

KIRIM- KONGO KANAMALI ATEŐİ

Nasıl Tanırım?
Nasıl Tedavi Ederim?

Doç Dr Aysel Kocagöl Çelikbaş

ANKARA NUMUNE EĞİTİM VE ARAŐTIRMA HASTANESİ
ENFEKSİYON HASTALIKLARI VE KLİNİK MİKROBİYOLOJİ KLİNİĞİ

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27.03.2013



Kanamalı Ateş Virüsleri

Filoviridae

- Marburg Kanamalı Ateşi
- Ebola Kanamalı Ateşi

Arenaviridae

- Lassa ateşi
- Arjantin Kanamalı Ateşi
- Bolivya Kanamalı Ateşi
- Venezuela Kanamalı Ateşi
- Brezilya Kanamalı Ateşi

Flaviviridae

- Sarı humma
- Dang Kanamalı Ateşi
- Kyasanur Ormanı hastalığı

Bunyaviridae

- Hanta virüs RS
- Hanta virüs PS
- Rift vadisi ateşi
- Kırım Kongo Kanamalı ateşi

Viral haemorrhagic fevers

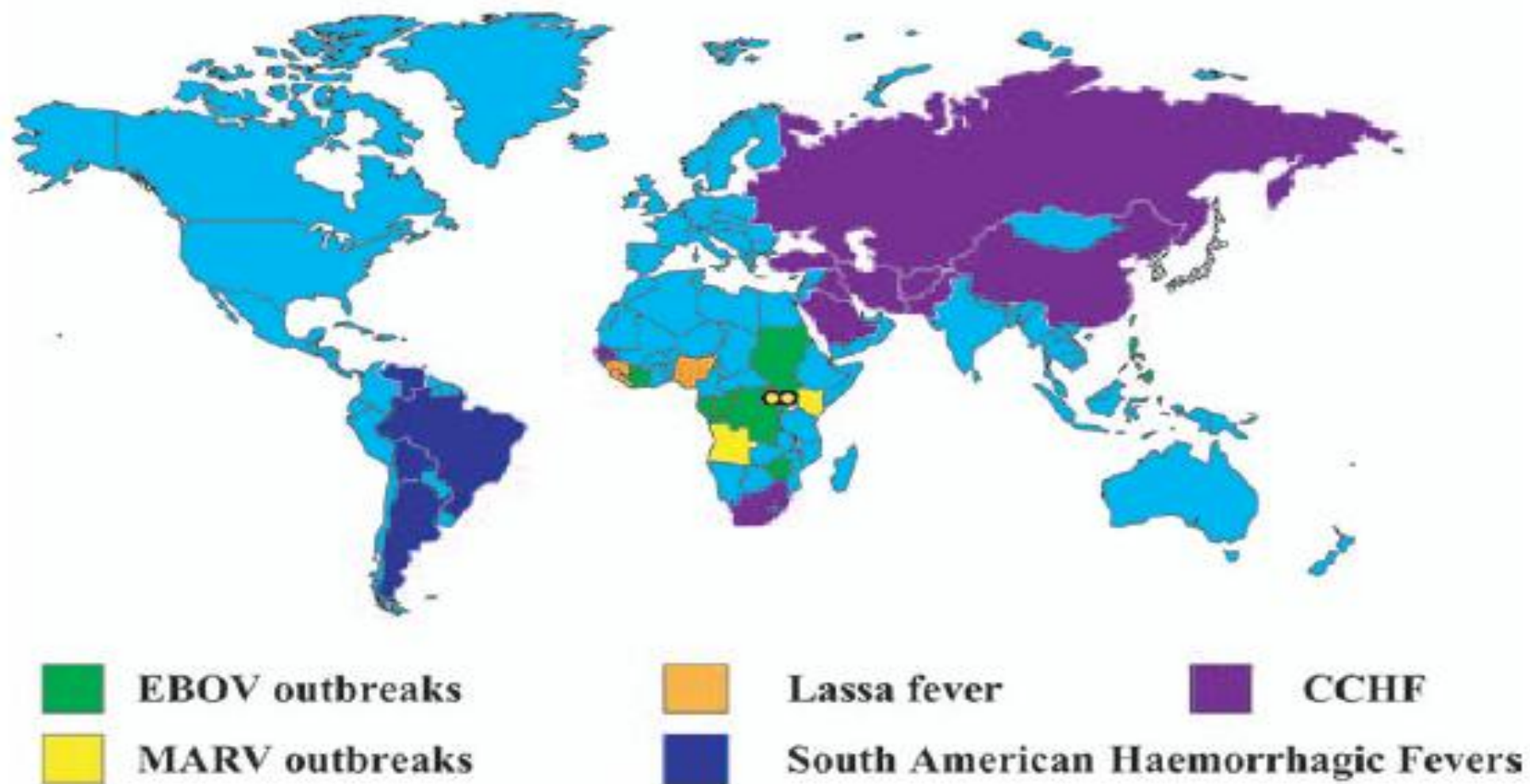


Fig. 1 Map of the world showing those countries known in 2005 to be affected by viral haemorrhagic fever (VHF) viruses. All those marked produce nosocomial outbreaks, with the exception of the South American haemorrhagic fever viruses. CCHF, Crimean–Congo haemorrhagic fever; EBOV, Ebola virus; MARV, Marburg virus.



Viral Kanamalı Ateş (VKA)

2002 2004

Kırım
Kongo
Kanamalı
Ateşi

2013





Tokat, Yozgat, Sivas, Erzurum, Erzincan,
Çorum, Çankırı, Bolu, Kastamonu, Karabük

İran 1975

Am J Trop Med Hyg. 1975 Mar;24(2):353-7.

Crimean hemorrhagic fever-Congo (CHF-C) virus antibodies in man, and in domestic and small mammals, in Iran.

Saidi S. Casals J. Faghih MA.

