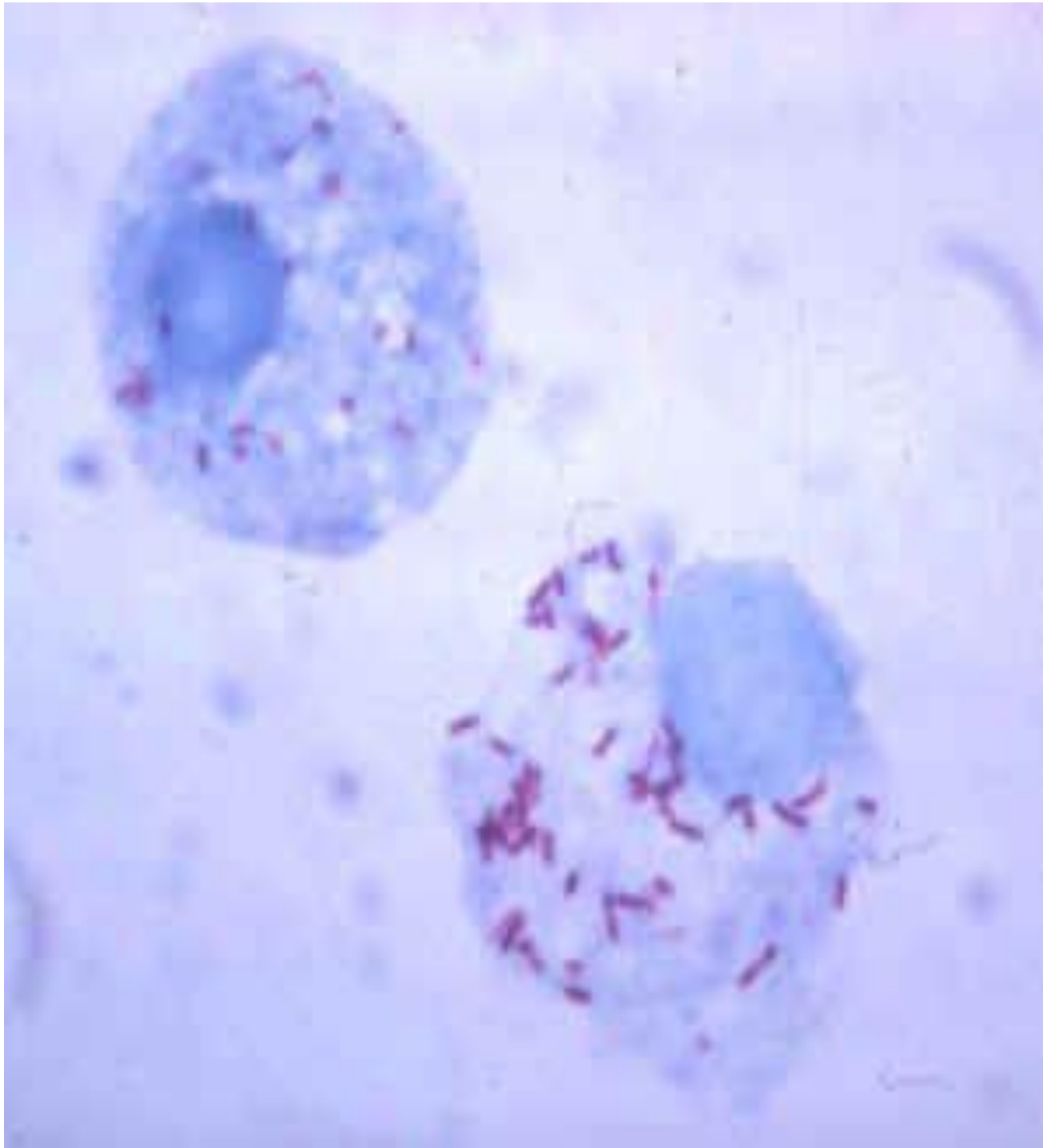


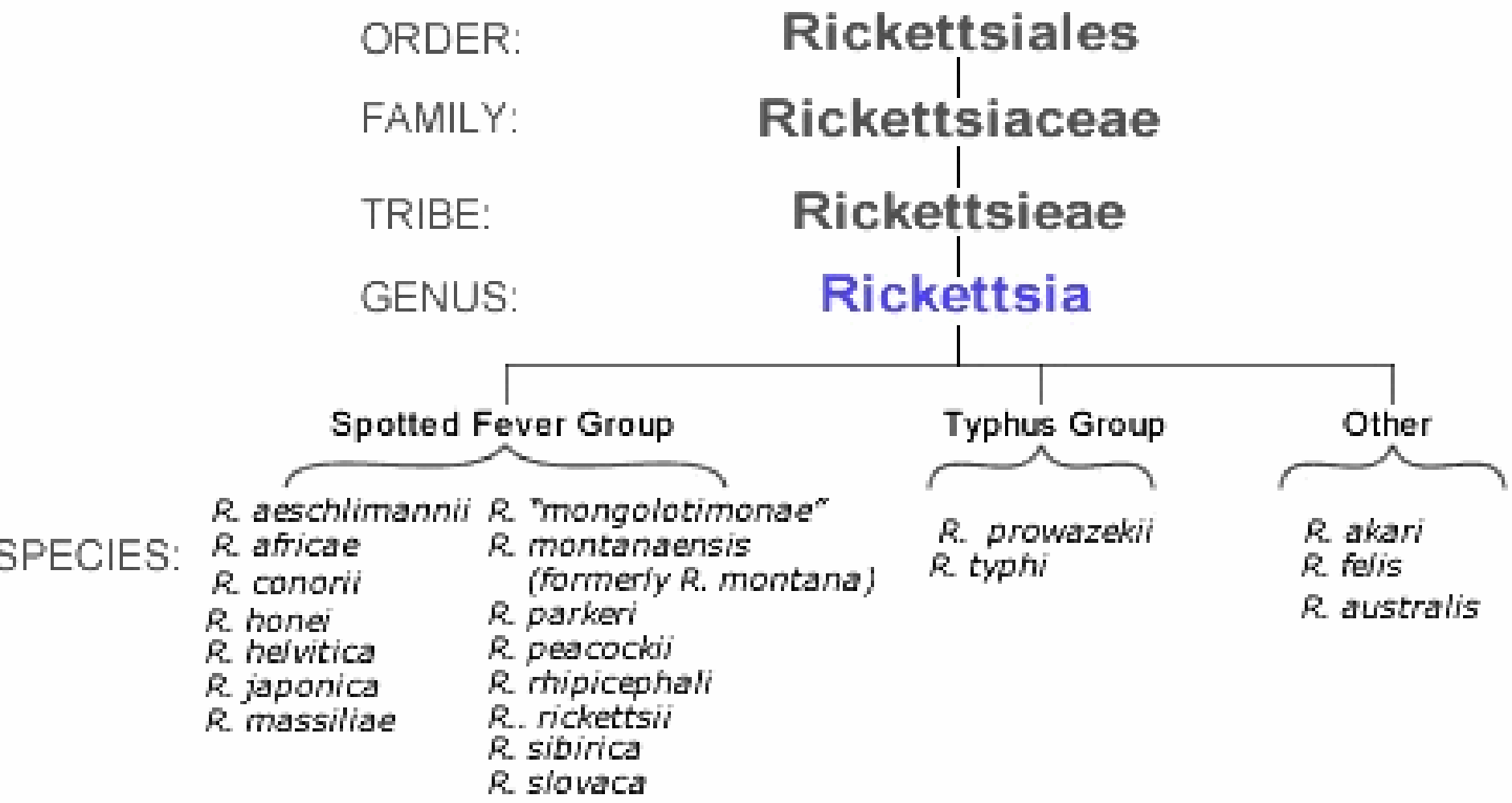
Clinical Symptoms

Incubation: 7-14 days

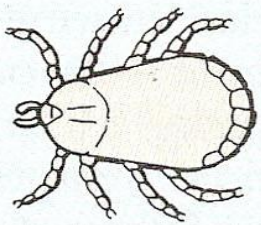
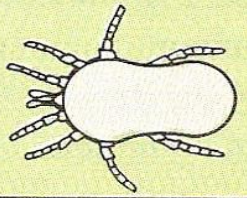
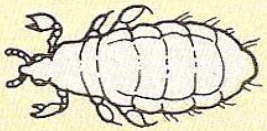
High fever, chills, headache, cough, myalgia
May lead to coma

Macular eruption
5-6 days after onset
Initially on upper trunk, spreads to entire body
Except face, palms and soles of feet




