Le infezioni nella Storia della Medicina

Infections in the History of Medicine

Demystifying the epidemic among Achaeans during the Trojan War

Demistificazione dell'epidemia tra gli Achei durante la guerra di Troia

Gregory Tsoucalas, Konstantinos Laios, Marianna Karamanou, George Androutsos
History of Medicine Department, University of Athens, Greece

INTRODUCTION

Greek classical literature contains numerous references to plagues and pestilences. During the Trojan War, in the Achaeans camp, burst a deadly pestilence. Homer in his epic poem gave no symptoms at all. He had only stated that mules and dogs died and men followed.
The disease therefore could not have been malaria, bubonic plague or typhus, as man is susceptible to all three but equines and dogs are not equally susceptible. Various infectious diseases could cause an epidemic both in human and animal populations.
Our quest to determine the best candidate includes Hendra virus, Nipah virus, anthrax, Bornaviruses, brucellosis, West Nile virus, Burkholderia bacteria, Japanese encephalitis virus, leptospirosis, rabies, tetanus, salmonellosis, vesicular stomatitis, Influenza A virus strains, and Alphaviruses strains.
Transmission between species and individuals occurs mainly via mosquitoes, and sometimes from soil, air, plantation, rats, bats, dead animal's excretions and fluids, due to broken skin barrier, poor hygiene, compromised immune system, contaminated water sources. However, in ancient world it was believed that gods' wrath triggered infections.

Corresponding author
Ioannis Tsoucalas
E-mail: gregorytsoucalas@yahoo.gr

SMINTHIAN APOLLO, THE GOD OF PESTILENCES

The Delphic Apollo sided with Lacedemonians (Spartans) during the Peloponnesian War [1]. During the siege of Troy Apollo was invoked as Smintheus by his priest, Chryses. Two times has been invoked and on both occasions a pestilence ensued [2].
Most plagues in the past had as entry gates the harbors and as vectors the rats. Ships carrying infected rodents disseminated the bubonic plague and other infectious diseases which usually originated in ports. All Sminthia (temples dedicated to the Mouse god Apollo) mentioned by Homer and Strabo were on the islands or coast [3]. Sminthia most probably were strategically placed at ports, so that the worshippers could plea the god for protection against the plagues brought to them by ships. The god who controls the rodents can inflict not only a pestilence, but starvation and defeat in battle as well. There was a time when Aeolians and Trojans were threatened by starvation as mice were eating their crops. During that time a prophecy was asked by the temple at Delphi. The answer was a sacrifice to Apollo Smintheus, who thereupon reduced the mouse population [4]. There can be little doubt therefore that Apollo Smintheus was the god of all severe pestilences [2, 5].

THE TROJAN EPIDEMIC

In the epidemic during the siege of Troy rodents played no part at all. The arrows

launched by the hand of the god Apollo Smintheus were the direct transmitter of the infectious disease. Equines and dogs were the first victims, while humans died with an interval [6]. In modern medicine, mosquitoes are playing the most vital part during a virus epidemic, being the main vector and infecting the bitten organisms. The sound of the thrown arrows is rather similar to the terrifying sound made by thousands bloodthirsty mosquitoes attacking their victims to achieve their reproduction. Homer describes this sound as "twang" (Greek: κλαγγή), produced by vibration. Could it be mosquitoes wings? It is certain that arrows sound not as vibrating objects, and Homer could have used here a metaphor to give emphasis to the power of the gods. The word "κλαγγή" for the arrows was used by Homer only before an outbreak of pestilence; on the contrary, when Apollo's arrows were used for other lethal purposes no emphasis was placed on the sound. It is intriguing the fact that mosquitoes were only recognized as virus transmitters during the nineteenth century, thus Homer instead of writing of an unexplained mosquito attack, could have imagined and put to paper the divine intervention. The word "εχεπευκές" used by Homer means "stinging", a rather unusual quality for an arrow [2, 6].