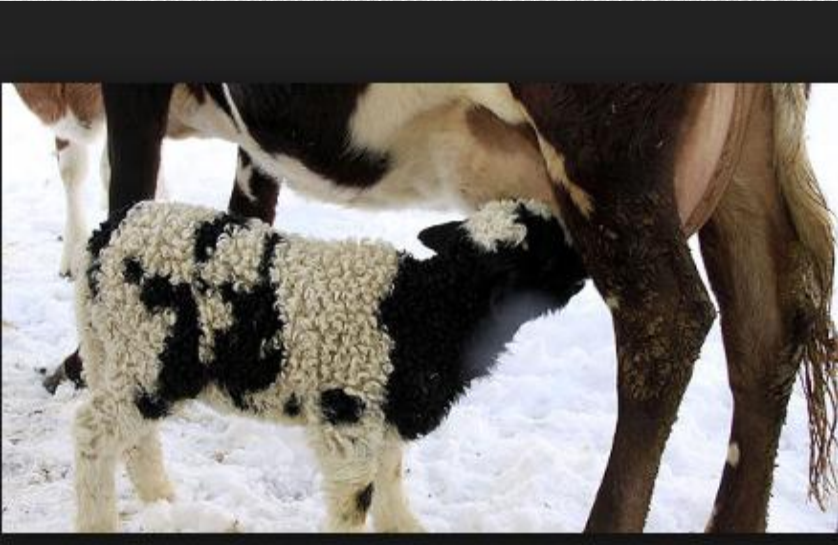
Abstract

A Crimean hemorrhagic fever-Congo (CHF-C) virus antibody survey was carried out in Iran with sera from man and several animal species; this survey was done by means of agar gel diffusion precipitation (AGDP) test with the following results (percent positive of number tested): men, 13% of 351; sheep, 38% of 728; goats, 36% of 135; cattle, 18% of 130; camels, 0% of 157; small mammals, 3% of 274. A number of sera were tested by complement-fixation (CF), neutralization (N), and hemagglutination-inhibition (HI) tests in addition to the AGDP test. A good correlation was found in the results with 105 sera tested by AGDP, HI, and N, with approximately 70% to 75% positive in all three tests; by CF, only 20% were positive. Of 55 human sera, of which 15 could be tested by N test, about half were positive by AGDP and only 10% by HI at low titers; none was positive by N and CF tests. These results suggest that any one of the three serological tests (N, HI, and AGDP) can be used to survey the antibody prevalence in sera from domestic animals; the CF test, not unexpectedly, was less suitable. Our results, however, are inconclusive in regard to the human sera.

Agar jel diffüzyon presipitasyon

- ❖ İnsan serumlarında %13
- ❖ Koyun %38
- ❖ Keçi %36
- ❖ Sığırlar %18
- ❖ Develer % 0
- ❖ Küçük memeliler %3

Bulaş





02 Ağustos 2012, 13:24

DİKKAT! TBMM Raporuna Göre Kene Virüsü Ajan Olabilir!:

TBMM uzmanlarının Kırım
Kongo Kanamalı Ateşi ile

ilgili hazırladığı rapordan: Biyoterörizm veya biyolojik savaş ajanı olarak kullanılmasından korkulmaktadır.

KKKA- Risk Grupları

- ❖ Endemik bölgede yaşayanlar
- ❖ Endemik bölge
- ❖ Kasaplar, mez
- ❖ Çobanlar
- ❖ Veteriner hek
- ❖ Sağlık çalışan
- ❖ Laboratuvar g
- ❖ Endemik bölge
- ❖ kuranlar, piknikçiler
- ❖ Avcılar



Initial high rate of misdiagnosis in Crimean Congo haemorrhagic fever patients in an endemic region of Turkey

N. TASDELEN FISGIN*, L. DOGANCI, E. TANYEL AND N. TULEK

Retrospektif çalışma
2004 -2008,

140 konfirme erişkin o

95 olgu başlangıçta KK

Olguların % 23'ü antibi

% 32 KKA

% 45 Üst Solunum Yolu Enfeksiyonu

% 5 Gastrointestinal Sistem Enfeksiyonu

% 5 Alt Solunum Yolu Enfeksiyonu

% 4 Etiyolojisi Bilinmeyen Pansitopeni

% 2 İdrar Yolu Enfeksiyonu

%1.5 Gastrointestinal hemoraji

%1.5 Leptospirozis

Kırım Kongo Kanamalı Ateşini Nasıl Tanırım ?-1

Anamnez

- Hastanın geldiği yer (endemik bölgelerin bilinmesi ve sorgulanması)
- Çevrede benzer hastalık ?
- Kene teması: Kene tutması
- Enfekte çiftlik hayvanları ile temas:
 - Hayvanlardan çıplak ellerle temas
 - Hayvan kesme
 - Et doğrama



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From: [Emerg Infect Dis. 2012 April; 18\(4\): 640–642.](#)

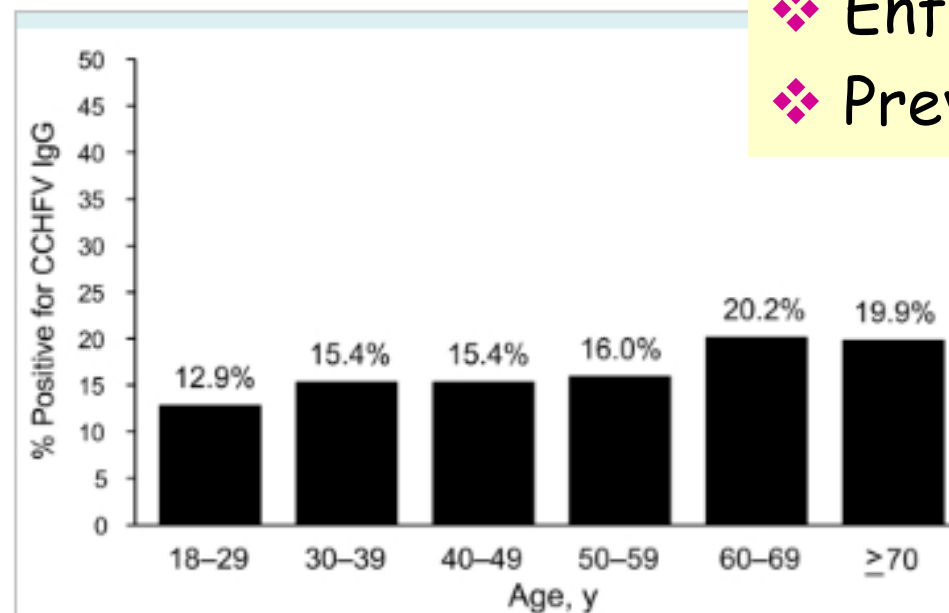
doi: [10.3201/eid1804.111374](#)

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PMC3309668

Figure 2



Distribution of Crimean-Congo hemorrhagic fever virus (CCHFV)–positive persons, by age group, Turkey, January–April 2009.

- ❖ Endemik Bölgede seroprevalans %10
- ❖ Enfeksiyonun %88'i asemptomatik
- ❖ Prevalans yaşla artıyor