ORDER:
Rickettsiales
FAMILY:
Rickettsiaceae
TRIBE:
Rickettsieae
GENUS:
Rickettsia
Spotted Fever Group
Typhus Group
Other
SPECIES:
R. aeschlimannii
R. africae
R. conorii
R. honei
R. helvitica
R. japonica
R. massiliae
R. "mongolotimonae"
R. montanaensis
(formerly R. montana)
R. parkeri
R. peacockii
R. rhipicephali
R.. rickettsii
R. sibirica
R. slovaca
R. prowazekii
R. typhi
R. akari
R. felis
R. australis

DISEASES	**RICKETTSIAL AGENT**	**INSECT VECTOR**	**MAMMALIAN RESERVOIR**
TYPHUS GROUP			
a) Epidemic typhus	R. *prowazekii*	Louse	Human
b) Murine typhus (Endemic typhus)	R. *typhi*	Flea	Rodents
c) Scrub typhus)	R. *tsutsugamushi*	Mite	Rodents

Disease	Organism	Vector	Reservoir
Rocky Mountain spotted fever	*R. rickettsii*	Tick-borne 	Ticks, wild rodents
Ehrlichiosis	*E. chaffeensis*		Ticks
Rickettsialpox	*R. akari*	Mite-borne 	Mites, wild rodents
Scrub typhus	*R. tsutsugamushi*		Mites (chiggers), wild rodents
Epidemic typhus	*R. prowazekii*	Louse-borne 	Humans, squirrel fleas, flying squirrels
Trench fever	*R. quintana*		Humans
Murine typhus	*R. typhi*	Flea-borne 	Wild rodents
Q fever	*C. burnetii*	None*	Cattle, sheep, goats, cats

*Tick vectors may be responsible for animal-to-animal transmission.

FIGURE 38-3 Epidemiology of common Rickettsiaceae infections.

Typhus Fever

Typhus Fever group

1. Epidemic Typhus

2. Recrudescent typhus (Brill Zinsser’ disease)

3. Endemic typhus

Rickettsia Prowazekii
(Von Prowazekii)

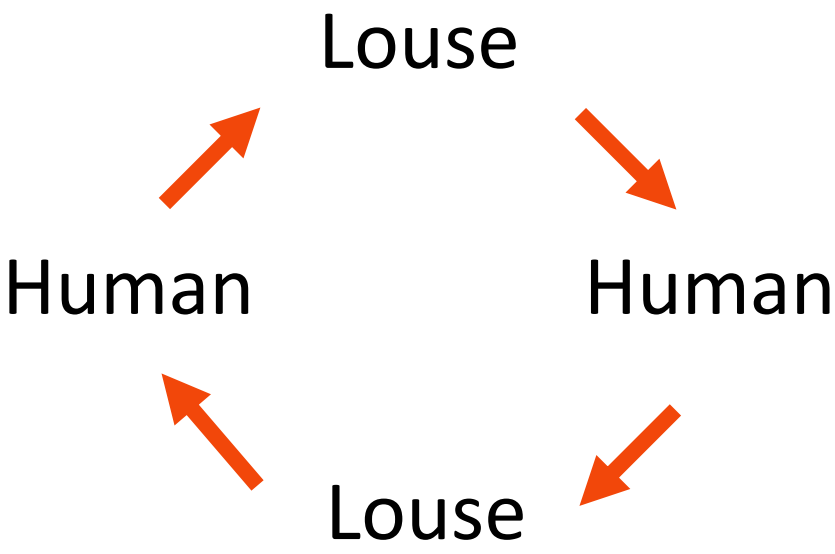
- Humans - natural vertebrate hosts
- Vector - Human body louse,(Pediculus humans corporis)

- Lice get infected from patients.
- Life cycle –multiplies in gut - 1 week

- Person – person contact.
- Lice bite causes itching and scratching
- May enter through respiratory tract / Conjunctiva

- Incubation 5- 15 days

R. Prowazekii



Abandons host with temp>40° or cooling carcass

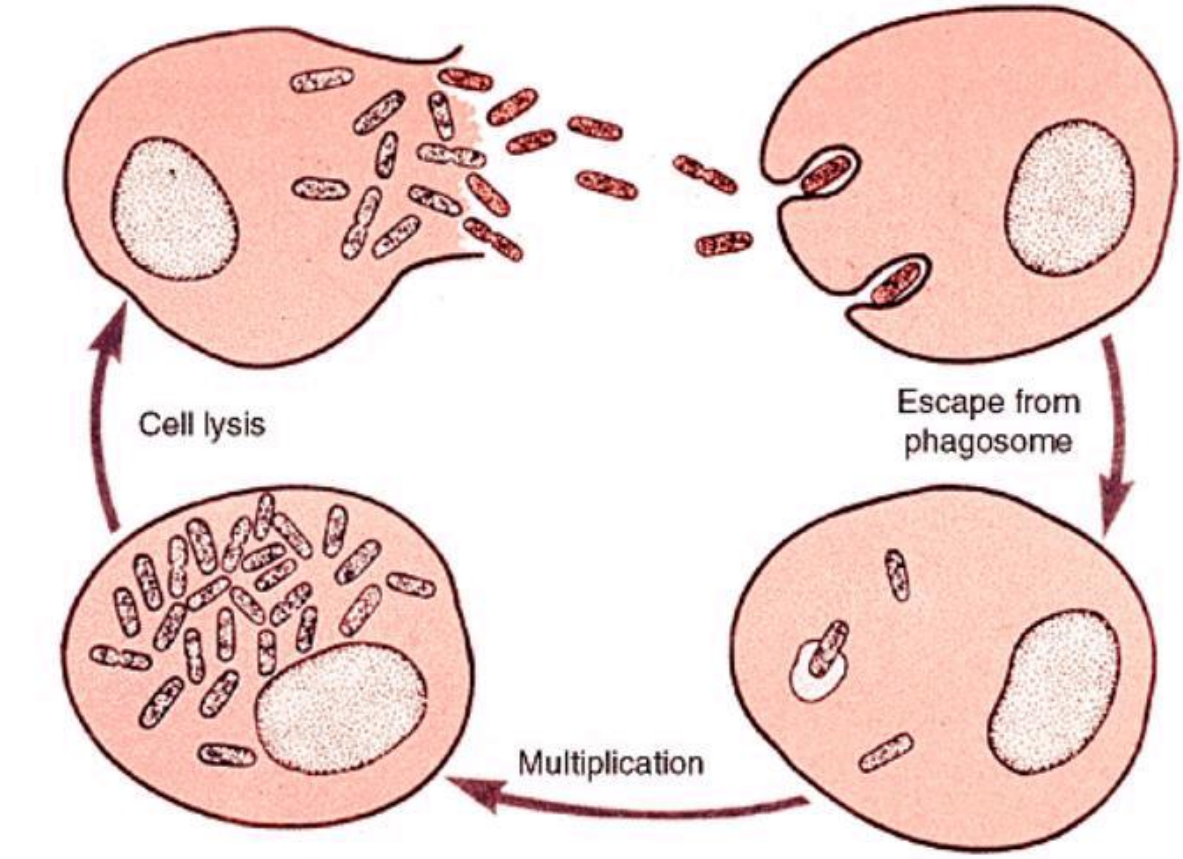
Epidemic typhus

Epidemic Typhus

- louse borne typhus – Pediculus humanus corporis, capitis not pubic louse
- body louse -dies of its infection with Rickettsia prowazekii in three weeks
- This is a serious disease consisting of fever, severe headache, myalgia, and central rash
- Untreated, the mortality ranges from 20-40%
- Major killer in concentration camps of WW II

May act as non human reservoir R prowazekii

Life Cycle of Rickettsia



Life Cycle of *Rickettsiae*

PATHOLOGY

Multiply in endothelial cells of small blood vessels

↓

Vasculitis

↓

(skin – rashes; other organs – DIC & vascular occlusion)

↓

Swollen & necrotic

↓

Thrombosis of the vessels

Clinical Symptoms

- Incubation: 7-14 days
- High fever, chills, headache, cough, severe myalgia
  - May lead to coma
- Macular eruption
  - 5-6 days after onset
  - Initially on upper trunk, spreads to entire body
    - Except face, palms and soles of feet

Clinical Features

- Fever, chills
- Rash on 4 th day; Spread from Trunk to Limbs not face palms, sole.
- In 2 nd week may into stuporous,delirious state
  May reach 40 % fatality
- Bacteria remain latent in Lymphoid tissue, cloudy state. (Typhus). Patchy pneumonia and gangrene.

