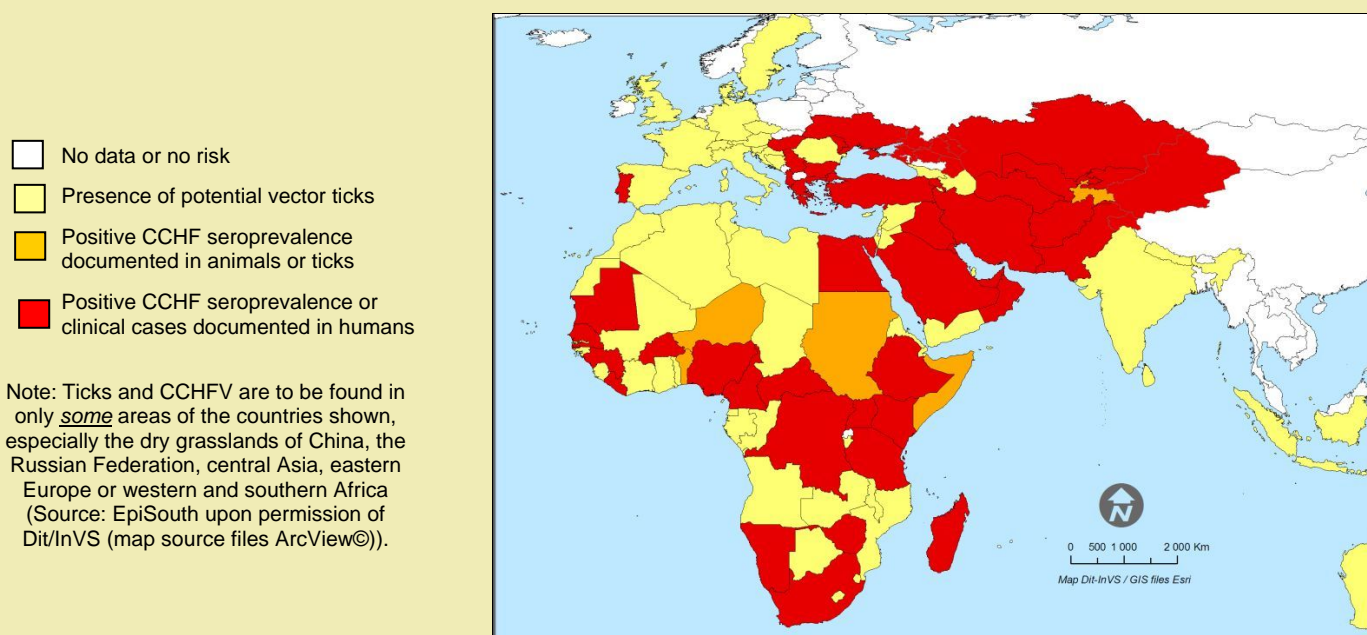


Epidemiology of Crimean–Congo haemorrhagic fever virus: Albania, Bulgaria, Greece, Islamic Republic of Iran, Kosovo, Russian Federation, Turkey.

1st October 2008

This document was jointly developed by EpiSouth and the World Health Organization Regional Office for Europe.

Fig. 1. Distribution of vector tick species and known areas of Crimean–Congo haemorrhagic fever (CCHF) seroprevalence, 1944–2008.



Crimean–Congo haemorrhagic fever (CCHF) virus is present in many countries. Available data show that CCHF is circulating with particular intensity in 2008 in Turkey, Islamic Republic of Iran, several Balkan countries and southern districts of the Russian Federation. This document focuses on the epidemiology of CCHF in these countries.

1. BACKGROUND

- CCHF virus is a Nairovirus of the *Bunyavirus* family identified in 1956 in the Congo and in 1967 in what is now Uzbekistan.
- CCHF virus is enzootic in the southern part of Europe (Balkans), Turkey, the southern Russian Federation, and in several countries in the Middle East, of sub-Saharan Africa, central Asia and the western part of China (Fig 1).
- **Reservoir:** Several species of ixodid ticks (mainly *Hyalomma* and *Amblyomma*) which are endemic to the semi-desert zones of a yet greater number of countries can transmit CCHF by bite. Animals such as wild rodents and livestock serve as amplifiers.