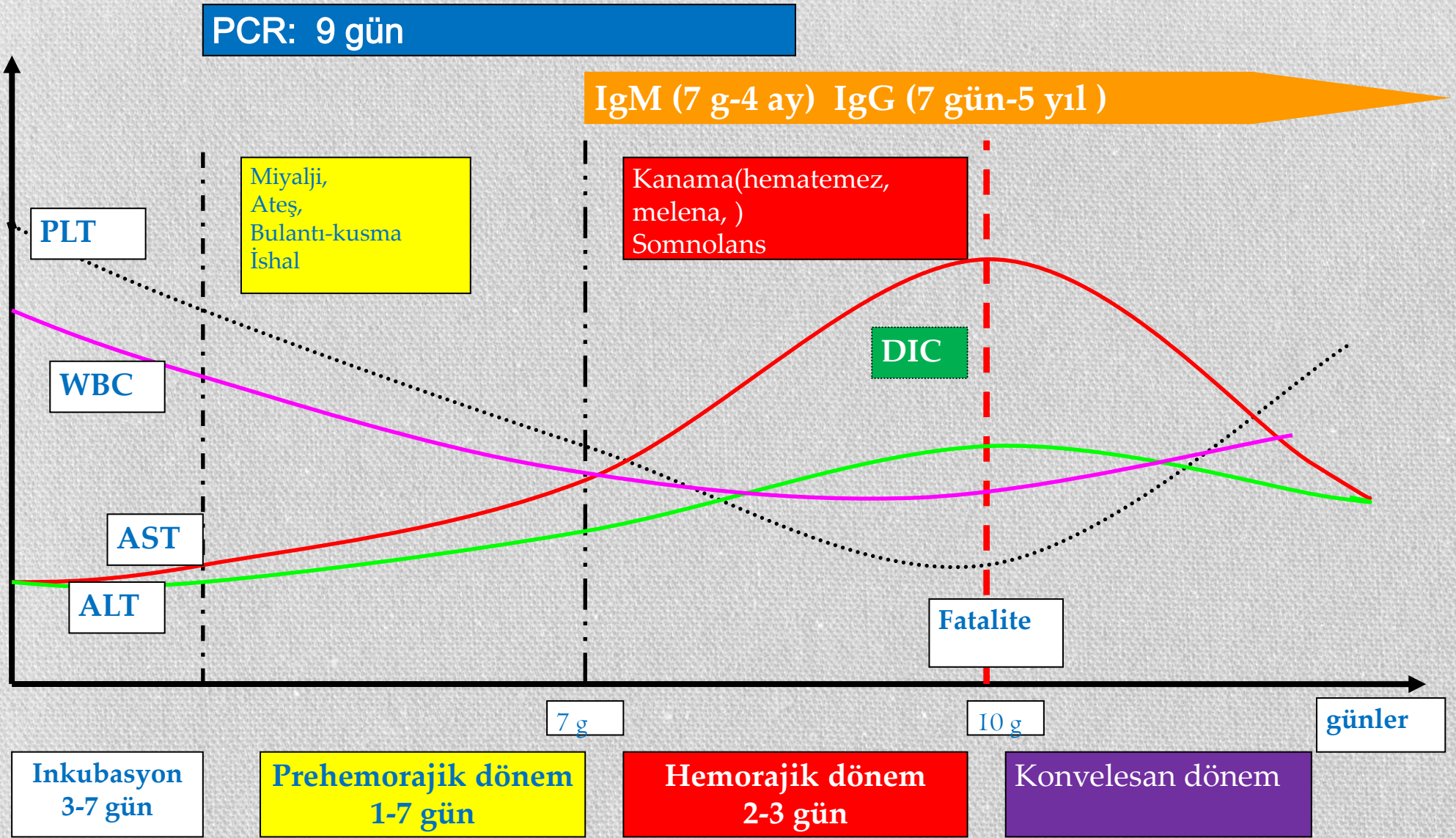
[Go to:](#)

[Epidemiologic
outbreak
in Turkey.](#)

[uses,](#)

Klinik Seyir

- ❖ İnkubasyon
- ❖ Prehemorajik dönem
- ❖ Hemorajik dönem
- ❖ Konvelesan dönem



KKKA - Semptomlar

- ❖ Ateş
- ❖ Üşüme - titreme
- ❖ Baş ağrısı
- ❖ Baş dönmesi
- ❖ Karın ağrısı
- ❖ Bulantı-kusma
- ❖ İshal
- ❖ Halsizlik
- ❖ Miyalji

KKKA- Klinik Bulgular

❖ Ateş (38°)

❖ Konjunktival hiperemi

❖ Hepatomegali -splenomegali

❖ Döküntü

Peteşi

Makulopapüler

❖ Kanama

Epistaksis

Hematemez

Melena

Hematüri

Hemoptizi

İntraabdominal

Vajinal

❖ Stupor (İntrakranial kanama)

❖ Ral (ARDS, Hemotoraks)

❖ Sarılık

❖ Böbrek yetmezliği



Hastalık Seyri

Prehemorojik Dönem

1-7 gün, ~3 gün

Ani ateş yükselmesi (4-5 gün sürer)

Baş ağrısı

Kas ağrısı

Halsizlik

İshal

Bulantı

Kusma

Yüzde hiperemi

Konjonktivit













KKKA- Laboratuvar Testleri

- ❖ Lökopeni
- ❖ Trombositopeni
- ❖ Transaminaz yüksekliği
- ❖ LDH yüksekliği
- ❖ CPK yüksekliği
- ❖ PT, aPTT uzaması

Kırım Kongo Kanamalı Ateşini Nasıl Tanırım ?-2

- Fizik muayene
- Klinik seyir
- Hemogram ve biyokimyasal testler esliğinde
- Vaka tanımlarının gözden geçirilmesi



KKKA - Vaka Tanımı

Klinik Tanımlama

- ❖ Ateş, baş ağrısı, myalji, halsizlik, bulantı/kusma, karın ağrısı / ishal
- ❖ Lökopeni, trombositopeni, yüksek AST-ALT-LDH-CK

Destekleyici bulgular

- ❖ Hemorajik - purpurik döküntü
- ❖ Diğer hemorajik semptomlar.

Epidemiyolojik hikaye

- ❖ Kene ısırması
- ❖ Hayvanlarla yakın temas
- ❖ Kırsal alanda yaşama/ seyahat
- ❖ Hayvan doku-kanı ile temas
- ❖ Laboatuvar çalışanı
- ❖ Çevrede benzer hasta

Şüpheli vaka

- ❖ Klinik tanımlamaya uyan, başka nedenle açıklanamayan vaka

Olası vaka

- ❖ Klinik tanımlamaya uyan ve en az 2 destekleyici bulgu
- ❖ Bölgede birden fazla vaka varsa destekleyici bulgu olmaksızın klinik tanımlamaya uyan

Kesin vaka

Klinik tanımlama +

- ❖ Kan- doku örneğinde viral RNA'nın gösterilmesi
 - ❖ Spesifik IgM pozitifliği
 - ❖ Spesifik IgG titresinde 4 kat artış
- Kesin tanı almış vaka ile epidemiyolojik bağlantı

KK

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Biosafety Level 4 Labs and BSL Information

This map displays major Biosafety Level 4 (BSL-4) facilities around the world according to data collected by FAS in 2010 and 2011. These high-containment facilities are used to conduct beneficial research on dangerous and emerging pathogens.



KKKA - Laboratuvar Tanı

Seroloji

- ❖ ELİSA
- ❖ İFA
- ❖ PCR
- ❖ Kompleman Birleşme Reaksiyonu
- ❖ İmmünodifüzyon
- ❖ Reverse Pasif Hemaglütinasyon



BSL 3

KKKA: Virüs/Antikor Kinetikleri



IgM pozitifliği: 2-3 aydan 6 aya

Zeller H

Sonuç Olarak;

- ❖ Hastalığı bilmek ve akılda tutmak
- ❖ Anamnez
- ❖ Fizik Muayene
- ❖ Serolojik test (ELISA ve PCR) sonuçları tanı için yeterli



Kırım Kongo Kanamalı Ateşini
Nasıl Tedavi Ederim?

