

## Crimean Congo Hemorrhagic Fever: Experience in Turkey



Prof. Hakan Leblebicioğlu, MD

[hakanomu@yahoo.com](mailto:hakanomu@yahoo.com)

Department of Infectious Diseases & Clinical Microbiology  
Ondokuz Mayıs University, Medical School, Turkey



## Disclosure

- I have no actual or potential conflict of interest in relation to this presentation



Birthplace of the founder of Turkey, Atatürk in Thessaloniki



## Crimean-Congo hemorrhagic fever in Turkey: Current status and future challenges

Hakan Leblebicioglu<sup>a,\*</sup>, Resat Ozaras<sup>b</sup>, Hasan Irmak<sup>c</sup>, Irfan Sencan<sup>d</sup>

<sup>a</sup>Department of Infectious Diseases and Clinical Microbiology, Ondokuz Mayıs University Medical School, Samsun, Turkey

<sup>b</sup>Department of Infectious Diseases and Clinical Microbiology, Istanbul University Cerrahpaşa Medical School, Istanbul, Turkey

<sup>c</sup>Republic of Turkey Ministry of Health, Ankara, Turkey

<sup>d</sup>Department of Infectious Diseases and Clinical Microbiology, Düzce Vahdettin Keyifli Education and Research Hospital, Düzce, Turkey

### ARTICLE INFO

#### Article history:

Received: 17 September 2013

Received in revised form:

8 December 2013

Accepted: 10 December 2013

Available online: 13 December 2013

### ABSTRACT

Crimean-Congo hemorrhagic fever (CCHF) is a tick-borne viral disease of humans that affects a wide geographic area of Africa and Eurasia, including Turkey, Iran, Pakistan, Afghanistan and Russia. Since the first detection of CCHF cases in Turkey in 2002, more than 9700 patients have been reported, with an overall mortality rate just under 35. This article assesses the present epidemiological situation of CCHF in Turkey, with an updated literature review, describes national practices and summarizes lessons learned in preparation for future outbreaks.



## Background

- The first reported cases were in Tokat district of Turkey in 2002
- Common clinical and laboratory features including flu-like complaints, petechial rash, thrombocytopenia, leukopenia and high liver enzymes
- The vector is *Hyalomma marginatum marginatum*



## Is Q fever an emerging infection in Turkey?

B. Gozalan,<sup>1</sup> B. Esen,<sup>2</sup> J. M. Rolain,<sup>3</sup> L. Akou<sup>4</sup> and D. Raoult<sup>5</sup>

هل هي Q غفلى عدوى متجددة في تركيا؟

أيسطون غوزالان،<sup>1</sup> بوزن إيسن،<sup>2</sup> جان مارك رولان،<sup>3</sup> ليفاك أكوك،<sup>4</sup> دانييل راؤول<sup>5</sup>

الخلاصة: تم الإبلاغ أيضا عن تفشي المرض في أيار/مايو والتم من أيار/سبتمبر 2002، عن 46 حالة حتى حادة بالقرب من منطقة البحر الأسود في شمال تركيا. وتم علاج المرضى بسرعة وبمجاح باستخدام ادم سيكلين، مما جعل التشخيص السريري (الإصابة بالريكتسيا أو الإبرليكيوسيس) أو الإبرليجات يوجد في الحضانة. وقد أمكن للتحليل النسخي لعينات الدم التي أخذت من 19 مريضاً أن يحدد الجرثومة المسببة للعدوى حتى أنها *Coxiella burnetii*. وقد أبلغ عن سبع حالات بوصفها حالات حادة من هي Q، وثلاث حالات عظمى أنها إصابة بالعدوى. العدوى شائعة. وقد كان أكثر الأمراض المسببة شيوعاً في الحالات الحادة: القيء (100.0%)، والغثاس (78.7%)، والسعال (79.1%)، والحمى (42.9%)، والام البطن (42.9%)، والقىح (42.9%)، وكانت الإبريات شديدة من أربعة لثمن جميع المرضى. ويرى الباحثون أن الاستقصاءات الوبائية حتى هي Q، مبررات تكونت ضرورية في المنطقة التي حدثت بها الإصابة.