The origin of the thousands of the mosquitoes could be explained firstly by the position where Greeks settled their camp, in the sores of the Scamander river [7]. Secondly, close to the camp, 700 meters from the conjunction between Scamander and Simois River, a plethora of swamps could be found, as shown in the map of the Heinrich Schliemann's book, the archeologist who discovered Troy [8]. Thirdly, all camp's and Troy's waste and sewage system could be calculated as breeding places for any species of mosquitoes. All the ingredients, water, swamps, bad hygiene, mosquitoes, were present, capable to cause an epidemic.

Since the simultaneous death of humans and animals could have given a more devastating impression, the interval must have had an impact. Homer included mules and dogs not just to emphasize the severity and terror of the epidemic, but also when noting the interval he accomplished to give a more detailed description. Questing the deadly virus responsible for the epidemic among the Achaeans, a thorough research among zoonotic diseases which can be transmitted to humans, equines and dogs, could probably reveal the mystery virus.

THE QUEST FOR THE MATCHING VIRUS

Hendra virus has so far only been recognized in horses and humans. However, there is potential for other species to be infected [9]. Recently Hendra virus was identified in dogs [10]. Flying foxes and fruit bats develop a viraemia then excrete the virus in their urine, faeces and saliva for approximately one week. Hendra causes a severe respiratory illness in horses which is very frequently fatal. The human infections are caused due to direct exposure to tissues and secretions from infected horses. Symptoms of Hendra virus infection of humans may be respiratory, including haemorrhage and oedema of the lungs, or encephalitic, resulting in meningitis. In horses, infection usually causes pulmonary oedema, congestion and/or neurological signs [9]. The incubation period of 9-16 days makes the virus potential rather impossible for Hendra to have been the fatal infection among the Acheans in Troy.

Nipah virus, also a member of the family Paramyxoviridae, is related but not identical to Hendra virus. The disease presented mainly as acute encephalitis with usually a short incubation period of some days to less than two weeks, with symptoms of fever, headache, and giddiness followed by seizures, and inability to maintain breathing, coma and eventually death. Distinctive clinical signs include areflexia, hypotonia, hypertension, tachycardia and segmental myoclonus. These signs and symptoms can progress to coma within 24 to 48 hours. Nipah virus is being transmitted to humans, cats, and dogs through close contact with infected pigs and bats or by the consume of the contaminated fruits [11-12]. Nipah virus could kill equines, humans and dogs, and has a short incubation period. It represents a potentially deadly agent for the epidemic that killed the Greeks.

Anthrax is a zoonotic disease caused by *Bacillus anthracis*. It is an acute infectious disease that commonly occurs in wild and domestic lower vertebrates such as cattle, sheep, goats, horses, camels, antelopes, and other herbivores [13]. Dogs are generally at low risk of developing disease following exposure to anthrax. When disease does occur, it appears associated with oral exposure to the bacteria leading to massive swelling of the head, neck, and mediastinal regions. Death is due to toxemia and shock. Almost in the same way die the horses too [14]. It is potentially fatal and highly contagious dis-

ease. Herbivores are the natural host. Human acquire the disease incidentally by contact with infected animal or animal products. Respiratory infection in humans initially presents with cold or flu-like symptoms for several days, followed by severe and often fatal respiratory collapse. Gastrointestinal infection in humans is most often caused by consuming anthrax-infected meat and is characterized by serious gastrointestinal difficulty, vomiting of blood, severe diarrhoea, acute inflammation of the intestinal tract, and loss of appetite. Cutaneous anthrax infection in humans shows up as a boil-like skin lesion that eventually forms an ulcer with a black center [13]. With an incubation period of 2.5 to 10.3 days, anthrax is among the killer candidates of the epidemic in Troy [15].

Bornaviruses belong to the order of Mononegavirales and are characterized by highly neurotropic and noncytopathic infections combined with high mortality. Borna disease virus, the prototype of the Bornaviridae family, infects a wide variety of mammalian species and causes a meningoencephalitis in naturally infected horses and sheep [16]. According to current knowledge, Bornaviruses also infect several other species, including humans at least occasionally. The epidemiology of Bornaviruses is largely unknown, but accumulating evidence indicates vectors and reservoirs among small wild mammals [17]. Rarely dogs can be infected as well [18]. The incubation period, which lasts a few weeks to several months, as well as the rarity of dog's infection, excludes Bornaviruses from our search for the fatal factor [19].