Viral yük $10^9 \uparrow$ mortal

Viral Load as a Predictor of Outcome in Crimean-Congo Hemorrhagic Fever

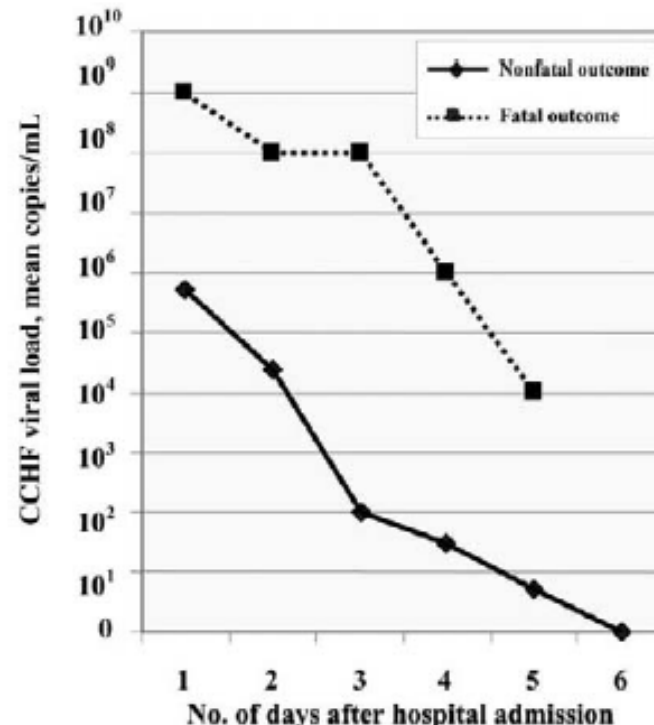
Mustafa Aydın Çevik,¹ Ayşe Erbay,¹ Hürrem Bodur,¹ Selim Sirri Eren,¹ Esragül Akinci,¹ Kenan Şener,² Pinar Öngürü,¹ and Ayhan Kubar²

¹Infectious Diseases and Clinical Microbiology Department, Ankara Numur Education and Research Hospital, and ²Department of Virology, Gulhane Military Medical Academy, Ankara, Turkey

Crimean-Congo hemorrhagic fever (CCHF) is a potentially fatal disease affecting multiple organ systems. To determine the association between viral load and severity of CCHF infection, quantitative measurement of CCHF virus was performed using 1-step reverse-transcriptase polymerase chain reaction for 36 patients with CCHF infection. Viral load ranged from 1.1×10^3 copies/mL to $\geq 9.9 \times 10^9$ copies/mL. Nine (25%) of 36 patients died. In 8 of the 9 patients with fatal outcomes, viral loads were detected that $\geq 1 \times 10^9$ copies/mL, whereas in 25 of the 26 patients with nonfatal outcomes, viral loads were detected that $< 1 \times 10^9$ copies/mL ($P < .001$). A viral load $\geq 1 \times 10^9$ copies/mL can be considered to predict a fatal outcome with a positive predictive value of 80%, with 88.9% sensitivity and 92.6% specificity. We suggest that viral load is a measure of the severity of CCHF.

first reported in Turkey in 2002 [10–12]. By the end of 2006, there were 1103 confirmed cases and 59 deaths (a case-fatality rate of 5.4%) in Turkey [4].

The usual approach for CCHF diagnosis combines the detection of the viral RNA genome and/or the antigen and the



referred from surrounding hospitals to the Infectious Diseases

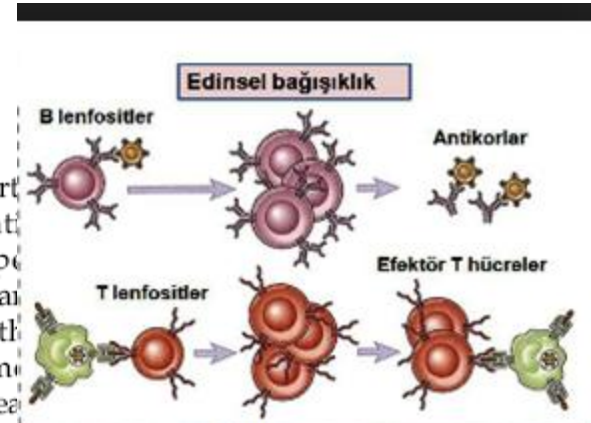
Fatal Seyirli Olgularda Güçlü bir Antikor Cevabı Gelişmiyor

O. Ergonul, A. Celikbas, N. Baykam, S. Eren and B. Dokuzoguz

Ankara Numune Education and Research Hospital, Infectious Diseases and Clinical Microbiology Department, Ankara, Turkey

