

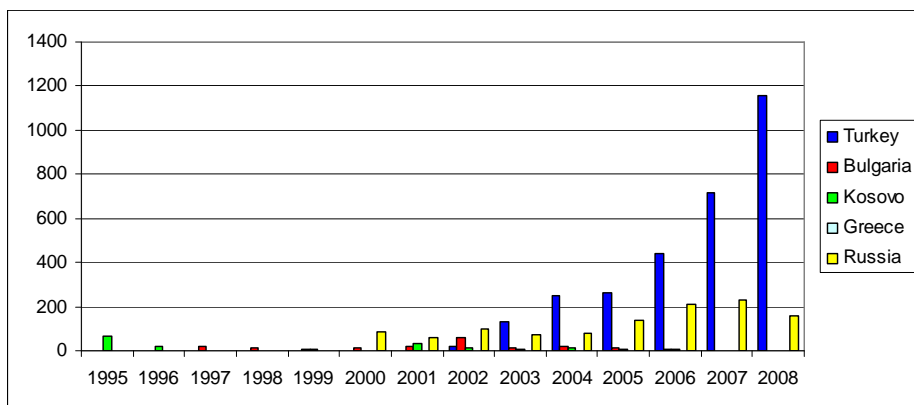
Crimean-Congo Hemorrhagic Fever

Onder Ergonul, MD, MPH

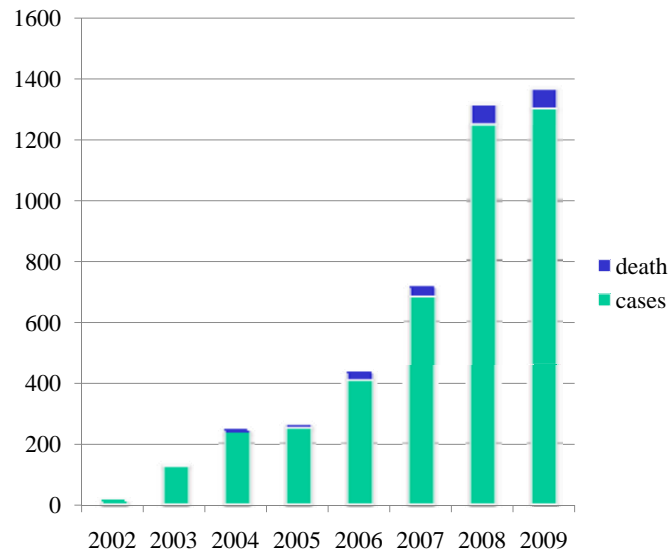
Marmara University, School of Medicine
Infectious Diseases Epidemiology Research Center
Istanbul, Turkey

April 28 2010, Verona

CCHF in Europe



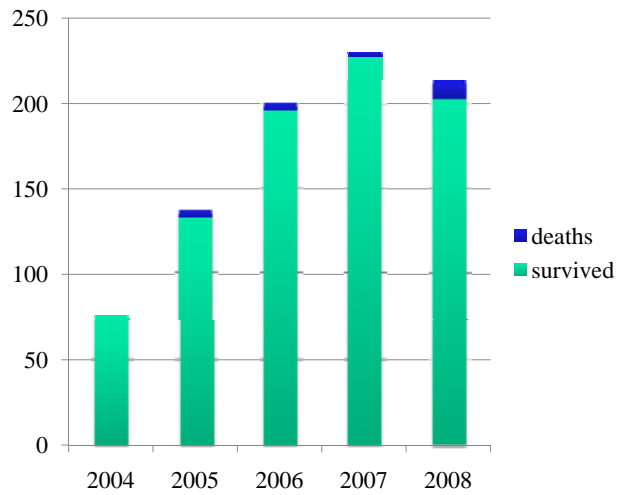
CCHF cases in Turkey



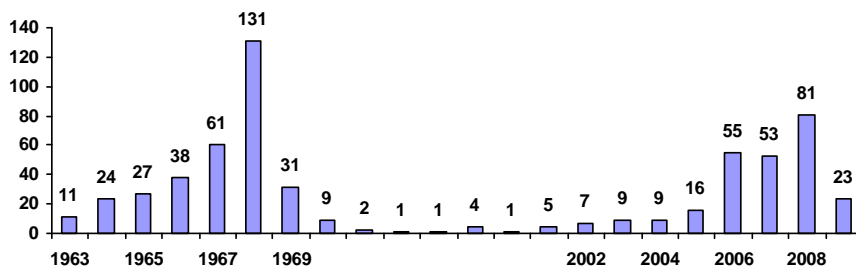
Unexpected deaths (young people) in 2009 in Turkey

- CCHF : 65
- Pandemic H1N1 : 600
- Occupational accidents in dockyards : >40
- Honor crime (all women) : >100
- Traffic accidents : 5000

