

Non-Foodborne Swine Zoonotic Diseases

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Abstract

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The aim of this paper is to give an overview of novel swine non-foodborne zoonotic diseases that have been prominent in the last decade in swine industry. The number of swine present worldwide and the large percentage of population that consume pork, swine represent significant reservoir of potential zoonoses. Numerous of human cases of swine non-foodborne zoonoses were reported all over the world. Although much progress is made to control swine non-foodborne zoonoses, we must remain vigilant to identified and control novel swine emerging zoonoses.

Introduction

Any disease which is naturally transmissible from vertebrate animals to humans is defined as a zoonosis [1]. Zoonotic diseases can be transmitted in variety of ways: via contaminated food, direct contact or close proximity, vectors and airborne transmission. From this point of view zoonotic diseases can be divided into foodborne and non-foodborne. About 75 % of new emerged diseases over past 10 years that affected humans have originated from animals or animal products [2]. This number is expected to increase due to intensive changes in agricultural practice, human population growth, evolution of pathogens and international trade [3]. Swine have been included in transmission of many infectious agents to humans acting as primary or intermediary source and reservoir of infection [4]. Swine industry has expanded its production units all over the world, because of increased consumption of pork as a central source of protein. It is estimated that about 99

million metric tons of pork was consumed worldwide in 2006 [5]. Therefore, the risk from transmission of potential pathogens from swine and their products is much higher in individuals who work as caretakers on farms, butchers and veterinarians who are in direct contact with live animals and carcasses and the consumers via contaminated food. The definition about non-food borne zoonotic disease is: any disease which can be transmitted from animals to humans primarily via methods that do not include a food vector [6]. Despite already known swine foodborne zoonotic diseases (*Salmonellosis*, *Yersinia enterocolitica*, *Toxoplasma gondii*, *Campylobacter* spp. etc.) there are many non-foodborne zoonotic diseases. Swine influenza virus has emerged as a non-foodborne zoonotic agent in previous several years, but new pathogens like methicilin-resistant *Staphylococcus aureus* (MRSA), *Clostridium difficile*, *Streptococcus suis* and some others have implicated swine as a potential vehicle of transmission [4]. The aim of this paper is to give an overview of selected

novel swine non-foodborne bacterial and viral zoonoses that have been prominent in the modern swine production units in the last decade.

Methicillin-resistant *Staphylococcus aureus* (MRSA)

Staphylococcus aureus is a common organism found on the skin and mucous membranes of animals and humans. It can function as an opportunistic pathogen causing superficial and/or invasive infections [6]. It is Gram positive and forms white to golden opaque colonies with a double zone of haemolysis on sheep blood agar. Methicillin resistant *Staphylococcus aureus* (MRSA) colonization has recently been identified in pigs and people who work with pigs, raising concerns about the role of pigs as reservoirs of MRSA for human infection [7]. Besides skin infections, *S. aureus* has also been associated in swine with septicemia, mastitis, vaginitis, metritis, osteomyelitis and endocarditis [8]. Subset of *S. aureus* (MRSA) are resistant to methicillin with this resistant encoded by the *mecA* gene, which codes for penicillin-binding protein 2a that confers resistance to all beta-lactam antimicrobials [9]. First it was thought that transmission of MRSA was only from human to animal, with direct contact of the hands of human and anterior nostrils of the animal. Today there is strong evidence that MRSA can be transmitted in both directions. When once exposed to MRSA animal become colonized and may serve as reservoirs for infection to other animals and their human handlers respectively [10, 11].

Table 1: Recently published reports of ST398 MRSA infections in humans with close contact to positive pigs and their family members.