Brill-Zinsser Disease

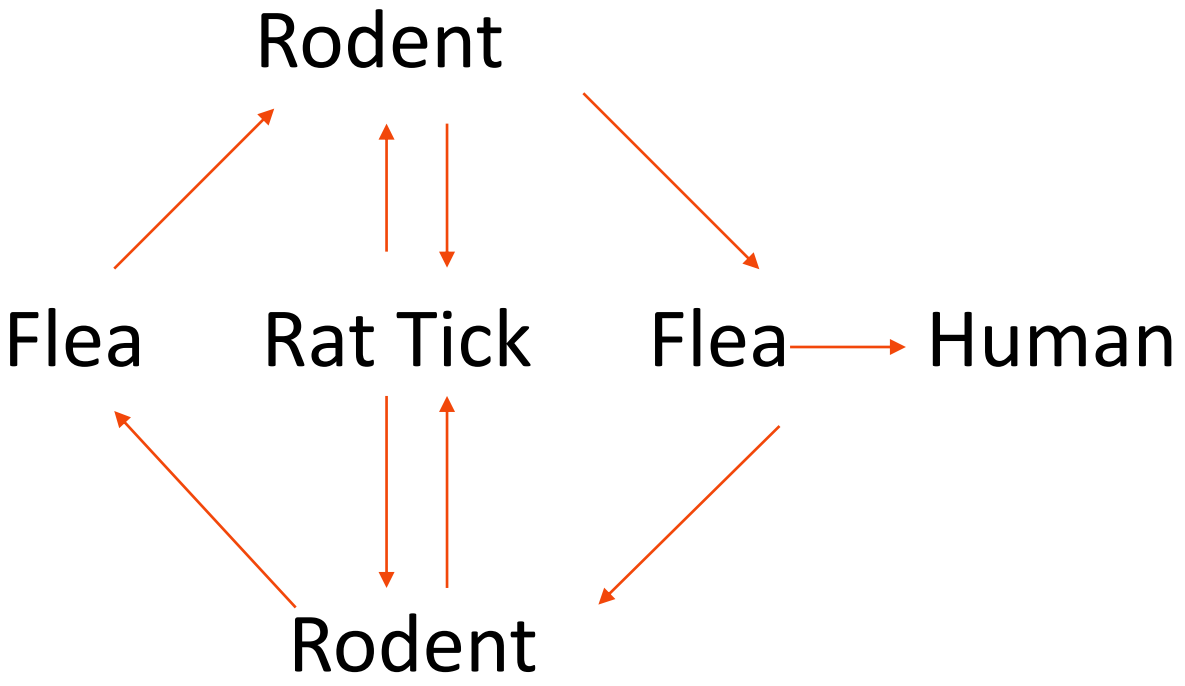
- Occurs years after primary attack
  - Person previously affected or lived in endemic area
  - Viable retained organisms in lymphoid tissue or organs
  - Milder symptoms
    - Febrile phase 7-10 days
  - Rash often absent
  - Low mortality rate
  - Lice may get infected after feeding on infected host

Endemic (Murine) Typhus

R.typhi

- Also called as Murine or Flea borne typhus
- From Rats -Transmitted by Rat flea
- Rickettsia multiplies in Gut and shed in feces
- Humans bitten by infected Rat fleas.
- Saliva or feces rubbed on bitten area, may lead to infection.

R. Typhi



Murine typhus
(much milder than epidemic typhus)

Clinical features

- Mild disease
- Vector – Rat flea -Xenopsylla cheopsis
- Rat flea bites rat;
- Multiplies in the gut of the rat
- Fleas unaffected. No transovarial transmission
- Man gets infected accidentally

Neill-Mooser Reaction

- Male guinea pig inoculated intra peritioneally with blood of patients, or isolates of R.typhi produce
- – Fever, and scrotal swelling, enlarged tests, and cannot be pushed back.-due inflammation and adhesions between layers of Tunica vagina
- Test positive in R.typhi

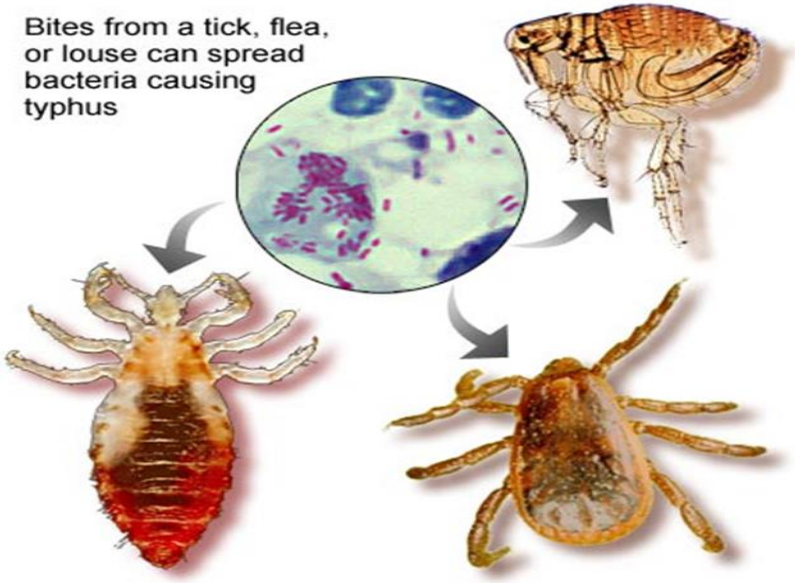
Treatment

- Tetracycline
  - Doxycycline 200mg
- Chloramphenicol
- Vaccine
  - Developed after World War II
  - Live attenuated, formalin inactivated.

DISEASES	RICKETTSIAL AGENT	INSECT VECTOR	MAMMALIAN RESERVOIR
SPOTTED FEVER GROUP			
a) Indian tick typhus	R. *conorii*	Tick	Rodent, Dog
b) Rocky mountain spotted fever	R. *rickettsii*	Tick	Rodents, Dogs
c) Rickettsial pox	R. *akari*	Mite	Mice

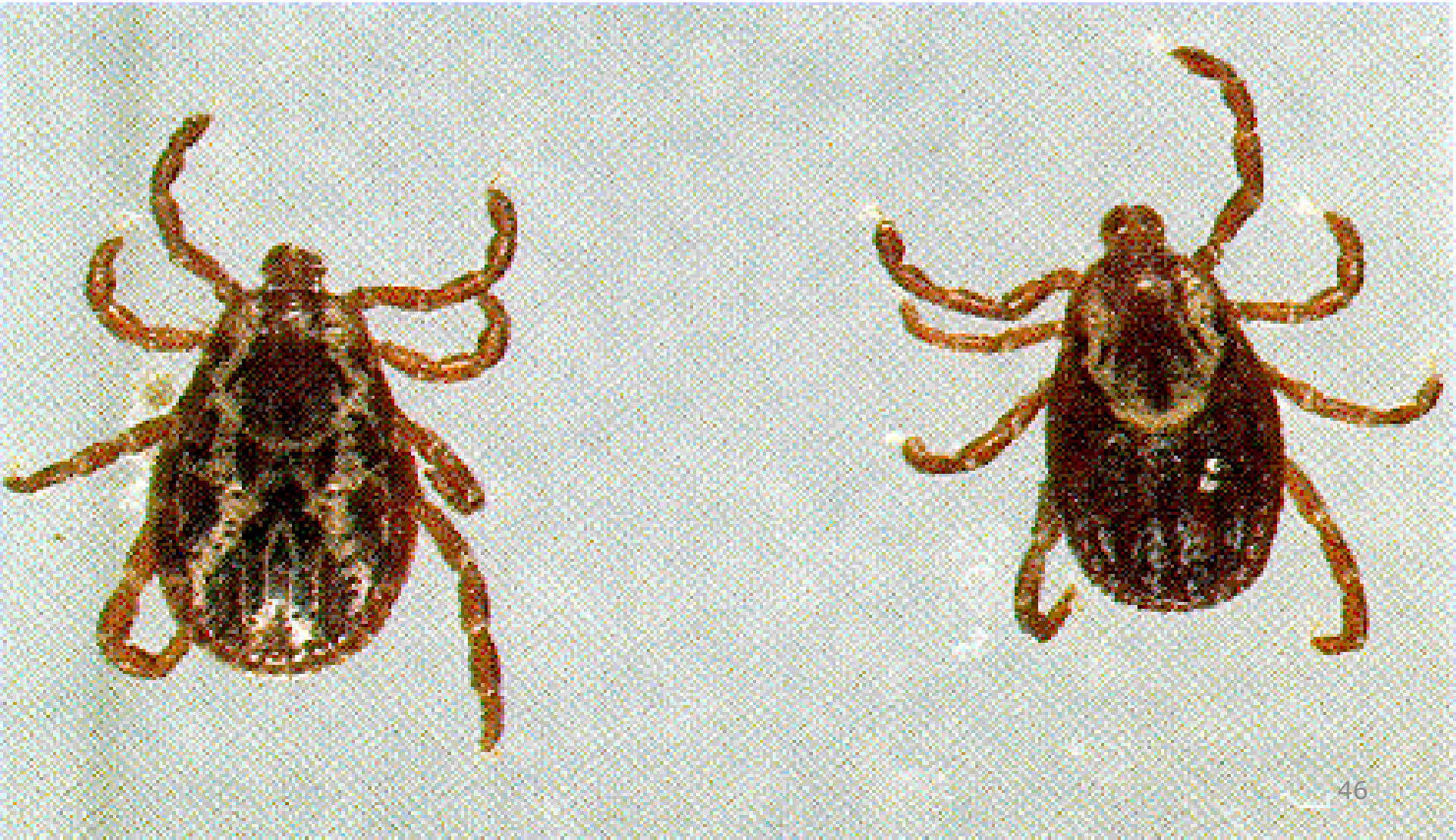
Tick Typhus

- R.rickettsii Rock mountain spotted fever
- R.siberica
- R.conori
- R.australis.