- **Transmission:** The virus causes sporadic cases in humans, essentially linked to tick bites during farming or cattle-raising activities.
- **Clinical presentation:** In most cases, infection in humans causes few or no symptoms, although CCHF virus may cause a severe viral haemorrhagic fever. Person-to-person transmission to carers occurs, including in the health care setting.
- **Incubation:** 1–7 days (on average 3–5 days).
- **Viraemia:** appears with clinical symptoms and lasts around 10 days.
- **Case-fatality rate (CFR)**
 - ✓ The literature describes CFRs as high as 40–50%, especially in severe forms diagnosed during epidemics in resource-poor settings.
 - ✓ Global CFR in hospitalized patients (all grades of severity), however, is closer to 2–6% according to recent data collected in Turkey, the Islamic Republic of Iran and the Russian Federation.
 - ✓ Data from South Africa, Turkey or the Islamic Republic of Iran show that the CFR can be significantly higher in patients with biologically confirmed CCHF who present clinical and biological criteria of severity.

- Non-specific supportive treatment may be effective.
- WHO has approved ribavirin as a specific treatment, based on limited circumstantial data in the endemic setting and experimental evidence.
- A vaccine has been developed in Bulgaria for use in humans.
- Discrepancies in global CFR in hospitalized patients during epidemics may therefore be explained by differences in:
 - ✓ the performance of surveillance systems in detecting less-severe cases;
 - ✓ the sensitivity and specificity of case definitions used and their positive predictive value during epidemics; and
 - ✓ diagnostic and therapeutic management.

2. MID-2008 CCHF SITUATION: TURKEY, RUSSIAN FEDERATION, ISLAMIC REPUBLIC OF IRAN, BULGARIA, ALBANIA, KOSOVO¹ AND GREECE

2.1. Turkey

- In 1974, seroepidemiological studies found evidence of anti-CCHF antibodies in 26 (2.4%) of 1100 sera tested in Turkey.²
- The first symptomatic human case of CCHF in Turkey was identified in 2002.
- Between 2002 and 2007, the number of confirmed CCHF cases reported in Turkey regularly increased, especially in eastern and north-eastern rural areas (Table 1 and Fig. 2).
- An epidemic is now reported each year in Turkey. It is most active from April to September.
- Between 1 January and 30 June 2008, a total of 688 confirmed cases (with 41 deaths, CFR: 6.0%) have been reported in Turkey.
- Cases are essentially described in adults exposed to tick bites during rural activities in north-central Anatolia (Fig. 10).
- Some sporadic cases occur in other areas of Turkey.
- One case was described in Kirklareli (north-west of Istanbul) in 2007.
- Since 2003, 8 cases have been documented in health care workers (HCW) (with 1 death) following accidental exposure to blood or body fluids.
- In some instances (study protocols), cases were treated with ribavirin.

Table 1. Confirmed CCHF cases and deaths in Turkey, 2002–2008 (Source: Ministry of Health)

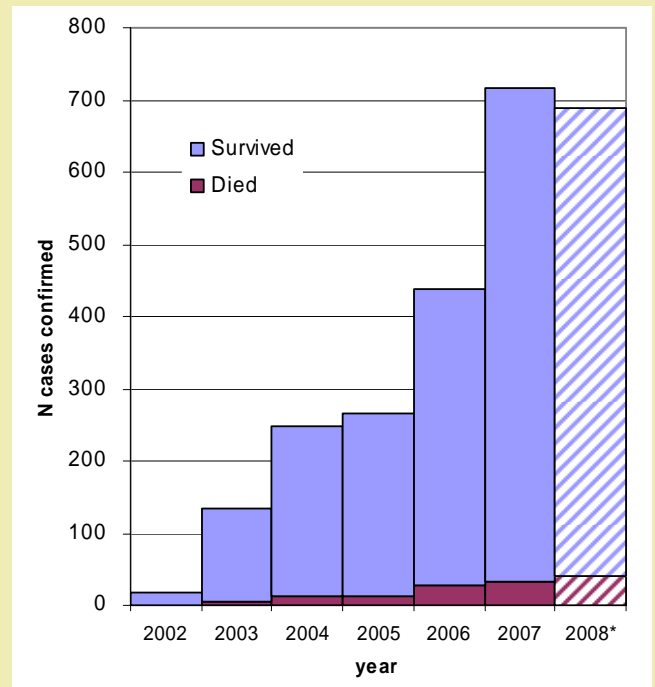
| Year | Cases | Deaths | CFR (%) |
|--------------|-------------|------------|------------|
| 2002 | 17 | 0 | 0.0 |
| 2003 | 133 | 6 | 4.5 |
| 2004 | 249 | 13 | 5.2 |
| 2005 | 266 | 13 | 4.9 |
| 2006 | 438 | 27 | 6.2 |
| 2007 | 717 | 33 | 4.6 |
| 2008* | 688 | 41 | 6.0 |
| Total | 2508 | 133 | 5.3 |

¹ Throughout this document, "Kosovo" means Kosovo in accordance with Security Council resolution 1244 (1999).