Brucellosis remains as a widespread zoonosis, with the potential to create disease in humans and animals. Domestic livestock goats, sheep, and cattle could be infected, as well as equine, dogs and humans. The symptoms are like those associated with many other febrile diseases, but with emphasis on muscular pain and sweating. The focalizations of brucellosis usually occur in bones and joints and spondylodiscitis of lumbar spine accompanied by sacroiliitis is very characteristic of this disease.

Orchitis is also frequent in men [20]. Mortality rate due to brucellosis is low, mostly secondary to endocarditis and central nerve involvement of disease [21]. Low mortality and incubation period of 2 to 4 weeks, eliminate brucellosis as the main infection factor that killed Acheans [22].

West Nile fever is an important zoonotic infection caused by West Nile virus, a member of the Flaviviridae. Human and equine West Nile Virus infections, occurring concurrently, could be manifested as central nervous system infections. The specific neurological diseases which may occur are West Nile encephalitis, West Nile meningitis, and West Nile poliomyelitis which may cause acute flaccid paralysis [23]. The same infection occurs in horses and rarely in dogs [24, 25]. The incubation period is typically between 2 and 15 days and the significant mortality rate combined with the rarity of dogs infection (4,6%) make the West Nile virus an average candidate for the epidemic in Troy.

Members of the genus Burkholderia can form associations with plants and are also able to cause disease in animals and humans. Equines, dogs, goats, cats, mice and pigs could be affected as well as humans [26]. Although most of the species in the genus Burkholderia are not pathogenic for healthy individuals, a few that include *B. pseudomallei*, *B. mallei,* and *B. cepacia*, are capable of causing severe, life-threatening infections in both normal and immunocompromised individuals. The mortality rate is high up to 95%. Melioidosis, caused by these members, presents as a broad range of conditions from acute fulminant pneumonia and septicemia acquired by inhalation to wound infections acquired through inoculation of the bacteria from soil through skin abrasion. Regardless of therapy, rapid progress of acute melioidosis to sepsis, followed by death within 48 h of clinical onset has been reported. The disease is named "Glanders" and is one of the oldest known equine diseases of horses, mules and donkeys. It can be spread from horses to humans [27]. Mules are more sensitive to Glanders, with high rate of mortality, but usually the disease lasts up to years. Therefore, since the incubation period of the reactivation can vary from weeks to many years, these bacteria should be excluded as a possibility to cause the epidemic [26].

Japanese encephalitis virus, a mosquito-borne zoonotic pathogen, is capable of causing serious infection of the central nervous system of humans [28]. Swine are very susceptible to the infection and are also amplifiers of the virus. Less frequently, horses become infected with the disease, and rather rarely dogs [29]. Mortality rate is up to 20 to 30%, the incubation period is of 5 to 15 days [30] and virus' potential to much our criteria is null.

Leptospirosis is a disease that affects humans and many animal species. Outbreaks usually result from exposure to water contaminated

with the urine of infected animals. Rats are the major reservoirs of leptospirosis. Organisms have been found in cattle, pigs, horses, dogs, rodents and wildlife. Animal's mortality is around 5% [31]. Approximately 10% of patients with leptospirosis develop severe disease, the Weil' syndrome, with ictericia, acute kidney injury and pulmonary hemorrhage, with high mortality. The duration of the incubation period is 5 to 10 days [32]. The low mortality rates in both human and animals along with the long incubation period exclude Leptospirosis too.

Rabies is a viral disease that causes acute encephalitis in warm-blooded animals. The disease is zoonotic, meaning it can be transmitted from one species to another, such as from dogs to humans, or from dogs to rats or the opposite, commonly by a bite from an infected animal [33]. The incubation period among equines is 6 weeks, the exposure is only 5% among their populations and the symptoms usually progress quickly over five to seven days resulting fatal [34]. The incubation period among humans is up to a few months, with fatal results if no treatment is administered [33]. The extensive incubation period and the absence in Homer's narration for animal bites, which could give a more epic conclusion, makes rabies a non-candidate for the epidemic.

