Overview of Zoonotic Diseases in Turkey: The One Health Concept and Future Threats -1

Zoonotic diseases are contagious or non-contagious infections with emerging and/or re-emerging characteristics and naturally transmissible from vertebrate animals to humans and vice-versa via contact, food, water, and by vectors in the human and animal ecosystems; their increasing risks affect global health security (1-3). These infections are caused by all types of pathogens, including bacteria, fungi, parasites, viruses, and unconventional agents such as prions. Prior to the 20th century, the best known zoonoses were rabies, anthrax, glanders, tuberculosis, plague, yellow fever, influenza, and certain zoonotic parasitic diseases (4). Sixty percent of 300 infectious agents identified between 1940 and 2004 have been classified as zoonoses, and most of these infections belong to the neglected diseases (5, 6). More than 200 zoonoses have previously been described to date, and their epidemiological appearance and distributions occur in sporadic, endemic, epidemic, and pandemic forms in the world causing deaths among humans, livestock, as well as wildlife. Zoonotic infections also result in great economic losses (5, 7) and could be one of the major reasons of poverty (6-8). The public health impact and financial consequences of these diseases can devastate the already overburdened economic conditions in developing countries as well as in Turkey (9, 10). Over the last decade, the global economic impact of zoonotic diseases has been estimated as more than $220 billion ($20 billion from direct costs and $200 billion from indirect losses) (11, 12). In the second-half of the last century, the control and/or elimination of zoonotic diseases has been successful in several industrialized countries through expensive infrastructural investments and meticulous coordinated interventions, including “test and cull of animals,” feed bans, mass vaccination of domestic animals and wildlife, health education, and milk pasteurization. Naturally, these highly effective methods for elimination of zoonotic diseases involve legal and financial collaterals. However, in most developing countries, livestock practices have primarily focused on implementing prevention and eradication measures with much less emphasis on the effect of mitigation (transmission control) strategies, considering the economic and development impacts at the macro (national economy and environment) or micro (health, livelihoods, and food security of smallholder farmers) levels. Thus, in most developing countries, the surveillance of zoonotic diseases is not recognized in the One Health context between veterinary medicine and human medicine. In addition, many countries lack diagnostic capacity and health infrastructure (7). Meanwhile, the global increase in zoonotic diseases was reported as 22% in 1990–2000 and 21% in 2000–2010 (13). The zoonotic infections that have emerged or re-emerged globally are Severe Acute Respiratory Syndrome (SARS) in 2003, Influenza A H1N5 (avian influenza) in 2003, Influenza A H1N1 (pandemic influenza or swine flu) in 2009–2010, Middle East Respiratory Syndrome (MERS) in 2012, Influenza A H7N9 in 2013, Ebola in 2014, and Zika virus in 2015–2016. To combat of zoonoses, the One Health concept has been defined by the World Health Organization (WHO) as a worldwide strategy that would expand interdisciplinary collaborations and communications in all aspects of health care for humans, animals, and environment Turkey is geographically located in Eurasia and represents a natural bridge for the transmission of many zoonotic infections that involve the movement of animals (particularly bird immigrations) and humans (illegal transport of humans or mass immigrations of populations) among the continents of Europe, Asia, and Africa. Turkey has a population of over 80 million and a livestock population of over 50 million, and its economic structure currently depends on a mix of industrial and agricultural products (10). Currently, Turkey has been affected from illegal animal and human movements. In particular, regional conflicts in the countries neighboring Turkey has led to massive refugee and illegal human movements during the past 30 years (15-17). In addition, Turkey has highly variable climatic conditions, vegetation structures, wildlife, and particularly many sanctuaries for immigrant birds. The geographic structure of Turkey also allows suitable habitats for various vector arthropods, such as bloodfeeding insects and ticks, throughout the four seasons of the year (10, 18-21). Thus, several zoonotic diseases are endemic throughout the country and affect humans and animals (22-24) with economic losses (25-30). In this review, an overview of the zoonotic diseases (Figure 1) in Turkey are described in the One Health concept and future threats perspectives.