² Hoogstraal H. J Med Entomol 1979; 15(4):307–417.

*Preliminary data to 30/06/08.

Fig. 2. Confirmed CCHF cases and deaths in Turkey, 2002–2008 (Source: Ministry of Health)



*Preliminary data to 30/06/2008 (hashed).

2.2. Russian Federation

- Data presented here originate from the Federal Service for Surveillance on Consumer Rights Protection and Wellbeing, Ministry of Health and Social Development of the Russian Federation ([Rospotrebnadzor](#)).
- Cases are described each year in the Southern Federal District (*Okrug*) (Fig. 3).
- Cases occur mainly in 3 of the 13 zones of this District: Republic of Ingushetia, Rostov *oblast* and Stavropol *kraj* (Fig. 4).
- The number of cases reported has risen progressively since 2002 (Table 2).
- A total of 839 confirmed cases (with 27 deaths) has been recorded since 2002.
- The yearly CFR in confirmed cases ranges from 1.7% to 11.1% with a global CFR of 3.2% for the period 2002–2008 (based on preliminary data for 2008).

Fig. 3. Southern Federal District, Russian Federation (in red) (Source: EpiSouth)



Note. Bela = Belarus; Ukr. = Ukraine; Geo. = Georgia; Az. = Azerbaijan.

Fig. 4. Detail of affected areas, Southern Federal District: Republic of Ingushetia, Rostov *oblast* and Stavropol *kraj*, Russian Federation (Source: EpiSouth)

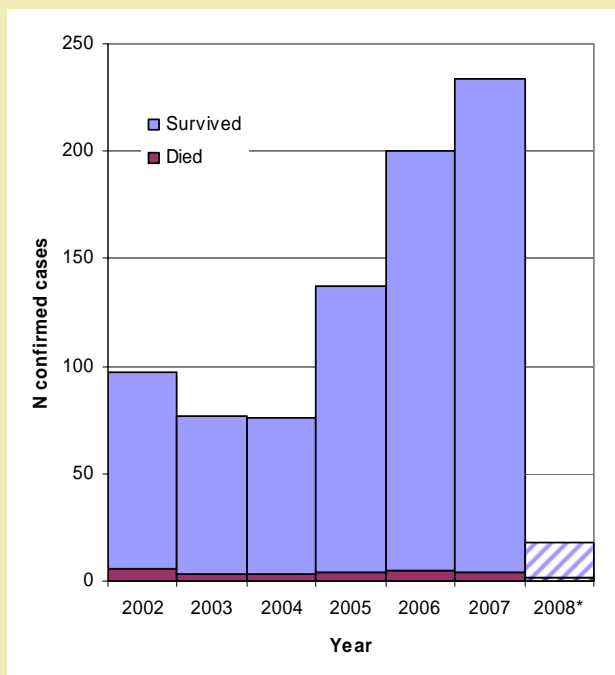


Table 2. Confirmed CCHF cases and deaths in the Southern Federal District, Russian Federation, 2002–2008 (Source: Rospotrebnadzor)

| Year | Cases | Deaths | CFR (%) |
|--------------|------------|-----------|------------|
| 2002 | 97 | 6 | 6.2 |
| 2003 | 77 | 3 | 3.9 |
| 2004 | 76 | 3 | 3.9 |
| 2005 | 137 | 4 | 2.9 |
| 2006 | 200 | 5 | 2.5 |
| 2007 | 234 | 4 | 1.7 |
| 2008* | 18 | 2 | 11.1 |
| Total | 839 | 27 | 3.2 |

*Preliminary data to 12/05/2008.

Fig. 5. Confirmed CCHF cases and deaths in the Southern Federal District, Russian Federation, 2002–2008 (Source: Rospotrebnadzor)



*Preliminary data to 12/05/2008 (hashed).

2.3. Islamic Republic of Iran

- Between 7 June 2000 and 10 May 2008, 1550 suspect or confirmed cases of CCHF were reported in the Islamic Republic of Iran (Table 3). Of these, a total of 434 cases (with 64 deaths, CFR: 14.7%) were confirmed at the Pasteur Institute in Tehran.
- Cases are reported mainly between March and November. Most cases are documented in the provinces of Sistan and Baluchestan, Tehran and Hormozgan (Fig. 11).