Tetanus, caused by the anaerobic bacterium *Clostridium tetani*, is an uncommon but often fatal disease that affects the central nervous system. The bacteria gain entry to the body through a wound or cut exposed to contaminated soil, dust, or manure. The spores are widely distributed in the intestines and feces of many non-human animals such as horses, sheep, cattle, dogs, cats, rats, guinea pigs, and chickens. Horses and humans are the most susceptible of all the animal species to tetanus. The development of dyspnoea, recumbency, and their combination with dysphagia, could be observed significantly in horses and mules within 2 days [35]. Tetanus among human has an incubation period mainly from 8 hours to 8 minus/or plus 3 days [36]. These two periods combined could place tetanus as a weak candidate, as it is rather impossible that all mules, dogs and humans were wounded and contaminated at the same time. It is also a certainty that Homer knowing about the severe and characteristic symptomatology of the virus, should have written some details to emphasise the facts. On the other hand, the long time fighting, the daily battles and the pour hygiene after such days could inflict such an uncommon epidemic.

Salmonellosis disease is frequently associated with poultry. However, strains of salmonella can infect horses and they constitute a risk for humans [37]. Dogs could also be affected [38]. Most outbreaks are foodborne and among immunocompromised adults after the long siege of Troy the mortality could be high [39]. The incubation period among humans is 8 to 72 hours and among equines 2 to 5 days, a fact that eliminates salmonella as the epidemic factor. The mortality among animals is about 20%. In the case of an acute equine infection, the symptoms appear within 6 to 24 hours [40]. This form of the disease gives some potential to Salmonella, strengthened by the fact that salmonella could contaminate water resources [41]. In that case all humans, equines, dogs and domestic animals could be simultaneously infected after drinking from the same water source with extremely high viremia. If all species infected followed the same disease pattern, death could have been occurred due to high fever, diarrhea and dehydration.

Vesicular stomatitis is another disease that is common to cattle, sheep, swine and horses as well as humans. Serological evidence of infection has been found in many other animals including deer, pronghorn antelope, bighorn sheep, bats, raccoons, opossums, lynx, bobcats, bears, coyotes, foxes, dogs, non-human primates, rabbits, rodents, turkeys and ducks. The clinical presentation of vesicular stomatitis resembles that of foot-and-mouth disease with vesicular lesions appearing on the mouth, tongue, teats and hooves [42]. Animals may show systemic signs such as anorexia, lethargy and pyrexia. Disease usually resolves within two weeks, and animals usually recover completely. Deaths from vesicular stomatitis are rare and usually due to secondary complications [43]. This infection is all bad fatal and so it should be excluded as well.

Equine influenza is the disease caused by strains of influenza A that are enzootic in horse species. Equine influenza is characterized by a very high rate of transmission among horses, and has a relatively short incubation time of one to five days [44]. The mortality rate is low [45]. Canine influenza virus is also caused by strains of influenza A [46]. The viruses can possibly cross the species barrier to cause an epizootic disease in humans. Human flu symptoms usually include fever, cough, sore throat,

muscle aches, conjunctivitis and, in severe cases, severe breathing problems and pneumonia that may be fatal, about 11% [47]. The mortality rates don't support Influenza Virus A strains to have been the main reason for the epidemic.
An Alphavirus belongs to the family of Togaviradae viruses. Members of this family are the Eastern Equine Encephalitis Virus, the Western Equine Encephalitis Virus and the Venezuelan equine encephalitis [48]. Alphaviruses provoke an acute viral disease that causes acute illness in equines and humans, with symptoms ranging from a mild, flu-like syndrome, myalgia, fatigue, vomiting, nausea, diarrhoea, pharyngitis, intracranial hypertension, and fever to encephalitis, brain, lung and gastrointestinal bleeding and death. The mortality among humans is 38%, with an incubation period ranging from 27.5 hours to four days, equine mortality begins from 35% and can reach 83% [49-52]. Other animals, such as cattle, swine, and dogs, can become infected. Such a virus who causes equines and human epidemics, and could also infect dogs, being hypothetically transmitted form mules with high levels of viremia, to human via mosquitoes, plantation where it might harbor enzootic foci with an incubation period of almost two days could present a perfect candidate for the epidemic that killed Acheans in the siege of Troy [53, 54].

