Crimean Congo Hemorrhagic Fever

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7 March 2016, Thessaloniki

Koç University
Objectives

- Epidemiology
- Clinical course
- Fatality
- Treatment
- Post-exposure prophylaxis
- Other options

<table>
<thead>
<tr>
<th>VHF virus</th>
<th>Geographic Distribution</th>
<th>Annual Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ebola</td>
<td>Africa</td>
<td>&lt;50; &gt;7000 in 2014</td>
</tr>
<tr>
<td>Marburg</td>
<td>Africa</td>
<td>&lt;300; increasing</td>
</tr>
<tr>
<td>Lassa</td>
<td>Africa</td>
<td>100,000-300,000</td>
</tr>
<tr>
<td>S.America</td>
<td>Argentine pampas</td>
<td>~300</td>
</tr>
<tr>
<td>Hantaan</td>
<td>Asia, Europe</td>
<td>50,000-150,000</td>
</tr>
<tr>
<td>Rift Valley</td>
<td>Africa</td>
<td>100-100,000</td>
</tr>
<tr>
<td>CCHF</td>
<td>Euroasia, Africa</td>
<td>&gt; 2000</td>
</tr>
<tr>
<td>Yellow F</td>
<td>Africa, South America</td>
<td>5,000-200,000</td>
</tr>
<tr>
<td>Dengue</td>
<td>Tropics, worldwide</td>
<td>DF: 100 million, DHF: 100,000-200,000</td>
</tr>
<tr>
<td>Omsk</td>
<td>Siberia</td>
<td>100-200</td>
</tr>
<tr>
<td>Kyasanur</td>
<td>Karnataka state, India</td>
<td>400-500</td>
</tr>
<tr>
<td>Alkhumra</td>
<td>Saudi Arabia</td>
<td>&lt;50</td>
</tr>
</tbody>
</table>
Crimean-Congo Haemorrhagic Fever Geographic Distribution

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

Greece (2008)
India (2011)

Epidemiologic characteristics

Rural area: 70% of the cases

Male/female ratio: 1.13/1

Tick bite history among patients: 69%

May, June, July: 84% of the cases

Migratory Birds, Ticks, and Crimean-Congo Hemorrhagic Fever Virus

To the Editor: In a recently published study, Estrada-Peña et al. reported the finding of Crimean-Congo hemorrhagic fever virus (CCHFV) in adult Hyalomma lusitanicum ticks from red deer (Cervus elaphus) in Spain during 2010 (1). Phylogenetic analysis showed that the virus was most likely of African origin. Here, we present a model for the transfer of CCHFV-infected ticks by migratory birds from Africa to Europe.

Stricto (s.s.), i.e., the principal vectors of CCHFV (2). Of 10 morphologically representative ticks, 9 were identified by molecular methods as H. rufipes and 1 as H. marginatum s.s. (6).

Ticks belonging to the H. marginatum complex are common in large parts of the African and Eurasian continents. The immature ticks feed mainly on birds and, to a lesser extent, on small mammals, whereas the adults actively seek larger mammals, including hares, wild and domesticated ungulates, or humans (4). In accordance with this pattern, 99% of the collected ticks in our study were larvae and nymphs.

On April 23, 2009, a woodchat
dubbed Lindeburg M. Emerg Infect Dis 2012

Different strains in Turkey

The Course of Infection in animals

Mild clinical symptoms
   Described by Shepherd et al in 1980s.
   No striking notes in recent outbreaks, since 2000.
Viremia
   Lasts for 7-10 days in mammals

Climate Change

Association or Causality?
Viral Hemorrhagic Fevers and Climate Change

El nino and the outbreaks:

– RVF (Linthicum et al. 1999)
– Dengue (Linthicum et al. 2008)

Climate change
- CCHF

Tick Borne Diseases and Climate

A complex network of environmental and human factors:
- independently,
- indirectly linked,
- synergistically, or
- antagonistically

Abiotic and biotic environmental changes: increase the abundance of infected ticks

Changes in human activities associated with increases in greater contact between people and tick-infested forests.

Randolph SE & Ergonul O. Future Virology 2008
In April (1990-2004), number of days >5 °C

Ergonul O, et al. ECCMID 2005, P 1147

CCHF cases in the Rostov region for 1963-2008

Cold winters in late 1960s; Hoogstral, 1979
Changes in Biotic Environment

- De-population
- Increase in vectors and reservoirs
- Re-population
- Sudden Exposure
Circulation of CCHFV in Southwestern Europe

The close affinity of the strain from Spain with strains circulating in western Africa.