 The dynamic interactions of zoonoses among humans, animals, and pathogens in the same environment could be evaluated within the “One World-One Health” concept with a holistic perspective. Actually, this approach dates back to the ancient periods of humankind (31). Prior to the discovery and application of sanitation and hygiene, particularly sterilization and antibiotics, bacterial zoonotic diseases, such as bovine tuberculosis, bubonic plague, and glanders, caused millions of human deaths in the world as well in Turkey (32). The discovery and application of insecticides and acaricides, and entomopathogens led to the reduction of vector-borne infections in the last century in Turkey as well globally (33). Effectively implemented control measures have resulted in a decrease in many community-acquired infections, including bacterial and parasitic diseases, such as tuberculosis and malaria, which constituted major public health problems until a few decades ago. Meanwhile, the frequent use of antibiotics in human medicine and veterinary purposes have led to the emergence of antimicrobial resistance in various nosocomial isolates of gram-positive and gram-negative bacteria. However, recent guidelines limiting antibiotic applications have been promising (34). In addition, over 50 vector-borne infections (19 tick-borne diseases [TBDs]) caused by different pathogens have been reported in farm animals and humans (20, 21) and in cats and dogs (35). A total of 47 tick species (38 ixodid and 9 argasid) have also been reported in the last century in Turkey (10), and these zoonotic diseases have a significant impact on the livestock industry of the country (26, 29, 30). Modes of transmission for zoonotic diseases between animals and humans involve several routes: (i) via blood-feeding arthropods, such as ticks, mites, fleas, biting midges, mosquitoes, and sand flies; (ii) via contaminated food (food-borne) and/or contaminated water (water-borne); (iii) via direct contact (ie, farmers, workers, and veterinarians at increased risk to exposure with zoonotic agents); (iv) via soil contaminated with manure; (v) via animal bites and/or animal scratches; and (vi) invasion with active penetration (36). In addition, some zoonotic diseases can be transmitted from patients to health care workers and health professionals (physicians, nurses, and other health staffs) (37). Bacterial Zoonotic Diseases in Turkey Bacterial zoonoses are grouped based on the infection routes described above. Most of the vector-borne bacterial zoonotic diseases are classified depending on the biological vector involved in its transmission, such as tick-, mite-, flea-, and insectborne. In addition, mechanical transmission of some bacterial zoonoses are also possible by iatrogenic or by insects, whereas a few zoonotic bacterial pathogens can be transmitted by the ingestion of trematodes and caddishflies as well. Particularly, tick-borne bacterial zoonoses are complex and have been grouped as rickettsial (38) and non-rickettsial (39). The reported bacterial zoonotic diseases in Turkey are shown in Table 1. Anaplasmosis is an opportunistic rickettsial vector-borne disease of humans and animals, caused by Anaplasma species including A. marginale, A. centrale, A. bovis, and A. ovis for ruminants; A. platys for canines; and A. pagacytophilum for human and domestic animals such as horses. The infection is widespread and transmitted iatrogenically and mainly intrastadially by male ticks; the disease is called Human Granulocytic Anaplasmosis or Human Granulocytic Ehrlichiosis (HGE) in man. The etiologic agent of HGE A. phagocytophilum is transmitted by Am. americanum ticks in endemic areas (40). A. phagocytophilum was determined in farm animals (41, 42) and in humans (43, 44) in Turkey. Additionally, A. phagocytophilum was detected in Ixodes ricinus ticks isolated from humans (45). A few bovine anaplasmosis outbreaks were also reported in cattle from some areas (35, 46-49) and one A. platys infection was reported in a dog in Turkey (50). Ehrlichiosis is caused by A. phagocytophilum, Ehrlichia chaffeesis, and E. ewingii in humans and is called Human Monocytotropic Ehrlichiosis and by A. phagocytophilum and E. canis in dogs and is called Canine Monocytotropic Ehrlichiosis (CME). The diseases are transmitted by ixodid ticks and are of public health and veterinary importance (38). In Turkey, the studies on CME are very limited but few reports have documented seropositivity (51), clinical cases, treatment (52), and molecular prevalence (53, 54). Typhus (Epidemic Typhus) is an arthropod-transmitted infection in humans and animals caused by Rickettsia