CHAPTER 9

CRIMEAN-CONGO HEMORRHAGIC FEVER IN RUSSIA AND OTHER COUNTRIES OF THE FORMER SOVIET UNION

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9.1. HISTORICAL ASPECTS

In the Compendium of the Sheikh of Khorezm by Dzhurzhoni in the 12th century, written in the Tajik language, the physician Zayn ad-Din abu Ibrahim Ismacil ibn Muhamad al-Husayini al-Jurjani described a hemorrhagic disease, now considered to have been Crimean-Congo hemorrhagic fever (CCHF), from the area that is presently Tajikistan [29]. The signs were presence of blood in the urine, rectum, gums, vomit, sputum, and abdominal cavity. The arthropod causing the disease was said to be tough, small, related to a louse or tick, and normally parasitizing a blackbird. Treatment that was sometimes ineffectual was application of *bodzkhar* and essence of red sandalwood at the site of the bite and feeding the patient fresh goat milk together with butter, *khot'ma* flowers (Malvaceae) and leaves or essence of *khovre* and essence of flax seeds, chicory, and gourd.

CCHF was also recognized for centuries under at least three names by indigenous peoples of southern Uzbekistan [18, 30]. In the opinion of Drobinsky [24], cases of CCHF had probably been seen in Romanian hospitals in occupied Crimea in 1942. Sipovsky [51] described 18 cases of peculiar gastrointestinal bleeding that occurred in the former Stalinabad (Dushanbe, Tajikistan Republic). This disease was called acute infectious capillary toxicosis, and *post factum* analysis clearly shows that this illness and CCHF resemble each other.

Crimean hemorrhagic fever, as originally named, was first fully described by Chumakov and coauthors [14, 15] who analyzed the data collected from the first outbreak of human disease in 1944, when about 200 members of the Soviet military were infected while assisting peasants in war-devastated Crimea (Ukraine SSR).

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9.2. HISTORY OF STUDIES ON THE ETIOLOGY OF CCHF

Chumakov and colleagues established the viral etiology of CCHF by inducing disease in psychiatric patients for whom pyrogenic therapy was prescribed. An infectious agent was found in both the blood of CCHF patients and in suspensions of *Hyalomma plumbeum* (*Hyalomma marginatum marginatum*) ticks. These authors showed its ability, after being filtered through bacterial filters, to cause disease with typical clinical features of CCHF in humans. Multiple species of laboratory animals, including adult white mice, guinea pigs, monkeys, and cats were found to be refractory to infection. Later, in 1955, Chumakov and coauthors similarly showed the viral etiology of CCHF in the Astrakhan region of Russia. A decade later several reports of the isolation of CCHF virus (CCHFV) using different types of cell cultures appeared in the literature [16]. These isolated viruses turned out to be nonpathogenic for newborn white mice and golden hamsters, and the attribution of these isolates to CCHFV was questionable.

Intracerebral inoculation of newborn white mice was first used for virus isolation in the USSR in 1967. Obviously at that time, this model was very useful for isolation of numerous arboviruses from around the world. Two groups of virologists from the Laboratory of Hemorrhagic Fevers, Institute of Poliomyelitis and Viral Encephalitides (USSR Academy of Medical Sciences), headed by Chumakov, were involved in this work. One group (Butenko and colleagues) worked in Astrakhan and another (Shalunova and colleagues), in Moscow. As a result, nine strains of CCHFV were isolated and identified. One strain (Drozdov) was isolated from a CCHF patient from the Astrakhan region; seven strains were recovered from patients in the neighboring Rostov region and one from Samarkand in Central Asia [10, 20].