The lack of similarity with isolates from eastern Europe.

Migratory movements of birds

Less likely; trade movements of domestic from eastern Europe.

Estrada Peña A. Emerg Infect Dis 2012

Known records of *Hyalomma marginatum*

The predicted climate suitability for the tick *H. marginatum* in the area of analysis with current (1970-2000) climate conditions

The predicted climate suitability as projected for the year 2050, using the same set of variables.

Estrada-Pena 2009
Which one do you expect in CCHF?

a. Low platelet
b. Low leukocyte
c. High procalcitonin
d. High ESR
e. High CRP

Case

37 years old male came to the outpatient clinic. He has myalgia, sometimes high fever. As the first step CBC was done. His plt count was 78,000/ml, leukocyte count was 3800/ml, his CRP was 60, procalcitonin level was 0.8.
Your differentials?

• CCHF
• West Nile
• Chikungunya
• Zika
• Sandfly
• Hanta virus
• Influenza
• Dengue

What is your next step?

• History
  – Drug
  – Travel
  – Etc.
• Lab tests
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.
Crimean-Congo Hemorrhagic Fever

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.

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).

The attack and the infection rates of CCHFV Infection in an endemic region
Önder Ergönül, Herve Zeller, Şirin Menekse, Ayşel Celikbaş, Şebnem Eren, Nurcan Baykam, Başak Dokuzoğuz
ECCMID 2006, Nice

IgG (+)
6 / 35 without tick bite history
6 / 19 with tick bite history

55 individuals in endemic region, 30 dealing with husbandry
19 individuals with history of tick bite
6 individuals without history of tick bite
11 patients
SEIR Model for CCHF

Fig. 15-2. Schematic diagram of a dynamic compartmental SEIR model.


Fig. 15-3. Output from the SEIR model when mean infectious period (1/\(\gamma\)) is 10 days, mean latent period (1/\(\theta\)) is 5 days, \(\mu = 0.0005\) and \(b = 0.02\).
The Parameters to be included to the model

- Susceptible human population:
  - $R_0$, herd immunity
  - Newborns, migration
- Tick population
  - Tick abundance
  - Climate change
- Plant reservoir
- Animal reservoir

Clinical Features
Clinical and Laboratory Course

Polymerase Chain Reaction: The first 2 weeks

Flu like Illness:
- Myalgia,
- Fever,
- Nausea-vomiting
- Diarrhea

IgM (7 days-4 months) and IgG (7 days-5 years)

Specific symptoms

Fatality happens

Incubation 3-30 days

Prodromal period 1-7 days

Specific symptoms 2-7 days

Convelescence
Host Dynamics
From Epidemiology to Immunology

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


**Why The Case Fatality Rate Differs?**

1. Different strains

2. Co-existent infection
   very rare; Malaria, Iran, 2012; Leishmania, Turkey, 2011

3. Health care facility
   - Access
   - Quality

4. The sensitivity threshold for the symptoms:
   inclusion of the milder cases inflates the denominator
Viral Load is Higher Among Fatal Cases


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

Onder Ergenul,1 Semru Tencelie,2 Nurcan Bagışan,1 Ayse Celikbas,2 and Basak Dokuzoguz4
1Infection Diseases and Clinical Microbiology Clinic, Ankara Numune Education and Research Hospital, and 4Biom Laboratories, Ankara, Turkey

J Infect Dis 2006; 193: 941-4
**Fatality Among Hospitalized Children**

50 children in Turkey; 0% (Tuygun N, et al. Pediatr Int 2011)

Cytokine Levels of Different Severity Groups for First Five Days

Multivariate analysis of HLA types for the prediction of severe cases among CCHF patients.

n=114, mild and severe confirmed CCHF patients

<table>
<thead>
<tr>
<th></th>
<th>Odds ratio</th>
<th>Confidence interval</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Q6</td>
<td>4.9</td>
<td>2.03-12.1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Q7</td>
<td>5.2</td>
<td>1.51-18.03</td>
<td>0.009</td>
</tr>
<tr>
<td>DR14</td>
<td>7.1</td>
<td>2.4-12.39</td>
<td>&lt;001</td>
</tr>
<tr>
<td>C12</td>
<td>1.7</td>
<td>0.72-4</td>
<td>0.225</td>
</tr>
</tbody>
</table>
The goal of the therapy is the prevention of fatality.