Ticks transmits bite- Trans ovarian spread

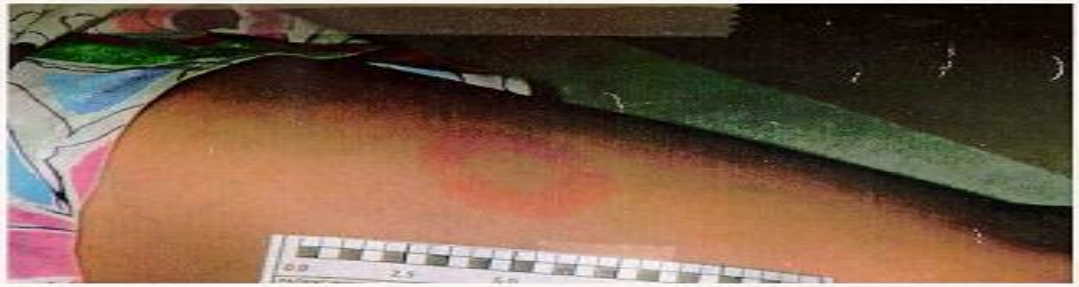
Ticks acts as vectors and reservoirs of Infection

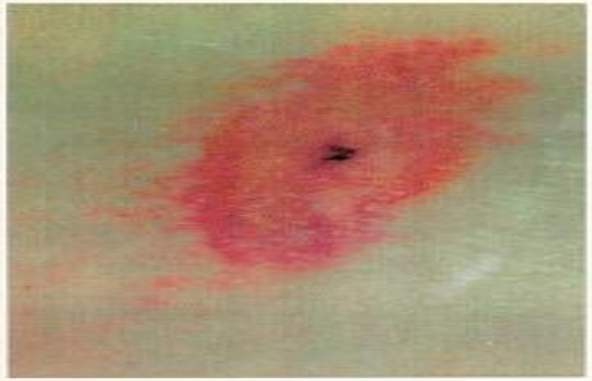


Clinical Features

- Incubation period – 1 week
- Fever, headache,myalgia,anorexia, n&V, diarrhea, photophobia, cough
- Bite site- Eschar
- Rash- wrists, ankles,palms,soles- generalized
- Maculopapular- petechial and haemorrhagic
- Hypotensive hypovolemic shock
- CFR-6-70%

Rocky Mountain spotted fever





Rocky mountain spotted fever

Rocky Mountain spotted fever

Rocky Mountain spotted fever

Ricketisial pox

- Transmitted by mites,
- Similar other spotted fever
- Headache ,fever
- Escher at the site of bite by mite.
- Maculopapular rash, can be vesicular resembling chicken pox
- Fever lasts for 1 week
- Transovarial transmission

Rickettsialpox

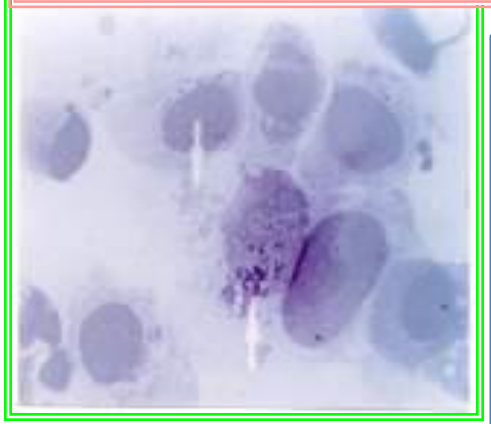
- Caused by ***Rickettsia akari***
- Transmitted from the bite of a **mite** that lives on **mice**
- **Not** transmitted by a tick
- Red, firm nodule that turns into **eschar**
- **Systemic symptoms** develop after eschar formation
- **Self-limited**, but **doxycycline** hastens resolution

Scrub Typhus

- Scrub typhus caused by Orientia tsutsugamushi
- Mild to fatal
- 6-18 days after bite of Mite ,an Escher is formed at the site of bite
- Enlargement of Lymph nodes, Interstitial pneumonitis,lymphadenopathy, splenomegaly, Encephalitis, Respiratory failure, circulatory failure

Scrub Typhus: A Rickettsial Disease

Pathogen: *Orientia tsutsugamushi*
Rickettsial bacteria



An acute febrile, rickettsial disease caused by a gram-negative, rod-shaped (cocco-bacillus) bacterium, known as *Orientia (Rickettsia) tsutsugamushi.*

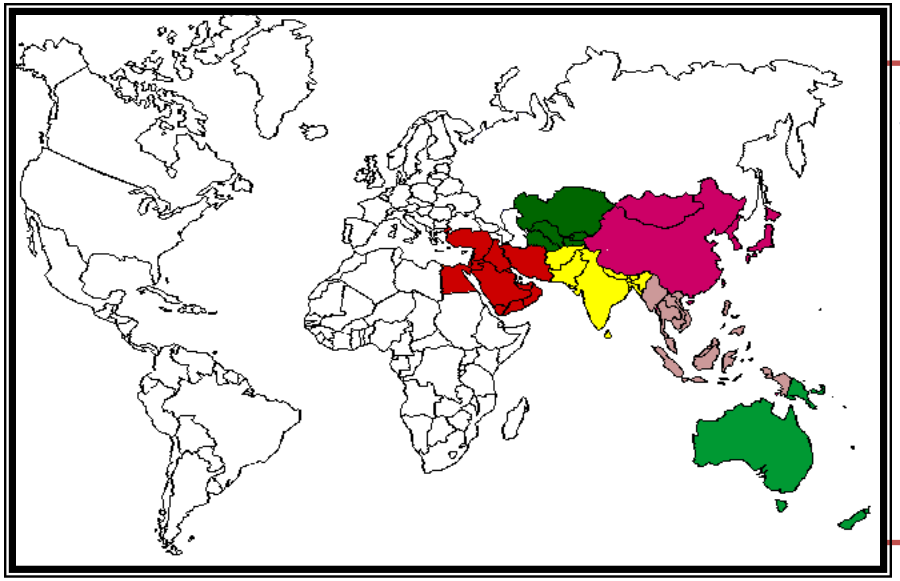
Vector: *Leptotrombidium*
Chigger-Mite

***O. tsutsugamushi* is transmitted to vertebrate hosts (rodents-primary host & humans-secondary or accidental host) by the bite of larval mites (chiggers) of the genus *Leptotrombidium*, e. g. *L. deliense, L. dimphalum*, etc.**

Epidemiology

- **Source of infection-------- Field mice,Rat, migratory birds**
- **Route of transmission-----Trombiculid mites**
- **Susceptible population----All susceptible**
- **Epidemic features----------Tsutsugamushi triangle**
- **CFR 10-60%**