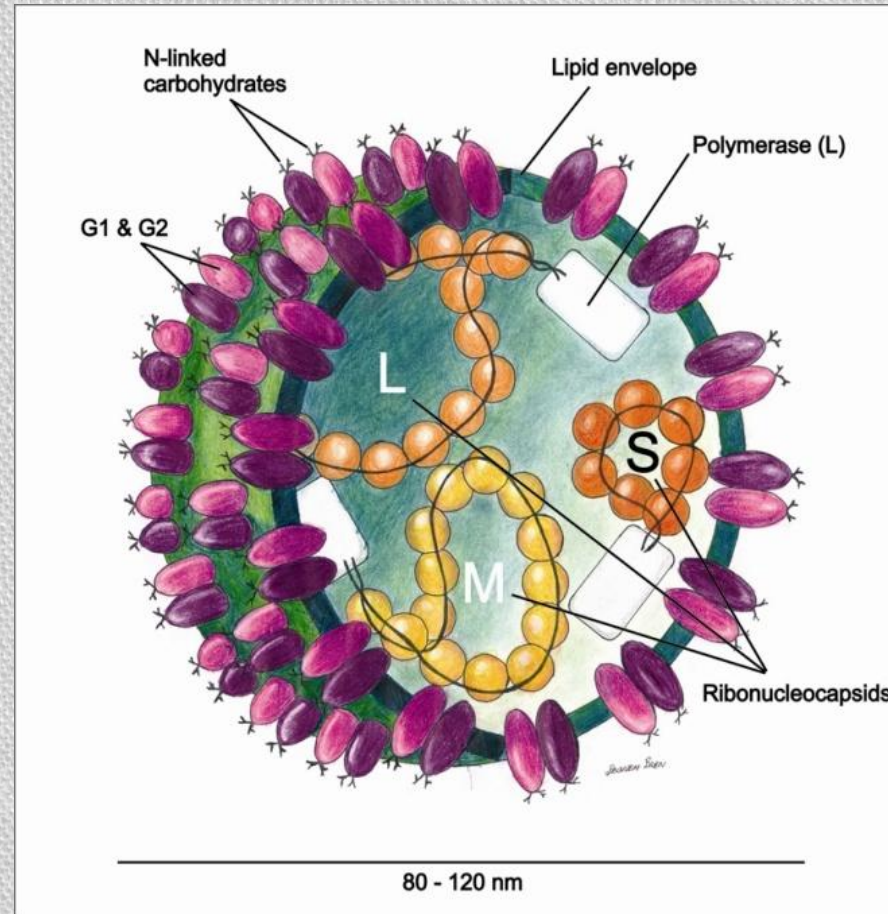
ABSTRACT

The aim of this study was to determine the predictors of mortality in patients with Crimean-Congo haemorrhagic fever (CCHF) virus. Among patients characterised by malaise, bleeding, leukopenia and thrombocytopenia during the spring and summer of 2002–2004, 54 had positive IgM antibody in blood or tissue. The overall case fatality rate was 7.4%. Among the patients with melaena ($p = 0.001$) and somnolence ($p = 0.022$) were more common. The mean platelet count was significantly lower in the fatal group (10 600/mL vs. 20 000/mL; $p = 0.038$), the mean



	Yaşayan olgular		Fatal olgular	
	n= 50	%	n=4	%
IgM pozitifliği	47	(94)	1	(25)
Ig G pozitifliği	31	(62)	0	(0)
PCR pozitifliği	19	(48)	3	(75)

Amaç 1: Viral Yükü Baskılamak !



Ribavirin

- ❖ Vero hücrelerinde in vitro viral replikasyonu inhibe eder
- ❖ Hayvan modelleri; ortalama yaşam süresini uzatır

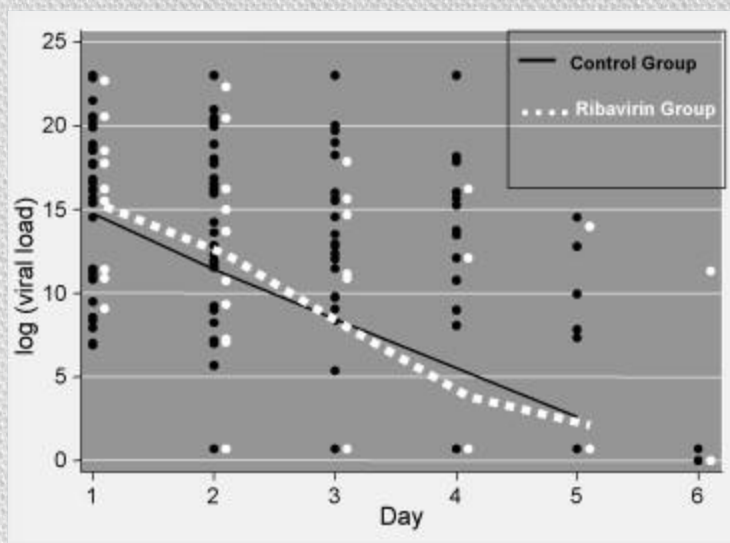
Ribavirin

- ❖ Gastrointestinal kanamaları olan hastalarda oral ilaç alımı sorunlu olabilmekte ve ilacın etkinliği açısından kuşkular gelişebilmektedir
- ❖ En önemli yan etki **anemidir**, tedavi tamamlandıktan düzelir
- ❖ Tedavinin etkinliği açısından erken tanı çok önemlidir, ciddi komplikasyonlar geliştikten sonra ribavirin tedavisinin etkinliği azalmaktadır



Effect of oral ribavirin treatment on the viral load and disease progression in Crimean-Congo hemorrhagic fever

Hürrem Bodur^{a,*}, Ayşe Erbay^a, Eşragül Akıncı^a, Pınar Öngürü^a, Nurhayat Bayazıt^a,



	Yaşayan n %	Ölen n %	Toplam n
Ribavirin +	8 (80)	2 (20)	10
Ribavirin -	34 (85)	6 (15)	40
Toplam	42	8	50

Viral yük 10^8

Eur J Clin Microbiol Infect Dis. 2009 Aug;28(8):929-33. doi: 10.1007/s10096-009-0728-2. Epub 2009 Mar 20.

The role of ribavirin in the therapy of Crimean-Congo hemorrhagic fever: early use is promising.

Tasdelen Fisgin N, Ergonul O, Doganci L, Tulek N.

- ❖ **Semptomların ilk 4 gününde başladığında**
- ❖ **Laboratuvar parametreler daha erken normale dönüyor**
- ❖ **Ribavirin tedavisine erken dönemde başlanmalı**

Original Article

**Evaluation of the Efficacy of Ribavirin Therapy on Survival of
Crimean-Congo Hemorrhagic Fever Patients: a Case-Control Study**

Shahrokh Izadi* and Masoud Salehi¹

Table 5. Temporal relationship between ribavirin prescriptions and disease events

Variable	Cured No. (%)	Deceased No. (%)	Odds ratio (95% CI)	<i>P</i>
----------	------------------	---------------------	---------------------	----------

Ölen 16 olgu

Yaşayan 47 olgu

- ❖ Yaşayan olgulara ribavirin ölenlerden 24 saat önce başlanmış
- ❖ Yaşayanlardan kanaması olmayanlara,
kanaması olanlardan 48 saat önce başlanmış
- ❖ Hastalığın ilk 4 gününde başlanırsa etkili

KKKA - Tedavi

Spesifik tedavi yok

Ribavirin ??

Yükleme.... 30 mg / kg

4 gün..... 15 mg / kg /gün (6 saat)

6 gün.....7.5 mg / kg /gün (8 saat)
(DSÖ)

Amaç 1: Uygun Desteği Sağlamak !