Which can be used in treatment?

a. Supportive tx (FFP, fluids, etc)
b. Oseltamivir
c. Ganciclovir
d. Ribavirin
e. Convalescent plasma
Universal precautions

Hospitalization

Isolation

Avoid from the trauma that could cause bleeding

Watch for bleeding

Protect oral cavity
  Remove crusts from the oral cavity,
  Brush teeth carefully,
  Keep mouth and lips clean

Hematologic support

Fluid and electrolyte balance should be sustained

If necessary;
  Blood,
  Trombocyte suspension,
  Fresh frozen plasma
Ribavirin: A Broad Spectrum Antiviral
Only Drug for VHF

<table>
<thead>
<tr>
<th>Arenaviridae</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lassa Fever</td>
</tr>
<tr>
<td>South America HF</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Bunyaviridae</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hanta</td>
</tr>
<tr>
<td>Rift Valley</td>
</tr>
<tr>
<td>CCHF</td>
</tr>
</tbody>
</table>

**Ribavirin is effective in vitro**

Effective in vitro

Inhibits viremia among rats

The most effective among the alternatives
Clinical Observations: Case series, historical control

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

Problems in Study Design: What We Learned?

A. Study Design
1. Inclusion criteria
   1. Severity
   2. Confounding by indication
2. Number of days from onset of symptoms
   1. Prehemorrhagic
   2. Hemorrhagic
3. Ineffective application:
   GIS symptoms in oral use (hematemesis)
4. Duration of treatment

B. Statistical Analysis
1. P value is not everything; sample size is important
2. Meta-analysis: oranges & apples; early vs late
Characteristics of Patients with Crimean-Congo Hemorrhagic Fever in a Recent Outbreak in Turkey and Impact of Oral Ribavirin Therapy

Onder Erginol, Ayse Colakbas, Basak Dokuzoguz, Sebnem Ero, Nuran Bayram, and Hazira Emen.
Infectious Diseases and Clinical Microbiology Department, Ankara Numune Education and Research Hospital, Ankara, Turkey.

Patients infected with CCHF virus is suggested, which will be helpful for future outbreaks.

Patients and methods. Ankara Numune Education and Research Hospital (Ankara, Turkey) is one of the largest referral-based tertiary care community hospitals in Turkey. Patients with acute febrile syndrome characterized by petechial bleeding, leukopenia, and thrombocytopenia were admitted to our clinic during the spring and summer of 2003 and 2004. Patients who had IgM antibodies or PCR results positive for CCHF virus in blood or tissue specimens were included to the study. Written informed consent was obtained from patients.

Table 3. Univariate and Adjusted Analysis for Prediction of Death

<table>
<thead>
<tr>
<th>Factor</th>
<th>Univariate Analysis</th>
<th>Adjusted Analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>OR (95% CI)</td>
<td>P-Value</td>
</tr>
<tr>
<td>SSI</td>
<td>2.49 (1.82-3.41)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Ribavirin use</td>
<td>0.68 (0.23-1.93)</td>
<td>.75</td>
</tr>
<tr>
<td>Corticosteroid use</td>
<td>5.65 (2.31-13.77)</td>
<td>.001</td>
</tr>
</tbody>
</table>

Abbreviations: CI, confidence interval; OR, odds ratio; SSI, severity scoring index.

Severity Scoring Index for Crimean-Congo Hemorrhagic Fever and the Impact of Ribavirin and Corticosteroids on Fatality

Başak Dokuzoguz,1 Ayse Kocaçil Colakbas,1 Sebnem Ero Gök,1 Nuran Bayram,1 Mustafa Nacif Erten,1 and Onder Erginol1
1Clinical Microbiology and Infectious Diseases Clinic, Ankara Numune Education and Research Hospital, Ankara, and Infectious Diseases and Clinical Microbiology, Kırıkkale University, College of Medicine, Kırıkkale, Turkey.

