CHAPTER 10

CRIMEAN-CONGO HEMORRHAGIC FEVER IN THE XINJIANG UYGUR AUTONOMOUS REGION OF WESTERN CHINA

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10.1. INTRODUCTION

Certain regions of China are well known as Crimean-Congo hemorrhagic fever (CCHF)-endemic areas, particularly the western part of the Xinjiang Uygur Autonomous Region (Xinjiang) in western China. Xinjiang is unique in terms of CCHF virus (CCHFV) infections because this region forms the eastern boundary of CCHF endemic region and borders Pakistan, Afghanistan, Tajikistan, and Kyrgyzstan. These neighboring countries also have CCHF-endemic areas. The study of CCHFV infections in this region can, therefore, provide important insights into CCHFV infections.

10.2. HISTORICAL ASPECTS OF CCHF IN XINJIANG, CHINA

10.2.1. CCHF known as "Xinjiang Hemorrhagic Fever"

An outbreak of a disease similar to that in Crimea was first documented in Bachu County in the westernmost region of Xinjiang in 1965 (Fig. 10-1). The disease was named Xinjiang hemorrhagic fever. The etiological agent for Xinjiang hemorrhagic fever was isolated from the blood of patients and from pasture ticks by the Hygiene and Epidemic Prevention Station of Xinjiang [32] and was named Xinjiang hemorrhagic fever virus. Since the first documented outbreak of Xinjiang hemorrhagic fever in 1965, Bachu County has been struck by Xinjiang hemorrhagic fever almost every year. In 1985, it was first reported that the Xinjiang hemorrhagic fever virus was indistinguishable from CCHFV by serological analyses, indicating that Xinjiang hemorrhagic fever is similar to

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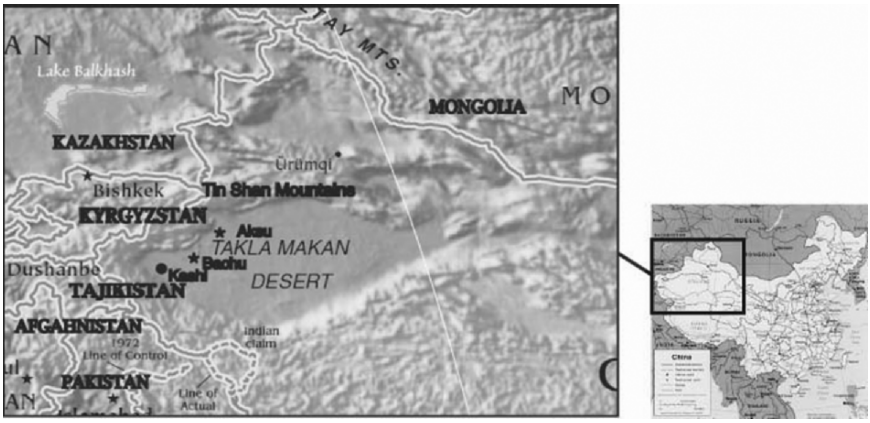

Fig. 10-1. Geography of Xinjiang, China. Patients with CCHF in Xinjiang have been reported in Bachu and Aksu Counties. The neighboring countries such as Kazakhstan, Kyrgyzstan, Afghanistan, and Pakistan also have endemic regions of CCHF.

CCHF [32]. It has now been confirmed by serological and molecular analyses that Xinjiang hemorrhagic fever virus is a CCHFV. Although the disease, Xinjiang hemorrhagic fever, was first recognized as a clinical entity in 1965, there is no doubt that the disease had been present in the region since antiquity.

10.2.2. History of CCHFV isolation in China

Since the first isolation of CCHFV in Xinjiang in 1966, CCHFV isolates have been recovered by inoculating materials collected from patients, ticks, sheep, and long-eared jerboa into the brains of suckling mice (Table 10-1). The latest isolation of CCHFV from a patient occurred in 1988. Although the number of CCHFV isolates is relatively small, studies on CCHFV infections in the region have progressed thanks to the isolation of the virus from patients, ticks, and vertebrates in the region.

10.2.3. Recent progress of studies on CCHF in Xinjiang, China

The first research articles written in Chinese that described Xinjiang hemorrhagic fever were published in 1983 [11, 28, 29]. Since 2000, collaborative research on CCHFV infections has been initiated by China and Japan, and recombinant protein-based diagnostic systems for CCHF have been developed [16, 17, 20, 24, 25]. Field studies on CCHF in Bachu County in Xinjiang were then initiated using these newly developed diagnostic systems. Furthermore, molecular epidemiological studies of CCHFV infections in this region were also carried out [14, 26]. Studies on CCHFV infections in Xinjiang have progressed dramatically in recent years.

