

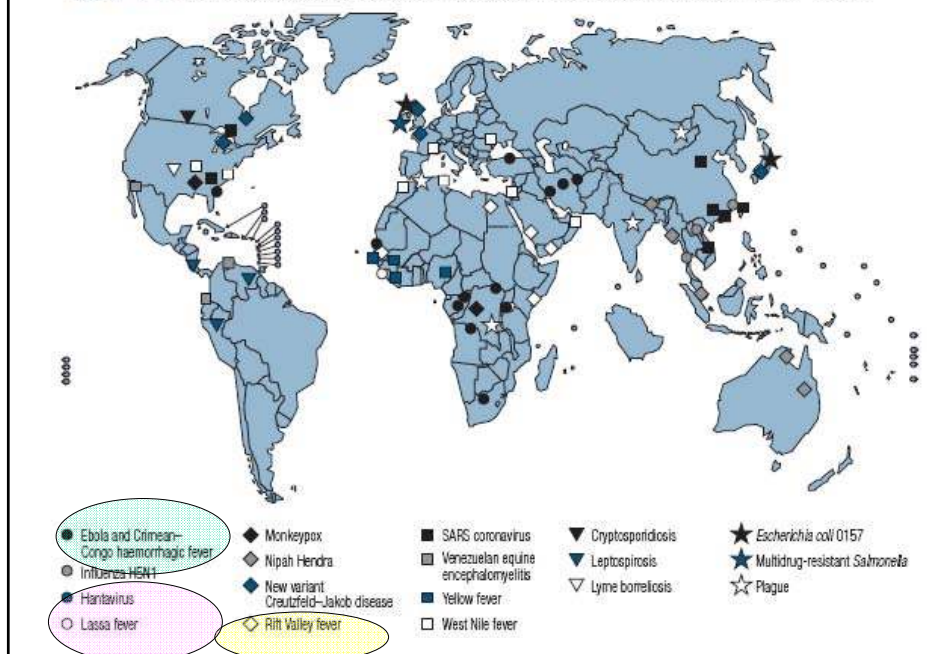
Crimean- Congo Hemorrhagic Fever

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Infectious Diseases Department
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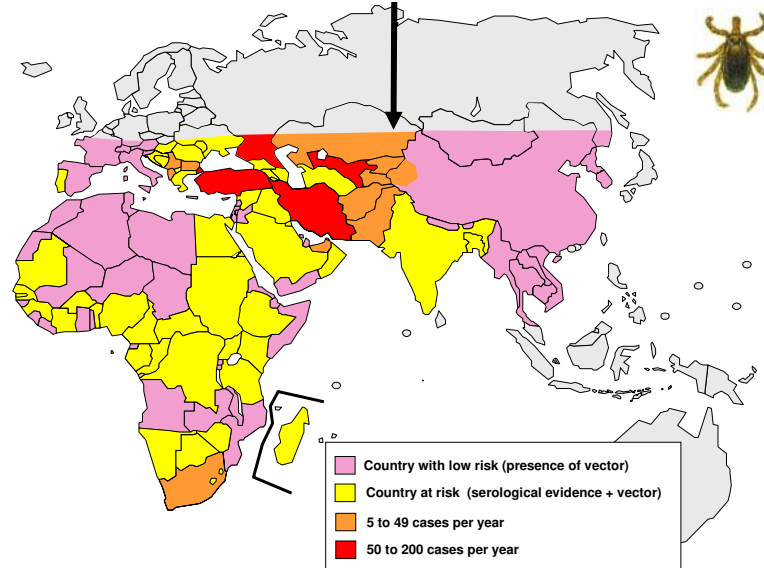
29 November 2008, Lelystad, Netherlands

Figure 1.4 Selected emerging and re-emerging infectious diseases: 1996–2004



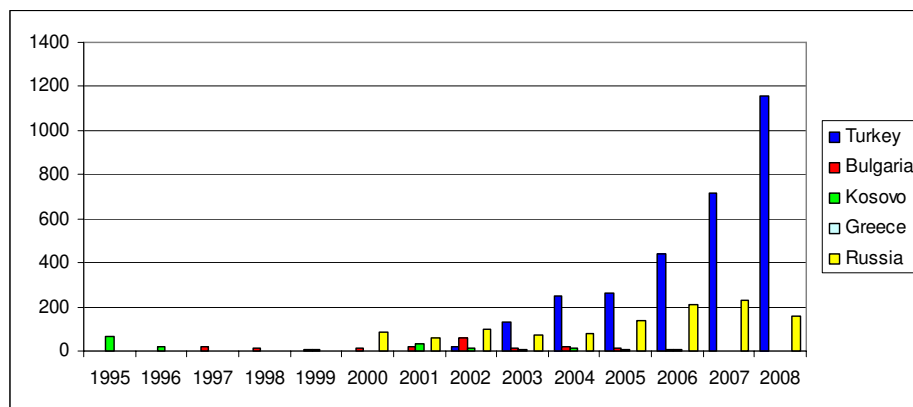
Crimean-Congo Haemorrhagic Fever Geographic Distribution