CONCLUSION

SINCE Homer did not describe symptoms, it is impossible to determine the responsible virus for the epidemic among the Achaeans in Troy. Furthermore is rather difficult to confirm that present day viruses differ or not from the ancient ones. Mutations often occur in viruses changing their characteristics. Occasionally another insect vector can transmit them, adding species to a plethora of vectors. Some viruses present the potential to have been the cause for the epidemic; however the perfect candidate in our opinion should be the Alphaviruses family. The symptomatology, the mortality rates, the incubation period, plus the fact that is the only modern disease during which animals die first, give an ideal surrounding for Homer's narration to be completed.
Although Alphaviruses at the present are confirmed to the Western hemisphere, strains have been isolated in China, Russia, and Czech Republic [55-57]. Equine encephalitis is a relatively new virus and the fact that a virus can jump from equines to humans is even newer knowledge. It may or may not have been a disease of the ancient world. It could have been a progenitor of the known virus, it could have been a completely different, or unknown, or an extincted one. The only thing that is certain is the environment and surroundings during the siege. River strains of Scamander and Simois rivers, swamps in the territory of Troy, contaminated water strains from the drainage system of Troy, mosquitoes, bats from the mountain Ida, rats from the besieged city and the Greek camp, domestic animals, equines, dogs, poor hygiene, continuous rough battle, wounded men, crowding, are all possible causes for an epidemic to be burst. At the end only two lines remained to describe a significant event: equines and dogs died, men followed some days later.

Keywords: Homer, Trojan war, Achaeans, pestilence, Alphaviruses.

SUMMARY

Although some modern scholars believe that Homer had at least a basic medical education, given that a plethora of medical terms may be found in his poems, in the case of the pestilence that killed the Achaeans (one of the Hellenic peoples believed to have inhabited the Peloponnese) at Troy, his reference was simply informative. No symptoms were mentioned and the only thing known was that mules and dogs were the first to die. While Delphic Apollo was usually on the side of Peloponnesians, during the Trojan War Apollo Smintheus (the Mouse God) sided with the Trojans. Apollo was invoked as Smintheus by his priest Chryses two times and on both occasions a pestilence ensued.
In our paper we try to clarify whether this pestilence, as we believe, was caused by a member of the Alphavirus genus, which can inflict a serious epidemic both on human and animal species, especially in equines.

RIASSUNTO

Nonostante alcune moderne scuole di pensiero ritengano che Omero possedesse conoscenze mediche quanto meno basilari, considerata la numerosità di termini medici che ricorrono nei suoi poemi, nel caso della pestilenza che colpì gli Achei (uno dei popoli ellenici che si ritiene abitassero nel Peloponneso) a Troia, le sue fonti erano solo divulgative. Non viene citato nessun sintomo e l'unico elemento noto consiste nel fatto che primi a morire furono muli e cani. Generalmente, Apollo delfico era dalla parte dei lacedemoni ma, durante la guerra di Troia, Apollo Sminteo (il dio topo) stava dalla parte dei Troiani. Apollo venne invocato come Sminteo dal suo sacerdote Crise due volte e in entrambe le occasioni si verificò una pestilenza. Nel nostro articolo tenteremo di chiarire se a provocare quella pestilenza sia stato, come noi riteniamo, un membro del genere Alphavirus, in grado di infliggere una seria epidemia sia alla specie umana che a quella animale, e in particolare agli equini.

REFERENCES

[1] Thucidides. Historiae, ed. H.S. Jones and J.E. Powell, Thucydidis historiae, 2 vols. Oxford: Clarendon Press, 1.118, 1942. (Cod: 153,260: Hist.)