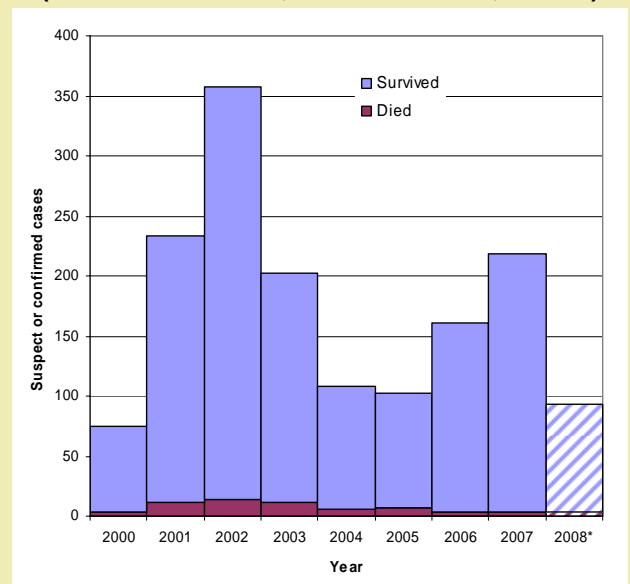
Table 3. Suspect or confirmed cases of CCHF and deaths in the Islamic Republic of Iran, 2000–2008 (Source: S. Chinikar, Pasteur Institute, Tehran³)

| Year | Suspect or confirmed cases | Death | CFR (%) |
|--------------|----------------------------|-----------|------------|
| 2000* | 75 | 4 | 5.3 |
| 2001 | 233 | 11 | 4.7 |
| 2002 | 358 | 14 | 3.9 |
| 2003 | 202 | 12 | 5.9 |
| 2004 | 108 | 6 | 5.6 |
| 2005 | 102 | 7 | 6.9 |
| 2006 | 161 | 3 | 1.9 |
| 2007 | 218 | 4 | 1.8 |
| 2008** | 93 | 3 | 3.2 |
| Total | 1550 | 64 | 4.1 |

* Data for 2000 starting 07/06/2000

**Preliminary data to 10/05/2008

Fig. 6. Suspect or confirmed cases of CCHF and deaths in the Islamic Republic of Iran, 2000–2008. (Source: S. Chinikar, Pasteur Institute, Tehran)



*Preliminary data to 10/05/2008 (hashed)

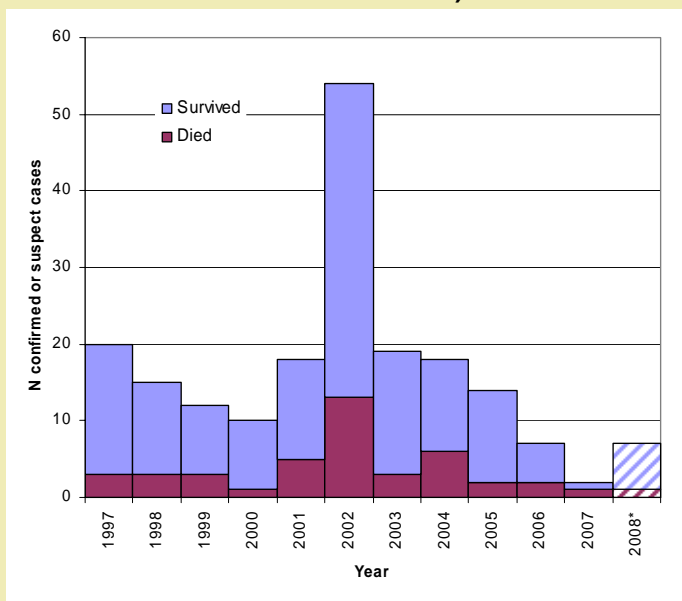
- The yearly CFR for suspect or confirmed cases of CCHF ranges from 1.8% to 6.9% with a global CFR of 4.1% for the 2000–2008 period (preliminary data to 10/05/2008).
- CCHF cases in Islamic Republic of Iran have access to oral treatment by ribavirin.

³ Presentation at the European Society of Clinical Microbiology and Infectious Diseases conference on VHF, Istanbul, 27–28 June 2008 and Chinikar S. et al. « Surveillance and laboratory detection of CCHF in Iran » accepted for publication, J. Vasc Access 2008 and Transboundary and Emerging Diseases journal. 2008 ; 55(5–6): 200–204.