50° North limit for the geographic distribution of genus *Hyalomma* ticks



Pierre Formenty, et al. In Ergonul & Whithouse, CCHF, Springer, 2007

CCHF in Europe and the neighborhood

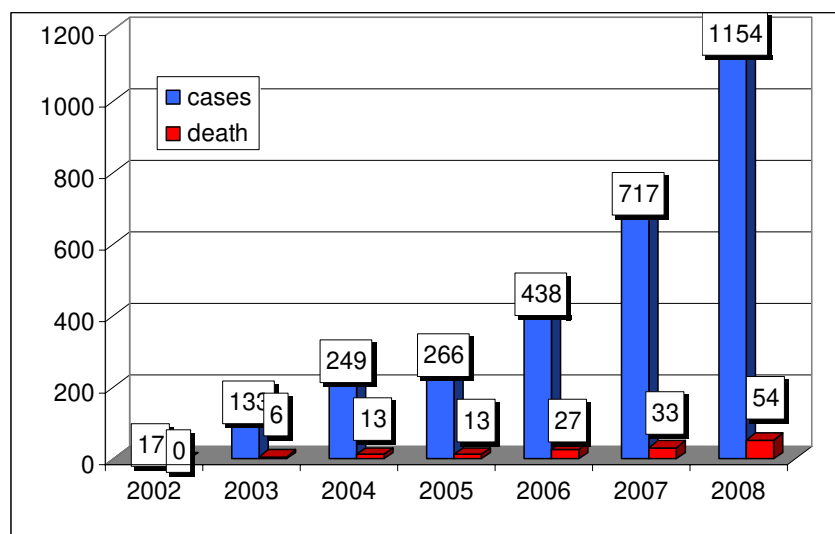


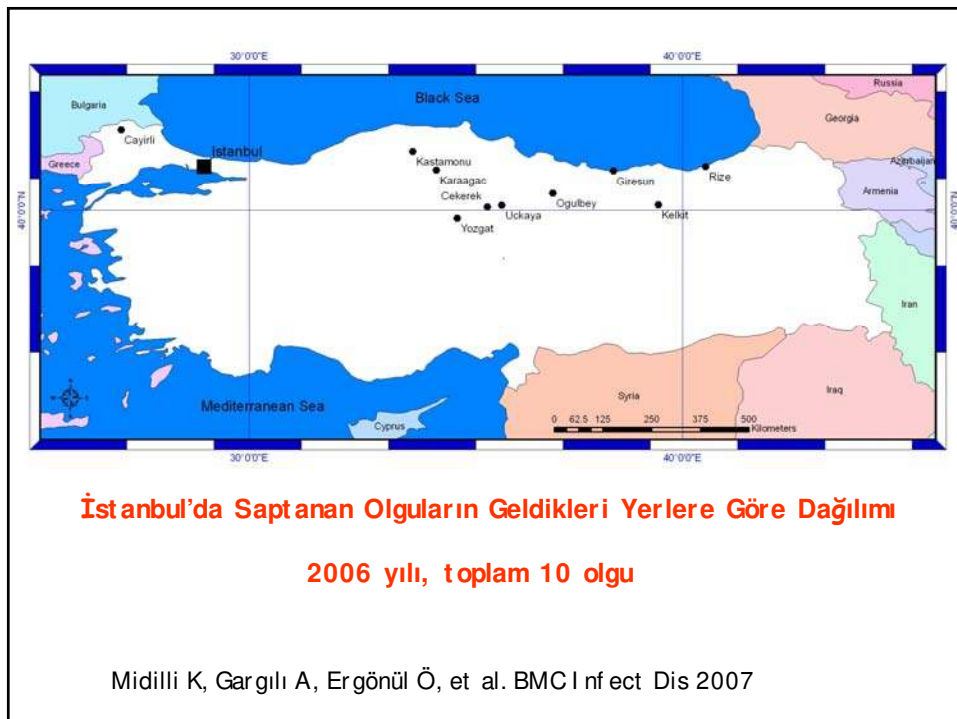
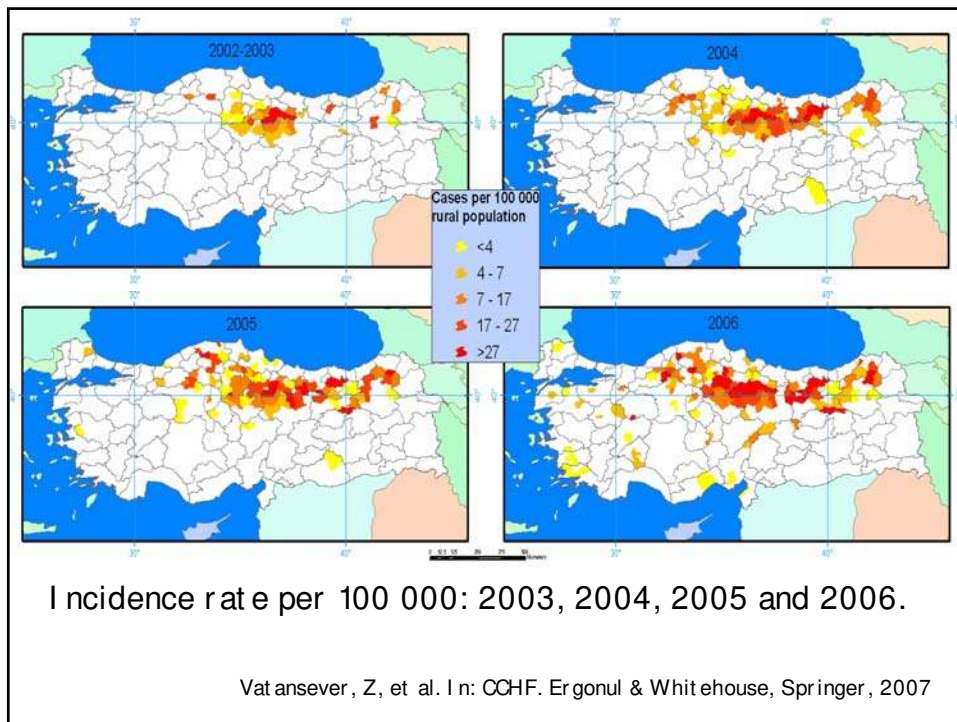
FIGURE