[2] Bernheim F., Zener A.A. The Sminthian Apollo and the epidemic among the Achaeans at Troy. *Transactions of the American Philological Association*. 108, 11-14, 1978.

[3] Farnell L.R. Cults of the Greek States IV. Clarendon Press, Oxford. 165, 1907.

[4] Aelian. De natura animalium, ed. R. Hercher, Claudii Aeliani de natura animalium libri xvii, varia historia, epistolae, fragmenta, vol. 1. Teubner, Leipzig. (repr. Graz: Akademische Druck- und Verlagsanstalt, 1971), 3-436, 1864. (Cod: 107,271: Nat. Hist., Paradox.)

[5] Krappe A.H. Apollon Smintheus and the Teutonic Mysing. *ARW* 33, 40, 1936.

[6] Ilias, ed. T.W. Allen, Homeri Ilias, vols. 2-3. Clarendon Press, Oxford. 1, 43-67, 1931. (Cod: 115,477: Epic.).

[7] Ilias, ed. T.W. Allen, Homeri Ilias, vols. 2-3. Clarendon Press, Oxford. 2, 1-356; 3, 1-370, 1931. (Cod: 115,477: Epic.).

[8] Schliemann H. Ilios. City and Country of the Trojans. Harper and Brothers, New York. 82, 1881.

[9] Hazelton B., Ba Alawi F., Kok J., Dwyer DE. Hendra virus: a one health tale of flying foxes, horses and humans. *Future Microbiol.* 8, 461-474, 2013.

[10] http:// news.discovery.com /animals /hendra-virus-dog-110726. htm. Last accessed April 13, 2013.

[11] Arif S.M., Basher A., Quddus M.R., Faiz M.A. Re-emergence Nipah - a review. *Mymensingh Med. J.* 21 (4), 772-779, 2012.

[12] Chua K.B., Goh K.J., Wong K.T., et al. Fatal encephalitis due to Nipah virus among pig-farmers in Malaysia. *Lancet* 354,1257-1259, 1999.

[13] Kamal S., Rashid A.M., Bakar M., Ahad M. Anthrax: an update. *Asian Pac. J. Trop. Biomed.* 1 (6), 496-501, 2011.

[14] Langston C. Postexposure management and treatment of anthrax in dogs-executive councils of the American Academy of Veterinary Pharmacology and Therapeutics and the American College of Veterinary Clinical Pharmacology. *AAPS J.* 7 (2), E272-E273, 2005.

[15] Wilkening D.A. Modeling the incubation period of inhalational anthrax. *Med. Decis. Making*. 28 (4), 593-605, 2008.

[16] Fujino K., Horie M., Honda T., et al. Evolutionarily conserved interaction between the phosphoproteins and X proteins of bornaviruses from different vertebrate species. *PLoS One*. 7 (12), e51161, 2012.

[17] Kinnunen P.M., Palva A., Vaheri A., Vapalahti O. Epidemiology and host spectrum of Borna disease virus infections. *J. Gen. Virol.* 94 (Pt 2), 247-262, 2013.

[18] Zhan Q.L., Zhang Y.Y., Xu M.M., et al. Epidemiological investigation on natural infection of different canine breeds with Borna disease virus in Ili, China. Zhonghua *Liu Xing Bing Xue Za Zhi* 30 (10), 993-997, 2009.

[19] Richt J.A., Rott R. Borna disease virus: a mystery as an emerging zoonotic pathogen. *Vet. J.* 161 (1), 24-40, 2001.

[20] Kursun E., Turunc T., Demiroglu Y., Arslan H. Evaluation of four hundred and forty seven brucellosis cases. *Intern. Med.* 52 (7), 745-750, 2013.

[21] Ulu-Kilic A., Metan G., Alp E. Clinical presentations and diagnosis of brucellosis. *Recent Pat. Antiinfect. Drug Discov.* 8 (1), 34-41, 2013.

[22] De Massis F., Di Girolamo A., Petrini A., Pizzigallo E., Giovannini A. Correlation between animal and human brucellosis in Italy during the period 1997-2002. *Clin. Microbiol. Infect.* 11 (8), 632-636, 2005.

