KIRIM- KONGO KANAMALI ATEŞİ

Doç Dr Aysel Kocagül Çelikbaş

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

ayselcelikbas@gmail.com

01.03.2013

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

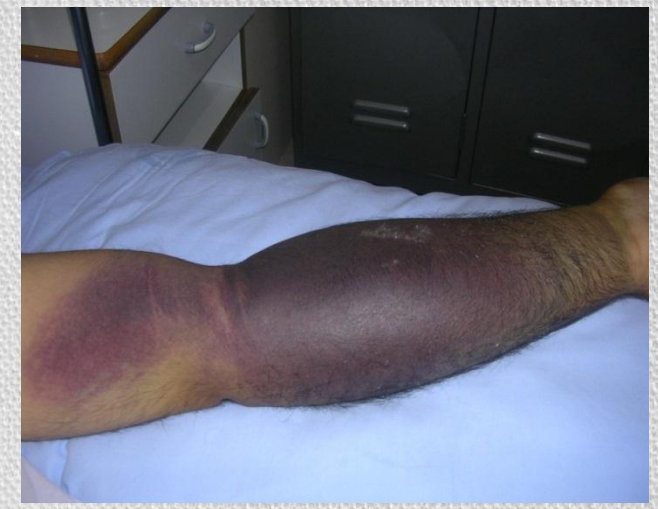
Viral Hemorajik Ateşlerde Ortak Klinik Tablo

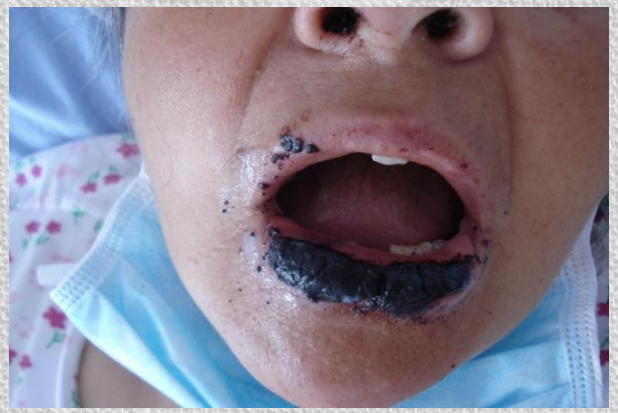
Başlangıç: ateş, halsizlik, baş ve kas ağrıları

Ciddi olgularda: Cilt altı
GIS
Ağız boşluğu
Genitoüriner sistem
Göz
Burun

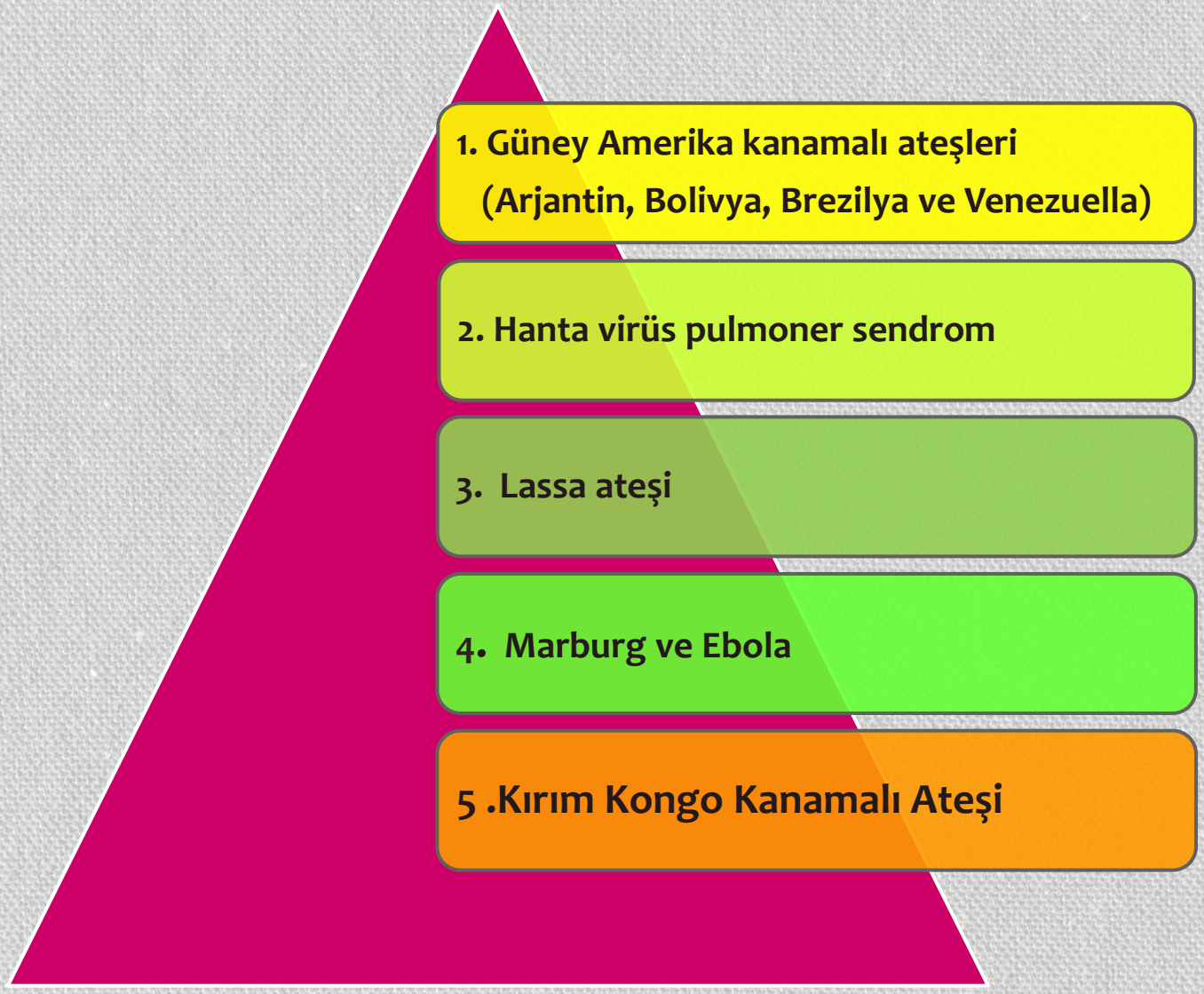
Kanamalar

Mortalite yüksek



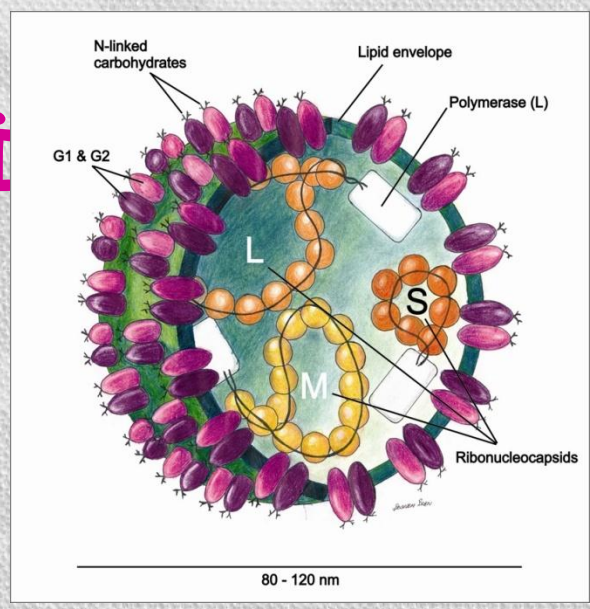


İnsandan İnsana Bulaşabilen Viral Kanamalı Ateşler



Bunyaviridae- Nairovirus

KIRIM-KONGO KANAMALI ATEŞİ



- RNA virusu
- 1944 - 45 Kırım

  (Kene süspansiyonları,hasta kanlarında viral bir etiyoloji !)
- 1956 Kongo
- 1967 Virüsün izolasyonu
- 1969 Kırım – Kongo

Dr. Şebnem Eren, ANEAH

Casals J Proc Soc Exp Biol Med 1969 May;131(1):233-6 Antigenic similarity between the virus causing Crimean hemorrhagic fever and Congo virus.
Chumakov MP Acta virol 1970 Jan;14(1):82-5 Relationship between strains of Crimean haemorrhagic fever and Congo viruses..

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

Arch Virol (1990) [Suppl 1]: 323–340

Epidemiology of Crimean-Congo hemorrhagic fever in Senegal: temporal and spatial patterns

M. L. Wilson[1,2], J.-P. Gonzalez[1,3], B. LeGuenno[1], J.-P. Cornet[3], M. Guillaud[4], M.-A. Calvo[1], J.-P. Digoutte[1], and J.-L. Camicas[3]

[1]Institut Pasteur, Dakar, Senegal
[2]Departments of Population Sciences and Tropical Public Health, Harvard School of Public Health, Boston, Massachusetts, U.S.A.
[3]Institut Francais de Recherche Scientifique pour le Developpement en Cooperation (ORSTOM), Laboratoire ORSTOM de Zoologie medicale, Dakar, Senegal
[4]Institut d'Elevage et de Medecine Veterinaire des Pays Tropicaux, Maisons Alfort, France

Accepted April 15, 1990

Summary. Aspects of the spatial and temporal patterns of transmission of Crimean-Congo hemorrhagic fever (CCHF) virus were studied in Senegal, West Africa. A country-wide serological survey of domestic animals indicated that transmission was most intense in the northern dry sahelian zone and least in the southern, more humid guinean zone. Human IgG prevalence, ranging from nearly 20% to <1% among 8 sites throughout the region, also was greatest in the north. A fatal human case of CCHF from Rosso, Mauritania in 1988 was studied and an accompanying serosurvey of human contacts and domestic animals indicated epidemic transmission during that period. Systematic samples of adult ixodid ticks on domestic animals allowed us to analyze the distribution and relative abundance of potential CCHF virus vectors, demonstrating that *Hyalomma* spp. predominated in those biotopes where transmission was most intense. A prospective study of CCHF virus infection and tick infestation in sheep exposed a period of epizootic transmission in 1988 that corresponded temporally with increased abundance of adult *H. truncatum* and *H. impeltatum*. Four strains of CCHF virus were isolated from pools of these ticks and of *Rhipicephalus guilhoni*. Our results suggest that CCHF virus is focally endemic throughout the region, although highly variable in time and space, and that the relative abundance of *Hyalomma* ticks may be the primary determinant of epidemic transmission.

Senagal 1990

- 8 Bölge
- Koyunlarda seroprevalans %10-20
- İnsanlarda % 1- 20
- Vektör ağırlıklı olarak Hyalomma spp

H truncatum

H impeltatum

Rhipicephalus

SANCO/B3/R11/1999

EUROPEAN COMMISSION
HEALTH & CONSUMER PROTECTION DIRECTORATE-GENERAL
Directorate B – Scientific Health Opinions
Unit B3 – Management of scientific committees II

Diagnostic T
for Crimean Congo Haemor
in Ratite

Report of t
Scientific Committee on Animal H

Adopted 11 Octo

2.4. Geographical distribution

Capua (1998) lists 35 countries throughout Africa, the Middle East, Asia and some southern and eastern European countries where evidence of CCHF virus has been demonstrated. However, in some countries, especially France, Portugal and Turkey

the evidence is somewhat tenuous and requires confirmation. The distribution of CCHF virus appears to coincide with the geographical range of the chief vectors i.e. members of the *Hyalomma* tick genus. Countries where *Hyalomma* ticks are present, but are currently free of CCHF virus should be considered at risk. As suggested by Capua (1998), it would appear prudent for EU countries at risk to undertake surveillance of resident ratites for the presence of CCHF virus.

for countries of the European Union? Avian Pathology 27, 117-120.