2.4. Bulgaria

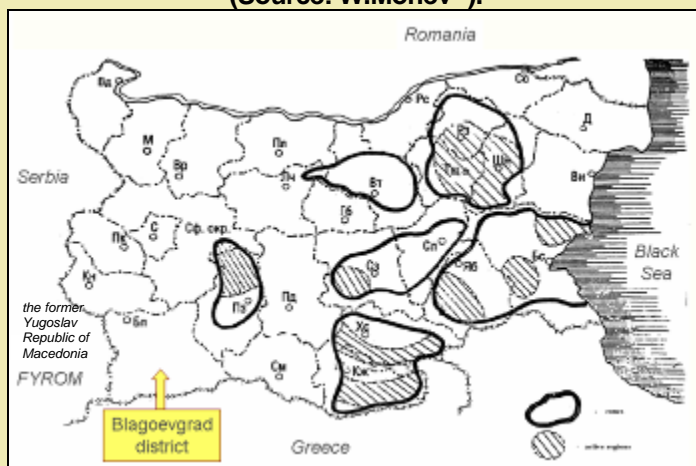
- Some areas of Bulgaria are endemic for CCHF. On average, 10–15 cases are reported each year.
- The most significant epidemic in the country occurred in 1954–1955 with a total of 487 cases (213 in 1954 and 274 in 1955). Approximately 300 of these cases were reported in the Shumen district, in the north-east of the country.
- Between 1953 and 1974, a total of 1101 CCHF cases were notified in Bulgaria (CFR 17%), of which 20 were acquired during health care.
- Between 1975 and 1996, the development and distribution of a human vaccine was associated with a reduction in notified cases: 271 cases (CFR: 11.4%).
- Since 1997, a total of 196 suspect or confirmed cases were notified (43 deaths, CFR: 22%) (Fig. 7).

Fig. 7: Suspect or confirmed CCHF cases in Bulgaria, 1997–2008* (Source: National Centre of Infectious and Parasitic Diseases)



*Preliminary data to 10/07/2008 (hashed)

Fig. 8. Zones where CCHF circulates in ticks and endemic zones in Bulgaria and Blagoevgrad, District Bulgaria (Source: W.Monev⁴).



⁴ W. Monev. Joint WHO-MZCP Intercountry Workshop on Crimean-Congo Haemorrhagic fever (CCHF) Prevention and Control, Istanbul, Turkey 6–8 November 2006.

- Between March 20 and July 10, 2008, national authorities identified 7 cases of CCHF:
 - ✓ 2 confirmed cases (acquired while delivering care) and 4 probable cases in Gotse Delchev county, Blagoevgrad district, in western Bulgaria (source: [Ministry of Health](#)) (Fig. 8).
 - ✓ An additional probable case was identified in Sliven district.

2.5. Greece

- Several seroepidemiological studies conducted in the 1970s and 1980s found evidence for the circulation of CCHF virus in Greece.
 - ✓ CCHF virus strain AP92 was isolated from ticks collected from goats in 1976 in Vergina village (80 km west of Thessaloniki). This strain seems to be low or not pathogenic to humans.
 - ✓ The virus was found in 4 (6.1%) of 65 residents of Vergina village (where strain AP92 was isolated)⁵ and 1.1% of over 3000 sera from apparently healthy individuals, mainly farmers and shepherds, sampled throughout Greece (0–6.2%, depending on the region)⁶.
 - ✓ The observation of higher sero-prevalence in departments close to Vergina village (Pella, Imathia, Karditsa), combined with the absence of CCHF cases, suggests that the detected antibodies were most probably against AP92 strain, which is genetically different from all other CCHF viral strains.⁷
- The first symptomatic case of CCHF diagnosed in Greece was confirmed in a woman who died on 25 June 2008. She was exposed to tick bites during farming activities in rural areas near Komotini (Rhodope department in the Thrace region) (Fig. 9).
- Tick control measures have been implemented and the surveillance of humans has been strengthened. Surveys on humans, domestic animals and ticks have been started. There are no other identified cases to date.

Fig. 9. Greece (Source: EpiSouth)



⁵ Antoniadis A, Casals J. Am J Trop Med Hyg 1982; 31(5):1066–1067.

⁶ Antoniadis et al. Arch Virol 1990; Suppl 1 :277–285.

⁷ Papa A. Personal communication July 2008.

2.7. Kosovo

- The first human cases were described in 1954 during an epidemic with 8 cases. Table 4 presents data on suspect and confirmed cases of CCHF between 1995 and November 2006.
- Available data indicate a seroprevalence of around 24% in the general population living in endemic areas (centre and south-western areas).