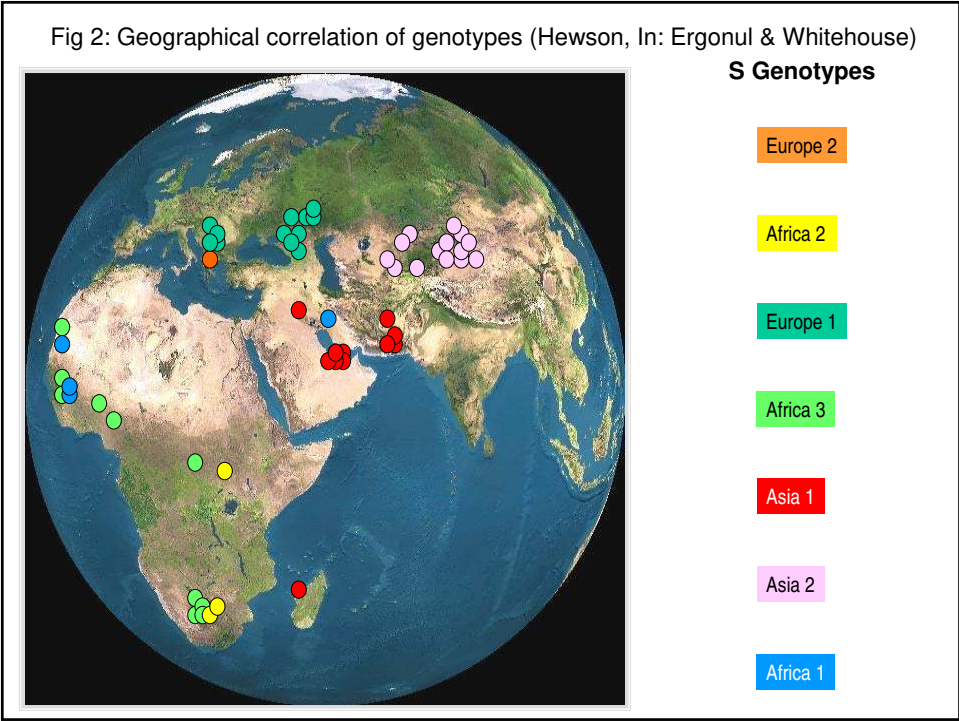
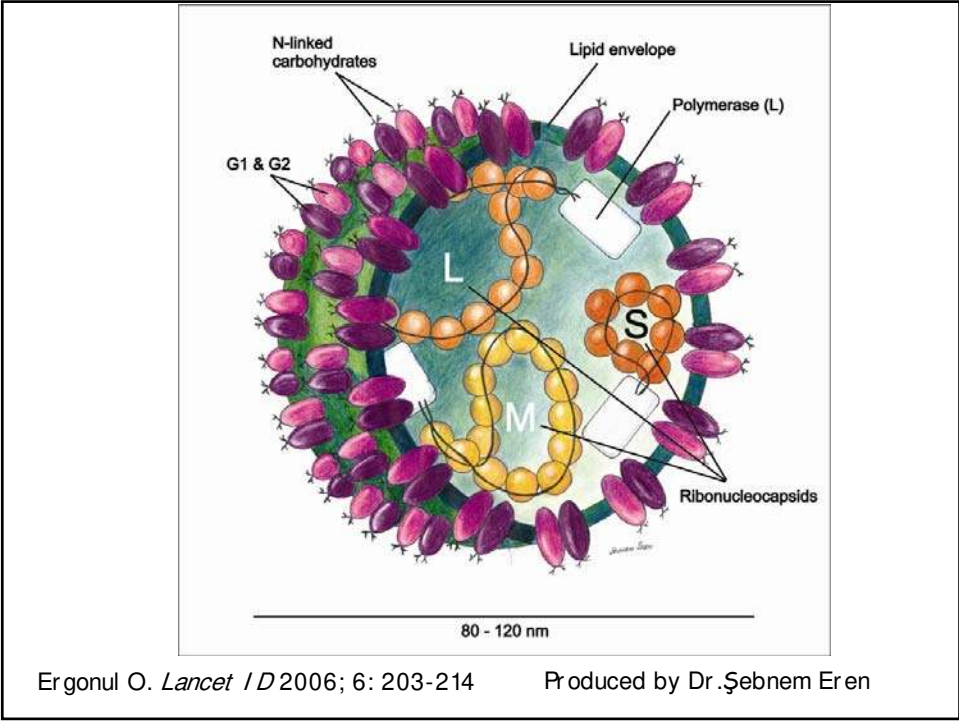
Map of Greece showing the area where a case of Crimean-Congo haemorrhagic fever was reported in June 2008

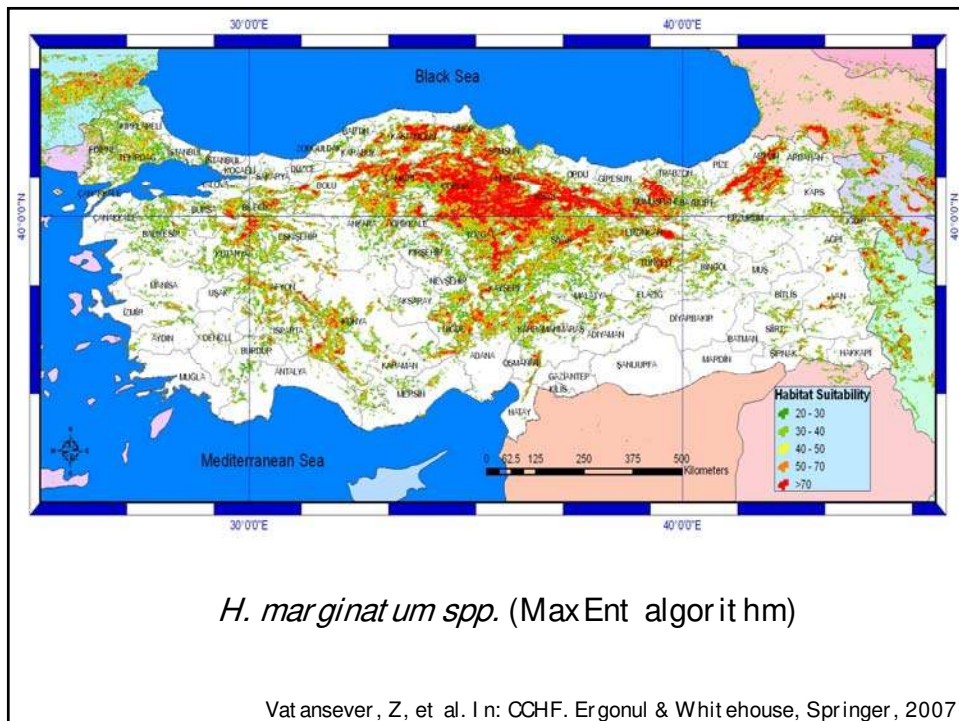
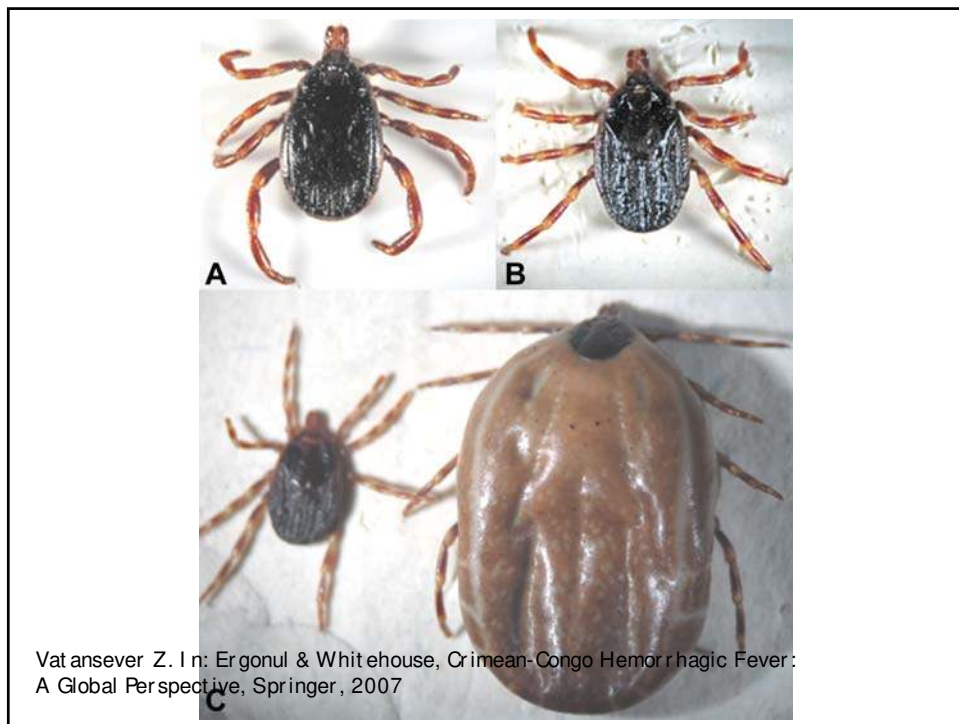