CCHF Cases in Russia

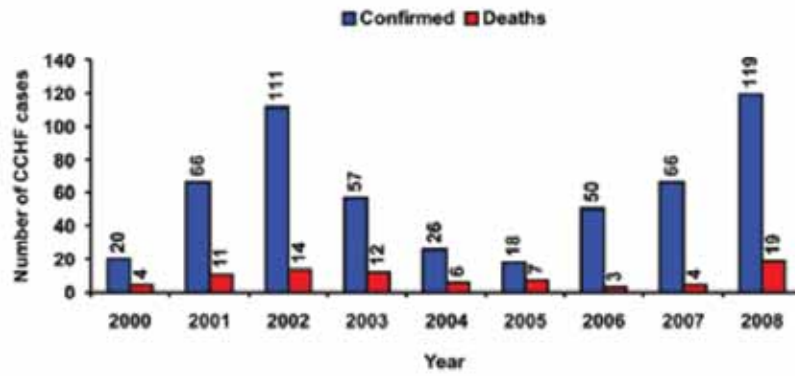


CCHF cases in the Rostov region for 1963-2008



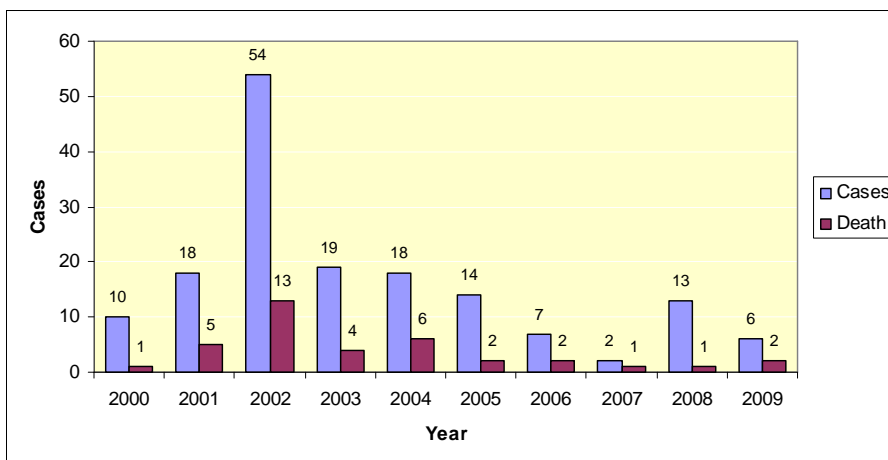
Cold winters in late 1960s; Hoogstral, 1979
Dr.Natalia Preschnekaya