Table 2. Effects of RBV and Additional Therapy on CFRs Among Patients With Crimean-Congo Hemorrhagic Fever, Stratified by SSI

<table>
<thead>
<tr>
<th>SSI Disease Severity</th>
<th>CFR, % (Proportion of Patients, by RBV Status)</th>
<th>P-Value</th>
<th>CFR, % (Proportion of Patients, by CS Status)</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>RBV</td>
<td>No RBV</td>
<td>CS</td>
<td>No CS</td>
</tr>
<tr>
<td>0-2; mild</td>
<td>0 (0/77)</td>
<td>0 (0/28)</td>
<td>0.0 (0/103)</td>
<td>0 (0/103)</td>
</tr>
<tr>
<td>3-6; moderate</td>
<td>1 (1/12.4)</td>
<td>17 (2/19)</td>
<td>0.01</td>
<td>4 (1/28)</td>
</tr>
<tr>
<td>10-13; severe</td>
<td>0 (0/16.4)</td>
<td>100 (1/21)</td>
<td>.296</td>
<td>99 (1/16)</td>
</tr>
</tbody>
</table>

Abbreviations: CFR, case-fatality rate; CS, corticosteroid; RBV, ribavirin; SSI, severity scoring index.
Confounding by indication

Fresh frozen plasma

<table>
<thead>
<tr>
<th>Survived cases</th>
<th>fatal cases</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image1" alt="Graph" /></td>
<td><img src="image2" alt="Graph" /></td>
</tr>
</tbody>
</table>

$p=0.002$

Thrombocyte suspension

<table>
<thead>
<tr>
<th>Survived cases</th>
<th>fatal cases</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image3" alt="Graph" /></td>
<td><img src="image4" alt="Graph" /></td>
</tr>
</tbody>
</table>

$p=0.001$

Ergonul, et al. *CMI 2006*
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

91 patients, 18 fatality

<72 hours
58 survived
2 died

>72 hours
15 survived
16 died

P<0.001

Early use of ribavirin is beneficial in Crimean-Congo hemorrhagic fever

The study included patients who were hospitalized between 2005 and 2010 at the Infectious Diseases Department of Kastamonu Dr. Münif İslamoğlu Hospital in the Kastamonu Province of Turkey. In total, 342 confirmed cases of Crimean-Congo hemorrhagic fever (CCHF) were included in the study.

The overall case fatality rate was 2.9%. In multivariate analysis, the patients that were admitted to the hospital within 2 days after onset of symptoms (odds ratio [OR]=5, confidence interval [CI] 0.31-0.86) and received oral ribavirin (OR=0.12, CI 0.05-0.26) were less likely to become more severe cases and less likely to be transferred to the tertiary care centers.
Early Use is More Effective
A randomised controlled trial of ribavirin in Crimean Congo haemorrhagic fever: ethical considerations
B Arda, A Aciduman, J C Johnston

CONCLUSION
There is universal agreement that placebo-controlled trials should be prohibited in life-threatening conditions if an existing treatment is effective at prolonging or preserving life. The available literature provides convincing evidence that CCHF may be effectively treated with prompt administration of ribavirin. It is the standard of care in several nations, and ratified by the Centers for Disease Control and WHO. Therefore, it would be decidedly unethical to conduct an RCT of ribavirin in patients harbouring this life-threatening disease.

J Med Ethics 2011

**Multiferon is more effective**

Two recombinant IFN-alpha preparations (Roferon A and Intron A) have significant antiviral activities against CCHFV.

Multiferon inhibits viral replication more efficiently than the two recombinant IFN alpha preparations.

No difference in fatality.

<table>
<thead>
<tr>
<th>VHF</th>
<th>Human to human transmission</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ebola</td>
<td>High</td>
</tr>
<tr>
<td>Marburg</td>
<td>High</td>
</tr>
<tr>
<td>Lassa</td>
<td>Moderate</td>
</tr>
<tr>
<td>S.America</td>
<td>Low</td>
</tr>
<tr>
<td>Hantaan</td>
<td>No</td>
</tr>
<tr>
<td>RV</td>
<td>No</td>
</tr>
<tr>
<td>CCCF</td>
<td>High</td>
</tr>
<tr>
<td>Yellow fever</td>
<td>No</td>
</tr>
<tr>
<td>Dengue</td>
<td>No</td>
</tr>
<tr>
<td>Omsk</td>
<td>Not reported</td>
</tr>
<tr>
<td>Kyasanur</td>
<td>Not reported</td>
</tr>
<tr>
<td>Alkhumra</td>
<td>Not reported</td>
</tr>
</tbody>
</table>
Transmission risk among HCWs

