



Bunyaviruses

Hantavirus Pulmonary Syndrome (HPS)

Rodents are reservoir

Virus airborne from rodent feces

Viral encephalitis

Crimean Congo Hemorrhagic Fever (CCHF)

Vector borne zoonosis

CRIMEAN-CONGO HEMORRHAGIC FEVER

- Caused by virus obtained from tick bites
 - Also contact with livestock or their carcasses
- Symptoms
 - Sudden onset of fever, muscle aches, dizziness, neck pain and stiffness, backache, headache, sore eyes and photophobia (sensitivity to light)
 - Severe symptoms and death possible
- Countermeasures Prevent tick bites
 - Use the DOD Insect Repellent System
 - Sleep under a permethrin treated bed net
 - Regular examination of clothing and skin for ticks; promptly remove attached ticks

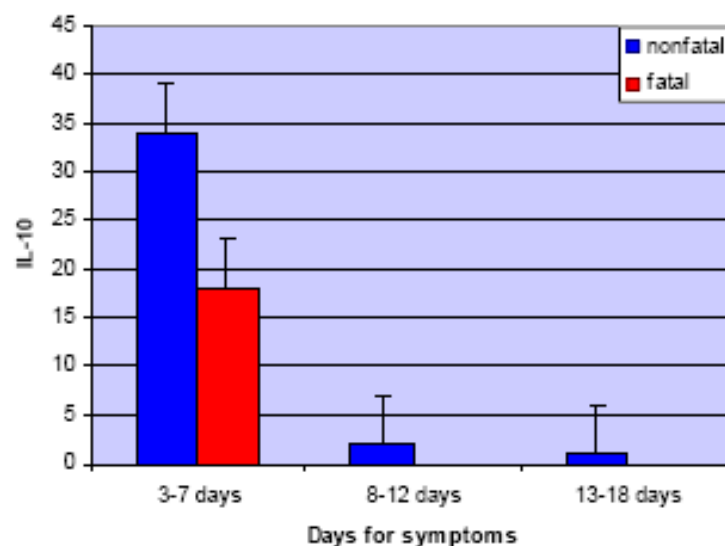
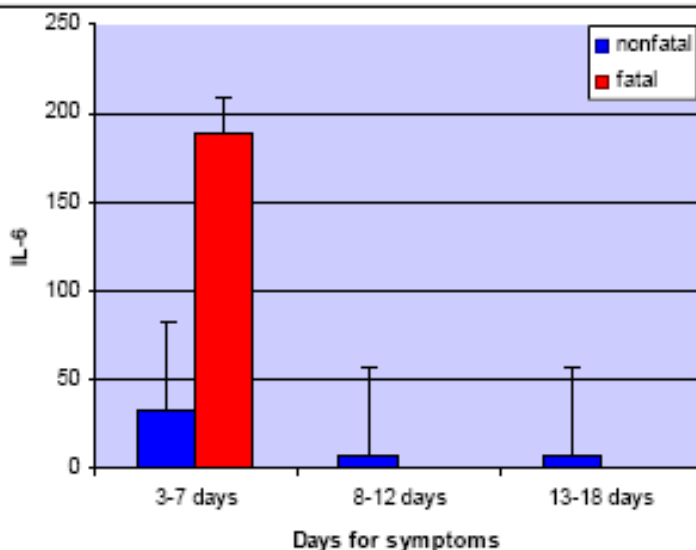
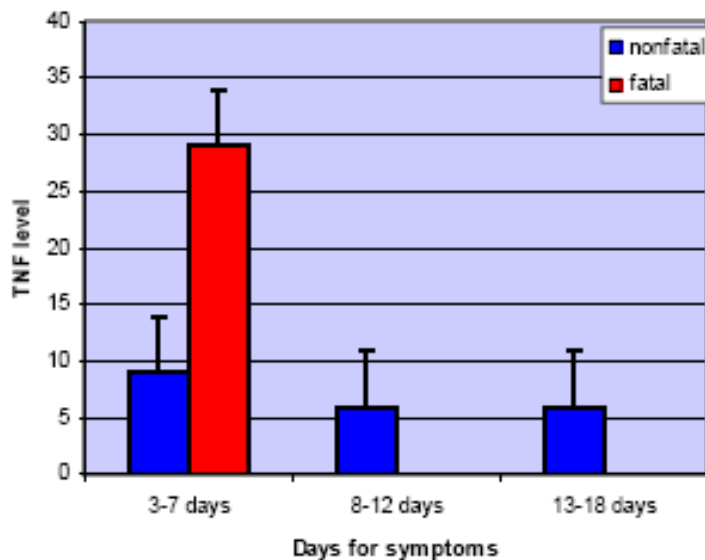
Pathogenesis