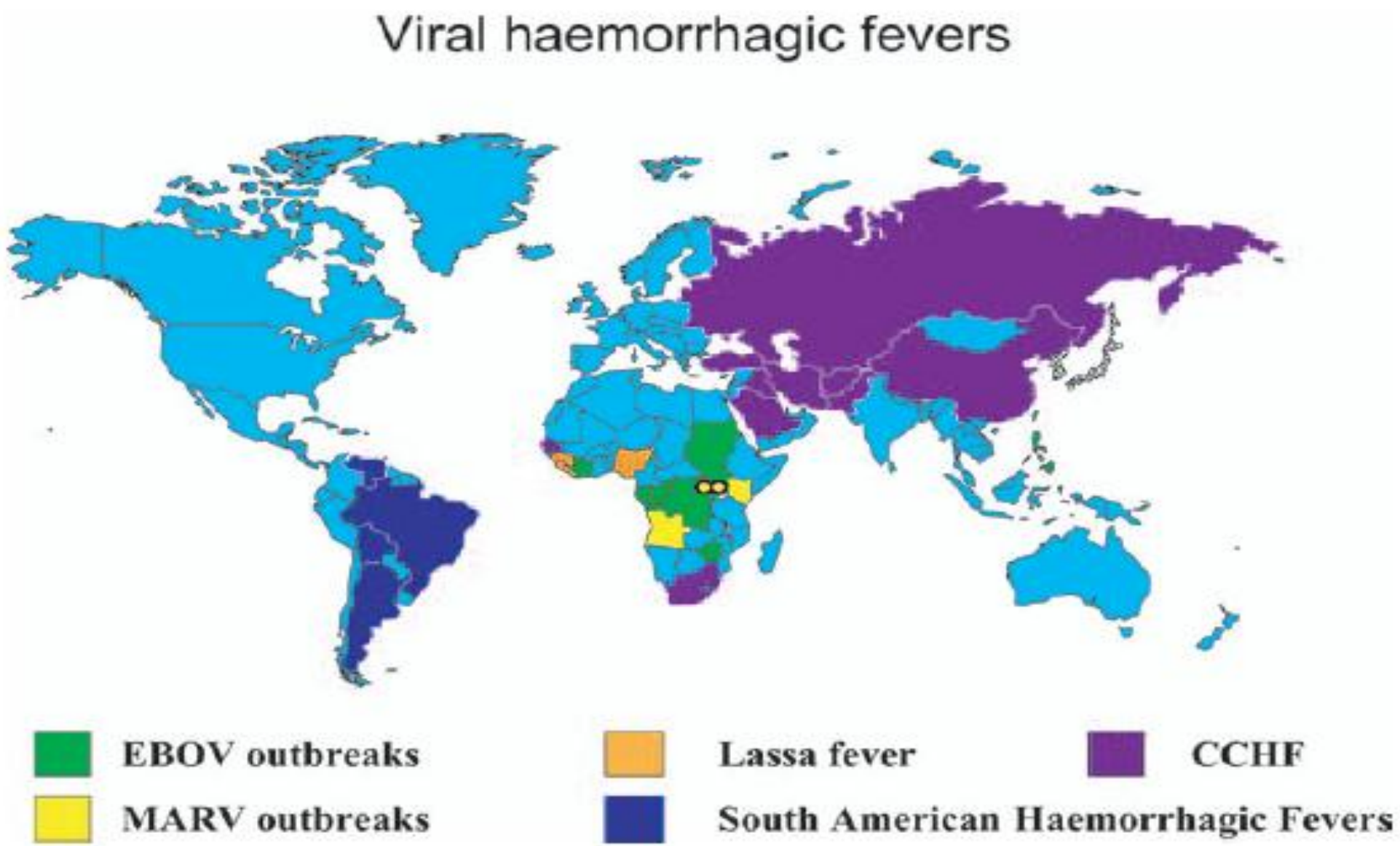


Fig. 1 Map of the world showing those countries known in 2005 to be affected by viral haemorrhagic fever (VHF) viruses. All those marked produce nosocomial outbreaks, with the exception of the South American haemorrhagic fever viruses. CCHF, Crimean–Congo haemorrhagic fever; EBOV, Ebola virus; MARV,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

Ön tanılar;

Febril nötropeni

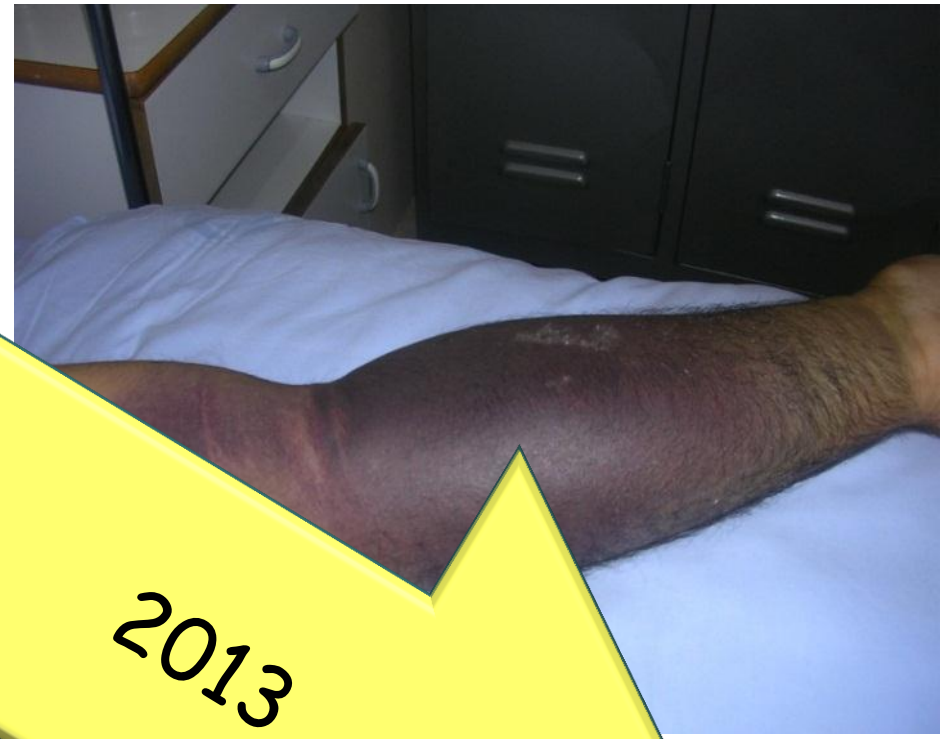
Q ateşi

Ehrlichiosis

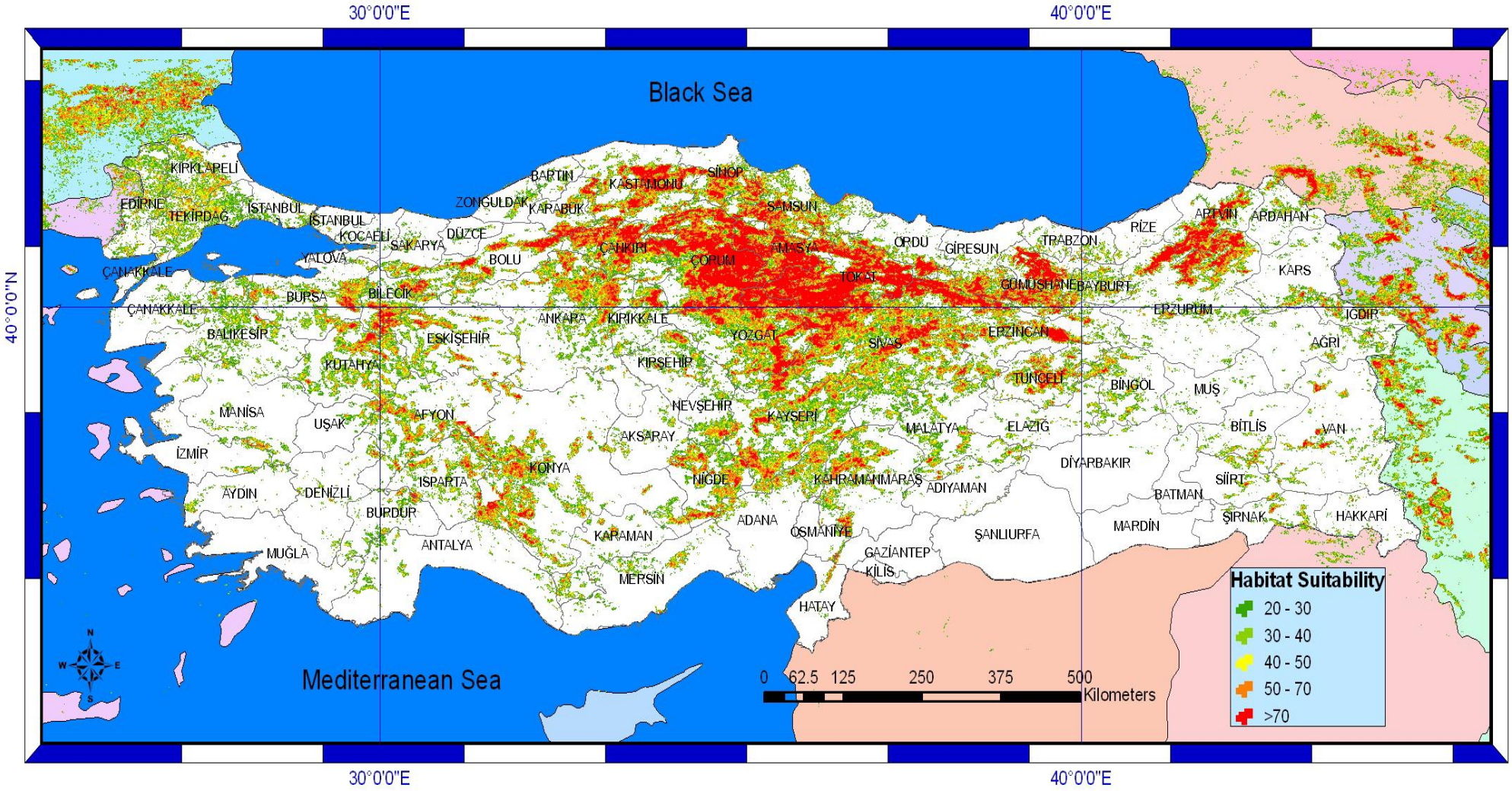
Bruselloz

Viral Kanamalı Ateş (VKA)

2002 2004 2013



Kırım Kongo Kanamalı Ateşi



H. marginatum spp. **(MaxEnt algorithm)**

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

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

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.

Bakanlık Keneye Karşı Keklik ve Sülünle Mücadele Edecek

Türkiye'de yaz ayların gelmesiyle sıkça görülen kene ölümleri vatandaşları tedirgin ederken, tabiata salınan beç tavuğu, sülün ve kekliklerle, Kırım Kongo Kanamalı Ateşi (KKKA) hastalığından kaynaklanan ölümlerin önüne geçilmesi hedefleniyor.

Türkiye'de yaz ayların gelmesiyle sıkça görülen kene ölümleri vatandaşları tedirgin ederken, tabiata salınan beç tavuğu, Sülün ve kekliklerle, Kırım Kongo Kanamalı Ateşi (KKKA) hastalığından kaynaklanan ölümlerin önüne geçilmesi hedefleniyor. Orman ve Su

KKKA - Vaka Tanımı

Klinik Tanımlama

- Ateş, başağrısı, 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

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

/ /	/ /

döküntü										
Hepatomegali										
Splenomegali										
İkter										

KKKA- Risk Grupları

- Endemik bölgede yaşayanlar
- Endemik bölgede tarım ve hayvancılık yapan çiftçiler
- Kasaplar, mezbaha çalışanları
- Çobanlar
- Veteriner hekimler
- Sağlık çalışanları
- Laboratuvar çalışanları
- Endemik bölgede kırsal alana gezi yapanlar, kamp kuranlar, piknikçiler
- Avcılar

Epidemiyolojik Özellikler

Erkek cinsiyet % 50

Çiftçi % 90

Kene tutma öyküsü % 60

Ergönül Ö ve ark	*Clin Infec Dis*	2004
Kartı SS ve ark	*Emerg Infect Dis*	2004
Bakır M ve ark	*J Med Microbiol*	2005
Özkurt Z ve ark	*J Infect*	2006
Ergönül Ö ve ark	*Clin Microbiol Infect*	2006

KKKA - Bulaş

Hastalanma olasılığı: 0.215

Goldfarb LG,1980

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

Bulgular: Enfeksiyon oranı 0.27 (14/55)

Kene ısırığı öyküsü olanlarda enfeksiyon oranı 0.42 (p=0.046).

Atak hızı: 0.20 (11/55).

Sonuç

Endemik bölgede yaşayan her 5 kişiden biri, kene ısırığı öyküsü her iki kişiden biri enfekte olmaktadır. Enfeksiyon hızı ve atak hızı diğer hastalıklarla karşılaştırıldığında oldukça yüksektir.

EMERGING INFECTIOUS DISEASES®

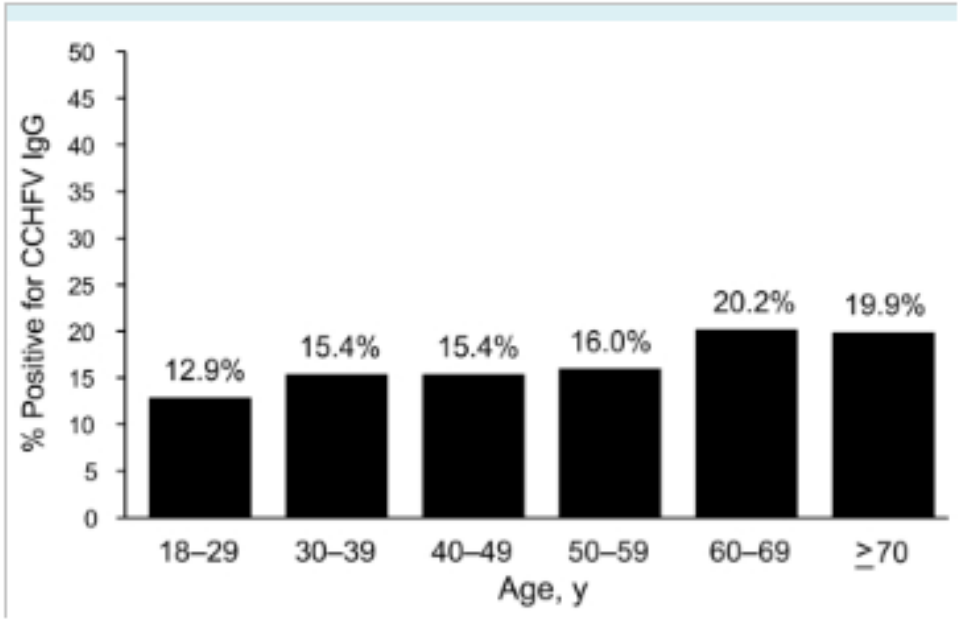
Emerg Infect Dis. 2012 April; 18(4): 640–642.