Scrub Typhus

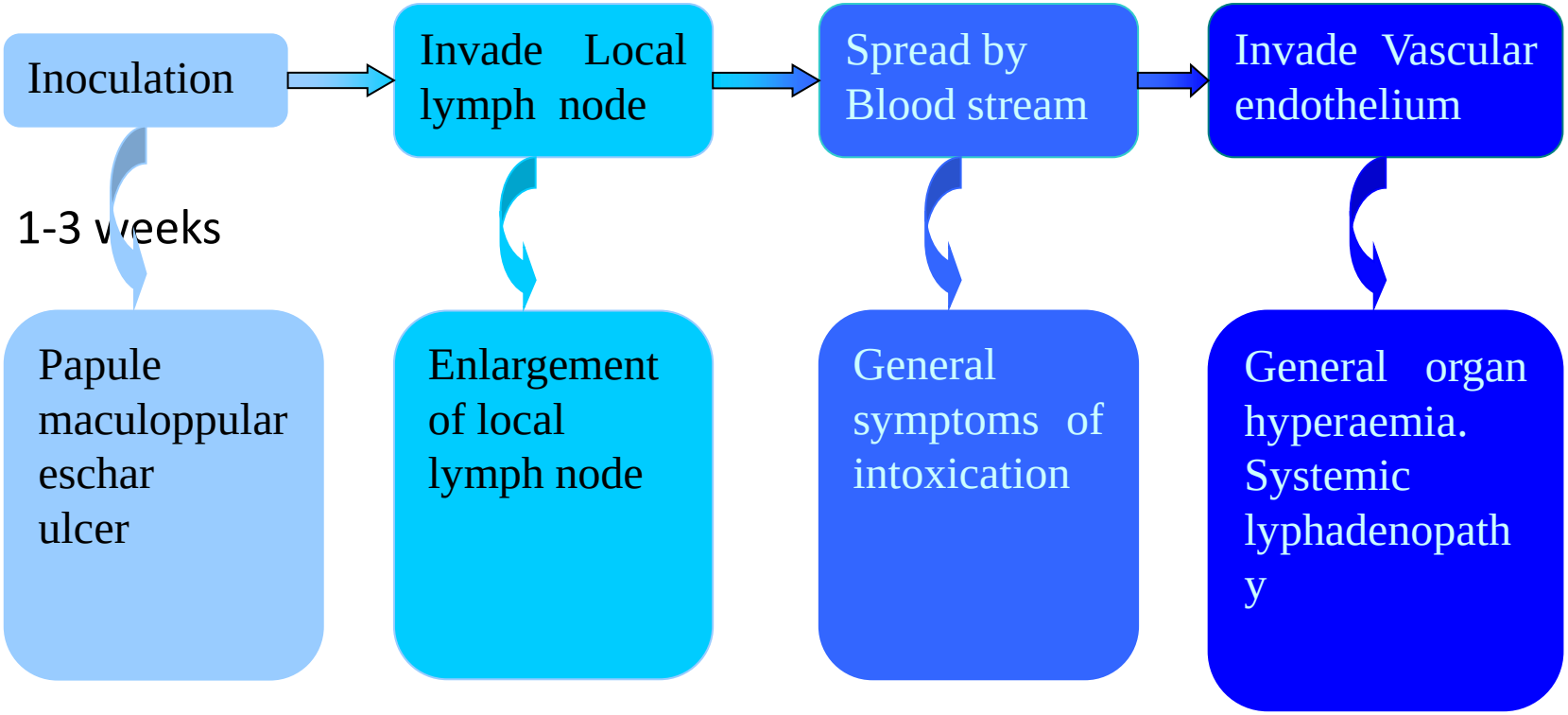


An important vector-borne disease, first described in 1899 in Japan.

During World War II, this disease killed thousands of soldiers who were stationed in rural or jungle areas of the Pacific theatre.

The disease occurred and threatened people throughout Asia & Australia. The range stretches from the Far-east to the Middle-east (from Japan and Korea, Southeast Asia, Pakistan, India, to Arab countries and Turkey). There are approx. 1 million cases each year world-wide, & over 1 billion people at risk.