- Capillary fragility
 - "capillary toxicosis", Soviet scientists
 - Infection of endothelium
- Coagulopathy
- Multiple host induced mechanisms
 - Massive apoptosis of lymphocytes
 - Induction of proinflammatory cytokines
 - Dysregulation of coagulation cascade
 - DIC

Evaluation of Serum Levels of Interleukin (IL)-6, IL-10, and Tumor Necrosis Factor- α in Patients with Crimean-Congo Hemorrhagic Fever

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Incubation Period

- The incubation period is influenced by the route of exposure. Infections acquired via tick bites usually become apparent after 1 to 3 days

- the longest incubation period reported by this route is **nine days**. Exposure to blood or tissues usually results in a longer incubation period

- Current estimates suggest that these infections become apparent, on average, after 5 to 6 days, but incubation periods up to 13 days are known

Clinical Signs

- The first sign of Crimean-Congo hemorrhagic fever is a sudden onset of fever and other nonspecific symptoms including chills, severe headache, dizziness, photophobia, neck pain, myalgia and arthralgia. The fever may be very high

- **Gastrointestinal symptoms**
including nausea, vomiting, non-bloody diarrhea and abdominal pain are also common

- Sharp mood changes,
confusion and aggression
have been reported in some
cases

- Cardiovascular changes such as bradycardia and low blood pressure can also occur

- This **early stage** of disease is called the **prehemorrhagic** phase. It is followed, after several days, by the hemorrhagic phase

- The hemorrhagic phase develops suddenly. It is usually short, lasting on average 2 to 3 days. A petechial rash may be the first symptom. The rash is followed by petechiae, ecchymoses and large bruises on the skin and mucous membranes

- Hematemesis, melena, epistaxis, hematuria, hemoptysis and bleeding from venipuncture sites are also common. Bleeding can occur in other locations, including the brain. In one case, internal bleeding mimicked acute appendicitis

- **Hepatitis** occurs in some patients, and may result in jaundice and hepatomegaly

- **Splenomegaly** can also be seen. Some patients die from hemorrhages, hemorrhagic pneumonia or cardiovascular disturbances

- In patients who survive,
recovery begins 10-20 days
after the onset of illness

- The **convalescent phase** is characterized by generalized weakness, a weak pulse and tachycardia. Other symptoms including sweating, dryness of the mouth, headache, dizziness, nausea, poor appetite, labored breathing, polyneuritis, poor vision, loss of hearing, and memory loss have also be seen. **Some patients temporarily lose all of their hair**

- **Hepatorenal insufficiency** has been reported in some countries but not others

- **Recovery** is usually complete but slow, and can take up to a year. **Subclinical infections** can occur, but are thought to be uncommon. **Mild febrile cases** without hemorrhages are also seen

Clinical Features







The Suspected Case

1. Individuals, who had fever, myalgia, malaise, diarrhea, and
2. History of being in endemic area
 - Tick exposure history and/or
 - Residency or travel to CCHF endemic region