**ABSTRACT** Between 4 May and 8 August 2002, 46 cases of acute fever were reported within a black sea region in northern Turkey. The infection was treated rapidly and successfully with tetracyclines. The clinical diagnosis of rickettsial or ehrlichial infection was considered. Analysis of serum and blood samples taken from 19 patients identified five causative organism as *Coxiella burnetii*. 7 cases were reported as acute Q fever and 8 as seropositive for past infection. The most common clinical symptoms among the acute cases were vomiting (100.0%), nausea (85.7%), diarrhoea (87.1%), fever (42.9%), abdominal pain (42.9%) and headache (42.9%). Liver enzymes were elevated in all patients. It is considered that epidemiological inves-

Doxycycline recommended

## International collaboration

- Diseases
  - Q fever, leptospirosis, rickettsiosis, ehrlichiosis, CCHF
- Collaborating centers
  - National Institute of Infectious Diseases, Laboratory of Rickettsia and Chlamydia, Department of Virology, Tokyo, Japan
    - Rickettsiosis, ehrlichiosis
  - WHO Collaborative Centre for Rickettsial Reference and Research, Marseille, France
    - Rickettsiosis, ehrlichiosis, *Coxiella burnetii* (+)
  - WHO Collaborating Center for Arboviruses and Viral Hemorrhagic Fever, Lyon, France
    - Crimean-Congo hemorrhagic fever (+)

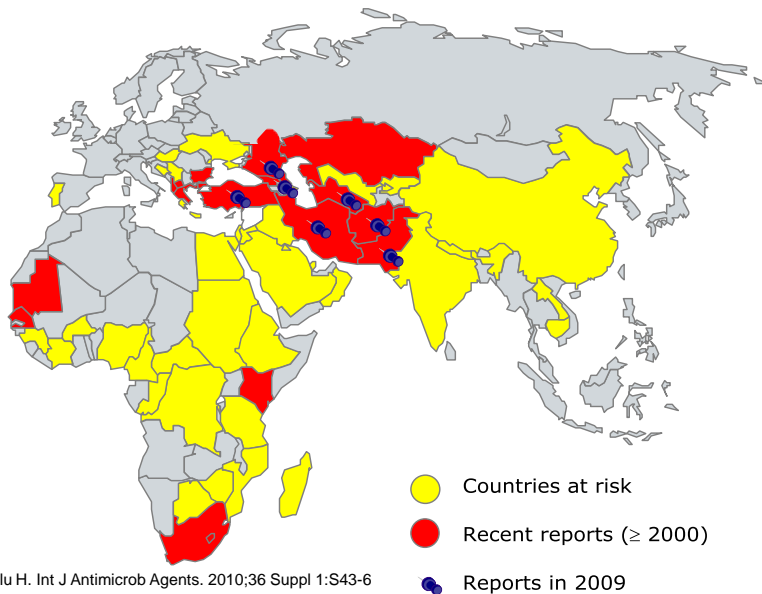
## Crimean-Congo Hemorrhagic Fever in Turkey