Pathogenesis and pathology

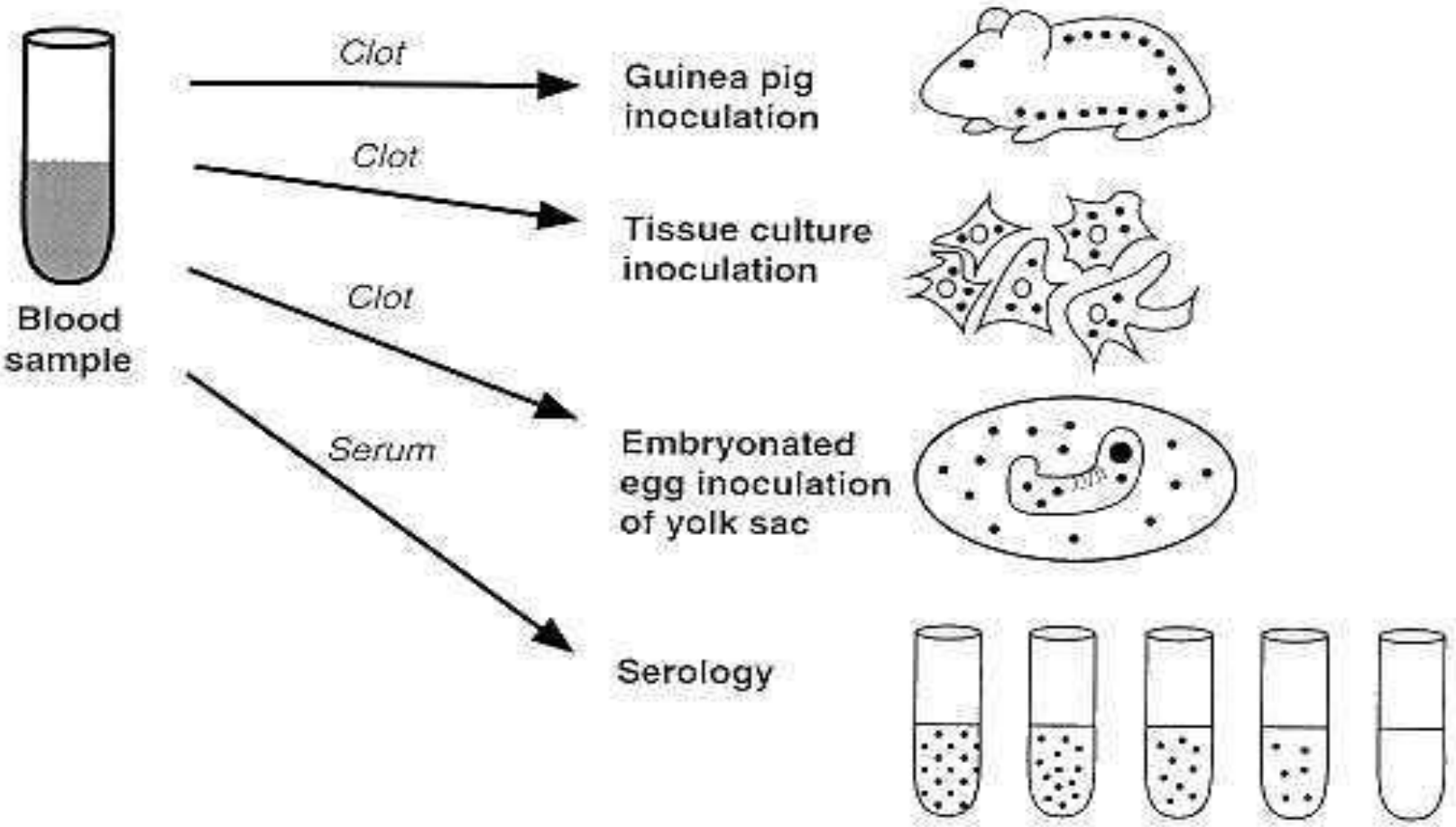


Skin Lesion (Eschar) Mite

Laboratory Diagnosis of Rickettsial diseases

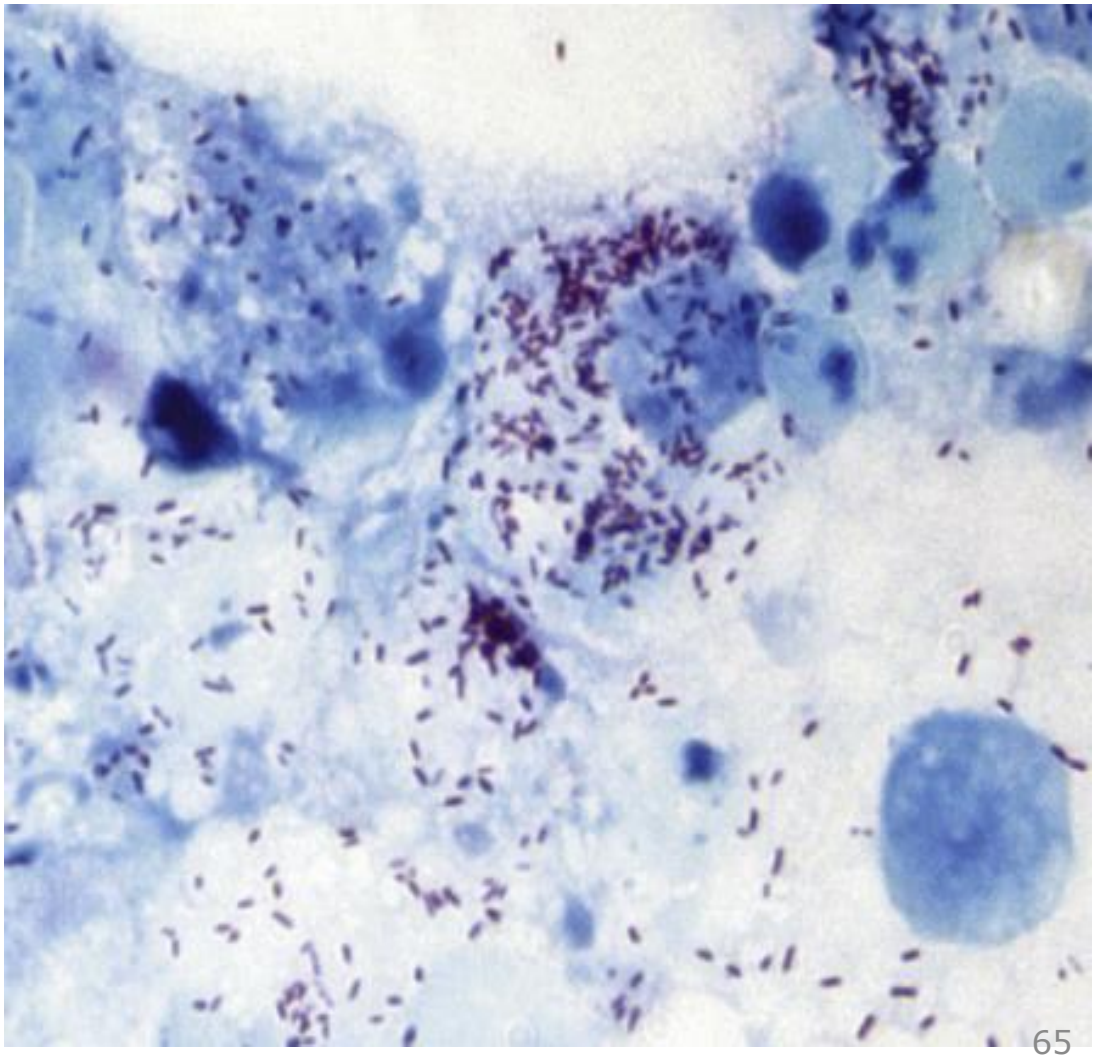
- Isolation- can be dangerous if not under proper biosafety precautions.
- Direct Detection- Microscopy
- Molecular- PCR
- Serology
- R.typhi R.conori, R.akari causes tunica reaction

Different Methods of Diagnosis



Culture

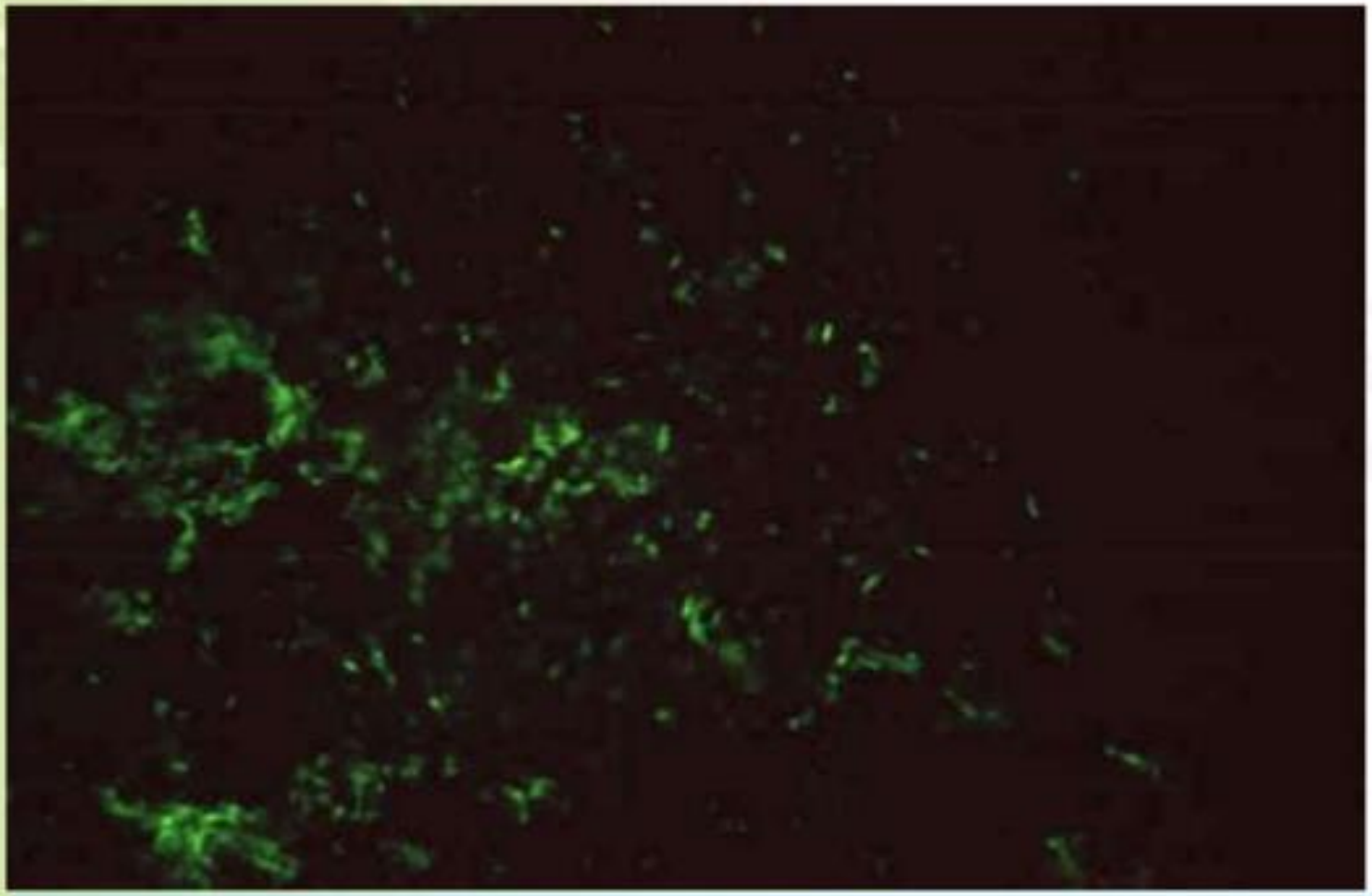
- Tissue cultures
- Vero
- MRC – 5



Newer & Safer

- Indirect Immunoflourescence
- Latex agglutination

Immunofluorescent antibody technique



Immunofluorescent Antibody Technique

(utilizes fluorescent antibody to detect rickettsial antigen in infected tissues)