PMCID: PMC3309668

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

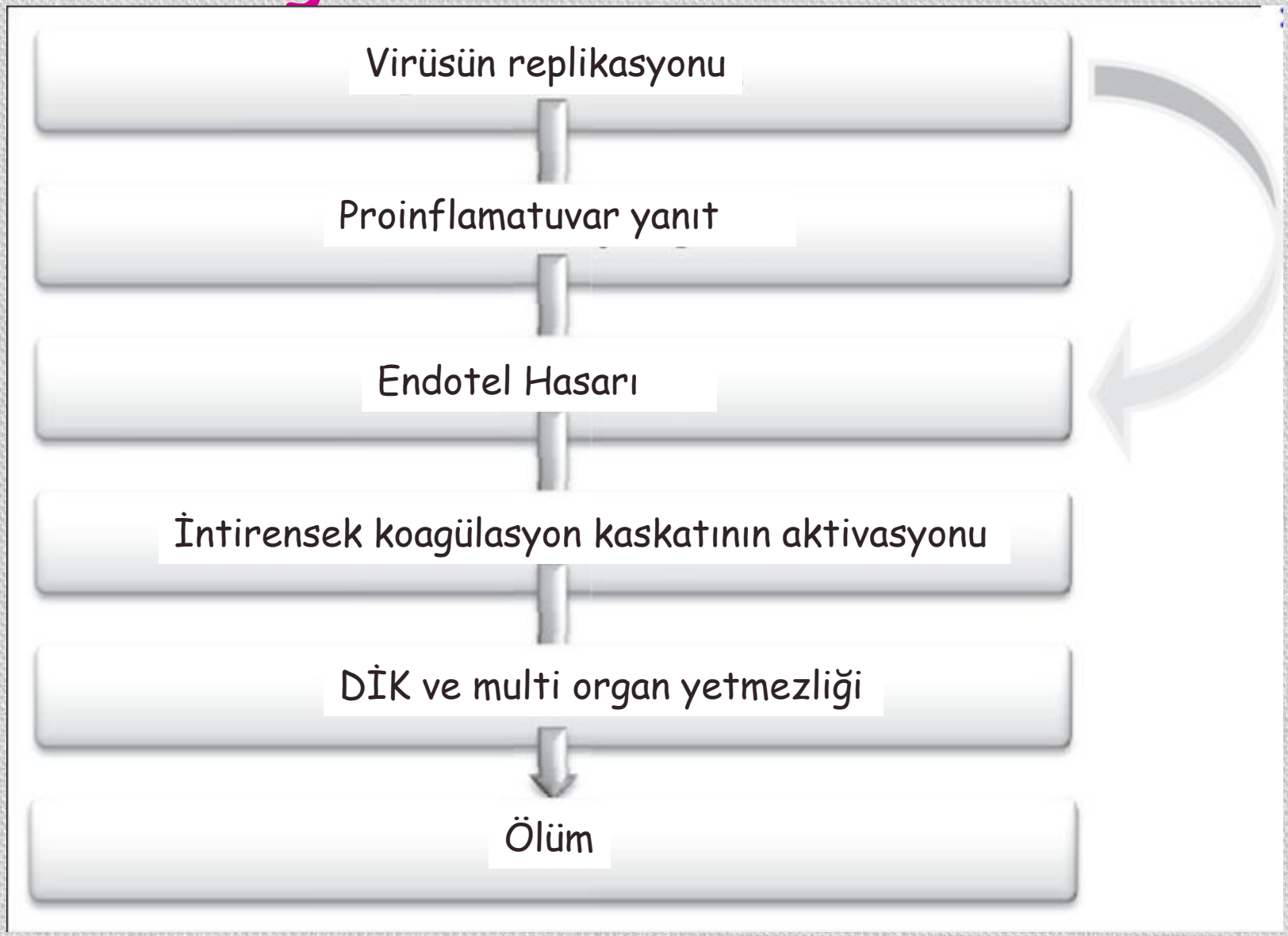
doi: 10.3201/eid1804.111374

Figure 2



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

KKKA- Patogenez



KKKA- Patogenez

BRIEF REPORT

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 Dokuzoguz[1]

[1]Infectious Diseases and Clinical Microbiology Clinic, Ankara Numune Education and Research Hospital, and [2]GENOM Laboratories, Ankara, Turkey

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 cytokines with respect to CCHF are lacking, and they are needed 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 infection, we examined serum levels of cytokines in patients

BRIEF REPORT

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

Mustafa Aydin Çevik,[1] Ayşe Erbay,[1] Hürrem Bodur,[1] Selim Sirri Eren,[1] Esragül Akinci,[1] Kenan Şener,[2] Pinar Öngürü,[1] and Ayhan Kubar[2]

[1]Infectious Diseases and Clinical Microbiology Department, Ankara Numune Education and Research Hospital, and [2]Department of Virology, Gulhane Military Medical Academy, Ankara, Turke

Viral yük 10^9 ↑ mortal

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 loads 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 were $\geq 1 \times 10^9$ copies/mL, whereas in 25 of the 26 patients with nonfatal outcomes, viral loads were detected that were $<1 \times 10^9$ copies/mL ($P < .001$). A viral load $\geq 1 \times 10^9$ RNA 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 detection of specific IgM antibodies in human serum or blood samples. In the acute stage of the illness, serological tests are efore humoral immune re- sensitive assay for detection d on RT-PCR for the early stage of infection [13]. This study aimed to determine the association between viral load and the severity of CCHF.

Patients and methods. A prospective study was performed at Ankara Numune Education and Research Hospital, a referral and tertiary-care hospital in Ankara, Turkey, during the spring and summer of 2006. Fifty-one patients who had an epidemiologic risk factor (i.e., a history of tick exposure and/or residence in or travel to an area of CCHF endemicity) and acute febrile syndrome characterized by malaise, bleeding, thrombocytopenia (platelet count, <150,000 platelets/mm^3), and elevated aspartate transaminase, alanine transaminase, lactic dehydrogenase, and creatinine phosphokinase levels were referred from surrounding hospitals to the Infectious Diseases

KKKA- Patogenez

Yüksek viral yük
Düşük antikor cevabı
IL10 artışı
IF gama artışı

CLINICAL AND VACCINE IMMUNOLOGY, July 2010, p. 1086–1093 Vol. 17, No. 7
1556-6811/10/$12.00 doi:10.1128/CVI.00530-09

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

Ana Saksida,[1] Darja Duh,[1] Branka Wraber,[1] Isuf Dedushaj,[2] Salih Ahmeti,[3] and Tatjana Avšič-Županc[1]*

Institute of Microbiology and Immunology, Faculty of Medicine, University of Ljubljana, Ljubljana, Slovenia[1]; Faculty of Medicine, University of Pristina, Pristina, Kosovo[2]; and Clinic of Infectious Diseases, Pristina, Kosovo[3]

Received 24 December 2009/Returned for modification 20 January 2010/Accepted 12 May 2010

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

Journal of Medical Microbiology (2007), 56, 1126–1128 DOI 10.1099/jmm.0.46910-0

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 Eraksoy[1] and Semra Calangu[1]

Correspondence
Atahan Cagatay
atayon@yahoo.com

[1]Department of Infectious Diseases and Clinical Microbiology, Istanbul Faculty of Medicine, Istanbul University, Istanbul, Turkey

[2]Department of Internal Medicine, Division of Hematology, Istanbul Faculty of Medicine, Istanbul University, Istanbul, Turkey

[3]Department 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 fa
80 %. A patient dwelling in an endemic region for CCHF was admitted with feve
bleeding diathesis and pancytopenia. Despite no history of tick exposure, CCHF
suspected. With an oral ribavirin therapy, clinical and laboratory improvements wer
diagnosis was confirmed by detection of IgM antibody to CCHF virus and positi
Although the main pathogenesis of CCHF infection is not elucidated yet, haemo
symptom rarely reported in viral haemorrhagic fevers, was observed in this case.
Haemophagocytosis is suggested to have a role in the development of pancytop
the mechanism of which still needs to be investigated, probably with cytokine st
with clinical symptoms and patient history, haemophagocytosis may be an indica

Received 22 August 2006
Accepted 7 May 2007

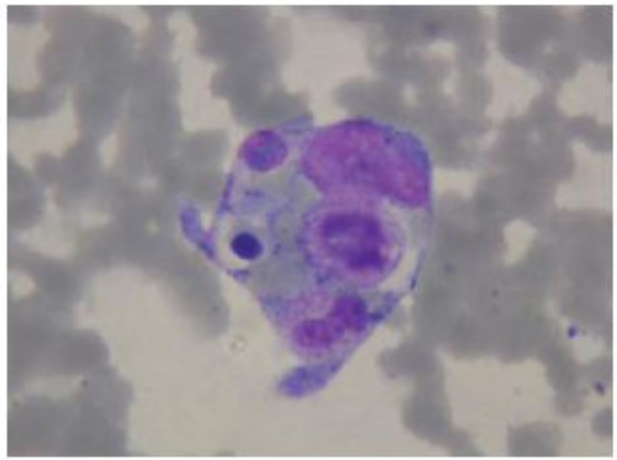


Fig. 1. Haemophagocytosis of neutrophils, erythrocytes, platelets and erythroblasts by a histiocyte in a bone marrow aspiration smear (May-Grunwald–Giemsa stained, magnification ×1000).

Crimean-Congo hemorrhagic fever: Five patients with hemophagocytic syndrome

Nuriye Tasdelen Fisgin,[1]* Tunc Fisgin,[2] Esra Tanyel,[1] Levent Doganci,[1] Necla Tulek,[1]