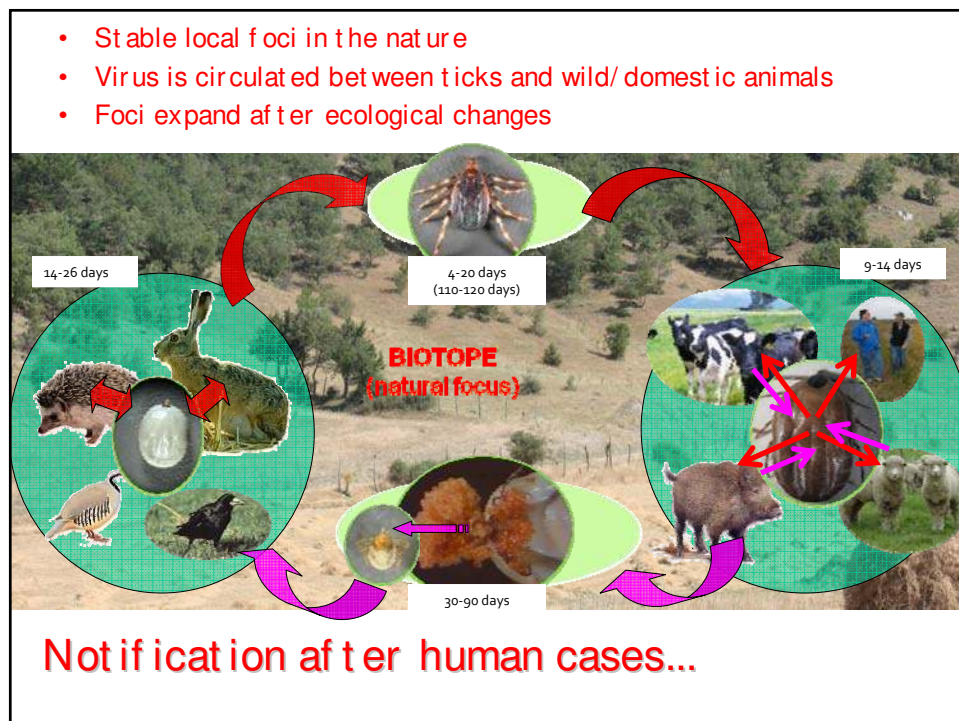
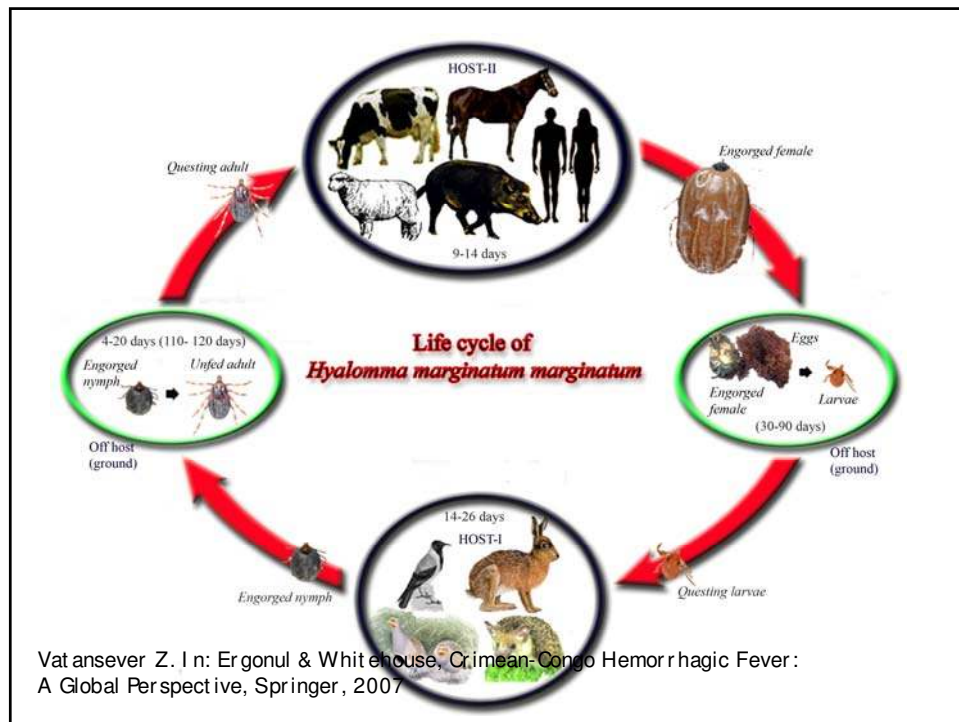
The Number of the CCHF cases in Turkey