Evidence of the role of these agents in the etiology of CCHF included regular detection of seroconversion of specific antibodies in patients with typical CCHF and virus isolation from patient's blood during the acute period of disease. Using serological tests, CCHFV was differentiated from nine spontaneous murine viruses, Omsk hemorrhagic fever virus, the virus of hemorrhagic fever with renal syndrome, and ten other arboviruses. The prominent American scientist Harry Hoogstraal, in his review of CCHF [30] wrote "… it was only in 1967, when Soviet workers first used the generally accepted newborn white mouse (NWM) inoculation technique for CCHF virus isolation and study, that the etiologic agent could be characterized antigenically, physiochemically, and morphologically." In 1968, the CCHFV (Drozdov strain) was transferred to the Yale Arbovirus Research Unit (YARU). In October 1968, Jordi Casals from YARU wrote in a letter to Chumakov, "as you can see, it appears that by complement-fixation your strain Drozdov is indistinguishable from three strains of Congo virus – Ug K 2/61, Congo 3010 and Pak JD 206. The fact that the serum pool from persons who have had Crimean hemorrhagic fever, which serum you sent me in your first shipment of materials, reacts with Congo virus (strain 3010) antigen with the same titer, 1:8, as it does with the Drozdov antigen, is of crucial importance and significance. We all believe here at YARU that these results are very exciting; whether or not Drozdov strain and Congo virus will turn out to be identical by neutralization test remains to be seen. I am planning to run the neutralization tests in 4 or 5 days and will let you know the result. If your strains of Crimean hemorrhagic fever virus turn out to be indistinguishable or very close to Congo virus, then the latter becomes a pathogen of exceptional interest, not just to you in the Soviet Union where you already knew it in the form of a very serious human illness, but also to the other areas in the world where it has been recognized heretofore."

Soon, both Russian and American investigators obtained additional data on identity of the Crimean and Congo viruses [12, 21]. Hoogstraal, in his 1979 review [30] declared, "The Drozdov strain of CCHF virus, isolated by this method from a patient (Drozdov) in Astrakhan, became the now-famous prototype CCHF strain for much experimental work in the USSR and abroad. Following the publication of Congo virus in 1967 [54], some have argued that the common name of the virus should be Congo virus, but Soviet authorities have insisted that the long recognized name Crimean hemorrhagic fever virus should be retained. As a compromise between 'unofficial' historical antecedents and 'official' Registry criteria, J. Casals et al. [13] suggested CHF-Congo virus as an accepted common name." For more on the controversy over the naming of CCHFV, see Chapter 3.

Major results of intensive research during the years since 1967 have included the development of cell culture techniques for virus isolation, which has allowed the identification of the virus in endemic regions of Europe, Asia, and Africa. This has also allowed for the identification of biological and morphological properties of the virus making it possible to classify it as a member of the family *Bunyaviridae* [23]. Plaque formation, hemagglutination, interference phenomena, and some peculiarities of cultivation of the virus in cell cultures were discovered. The spectrum of pathogenicity of CCHFV for laboratory and domestic animals was studied, as well as possibilities of laboratory techniques for serological diagnosis and experimental investigations. Serological methods, of course, have been highly beneficial in the areas of CCHFV laboratory diagnostics and research, for example, by placing CCHFV in the genus *Nairovirus*, and together with Hazara virus isolated from *Ixodes redikorzevi* ticks from Pakistan, forming the CCHFV antigenic group [2, 3].

9.3. EPIDEMIOLOGY

Although many of the fundamental epidemiological parameters of CCHF in the southern territories of the USSR and Bulgaria have been identified previously, after 1967 new data radically expanded our knowledge of the geographical distribution of natural foci, host reservoirs, and tick species associated with CCHFV. The virus is distributed in the following regions in Europe: Russian Federation (Astrakhan, Rostov, Volgograd regions, Kalmykia, Krasnodar and Stavropol territories, Dagestan, Ingushetia), Ukraine (Crimea, Lugansk region) Azerbaijan, Armenia, Georgia (?), Bulgaria, Greece, Hungary (?), Republics of former Yugoslavia, Albania, France (?), and Portugal. In Asia, the virus occurs in all the former Soviet Union republics of Central Asia, Kazakhstan, China (western provinces), Afghanistan, Pakistan, India, Iran, Iraq, United Arab Emirates, Kuwait, and Turkey.

9.4. INCIDENCE OF DISEASE

The total number of registered CCHF cases in the world is about 5,000, with more than 200 cases in the Crimea, 1,154 in the Russian Federation (Fig. 9-1), some 700 in Central Asia, more than 550 cases in Uzbekistan, about 150 in Tajikistan, a single case in Kyrgyzstan, about 200 in Kazakhstan, 1,500 cases in Bulgaria, nearly 50 in territories of the former Yugoslavia (mainly in Kosovo), 40 cases in the Middle East countries and Pakistan, over 1,000 cases in Turkey, and approximately 200 cases in Africa – half of them reported from the Republic of