Hemofagositoz sendromu tanı kriterleri

Klinik kriterler

Ateş

Three pedia … nduced
hemophago… he Mid-

…erleri

… seriden ≥2 sinin etkiler…

…mi

…iterler

…ezi biyopsilerinde hemo…

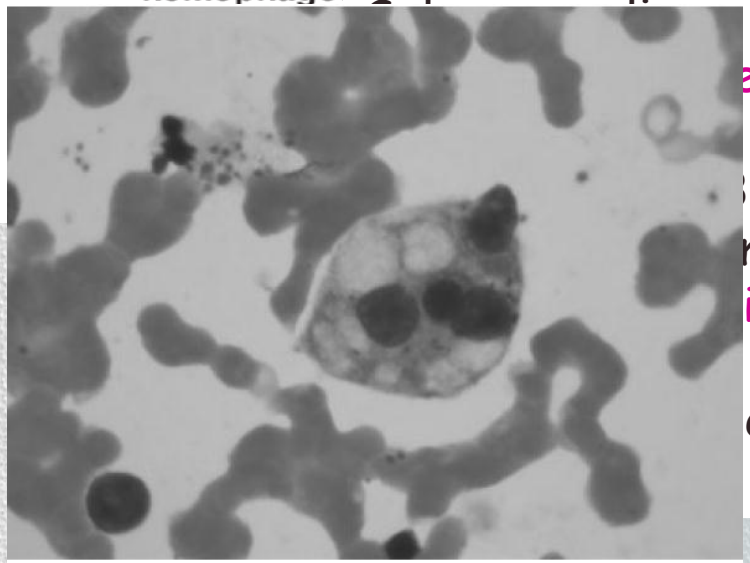
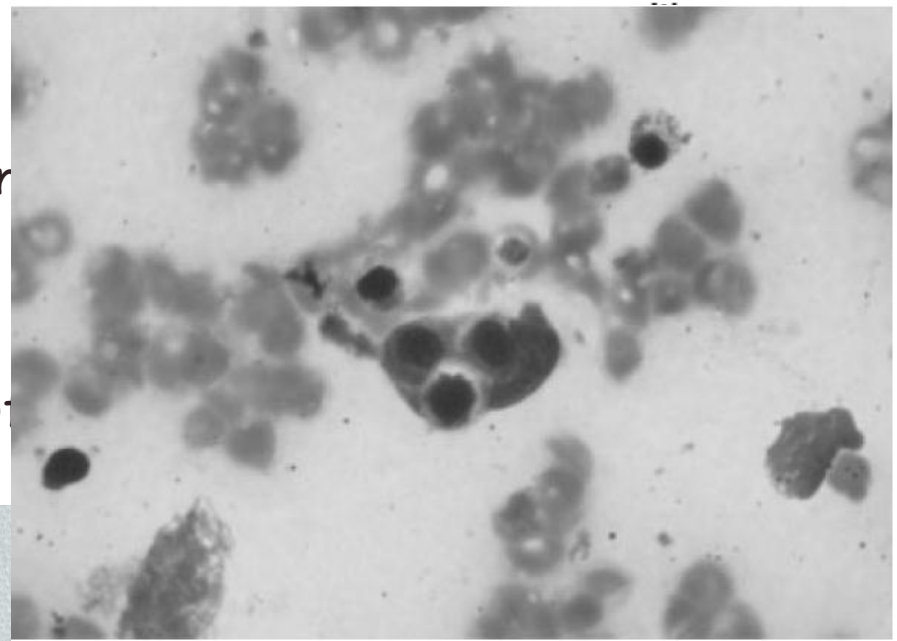
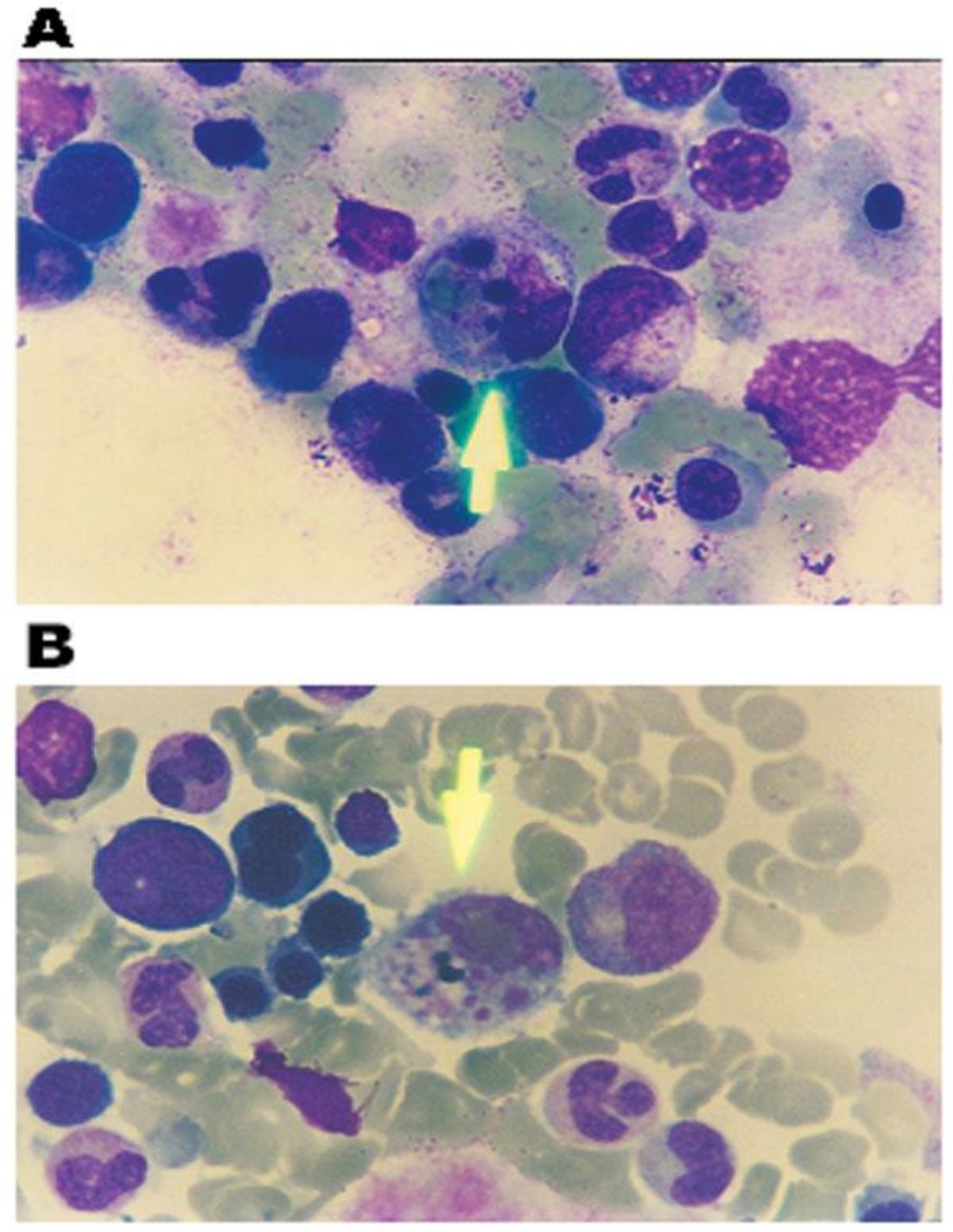


Figure 5. Hemophagocytosis in the bone marrow aspiration smears in Patient 5.





Kemik iliği aspirasyonu

hemofagositoz

A) Eritrositin fagositozu

B) Trombositin fagositozu

Karti SS, et al. Emerg Infect Dis 2004

Viral yükle parelel olarak CD3- CD8 T hücreler artıyor.
Ancak hayatta kalanlarla ölenler arasında anlamlı fark yok.

Int J Infect Dis. 2009 Sep;13(5):560-3. doi: 10.1016/j.ijid.2008.08.027. Epub 2008 Dec 27.

Analysis of lymphocyte subgroups in Crimean-Congo hemorrhagic fever.

Akinci E, Yilmaz M, Bodur H, Ongürü P, Bayazit FN, Erbay A, Ozet G.

Clinic of Infectious Diseases and Clinical Microbiology, Ankara Numune Education and Research Hospital, Samanpazari, Ankara, Turkey. esragulakinci@yahoo.com

Abstract

OBJECTIVES: This study examined the association between lymphocyte subgroups and mortality in patients with Crimean-Congo hemorrhagic fever (CCHF) in Turkey.

METHODS: During the spring and summer of 2007, peripheral blood was collected from hospitalized patients with suspected CCHF. Lymphocyte subgroups were characterized by fluorescence-activated cell sorting. CCHF cases were confirmed by detecting viral RNA by PCR and/or IgM antibodies by ELISA. Lymphocyte subgroups were compared between fatal and non-fatal cases. The correlation between lymphocyte subgroups and viral loads was also investigated.

RESULTS: Seventy-seven confirmed cases of CCHF were included in this study (five cases were fatal (6.5 %)). No differences in lymphocyte subgroups were found between fatal and non-fatal cases, except for significantly higher CD3+CD8+ T cells in the fatal cases (p=0.017). A positive correlation between viral load and CD3+CD8+ T cells was also detected (p=0.044). There was no correlation between other lymphocyte subgroups and viral load.

CONCLUSIONS: Higher levels of CD3+CD8+ T lymphocytes were detected in fatal compared to non-fatal CCHF cases. Despite this cytotoxic immune activation, a fatal outcome could not be prevented. We hypothesize that high viral load and other factors may influence this outcome, although more studies are required to explain the pathogenesis of CCHF.

KKKA- Patogenez

Hematological aspects of Crimean-Congo hemorrhagic fever

Kırım-Kongo kanamalı ateşinin hematolojik yönleri

Immunological

Increased levels of cytokines (TNFα, IL-1,IL-6, IL-10)

Increased serum neopterin

Increased absolute number of peripheral blood natural killer cells

Feride Duru, Tunç Fışgın
Department of Pediatric Hematology, Ondokuz Mayıs University, Faculty of Medic

Abstract

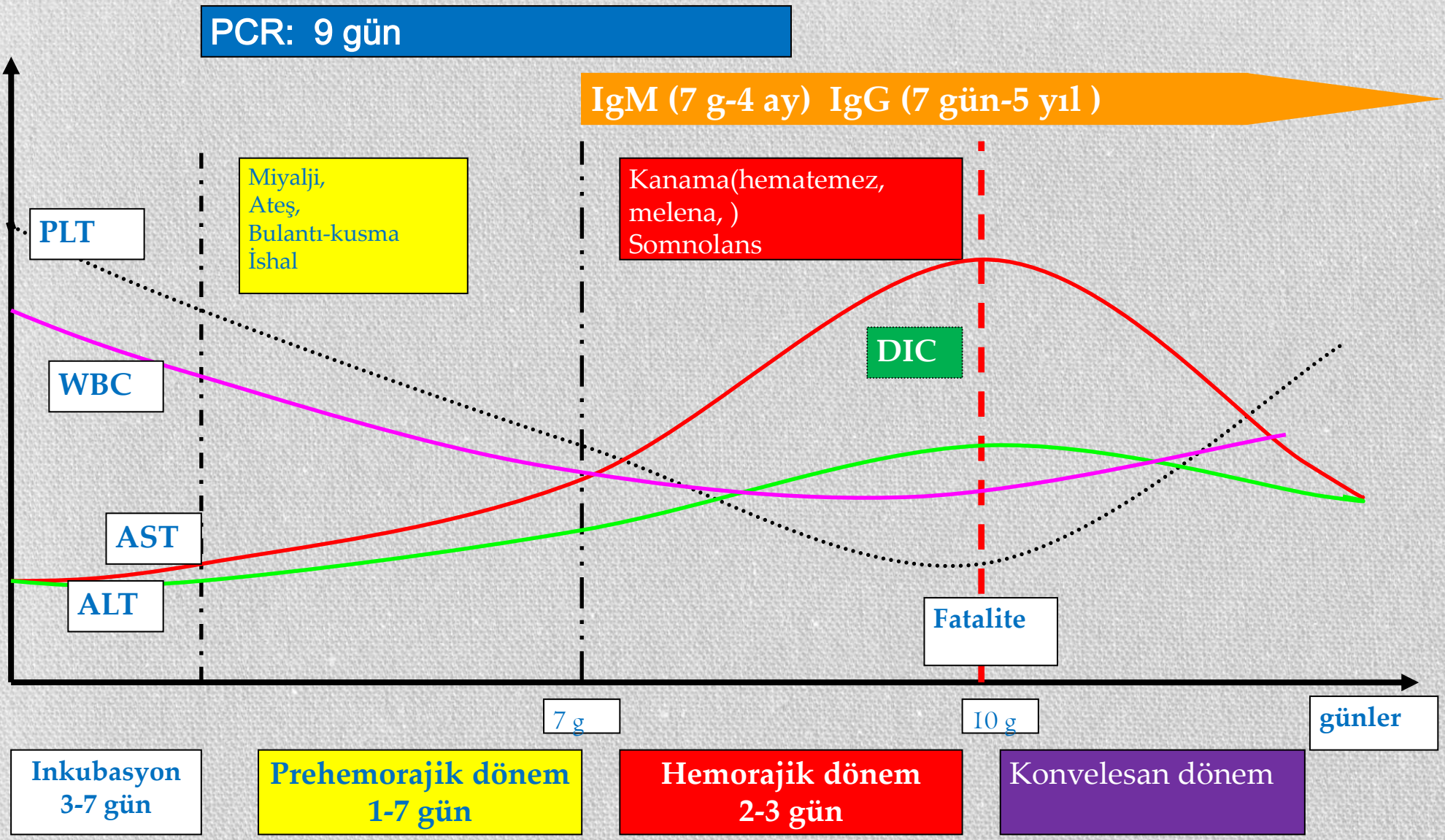
Crimean-Congo hemorrhagic fever (CCHF) is an acute tick-borne viral disease transmitted to humans by Hyalomma ticks or by direct contact with the blood of infected humans or domestic animals. In certain areas of the world, including Africa, Asia, South East Europe and Middle East, sporadic cases or outbreaks of CCHF have been reported. During the last six-year period from 2003 to 2009, CCHF has also occurred endemically in Turkey, particularly during spring and summer, with a case-fatality rate of approximately 5%. The disease is characterized by acute fever, naus

Turk J Hematol 2009; 26: 161-6

Klinik Seyir

- İnkubasyon
- Prehemorajik dönem
- Hemorajik dönem
- Konvelesan dönem

Hoogstraal,H. J med Entemol 1979; 307-417



Ergönül Ö. *Lancet ID* 2006; 6: 203-214

KKKA-İnkubasyon

- Kene ezilmesi
- Kene tutması

İnkubasyon: 3.4 (2- 7) gün

- Enfekte çiftlik hayvanlarının
- Akut infekte hastaların

Kan -vücut sıvıları - dokuları

İnkubasyon: 4.7 (2- 9) gün

Swanepoel R. et al. Rev Infect Dis. 1989, vol 11,suppl 4

KKKA- Semptomlar

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

KKKA- Klinik Bulgular

- Ateş (38°
- Konjuktival 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)