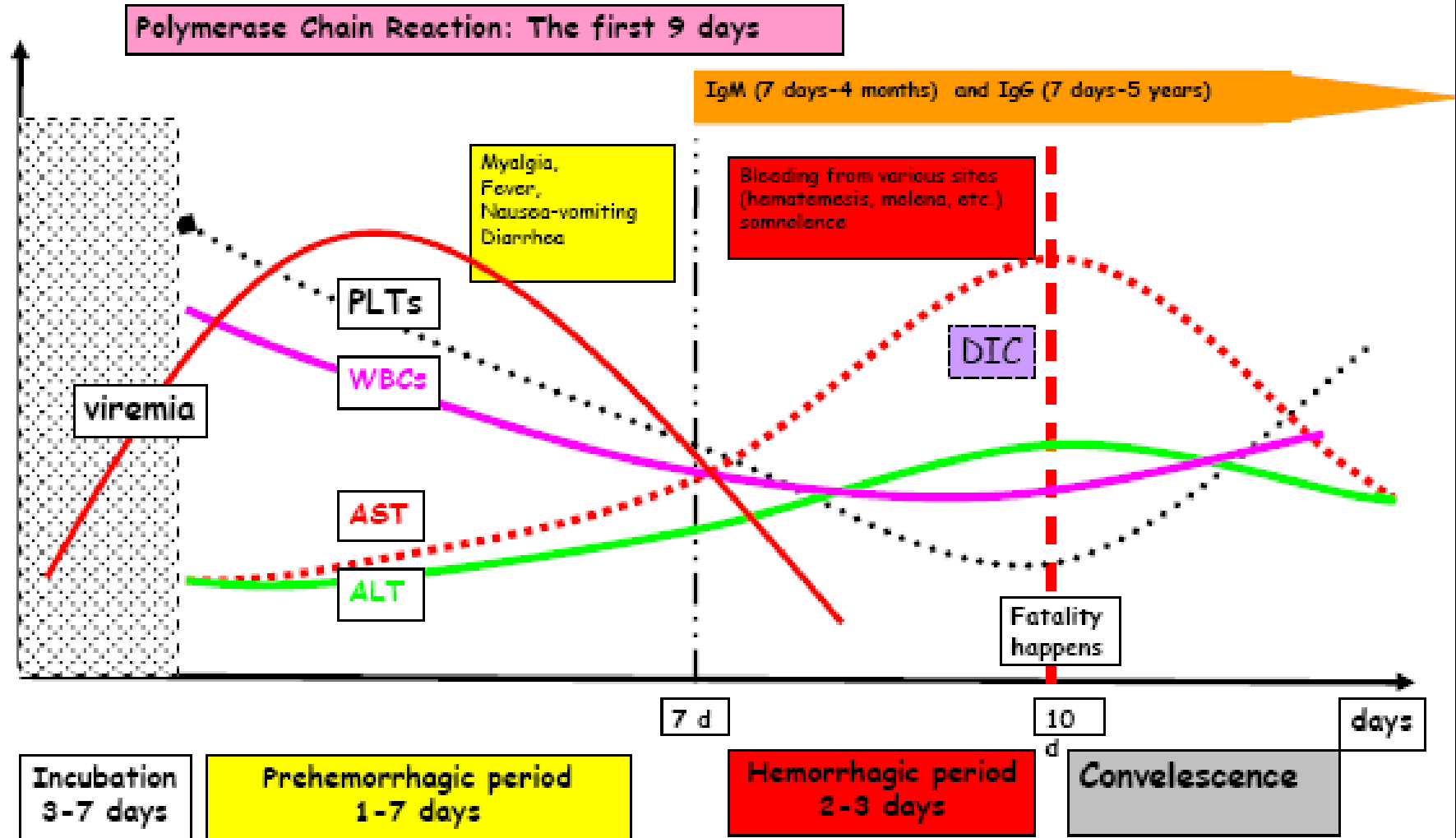
The probable case

Patients who had leukopenia, thrombocytopenia, elevated AST, ALT, and LDH levels.