CCHF in Iran

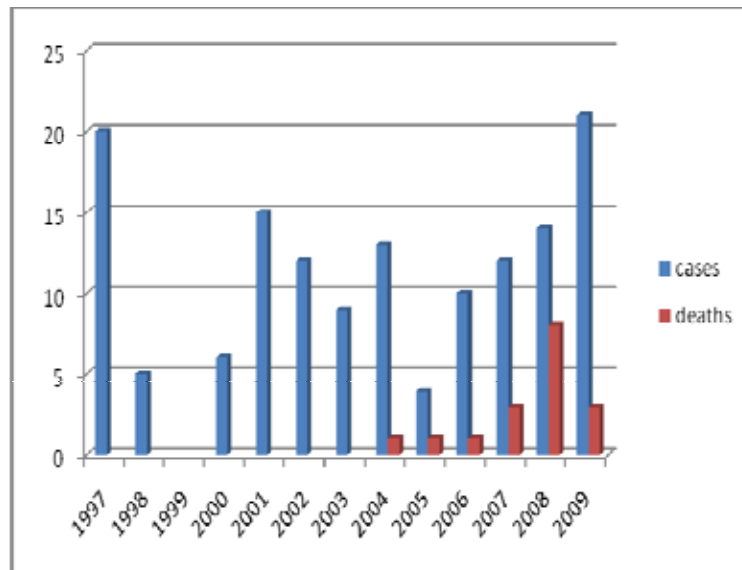


Chinikar S. Arboozonet, newsletter 02

CCHF in Bulgaria



CCHF in Tajikistan

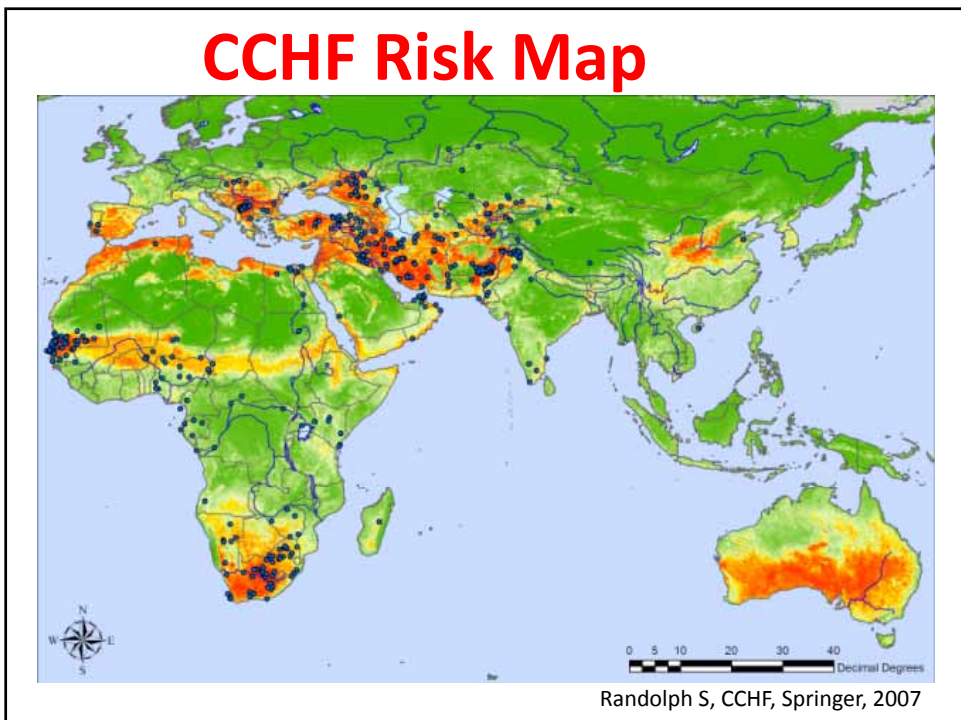
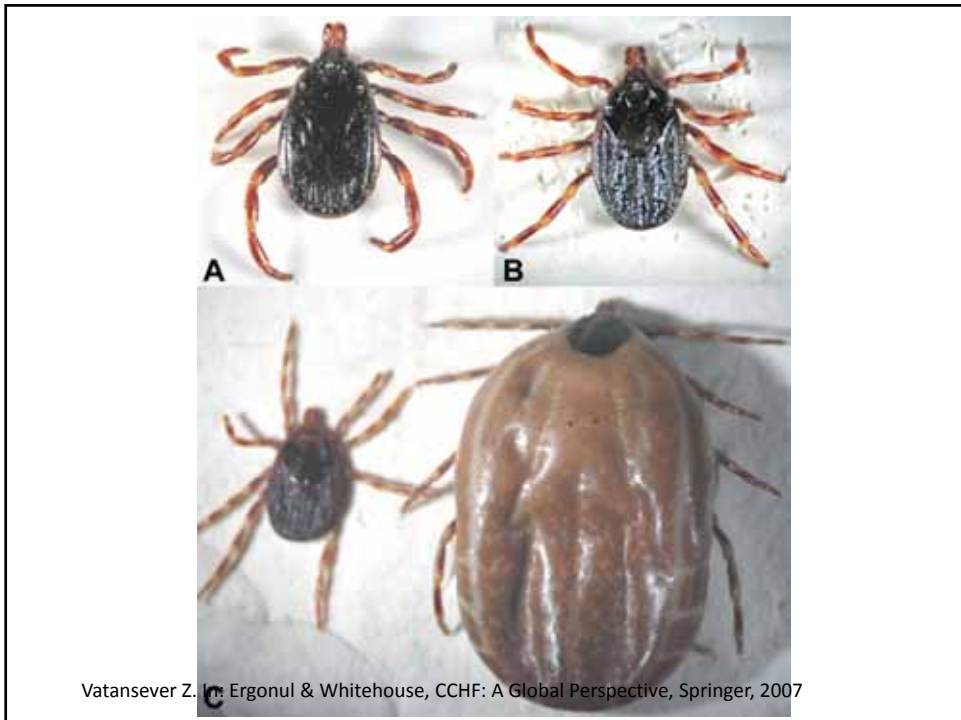


The First Clinical Case in 2008 in Greece

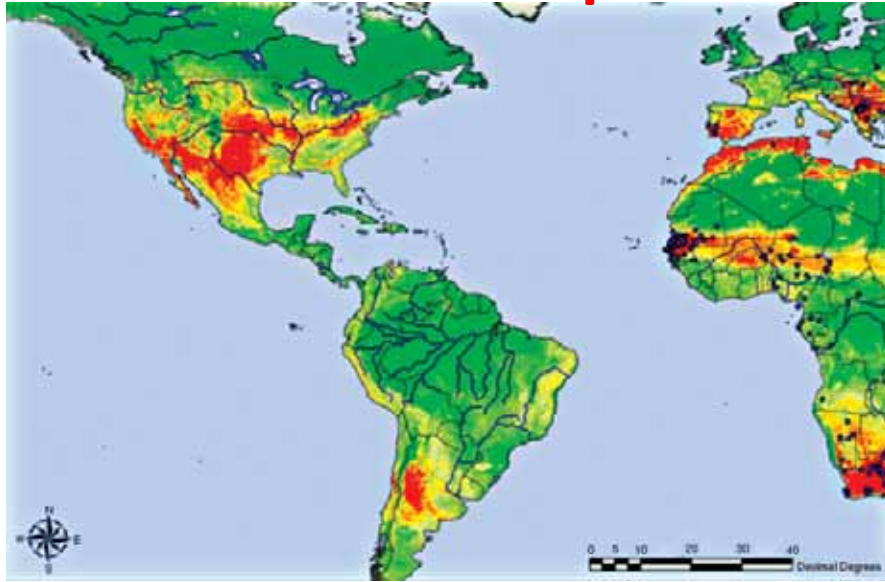
FIGURE
Map of Greece showing the area where a case of Crimean-Congo haemorrhagic fever was reported in June 2008