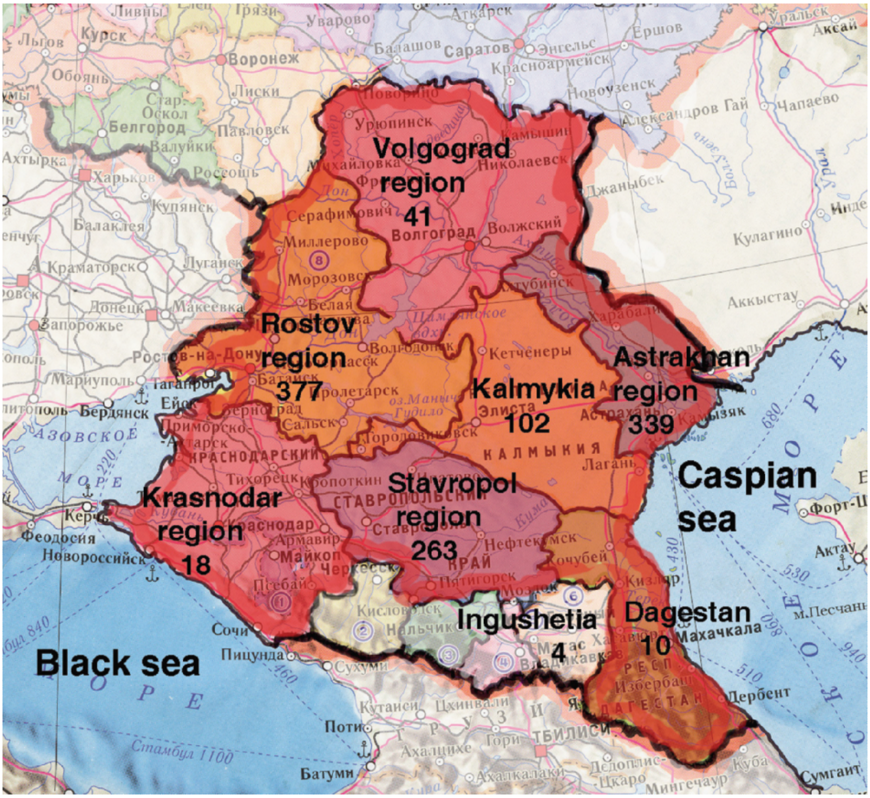

Fig. 9-1. Map of the Russian Federation showing the total number of CCHF cases for 1948–2005.

South Africa. The situation in the latter country is interesting, because, unlike other African countries, clinical and epidemiological features in South Africa strongly resemble those in classical foci in Central Asia; mortality rates are up to 30%, modes of transmission include ticks bites, direct contact with crushed infected ticks, contacts with infected human, bovine and sheep blood.

9.4.1. Incidence of CCHF in the countries of the former Soviet Union

Three hundred thirty-nine cases of CCHF were registered in the Astrakhan region of Russia in the period from 1953 to 2005; 377 cases in the Rostov region from 1963 to 2005; 263 cases in the Stavropol region from 1953 to 2005. In 1948, 18 persons became ill in the Krasnodar region. From 2000 to 2005, 102, 41, and 10 cases occurred in Kalmykia, the Volgograd region, and Dagestan, respectively [8, 9]; four cases were identified in 2004 from Ingushetia [49]. The most cases (230 patients) occurred in the Astrakhan region from 1953 to 1967. Only nine cases were registered from 1970 to 1983 and only a single case in 1984–1999. In the following 4-year period ending in 2004, 50 persons became ill. An additional 37 cases were recognized in 2005.

After the first description of CCHF in the Rostov region in 1963, the number of human cases in the region during the following 8 years (to 1970) was 338. The highest incidence of disease was recorded in 1968 (138 cases; 23.4 per 100,000 population). In the other years of the same 8-year period (1963–1970), incidence varied between 8.9 and 17.0 cases per 100,000 population. Twenty-eight cases were reported in 2001–2004, with an additional ten cases in 2005.

The number of cases recorded from the Stavropol region from 1953 to 1968 was 25. There were one and two cases in 1970 and 1972, respectively. However, from 1999 to 2005, the total number of cases increased to 237 [9]. Eighteen cases were reported in the Krasnodar region in 1948 [33]; however, no other information of additional cases from this region is available.

During the initial outbreak of CCHF on the Crimean peninsula in 1944, approximately 200 cases of disease were recorded. Only small outbreaks and sporadic cases have been seen there in the years that followed [8, 9]. Additionally, three laboratory-confirmed cases were reported from the Lugansk region in Ukraine in 1969 [32].