[23] Ozkul A., Ergunay K., Koysuren A., et al. Concurrent occurrence of human and equine West Nile virus infections in Central Anatolia, Turkey: the first evidence for circulation of lineage 1 viruses. *Int. J. Infect. Dis.* 17 (7), e546-e551, 2013.

[24] Ibarra-Juarez L., Eisen L., Bolling B.G., et al. Detection of West Nile virus-specific antibodies and nucleic acid in horses and mosquitoes, respectively, in Nuevo Leon State, northern Mexico, 2006-2007. *Med. Vet. Entomol.* 26 (3), 351-354, 2012.

[25] Lan D., Ji W., Yu D., et al. Serological evidence of West Nile virus in dogs and cats in China. *Arch. Virol.* 156 (5), 893-895, 2011.

[26] Chin J. In Control of Communicable Diseases Manual (17th Edition) 2000. American Public Health Association, Washington D.C.
[27] Choh L.C, et al. Burkholderia vaccines: are we moving forward? *Front. Cell. Infect. Microbiol.* 3, 5, 2013. doi: 10.3389/fcimb.2013.00005, 2013.
[28] Hu Q., et al. Recurrence of Japanese Encephalitis Epidemic in Wuhan, China, 2009-2010. PLoS One. 8, 1, e52687, 2013. doi: 10.1371/journal.pone.0052687.
[29] Shimoda H., Ohno Y., Mochizuki M., Iwata H, Okuda M., Maeda K. Dogs as Sentinels for Human Infection with Japanese Encephalitis Virus. *Emerg. Infect. Dis.* 16, 7, 2010.
[30] Partridge J., Ghimire P., Sedai T., Bista M.B., Banerjee M. Endemic Japanese encephalitis in the Kathmandu valley, Nepal. *Am. J. Trop. Med. Hyg.* 77 (6), 1146-1149, 2007.
[31] Roqueplo C., Cabre O., Davoust B., Kodjo A. Epidemiological study of animal leptospirosis in New Caledonia. *Vet. Med. Int.* 826834, 2013. doi: 10.1155/2013/826834
[32] Seguro A.C., Andrade L. Pathophysiology of Leptospirosis. *Shock*. 39, Suppl. 1, 17-23, 2013.
[33] Tenzin T., Ward M.P. Review of rabies epidemiology and control in South, South East and East Asia: past, present and prospects for elimination. *Zoonoses Public Health* 59, 7, 451-467, 2012.
[34] Retrieved from http://www.uky.edu/Ag/AnimalSciences/pubs/asc125.pdf. Last accessed April 13, 2013.
[35] Van Galen G., Delguste C., Sandersen C., Verwilghen D., Grulke S., Amory H. Tetanus in the equine species: a retrospective study of 31 cases. *Tijdschr. Diergeneeskd.* 133, 12, 512-517, 2008.
[36] Weng W.C., et al. Clinical characteristics of adult tetanus in a Taiwan medical center. *J. Formos Med. Assoc.* 110, 11, 705-710, 2011.
[37] Jay-Russell M.T., Madigan J.E., Bengson Y., et al. Salmonella Oranienburg isolated from horses, wild turkeys and an edible home garden fertilized with raw horse manure. *Zoonoses Public Health*. 61 (1), 64-71, 2014.
[38] Tupler T., Levy J.K., Sabshin S.J., Tucker S.J., Greiner E.C., Leutenegger C.M. Enteropathogens identified in dogs entering a Florida animal shelter with normal feces or diarrhea. *J. Am. Vet. Med. Assoc.* 241 (3), 338-343, 2012.
[39] Gordon M.A. Salmonella infections in immunocompromised adults. *J. Infect.* 56 (6), 413-422, 2008.
[40] http://www.nj.gov/agriculture/divisions/ah/diseases/nontyphoidal salmonellosis.html. Last accessed April 13, 2004.
[41] Ailes E., Budge P., Shankar M., et al. Economic and health impacts associated with a *Salmonella typhimurium* drinking water outbreak-Alamosa, CO, 2008. *PLoS One* 8 (3), e57439, 2013.