❖ Transfüzyon

Trombosit

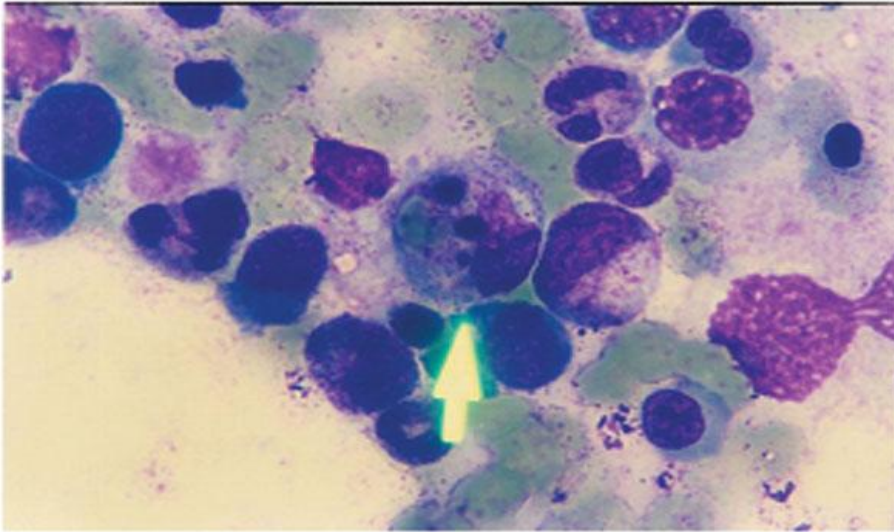
Eritrosit

Tam kan

Taze donmuş plazma

❖ Organ yetmezliğine yönelik destek

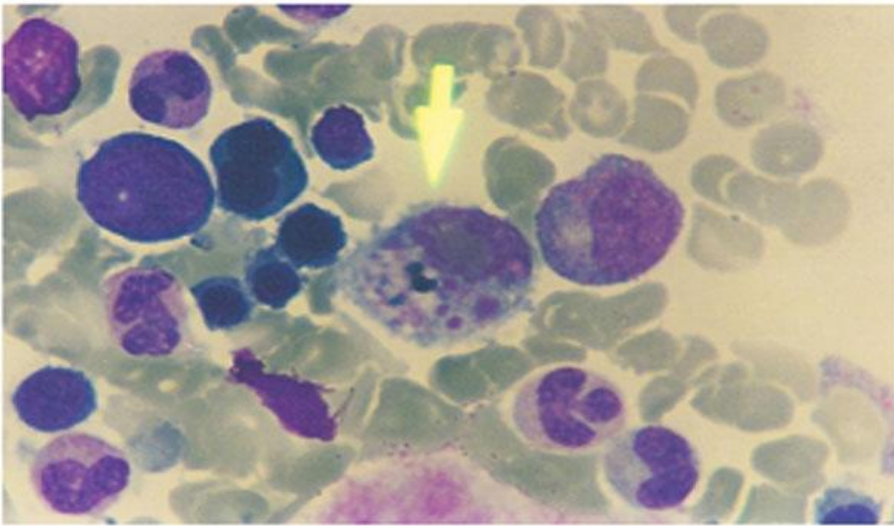
A



Kemik iliği aspirasyonu **Hemofagositoz**

A) Eritrositin fagositozu

B



B) Trombositin fagositozu

Case Report

Haemophagocytosis in a patient with Crimean–Congo haemorrhagic fever

Atahan Cagatay,¹ Mahir Kapmaz,¹ Asli Karadeniz,¹ Seniha Basaran,¹ Mustafa Yenerel,² Selim Yavuz,² Kenan Midilli,³ Halit Ozsut,¹ Haluk Eraksoy¹ and Semra Calangu¹

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³Department of Microbiology and Clinical Microbiology, Cerrahpasa Faculty of Medicine, Istanbul University, Istanbul, Turkey

Crimean–Congo haemorrhagic fever (CCHF) is a severe disease with a case fatality rate of 80%. A patient dwelling in an endemic region for CCHF was admitted with fever, bleeding diathesis and pancytopenia. Despite no history of tick exposure, CCHF was suspected. With an oral ribavirin therapy, clinical and laboratory improvements were observed. The diagnosis was confirmed by detection of IgM antibody to CCHF virus and positive PCR. Although the main pathogenesis of CCHF infection is not elucidated yet, haemophagocytosis, a symptom rarely reported in viral haemorrhagic fevers, was observed in this case. Haemophagocytosis is suggested to have a role in the development of pancytopenia. The mechanism of which still needs to be investigated, probably with cytokine studies. With clinical symptoms and patient history, haemophagocytosis may be an indicator for CCHF.

Received 22 August 2006
Accepted 7 May 2007

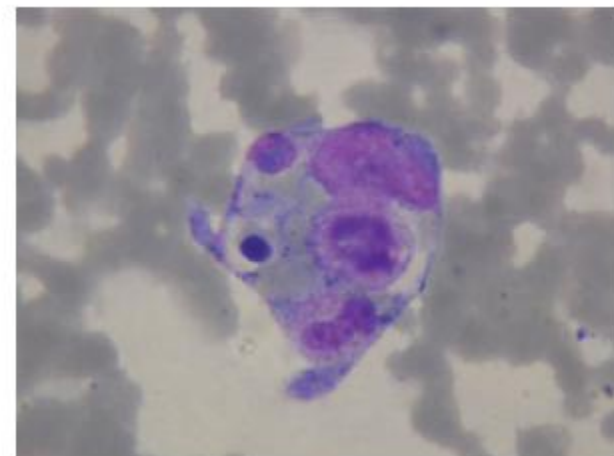


Fig. 1. Haemophagocytosis of neutrophils, erythrocytes, platelets and erythroblasts by a histiocyte in a bone marrow aspiration smear (May-Grunwald–Giemsa stained, magnification $\times 1000$).

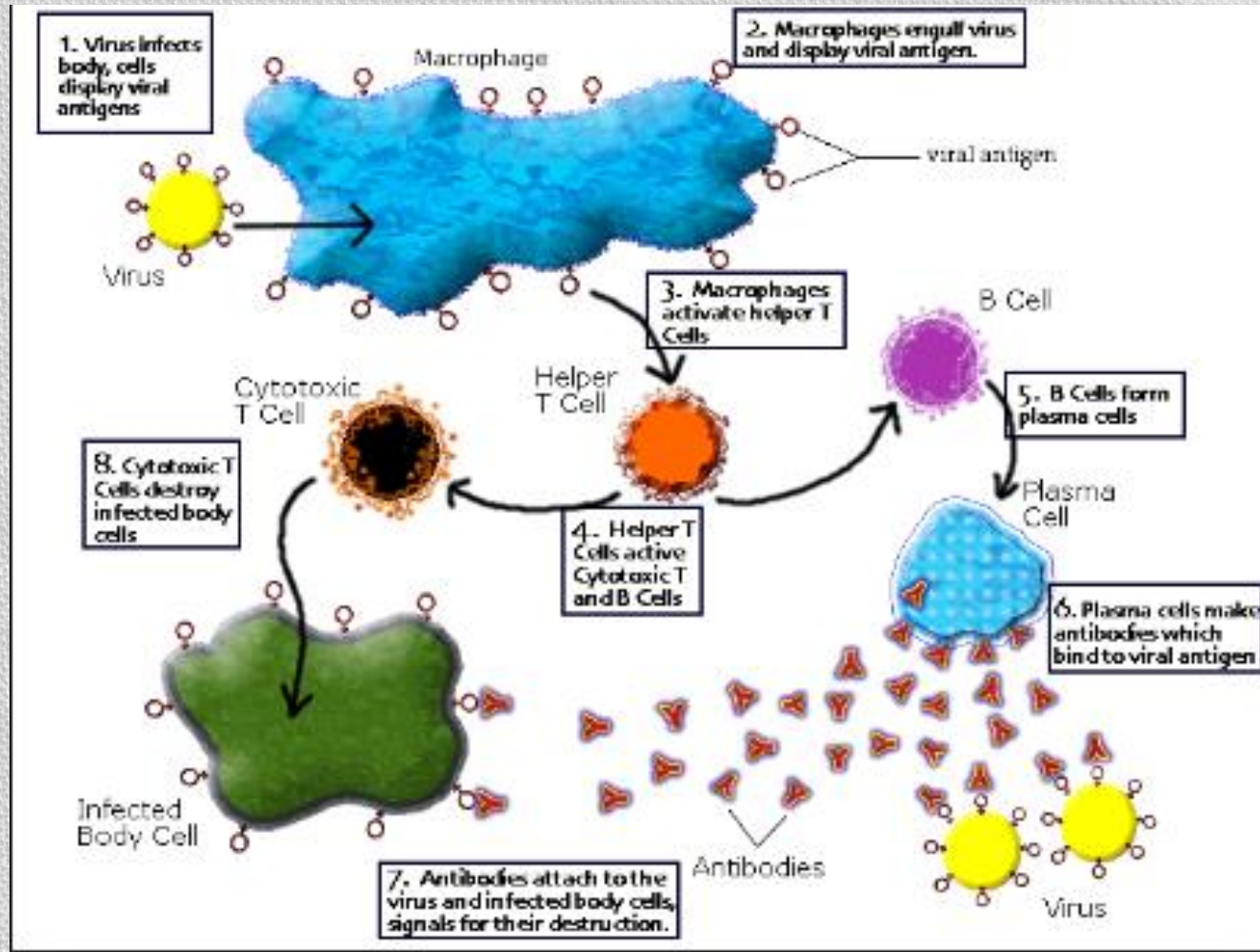
Tedavi	Endikasyon	Doz
Trombosit	▶ Kanama (hematemez, melen a, epistaksis gibi) ve PLT<50 000 /mm³ ▶ PLT<50 000 /mm³ ve invazif girişim ▶ PLT<20 000 /mm³ ve hemostaz parametrelerinde sorun, ateş ▶ PLT<10 000 /mm³ ve koagölasyon parametreleri normal, ateş yok	▶ 1 U aferez - veya ▶ 1 U PLT/15 kg