Table 10-1. Description of nucleotide sequences of the partial S segment of CCHFV isolates in the Xinjiag Uygur Autonomous Region used in the present study

CCHFV	Origin	Place of isolation (county)	Year of isolation	Accession no. for S-segment sequence	Accession no. for M-segment sequence
66019	Human	Bachu	1966	AJ010648	AB069669
68031	Sheep	Bachu	1968	M86625	Not reported
HY-13	Tick (*Hyalomma asiaticum asiaticum*)	Bachu	1968	U88413	AY900145
7001	Human	Bachu	1970	AF415236	AB069670
75024	Human	Aksu	1975	AF362080	AB069671
7803	Human	Bachu	1978	AF354296	AB069672
79121	Long-eared jerboa	Bachu	1979	AF358784	AB069673
8402	Tick (*H. asiaticum asiaticum*)	Bachu	1984	AJ010649	AB069674
88166	Human	Bachu	1988	AY029157	AB069675

10.3. LIFE CYCLE OF CCHFV IN XINJIANG, CHINA

10.3.1. Vector and host

CCHFV is maintained in nature in Xinjiang through cycles of asymptomatic infection between tick (*Hyalomma asiaticum asiaticum*) and mammals including livestock such as sheep and goats (Fig. 10-2).

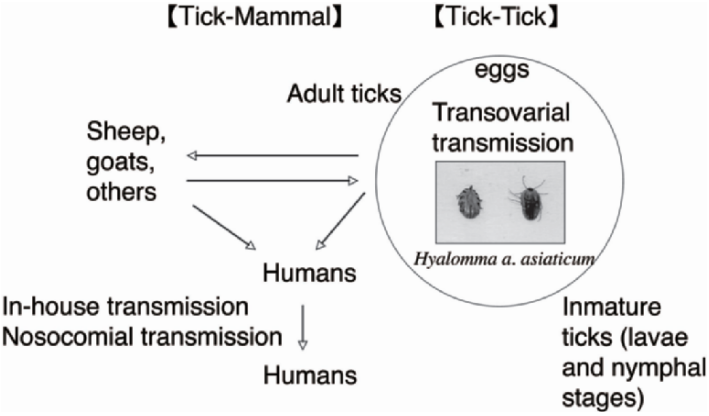

Fig. 10-2. Life cycle of CCHFV and infection routes of CCHFV to humans in Xinjiang. The main tick vector in the region is *Hyalomma asiaticum asiaticum*. Inhabitants in Xinjiang depend on sheep for nutrition, economic well-being, and religious activities. Inhabitants are usually infected with the CCHFV through close contact with the viremic tissues of sheep or through tick bites.

10.3.1.1. Ticks

CCHFV strains 8402, 68013, and HY-13 were isolated from *H. asiaticum asiaticum* ticks. The partial genome of the S segment of CCHFV was amplified from *H. asiaticum asiaticum* ticks, collected from the endemic area during the outbreak seasons in 2001 and 2002 [26]. The tick species, *H. asiaticum asiaticum*, certainly plays a key role in CCHF outbreaks in Xinjiang; however, little information on tick species that are associated with CCHFV infections in Xinjiang have been collected to date. Further studies are needed on the maintenance of CCHFV in nature in Xinjiang and on the relationship between the habits of these ticks with CCHF outbreaks in the region.

10.3.1.2. Vertebrates

Since the first documented outbreak of CCHF in Xinjiang in 1965, CCHFV isolates have been recovered not only from patients but also from sheep and long-eared jerboa [32] (Table 10-1). It was reported that 37 out of 125 sheep (30%) in the Bachu County in Xinjiang showed a positive reaction in a complement fixation assay for the detection of antibodies to CCHFV [32]. Recently, we conducted a similar study and found that approximately 60% of adult sheep showed a positive reaction in indirect immunofluorescent and immunosorbent assays for the detection of immunoglobulin G (IgG) antibody to CCHFV [24]. These results strongly suggest that sheep are commonly infected with CCHFV. *Hyalomma* tick infestations are also common in sheep in the region (Fig. 10-3), and these two factors indicate that sheep are important to the life cycle of CCHFV in Xinjiang. Unfortunately, no seroepidemiological studies on CCHFV infections in other mammals in the region have yet been conducted. The fact that CCHFV was isolated from a small mammal such as long-eared jerboa suggests that small mammals may also play an important role in the maintenance of CCHFV in nature in the region. It is suggested that CCHF outbreaks among people in the region are associated with CCHFV infections in sheep based on the fact that sheep in the region are commonly infected with CCHFV and that the residents in the CCHF-endemic region have close contact with sheep in their daily life. Epidemiological studies on CCHFV infections among vertebrates other than sheep are needed to clarify the ecology of the CCHFV in nature in the region and the risk to residents to CCHFV infection in Xinjiang.