Country	Positive humans %	Positive Pigs and pig farms	Author-year
Netherlands	>20 %	39 % pigs	Wulf and Voss 2008 (14)
Belgium	38 % (49)	44,2% (663/1500) pigs	Denis et al. 2009 (15)
Ontario, Canada	25 % (5 of 25)	45% (9/20) pig farms	Khanna T et al. 2008 (7)
Germany	86% (97), 5% (4) their family members	In a study in 47 positive farms	Cuny C et al. 2009 (16)
U.S.A	45% (9/20)	49% (147/299) pigs	Smith and al.2009 (17)

In 2005, a new MRSA strain was identified in Netherlands that was resistant to digestion with the restriction endonuclease *Sma*I when typing with pulsed-field gel electrophoresis (PFGE) was attempted, and was associated with contact with pigs.

This strain belongs to a multilocus sequence type ST398 [12]. Microbiological testing in Denmark confirmed that pigs were source of MRSA CC398 (ST398) [13]. Recent studies (summarized in table 1) have shown high prevalence of ST 398 MRSA strain among humans and pigs [7, 14-17]. In the Netherlands, Germany, Denmark and China infection with ST398 in humans have been described including mastitis [10], endocarditis [18], ventilator-associated pneumonia [19], wounding infections [10] and skin and soft tissue infection (SSTI) [20].

Transmission of ST 398 MRSA from farmworkers to their family members has been reported, but spread into the general community seems to be infrequent [16, 21]. High frequency of MRSA among the group of pig farmers (760 times greater than general Dutch population) indicated that their profession put them at risk for MRSA colonization [12]. Wasswberg et al. reported 72 % less transmission of ST 398 MRSA strain in Dutch Hospitals compared with other MRSA genotypes. The lower transmission may be due to different pathogen-related and patient-related characteristic [22]. Transmission between humans and pigs with ST398 were reported in three family members, two workers, farmer and his pigs. All cases except initial case (mother with mastitis) were solely colonized without clinical signs [10]. ST398 MRSA usually is associated between livestock infected pigs and people exposed to animals [23]. Surprisingly high prevalence of ST398 (17.1%) was found in prospective cohort in adults in four hospital in Beijing, China. No apparent contact with animals in all positive cases was found [20]. Two ST398 strains in Hong Kong were isolated from patients with bacteremia without previous relation with pig farming [24]. That high prevalence of community acquired ST398 MRSA in this region is probably because whole genome sequencing of European ST398 has revealed that it lacked virulence factors such as enterotoxins and phage-encoded toxins [20]. Although ST398 was found in a number of medical and surveillance reports in many countries (Hong Kong, China, Italy, Germany, Denmark, The Netherlands, Sweden, Dominican, Scotland, Austria, Spain, Belgium, Norway and Canada) the clinical importance is not to much significant as other human strain in the community and hospitals [23]. Most prevalent strains associated with community-associated MRSA (CA-MRSA) human infection is USA300 and USA100 for hospital-associated MRSA HA-MRSA respectively [25]. ST 398 compared with other MRSA strain is susceptible to most of antibiotics but it show almost universal resistance to the tetracyclines [13]. Hypothetically the diversity of ST 398 all over the world may be linked with high amount of tetracyclines used as growth promoters in pig farming. The low prevalence ST 398 infections in the community in the european region (The Netherlands) compared with asian region, also can be explained with the national policy that enforce strict screening and isolation of all cases who are

considered at high risk for MRSA when admitted in to a hospital [12].

Public health agencies in the United States and Europe have not found evidence that contaminated meat contribute to an increased risk of MRSA [6]. From the studies about LA-MRSA ST 398 strain it is still unknown whether this is novel MRSA strain or is already has been previously present on livestock farms. Additional research should be done with aim to investigate spectrum and spread of this MRSA strain in general population and to identify other potential zoonotic MRSA strains [4].