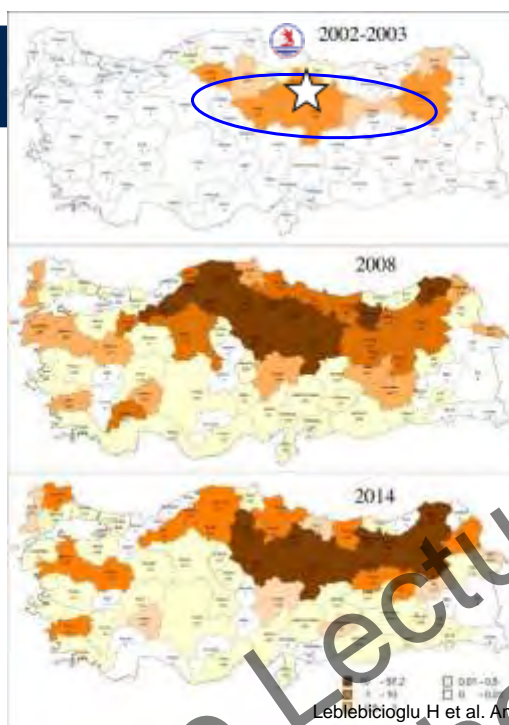
S. Sami Karti,\* Zekaver Odabasi,† Volkan Korten,† Mustafa Yilmaz,\* Mehmet Sonmez,\*  
Rahmet Ceylan,\* Elif Akdogan,\* Necmi Eren,\* Iftihar Koksak,\* Ercument Ovali,\* Bobbie R. Erickson,‡  
Martin J. Vincent,‡ Stuart T. Nichol,‡ James A. Comer,‡ Pierre E. Rollin,‡ and Thomas G. Ksiazek‡

Emerging Infectious Diseases • www.cdc.gov/eid • Vol. 10, No. 8, August 2004

EMERGING INFECTIOUS DISEASES®

### Geographic distribution of CCHF





Leblebicioglu H et al. Antiviral Research 2016;126:21-34

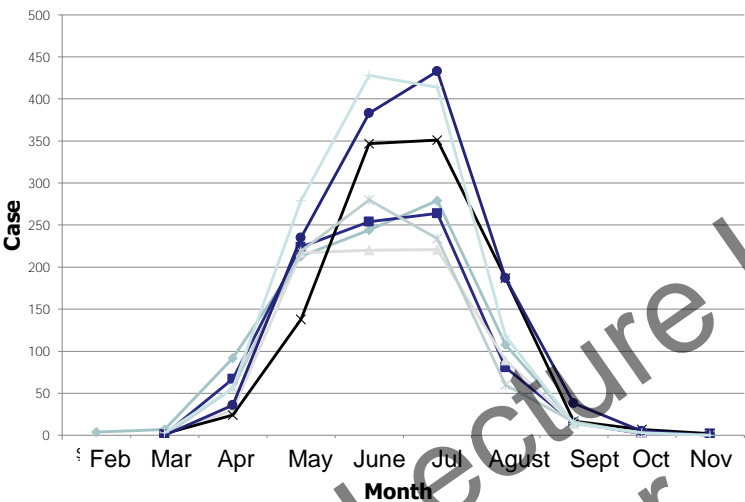
## The region

- Winter is temperate
- Land structure is more fragmented
- The altitude is around 1000 m.
- Generally the disease is not seen at sea level and touristic coastal regions in Turkey
- Agriculture, backyard farming and animal husbandry are common
- Risk factors
  - Older age, less schooling, farming, history of tick bites, tick removal from animals, farming, animal husbandry, contact with animals and living in a rural area



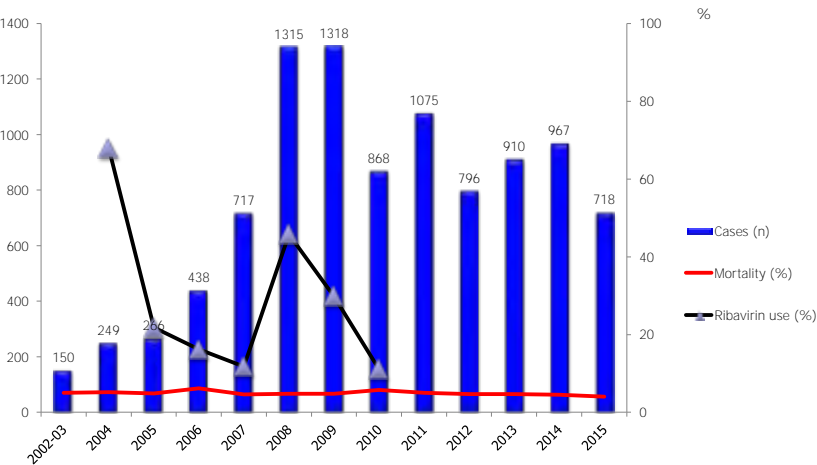
Leblebicioglu H et al. Antiviral Research 2016;126:21-34