Transmission risk
- Contaminated blood 8.7%
- Needle stick 33%


In an endemic region in Africa;
Seroprevalence among HCWs <1% (1/128)

Nosocomial Infection in Tajikistan, 2009

Index case
50, male, FATAL

Physician
47, m, FATAL

Wife
47, m, survived

Brother
42, m, FATAL

39 contacts
27 HCWs

Transmission of CCHF to HCWs

3 out of 5 (60%) died
No ribavirin use 10 years ago in Iran

What precautions should be used for HCW?
Hand hygiene and use of PPE based on risk assessment

- Always before and after patient contact, and after contact with contaminated environmental surfaces or equipment
- If direct contact with patient’s blood and body fluids, secretions, excretions, mucous membranes or non-intact skin
- If there is a risk of spills onto the health-care worker’s face
Is Ribavirin Prophylaxis Effective for Nosocomial Transmission of Crimean-Congo Hemorrhagic Fever?

Conclusions

In preventing the transmission of CCHF, it should always be kept in mind, especially in serious CCHF cases, that there can always be bleeding. Barrier precautions should never be neglected. Ribavirin is the drug of choice currently available and seems effective in cases of nosocomial transmission of CCHF.
Crimean-Congo Hemorrhagic Fever among Health Care Workers, Turkey

Table 1: Clinical and laboratory findings of HCWs in whom Crimean-Congo hemorrhagic fever developed after occupational exposure, Turkey, 2004-2011

<table>
<thead>
<tr>
<th>Body</th>
<th>Temperature, °C</th>
<th>Bleeding</th>
<th>Leukocytes, x10^9/mm³</th>
<th>Platelets, x10^9/mm³</th>
<th>AST</th>
<th>ALT</th>
<th>Alkaline phosphatase</th>
<th>Bilirubin</th>
<th>SII</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. survived</td>
<td>36.5</td>
<td>No</td>
<td>120</td>
<td>42,000</td>
<td>425</td>
<td>346</td>
<td>3</td>
<td>225</td>
<td>Moderate</td>
</tr>
<tr>
<td>2. survived</td>
<td>37.2</td>
<td>No</td>
<td>120</td>
<td>53,000</td>
<td>145</td>
<td>61</td>
<td>1</td>
<td>270</td>
<td>Severe</td>
</tr>
<tr>
<td>3. died</td>
<td>40.5</td>
<td>Ecchymoses, hemorrhage, meningitis, hemorrhitits</td>
<td>11,100</td>
<td>40,000</td>
<td>261</td>
<td>277</td>
<td>59</td>
<td>171</td>
<td>Severe</td>
</tr>
<tr>
<td>4. survived</td>
<td>40.5</td>
<td>No</td>
<td>2,900</td>
<td>70,000</td>
<td>900</td>
<td>37.4</td>
<td>125</td>
<td>250</td>
<td>Mild</td>
</tr>
<tr>
<td>5. survived</td>
<td>39</td>
<td>Epistaxis</td>
<td>1,600</td>
<td>50,000</td>
<td>143</td>
<td>64</td>
<td>121</td>
<td>218</td>
<td>Moderate</td>
</tr>
<tr>
<td>6. survived</td>
<td>40.5</td>
<td>No</td>
<td>1,500</td>
<td>44,000</td>
<td>123</td>
<td>216</td>
<td>40.5</td>
<td>165</td>
<td>Moderate</td>
</tr>
<tr>
<td>7. survived</td>
<td>39.1</td>
<td>No</td>
<td>3,100</td>
<td>52,000</td>
<td>146</td>
<td>132</td>
<td>40.8</td>
<td>170</td>
<td>Moderate</td>
</tr>
</tbody>
</table>

1. HCW = health care worker; AST = aspartate aminotransferase; ALT = alanine aminotransferase; ALP = alkaline phosphatase; B = bilirubin; SII = severity score index.
2. Reference values: Leukocytes, 4,000–11,000/mm³; platelets, 150,000–400,000/mm³; AST, <50 U/L; ALT, <50 U/L; ALP, <24 U/L; creatinine, 80–100 mg/dL.