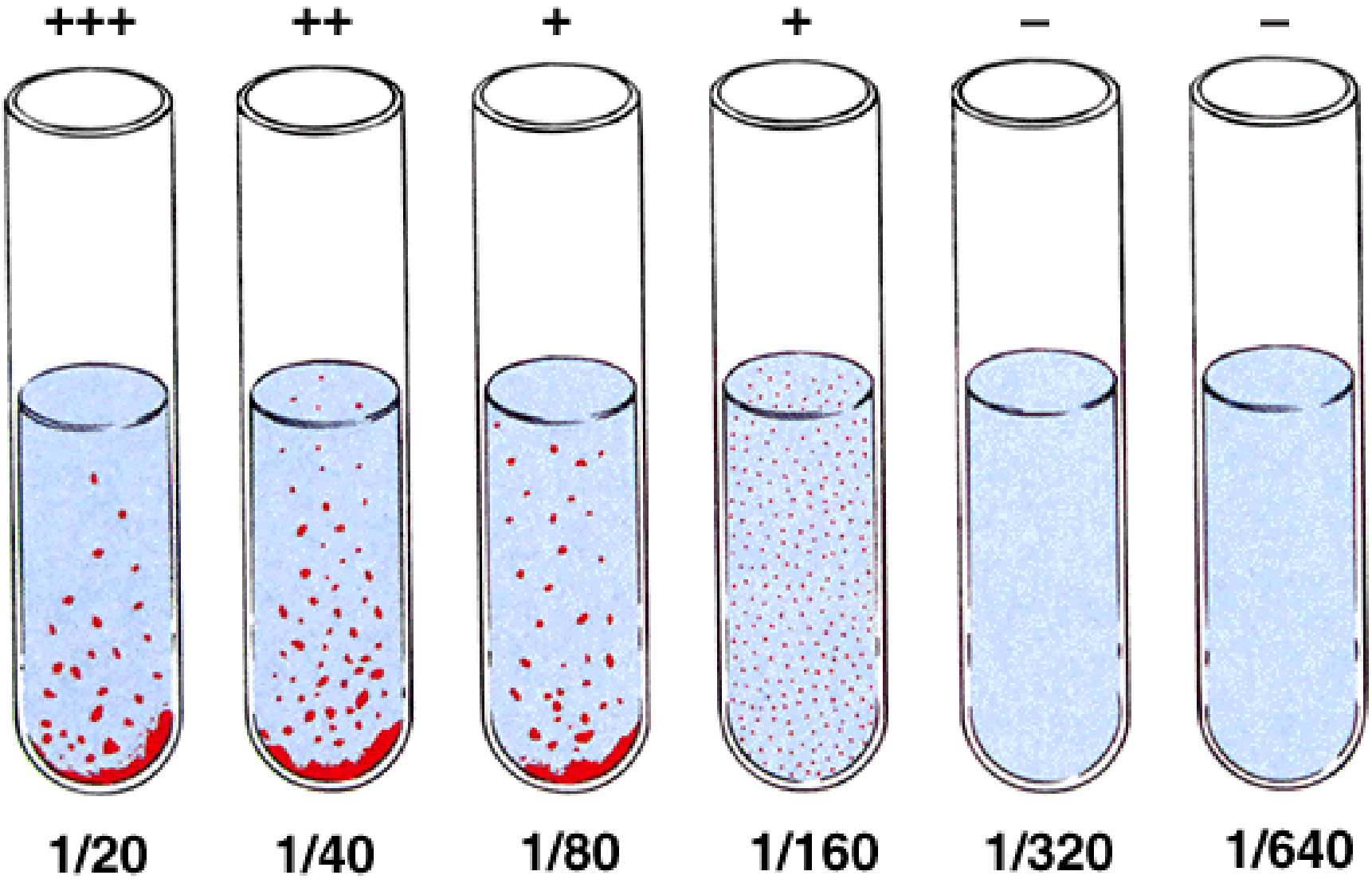
Weil – Felix Test

Test based on principle of Heterophile agglutination tests

- Non motile strains of Proteus are selected.
- OX19,OX2,OXK

- Sharing alkali stable carbohydrate antigen by some Rickettsia with certain strains of Proteus vulgaris OX19,OX2, and Proteus mirabilis OXK.

DISEASE	WEIL-FELIX		
	OX19	OX2	OXK
Epidemic typhus	+++	+	-
Endemic typhus	+++	+/-	-
Scrub typhus	-	-	++
RMSF	+	+	-
Rickettsial pox	-	-	-
Q fever	-	-	-
Trench fever	?	?	?

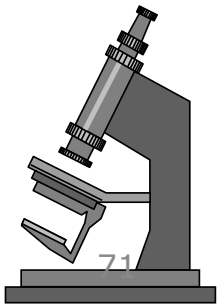

+++
++
+
+
–
–
1/20
1/40
1/80
1/160
1/320
1/640

Prevention

Breaking the infection chain (controlling and killing the vectors and reservoir hosts)

Inactivated vaccine has protective effect (not good enough)

Live attenuated vaccine (causes mild disease)



Family Anaplasmataceae

- Ehrlichia
- Neorickettsia
- Anaplasma
- Multiply in vacuoles in mononuclear cells and granulocytic phagocytes(Morula)

Human Monocytic Ehrlichiosis

- Caused by ticks, E.chaffensis.
- Leucopenia Thrombocytopenia
- Non necrotizing granulomas in bone marrow & liver
- Liver is involved.
- Doxycycline

Neorickettsia

- Small – Gram negative , obligate intracellular pathogens,
- infects Phagocytic cells.
- Called as Glandular fever
- Neorickettsia sennetsu.
- Cause atypical lymphocytosis
- No arthropod vector
- Eating fish infected with flukes infected by these bacteria.

Lab Diagnosis

- Giemsa
- Immunofluorescence
- PCR

Q Fever

- Occurs in veterinarians, ranchers, and animal researchers who are in contact with infected placenta from sheep, cattle, or goats (no arthropod vector)
- Incubation period is 10-28 days
- Fever and headache are common; 50% will develop pneumonia after inhaling the organism; hepatitis & endocarditis are rare
- Specific serology establishes the diagnosis
- Bioterrorist threat?

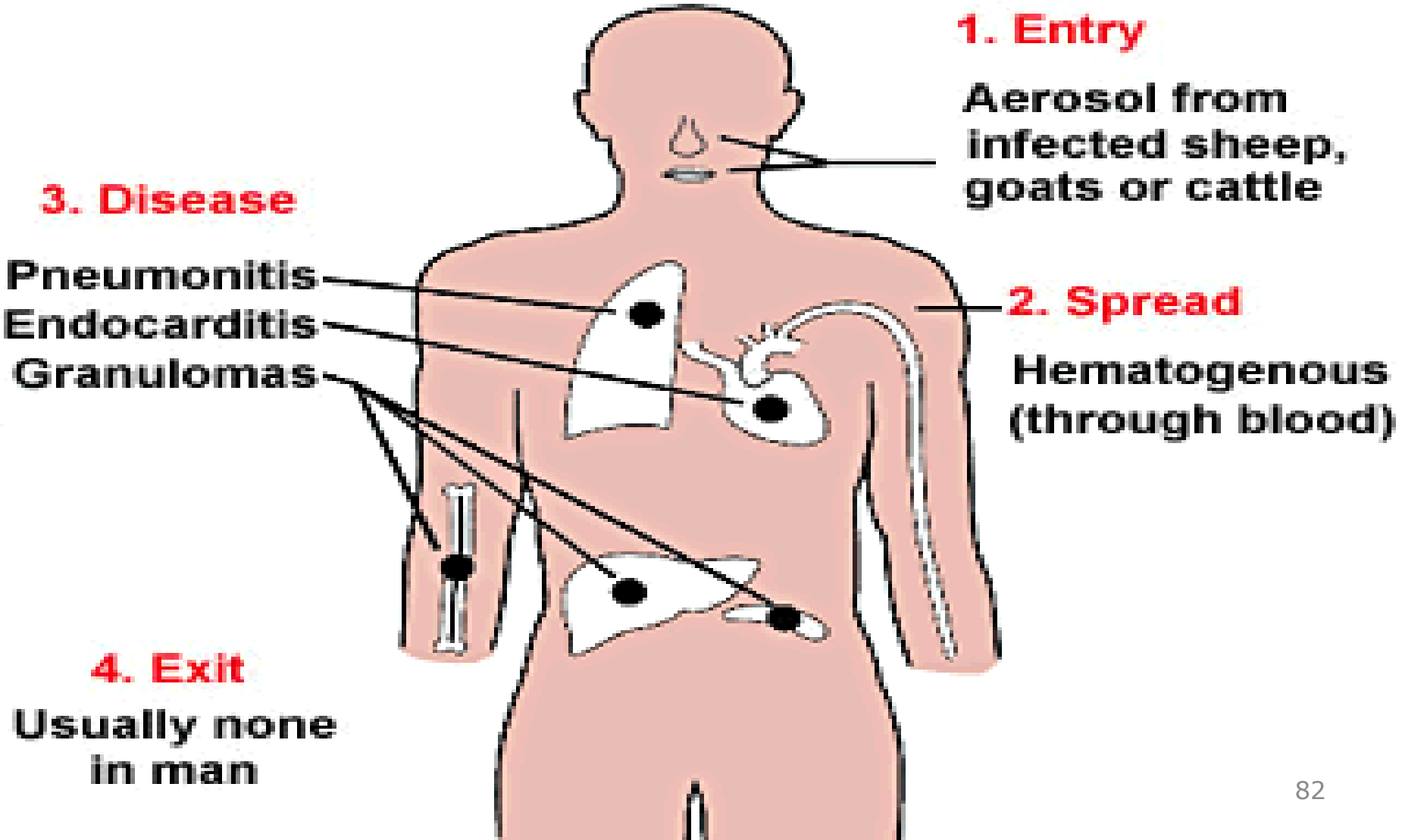
Coxiella Burnetii

- Self-limiting flu-like syndrome with high fever (40℃)
- Primary reservoirs are wild (cattle, sheep, goat etc.)
- Non-cross reactive antigen with non-motile Proteus (Weil-Felix reaction negative)
- Live in phagolysosome macrophages of vertebrate host

Q Fever

- Etiological agent ? “Query”
- **Small in size -Coxiella burnetti**
- Air borne transmission
- Domestic live stock get infected.
- Survive in dried feces, Milk, urine, placental products
- Cause Human infection. No skin rash

Q - Fever


1. Entry
Aerosol from infected sheep, goats or cattle
2. Spread
Hematogenous (through blood)
3. Disease
Pneumonitis
Endocarditis
Granulomas
4. Exit
Usually none in man

Q Fever

- Wool hides, Meat, Milk
- Enters through abrasions
- System infection through Intestine, pulmonary,
- Can cause serious infection, Hepatitis and meningitis,
- May last for 2 – 3 years as chronic condition
- Infects Monocytes and Macrophages,

Pasteurization of Milk Which method is better ?