10.4. CLINICAL ASPECTS OF CCHF IN XINJIANG, CHINA

10.4.1. Patients

Patients with CCHF have been reported only in Bachu and Aksu counties in Xinjiang (Fig. 10-1). In 2001 and 2002, field studies on CCHFV infections in Bachu County in Xinjiang were conducted using virological examinations. Forty-six and 12 patients diagnosed as having CCHF based on clinical symptoms such as fever, backache, joint pain, bleeding from body orifices, and/or

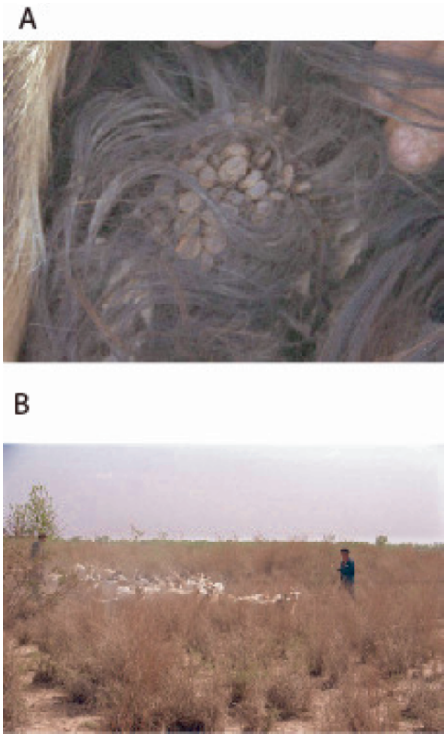

Fig. 10-3. Picture shows ticks (*Hyalomma asiaticum asiaticum*) infesting sheep (*arrow* indicates ticks (A) and with shepherds (B) in the rural and desert areas in Bachu County, Xinjiang.

purpura were registered with the local health authority in 2001 and 2002, respectively. However, one third of the 46 patients and one half of the 12 patients registered in 2001 and 2002, respectively, were confirmed to have CCHFV infections by virological assays such as serology, CCHFV antigen detection and reverse transcription polymerase chain reaction (RT-PCR) for amplification of virus genome. In the 2001 outbreak, three males died of hemorrhagic symptoms and multiple organ failure possibly due to CCHFV infection. From the 16 of the patients with CCHF diagnosed through virological examination, information on age, sex, clinical manifestations, and occupation were available for analyses. Male to female ration was 10:6. Age of the patients varied from 4 to 70 years with an average age of 31. Seven and four out of the 16 were farmers and shepherds, respectively. Of the six female patients, three had had close contact with sheep through raising sheep. The youngest patient was a 4-year-old girl and her mother also suffered from CCHF. The girl developed fever on the 5th day after the onset of infection in her mother. The partial genome of the CCHFV amplified from the girl was identical to that from her mother. It is speculated that the girl may have been infected with CCHFV through contact with her mother [18].

The area of CCHF outbreak in Bachu County is restricted to some small villages. Although no outbreaks of CCHF have been reported in urban areas where commercial activities associated with sheep and lambs, such as slaughter, marketing and preparation for human consumption in restaurants, are conducted, there is a great potential risk of CCHF outbreaks in such areas.

10.4.2. Clinical manifestations

The symptoms of patients with CCHF range in severity from fever only or fever with flu-like symptoms to hemorrhage with multiple organ failure resulting in death. All patients developed fever and joint pains. Orbital pain, backache, and headache are common symptoms in patients. One patient, a 28-year-old shepherd, with severe symptoms of hemorrhage from gingiva, nostrils, and rectum was reported [25] (Fig. 10-4). He eventually recovered without any sequelae. In severe cases such as this, elevation of liver enzymes is often seen. Furthermore, oliguria was a common symptom and it was presumably associated with renal failure caused by the direct influence of CCHFV infection or by indirect influence through hypovolemic shock.

10.4.3. Treatment

Basically, maintenance therapies such as hydration, blood transfusion, and other specific therapies, i.e. administration of diuretics and/or antibiotics (if necessary), should be initiated as soon as possible. However, it is usually difficult for patients with CCHF to receive such treatment due to populations in the endemic region being economically disadvantaged and having limited access to a regional hospital. Once patients with suspected CCHF are hospitalized, they should be treated with of ribavirin as well as supportive therapies.