Table 4. Suspected and confirmed CCHF cases in Kosovo, 1995–2006
(Source: Institute of Public Health⁸).

| Year | Suspected cases | Confirmed cases | Deaths |
|--------------|-----------------|-----------------|-----------|
| 1995 | 122 | 46 | 7 |
| 1996 | 23 | 9 | 5 |
| 1997 | 0 | 0 | 0 |
| 1998 | 1 | 1 | 0 |
| 1999 | 7 | 3 | 2 |
| 2000 | 2 | 1 | 0 |
| 2001 | 115 | 31 | 7 |
| 2002 | 114 | 14 | 3 |
| 2003 | 6 | 6 | 3 |
| 2004 | 17 | 12 | 2 |
| 2005 | 12 | 6 | 2 |
| 2006 | 11 | 5 | 2 |
| Total | 430 | 134 | 33 |

2.6. Albania

- The first human case of CCHF was described in Albania in 1986.
- A total of 35 suspect or confirmed cases were reported between 1986 and 1990.⁹
- From 2001 to 2006, a yearly average of 10 suspect and 5 confirmed cases have been reported (Table 5).
- Seven family clusters were discovered within six years accounting for 50% of the cases.
- Ticks were responsible (only when discovered) in 8 cases (17.3%) and the only fatal case was related to a tick bite.

Table 5: Suspect and confirmed cases of CCHF in Albania, 2001–2006
(Source: Public Health Institute)

| Year | Suspect cases | Confirmed cases |
|--------------|---------------|-----------------|
| 2001 | 11 | 8 |
| 2002 | 9 | 4 |
| 2003 | 11 | 10 |
| 2004 | 15 | 9 |
| 2005 | 9 | 0 |
| 2006* | 5 | 1 |
| Total | 60 | 32 |

*Preliminary data to 06/11/2006

⁸ I. Dedushaj, Joint WHO-MZCP Intercountry Workshop on Crimean-Congo Haemorrhagic fever (CCHF) Prevention and Control, Istanbul, Turkey 6–8 November 2006.

⁹ S. Bino. Joint WHO-MZCP Intercountry Workshop on Crimean-Congo Haemorrhagic fever (CCHF) Prevention and Control, Istanbul, Turkey 6–8 November 2006.

- Most cases are reported in Kukës and Has districts, in the north-eastern part of the country, although there are few cases reported from other areas.
- Anti-CCHF antibodies were found in 1.3% of 233 sera sampled in the general population.
- CCHF virus was identified only in two of 2586 collected ticks (*Hyalomma. Spp.*)

3. COMMENTS

CCHF virus is the causative agent of the viral haemorrhagic fever with the widest geographical area of circulation in the world. Among other areas, it is present in the WHO European Region (Greece, Bulgaria, Turkey, Albania, Kosovo, southern part of the Russian Federation). Evidence of CCHF circulation can also be found in most countries on the Black Sea coastline.

Low-intensity circulation of CCHF was established in Turkey and Greece over 30 years ago. The virus has recently emerged on a larger scale in Turkey. This could be due to the multiplication of vectors and reservoir animals (hares, boars) in rural areas. Temperature changes may also play a role.

Data collected in Turkey, the Islamic Republic of Iran and the Russian Federation show lower CFRs than those initially documented in endemic settings. This is due to the quality of diagnostic and medical management of cases, and to a sensitive system of detection through systematic screening of people referred for tick bites in endemic areas. Some continue to debate the usefulness of ribavirin treatment in the early stages of infection.

In all countries concerned, the vast majority of cases are reported in known endemic areas. The occurrence of human CCHF cases, even in clusters, with a documented exposure to tick bites or to blood or body fluids of confirmed or suspect cases, is not an unexpected event and does not require specific measures other than those implemented by national authorities and informing tourists of available preventive measures.

Simple precautions can be observed to prevent tick bites (repellents, wearing long garments, careful removal of ticks using forceps in case of bite¹⁰).

No case has been reported in a tourist visiting any of the countries discussed here. To date, a single case of imported CCHF to a non-endemic country has been described ([France, 2004](#)).

The period during which transmission is highest is late spring–summer in the endemic zones of the countries mentioned. The number of suspected or confirmed cases in these endemic zones is therefore highly likely to increase in the coming weeks.

The Annex lists several WHO publications useful for the surveillance and control of CCHF and clinical management.

¹⁰ Useful links on tick removal :

- [Eurosurveillance](#)
- [Purdue](#)
- [Turkish Ministry of Health](#)

Fig. 10. Confirmed cases of CCHF in Turkey, 2002–2008
(Source: Ministry of Health of Turkey)