Confirmed case

CCHF IgM or PCR positivity in the blood or body fluids of the patient.

The Clinical Course of Crimean-Congo Hemorrhagic Fever



The Predictors of Fatality

Viral factors

High viral load
shown by recent studies for many VHFs

Cevik, et al. CID 2007

Host factors

Cytokines: TNF alfa, IL1, IL6

Ergonul, et al. JID 2006

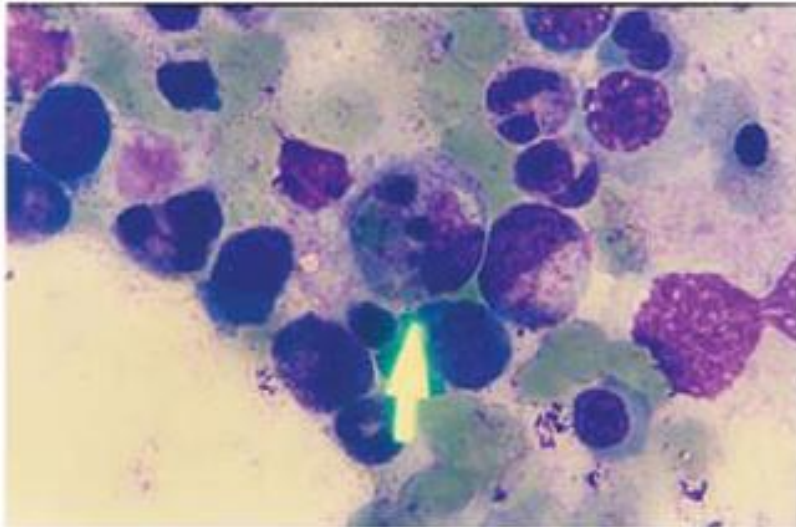
Why The Case Fatality Rates Are Different?

- 1) Different strains
- 2) Co-existent infections
- 3) Host factors
- 2) Health care facility
 - Access
 - Quality
- 3) Public awareness

Antibody production is weaker among fatal cases

	Patients survived n=50	Patients died n=4
IgM positives	37/40 (93)	$\frac{1}{4}$ (25)
IgG positivity	27/40 (68)	0/4 (0)
PCR positivity	19/40 (48)	3/4 (50)

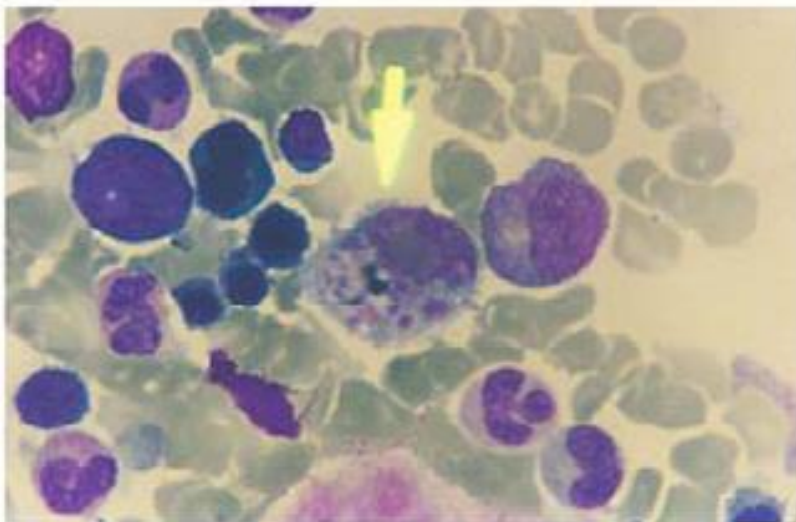
A



Bone marrow aspiration smear,
stained with Wright, showing
hemophagocytosis

A) phagocytosis of an
erythrocyte and nuclear
remnants by a macrophage.

B



B) phagocytosis of platelets by a
macrophage.