Streptococcus suis

Streptococcus suis is an emerging zoonotic agent that has increased in importance in the last 5 years. Natural habitat of *Streptococcus suis* is the upper respiratory tract, particularly the tonsils and the nasal cavities of the pigs [26]. *Streptococcus suis* is common in domestic swine worldwide and 35 various serotypes have been described [27]. Clinical signs in pigs include central nervous system signs (head tilt and paddling), arthritis and polyserositis [6]. In humans *S. suis* usually produces purulent meningitis, although endocarditis, cellulitis, peritonitis, rhabdomyolysis, arthritis, spondylodiscitis, pneumonia, uveitis, and endophthalmitis have also been reported [28]. Most of human infections are occurring among veterinarians, pork handlers and slaughterhouse workers who are in direct contact with swine, raw pork or pig viscera. Transmission of infection is usually through the skin via cut, infected wound or abrasion [29].

First case of human infection was reported in Denmark in 1968 [30]. *S. suis* serotype 2 is the most frequently associated in humans and pigs and it is the most prevalent serotype that has been isolated from clinical material from pigs in Europe [31]. *Streptococcus suis* in pigs is spread worldwide: North America, Brazil, Europe, Australia and New Zealand [32]. Since, first reported case of human infection with *S. suis*, increasing number of humans infections have been reported in many countries [30]. First case of human infection in North America was reported in 2006 in 59 year old male farmer [33]. The number of reported human *S. suis* cases has increased significantly in past few years. In review published in 2007 409 cases were reported [30], but in 2009 this number has increased to >700 cases, where the most cases originate from Southeast Asia (Table 2). Total of 215 cases, including 38 deaths of *S. suis* human infections, occurred in China. All of the infected people had contact with pigs infected with *S. suis* type 2 [34]. *S. suis* was detected in 151 (33.6 %), from total of 450 patients with suspected bacterial meningitis in one prospective study [35]. Serotype 2 was the most commonly detected organism in Viet Nam, and is responsible for acute meningitis in adults [36].

Table 2: *S. suis* human cases reported worldwide, by country and number of new cases reported in two year period.

Country	Pre- 2006	Till 2008	New cases from 2006 to 2008
China	283	332	49
Vietnam	0	293	293
Thailand	47	118	71
Netherlands	34	41	7
UK	6	15	9
Germany	6	7	1
Spain	6	6	0
France	5	7	2
Croatia	4	2	0
Denmark	3	12	9
Belgium	2	2	0
Japan	2	2	0
Italy	2	2	0
USA	1	1	0
Argentina	1	1	0
Austria	1	1	0
Canada	1	1	0
Hungary	1	1	0
Greece	1	2	1
New Zealand	1	1	0
Singapore	1	1	0
Sweden	1	1	0
Total	407	849	442

Human *S. suis* cases are most often reported from countries where density of pigs is high (Figure1) and where pig-rearing is common practice [28]. Human *S. suis* infections have been described including multiorgan failure, deafness, purulent meningitis, subacute meningitis, spondylodiscitis and septicaemia. All of this cases were associated with exposure to pigs [37-40].

Serological studies have shown that the infections with this organism are common in swine-exposed individuals (veterinarians, farm workers, veterinary inspectors) [41, 42], and it has been shown that laboratory misidentify of this organism may be the reason for the lack of reports of human cases in the United States [43].

Streptococcus suis is an important emerging pathogen responsible for causing meningitis and septicaemia in humans and pigs. Diseased pigs with and without clinical symptoms play an important role in the transmission between humans. Sporadic infections with *S. suis* in humans have been reported worldwide. Most of the infections occur between individuals who have direct contact with live pigs, pork and pig viscera. In North America, human *S. suis* infections are quite rare in contrast to infections in Southeast Asia. This finding can be explained with the fact that pig density in Southeast Asia is very high, as well as absence of preventive measures in slaughtering practice and consumption of undercooked pig products. Traditional consumption and differences in swine husbandry also play significant role for the transmission of this pathogen [4].