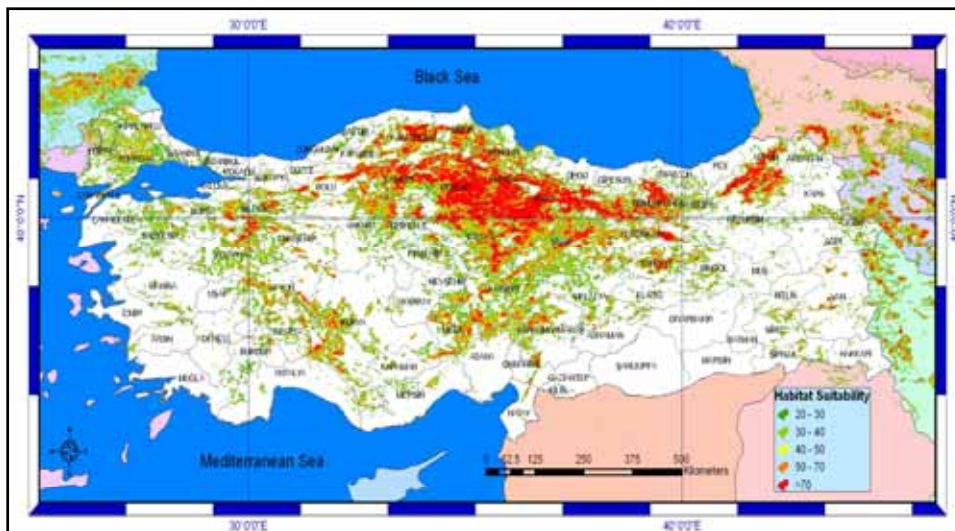
Papa A, Maltezou HC, et al. Euro Surveill 2008



CCHF Risk Map

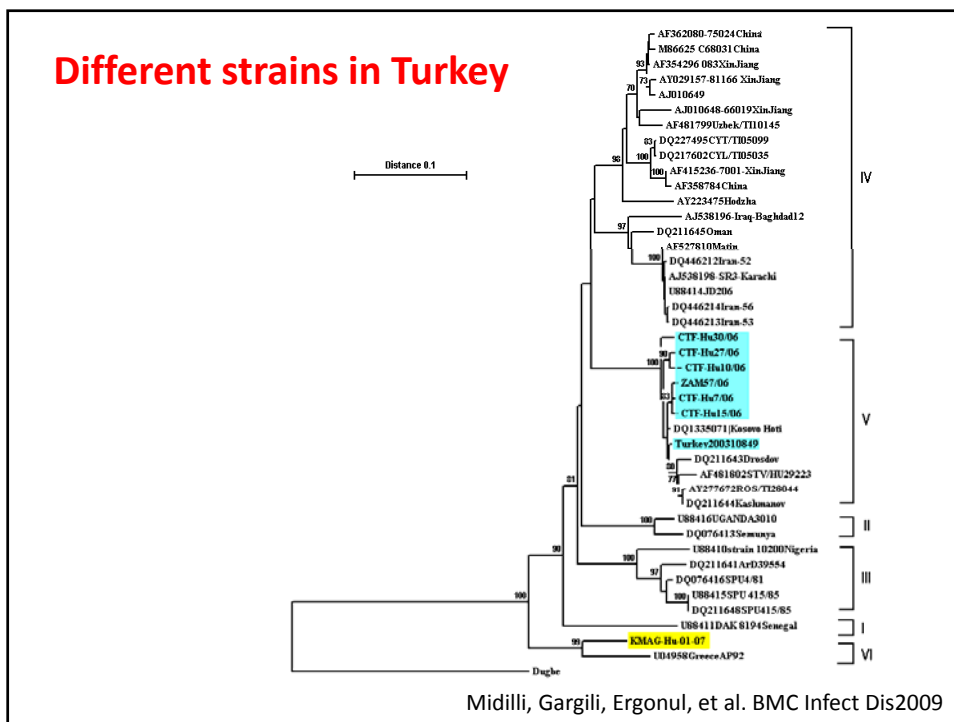
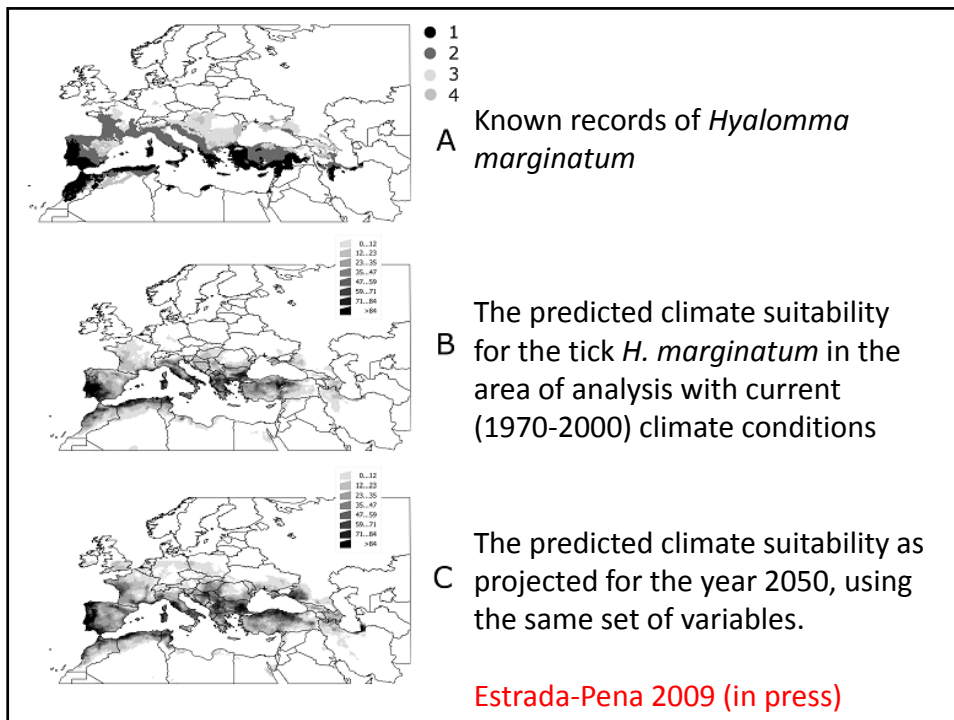