Fig. 10-4. Hemorrhagic symptoms in a patient with CCHF. The clinical course and virological data for this patient have been reported [25]. This patient was treated with an intravenous administration of ribavirin and recovered without any sequelae. [Au1]

10.4.4. Infection route for CCHFV in humans

Most patients with CCHF in Xinjiang were shepherds or farmers. The residents living in the endemic area usually have close contact with sheep in their daily lives and some inhabitants even share their houses with the sheep they are raising. Sheep in the endemic area were closely observed for tick infestations during the endemic season, and it was quite easy to find sheep infested with ticks (Fig. 10-3). The people in the region in Bachu County appear to be infected with CCHFV through close contact with tissues, blood or bodily fluid of viremic sheep, including lambs, or the bite of CCHFV-infected ticks (mainly *H. asiaticum asiaticum*). Cultivating cotton is also a major economic activity in the area. When farmers are working in the cotton fields or on farms on which vegetables are grown, the chance of infection with CCHFV through tick bite is increased. Although there have not yet been any reported cases of nosocomial and in-house CCHF outbreaks in Xinjiang except for one case in which a child might have been infected from her mother, the human-to-human transmission of CCHFV might be one of major routes of CCHFV infection in humans [18]. The mode of infection of CCHFV in people within their region should be clarified in order to develop an efficacious strategy for reduction of patients with CCHF.

10.5. PREVENTION

10.5.1. Education

The reduction of the number of patients with CCHF in the CCHF-endemic regions in Xinjiang is of great importance. Most patients with CCHF in this region are aged between 15 and 40 years, indicating that they are of a working age. For this reason, preventive measures are important. Surveillance of CCHFV infections, development of diagnostics for CCHF, and assessment of risk factors in CCHFV, and so on, must be undertaken.

The risk factors for CCHFV infections must be clarified for each region in which outbreaks occur in order to establish an efficacious strategy to limit CCHF outbreaks. The life of the residents is closely associated with the raising of sheep. When people work on farms, they have a high risk of tick bite, thus increasing the risk of CCHFV infections. The economic activities associated with raising sheep and work in the field may pose a great risk of CCHFV infections. It is speculated that the number of patients can be reduced if proper education for residents on preventive measures of CCHFV infections are implemented. As discussed below, CCHF outbreaks occur in spring from March to July in the region. Therefore, such education should be implemented especially during the endemic season. However, prevention of CCHF in the region is unfortunately very difficult as the lives of many of the inhabitants depend on very activities that pose a risk of CCHFV infection.

10.5.2. Development of diagnostic systems for CCHF

CCHFV is classified as a biosafety level-4 pathogen, indicating that infectious virus must be manipulated in a high-containment (BSL-4) laboratory. This fact suggests that the development of antibody-detection systems using authentic CCHFV antigens is difficult in an institute without a BSL-4 laboratory. To overcome this difficulty, recombinant CCHFV-nucleoprotein (NP)-based antibody detection systems have been developed [13, 16, 17, 19, 20, 24, 25]. The recombinant CCHFV-NP was expressed in a recombinant baculovirus system from the cDNA of S segment of the CCHFV Chinese strain 8402 and then purified. A recombinant CCHFV-NP-based enzyme-linked immunosorbent assay (ELISA) for the detection of IgG and IgM antibodies was developed and shown to have high sensitivity and specificity [16, 20, 24, 25]. A recombinant NP-based ELISA for the detection of IgG antibodies to CCHFV in sheep sera [24] and, a recombinant CCHFV-NP-based indirect immunosorbent assay have also been developed [17]. Furthermore, a CCHFV antigen detection sandwich ELISA was developed using a novel monoclonal antibody [19]. The advantage of these recombinant protein-based diagnostic systems is that these diagnostics can be employed in regional institutes without a BSL-4 laboratory.

As the CCHF outbreak area in Xinjiang is a remote and economically disadvantaged region, it is difficult to equip local laboratories with these diagnostic systems for CCHF. However, to combat outbreaks of CCHF and reduce the mortality and morbidity of CCHF in such regions, precise diagnosis of CCHF is necessary. The establishment of diagnostic systems for CCHFV infections in a regional laboratory near the site of CCHF outbreaks is, therefore, an issue to be settled in the future.

10.5.3. Assessment of risk factors for CCHFV infection

The assessment of risk factors for CCHFV infection in the endemic area in Xinjiang is still to be performed. Most people in the endemic region are Muslim and their life depends heavily on raising sheep. They also cultivate cotton and vegetables in fields where ticks including *H. asiaticum asiaticum* are abundant. There is no doubt that raising sheep is one of the occupational activities with a high risk of infection. The slaughter of lambs and sheep is also a job with a high risk of CCHFV infections. CCHFV were isolated from ticks, *H. asiaticum asiaticum*, and CCHFV genomes were amplified by nested RT-PCR in 4 of 16 tick pools (a total of 80 ticks) and in 3 of the 65 tick pools (a total of 280 ticks) collected in the 2001 and 2002 outbreak seasons, respectively. Manipulation of ticks infesting sheep (including lambs) may increase the risk of CCHFV infection. Therefore, in order to prevent CCHF outbreaks in the CCHF-endemic region, clarification of risk factors for CCHFV infections is needed (See Chapter 21).