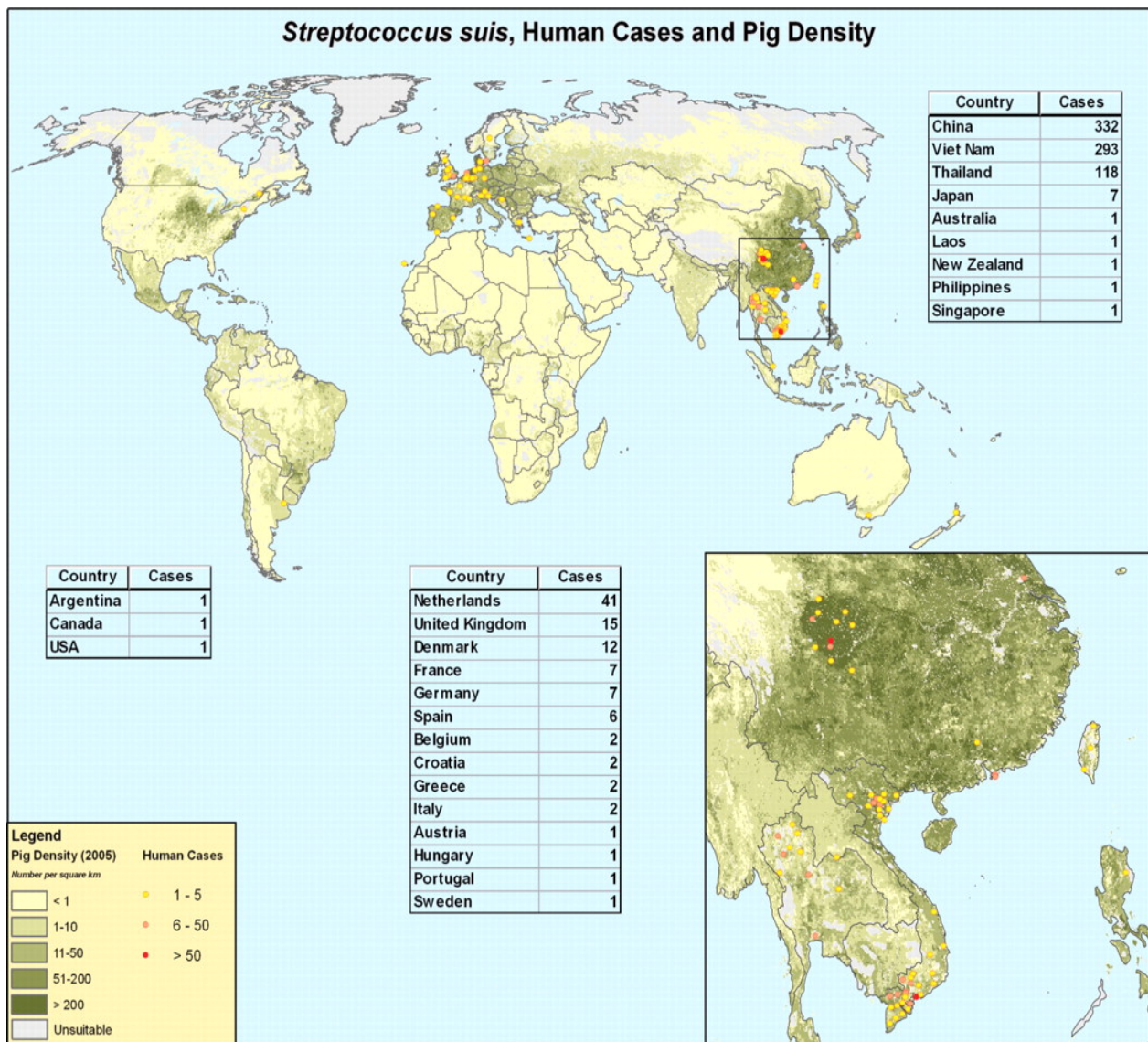


Figure 1: World map of human *Streptococcus suis* cases with background pig density data.