Başağrısı

Kasağrısı

Halsizlik

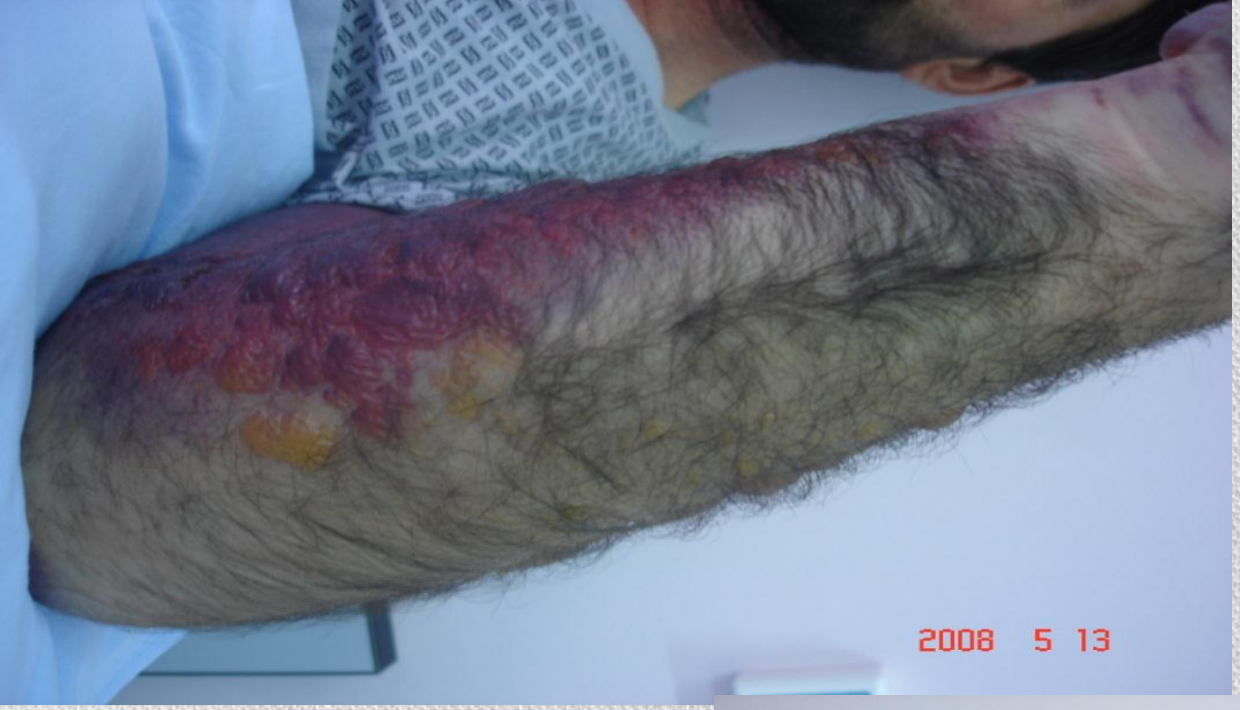
İshal

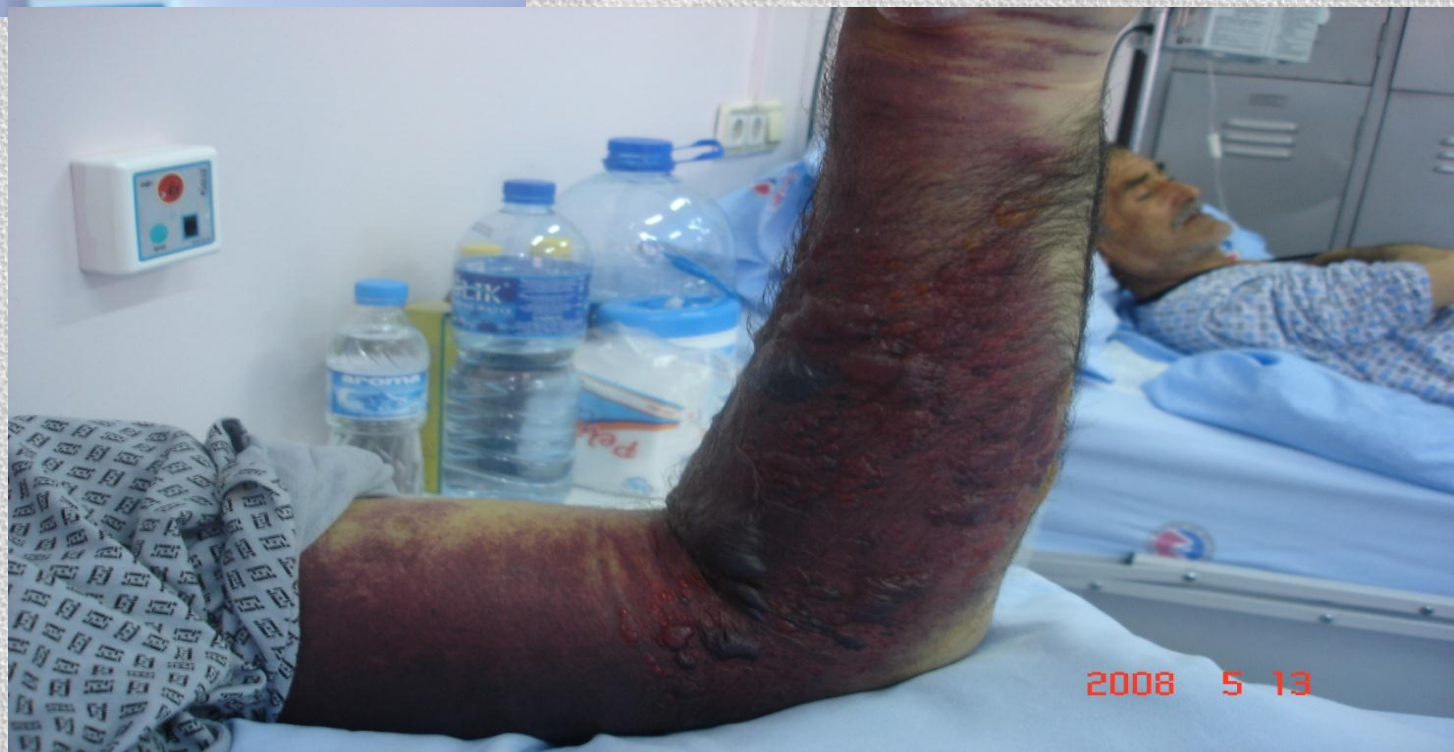
Bulantı

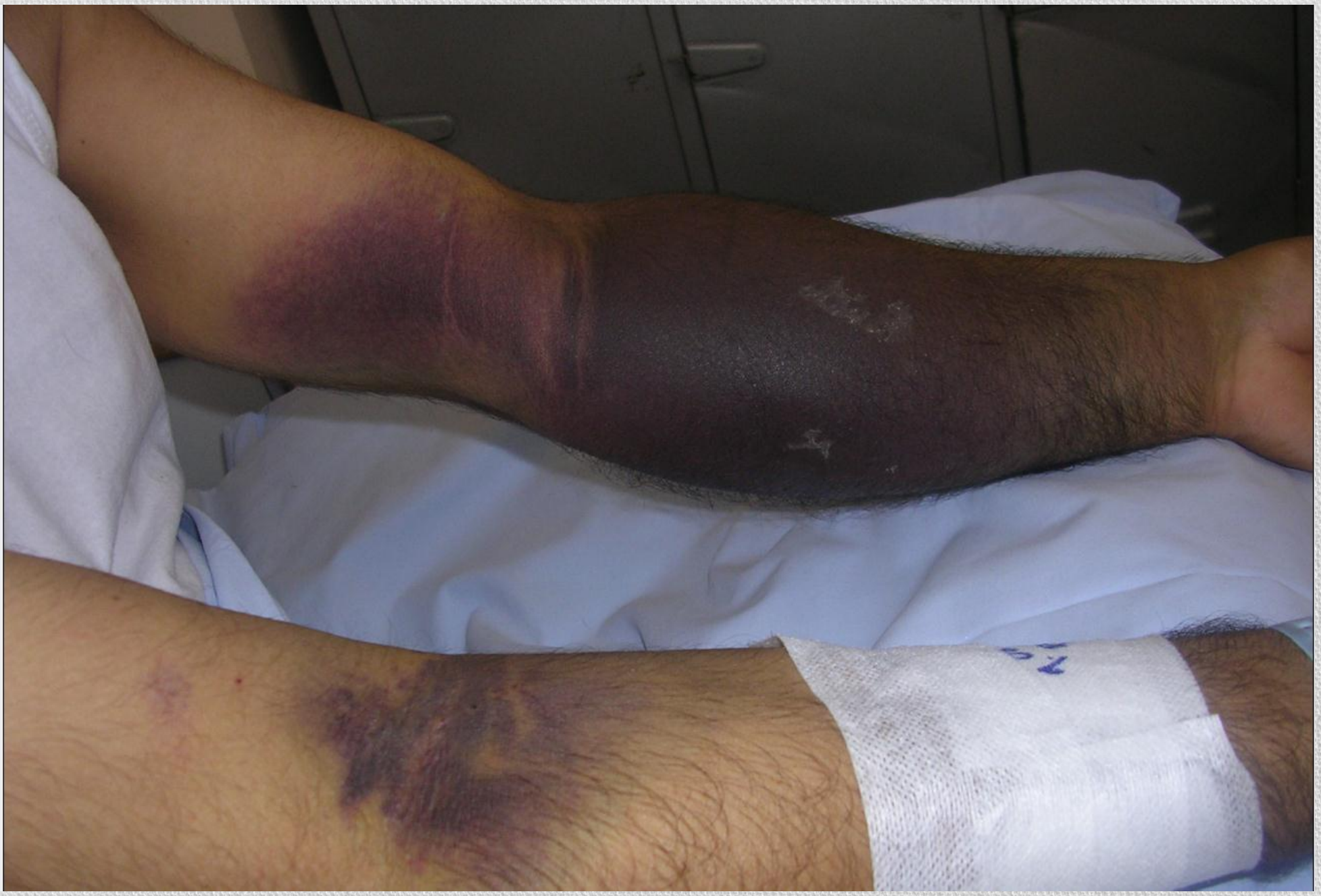
Kusma

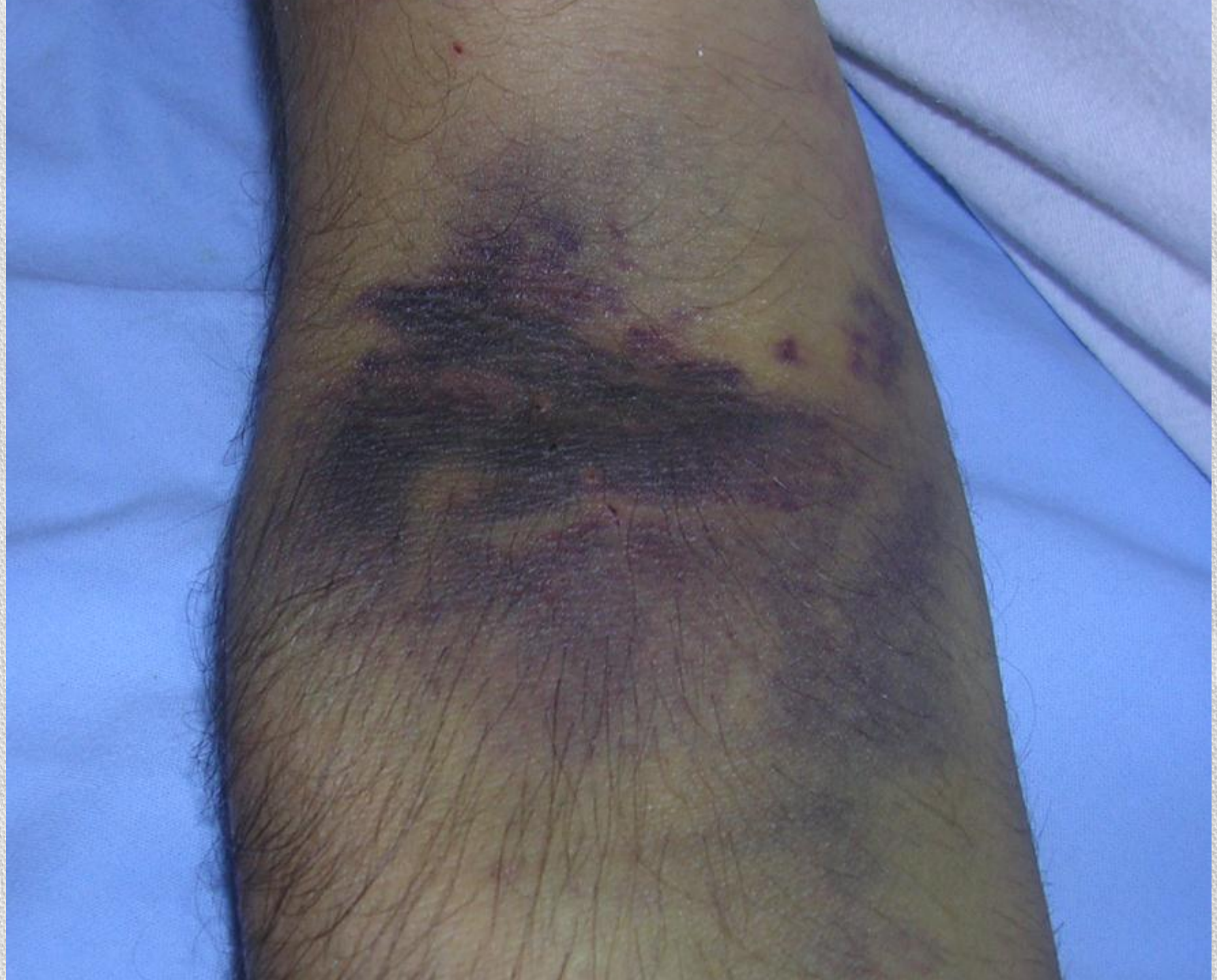
Yüzde hiperemi

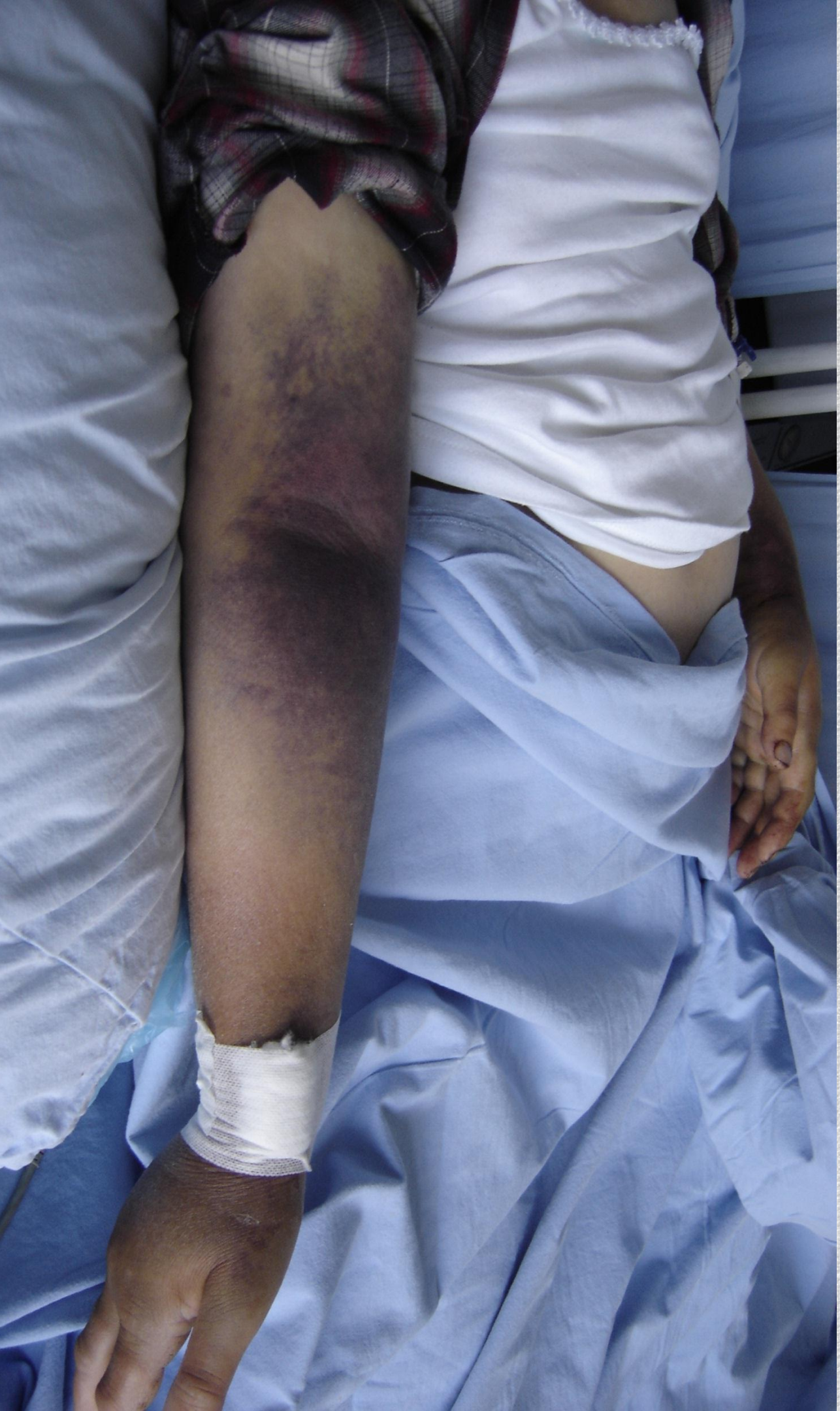
Konjonktivit

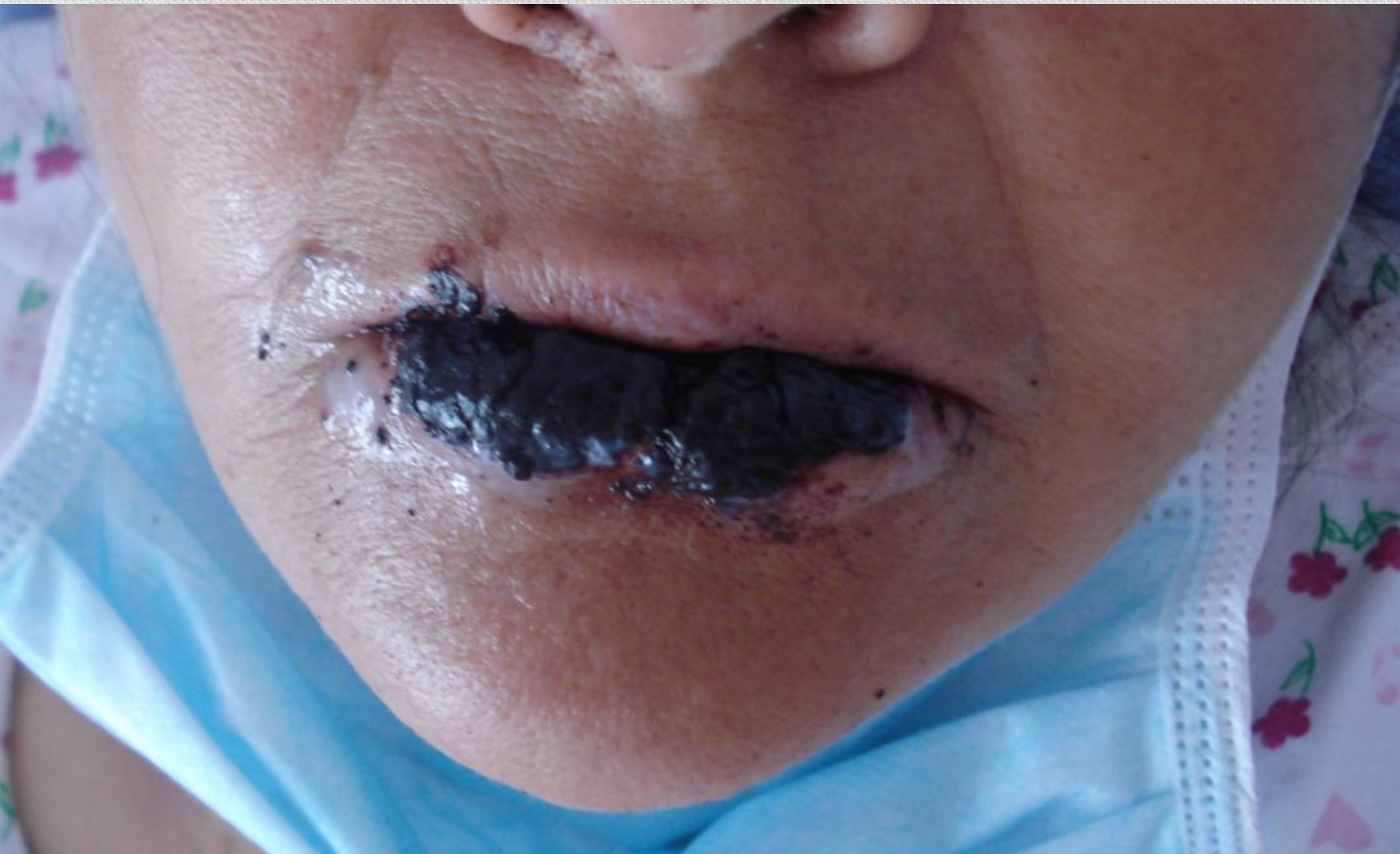

2008 5 13

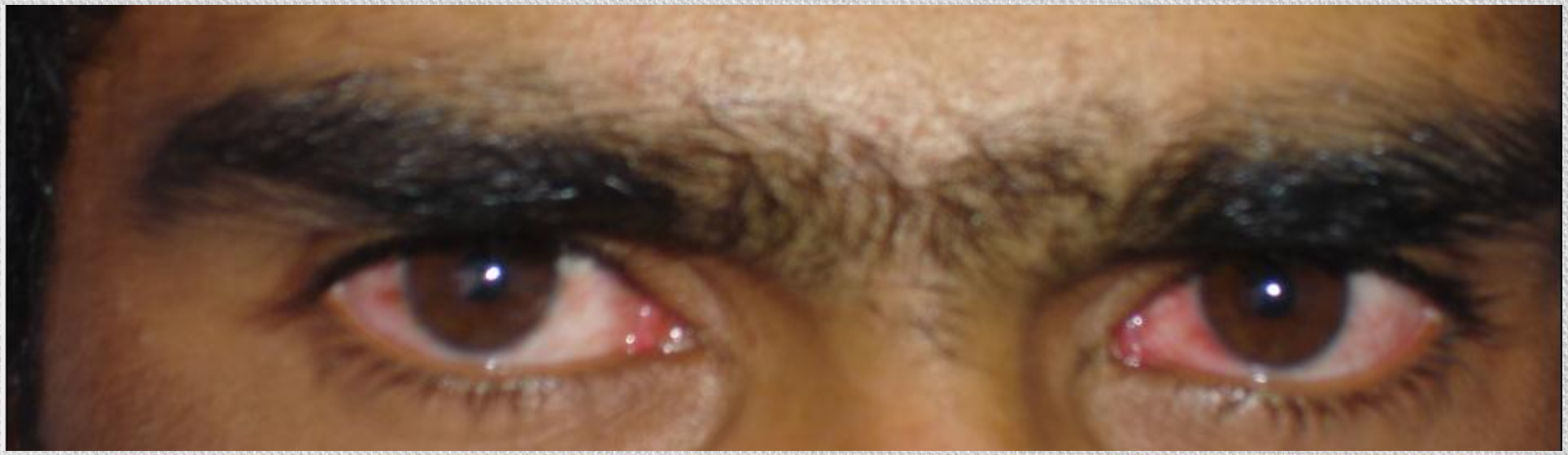

2008 5 13











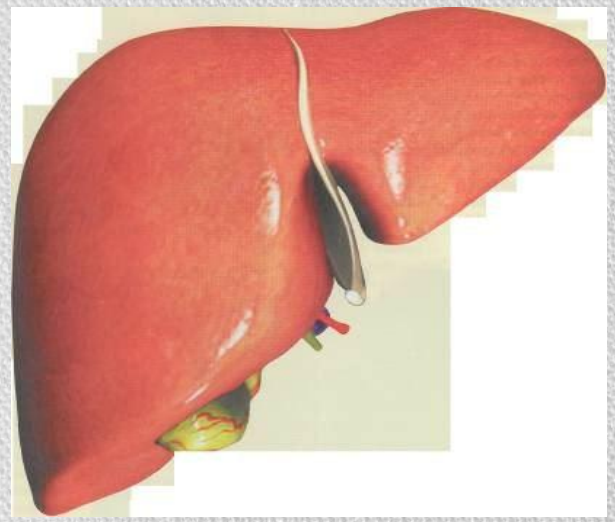
Fizik Muayene Bulguları

	Yaşayan hastalar n= 50 (%)	Ölen hastalar n=4 (%)	*p*
Ateş 38 C°	21 (42)	2 (50)	0.755
Kanama			
Hematemez	13 (26)	4 (100)	0.009
Melena	7 (14)	4 (100)	0.001
Burun kanaması	20 (40)	3 (75)	0.301
Hemoptizi	4 (8)	1 (25)	0.341
Hematüri	8 (16)	0 (0)	0.509