Peki Biz ne yapıyoruz ?

- ❖ Kanama yoksa 10000 altına inene kadar trombosit vermiyoruz
- ❖ APTT 35-45 arasında 2x 10 mg/kg TDP
- ❖ Fibrinojen 160 altında kriopresipitat

Amaç 3: İmmün Yanıtı Düzenlemek !

DIK'i önlemek!



Vero Hücreleri

Crimean-Congo Hemorrhagic Fever Virus Activates Endothelial Cells[▽]

Anne-Marie Connolly-Andersen,^{1,2} Guido Moll,³ Cecilia Andersson,^{1,2} Sara Åkerström,^{1,2}
Helen Karlberg,^{1,2} Iyadh Douagi,⁴ and Ali Mirazimi^{1,2*}

- ❖ Monosit derivesi dendritik hücreler (moDCs) ve makrofajları infekte ediyor
- ❖ Bu hücrelerden sitokinler salınıyor
- ❖ Virus endotelial hücrelerini hem direk hemde sitokinler aracılığı ile etkiliyor
- ❖ Virüs dozu arttıkça ICAM-1 düzeyi artıyor
- ❖ Lökosit adezyon moleküllerinin regülasyonu bozuluyor

J Med Virol. 2008 Aug;80(8):1397-404. doi: 10.1002/jmv.21222.

Crimean-Congo hemorrhagic fever virus delays activation of the innate immune response.

Andersson I, Karlberg H, Mousavi-Jazi M, Martínez-Sobrido L, Weber E, Mirazimi A.

KCB/Swedish Institute for Infectious Disease control, Solna, Sweden.

- ❖ Doğal bağışıklığın antiviral etkinlik basamağı 48 saat kadar geç başlıyor
- ❖ Çünkü virüsle enfekte hücrelerden interferon salınımı gecikiyor



İnterlökin 6 ve TNF alfa yüksek

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

Onder Ergonul,¹ Semra Tuncbilek,² Nurcan Baykam,¹ Aysel Celikbas,¹ and Basak Dokuzoguz¹

¹Infectious Diseases and Clinical Microbiology Clinic, Ankara Numune Education and Research

infection is one of the important public health issues in Turkey, because of its high case fatality rate.

During viral hemorrhagic fevers, inflammatory processes are key elements of the immune response, and the release of proinflammatory cytokines—in particular, of interleukin (IL)-1, IL-6, and tumor necrosis factor (TNF)- α —have been suggested to be related to the disease course [6, 7]. However, studies of

The Journal of Infectious Diseases 2006; 193:941–4

to achieve a better understanding of the pathogenesis of the disease caused by CCHFV infection [8]. To define the possible role that inflammatory responses play in the control of the

Emergence of Crimean–Congo haemorrhagic fever in Greece

A. Papa¹, V. Dalla², E. Papadimitriou¹,
G. N. Kartalis², A. Antoniadis¹

Article first published online: 20 OCT 2009

DOI: 10.1111/j.1469-0691.2009.02996.x

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European Society of Clinical Microbiology and
Infectious Diseases

Issue



**Clinical Microbiology and
Infection**

**Volume 16, Issue 7, pages
843–847, July 2010**

İnterlökin 8 yüksek

Serum nitric oxide levels in patients with Crimean-Congo haemorrhagic fever



E. EDİZ TÜTÜNCÜ, YUNUS GURBUZ, BARIS OZTURK, FERIT KUSCU & IRFAN SENCAN

Scand J Infect Dis. 2010 May;42(5):385-8

DIK



Journal of Infection

Volume 56, Issue 5, May 2008, Pages 366–370



High serum levels of neopterin in patients with Crimean–Congo hemorrhagic fever

Journal of Infection (2007) 55, 184–187

Pınar Onguru^a, Emin Öz
Erbay^a, Fatma Nurhayat Baya



www.elsevierhealth.com/journals/jinf

Plasma activity of thrombin activatable fibrinolysis inhibitor in Crimean-Congo hemorrhagic fever

Mehmet Sonmez^{a,*}, Kemalettin Aydın^b, Ahmet Durmus^a, Nurgul Sucu^b,
Mustafa Yilmaz^a, Elif Akdogan^a, Iftihar Koksall^b, Ercument Ovali^a,
Serdar Bedii Omay^a



The Treatment of Crimean-Congo Hemorrhagic Fever With High-dose Methylprednisolone, Intravenous Immunoglobulin, and Fresh Frozen Plasma

Erol Erduran, MD, Ayseur Bahadir, MD,* Nil Palanci, MD,† and Yusuf Gedik, MD†*

Metil prednizolon (MP) (5-30 mg/kg/gün): Makrofaj aktivasyonunun süpresyonu ve reaktif hemofagositik lenfhistiyositozisin (HLH) tedavisi

Taze donmuş plazma (TDP) : DİK tedavisi

İntravenöz immünoglobulin (IVIG): Makrofaj aktivasyonunun ve sitokin fırtınasının süpresyonu

KKKA - Patogeneze

IL10 artışı
IF gama artışı
Ölen hastalarda
Viral yük yüksek
Antikor cevabı düşük

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Interacting Roles of Immune Mechanisms and Viral Load in the Pathogenesis of Crimean-Congo Hemorrhagic Fever[▽]

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Until now, the pathogenesis of Crimean-Congo hemorrhagic fever (CCHF) has not been well described. However, it has been hypothesized that it could be a result of the direct injury of virus-infected tissues in combination with the indirect effects of host immune responses, including cytokines. To shed more light on the role of viral load and cytokines, differential influences of CCHF virus (CCHFV) RNA load, antibody response, and cytokine production on severity and outcome of the disease were studied in sera of 46 patients with confirmed acute CCHF from Kosovo. In this study, viral load proved to be strongly related to the severity and

Tedavide Hiperimmunglobulin?