Emerg Infect Dis 2014
Health Care Response to CCHF in US Soldier and Nosocomial Transmission to Health Care Providers, Germany, 2009

Natalia Yurievna Pshenichnaya, Natalya Alekseevna Nenasheva, Viktoriya Kirillovna Kononova, Alina Emirlanovna Yagupova, Alina Konstantinovna Tushinova, Natalia Nikolaevna Dronova, Elizaveta Nikolaevna Sokolovskaya, Svetlana Alexeevna Ovchinnikova, and Mark G. Kortepeter

Table 3. Surveillance criteria and PPE, by exposure risk, for contacts of US soldier with fatal Crimean–Congo hemorrhagic fever (CCHF) acquired by a US soldier in Afghanistan, 2009

<table>
<thead>
<tr>
<th>Group no.</th>
<th>No. of contacts</th>
<th>N95 PPE utilized</th>
<th>Blood and body fluid exposure</th>
<th>Body temperature</th>
<th>Diarrhea</th>
<th>Hepatic failure</th>
<th>Management</th>
<th>Outcome</th>
</tr>
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<td>1</td>
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<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>2</td>
<td>5</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>3</td>
<td>5</td>
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<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
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</tbody>
</table>

†Proper PPE for aerosol exposure included gown, gloves, N95 respirator, and protective eyewear; powered air-purifying respirators and full biohazard suits were required during bronchoscopies and chest tube placements by the physician performing the procedure.

Perspective

Probable Crimean–Congo hemorrhagic fever virus transmission occurred after aerosol-generating medical procedures in Russia:

nosocomial cluster

Natalia Yurievna Pshenichnaya, Svetlana Alexeevna Nenasheva

This case of airborne transmission of CCHF demonstrates that during performance of any AGMPs for any CCHF patient, airborne precautions should always be added to standard precautions (particulate respirator protective to N95 or equivalent standard, eye protection, single airborne precaution room or well-ventilated setting, etc.) according to WHO guidelines for all HCWs who are in a patient’s room. Access to any room where the aerosol-generating procedures are performed should be extremely limited.
Exposure to Crimean-Congo Hemorrhagic Fever Infection among Health Care Workers

The authors recommend oral ribavirin postexposure prophylaxis for Lassa fever exclusively for definitive high-risk exposures.

**Table 1. Results of tick-detachment techniques**

<table>
<thead>
<tr>
<th>Technique</th>
<th>Detached as a whole, n (%)</th>
<th>Detached broken, n (%)</th>
<th>Undetached, n (%)</th>
<th>Total</th>
<th>Application time, s (minimum-maximum)</th>
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</thead>
<tbody>
<tr>
<td>Card-detachment technique</td>
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<td></td>
</tr>
<tr>
<td>Immature ticks</td>
<td>0</td>
<td>0</td>
<td>20 (50)</td>
<td>20</td>
<td>60 (40-80)</td>
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<tr>
<td>Adult ticks</td>
<td>3 (7.5)</td>
<td>5 (12.5)</td>
<td>12 (30)</td>
<td>20</td>
<td>90 (60-140)</td>
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<td>Lassoing technique</td>
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<td>3 (7.5)</td>
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<td>30 (10-45)</td>
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<td>18 (45)</td>
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<td>Freezing technique</td>
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<td>20 (50)</td>
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<td>30 (10-50)</td>
</tr>
<tr>
<td>Adult ticks</td>
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<td>20 (50)</td>
<td>20 (50)</td>
<td>20</td>
<td>30 (10-50)</td>
</tr>
<tr>
<td>Technique using tweezers</td>
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<tr>
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<td>20</td>
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</tr>
<tr>
<td>Adult ticks</td>
<td>18 (45)</td>
<td>2 (5)</td>
<td>0</td>
<td>20</td>
<td>45 (40-50)</td>
</tr>
</tbody>
</table>
Potential Responses to “So What?” Question

1. Understanding of the disease dynamics; to improve our intuition (Description).
   **Picture of global burden**

2. Highlights the key uncertainties and gaps in our knowledge; to suggest observational or experimental studies (hypothesis generation).
   **New clinical and epidemiological studies**

3. Models can help in the selection of control policies (intervention).
   **Drugs, vaccine or repellent?**

4. Forecasting the future of epidemics (prediction).
   **What will happen next year?**

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