# Distribution of CCHF cases by months 2008-2014



Republic of Turkey Ministry of Health

# CCHF in Turkey between 2002-15



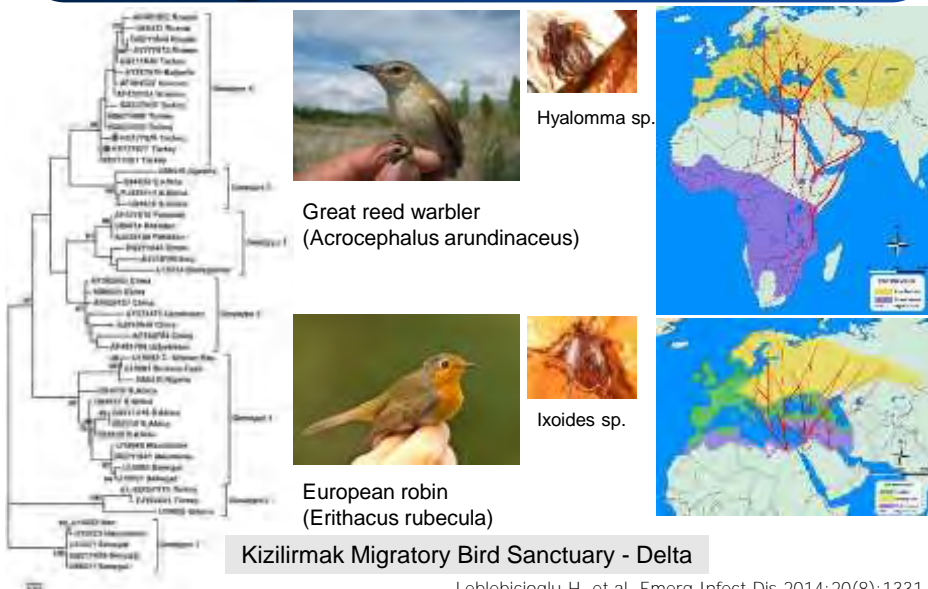


## Emergency of CCHF



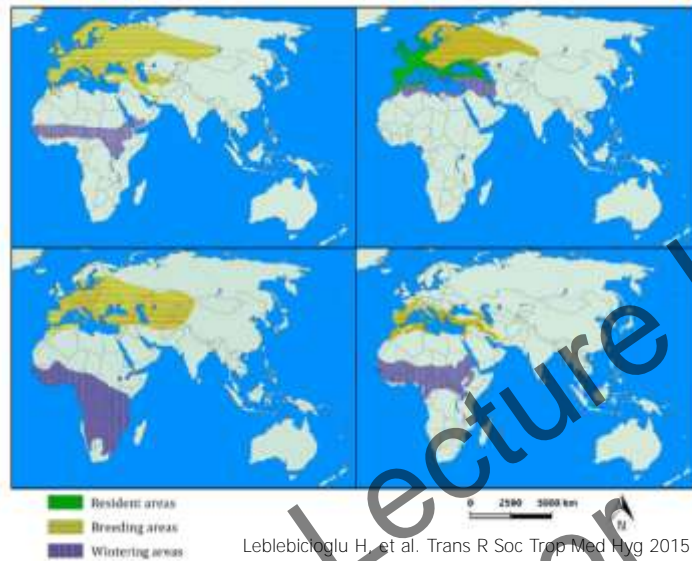
Ergonul O. Lancet Infect Dis 2006;6(4):203-14  
 Leblebicioglu H. Int J Antimicrob Agents 2010;36 Suppl 1:S43-6