Makülopapüler rash	15 (30)	1 (25)	0.640
Konjunktival hiperemi	21 (42)	1 (25)	0.638
Somnolans	17 (34)	4 (100)	0.022
Sarılık	5 (10)	1 (33)	0.330
Diare	17 (34)	2 (50)	0.607
Hepatomegali	17 (35)	0 (0)	0.293

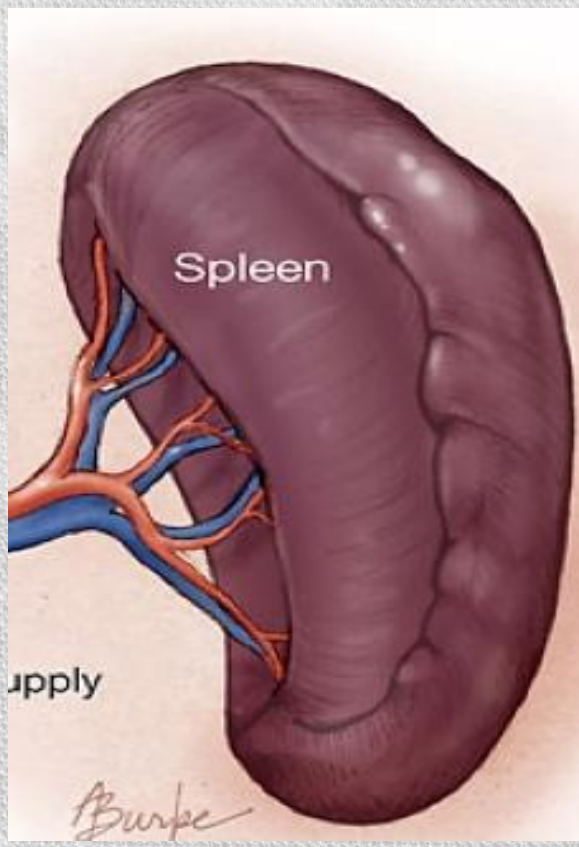
Ergönül ve ark. *Clin Microbiol Infect 2006*

Şuur bozukluğu ve splenomegali,

Bakır M, ve ark. *J Med Microbiol* 2005



Organlardaki değişiklikler



Crimean-Congo hemorrhagic fever: does it involve the heart?

- **Amaç**: KKKA ile takip edilen hastaların kardiyak fonksiyonlarını değerlendirmek.
- **Metod**: 2007 yılı hastaları

  Prospektif

  Hospitalizasyonun ilk 24 saati içinde transtorasik EKO
- **Bulgular**:17 hasta ciddi 27 hasta hafif seyirli

  5 hasta mortal seyretmiş.