The Course of Infection in animals

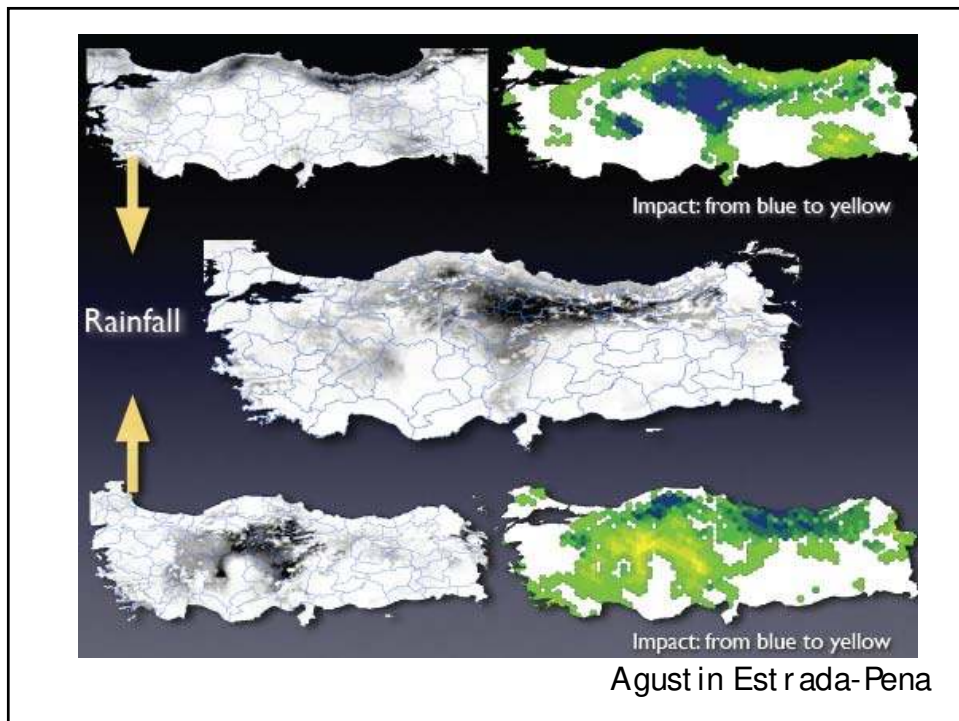
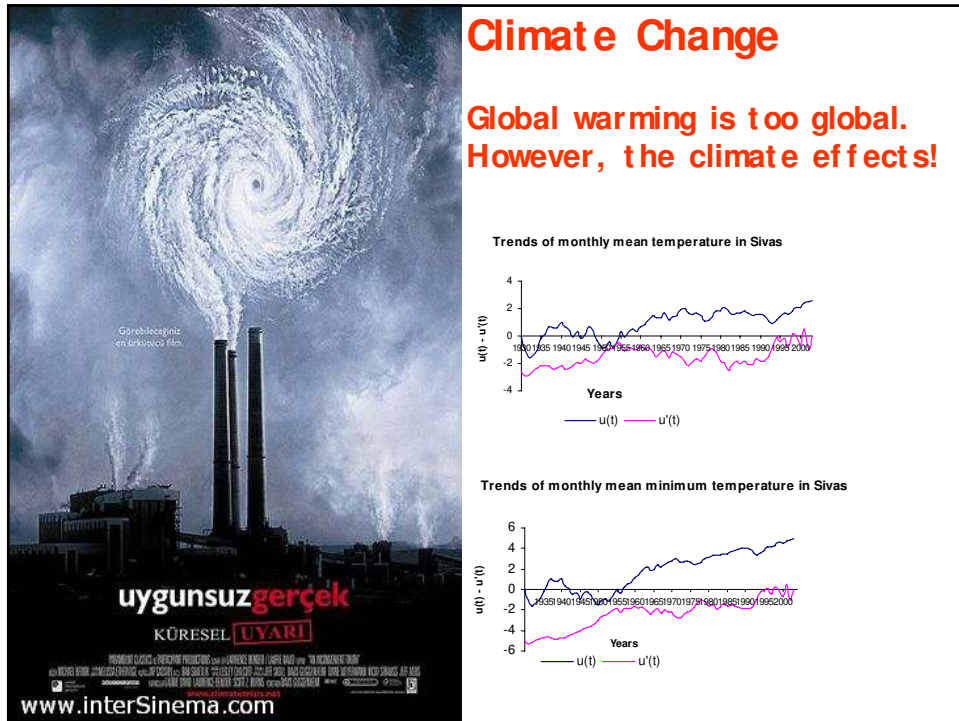
- No clinical symptoms
 - Not known in veterinary medicine
- Viremia
 - Lasts for 7-10 days in mammals

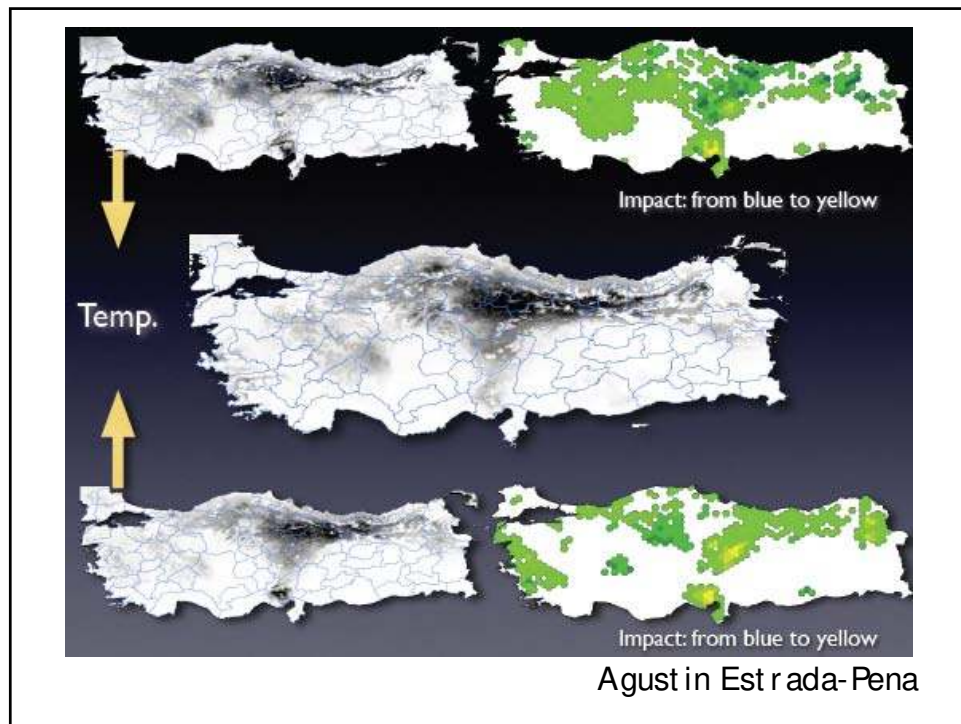


Seropositive and/ or PCR+ Animals in Turkey

- Cattle
- Sheep
- Wild boars
- Hares
- Ground feeding birds
 - Partridges etc.