The only case of CCHF in Armenia was reported in 1974 [50]. Local physicians reported 72 cases of CCHF in the Chimkent region of Kazakhstan from 1948 to 1975, although 49 patients were reported in the entire Republic from 1965 to 1982. An outbreak involving 90 patients occurred in 1989 in the Kyzyl-Orda, Chimkent, and Djambul regions of Kazakhstan; morbidity rates ranged from 0.01 to 0.09 per 100,000.

From 1948 to 1963, in Uzbekistan, a total of 525 CCHF cases were reported. However, from 1973 to 1983, only 28 cases were reported. Ninety-three CCHF cases were reported in Tajikistan from 1943 to 1970. By 1974, the number of cases reached 121, and during 1975–1983, an additional 23 cases were seen. Morbidity rates varied from 0 to 0.27 per 100,000 (in 1975) [8, 9].

The hospital-acquired outbreak in Turkmenistan in 1946 involved seven persons [41]. In the years that followed, only sporadic cases occurred. Two cases were recorded in 1953, and one in 1971, in the Osh region of Kyrgyzstan [31].

As shown by seroepidemiological studies, the level of naturally acquired specific immunity to CCHFV in all endemic territories is extremely insignificant, and so, the overwhelming majority of both local and newly arrived population is susceptible to CCHF. The morbidity in all of the endemic regions over the years has been very sporadic. Even during the significant outbreaks, only single cases were noticed in the same territories, and not every year. For example, during the epidemic period from 1963 to 1971, in the Rostov region, 169 settlements in 18 administrative regions were affected by CCHF with a mean number of reported patients from 1.0 to 1.42 [1].

9.5. SEASONAL ACTIVITY

Not surprisingly, the seasonality of CCHF cases corresponds to the months of the year when the tick vectors are most active. The first cases of CCHF during the initial outbreak in 1944–1945 in the Crimean peninsula were noticed in April and the last in September, with the highest number occurring in July (53% of all cases) [30, 34]. The earliest CCHF case in the Astrakhan region was reported in March, with the last one reported in August. In fact, the majority of cases occurred between the first week of May and the second week of June [8, 9, 35, 52]. The first CCHF cases in the Rostov region appeared at the end of May and the morbidity reached its maximum (as in Astrakhan region) at the end of May/beginning of June. The last cases were usually seen by the end of August. Only two patients acquired the disease in September in the Rostov region. The data of 1963–1969 shows the seasonal dynamics of CCHF morbidity in the Rostov region as follows: 0.9% of all cases were in April, 34.2% in May, 41% in June, 17.9 in July, 5.3% in August, and 0.6% in September. Two hundred fifty-one patients were recorded in May and June during the period from 1963 to 1970, comprising 72.4% of all cases (338) [1, 44].

Based on data from 1950–1969, CCHF cases in the Samarkand region of Uzbekistan were noticed year-round, nevertheless, the majority of infections occurred during the summer months (June, July, and August). During 1948–1975 in the Chimkent region of Kazakhstan, the first cases of the disease were seen in January, which was highly unusual. The distribution of CCHF cases by season was as follows: 61.4% summer, 24.2% autumn, 11.6% spring, and 2.8% in the winter (January) [8, 9, 30].

9.6. EPIDEMIOLOGY

The age range of the majority of the CCHF cases in the Rostov region was 20–60 years. The risk groups in the Rostov region, as well as in other endemic regions, comprising up to 70% of all CCHF cases, included milkmaids, cattle farm workers, agricultural workers, and housewives. Regional epidemiologists often stated that there is no strict association of CCHF with a particular trade in the rural area. Nevertheless, it was clear that the incidence of disease was highest among those who work in the open steppe environment [1, 44].

Likewise, in the Astrakhan region, approximately 80% of the patients were 20–60 years old; again, most were agricultural worker, and males (54.2%) were more likely to become infected than females (45.8%) [35, 52].

Adult rural residents made up 68% of all those infected with CCHFV in Kazakhstan, being cattle breeders and farm hands. Two persons who lived in an urban environment also became infected; one worked on the slaughtering floor of a meatpacking factory, and the other was a miner, who occasionally visited the endemic area. It is noteworthy that the numbers of shepherds and health-care workers infected with CCHFV were relatively high (38.8% and 16.3%, respectively) in Kazakhstan [53].

In Tajikistan, the breakdown of CCHF patients by profession was as follows: 28% agricultural workers, 19% shepherds, 14% housewives, 13% health-care workers, 11% farm machine operators, 8% teachers or students, and 6% dairy farm workers [42].