  Ciddi olgularda ve özellikle mortal olgularda sol ventrikül ejeksiyon fraksiyonu (p=0.04) düşük, pulmoner arter sistolik basıncı (p=0.02)yüksek, sıklıkla perikardiyal efüzyon (p<0.001) saptanmış..
- **Sonuçlar: Kardiyak fonksiyonlar mortal ve ciddi seyreden olgularda bozulmuş.**

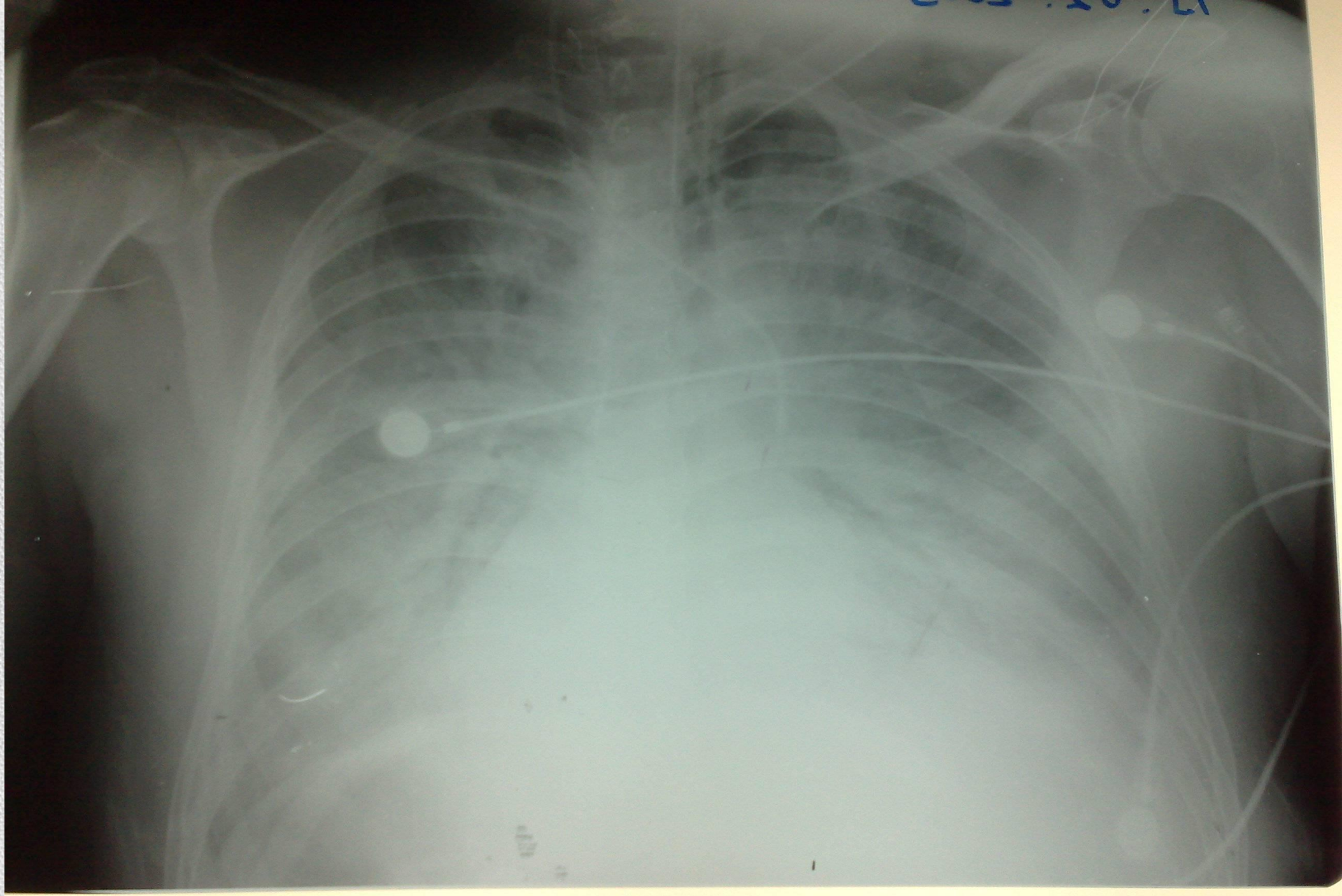
  Virus kalp kaslarının direkt invazyonu veya kardiyak yapılarda endotel hasarının bunda rolü olabilir

Engin A, Yılmaz MB,Elaldı N et al. IJID

Crimean Congo Hemorrhagic Fever and Diffuse Alveolar Haemorrhage

- Olgu sunumu: Gross hemoptizi olmadan diffüz bilateral alveolar hemoraji ile seyreden oral ribavirin tedavisi sonrasında klinik ve radyolojik olarak hızla düzelen bir olgu sunulmuş
- Alveoler hemoraji endotel hasarına bağlanmış

Doğanci L. Trop Doct. 2008 Oct;38(4):252-4



Respiratory lesions in Congo-Crimean hemorrhagic fever

- **Amaç:** KKKA olgularında akciğer bulgularının,
- **Metod:** 283 hastanın klinik, laboratuvar ve radyolojik görünümleri değerlendirilmesi, proinflamatuvar sitoki düzeylerinin belirlenmesi
- **Bulgular:** Pulmoner lezyonlar acute respiratory distress syndrome (ARDS)ile uyumlu bulunmuş

  Hemorajik periyodda bulgular kan tükürme, pulmoner hemoraji ve plevraya kanama. Hastalığın ciddiyeti proinflammatory sitokineler ile korele
- **Sonuç:** KKKA nin her döneminde Respiratuvar bulgular görülebilir. Hemorajik dönemde sistemik inflamatuvar reaksiyonla ilişkili olarak ARDS görülebilir

Sannikova IV. Ter Arkh. 2007;79(11):20-3

Transfüzyon İlişkili Akut Akciğer Hasarı

İmmünkomplekslerin oluşması ve pulmoner vasküler yatağa geçmesi sonucu vazoaktif maddeler salınır ve bunun sonucunda

- Alveoler bölgeye sıvı kaçağı,
- Kompleman aktivasyonu,
- Lökositoz
- Polimorfnükleer nötrofillerde aktivasyon olur
- . Her ünite kan transfüzyonu TRALI riskini arttırmaktadır

Transfusion 1997;37:719–726.
J Clin Invest 1998;101:1458–146
Sanchez R. Am J Clin Pathol. 2007 ;128(1):128-34

J Infect 2005

CASE REPORT

Crimean Congo hemorrhagic fever infection simulating acute appendicitis

Aysel Çelikbaş[a], Önder Ergönül[a,*], Başak Dokuzoğuz[a], Şebnem Eren[a], Nurcan Baykam[a], Arife Polat-Düzgün[b]

[a] *First Infectious Diseases and Clinical Microbiology Clinic, Ankara Numune Education and Research Hospital, Ankara, Turkey*
[b] *Third General Surgery Clinic, Ankara Numune Education and Research Hospital, Ankara, Turkey*

Accepted 29 May 2004

KEYWORDS
Crimean Congo hemorrhagic fever; Acute abdomen; Transmission

Summary An unusual cause of acute abdominal pain simulating acute appendicitis is presented. The patient was admitted with complaints of fever, malaise, headache, nausea, vomiting, diarrhoea, and severe bleeding. Based on the clinical and epidemiological findings, a diagnosis of Crimean Congo hemorrhagic fever virus infection was suspected, and ribavirin therapy was started. While her clinical condition was improving, she experienced a sudden pain at her right lower quadrant of the abdomen. Explorative laparotomy revealed haemorrhage within the abdominal muscles. Her CCHF IgM was found to be positive.

KKKA- Laboratuvar Testleri

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

Laboratuvar Bulguları

	Yaşayan hastalar ortalama (min-max) n=50	Ölen hastalar ortalama (min-max) n=4	*p*
Uzamış Prothrombin zamanı, /s	16 (10-42)	27 (18-33)	0.002
Uzamış aktive parsiyel tromboplastin zamanı, /s	44 (25-74)	73 (55-92)	<0.001
Trombosit sayısı / mm^3	27,000 (3,500-108,000)	11,000 (6,000-15,000)	0.038
Lökosit sayısı / mm^3	1,880 (150-13,000)	1,800 (1,200-3,000)	0.595
Alanine transferase, U/L	331 (38-1,443)	1,125 (219-1,785)	<0.001
Aspartate transferase, U/L	913 (65-7,150)	3,200 (773-7,700)	0.004
Lactic dehydrogenase, U/L	2,545 (283-26,000)	4,019 (1,980-9,480)	0.478
Creatinine phosphokinase, U/L	1277 (10-21,189)	1823 (1388-2164)	0.736

Ergönül, ve ark. *Clin Microbiol Infect 2006*

Ciddi Seyir Kriterleri

Swanepoel; Ciddi seyir kriterleri.

Hastalığın ilk 5 gününde

- Lökosit sayısı ≥10 000/mm3, veya
- Trombosit sayısı ≤20 000/mm3, veya
- AST ≥ 200 U/L, veya
- ALT ≥150 U/L, veya
- aPTT ≥60 saniye, veya
- Fibrinojen ≤ 110 mg/dL

Swanepoel R. et al. Rev Infect Dis. 1989, vol 11,suppl 4

Ciddiyet Kriterleri
Hangi laboratuvar testleri fatalitenin göstergesi ?

ORIGINAL ARTICLE 10.1111/j.1469-0691.2006.01445.x

Analysis of risk-factors among patients with Crimean-Congo haemorrhagic fever virus infection: severity criteria revisited

		Sensitivite (%)	Spesifite (%)	PPV (%)	NPV (%)
	Lökosit sayısı, 10,000/mm^3	100	94	25	100
AST	≥ 200 U/L, Swanepoel	9	100	100	18
	≥ 700 U/L, alternatif	16	100	100	58
ALT	≥150 U/L, Swanepoel	10	100	100	28
	≥900 U/L, alternatif	43	98	75	92

not possible because of haematemesis and melaena. Higher levels of AST (≥ 700 U/L) and ALT (≥ 900 U/L) are suggested for use as severity criteria. Oral ribavirin was not effective for patients with haematemesis, and intravenous ribavirin is necessary for treatment of CCHF.

Keywords Crimean-Congo haemorrhagic fever virus, diagnosis, ribavarin, risk-factors, severity criteria

Original Submission: 5 May 2005; **Revised Submission:** 16 November 2005; **Accepted:** 24 November 2005

KKKA- Tanı

- Virüs izolasyonu
  - Fare beyni inokülasyonu
  - Hücre kültürü
- Seroloji
  - ELİSA
  - İFA
  - PCR
  - Kompleman Birleşme Reaksiyonu
  - İmmünodifüzyon
  - Reverse Pasif Hemaglütinasyon

BSL 3

HSE

DH Department of Health

The ACDP Hazard Group 4 viral haemorrhagic fevers viruses

ARENAVIRIDAE

Old World arenaviruses

Lassa

Lujo

New World arenaviruses

Chapare

Guanarito

Junín

Machupo

Sabiá

BUNYAVIRIDAE

Nairoviruses

Crimean Congo haemorrhagic fever

FLAVIVIRIDAE

Kyasanur forest disease

Alkhurma haemorrhagic fever

Omsk haemorrhagic fever

FILOVIRIDAE

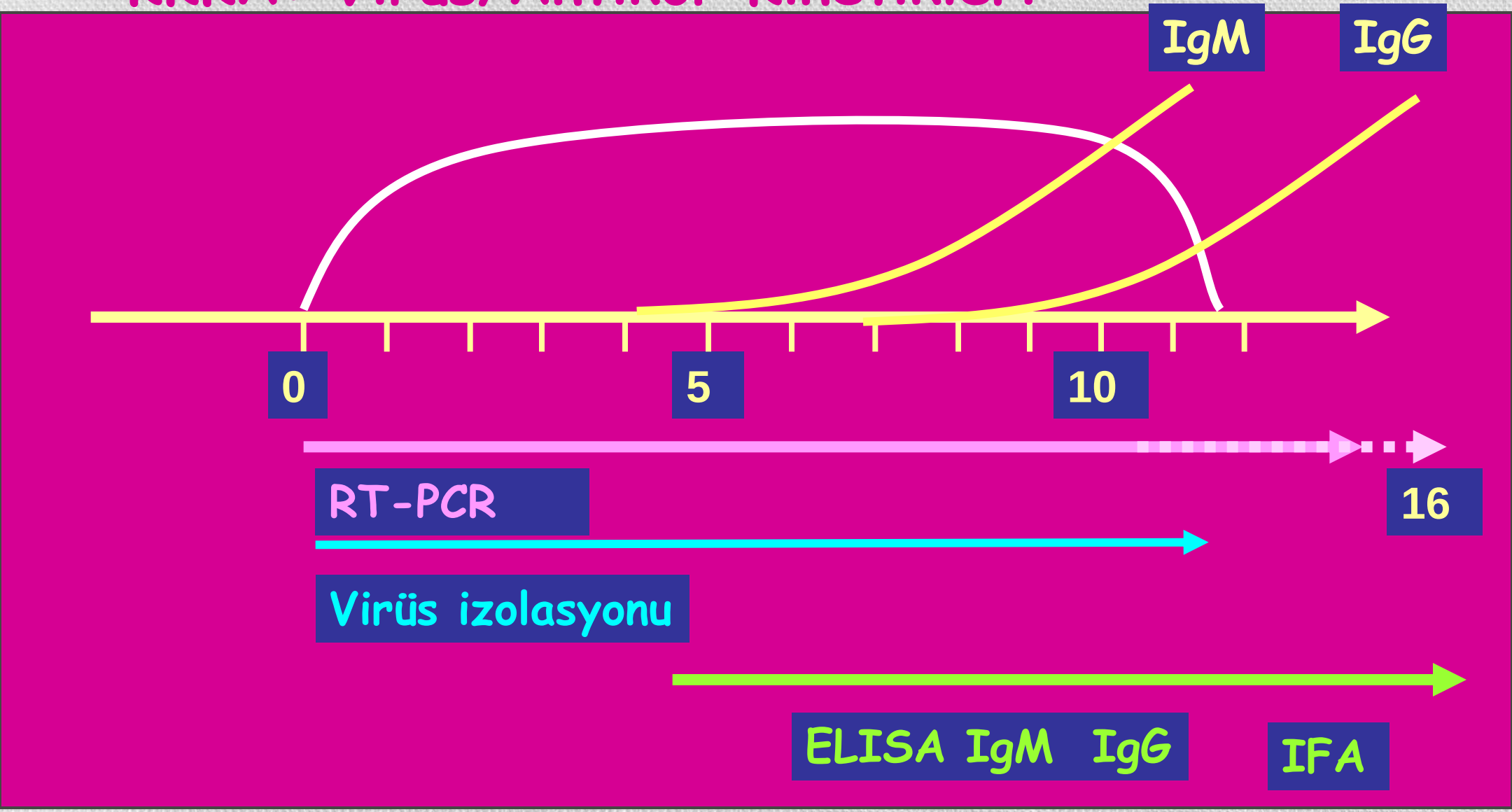
Ebola

Marburg

4 viral haemorrhagic fevers and similar human infectious diseases of high consequence