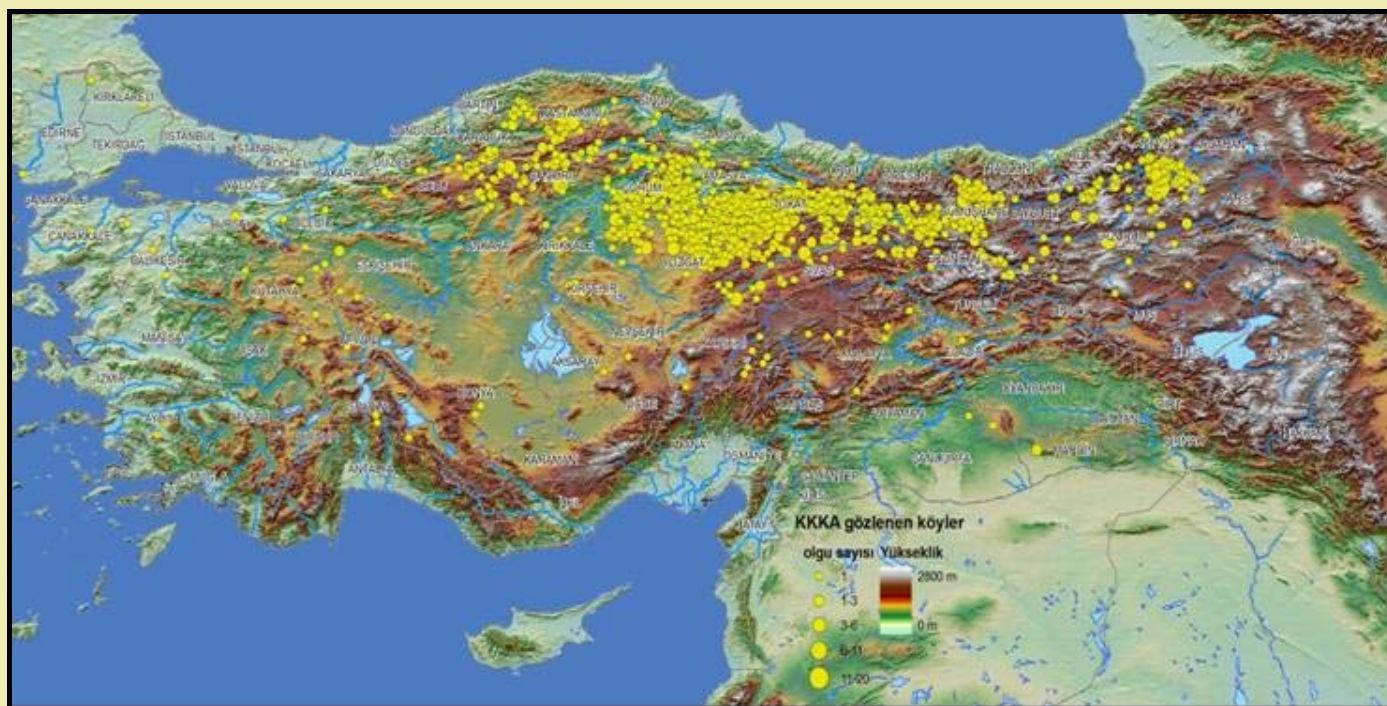
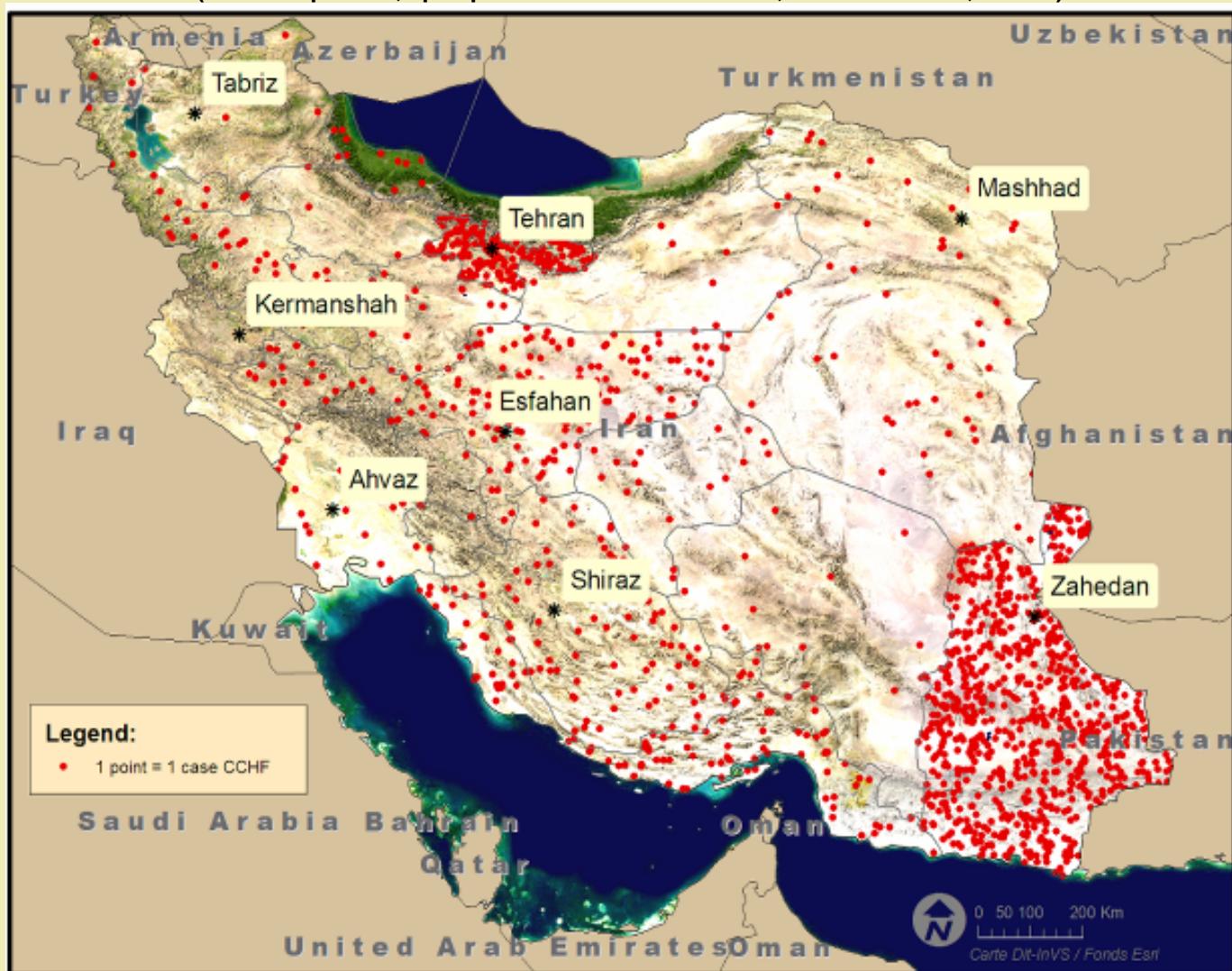