Randolph S, CCHF, Springer, 2007



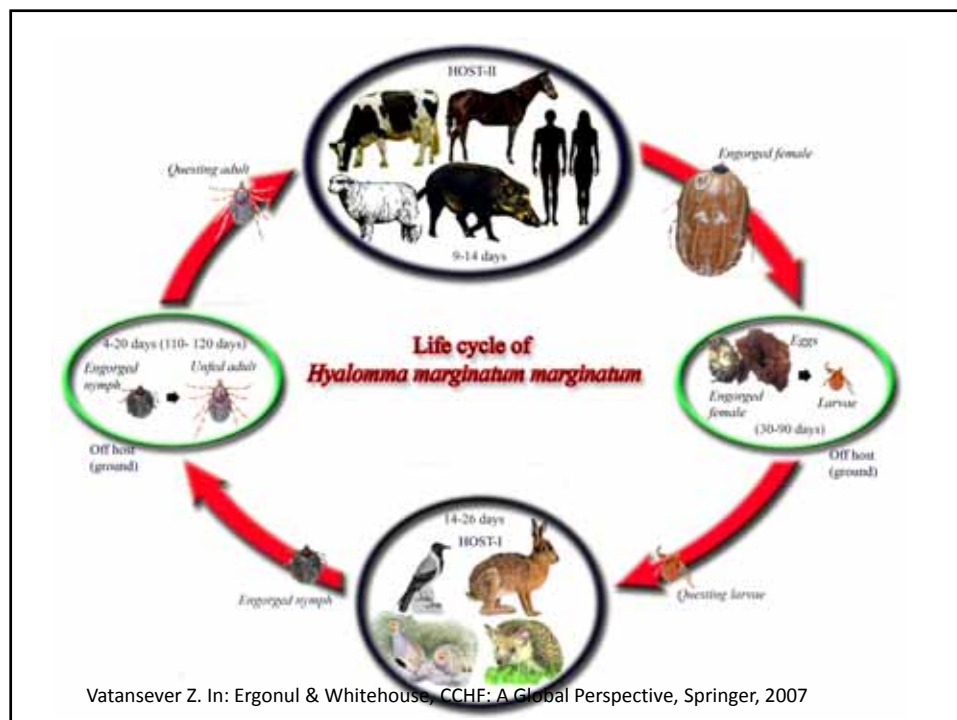
H. marginatum spp. (MaxEnt algorithm)

Vatansever, Z, et al. In: CCHF. Ergonul & Whitehouse, Springer, 2007



Why The Case Fatality Rate Differs?

1. Different strains
2. Co-existent infections ?
3. Health care facility
 - Access
 - Quality
4. The sensitivity threshold for the symptoms:
inflation of denominator by milder cases
5. Public awareness