prowazekii. At least two strains of the agent can be distinguished by genetic analysis. One strain is found only in humans worldwide, while the other also occurs in flying squirrels (Glaucomys sabrinus and G. volans) in the USA (55). The primary vector of person-to-person transmission is the human body louse (Pediculus humanus corporis). Lice are infected when they feed on the blood of infected patients and excrete R. prowazekii in the feces as they feed on a new host. Transmission occurs when organisms in the louse feces are rubbed into the bite wound or other breaks in the skin (55). The rickettsia is also infectious by inhalation or contact with the mucous membranes of the mouth and eyes. In most parts of the world, humans are the only reservoir host for R. prowazekii. Infections can become latent and later recrudesce; humans with recrudescent typhus are capable of infecting lice and spreading the disease (56). It was reported that typhus epidemics were seen in Erzurum and nearby cities during the years of World War I in Turkey (57). Tick-borne Typhus is one of the oldest rickettsial diseases also called Boutonneuse fever or Mediterranean Spotted Fever (MSF). In Turkey, several cases of MSF associated with R. conorii have been reported in humans (58-63). Recently, R. hoogstraali and two human pathogenic species (R. aeschlimannii and R. slovaca) were detected in ixodid ticks in Turkey (64, 65). In addition, in the Thrace region of Turkey, R. conorii was also isolated from the skin lesions in three of 10 patients with MSF and was identified molecularly in the biopsy materials from 9 of 10 patients (66); Rickettsia spp. were found positive in the pools of ticks collected from tortoises (67). Rickettsialpox is a mite-transmitted bacterial zoonotic disease. The causative agent is Rickettsia akari, a member of the spotted-fever group of rickettsiae. The disease causes mild, self-limited, febrile illness characterized by eschar formation at the mite bite site, followed by the onset of systemic symptoms and a more generalized papulovesicular rash. The pathogen is originally found in mice (usually the house mouse), and humans may be infected by the bite of an infected mite, Liponyssoides sanguineus (68). In Turkey, a clinical rickettsialpox case has been described in a 9-year-old boy from the Nevsehir province (69). Murine typhus is a zoonotic infection in rats, cats, and humans caused by Rickettsia typhi and occurs worldwide. Recently, the infection is also described as a disease of travelers (70). The causal agent may be transmitted to humans by the bite of infected rodent fleas (Xenopsylla cheopis) and possibly cat fleas (Ctenocephalides felis). Two clinical cases of endemic or murine typhus were also reported in Istanbul, Turkey (71). Wolbachia endobacteria are the most widespread intracellular endosymbiont of arthropods and nematodes. Their interactions with their hosts are often mutualistic rather than parasitic (72). Recently, the prevalence of Wolbachia endobacteria were determined via molecular techniques in the mosquito populations in Turkey (73, 74) and in the chewing lice species collected from the Angora goats (75). Candidatus Rickettsia vini is a newly named rickettsial bacterium belonging to the spotted-fever group that has been molecularly detected in Ixodes arboricola ticks (76). In Turkey, Candidatus R. vini was detected in I. arboricola ticks collected from birds in the Kizilirmak Delta (77). Lyme Disease (LD), the most common tick-borne zoonotic infection with clinical significance of humans and domesticated animals in the northern temperate zone, was first described in the USA in the late 1970s, and the causal agent was described as a tick-borne spirochete Borrellia burgdorferi in 1982. The environmental risk of LD is measured by the density of infected questing ticks and more specifically by the density of infected nymphs of genus Ixodes, as nymphs appear to be the most important epidemiological stage (39). In Turkey, Lyme borreliosis is also one of the most important tick-borne zoonotic disease, and its causal agent Bor. burgdorferi was isolated from I. ricinus ticks collected from cattle in the Black Sea region in 1998 (78). The spirochetes of Borrelia were present in an unfed tick nymph (79). Meanwhile, some Bor. burgdorferi sensu lato strains were characterized molecularly (80), and a novel Borrelia sp. was also isolated from H. aegyptium ticks collected from tortoises (Testudo graeca) (81), and the spirochete was named as Bor. turcica sp. nov (82). A clinical Lyme case was observed in a dog in 2007 (83), and antiBor. burgdorferi antibodies were also detected in