10.6. EPIDEMIOLOGY OF CCHF IN XINJIANG, CHINA

10.6.1. Geographical prevalence of CCHFV

Patients with CCHF have been reported from Central Asian countries that have borders with Xinjiang, China, such as Kazakhstan, Kyrgyzstan, Tajikistan, Afghanistan, and Pakistan. No patients with CCHF have been reported within China excluding the Xinjiang region. Xinjiang is divided into northern and southern Xinjiang by the Tian Shan Mountains (Fig. 10-1). All patients in Xinjiang were from the southern region and most patients were reported in a small village near Bachu County in the Kashi district (Fig. 10-1).

10.6.2. Seroepidemiology of CCHFV infections in the endemic region

Seroprevalence to CCHFV was investigated in residents living in the CCHF-endemic village near Bachu County in 2001. Serum samples were collected from 70 residents of various ages under informed consent. The antibody to CCHFV was detected by the recombinant NP-based IgG-ELISA [16] in approximately one fourth of participants. Furthermore, 60% of the participants over 50 years of age showed a positive reaction. There was no significant difference in the antibody positive rate to CCHFV between males and females. Together with that fact that 60% of the sheep in the region showed a positive reaction in the IgG-ELISA [24], these results indicate that residents living in the village within Bachu County are at high risk of CCHFV infection.

10.6.3. Environment of the region in which CCHF is endemic in Xinjiang

10.6.3.1. Environment

The CCHF endemic regions, Bachu and Aksu counties, in Xinjiang are located on the Silk Road in the Taklamakan desert, which is arid and receives little rain throughout the year (Figs. 10-1 and 10-3).

10.6.3.2. Lifestyle of people in the endemic region

More than 80% of people living in Xinjiang are Muslim, as are most residents in the CCHF endemic region within Xinjiang, and their lives are closely associated with the cultivation of domestic livestock of sheep. They depend on primary industry such as raising sheep and farming cotton and vegetables. Some of the adult males work as shepherds (Fig. 10-3). Their socioeconomical status is usually not high. Therefore, the residents usually live in the same accommodation in which the sheep are raised. *H. asiaticum asiaticum* ticks are abundant in the region, and it is not difficult to find these ticks moving on the ground.

10.6.3.3. Economic activities associated with CCHF outbreaks in the endemic region

The economic activities associated with sheep such as cultivating sheep, shearing, slaughter, and the cooking of sheep meat, pose a risk of CCHFV infection. Furthermore, as sheep are usually infested with ticks and are routinely sold at supermarkets in urban areas as well as being slaughtered for meat, there is a possibility that CCHF outbreaks will occur not only in the remote villages, but also in urban areas in the region. Nosocomial infections of CCHF among healthcare workers have been reported in several countries [2–4, 9, 27]. Although no nosocomial outbreaks of CCHF have been reported in Xinjiang, the management of febrile patients poses a risk of CCHFV infections among the healthcare workers in the region. They must always be careful in the treatment of febrile patients to prevent infection.

10.6.4. Seasonality of CCHF outbreaks in Xinjiang

Most patients contract CCHF in spring, between March and July, each year. Very few cases are observed at other times of the year. There may be risk factors for residents in the regions for infection with CCHFV in this season. It is expected that the virus load in the region may increase in spring. As indicated above, sheep are commonly infected with CCHFV and ticks harbor the CCHFV. The number of newborn lambs increases in spring in the region. Newborn sheep that are negative for CCHFV antibodies are naïve to CCHFV infections, suggesting that the viremia of the CCHFV occurs in the newborn sheep once they are infected with the CCHFV through tick bites. Therefore, the CCHFV load is expected to increase in the endemic region in spring each year, according to the increase in the number of newborn sheep. Furthermore, ticks become active in spring in the region. Based on these facts, the increase in the number of patients with CCHF may be due to both factors, the increase in CCHFV load in sheep, especially newborn sheep, and the increase in tick activity in the region.