Advisory Committee on Dangerous Pathogens

KKKA: Virüs/Antikor Kinetikleri



IgM pozitifliği: 2-3 aydan 6 aya

Zeller H

Ayırıcı Tanı

Bilinen Enfeksiyonlar

Bruselloz
Q Ateşi
Riketsiyoz
Erlichioz
Lyme
Leptospiroz
Salmonelloz
Malarya

Enfeksiyon dışı

B12 eksikliği
Febril nötropeni
Toksikasyon

Diğer VHF

Güney Amerika
Lassa
Rift Valley
Hanta
Ebola & Marburg
Sarı Humma
Dengue
Kyasanur
Omsk
Alkumra

KKKA- Tedavi

Destek tedavi

- Transfüzyon
  - Trombosit
  - Eritrosit
  - Tam kan
  - Taze donmuş plazma
- Organ yetmezliğine yönelik destek

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)

Ribavirin

- FDA onayı yok
- Etkinlik açısından en önemli/ en çok tartışılan ilaç
- 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

Gözleme Dayalı Çalışmalar

Pakistan,

3 saglık çalışanı (2 cerrah 1 yardımcı personel)

oral ribavirin 4 g/gün X 4 gün ve 2.4 g/gün X 6 gün

3 hastanın tedavi öncesi;

- BK ve PLT sayıları düşük,
- AST ve ALT düzeyleri yüksek
- Hemostazı bozuk
- ölüm olasılığı %90.

Tüm değerler ribavirin başlandıktan 48 saat sonra normal

Fisher-Hoch SP, et al. Lancet. 1995 Aug 19;346(8973):472-5.

The efficacy of oral ribavirin in the treatment of crimean-congo hemorrhagic fever in Iran.

We compared the mortality rate among patients suspected of having Crimean-Congo hemorrhagic fever (CCHF) who received treatment with oral ribavirin and those who did not.
Ninety-seven (69.8%) of 139 treated patients suspected of having CCHF survived, and 61 (88.9%) of 69 treated patients with confirmed CCHF survived.
The efficacy of oral ribavirin was 80% among patients with confirmed CCHF and 34% among patients suspected of having CCHF.
Considering the limitations of observational studies, we conclude that oral ribavirin is an effective treatment for the hemorrhagic form of CCHF.

Mardani M, *Clin Infect Dis* 2003; 36: 1613-1618.

2002-2003

Orta şiddete olgular	5
Ciddi olgular	30
Ribavirin verilen	8
Ribavirin verilmeyen	22
Ölüm oranı	
Total	%2.8
Ribavirin verilmeyen	% 4.5

Ergonul O, et al. *Clin Infec Dis* 2004

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.

Faculty of Medicine, Department of Clinical Microbiology and Infectious Diseases, Ondokuz Mayis University, Samsun, Turkey. nurlyetf@omu.edu.tr

Abstract

Crimean-Congo hemorrhagic fever (CCHF) is a disease with high fatality. To demonstrate the effectiveness of ribavirin against CCHF. The first group of 21 patients received ribavirin within 4 days of the onset of symptoms (early use of ribavirin, EUR); the second group of 20 patients received ribavirin > or =5 days after the onset of the symptoms of the disease (late use of ribavirin, LUR); and the last group of 11 patients did not receive ribavirin (no use of ribavirin, NUR). At 5-10 days from the onset of symptoms the mean platelet counts of the patients in the EUR group were significantly higher than those of the patients in LUR group, and at 7-9 days, they were significantly higher than that of the patients in the NUR group. The mean aspartate transferase levels in the EUR group were significantly lower than of the NUR group on days 8 and 9, and the mean alanine transferase level was significantly lower on day 8 after the onset of the symptoms. There is a beneficial effect of ribavirin if given at an early phase of the CCHF. We suggest ribavirin use especially in the early phase of the disease.

Hastalığın ilk 4 gününde başlanan ribavirin tedavisi etkili

Tedavide Hiperimmunglobulin?

- KKKA den iyileşen hastalardan elde edilen serum Atların immünizasyonu ile elde edilen gama globulin
- Hastalığın erken döneminde faydalı

Hoogstral 1979 J. Med. Entomol 307-417

- Hastalıktan iyileşenlerden elde edilen "İmmün plazma"
- 7 hasta iyileşme
- Kontrolu olmayan bir çalışma

Vasilenko SM. Lancet 1990;335, 791-792.

Jpn. J. Infect. Dis., 64 (5), 439-443, 2011

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

Ayhan Kubar*, Mustafa Haciomeroglu[1], Aykut Ozkul[2], Umit Bagriacik[3], Esragul Akinci[4], Kenan Sener, and Hurrem Bodur[4]

Gulhane Military School of Medicine, Ankara; [1]Refik Saydam Hygiene Center, Ankara; [2]Ankara University, Ankara; [3]Gazi University, Ankara; and [4]Ankara Numune Training and Research Hospital, Ankara, Turkey

(Received May 10, 2011. Accepted August 9, 2011)

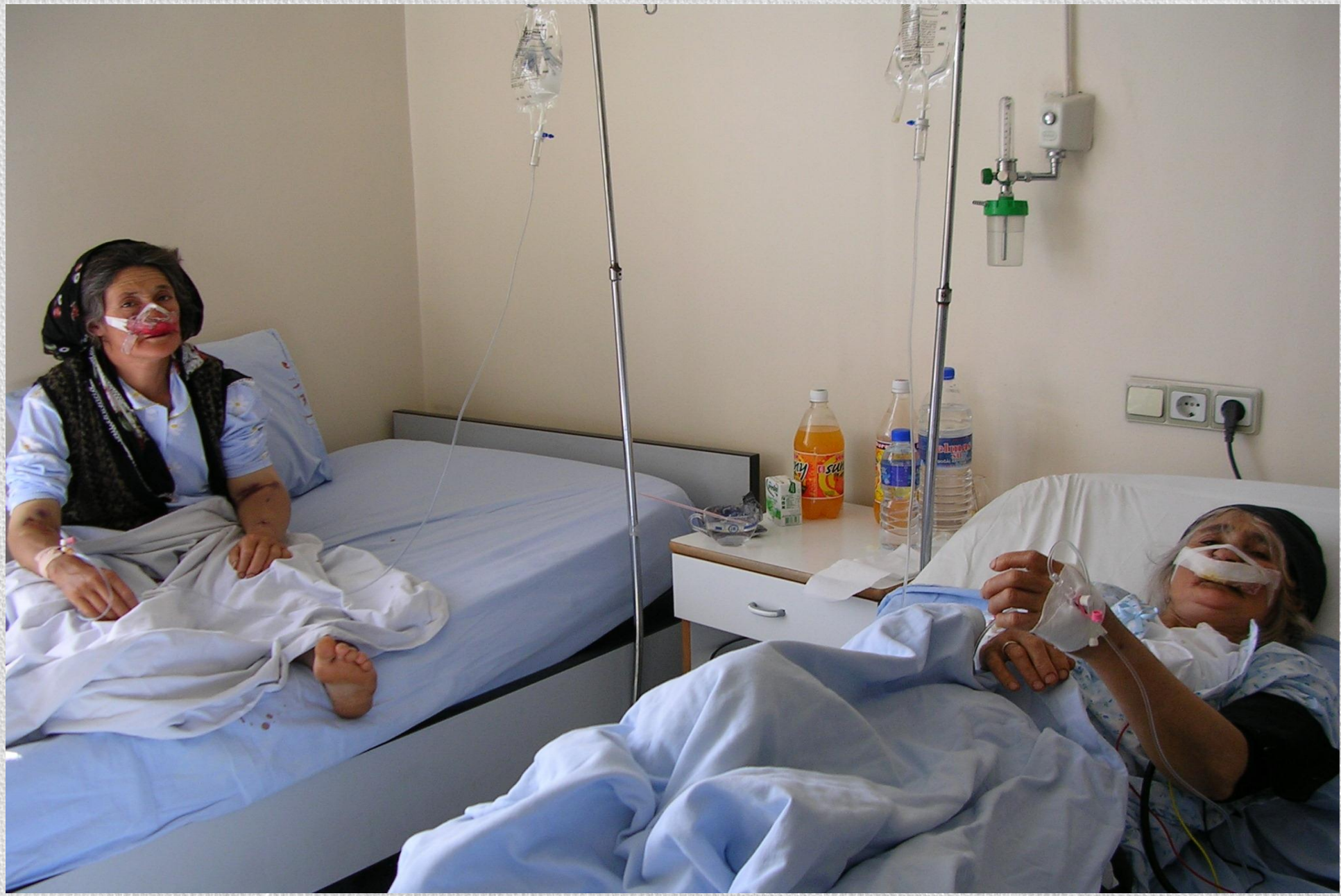
---

*Corresponding author: Mailing address: Gulhane Military School of Medicine, 06018 Ankara, Turkey. Tel: +90 312 3043414, Fax: +90 312 3043402, E-mail: akubar@hotmail.com

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 10^8 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.

Korunma

- Endemik bölgelerde yaşayanlar veya bu bölgelere seyahat edenler bahar ve yaz aylarında kenelere karşı önlem almalıdırlar.
- KKHA şüphesi olan vakaların kan ve vücut sıvıları ile perkütan veya mukokütanöz temas edildiğinde o bölge bol su ile yıkanmalıdır.
- Maruz kalanlar 10-14 gün boyunca KKHA belirtileri açısından yakın takip edilmelidir.



2007 CDC Viral Kanamalı Ateşlerde Korunma Önerileri

- Standart önlemler
- Temas önlemleri
- Damlacık önlemleri ve
- Göz koruma önerilir
- İnfekte aerosollerin ortama yayılmasını gerektiren girişimler sırasında solunum bulaşını önlemeye yönelik "izolasyon odaları" kullanılabilir

- Rutin hasta bakımında "Solunum Bulaşı Önlemleri" gerekmez

CDC
CENTERS FOR DISEASE CONTROL AND PREVENTION

http://www.cdc.gov/ncidod/dhqp/pdf/guidelines/Isolation2007.pdf

Kişisel Korunma Ekipmanları

Laboratuvar dışında gereksiz

Klinik takip sırasında

Eldiven, önlük

+

Aerosolizasyon olacak işlem yapılacaksa

Yüz koruyucu maske veya gözlük ile

N95 maske

http://www.health.state.mn.us/divs/idepc/dtopics/infectionco


ANEAH 1.Enfeksiyon Hast.Kliniği


ANEAH 1.Enfeksiyon Hast.Kliniği


ANEAH 1.Enfeksiyon Hast.Kliniği

Temas Sonrası Uygulamalar

- Hastanın kan ve vücut sıvıları ile temas edilmişse, temas edenin en az 14 gün kadar ateş, halsizlik, yaygın vücut ağrısı ve diğer belirtiler (lökopeni, trombositopeni vb.) yönünden ayaktan izlenmesi gerekmektedir
- KKKA hastalarına yapılan uygulamalar sırasında kazara iğne batması söz konusu olursa, iğnenin battığı yer sabun ve su ile yıkanarak dezenfektan ile silinmelidir
- Hastanın kan ve vücut sıvılarına yine kazara bir temas olması halinde, enfekte materyale maruz kalan bölge sabunlu su ile iyice yıkanır
- Göze enfekte materyal sıçramış ise, göz temiz su ile iyice

Sağlık Çalışanlarında Yaklaşım

Şüpheli enfeksiyon:
Hastanın kanına ya da vücut sıvılarına temas

1. Bir hafta boyunca günlük Tam Kan sayımı
2. Profilaksi (?)

14 gün sonunda normal tam kan sonuçları

Takip kesilmeli

Düşük trombosit ve lökosit düzeyi

1. Hospitalizasyon ve izolasyon
2. Hematolojik destek
3. Ribavirin

Kontamine Yüzey ve Aletlerin Dezenfeksiyonu

- Yer ve yüzeyler
- Tıbbi aletler (Vücut dereceleri, Steteskop)
- Hastanın eşyaları (Çatal, kaşık, bardak, tabak)
- Sürgü ve çöp kutuları

1:10 luk sodyum hipoklorit

TEŞEKKÜRLER