dogs and horses in Turkey (84). In contrast, a few reports on LD cases in humans have been documented in some parts of Turkey (85-88). The seropositivity rate was reported as 17% in the patients with a history of tick bite in Central Anatolia (89). However, a serological study showed that the seropositivity rate for LD was found to be 10% in 50 patients having symptoms compatible with LD at the Erciyes University Hospital in the Kayseri province (90). In the Marmara region, three LD cases have been confirmed serologically and by in vitro cultivation with two of the three cases detected in the residents of Istanbul, while the third was described in a tourist from the USA (88). Meanwhile, Bor. burgdorferi was also isolated from questing I. ricinus ticks sampled by flagging from parks and rural areas in the Thrace region of Turkey (44). In the same region of Turkey, another similar field study was performed on ticks, which were collected from tortoise and Rickettsia spp., and Bor. burgdorferi s.l. were molecularly detected in the tick pools (67). Meanwhile, another study was conducted to investigate the presence of Bor. burgdorferi in tick samples collected from humans, domestic and wild animals, and the ground as unfed (questing) in 12 different provinces, including Agri and Erzurum in Eastern Anatolia; Ankara, Cankiri, Yozgat, and Kirsehir in Central Anatolia; Artvin, Giresun, and Corum in the Black Sea Coast; Kocaeli and Bolu in Marmara; and Mardin in Southeastern Anatolia regions of Turkey. Bor. burgdorferi sensu stricto was also isolated from unusual tick species, such as H. marginatum, H. excavatum, Hae. parva, and nymphs of Hyalomma spp. (64). Epidemiologically, these results reveal that Turkey has a high-risk potential for zoonotic LD.

Tick-borne Relapsing Fever (TBRF) Can be either louse-borne (LBRF) or tick-borne (TBRF). LBRF is caused by a human-restricted pathogen, spirochete Borrelia recurrentis, and transmitted by the body louse Pediculus humanus, while TBRF is caused by Borrelia spp. and is associated with the bite or coxal fluid of argasid ticks of the genus Ornithodoros in a wider endemic geographic area of the world, spanning Africa, Asia, Europe, Eurasia, and the Americas with different Borrelia tick vector complexes implicated in the transmission in each area (39, 91, 92). In Turkey, the presence of relapsing fever with a spirochete of the Crocidurae group Bor. crocidurae was shown in Ornithodoros erraticus ticks collected from rodent holes in the southeastern areas near the Syria border (93). During the Balkan War and the First World War, some outbreaks were noted among the Ottoman and Turkish army (94). Tularemia is an important arthropod-transmitted zoonotic bacterial infection caused by the Francesilla tularensis and comprises a range of clinical syndromes ranging from mild to very severe intensity. The majority of cases occur in the northern hemisphere, particularly in the rural or semirural environments (39). In Turkey, tularemia is also an important disease, which has reemerged in 1988, and the first outbreak was recorded in 2005. Almost all cases were recorded as oropharyngeal tularemia due to the ingestion of contaminated food or water (95). The first case associated with the outbreak was diagnosed near Kayseri in 2009 in Central Anatolia, and the region was described as an endemic area for tularemia (96), but no positivity was detected using molecular techniques in the pools of mosquitoes and ticks collected near the Kayseri area (18). Bartonellosis or Cat Scrath Disease is another zoonotic vector-borne infection of humans and animals that is caused by an excluded rickettsilaes bacteria Bartonella spp. The causal agents Bar. bacilliformis and Bar. quintana are transmitted by sand flies (Lutzomyia spp) and by the human body louse, respectively, while the other agent Bar. henselae is commonly transmitted to humans through the bite or saliva-contaminated scratch of cats that are the natural reservoirs for the bacteria (97). Bar. henselae has a large distribution in the northern hemisphere (98). Domestic cats represent the main reservoir of the pathogen, and the main vector of the infection is the cat flea (99). However, the trans-stadial transmission of Bar. henselae by I. ricinus ticks was also shown (100). In Turkey, a case of bartonellosis in a domestic cat was reported (101). However, the seropositivity rates of Bar. henselae were 18.6% in cats (101), 6% in human blood donors (102), and 16.9% in kidney transplant patients (103) and 22.2% in cattle breeders and veterinarians (104), while the seroprevalence of Bar. vinsonii subsp. berkhoffii was recorded as 