Changes in Biotic Environment

De-population

Increase in vectors and reservoirs

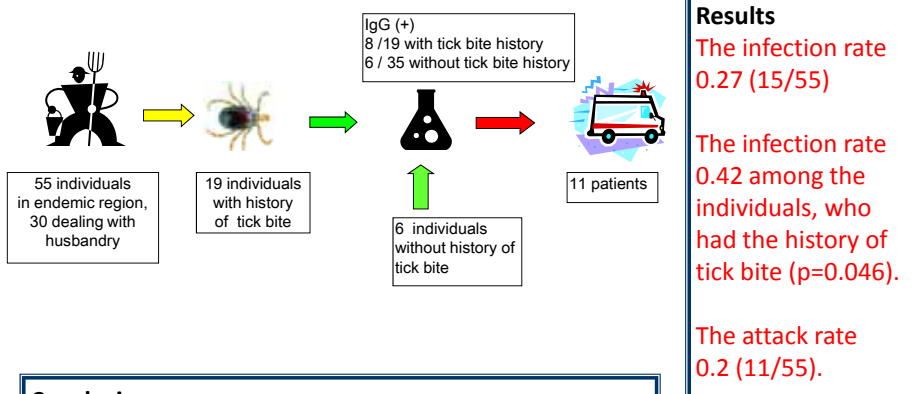


Re-population

Sudden Exposure

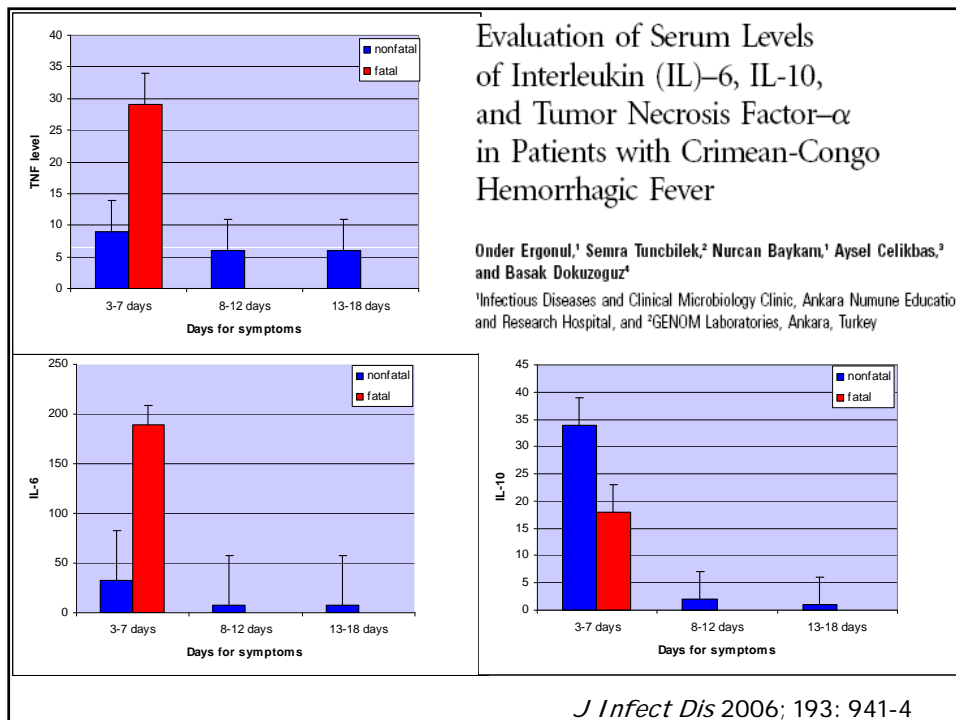
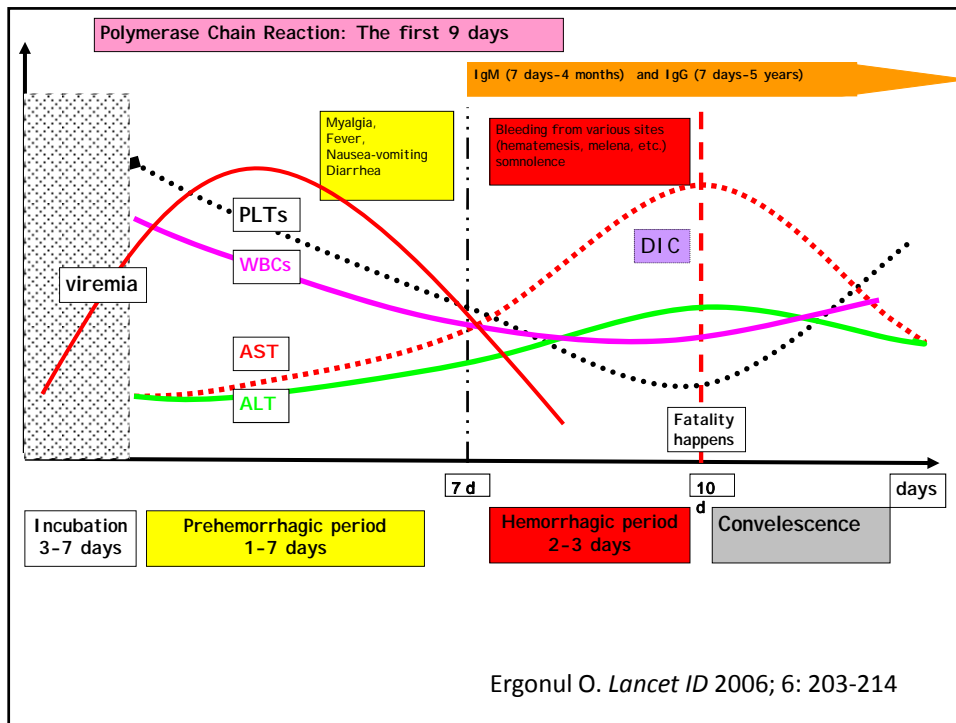


The attack and the infection rates of Crimean Congo Hemorrhagic Fever Virus Infection in an endemic region Önder Ergönül, Herve Zeller, Şirin Menekşe, Aysel Çelikbaş, Şebnem Eren, Nurcan Baykam, Başak Dokuzoğuz ECCMID 2006, Nice

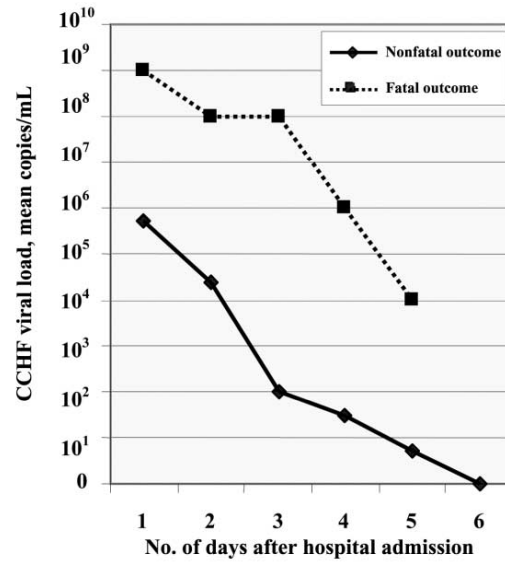


Conclusions

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.