The CCHF patients in Uzbekistan ranged from 2 to 74 years old, with the majority (83%) being between 15–50 years old. Sixty percent of the patients were farm workers, and 9% were school children brought to the fields to help gather the harvest [40].

9.7. MODES OF TRANSMISSION

As stated elsewhere, tick bites are the most common route of transmission of CCHFV to humans. In the original Crimean outbreak in 1944, 87.8% of patients reported that they had been bitten by a tick several days before onset of the disease; human-to-human transmission was not reported [14, 15, 24].

In the Astrakhan region, approximately 30% of CCHF patients have reported being bitten by a tick or have found one crawling on their body or clothes. A case from May 1962 of the simultaneous infection of both husband and wife who sheared sheep has been reported. That spring the weather in the Astrakhan region was dry and hot, and the fields were very dusty. Neither husband nor wife reported a tick bite, and, thus, it was suggested that the disease was acquired by inhalation of infected dust particles; although undetected tick bite or exposure to infectious blood or body fluids during the process of shearing is also a possibility. Such a possibility is highlighted by the case of a nurse at a regional hospital, who became infected following manipulation of the blood of CCHF patients. She had severe eczema of the hands, and presumably became infected through the multiple lesions on her hands [52].

CCHF has a long history of nosocomial spread (see Chapter 22). Three cases of nosocomial infection are known from the Rostov region, all of which were medical personnel who become infected from the blood of CCHF patients [30, 34]. In 1946, a CCHF patient in Turkmenistan was a source of infection for six other persons, medical attendants, and other patients hospitalized in the same ward (six of the patients died).

The transmission of CCHFV through contact with the blood of infected cows and sheep was repeatedly reported from the countries of Central Asia (Tajikistan and Uzbekistan); slaughtering-infected cattle posed the highest risk [8, 9].

Two cases of laboratory infections are known from Russia. Manipulation of infected material during viral isolation, preparation of viral antigen, and serologic analyses resulted in infection by direct contact through the small skin injuries, accidental skin puncture by syringe needles, or inhalation of aerosols. Both of the laboratory-acquired cases were very severe and one patient ultimately died [26].

The analysis of the data from Russia and other former Soviet Union countries suggest that the major risk factors for CCHFV transmission to humans are residence in endemic regions, exposure to tick vectors (such as agricultural and cattle-breeding workers, sheep herders, and dairy farmers), direct contact with CCHF patients, and working with the virus or virus-infected materials in the laboratory (for more on CCHF risk factors, see Chapter 21).

9.8. MORTALITY RATES

Various authors have reported the mortality rates of CCHF during the initial outbreak in Crimea in 1944 as 8–11%; whereas, in succeeding years, when only small outbreaks or sporadic cases were reported, up to 30% of the cases were fatal. A possible explanation for this disparity is the underreporting of milder cases [17, 30, 34]. Mortality rates in the Astrakhan region, in the epidemic period from 1953 to 1967, varied from 12% to 16%. Eleven of 25 (44%) CCHF patients from 1953–1968 in Stavropol region died [34, 35]. The average mortality rate in Kazakhstan was 32.6% (1965–1982); however, interestingly, very high mortality has also been seen in the Chimkent region of that country when patients were infected by the blood of CCHF patients (62.5%). Likewise, in Tajikistan, transmission of CCHFV by infected blood resulted in a 50% case fatality rate.

More recently, mortality rates in endemic regions of Russia (southern territories of European Russia) have significantly decreased when compared with previous years. For instance, in 2004, there were six fatalities of 68 patients (8.8% mortality), and in 2005, six of 130 cases (4.6%) had fatal outcomes. Such a decrease may be the result of three main causes: (1) wide distribution and availability of specific diagnostic methods that lead to laboratory confirmation of multiple milder cases without, or with only slight, hemorrhagic syndrome, (2) utilization of ribavirin for the treatment of patients, and (3) predominant circulation of less pathogenic viral strains in endemic regions.

9.9. ARTHROPOD VECTORS OF CCHFV

Approximately 30 species and subspecies of Ixodid ticks are ecologically associated with CCHFV virus (see Chapter 12). *H. marginatum marginatum* is the most important tick vector in the European part of Russia. In Central Asia, many other ticks in the genus *Hyalomma* are known to harbor the virus (see Table 12-1 in Chapter 12 for a complete list) [18, 30].