10.7. MOLECULAR EPIDEMIOLOGY OF CCHF IN XINJIANG, CHINA

10.7.1. Molecular epidemiology of CCHF determined with genetic information of the viral isolates

The molecular epidemiological studies on CCHFV infections have been conducted with genetic information from the partial S segment of CCHFV isolates [5, 7–10, 15, 22, 23, 30]. The phylogenetic analyses based on the nucleotide sequence of the partial S segment of CCHFV isolates around the world indicates that the Chinese CCHFV isolates as well as the Kazakhstan and Uzbekistan strains form a group independent from those consisting of the other CCHFV isolates from other part of the world (Fig. 10-5a). Even the Pakistani

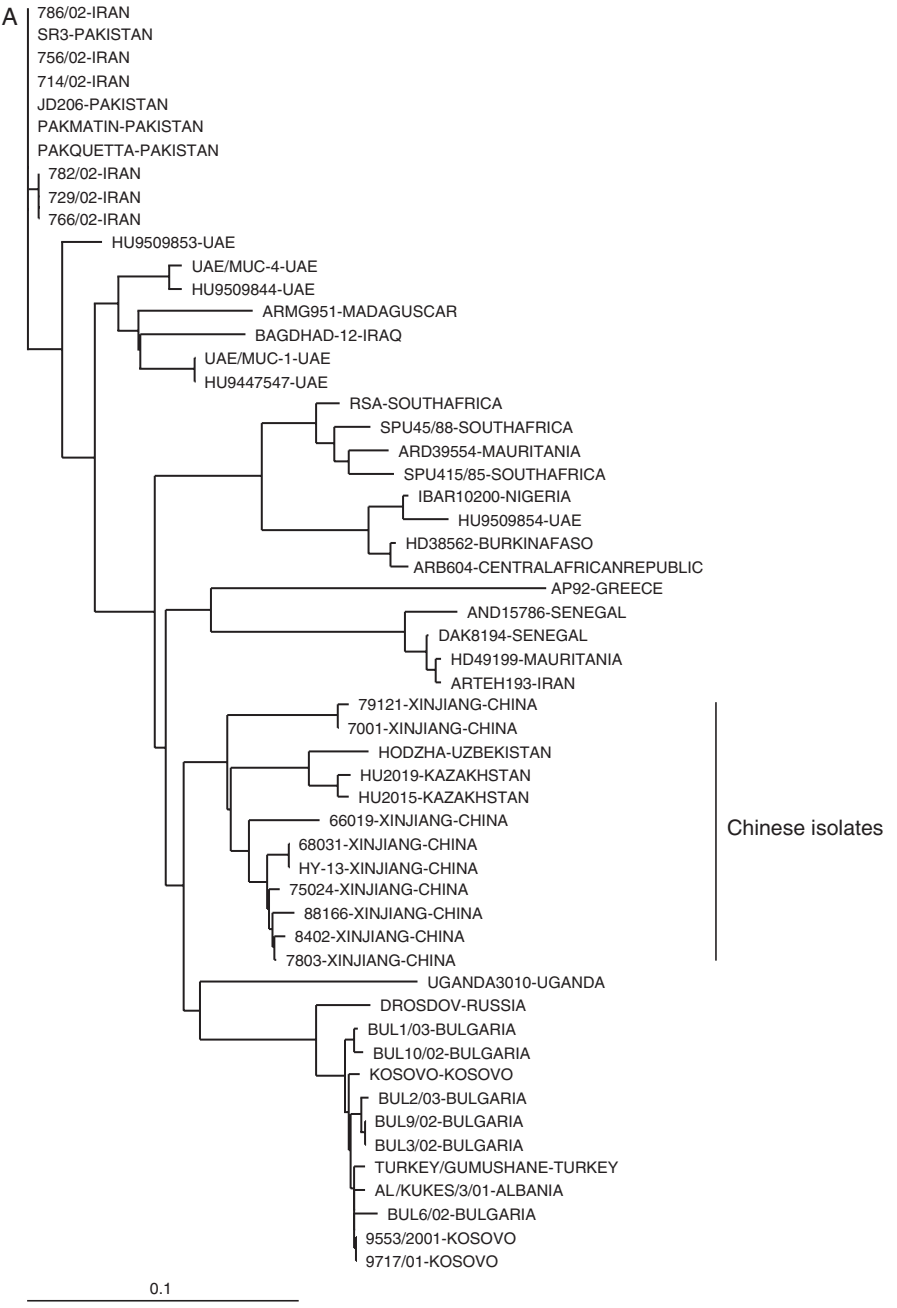

Fig. 10-5.