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

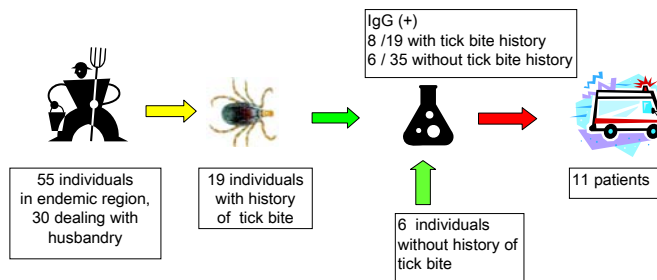
The probable case

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 attack and the infection rates of Crimean Congo Hemorrhagic Fever Virus Infection in an endemic region
 Önder Ergönül, Herve Zeller, Şirin Menekşe, Aysel Çelikbaş, Şebnem Eren, Nurcan Baykam, Başak Dokuzoğuz
 ECCMID 2006, Nice



Results

The infection rate
0.27 (15/55)

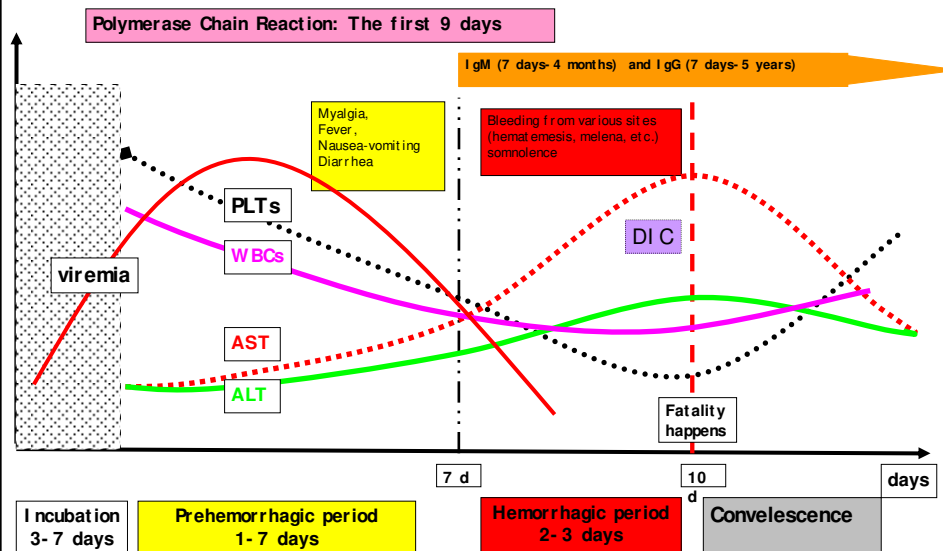
The infection rate
0.42 among the
individuals, who
had the history of
tick bite
($p=0.046$).

The attack rate
0.2 (11/55).

Conclusions

One of every five persons living in endemic area, and one of two persons with tick bite history in endemic area acquire the disease. The infection and attack rates are very high compared to other diseases.

The Clinical Course of Crimean- Congo Hemorrhagic Fever



Ergonul O. *Lancet ID* 2006; 6: 203-214



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 α , IL1, IL6

Ergonul, et al. JID 2006

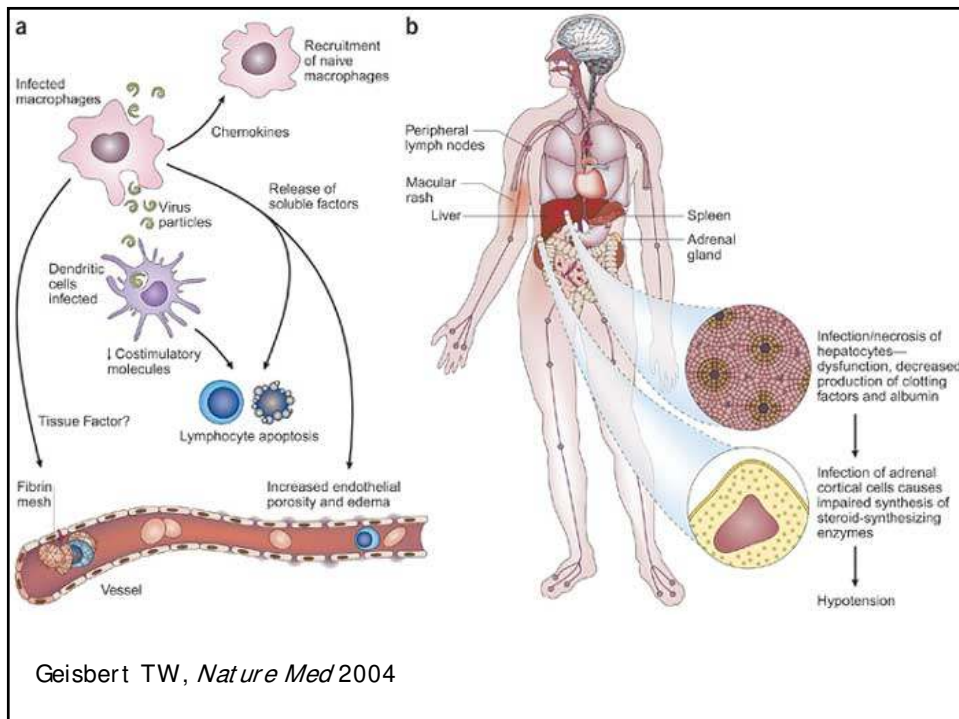
Why The Case Fatality Rates Are Different?