9.10. WARM-BLOODED HOSTS OF CCHFV

Natural hosts and reservoirs of CCHFV include hedgehogs, hares, ground squirrels, jerboas, and some species of rodents and ungulate animals (see Chapter 13). These animals may develop constant viremia, high enough to transmit the virus to feeding ticks. Adult ungulates, immunized by their first encounter with CCHFV, loose the ability to produce a high-titer viremia and thus became a dead-end host.

As many as 70% of the European hares in the Astrakhan region, which were examined for the presence of specific antibodies to CCHFV, were found to be positive. Similar data were obtained from the Rostov region and from Bulgaria. Experimental work showed the ability of hares to be the source of virus infection for *H. marginatum marginatum* larvae, which feed on them during the period of viremia [4, 19, 56]. Subcutaneously inoculated animals did not develop clinically evident infection, but viremia was prolonged (from day 1 to 10 postinoculation).

H. plumbeum (*H. marginatum marginatum*) tick larvae were found to become infected while feeding on experimentally infected big-eared (Asian) hedgehogs (*Hemiechinus auritis*); moreover, they were also able to transmit the virus transstadially. Neither the big-eared nor the European (*Erinaceus europaens*) hedgehogs presented any clinical signs of disease. Virus could not be detected in the blood of European hedgehogs 5–13 days postinoculation; whereas the big-eared hedgehog produced high-titered (10^4) viremia 4–6 days postinfection [5].

Small ground squirrels (*Citellus pygmaeus*) infected subcutaneously at the age of 4–6 weeks retained CCHFV without marked clinical signs. The virus was regularly recovered from blood and parenchymatous organs 2–7 days after inoculation. In some individuals, virus could be detected in the kidneys and brain. The amount of virus needed to produce viremia in ground squirrels was determined to be 10 mouse LD_{50} (50% lethal dose), and studies have shown that artificially infected ground squirrels are capable of transmitting CCHFV to feeding larval and nymphal ticks of multiple species [6].

9.11. CLIMATIC INFLUENCE ON THE ACTIVITY AND DISTRIBUTION OF CCHFV IN THE NORTHERN PART OF ITS NATURAL FOCUS

Worldwide, the occurrence of CCHF coincides with the natural foci of *Hyalomma* species ticks. In Russia, this is primarily *H. marginatum marginatum*, which has a northern geographic limit of 48° north latitude. Epidemic potential and disease incidence are strongly dependent on the abundance of the main tick vector (adult *H. marginatum marginatum*) in the spring and summer. And this, in turn, is dependent on the climatic conditions during the winter months in the northern limits of its habitat (for a more general discussion of the effects of climate on tick-borne diseases, see Chapter 14).

Since 1891, significant warming has been observed in the Astrakhan and Rostov regions. In the period from 1963 to 1968, the number of reported CCHF patients in the Rostov region increased (11 in 1963, 24 in 1964, 27 in 1965, 38 in 1966, 61 in 1967, and 131 in 1968) proportionally to the average seasonal rates of adult *H. marginatum marginatum* tick abundance. Likewise, beginning in 1995, the six winters that followed were mild, with increased average seasonal rates of *H. marginatum marginatum* tick abundance. This led to an increase in CCHF cases in 2001–2003. The number of administrative regions considered endemic for CCHF also increased from 2 to 14, as well as the overall area of the endemic regions (from 600 to 16,000 km^2). This expansion of endemic regions has been suggested to be due to the dissemination of virus-infected nymphs and larvae of *H. marginatum marginatum* by rooks (*Corvus frugilegus*) and other birds. In addition, perceptible warming in the last few years has led to the increase of epizootic and endemic activities of CCHF in the Rostov region, synchronously with that in the Astrakhan region.

The emergence of CCHF in the Volgograd region in 2000 is of special interest. This is evidence of the spreading of the natural focus of CCHFV, possibly as a result of global warming, and formation of abundant local populations of *H. marginatum marginatum* ticks, much further north than the known endemic regions [11].

9.12. MOLECULAR EPIDEMIOLOGY

In recent years, a large body of genetic data has become available for many CCHFV strains isolated from around the world, with many strains isolated from Russia and other countries of the former Soviet Union represented [22, 27, 28, 38, 39, 45, 55].

Attempting to analyze the molecular epidemiology of CCHFV strains isolated from the European part of Russia and the Central Asian republics of the former Soviet Union, we compiled all available sequences in GenBank. Based on the phylogeny of all three segments, strains from the European part of Russia grouped together with strains isolated from southern Europe. In addition, our data supported those of others [7, 25, 28, 43, 55] regarding the phylogeny of strains isolated from the Astrakhan, Rostov, Volgograd, and Stavropol regions. S-segment sequences of these strains reliably grouped with viruses isolated from Bulgaria, Kosovo, Albania, and Turkey. Similarly, 12 fragments of the L segment of strains isolated in the southern regions of Russia form a phylogenetic group with a Bulgarian isolate [38, 39].