Clostridium difficile

Clostridium difficile is a gram positive bacteria which is able to form spores. It was described for the first time in 1935 as a part of normal gut flora in human neonates [44]. *Clostridium difficile* in humans it is responsible for causing pseudomembranous colitis with severe gut diseases in some cases [45]. It is also a common agent of colitis in neonate pigs [46]. Many studies have suggested that risk factor for development of disease is exposure with antibiotics in both humans [47-49] and pigs [50, 51]. Antibiotics cause disruption of normal gut flora of the host and allow *Clostridium* spores to germinate. In the last decade epidemiology of *C. difficile* has dramatically changed. Several studies have examined the prevalence of *C. difficile* shedding among pigs in North America and worldwide [6]. Because *C. difficile* is an agent which causes enteritis in neonatal pigs (from birth to 7 days of age), prevalence of faecal

shedding in piglets is higher than in adult swine. There is a significant decrease in colonization over time with 74% in piglets on day 2, 56% on day 7, 40% on day 30, 23% on day 44 and 3.7% on day 62 [52]. An epidemic of high virulent strain of *C. difficile* was reported recently in Europe and North America. This strain was hypervirulent and capable to produce protein toxins A, B and so called binary toxin [53]. The same *C. difficile* strain caused outbreak of enteritis in neonatal piglets in Europe and USA and was identified with PCR as a ribotype 078 [46]. Several of *C. difficile* types have been described as enteric pathogen in animals (pigs, horses, goats, sheep, dogs, cats, cattle), but most prevalent strain in pigs (83%) and cattle (94%) was *C. difficile* ribotype 078 [54]. Also, this is the third most common strain found in humans in Europe [55]. First case of *C. difficile* ribotype 078 toxinotype V in pigs was found in Slovenia [56]. *Clostridium difficile* infection (CDI) can present a severe disease in humans particularly when it caused by hypervirulent

strain characterized as North American pulsed-field ribotype 27. Outbreaks of CDI associated with this strain have been reported in United States, Canada and Europe [57]. In a prevalence study on hospital strains performed in 2005 ribotype 078 was the 11th most prevalent type in Europe representing 2.8% (9/322) of all toxigenic strains. In total of 14 countries involved in study only in Greece ribotype 078 was represented with more than 10% of all strains [58]. The number of human infections with *C. difficile* ribotype 078 appears to be increasing associated with high levels of mortality similar as other hypervirulent strain *C. difficile* 027 [59]. Recently the prevalence of *C. difficile* ribotype 078 has increased from 3 to 13% in several countries in Europe [49]. In the USA the prevalence of ribotype 078 infections in humans has dramatically increased from 0.02% to 1.3% (pre-2001 to 2006), and ribotype 078 was increasingly associated with community-acquired CDI [60]. Goorhuis et al. have shown difference between infections in humans with ribotype 027 and 078 respectively. Patients infected with ribotype 078 were younger (67.4 vs. 73.5) and had more frequently community-associated CDI (17.5% versus 6.7%; odds ratio = 2.98; 95% confidence interval = 2.11–8.02) than patients infected with ribotype 027 [57]. High genetic similarity of *C. difficile* ribotype 078 was found between humans and pigs [56, 57]. Some studies suggest that *C. difficile* contaminate retail food including meat products, vegetables and salads. With abundant evidence that food contains toxigenic strains of *C. difficile*, it still remains that food-borne transmission is unproven [55].

Clostridium difficile is an emerging pathogen responsible for causing diarrhea in neonatal pigs and pseudomembranous colitis in humans. Many studies in Europe reported that strains of *C. difficile* in pigs and humans are genetically identical and confirmed the zoonotic potential [56]. The number of community-acquired *C. difficile* infections is increasing worldwide and the opinion that animals are a reservoir for human infection still stands. Besides the genetic homology of the *C. difficile* strains in pigs and humans, the question about the source and the transmission of the infection between humans and pigs still remains unanswered.

Swine A influenza viruses

Influenza viruses are members of the virus family *Orthomyxoviridae*. They are pleomorphic, enveloped viruses approximately 80–120 nm in diameter. Influenza viruses encode 10 or 11 viral proteins on eight separate segments of negative-sense RNA [61].