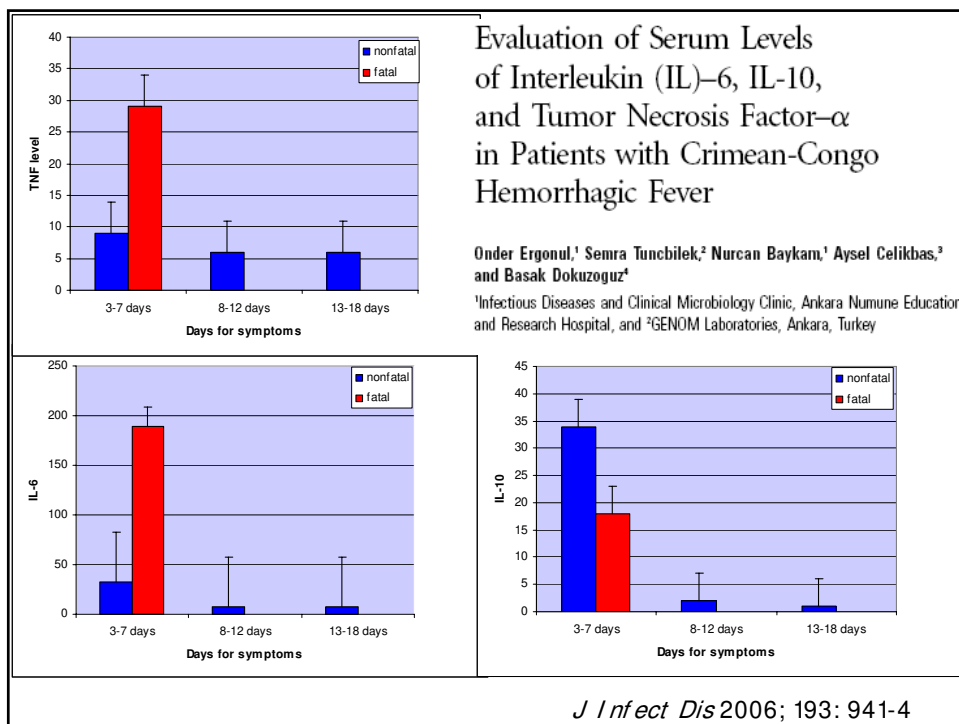
- 1) Different strains
- 2) Co-existent infections
- 3) Host factors
- 2) Health care facility
 - Access
 - Quality
- 3) Public awareness

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

Geisbert TW, *Nature Med* 2004 10: 110-121

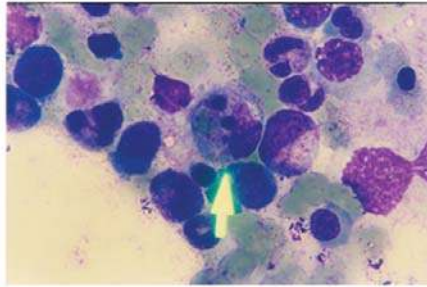




Antibody production is weaker among fatal cases

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

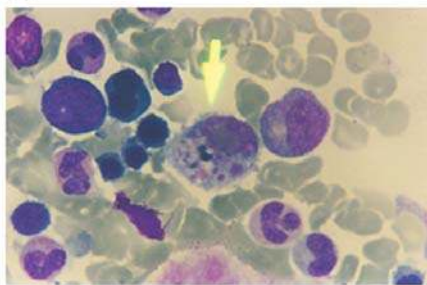
A



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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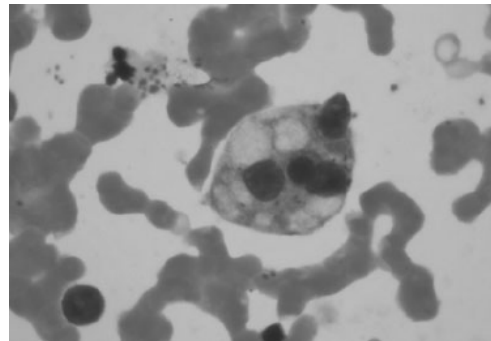
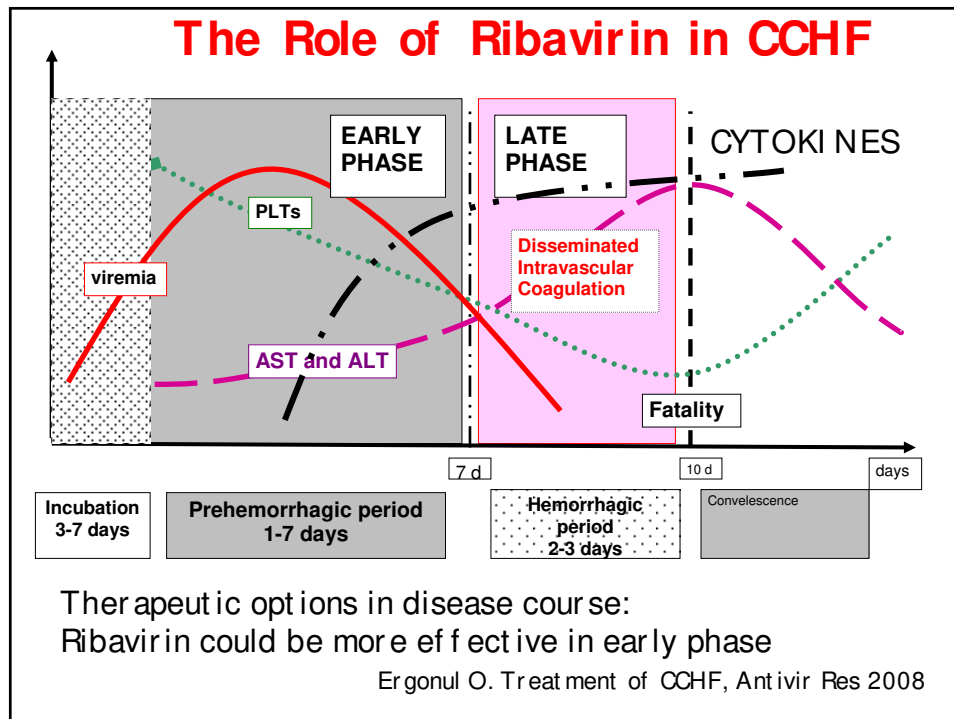