Phylogeny based on complete S segments show that viruses isolated from China, Tajikistan, Kazakhstan, and Uzbekistan group together (Asia 2); whereas, isolates from the Stavropol, Rostov, Volgograd, and Astrakhan regions, along with Bulgarian isolates form a distinct group (Europe 1) (Fig. 9-2). Thus,

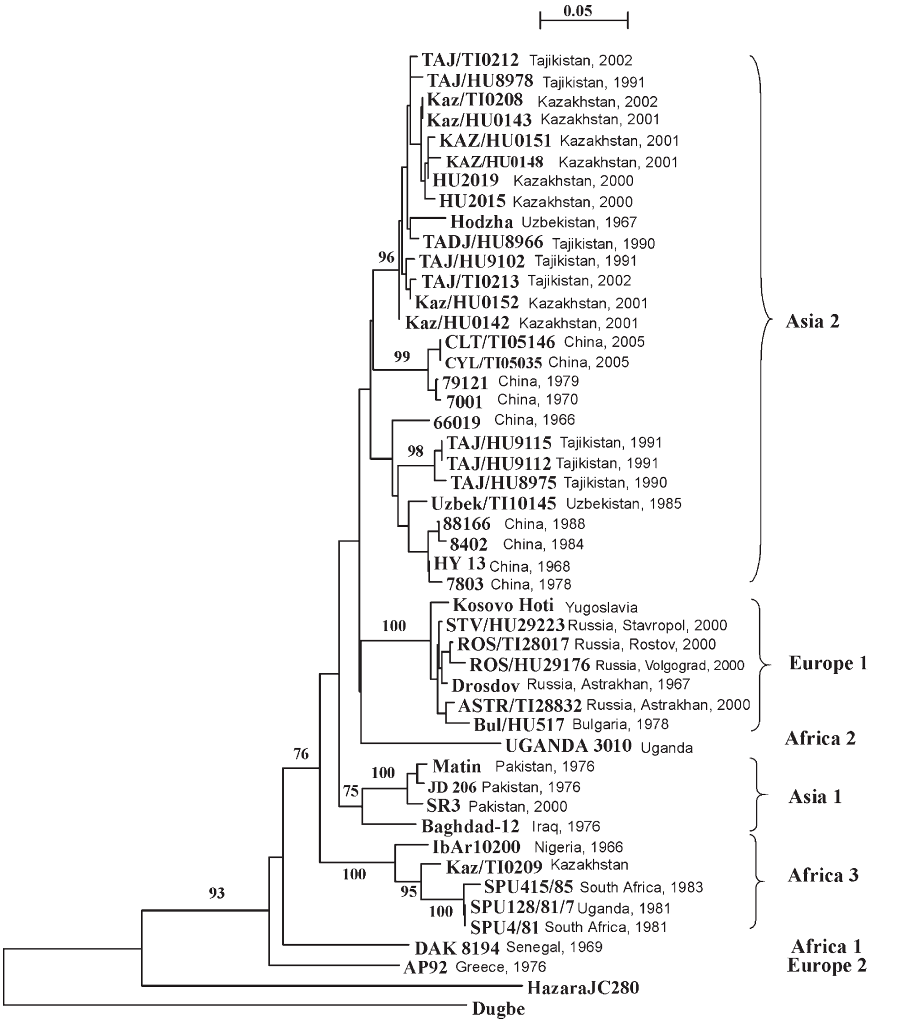

Fig. 9-2. Phylogenetic tree of a 294-nucleotide region of the S segment of CCHFV. Tree was constructed with CLUSTAL W software (version 1.83) using the neighbor-joining algorithm. Dugbe and Hazara viruses were included as out-groups. Bootstrap values from 1,000 replicates are shown at each branch point (only those of 70% and greater are shown).

one may find at least two genotypes of CCHFV circulating in Russia and the Central Asian Republics, one of which is genetically close to viruses circulating in China. For a more general discussion of the molecular epidemiology and phylogeny of CCHFV, see Chapter 5.