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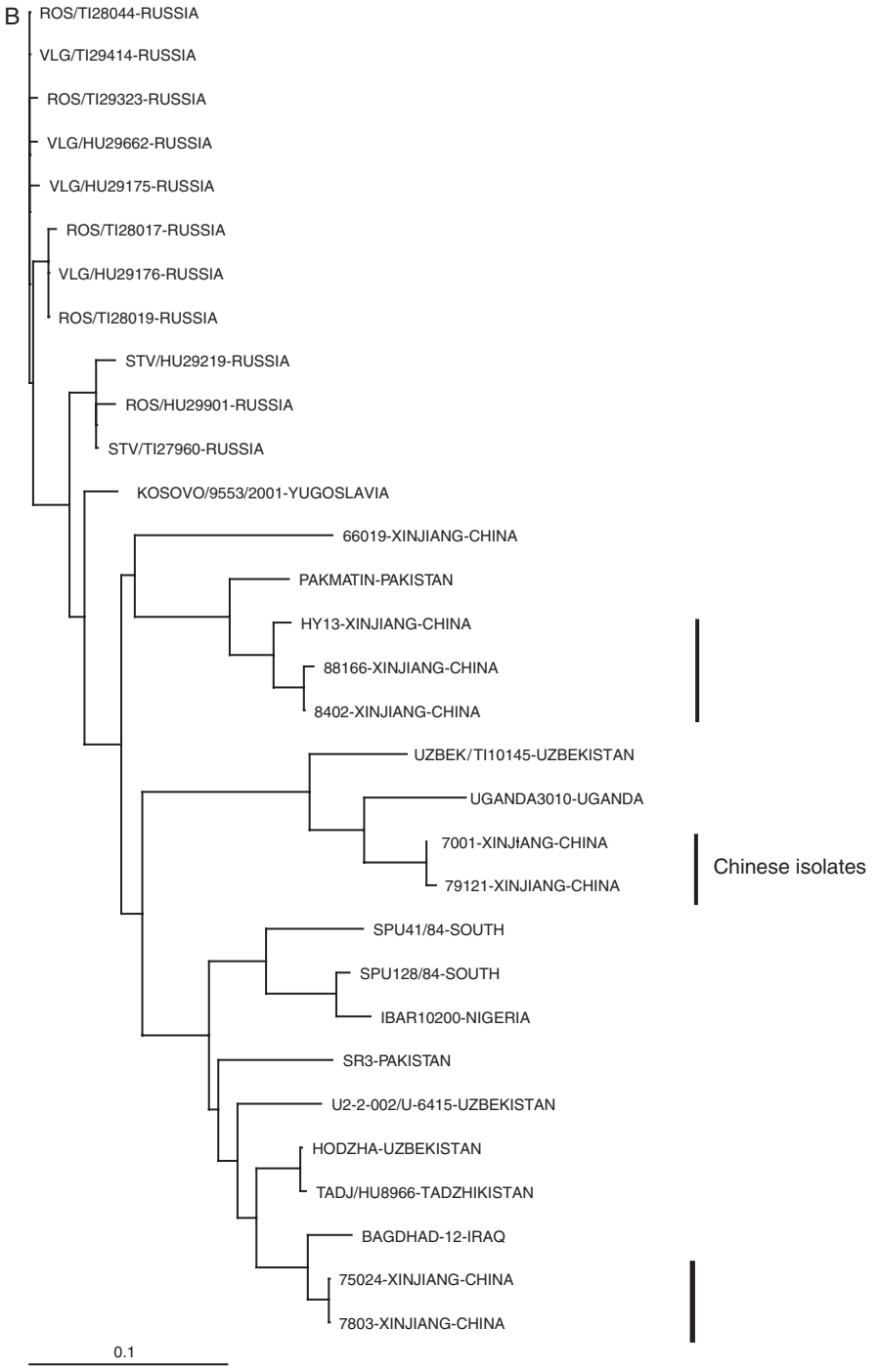

Fig. 10-5.

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CCHFV isolates form a different clade from that of the Chinese isolates. The CCHFV in Xinjiang have evolved in an independent manner possibly associated with the evolution of CCHFV-related tick species. The Chinese virus isolates 7001 and 79121 have a close relationship with the Kazakhstan CCHFV in the evolutional event.

Recently, genetic information on the M segment of CCHFV isolates including those of the Chinese virus isolates has become available. It is indicated that there is a hypervariable region and a relatively conserved region in terms of nucleotide sequence within the M segment [1, 14, 21]. Phylogenetic analyses have also been carried out based on nucleotide sequence of the conserved region of the partial M segment [5, 14, 31]. In contrast to the phylogenetic relationship analyzed using the partial S segment (Fig. 10-5a), the Chinese isolates of 66019, HY-13, 88166, and 8402, the Chinese isolates of 7803 and 75024, and the Chinese isolates of 7001 and 79121 form independent clades with the Pakistani isolate, Matin, the Pakistani isolate, SR3, the Tajikistani isolate, TADJ/HU8966, the Uzbekistani isolates, Hodzha and U2-2-002/U-6415, the