## CCHFV and birds



Leblebicioglu H, et al. Emerg Infect Dis 2014;20(8):1331-4

## Distribution map of the migratory bird species detected carrying ticks with CCHF



Leblebicioglu H, et al. Trans R Soc Trop Med Hyg 2015; 109: 676–678  
Messina JP, et al. Trans R Soc Trop Med Hyg 2015;109:503–13

## Governmental organization

- The Ministry of Health (MoH) has taken a lead role in the coordination of studies in diagnosis, treatment and prevention of CCHF in Turkey
- The Ministry of Food, Agriculture and Livestock (MoFAL) has also carried out control of CCHF in animals and the field
- Establishment of CCHF advisory board (2003)
  - Cross-departmental cooperation



## CCHF Advisory Board of Turkey

- Ministry of Health
- Ministry of Food, Agriculture and Livestock
- The National Reference Laboratory
- Specialists in Clinical Microbiology, Medical Microbiology, Virology, Parasitology, Entomology, Veterinary Medicine and Public Health
- Communications specialists, sociologists and pharmacologists have also provided expertise to the board as required

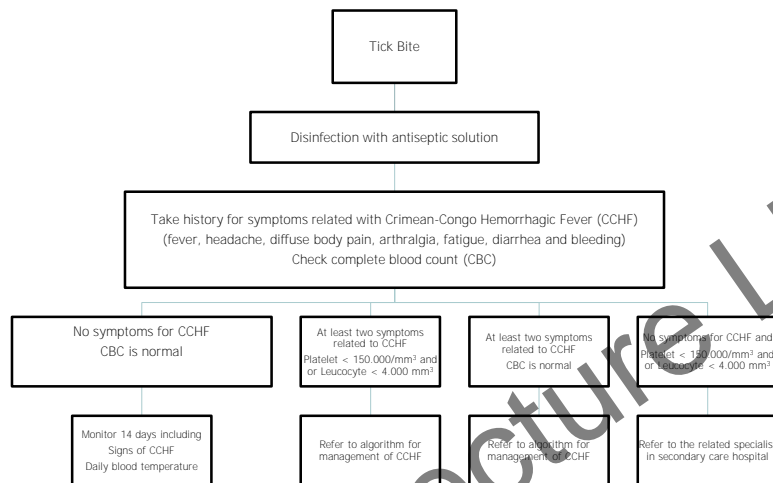
Republic of Turkey Ministry of Health

## CCHF Advisory Board of Turkey

- The Board meets at least biannually
- Guidance on describing case definitions
- Developing CCHF notification forms (2005)
  - Electronic recording system (2010)
- Algorithms
  - Approach to patients with tick bite" and "CCHF Case Management"
- Standards
  - Patient transfer or referral
  - Disinfection policies
  - Burial practice
- Reviews epidemiology, surveillance studies, effectiveness of preventative measures, current projects
- Coordination of educational activities