9.13. TREATMENTS USED IN RUSSIA AND OTHER COUNTRIES OF THE FORMER SOVIET UNION

Along with symptomatic therapy, specific antiviral treatment with 200 mg of oral ribavirin has been used for CCHF patients in the endemic regions of Russia. The loading dose of 30 mg per kg (2,000 mg for a 70 kg person) was established by experimental studies performed in the Stavropol region. A maintenance dose of 600 mg twice a day for those under 75 kg, and 500 mg twice a day for the persons over 75 kg, was also established, with a treatment length of 5–10 days. Maleyev et al. [37] presented data on their treatment of 20 CCHF patients. In 18 patients (90%), ribavirin was administered during the first 4 days after the onset of the disease. Clinical signs of hemorrhage were evident in only five patients; they presented with localized postinjection hematomata and petechiae. All patients demonstrated marked hypocoagulation. High fever resolved during the 2nd day after ribavirin administration. Blood tests performed 48 h after the initiation of therapy revealed white blood counts rising to normal levels in all patients. Two patients who developed nasal bleedings, gingival hemorrhages, and postinjection hematomata received hemostatic therapy, together with ribavirin, from the 2nd day of the disease. No fatalities were observed in this group of patients.

Ribavirin-Meduna (15 mg per kg) was also applied for the treatment of CCHF patients in the Astrakhan region (the clinical hospital of the Astrakhan Medical Academy). Normally, a 2-dose per day regimen of 1,000 mg was used (400 mg in the morning and 600 mg in the evening) and continued for up to 10 days. As a supplemental treatment, 0.5 g endogenous interferon (Cycloferon) was given on days 1, 2, 4, 6, 8, 10, and 12 after onset of disease [36].

Thus, the data from the Stavropol and Astrakhan regions suggest that the use of ribavirin is an effective treatment of CCHF, especially when administered before hemorrhagic manifestations (usually before the 5th day of the disease). For more on the use of ribavirin and other potential treatments for CCHF, see Chapter 20.

9.14. EPIDEMIOLOGICAL SURVEILLANCE AND INVESTIGATION IN ENDEMIC REGIONS

Epidemiological surveillance plays an important role in the overall control strategy of CCHF in Russia and other FSU countries. Various research institutions, Centers of Sanitary and Epidemiological Surveillance, Plague Control Institutions and Stations, and veterinary institutions collaborate on the surveillance of CCHF in Russia. It is compulsory for health authorities to inform their respective ministries of health on each suspected CCHF case. Isolation arrangements and a strict antiepidemic regimen for CCHF patients and their contacts are mandatory. Epidemiological investigation of each case or outbreak is carried out for the identification of the source of infection, transmission routes, and the identification of persons at risk of contracting the disease.

Editor's comments

Since 2005, there has been a marked expansion of CCHF cases in several regions of Russia, as evidenced by the following ProMED-Mail (www.promedmail.org) reports from 2006:

Date: 24 June 2006

As of 8 June 2006 there has been a marked expansion in the distribution of CCHF cases: new cases have been detected in the Zymovnikovskiy, Tsymlyanskiy, and Tselinniy districts of the Rostov region where no cases have been observed in recent years [46].

Date: 10 August 2006

[Thus far in 2006] a severe deterioration in the epidemiological situation for CCHF has been observed in the Southern Federal District of Russia. As of 8 August 2006, the Federal Service for Surveillance of Consumer Rights and Human Well-being reported that 192 cases of CCHF had been recorded in the southern federal district. This figure exceeds that for the corresponding period of (2005) by 43%. The greatest deterioration has occurred in the Republic of Kalmykia (65 cases of CCHF recorded) and in the Rostov region (53 cases of CCHF). CCHF has been diagnosed in 15 patients in the Astrakhan area, in 16 patients in the Volgograd area, and in 3 patients in the Republic of Dagestan. So far in 2006, five patients have died as a consequence of CCHFV infection, compared with four fatalities in the corresponding period of 2005. Two fatal cases were recorded in the Republic of Kalmykia, and one each in the Stavropol, Rostov, and Astrakhan regions [47].

Date: 31 August 2006

Forty-one cases of Crimean-Congo hemorrhagic fever (CCHF), including one fatality, have been recorded in 12 districts of the Stavropol region, according to the Territorial Management of Rospotrebnadzor (Federal Service on Surveillance of Consumer Rights and Human Well-being) in Stavropol. These figures are worse than those of 2005, when 38 cases were recorded in 15 areas of the region. The 334 people admitted to hospital with suspected CCHF exceeded by 46% of the number admitted to hospital in 2005 on suspicion of CCHF infection [48].

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