6.6% in dogs (105) in Turkey. In addition, the seropositivity rates of Bar. henselae in domestic cats varied in distinct provinces, such as Bursa, Adana, Aydin Burdur, Kayseri, and Istanbul, where they were 41.3%, 33.9%, 27.5%, 32.3%, 7.9%, and 12.5%, respectively; the average seropositivity of Bar. heselae in cats was found to be 27.9% in Turkey (106). Hemoplasmosis is one of the bacterial infections of humans and animals caused by the Mycoplasma spp. (107). Although the infection is mainly described as vector-borne and transmitted by blood-feeding arthropods, such as ticks and fleas, the disease might also be transmitted through other routes, such as mechanically with contaminated operation tools or blood transfusions and vertically in the intrauterine period (108). Rhipicephalus appendiculatus transmits the infection to dogs by co-feeding (109). In Turkey, a clinical case of feline hemoplasmosis associated M. haemofelis was reported (110). Q fever is caused by an excluded rickettsiales bacterium Coxiella burnetii. A number of hard and soft tick species, including Amblyomma, Dermacentor, Haemaphysalis, Hyalomma, Rhipicephalus, and Ornithodoros, have been documented to harbor the C. burnetii (111-113). Recent studies have shown that ticks harbor Coxiella-like bacteria, which are potentially tick-specific endosymbionts. For instance, Coxiella-like bacteria and possibly C. burnetii have been detected in the tick species Haemaphysalis bispinosa, Hae. hystricis, Dermacentor compactus, Der. steini, and Amblyomma sp., which were collected from wildlife and domesticated goats in different locations of Malaysia (114). Q fever is also an endemic and zoonotic infectious disease of humans and animals in Turkey. It was reported that cows, sheep, goats, and dogs might serve as reservoirs of C. burnetii, and Ornithodorus lahorensis ticks also harbor the agent; the disease is disseminated throughout Turkey, although the epidemics among humans are relatively rare (115). Recently, IgG seropositivity of C. burnetti in women with an abortion history and in women with healthy births in the central Black Sea region of Turkey was reported as 15.6% and 11.1%, respectively, (116). Plague or Black Death is another zoonotic bacterial disease transmitted from rodent to rodent and from rodent to man via flea bites. Humans can also be infected by direct contact with infected animal tissues. Pneumonic plague may result from direct human-to-human transmission. The causative agent of the disease is the bacterium Yersinia pestis. Urban plague describes the situation where plague circulates among wild rodents. The infection is maintained in the rat population by fleas, such as Xenopsylla cheopis (Asia, Africa, Europe, and the Americas), X. astia (southeast Asia), and X. brasiliensis (Africa, India, and South America). Rarely, plague is spread directly from person to person by fleas, such as Xenopsylla species and the so-called human flea Pulex irritans (117). The first recorded appearance of the plague in Europe was at Messina, Sicily, in the Middle Ages (October 1347). It is thought that it arrived on trading ships that likely came from the Black Sea, past Istanbul and through the Mediterranean. It is estimated that a quarter of the people living in Europe were killed from the Black Death at that time. Within the last decade, human plague cases have been reported from countries in Africa, America, and Asia. Between 1990 and 1996, there were 16,005 cases of plague and 1214 deaths (7.6%) reported to the WHO (117). It is noted that the last plague outbreak involving 32 human cases in Turkey was recorded in 1947 in Akcakale, a town located on the Turkish-Syrian border (15). There is no official record of plague in Turkey since then. Anthrax is an infection of humans and other mammals caused by the bacterium Bacillus anthracis, a Tier 1 biologic agent. Anthrax spores persist for a long time under changing environmental conditions and can be easily found in nature; they can also be produced in the laboratory. Although the vast majority of human cases are related to direct contact with infected carcasses or to handling of contaminated products from morbid animals, the transmission of the disease has been demonstrated by a wide variety of tabanid and mosquito species and with stable flies (Stomoxys spp) (118). The disease has wide distribution in the world and is also an endemic zoonosis in Turkey. A total of 967 (464 from animals and 503 from humans) anthrax cases were reported from Eastern Turkey between 1992 and 2004 (119). In contrast, a total of 26,954 human anthrax cases were recorded by the Turkish Ministry of Health