Karti SS, et al. *Emerg Infect Dis* 2004

Crimean-Congo hemorrhagic fever: Five patients with hemophagocytic syndrome

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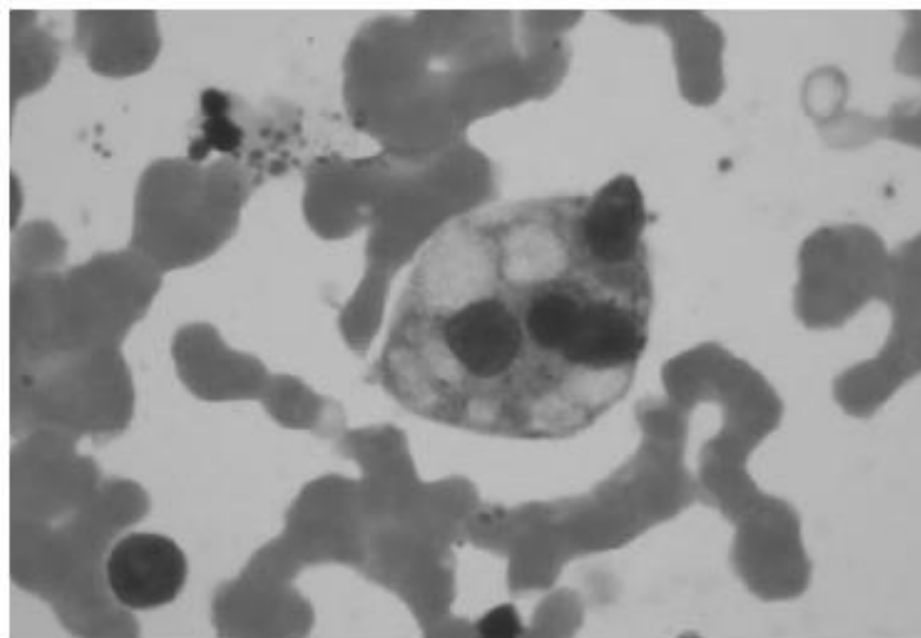
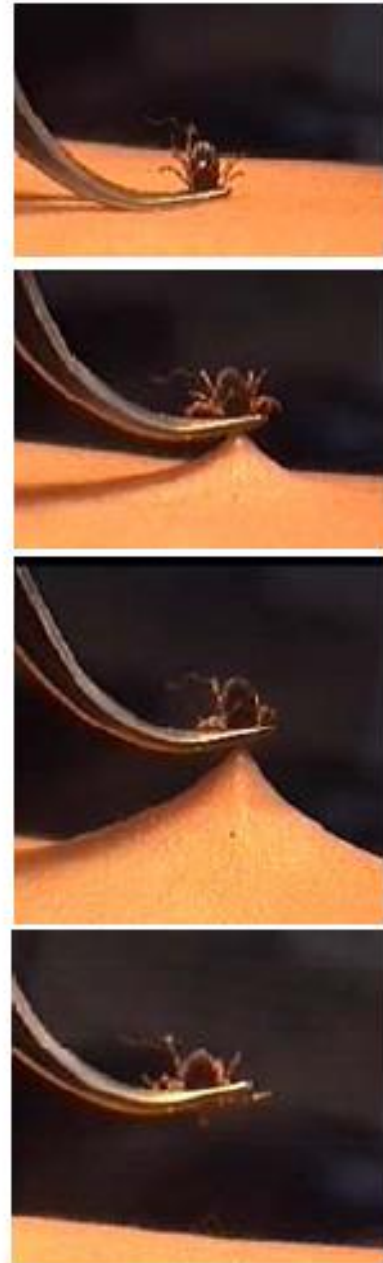


Figure 5. Hemophagocytosis in the bone marrow aspiration smears in Patient 5.

Am J Hematol 2007

Tick removal: What is the best way?

Vatansever Z, In: Ergonul & Whitehouse,
Crimean-Congo Hemorrhagic Fever:
A Global Perspective, Springer, 2007





The End