Pigs possess receptors for avian and human viruses and serve as potential danger for novel reassortment strains [62]. The well known pandemic of swine influenza was in 1918-1919. During this pandemic, there were outbreaks of influenza in swine

and humans that were caused from a single infection agent [4]. First influenza virus in swine was isolated in 1930 in North America [63]. In 2009, there was an outbreak of a novel pandemic H1N1 virus in humans. This strain originated from a reassortment between swine, avian and human lineages of influenza viruses [64]. In 2009, H1N1 outbreaks were reported in 69 countries with 21940 cases including 125 deaths [65]. Except the 2009 outbreak, human cases of pH1N1 influenza have been sporadically reported. Before the outbreak in 2009, another outbreak in 1976 occurred in Fort Dix (New Jersey), where 1 person died from 230 H1N1 infected soldiers [62, 66]. In the period between 1958 and 2007, 50 human cases of classical swine influenza were reported and most of them involved individuals which had close contact with swine [62]. From December 2005 till February 2009, 11 cases of triple-reassortant H1 infections in humans have been reported in the United States, including a report of pig-to-human transmission with a strain currently circulating in the pig population in U.S at the Ohio County Fair in 2007 [67, 68]. From the 11 infected patients, eight of them had contact with clinically ill pigs [67]. The number of pH1N1 influenza reports worldwide is small compared to the number of people that were in close contact with pigs [61]. Human H3N2 viruses also have been frequently recovered from pigs in Asia and occasionally from Europe and North America [61]. Influenza viruses of subtype H3N2 are endemic in most pig population world-wide, where they persist many years after antigenic counterparts disappeared from humans, and therefore present a reservoir of virus which may in the future transmitted to a human population [69]. During influenza outbreak in 1998 in four swine herds in U.S two antigenically distinct H3N2 viruses were isolated from infected animals: a double-reassortant virus containing genes similar to human and swine viruses, and triple-reassortant virus with genes similar to those of human, swine and avian influenza viruses [70]. The emergency of an H3N2 virus with triple-reassortant internal gene (TRIG) cassette consisting genes from human (HA, NA and PB1), avian (PB2 and PA) and swine (NP, M and NS) viruses and human H1N1 and H1N2 viruses in 2003 and 2005 in U.S. swine population exemplify influenza virus transmission from human to swine [70, 71]. In European swine H3N2 viruses were derived from descendants of the 1968 “Hong Kong” pandemic human virus, but they have evolved further in reassortant H3N2 viruses human-like and avian-like internal genes [61]. In contrast to U.S. in Europe H3N2 influenza viruses related to human strain continued to circulate in pig population long after they disappeared from the human population [69]. This sharp difference between high level of H3N2 infections in Europe to the low prevalence in pigs in North America may suggest that virus is not established in American swine population, but occurs only by infrequent introduction from infected human [69]. Situation in Asia is more complex than Europe and North America. H3N2 viruses have been

repeatedly transmitted from people to pigs since 1970s, and variants of Hong Kong/68 pandemic virus cocirculate in pigs with contemporary human H3N2 viruses [72-74]. Efficient transmission of human influenza viruses among pigs it seems requires adaptation to the new host species. Thus, H3N2 viruses that have been maintained in pigs in North America and Europe are reassortants with a mix of human and swine-adapted genes. Serological studies have shown that antibodies may be present up to 23% in humans exposed to pigs, but they are of limited value because of the difficulty to differentiate between swine and human influenza viruses [66]. The occurrence of influenza virus infections in pigs poses two important public health issues: infection of people with swine influenza viruses and the potential of pigs to serve as hosts for the creation of novel viruses of pandemic potential for the human population. Pigs remain important because of the genetic origin of the 2009 pH1N1 virus outbreak. This virus contains a unique combination of gene segments from North American and Eurasian lineages [75, 76].