between 1960 and 2005, with 6861 cases reported between 1990 and 2005 (120). Although the incidence rate of anthrax in humans is decreasing (≤150 cases per year between 2011 and 2016) in Turkey, regional outbreaks still present a risk to human and animal health. The prominent clinical form recorded is cutaneous anthrax (120, 121). Recently, in April 2017, two pumas died at the Kayseri Zoo Park, and the etiologic agent was identified as B. anthracis by laboratory examination. The source of the infection was considered consumption of a carcass of cattle that had died of unknown reasons (personal communication with Professor M Doganay). Brucellosis is a zoonotic infection with significant health and economic problems worldwide. The causal agents of the infection are Brucella abortus, B. melitensis, B. ovis, B. suis, and B. canis. The disease is mainly food-borne and is transmitted to humans through the consumption of unpasteurized/raw dairy products and rarely by eating undercooked meat. In addition, the bacteria may also enter the body by inhalation or by contact. In Turkey, brucellosis is a known disease since the First World War and its incidence has been increasing over the years. In 1999, 11,462 cases were notified to the Ministry of Health, with the incidence rate being 17.41/100,000. In the last decade, the annual recorded cases in human have been decreasing below 6,000. Predominant etiological agent is also B. melitensis (122). Although several control and eradication measures have been applied, brucellosis remains an endemic disease in many regions and leads to a large economic loss in cattle and in small ruminants with serious public health problems (23, 123). The prevalence of brucellosis was shown to be 32.9% in tested animals (124). Campylobacteriosis is a common food-borne zoonotic infection of humans with gastroenteritis. The causal agent of the disease is most commonly Campylobacter jejuni. The agent is transmitted to humans by ingestion of contaminated food (usually unpasteurized/raw milk and undercooked poultry) and drinking of contaminated water (water-borne). The infection is also transmitted by contact with contaminated poultry, livestock, or household pets, particularly puppies (125). Meanwhile, animals farmed for meat are the major source of campylobacter enteritis. In Turkey, campylobacter gastroenteritis has been reported as a more common disease in children (126). Clostridial diseases are caused by many clostridial bacteria both in humans and domestic animals, but these pathogens are seldom considered zoonotic agents. Clostridium botulinum and C. tetani lead neurotoxicoses in humans and domestic and wild animals, but there is no evidence for transmission among the species. C. septicum causes malignant edema in domestic animals and humans, and the signs and the lesions of infection are generally the same in both; however, there is no evidence for direct transmission between animals and humans. However, it was suggested that indirect transmission of entrotoxigenic C. peringes type C and C. difficile is possible via foods (i.e., in retail meats) (127). In Turkey, limited C. difficile infection cases have been reported in the patients with antibiotic-associated bloody diarrhea in some provinces such as Kayseri (128), Bursa (129), and Istanbul (130). Tetanus is also another clostridial disease characterized with muscle rigidity and spasms. The agent of infection is Clostridium tetani, which is generally found in soil, dust, and manure. The pathogens usually enter through a break in the skin, such as a cut or puncture wound by a dirty contaminated object. Tetanus in neonates is primarily related to insufficient sanitation and lack of hygiene. Neonatal tetanus is actually preventable by immunization in many developing countries, and it has already been eliminated in most of the developed countries. In Turkey, the incidence of tetanus cases in humans has been reduced by improving hygiene conditions and implementation of tetanus vaccine in the last decades (131, 132). Enterohemorrhagic Escherichia coli (EHEC) infection is an important coliform water-borne zoonotic disease seen worldwide. Cattle are important reservoirs of Shiga-like toxin-producing Escherichia coli (SLTEC) O157:H7 EHEC, which causes hemorrhagic colitis and hemolytic uremic syndrome in humans. The infected cattle can shed low levels of E. coli O157:H7 for a long term. The most important EHEC reservoir cattle can also carry unusual EHEC strains, such as EHEC O104:H4. Humans acquire EHEC by direct contact with carrier cattle or sheep, their feces, infected people, and contaminated soil or water or via the