Crimean Congo Hemorrhagic Fever: Experience in Turkey

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Disclosure

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

Birthplace of the founder of Turkey, Ataturk in Thessaloniki
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*
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


Emerging Infectious Diseases • www.cdc.gov/eid • Vol. 10, No. 6, August 2004

Geographic distribution of CCHF

Countries at risk
Recent reports (≥ 2000)
Reports in 2009
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
CCHF in Turkey between 2002-15

Distribution of CCHF cases by months 2008-2014

Republic of Turkey Ministry of Health

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

- Climate change
- Migratory birds
- Environment change
- Increase in tick density
- Decrease in host animals

CCHFV and birds

- Great reed warbler (Acrocephalus arundinaceus)
- European robin (Erithacus rubecula)

Kizilirmak Migratory Bird Sanctuary - Delta

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

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
  - Cross-departmental cooperation


Republic of Turkey Ministry of Health
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

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
Management of tick bite

Tick Bite

Disinfection with antiseptic solution

Take history for symptoms related with Crimean-Congo Hemorrhagic Fever (CCHF) (fever, headache, diffuse body pain, arthralgia, fatigue, diarrhea and bleeding)

Check complete blood count (CBC)

No symptoms for CCHF
CBC is normal

Monitor 14 days including
Signs of CCHF
Daily blood temperature

At least two symptoms related to CCHF
Platelet \(< 150,000/\text{mm}^3\) and/or
Leucocyte \(< 4,000/\text{mm}^3\)

Refer to algorithm for
management of CCHF

At least two symptoms related to CCHF
CBC is normal

CBC is normal

Platelet \(< 150,000/\text{mm}^3\) and/or
Leucocyte \(< 4,000/\text{mm}^3\)

Refer to the related specialist
in secondary care hospital

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 of PCR positivity in the blood or body fluids of the patient

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

Republic of Turkey Ministry of Health
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 online 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
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
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

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

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**ABSTRACT**

Crimean-Congo Hemorrhagic Fever (CCHF) is endemic in Eurasia, including Turkey, Pakistan, Afghanistan, and Iran. CCHF virus is spread by the Hyalomma alternata equi (H. a. equi) tick to cattle and sheep. Muslim countries in which Eid al-Adha celebrations are held are in the regions where CCHF is endemic. There has been an increase in CCHF cases in various countries during the past few years. In the CCHF risk zone, hunting or slaughtering stray animals, and handling hides of dead animals, are high-risk activities. CCHF is characterized by the abrupt onset of fever, which is one of the most common symptoms. Despite the severity of the disease, there is limited evidence of the clinical presentation and the effectiveness of specific patient care and prophylactic measures. CCHF can be transmitted through human-to-human contact, and it is essential to implement preventive measures to decrease the incidence of CCHF in the affected countries. The objective of this report is to review the available data regarding the risk of CCHF and to propose guidelines for the prevention of CCHF during the festival of Eid al-Adha. © 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.
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

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

Public Health
Agency of Canada

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