Republic of Turkey Ministry of Health

## Management of tick bite

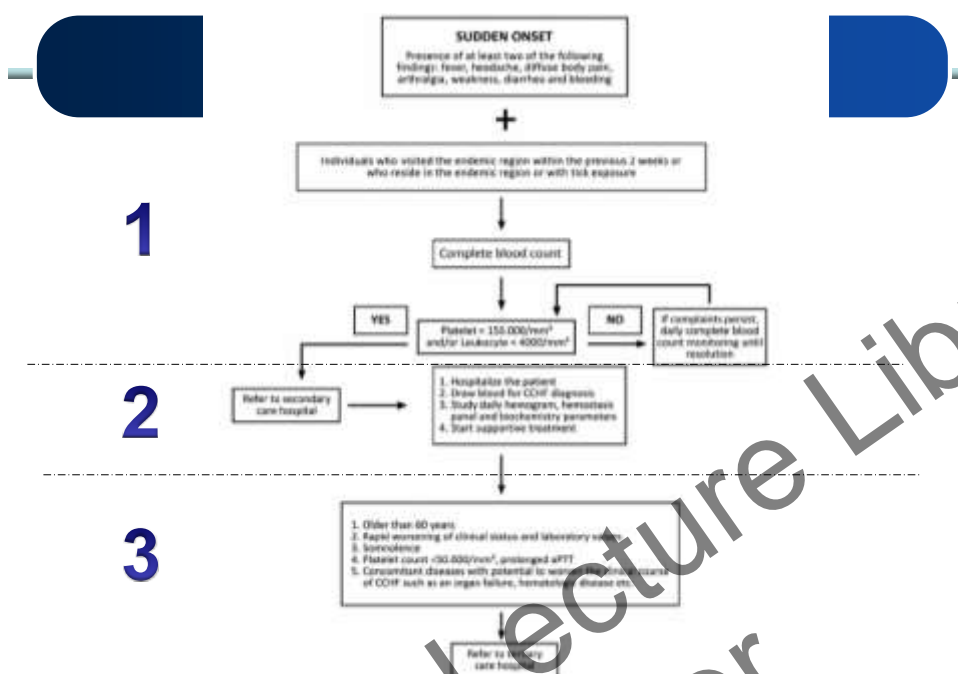


Republic of Turkey Ministry of Health

## Case definition

- **Suspected case**
- Individuals who had fever, myalgia, malaise, diarrhoea, and history of being in endemic area
  - ▪ Tick exposure history; and/or
  - ▪ Residency or travel to CCHF endemic region
  - ▪ Healthcare workers, exposure to blood and body fluids of a patient
- **Probable case**
- Suspected cases who had thrombocytopenia, elevated AST and ALT levels
- **Confirmed case**
- CCHF IgM or PCR positivity in the blood or body fluids of the patient

ECDC. Consultation on Crimean-Congo haemorrhagic fever prevention and control. 2008



Leblebicioğlu H, et al. Vector Borne Zoonotic Dis 2012;12(9):805-11

## Reference hospitals



- 19 provinces were identified
- Secondary and tertiary hospitals have been identified as reference centers for CCHF
- An emergency patient transfer service is managed by the MoH

## National Reference Laboratories



- In-house PCR then commercially available RT-PCR (2010)
- ELISA specific IgM, IgG
- Results are available in 24 hours
- Laboratories are integrated with on-line surveillance system

Republic of Turkey Ministry of Health

## Educational activities

- Public health education campaigns to increase citizens' awareness to avoid the disease
- Specific training for community leaders and religious personnel
- School education programs
- Face-to-face education of people under risk of CCHF
  - Geographic Information Systems (GIS) is used to map cases
- Continuous education program for healthcare workers
- Medical congresses, symposia
- Movies, documentaries, posters, brochures, leaflets, slide sets, coloring books

Republic of Turkey Ministry of Health

# KIRIM-KONGO KANAMALI ATEŞİ

## BULASMA YOLLARI

## BELİRTİLERİ

## KORUNMA

**UNUTMAYINIZ!**

T.C. SAĞLIK BAKANLIĞI  
Ulusal Sağlık Yürütme Kurulu Başkanlığı  
2017

### Kırım-Kongo Kanamalı Ateşi (KKKA) nedir?

KKKA, bulaşıcı mikropiy enfeksiyöz ve/veya toksik etkenlerle oluşan akut enfeksiyöz hastalıktır.

**Belirtileri:**

- 1. Hızlıca gelişen ateş
- 2. Kas ağrıları
- 3. Vücut ağrıları
- 4. Baş ağrıları
- 5. Kusma
- 6. İshal

**Dişilik belirtileri:** Hastanın bacak ve/veya ellerinde, bacakta (ayakta) ve/veya ellerde (ayakta) morluklar görülür.

**Ölüm:** Hastanın bacak ve/veya ellerinde, bacakta (ayakta) ve/veya ellerde (ayakta) morluklar görülür.

**Korunma:** Hastanın bacak ve/veya ellerinde, bacakta (ayakta) ve/veya ellerde (ayakta) morluklar görülür.

### KENEYİ HAFİFE ALMAYIN, TEDBİRİ ELDEN BIRAKMAYIN!

**Ölüm:** Hastanın bacak ve/veya ellerinde, bacakta (ayakta) ve/veya ellerde (ayakta) morluklar görülür.

**Ölüm:** Hastanın bacak ve/veya ellerinde, bacakta (ayakta) ve/veya ellerde (ayakta) morluklar görülür.



## Prevention in hospital

- Standard infection control practices
  - Isolation and/or cohort of patients
  - Hand hygiene
  - Use of personal protective equipment (PPE)
  - Safe injection practices
  - Before leaving the patient's room or cubicle, remove and discard PPE