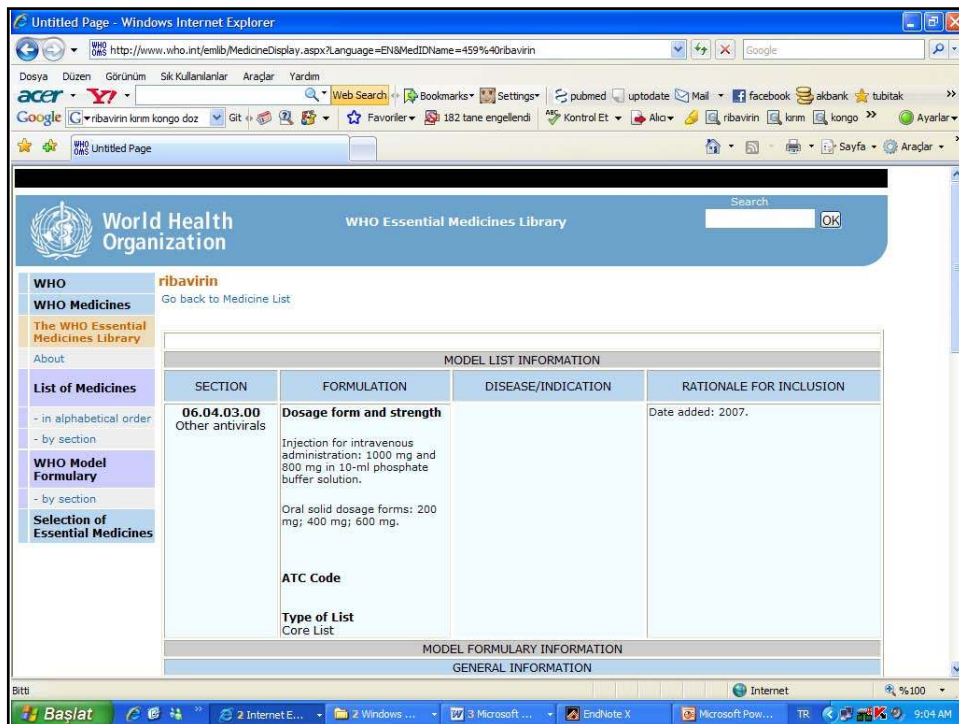
Figure 5. Hemophagocytosis in the bone marrow aspiration smears in Patient 5.

Am J Hematol 2007

Ribavirin: Only Drug for VHFs

Arenaviridae
Lassa Fever
South America HF
Bunyaviridae
Hanta
Rift Valley
CCHF





Confounders in Ribavirin use

1. Severity
2. Number of Days from onset of symptoms
 1. Prehemorrhagic
 2. Hemorrhagic
3. Ineffective application:
 - GI Symptoms in oral use (hematemesis)
4. Duration of treatment
5. Inclusion criteria

Health Care Workers infected by CCHF

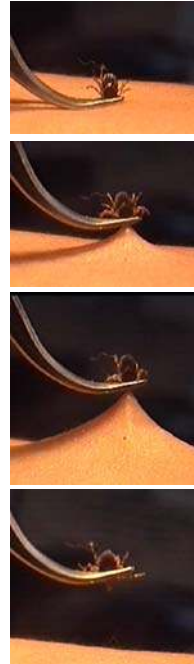
Country	Year	infected	fatal
Bulgaria	1950-1974	42	17
South Africa	1967	5	?
	1984	7	1
Pakistan	1976	4	2
	1994	3	?
	2002	2	1
Iraq	1979	2	2
United Arab Emirates	1979	5	2
Albania	2002	1	0
Moritania	2003	5	5
Turkey	2003	1 (?)	1
	2005	3	-
	2006	1	1
	2008	8	1
TOTAL		88	32

Case Management

Suspected case	Clinical symptoms History Biochemical tests
Preventive measures	Isolation of the patient Education of the HCWs Use of barrier precautions
Confirmation of dx	PCR ELISA
Decision for tx	Definition of severity criteria and ribavirin use Differential diagnosis and doxycycline Hematologic support Respiratory support
Follow-up	No recurrence HCWs

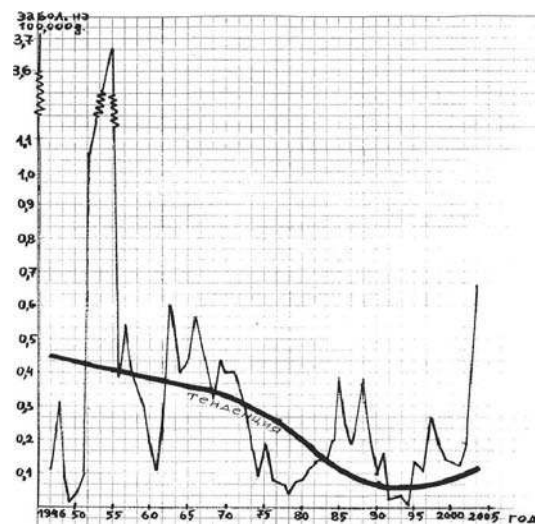
Ergönül O. *Lancet Infect Dis* 2006

Tick removal: What is the best way?



Vat ansever Z, I n: Ergonul & Whit ouse,
Crimean-Congo Hemorr hagic Fever :
A Global Perspect ive, Springer, 2007

Vaccination experience is limited to Bulgaria Efficacy: We need more clarity



Dr. Nikolai Kalvat chev

Bulgarian Experience

Passive simultaneous transfer of two different specific immunoglobulin preparations,

“CCHF-bulin” (for intramuscular use)

“CCHF-venin” (for intravenous use),

prepared from the plasma of CCHF survivor donors (Vassilenko et al., 1990).

Only 7 patients

Turkish Experience on CCHF

1. Acceleration phase of the epidemic curve:
Every year, more cases than a year ago.
2. Dissemination of the cases to the west.
3. More HCWs have been affected.
 1. Protection of HCWs
 2. Infection Control in Hospitals
4. Debate on ribavirin use: RCT?
5. Personal protection
 1. How to remove ticks?
 2. Repellents, permethrine

“I was tired, and what was the use? I must have examined the stomachs of a thousand mosquitoes by this time. But the Angel of Fate fortunately laid his hand on my head”

Sir Ronald Ross, 1857-1932

How long should we wait?

Thank you