Hepatitis E virus

Hepatitis E virus (HEV) is a single-stranded, positive-sense RNA virus of the genus *Hepevirus*. HEV is an important zoonotic pathogen causing more than 50% of all human cases of acute hepatitis in endemic countries [77]. Mortality rates are low in human population, except in Africa and Asia where in the third trimester of pregnancy, mortality can reach more than 20 % [78]. HEV is transmitted by faecal-oral route and is a public health concern in areas with poor sanitation and public health infrastructure [77]. Regardless the fact that HEV is endemic in human population, in pigs HEV is widespread in swine farms worldwide. The infection in pigs occurs at about 2 to 3 months of age and they have transient viremia for about 1 to 2 weeks. Feces from infected pigs contains large amount of virus and are likely the main source of infection [79]. Fecal shedding of the virus from the infected pigs lasts for about 3-7 weeks [79]. HEV was first isolated from domestic pigs in the Midwestern United States in 1997 [4]. There are five genotypes of HEV known to date. Genotypes 1 and 2 infect only humans, but genotypes 3 and 4 infect humans and animals including swine [77, 80]. First example of human infection with HEV genotype 3 was reported in United States and was similar with HEV genotype 3 isolated from a swine herd in United States [81, 82]. Genotypes 3 and 4 are less virulent in humans than genotypes 1 and 2 [83]. Molecular studies have shown that swine and human isolates from one geographical region are very similar and are different from those in other geographical regions [84, 85]. In developing countries where HEV is endemic, even genotype 3 and 4 are present in the local swine herds, virulent genotypes 1 and 2 were the most frequently recovered from human cases of hepatitis E [86]. In the industrialized countries where more

virulent genotypes 1 and 2 are not present, less virulent genotypes 3 and 4 have been frequently isolated from occasional cases of clinical hepatitis E [83]. In United States and Taiwan, people who are in close contact with swine are associated with increased risk from seroconversion but without clinical disease [87-89]. Swine veterinarians in USA are 1.51 times more positive for anti-HEV antibodies than other blood donors [88]. The prevalence of IgG anti-HEV is very high in some developing countries such as Egypt with more than 70% of the human population positive for IgG anti-HEV [79]. High prevalence of anti-HEV Ig in healthy individuals in nonendemic areas may be linked with inapparent infections with less virulent strains of HEV derived from swine or other domestic or wild animals [83]. The varieties between high seroprevalence and low frequency of hepatitis E infection in these areas indicate that zoonotic spreading of virus is at least partly responsible [77]. More than 20 % of pigs and pig production units excreting large quantity of HEV [78] in watercourses most probably as a consequence of run-off from outdoor pig farms [77]. HEV has been isolated in slurry lagoons from pig farms [78, 90] and from sewage works in pig slaughterhouses [91]. Those data suggested that hepatitis E infections in humans with limited pig contact in endemic areas may be associated with faecal contamination of waterworks and poor sanitary conditions. Swine veterinarians and pig farmers in both developing and developed countries are at high risk for HEV infection. Despite the fact that HEV is endemic in developing countries, sporadic infections were reported in North America, Japan, Australia, New Zealand and Europe [92, 93]. Numerous serological studies about exposure to HEV obtained in both developed and developing countries have confirmed that the infection is very common, but the clinical form is rare in developed countries [6].

Nipah virus

Nipah virus (NiV) is a negative-stranded RNA virus of the family *Paramyxoviridae*. Both Nipah and Hendra viruses are the sole members of the genus *Henipavirus* [94]. It is dangerous zoonotic agent, causes fever and headache in humans, and can lead to a deadly encephalitis. In pigs, signs are manifested with respiratory and febrile illness, tetanic spasms, lateral recumbence, spastic paresis and uncoordinated gait [95]. Between September 1998 and April 1999, after spreading as a unrecognised respiratory or encephalitic infection in Malaysian pigs, NiV appeared in the human population and caused fatal encephalitis [96]. Over 400 cases of NiV in humans were reported with approximately 200 deaths in Malaysia, Singapore, Bangladesh and India [96]. The virus, isolated in 1999 from cerebrospinal fluid (CSF) of human fatal cases was named as Nipah virus [97]. It is presumed that this outbreak is a result of virus 'jumping' species into farmed domestic pigs