- Pasteurization by holders method not effective (63°C X 30 min)

- Flash method effective. (72°C X 15-20 sec)

Laboratory Diagnosis

- Indirect Immunofluorescence methods
- Indirect Immunoperoxidase assay
- IgG IgM ELISA
- CFT
- Polymerase chain reaction
- Isolation of the organism is dangerous.

Treatment

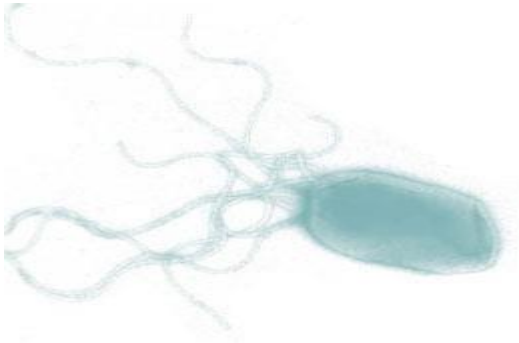
- Doxycycline

Bartonellaceae

- Gram – ve bacilli
- B.bacilliformis, B.quintana,B henselae
- Bartonella bacilliformis
- Also called as Oroya fever,
- A Medical student – Peruvian

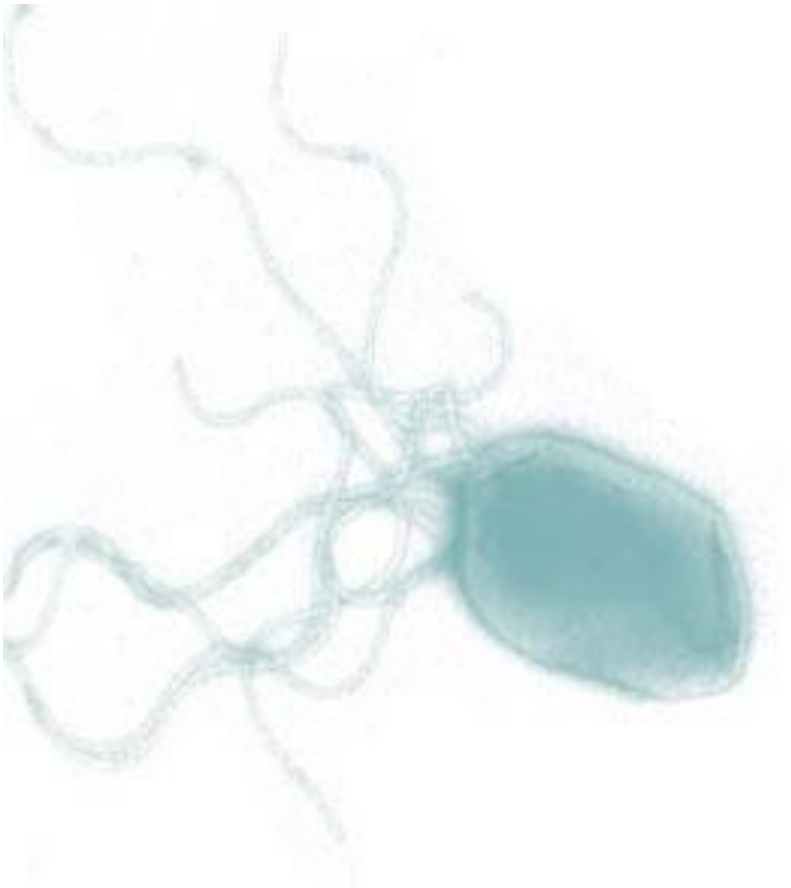
  Daniel Carrion Credited for isolation.

  Called as Carrions Disease



Bacterial Morphology

- B.bacilliformis
- Pleomorphic gram negative bacteria
- Carries 10 polar flagella.
- Strict aerobes
- Grow semi solid NA with rabbit serum & Hb



Clinical features

- Bacterial invasion of Erythrocytes
- Progressive Anemia,
- Carries high mortality
- Verruga peruana

- Treatment-Penicillin, Streptomycin, Tetracycline,Chloramphenicol.
- DDT

B quitana

- Called as trench fever (five day fever)
- Transmitted by body louse
- Grows in cell free culture media
- Fever,headache, mayalgia, back pain, roselar rash
- Chronic/Latent infections; Infection may last > 20 years

Bartonella henselae

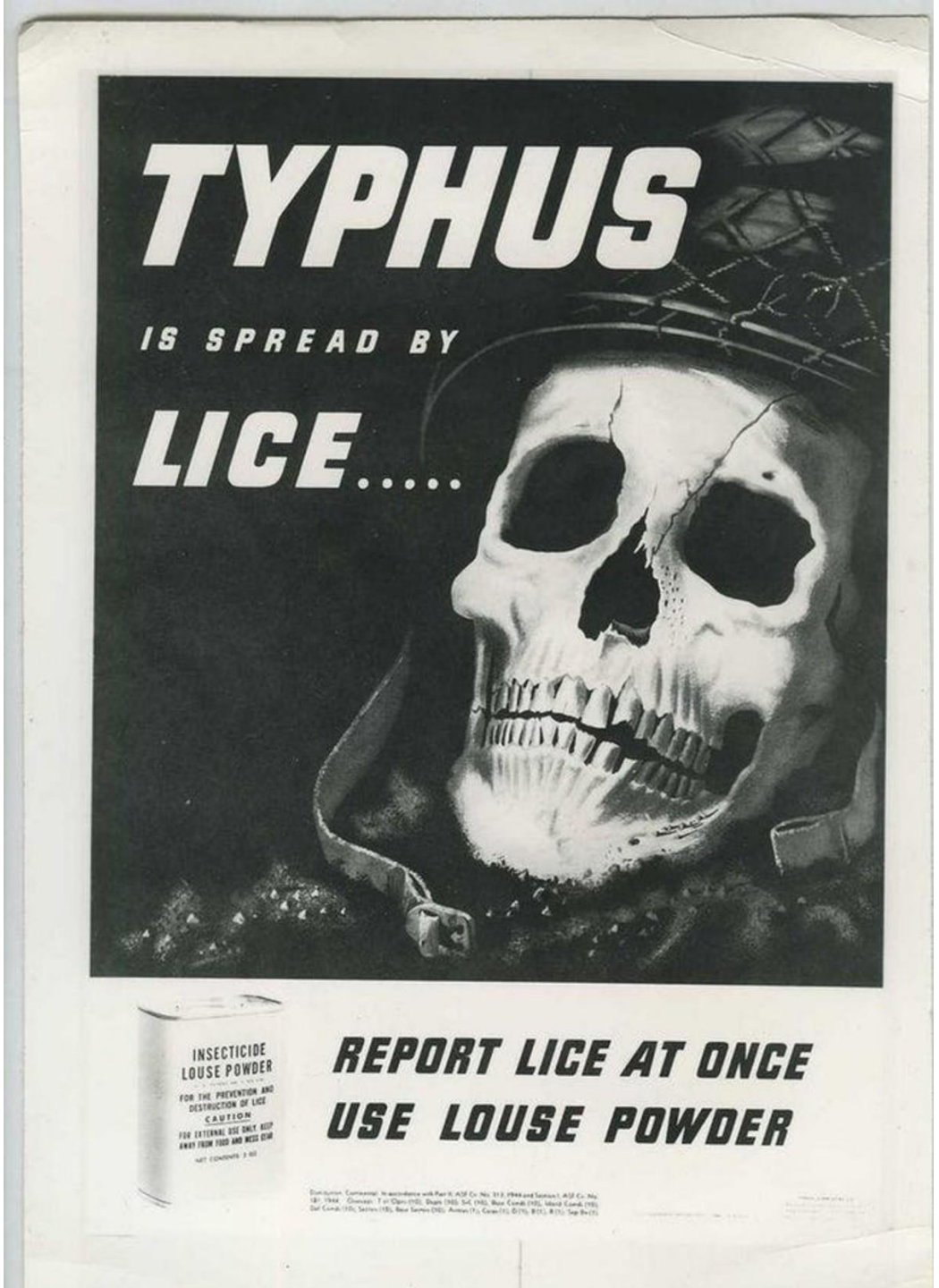
- Cat scratch disease (CSD)
- Weil-Felix reaction negative
- Infection by scratch or bite of infected cats or dogs
- “Parinaud” Eye-Lymph node syndrome

  The eye looks red, irritated, and painful, similar to conjunctivitis.

In AIDS patients causes bacillary angiomatosis

Prevention

- Use of repellents in endemic areas
- Protective clothing in endemic areas
- Careful inspection & quick removal of ticks
- Useful vaccine for RMSF is available for high risk groups such as forest rangers that work in endemic areas
- Weekly doxycycline may prevent scrub typhus infection in field workers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