ingestion of undercooked meat, other animal products, contaminated vegetables and fruit, and other foods (133). In Turkey, limited data are available regarding EHEC O157 in humans and animals. Although the incidence of E. coli O157:H7 has been reported as varying up to 40% in gastroenteritisassociated children (134, 135), verocytotoxin producing E. coli O157 was molecularly detected in only one case (136). In contrast, verocytotoxin producing E. coli O157 was also isolated from clinically healthy cattle samples in the Hatay province of the Mediterranean region (137) and in the carcasses of cattle and abattoir environment in Istanbul in the Marmara area (138). Erysipeloid is a rare skin bacterial infection of humans caused by Erysipelothrix rhusiopathiae and Ery. tonsillaru and occurs more commonly in individuals, who handle fish and raw meat. The disease has economic importance for farmed animals, including swine, turkeys, chickens, and sheep. People acquire the disease through contact with infected animals (particularly pigs), fish, or birds. The pathogen enters the body through existing skin wounds, such as cuts, scratches, punctures, or splinters. The infection does not spread from person to person (139). In Turkey, a few rare cases of erysipeloid in humans were reported (140, 141). Glanders or Malleus is one of the oldest known, highly contagious and re-emerging infections and often causes fatal zoonotic disease in equids, such as horses, mules, and donkeys. These solidungulate animals serve as a natural reservoir role for the pathogen. The causal agent of the disease is Burkholderia mallei (formerly Pseudomonas mallei). It was reported that this bacterium has been listed as a potential agent for biological warfare and bioterrorism under Center of Diseases Controlcategory B (142). The pathogen organism is transmitted to the animals either directly or indirectly from secretions and excretions of infected animals. The infection occurs subclinically in horses, and the agent organisms are found in the lesions and discharges of the skin and nasal mucosa. Thus, chronic infected horses can serve a carrier role for the epidemiology of the disease. Mules and donkeys are acutely infected animals, and the organisms are excreted in feces, urine, saliva, and tears. The major mode of transmission among solipeds is the respiratory route and ingestion of feed and water contaminated by nasal discharge, or sputum of sick animals, or direct contact with fomites. Glanders has been eradicated from many countries by statutory testing, elimination of infected animals, and import restrictions. However, it persists in some Asian, African, and South American countries. The infection should be considered a re-emerging disease and may be imported by pet or racing equids into glanders-free areas (143). The transmission of B. mallei from infected equines to humans is uncommon, and the person-to-person transmission is also rare. The main routes of zoonotic transmission of B. mallei in humans involve direct invasion of a cut, abrasion, or laceration of the skin and; inhalation; and by attack to mucous membranes (144). The first zoonotic human case was reported in a French veterinarian in 1793 (142), and recently, a clinical glanders case was determined in a microbiologist at the U.S. Army in 2000 (145). Professionals who are in close contact with sick horse, such as veterinarians, farmers, horse traders/fanciers, laboratory workers, and other workers in slaughterhouses and horse stable and soldiers are at occupational exposure to glanders. In Turkey, glanders is one of the compulsory notifiable diseases. To control and eradicate glanders, a national project was conducted by the Ministry of Agriculture between 2000 and 2001. In the project scope, a total of 235,286 equines were screened for glanders, and 3509 were found positive. All of the positives were culled as compensation. The economic impact of the disease was devastating for Turkey. In same period, no clinical cases of glanders were observed in tested horses and mules, while only one glanders case was reported from a donkey with clinical sings. In recent years, approximately 10,000 pedigree horse sera were tested using the complement fixation test (CFT) and all of the tested sera were found negative for glanders (146). It was reported that the history of human cases of glanders goes back to 1890s when some army and civil veterinarians became sick during the struggle programs against glanders between 1901 and 1934 and died of the disease (147). In the following decades, limited human cases of glanders were also reported from some parts of Turkey (148-150).