Viral Load is Higher Among Fatal Cases



Cevik, et al. Clin Infect Dis 2007
 Duh, et al. Emerg Infect Dis 2007

Antibody production is weaker among fatal cases

	Patients survived n=50	Fatal cases 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)

Ergonul, et al. CMI 2006

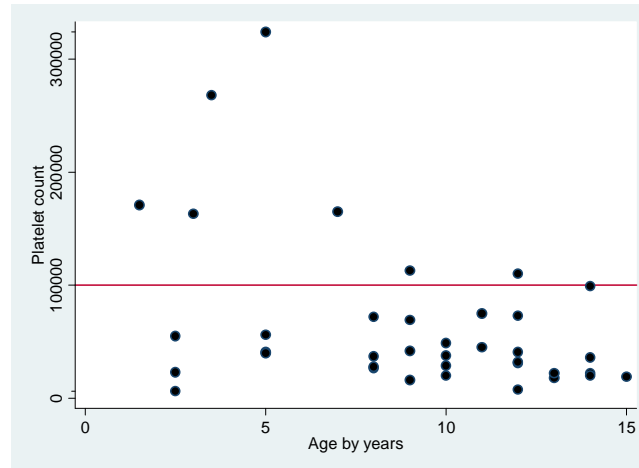
CCHFV delays activation of the innate immune response.

Andersson I, J Med Virol 2008

Fatality Among Children

33 children in Iran: 24% (Sharifi-Mood, et al. Ped Infect Dis J 2008)

42+16 children in Ankara: 0% (Etlik ve Dr.Sami Ulus, in press)



The goal of the therapy is
the prevention of fatality

Ribavirin Use in VHF

Arenaviridae
Lassa Fever
South America HF
Bunyaviridae
Hanta
Rift Valley
CCHF

Ribavirin is effective in vitro

Effective in vitro

Watts DM, et al. Am J Trop Med Hyg 1989

Inhibits viremia among rats

Tignor GH, et al. Antiviral Res 1993

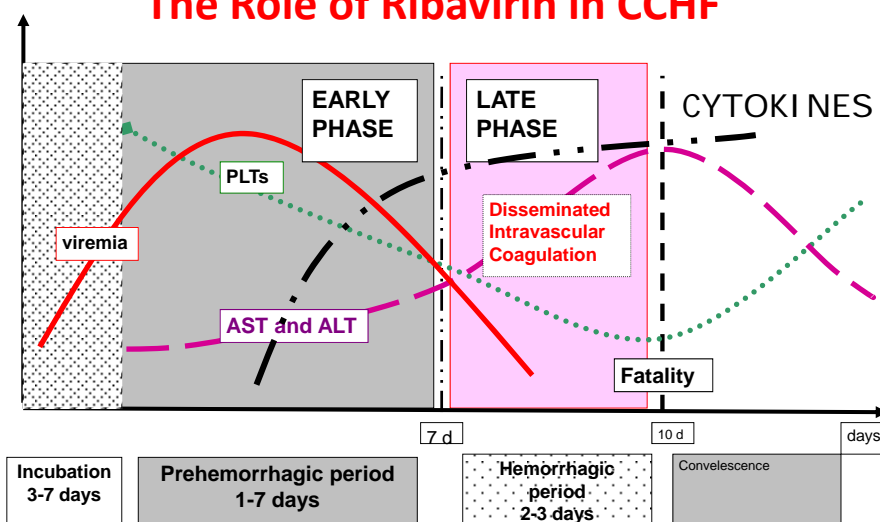
The most effective among the alternates

Paragas J, et al. Antiviral Res 2004

Clinical Observations: Case series, historical control

Author, year	Cases	Fatality in ribavirin group	Fatality in no ribavirin group
Fisher-Hoch 1995	3 SÇ	0/3 (0%)	-
Mardani 2003	69	42/139 (30%)	22/48 (46%)
Ergonul 2006	45	0/22 (0)	1/23 (4.3%)
Ozkurt 2006	26	2/22 (9%)	4/38 (10.5%)
Elaldi, 2009	218	126 (7.1%)	92 (11.9%)