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Short Communication

Prompt Administration of Crimean-Congo Hemorrhagic Fever (CCHF) Virus Hyperimmunoglobulin in Patients Diagnosed with CCHF and Viral Load Monitorization by Reverse Transcriptase-PCR

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Viral Yüku düşürüyor
Mortaliteye etkisi yok

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SUMMARY: Crimean-Congo hemorrhagic fever virus (CCHFV), a member of the genus *Nairovirus* of the family *Bunyaviridae*, causes a severe disease in humans with high mortality rates. In Turkey, the number of patients with CCHF has increased since 2002. Here, we aimed to treat CCHF patients with CCHFV hyperimmunoglobulin. We prepared a CCHFV hyperimmunoglobulin product from 22 individuals who survived CCHF infection. A total of 26 CCHF patients were enrolled into this study. For CCHFV hyperimmunoglobulin administration, a Kubar Unit (KU) was defined. As a standard therapeutic approach, 400 KU of hyperimmunoglobulin were given to each patient as a single dose before viral load was detected. We used one-step real-time reverse transcriptase-PCR to monitor the viral load of CCHF patients. According to the one-step real-time PCR results, 15 patients with a viral load of 10^3 copies/mL or more were defined as high risk. In this high-risk group, the survival rate was found to be 86.6% (13/15) and 2 patients died despite CCHFV hyperimmunoglobulin administration. CCHF is a very serious and highly fatal infection, particularly for patients in the defined high-risk group. Prompt administration of CCHFV hyperimmunoglobulin might be a very promising new treatment approach, especially for high-risk individuals.

Hangi Tedavi? Ne Zaman?



Kırım Kongo Kanamalı Ateşi

KAN GRUBU:

KKKA PCR:

IgM:

IgG:



Hastalık günü										
Tarih	/	/	/	/	/	/	/	/	/	/
Lökosit										
Trombosit										
Hemoglobin										
AST										
ALT										
LDH										
CK										
Amilaz										
Trigliserid										
Ferritin										
aPTT										
PT										
Fibrinojen										
D-Dimer										
INR										
C 3-5										
Diğer										
Klinik şiddet										

/...../.....

zarıklık

.....

☐ Hayır.

Yok

/	/	/

akıntı

Hepatomegali

Splenomegali

İkter

A new perspective to determine the severity of cases with Crimean-Congo hemorrhagic fever

Mehmet Bakir¹, Aynur Engin¹, Mustafa Gokhan Gozel¹, Nazif Elaldi¹, Saadettin Kilickap² & Ziyet Cinar³

Parametreler	Sınıflama	CSS puanlama
AST	5XNÜS	0
	≥5XNÜS	1
ALT	NÜS	0
	≥NÜS	1
LDH	3XNÜS	0
	≥3XNÜS	1
BK	10 000 hücre/μl	0
	≥10 000 hücre/μl	1
Hepatomegali	YOK	0
	VAR	1
Organ yetm	YOK	0
	VAR	1
Kanama	YOK	0
	VAR	1
Yaş	60	0
	≥60	1

Parametreler	Sınıflama	CSS puanlama
<u>DIC</u>		
PLT	≥100 000 hücre/μl	0
	50-100 000 hücre/μl	1
	50 000 hücre/μl	2
PT uzaması	3 sn	0
	3-6 sn	1
	≥6 sn	2
Fibrinojen	≥100 mg/dl	0
	100 mg/dl	1
D-dimer	Normal	0
	>NÜS ve 10X NÜS	1
	≥10XNÜS	2

A new perspective to determine the severity of cases with Crimean-Congo hemorrhagic fever

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İlk günlük CSS				Üçüncü günlük CSS			
	0-5	6-10	≥11		0-5	6-10	≥11
Yaşayan (n:224)	158 (100)	63 (90)	3 (33)	Yaşayan (n:213)	142 (100)	71 (95)	0 (0)
Ölen (n:13)	0 (0)	7 (10)	6 (67)	Ölen (n:7)	0 (0)	4 (5)	3 (100)

Severity Scoring Index for Crimean Congo Hemorrhagic Fever virus infection and the impact of Ribavirin and Corticosteroids on Fatality

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Severity Scoring Index SSI

		score
Platelet count (x10 ³ /mm ³)	>150	0
	150 -50	1
	49-20	2
	<20	3
aPTT (sec)	≤ 34	0
	35 – 45	1
	46 - 59	2
	> 60	3
Fibrinogen (mg/dl)	≥ 180	0
	179 – 160	1
	159 -120	2
	<120	3
Bleeding	No	0
	Petechia	1
	Echymosis	2
	Bleeding	3
Somnolence	No	0
	yes	1

Skor 0-2 Hafif olgu

Skor 3-9 Orta olgu

Skor 10-13 Ağır olgu

	Ribavirin			Corticosteroids		
	CFR/Given (%)	CFR/Not given (%)	p	Given (%)	not given (%)	p
Mild (0-2)	0/77 (0)	0/26 (0)	NA	0	0/103 (0)	NA
Moderate (3-9)	2/134 (1.49)	3/17 (18)	<0.001	2/30 (7)	3/121 (2)	0.251
Severe (10-13)	16/24 (67)	2/2 (100)	0.326	9/17 (53)	9/9 (100)	0.013

Peki Biz Ne Yapıyoruz ?

Skor 0-2 Hafif olgu



Takip

Skor 3-9 Orta olgu



Ribavirin

Skor 10-13 Ağır olgu



Ribavirin ± Steroid
Deksametazon 10mg/m²

Destek tedavi

- ❖ Kanama yoksa 10000 altına inene kadar trombosit vermiyoruz
- ❖ APTT 35-45 arasında 2x 10 mg/kg TDP
- ❖ Fibrinojen 160 altında kriopresipitat(Faktör VIII,Faktör XIII, Fib)

Sonuç Olarak;

- ❖ Tedavide konusunda tartışmalar devam ediyor
- ❖ Standart bir tedavi önerisinde bulunmak zor
- ❖ Olgu bazında değerlendirmeye ihtiyaç var
- ❖ Olgu bazında değerlendirmede ciddiyet skorlaması (SSI) yapılması yol gösterici olabilir
- ❖ Patogenezi aydınlandıkça tedavi hedefleri daha iyi belirlenebilir





TEŞEKKÜRLER