Fig. 10-5. cont'd. Phylogenic relationship of CCHFV Chinese isolates determined by the neighbor-joining method using the nucleotide sequence of the partial S segment (A) and the partial M segment (B). The accession number of the isolates used in the phylogenetic analyses for the partial S segment excluding those of Chinese isolates are as follows (Country, accession number): Pakquetta (Pakistan, U75677), Pakmatin (Pakistan, U75678), JD206 (Pakistan, U88414), 714/02 (Iran, AY366376), 756/02 (Iran, AY366378), 786/02 (Iran, AY366374), HU9509853 (UAE, U75672), 729/02 (Iran, AY366375), 766/02 (Iran, AY366373), 782/02 (Iran, AY366377), UAE/MUC-1 (UAE, S82580), HU9447547 (UAE, U75670), ArMg951 (Madagascar, U15024), UEA/MUC-4 (UAE, S82581), HU9509844 (UAE, U75668), IbAr10200 (Nigeria, U75674), HU9509854 (UAE, U75671), HD38562 (Burkina Faso, U15093), ArB604 (South Africa, U15092), SPU 45/88 (South Africa, U84637), ArD39554 (Mauritania, U15089), RSA (South Africa, U75675), HD49199 (Mauritania, U15023), ArTeh193 (Iran, U15022), DAK8194 (Senegal, U88411), AnD15786 (Senegal, U15020), AP92 (Greece, U04958), BUL6/02 (Bulgaria, AY550256), AL/Kukes/3/01 (Albania, AF449482), Turkey (Turkey, AY508485), BUL10/02 (Bulgaria, AY550258), 9553/2001 (Kosovo, AF428144), 9717/01 (Kosovo, AF428145), BUL9/02 (Bulgaria, AY550257), BUL3/02 (Bulgaria, AY550255), BUL2/03 (Bulgaria, AY550254), Kosovo (Kosovo, AF404507), BUL1/03 (Bulgaria, AY550253), Drosdov (Russia/Astrahan, U88412), UGANDA3010 (Uganda, U88416), HU2019 (Kazakhstan, AF362746), HU2015 (Kazakhstan, AF362744). The accession number of the isolates used in the phylogenetic analyses for the partial M segment excluding those of Chinese isolates are as follows: ROS/TI29323 (Russia/Rostov, AF401650), VLG/TI29414 (Russia/Volgograd, AY179961), VLG/HU29662 (Russia/Volgograd, AY093622), ROS/TI28044 (Russia/Rostov, AF401651), ROS/TI28019 (Russia/Rostov, AF401649), VLG/HU29176 (Russia/Volgograd, AY093621), ROS/TI29017 (Russia/Rostov, AF401648), VLG/HU29175 (Russia/Volgograd, AY093620), ROS/HU29901 (Russia/Rostov, AY093625), STV/TI27960 (Russia/Stavropol, AF401647), STV/HU29219 (Russia/Stavropol, AY093624), Uzbek/TI10145, Uzbekistan, AY093627), Matin (Pakistan, AF467769), IbAr10200 (Nigeria, U39455), CRI538199 (Pakistan, AJ538199), Tadi/HU8966 (Tajikistan, AY179962), CRI538197 (Iraq, AJ538197).

Iraqi isolate, Baghdad-12, and with the Uzbekistani isolate, Uzbek/TI110145, respectively (Fig. 10-5b). However, the Russian isolates of the CCHFV form an independent clade from those of other CCHFV isolates including the Chinese isolates. These results suggest that the CCHFV in Xinjiang has a close relationship with CCHFV in the neighboring countries such as Pakistan, Tajikistan, and Uzbekistan.

Xinjiang in China is a unique and important region for the study of CCHFV infections as it forms the eastern border of CCHFV infections and has long historical ties with the neighboring countries in terms of transportation, communications, and economic activities, which might have an influence on the evolutional events of CCHFV in the region. The discrepancy between the phylogenetic relationships based on the partial S segment and that based on the partial M segment may be due to a difference in the mutational rate between the S and M segments and/or more dynamic evolutional events such as recombination and reassortment [6, 12]. Further study on the molecular epidemiology of the CCHFV will provide a deeper insight into the evolutional events of the CCHFV.

10.8. SUMMARY

Xinjiang hemorrhagic fever, a form of CCHF, was first identified to be caused by the CCHFV in the early 1980s when the CCHFV was isolated from patients, small mammals and ticks in Xinjiang. These scientific achievements led us to understand the features of CCHFV infections in the region more precisely. However, there are still many questions to be resolved: the ecology of CCHFV, risk factors of CCHFV infection, surveillance of CCHF outbreaks, molecular epidemiology of CCHFV infections, effective preventive measures for CCHF outbreaks, efficacious treatment for patients with CCHF, development of diagnostics for CCHF that can be easily carried out at the site of the outbreak, development of efficacious vaccines, and so on. We strongly hope that these subjects will be resolved in the near future.

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