Fig. 11. Geographical distribution of suspect or confirmed CCHF cases in the Islamic Republic of Iran, 2000–2008
(Source: EpiSouth, upon permission of Dr S. Chinikar, Pasteur Institute, Tehran)



Annex

The following are WHO technical guidance and normative publications that are relevant for CCHF surveillance and control and available electronically, and other sources of information.

General aspects

- *Crimean–Congo haemorrhagic fever*, WHO fact sheet (<http://www.who.int/mediacentre/factsheets/fs208/en/>)
- Case definition for acute haemorrhagic fever syndrome in *WHO recommended surveillance standards*, 2nd ed. (WHO/CDS/CSR/ISR/99/2/EN) (http://www.who.int/csr/resources/publications/surveillance/WHO_CDS_CSR_ISR_99_2_EN/en/)

Case management – Use of ribavirin

- WHO model lists of essential medicines (<http://www.who.int/medicines/publications/essentialmedicines/en/index.html>)
- Essential medicines list and WHO model formulary (http://www.who.int/entity/selection_medicines/list/WMF2008.pdf)

Infection control

- Infection prevention and control of epidemic- and pandemic-prone acute respiratory diseases in health care. WHO interim guidelines (WHO/CDS/EPR/2007.6) (http://www.who.int/entity/csr/resources/publications/WHO_CDS_EPR_2007_6c.pdf)
- Infection control for viral haemorrhagic fevers in the African health care setting (WHO/EMC/ESR/98.2) (http://www.who.int/csr/resources/publications/ebola/WHO_EM_C_ESR_98_2_EN/en/)
- *Infection interim infection control recommendations for care of patients with suspected or confirmed filovirus (ebola, Marburg) haemorrhagic fever* (http://www.who.int/entity/csr/bioriskreduction/interim_recommendations_filovirus.pdf)

Laboratory investigation

- WHO Collaborating Centres for Arbovirus and Haemorrhagic Fever Reference and Research in the WHO European Region (http://www.who.int/whocc/List.aspx?cc_title=haemorrhagic&cc_region=EURO&);
- Guidance on regulations for the transport of infectious substances 2007–2008 (WHO/CDS/EPR/2007.2) (http://www.who.int/csr/resources/publications/biosafety/WHO_CDS_EPR_2007_2cc.pdf)

Outbreak communication:

- WHO outbreak communication guidelines (WHO/CDS/2005.28) (http://www.who.int/csr/resources/publications/WHO_CDS_2005_28/en/)
- Crimean–Congo haemorrhagic fever, Ministry of Health, Turkey (<http://www.kirim-kongo.saglik.gov.tr/>) (in Turkish)