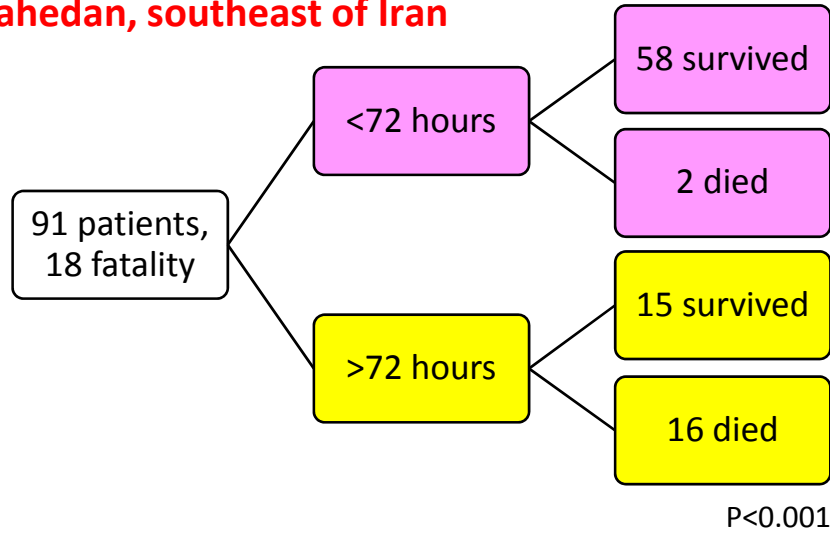
The Role of Ribavirin in CCHF



Ribavirin could be more effective in early phase

Ergonul O. Treatment of CCHF, Antivir Res 2008

**Early Ribavirin Use in CCHF:
Zahedan, southeast of Iran**



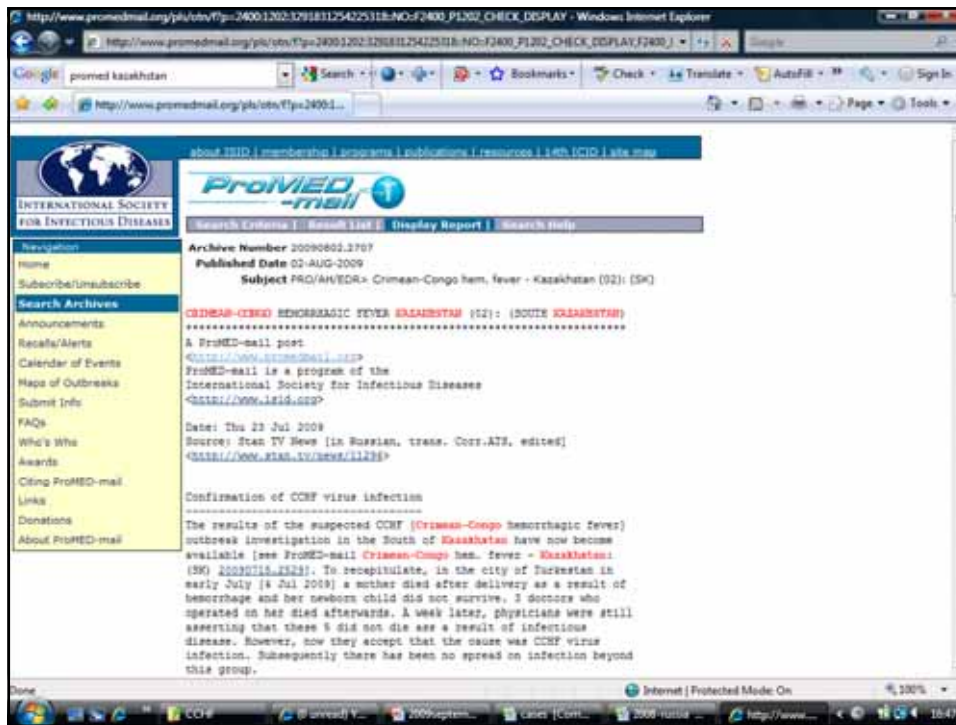
Sharifi-Mood B, et al. Arch Iran Med 2009

VHF	Human to human transmission
Ebola	High
Marburg	High
Lassa	Moderate
S.America	Low
Hantaan	No
RV	No
CCCF	High
Yellow fever	No
Dengue	No
Omsk	Not reported
Kyasanur	Not reported
Alkhumra	Not reported

Health Care Workers infected by CCHF

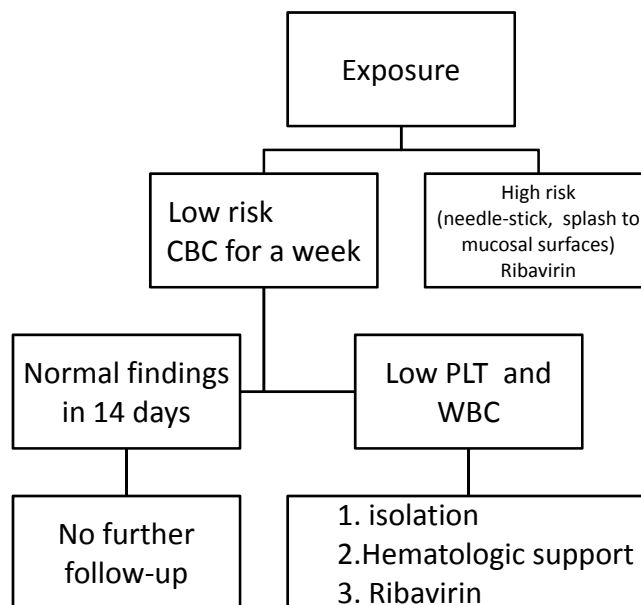
Country	Year	infected	fatal
Bulgaria	1950-1974	42	17
South Africa	1967	5	?
	1984	7	1
Pakistan	1976	4	2
	1994	3	?
	2002	2	1
Iraq	1979	2	2
United Arabic Emirates	1979	5	2
Albania	2002	1	0
Moritania	2003	5	5
Turkey	2003	1	1
	2005	3	-
	2006	1	1
	2008	8	1
	2009	1	1
Tajikistan	2009	1	1
Kazakhstan	2009	3	3







Post-exposure Prophylaxis



Areas for Improvement in Case Management

	Resource poor	Mid-income	Ideal conditions
Case detection	Lack of awareness, medical seek at the late stage	Moderate-High level of awareness	High level of awareness
CBC, ALT, AST	Not available or manual	Automated, available	Automated, available
Confirmation by PCR	Not available	Central, late result	On site, Rapid result
Blood products	Not available	Apheresis	apheresis
Antiviral	Not available	Available	Available
PPE	Not appropriate More deaths of HCWs	Appropriate in general	Appropriate

Problem areas	Needs	Limitations
Diagnosis	Standard case definitions Rapid and cheap diagnostic test	Lack of efficient international collaboration
Transmission dynamics	Ro Detection in nature Serosurveys	Difficulties with national authorities
Risk Prediction	Risk maps Models	Difficulties with national authorities
Treatment	No new antivirals Ribavirin RCT debate	Small market, No interest
Prevention	Vaccine	Small market, No interest
Vector control	Repellents	No money No study
Education	Realistic, convincing material with no panic	Lack of know how