[42] Rainwater-Lovett K., Pauszek S.J., Kelley W.N., Rodriguez L.L. Molecular epidemiology of vesicular stomatitis New Jersey virus from the 2004-2005 US outbreak indicates a common origin with Mexican strains. *J. Gen. Virol.* 88 (Pt 7), 2042-2051, 2007.
[43] Katz J.B., Eernisse K.A., Landgraf J.G., Schmitt B.J. Comparative performance of four serodiagnostic procedures for detecting bovine and equine vesicular stomatitis virus antibodies. *J. Vet. Diagn. Invest.* 9 (3), 329-331, 1997.
[44] Mavadiya S.V., Raval S.K., Mehta S.A., et al. Epidemiological survey of equine influenza in horses in India. *Rev Sci Tech.* 31 (3), 871-875, 2012.
[45] Smyth G.B., Dagley K. Internet-based survey of horse owners for mortality and morbidity related to equine influenza in the 2007 Australian epidemic. *Aust. Vet. J.* 89 Suppl 1, 23-25, 2011.
[46] Hilling K., Hanel R. Canine influenza. *Compend. Contin. Educ. Vet.* 32 (6), E1-E9, 2010.
[47] Peng W., Goldstein E., Ho L.M., et al. Excess mortality associated with influenza A and B virus in Hong Kong, 1998-2009. *J. Infect. Dis.* 206 (12), 1862-1871, 2012.
[48] Weaver S.C., Rico-Hesse R., Scott T.W. Genetic diversity and slow rates of evolution in New World alphaviruses. *Curr. Top. Microbiol. Immunol.* 176, 99-117, 1992.
[49] Bowen G.S., Fashinell T.R., Dean P.B., Gregg M.B. Clinical aspects of human Venezuelan equine encephalitis in Texas. *Bull. Pan. Am. Health Organ.* 10 (1), 46-57, 1967.
[50] Delfraro A., Burgueño A., Morel N., et al. Fatal human case of Western equine encephalitis, Uruguay. *Emerg. Infect. Dis.* 17 (5), 952-954, 2011.
[51] Garmashova N., Atasheva S., Kang W., Weaver S.C., Frolova E., Frolov I. Analysis of Venezuelan equine encephalitis virus capsid protein function in the inhibition of cellular transcription. *J. Virol.* 81 (24), 13552-13565, 2007.
[52] Deresiewicz R.L., Thaler S.J., Hsu L., Zamani A.A. Clinical and neuroradiographic manifestations of eastern equine encephalitis. *N. Engl. J. Med.* 336 (26), 1867-1874, 1997.
[53] Weaver S.C., Ferro C., Barrera R., Boshell J., Navarro, J. C. Venezuelan equine encephalitis. *Annu. Rev. Entomol.* 49, 141-174, 2004.
[54] Vander Kelen P.T., Downs J.A., Stark L.M., Loraamm R.W., Anderson J.H., Unnasch T.R. Spatial epidemiology of eastern equine encephalitis in Florida. *Int. J. Health Geogr.* 11, 47, 2012.
[55] Wang Z., Zhang X., Li C., et al. Vector competence of five common mosquito species in the People's Republic of China forWestern equine encephalitis virus. *Vector Borne Zoonotic Dis.* 12 (7), 605-608, 2012.
[56] Lvov D.K., Skvortsova T.M., Gromashevskiĭ V.L., Berezina L.K., Iakovlev V.I. Isolation of the causative agent of Karelian fever from Aedes sp. mosquitoes. *Vopr. Virusol.* 30 (3), 311-313, 1985.
[57] Kolman J.M., Minár J., Horák H. Serologic examination of birds from the area of Southern Moravia for the presence of antibodies against arboviruses of the groups alfa, flavo, Bunyamwera supergroup, and the virus Yaba 1-Lednice 110. I. Domestic fowls. *Zentralbl. Bakteriol. Orig. A.* 233 (3), 279-287, 1975.