## Vaccine for CCHF

- There is no approved vaccine for CCHF
- Inactivated Bulgarian vaccine
  - The neutralizing activity in these groups was low
- Animal study with CCHFV Turkey-Kelkit06 strain
  - Partially protection with a significant delay in time to death
- A vaccine based on CCHF virus glycoproteins using orthopox virus vector
  - Vaccine failed to protect the animals from lethal disease

Christova I et al. Probl Infect Parasit Dis 2010;37:7-8  
Canakoglu, N et al. PLoS Negl Trop Dis 2015;9:e0003579  
Dowall SD et al. Hum Vaccin Immunother 2015 (In press)



## Tick control in livestock

- The MoFAL have carried out the programs of treating animals with ectoparasitic drugs
  - Flumethrin, a fat-soluble pyrethroid insecticide
- The biggest obstacle in treating animals is backyard farming which is widespread in Turkey
- There is an idea among animal owners that the treatment reduces meat quality
  - This reduces the effectiveness of interventions

Republic of Turkey Ministry of Health



TR MoFAL regulation 2011. Slaughtering is prohibited in roadsides and backyards

Leblebicioglu H et al. Int J Infect Dis 2015;38:e9-e15

Review

Consensus report: Preventive measures for Crimean-Congo Hemorrhagic Fever during Eid-al-Adha festival

Hakan Leblebicioğlu<sup>a,\*</sup>, Mustafa Sunbul<sup>a</sup>, Ziad A. Memish<sup>b</sup>, Jaffar A. Al-Tawfiq<sup>c</sup>, Hurrem Bodur<sup>d</sup>, Aykut Ozkul<sup>e</sup>, Ali Gucukoglu<sup>f</sup>, Sadegh Chinikar<sup>g</sup>, Zahra Hasan<sup>h</sup>

<sup>a</sup> Department of Infectious Diseases and Clinical Microbiology, Medical School, Ondokuz Mayıs University, Samsun, Turkey

<sup>b</sup> Public Health Directorate, Ministry of Health, Riyadh, Saudi Arabia; <sup>c</sup> College of Medicine, Al-Faisal University, Riyadh, Saudi Arabia

<sup>d</sup> Jember Health Services Institute, Jember, East Java; <sup>e</sup> Istanbul University School of Medicine, Istanbul, Turkey

<sup>f</sup> Department of Infectious Diseases and Clinical Microbiology, Ankara University School of Medicine, Ankara, Turkey

<sup>g</sup> Department of Veterinary, Faculty of Veterinary Medicine, Ankara University, Ankara, Turkey

<sup>h</sup> Department of Food Hygiene & Food Safety, Faculty of Veterinary Medicine, Ondokuz Mayıs University, Samsun, Turkey

<sup>i</sup> Infectious and Viral Hepatitis, Pfizer Laboratory National Reference Laboratory, Federal Institute for Health, Berlin, Germany

<sup>j</sup> Pathology and Laboratory Medicine, The Aga Khan University, Karachi, Pakistan

ARTICLE INFO

Article history:

Received 14 April 2015

Received in revised form 24 June 2015

Accepted 20 June 2015

Keywords:

Crimean-Congo hemorrhagic fever

Eid-al-Adha

Consensus

Prevention

Measures

Measures

Measures

Measures

Measures

Measures

Measures

Measures

Measures

Measures

Measures

Measures

Measures

Measures

Measures

Measures

Measures

Measures

Measures

Measures

Measures

Measures

Measures

Measures

Measures

Measures

Measures

Measures

Measures

Measures

Measures

Measures

Measures

Measures

Measures

Measures

Measures

Measures

Measures

Measures

Measures

Measures

Measures

Measures

Measures

Measures

Measures

Measures

Measures

Measures

Measures

Measures

Measures

Measures

Measures

Measures

Measures

Measures

Measures

Measures

Measures

Measures

Measures

Measures

Measures

Measures

Measures

Measures

Measures

Measures

Measures

Measures

Measures

Measures

Measures

Measures

Measures

Measures

Measures

Measures

Measures

Measures

Measures

Measures

Measures

Measures

ABSTRACT

Crimean-Congo hemorrhagic fever (CCHF) is endemic in Eurasian countries such as Turkey, Pakistan, Afghanistan and Iraq. CCHF virus is spread by the Hyalomma ticks which feed mainly on cattle and sheep. Muslim countries, in which these animals are sacrificed during Eid-al-Adha, are among the countries where CCHF is endemic, and it has been observed that CCHF is associated with practices surrounding the Eid-al-Adha festival. The days for Eid-al-Adha are 10–13 days earlier in each year according to Islamic calendar, so previous year's Eid-al-Adha occurred in autumn-winter months however in the next 10–13 years it will be held during the summer months when CCHF is more prevalent. This may lead to a rise in the number of cases due to increased dissemination of CCHF virus with increased animal movements and human activities. This consensus report focuses on the variable practices regarding animal husbandry in different regions and possible preventative measures to reduce the incidence of CCHF. Surveillance, hygiene and personal protection are essential parts of prevention. There is a need for international collaborative preparedness and response plan for prevention and management of CCHF during Eid-al-Adha in countries where the disease is prevalent. © 2015 The Authors. Published by Elsevier Ltd on behalf of International Society for Infectious Diseases. This is an open access article under the CC-BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

International collaboration



World Health Organization



Food and Agriculture Organization of the United Nations



EpiSouth



Arbo-zoonet



SEVENTH FRAMEWORK PROGRAMME



Fighting Emergence of CCHF virus in Europe



Platform for European Preparedness Against (Re-)emerging Epidemics

## CCHF Research Network of Turkey

### CCHF-RNT



## Scientific publications

- Search with keyword CCHF
- As of November 3, 2015
  - 1117 publications
  - 243 of them (20.8%) originated from Turkey
    - 183 research studies, 28 case reports, 23 reviews, and 9 letters to the editor. Amongst the studies, 33 included pediatric cases
    - Themes; molecular studies, epidemiology, pathogenesis, clinical findings, diagnosis, prognostic factors, treatment, prevention



## Future research areas

- Identifying the drivers of increasing number of cases and the spread of infection to other districts in the region
- Improved understanding of the pathogenesis and drivers of emergence of CCHF
- Development of a standardized case definition for CCHF
- Development and validation of rapid diagnostic tests for CCHF with high sensitivity and specificity
- Prospective, randomized controlled trials investigating antivirals and immune therapy
- Prospective long-term, observational studies to identify the sequel of infection and the duration of natural protection after acute infection
- Period of infection control measures to be applied for patients diagnosed with CCHF and discharge criteria
- Further development and clinical trials of potential CCHF vaccines

## Conclusion

- CCHF is an emerging zoonosis in Turkey
- There is no approved antiviral drug for treatment and prophylaxis for CCHF
- The principle measures
  - Creation of early warning systems
  - Development of standard case definitions
  - Increasing laboratory capacity
  - Creation of an effective surveillance method
  - Cooperation with national and international organizations (One Health Approach)
  - Continuous and regular education of people and health care workers
  - Control of animal movement and tick control in livestock
- This approach to dealing with the emergence of CCHF in Turkey serves as an example for other countries that are at risk

Thank you



Turkish Institute of Public Health

National Reference Laboratory of Turkey

Turkish CCHF Research Network



Public Health  
Agency of Canada

wellcome trust