[94, 98-100]. In Malaysia, virus was primary spreading by movement of infected pigs between farms, states and internationally to Singapore, where abattoir workers became infected while processing pigs (95). The natural reservoir of the virus is fruit bats from the genus *Pteropus* [101]. Human infection with the virus is linked to direct contact with infected pigs and especially with their body fluids [97]. Parashar et al. in their findings confirmed that close contact with pigs especially with sick pigs (handling of pigs, feeding, treating, assisting with farrowing, treatment and removal of sick and death pigs), were strongly associated with infection in humans [102, 95]. Pigs are considered the amplifying host for human infection and it is believed that they are the main source of infection [101]. The major route of excretion of Nipah virus from pigs is via the airways. It is suggested that the larger drops via the sputum (rather than fine aerosol) are more likely linked with the transmission of the infection [103]. Besides pigs, other domestic animals are also susceptible to Nipah virus. Large numbers of clinically affected dogs died during these outbreaks in swine farms [94, 98]. In the outbreak in Malaysia, Nipah virus was isolated from the kidney of affected dog [94]. This may suggest that virus could be spread through urinary secretion by domestic carnivores. Cats are also susceptible to infection and they excrete the virus in urine [104]. Before the outbreak in Malaysia, the recent outbreaks of NiV infection in Bangladesh and India had higher fatality rates where human to human transmission was reported [105-108]. Transmission of the virus in humans with fatal encephalitis without close contact with pigs has been reported in Bangladesh in 2001, 2003 and 2004 [109].

Japanese encephalitis

Japanese encephalitis virus (JEV) is a zoonotic vector-borne viral disease which is mainly transmitted by the mosquito *Culex tritaeniorhynchus* [110]. It was first isolated in 1933 in Japan from humans cases with encephalitis [111]. Approximately 25% of clinical JEV cases are fatal, 50% have some form of neurological sequelae, such as quadriplegia or mental retardation, and 25% fully recover [112]. Wading birds are considered the primary endemic hosts of JEV, but pigs are important in the transmission cycle because they are the only known mammals to fulfill the criteria as an amplifying host for the virus [113]. They develop viremia that lasts 2-4 days and are capable to infect various mosquito species [114]. To date there is no evidence that human contact with blood from infected viremic pigs is a risk factor. In viremic state they only infect certain mosquito species. With biting those infected insects can cause infection in humans [112]. Seroprevalence rates in other animals such as dogs and sheep are high but too low to infect mosquitoes [115]. The distribution of JEV occurs mostly in East, Southeast and South Asia and in the South Pacific [116]. It is

believed that JEV is responsible for more than 40,000 annual cases of encephalitis with 10,000 deaths [112]. Besides pigs, horses and donkeys could serve as a reservoir for the virus. In some regions of Asia (Bangladesh, Cambodia, Indonesia, Laos, Myanmar, North Korea and Pakistan), increasing pig populations, intensified rice farming and lack of vaccination and surveillance have been linked to increasing human infections [115]. In Japan, that trend was reversed. During the last 40 years, the number of pigs in Japan has increased while the number of farms has decreased. Raising pigs in modern facilities drastically declined the number of JEV cases in humans [116].

Conclusion

We can conclude that swine represent a significant source of non foodborne zoonoses. Most of the infections occurring in areas where sanitation measures are poor and density of animals is high. Individuals with occupational contact with swine, like veterinarians, butchers, caretakers, farmers, have high risk for infection. Modernization of swine industry has showed that some swine zoonoses were drastically reduced. Our review is certainly incomplete. Additional pathogens such as Norovirus, Ebola reston virus and porcine endogenous retroviruses have also been implicated in zoonotic transmission between pigs and humans. Although much progress is made to control swine non foodborne zoonoses, we must remain provident to identify and control novel emerging swine zoonoses.

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