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The link between human and swine health: The challenge of emerging and re-emerging diseases in an era of changing ecosystems and swine management practices

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Introduction

Pigs have been important to the health and well being of humans since they were first domesticated—approximately 10,000 years ago (Dunlop & Williams, 1996). Today, pork is the most commonly consumed meat product in the world (FAO, 2004), and is a major source of animal protein in human diets. Pigs are also an important source of insulin for treatment of diabetes and heart valves for repair and replacement in humans. Manure from swine has been used as a source of fertilizer to improve crop production, again helping to protect food security for people. In addition, many people benefit economically from working in swine food and by-product (e.g., pigskin for leather, pig bristles for hair brushes, gelatin extracted from skin, etc.) industries— and with greater household income comes improved health (OECD & WHO, 2003). However, human health can be adversely affected by infectious diseases acquired through contact with pigs. Over 60 % of all infectious disease (Cleaveland, 2001), and 75% of emerging infectious disease pathogens (Taylor, 2001) can be transmitted to and cause disease in humans. There are several pathogens of swine, including viruses, bacteria, and parasites and protozoa, that are transmissible to humans (See **Table 1** for a subset), and that cause significant human morbidity and mortality. Several of these pathogens which are important to public health, are not associated with clinical signs or disease in pigs. Veterinarians and other animal health scientists and managers, who have responsibility to look after the health of swine, are also front line public health practitioners. This fits with the greater scope of responsibilities of veterinarians, who swear at graduation that they will use their scientific knowledge and skills for the benefit of society through the promotion of public health as well as the protection of animal health (AVMA, 2003). That public health concerns are considered a priority also fits with the goals of the pork industry, which understands that providing consumers with wholesome and safe food products that will not jeopardize human health is critically important to the success of the food industry.

A number of factors that facilitate the transmission of infectious disease agents from animals, including swine, to humans have been identified over the last decade. These include an increasing human population with human encroachment into food animal production and wildlife habitats; globalization of the food supply with intensification of the food production industry accompanied by changes in animal husbandry practices, changing climates and ecosystems; increasing international travel and trade; human-made and natural disasters; increased rapid movement of people and animals; and changes in human behaviors—such as the consumption of bush meat, and the importation and purchase of exotic animals for pets (IOM, 2003). This paper focuses on a subset of emerging zoonotic diseases of swine, which have emerged or re-emerged during the past 10-20 years, and describes the factors that have facilitated emergence of the disease, the current risks to human public health (including occupational risks), and important public health interventions to minimize those risks.

Animal husbandry practices and food borne disease

Worldwide, more than 2 million people die every year from diarrhea caused by consuming contaminated food and water. In the United States, there are approximately 76 million cases of foodborne disease annually, with 325,000 hospitalizations and 5,000 deaths (Meade et al, 1999). Intensification and globalization of the food supply have greatly increased the emergence of a number of food borne pathogens in swine including *Salmonella* spp.(Cole et al 2000), *Yersinea enterolytica* (Jones, 2003), *Escherichia coli* 0157:H7, (Nakazawa et al, 1999) and *Campylobacter* sp.(Pearce et al, 2003). Often pigs can harbor these pathogens without showing signs of clinical illness (Cole et al, 2000). Concentrated Swine Feeding Operations, where thousands of animals are raised in closed confinement, provide an environment where occupational transmission of these agents can occur. Depending on swine-associated waste management, these pathogens can contaminate the environment putting humans at risk of infection (Cole et al, 2000). Other animal husbandry practices, types of swine raising operations, farm management, political factors such as civil strife, and economic factors have led to a re-emergence and outbreaks of *Trichinella spiralis* (Djordjevic et al, 2003), *Toxoplasma gondii* (Olson & Guselle, 2000), *Taenia*

Table 1: Important selected emerging and re-emerging infectious zoonotic diseases of swine

Pathogen	Where agent resides in swine	Primary mechansism of transmission to humans	Biothreat agents of concern (CDC & (Korteoeter MG & Parker GW. 1999)
Parasites			
Trichinella spiralis	GI tract, muscle	Foodborne	
Taenia solium	GI tract, muscle	Foodborne	
Toxoplasma gondii	muscle	Foodborne	
Cryptosporidium pig genotype	GI tract	Foodborne	Yes – CDC Category B
Ascaris suum	GI tract	Foodborne	Yes
Bacteria			
Salmonella spp.	GI tract	Foodborne, occupational	Yes – CDC Category B
Campylobacter coli, jejuni	GI tract	Foodborne	
E. coli 0157:H7	GI tract	Foodborne	Yes – CDC Category B
Yersinia enterocolitica	Tonsils, oral cavity, GI tract	Foodborne, Occupational	Yes
Listeria monocytogenes	GI tract	Foodborne	
Brucella suis	Nonphagocytic and phagocytic cells	Contact, Ingestion Occupational	Yes - CDC Category B
Bacillis anthracis	Blood, lymph nodes, tonsils, tongue, throat	Contact, occupational, inhalation, foodborne	Yes – CDC Category A
Mycobacterium sp.	Cervical and mesenteric lymph nodes	Aerosol, Ingestion, occupational	
Clostridium perfringens type A	GI tract	Foodborne	
Erysipelothrix rhusiopathiae	Joints, lymph nodes, endocardium, liver	Small cuts, wounds, Occupational	
Streptococcus suis II	Tonsils	Occupational, skin injury; Contact, Ingestion	
Leptospira icteroheamorrhagiae and *Pomona*	Urine	Occupational Contact with infected urine	
Viruses			
Nipah Virus	Blood vessels, neurons, central nervous system	Contact w contaminated tissue / body fluids from infected animals; Occupational, other?	Yes – CDC Category C
Japanese B encephalitis	Blood system	Vector borne	
Rabies	Nerve and muscle cells, spinal cord, brain	Direct contact, bites	
Influenza	Lungs, respiratory tract	Respiratory, occupational	
Hepatitis E[B]	??Liver, small intestines, colon, lymph nodes	??Fecal/oral, Occupational	

[A]Swine shed cryptosporidium; transmission to humans from swine has not yet been proven
[B]Suggestive but not confirmed as a zoonoses; remains under investigation

solium (Olson & Guselle, 2000), and the emergence of *Cryptosporidium sp*.,(Xiao, 2002).

Relationships between swine and people also seem to have impacted on the pattern of antimicrobial resistant flora in humans. Several studies have shown that people working in occupations having direct contact with pigs, including farmers, pig breeders, and slaughterhouse workers, have a higher prevalence of antimicrobial resistant bacteria in their commensal flora (i.e., *Staphylococcus aureous*, nongroupable streptococci) compared to other occupational or community groups (Aubry-Damon et al, 2004). This situation could have important implications for the health of individuals or across populations (CDC, 1999).

Influenza A

Influenza A viruses causes significant morbidity and mortality in people in the US annually, causing approximately 25,000-35,000 deaths per year. Every 10-50 years, influenza pandemics in humans, caused by infections with influenza A viruses, have resulted in several hundred thousands to millions of deaths around the world. Wild aquatic birds, most notably ducks, have been identified as the reservoir for influenza A viruses (Webster 1992). All 16 serotypes of influenza A virus have been shown to replicate in the intestinal and respiratory tracts of these birds without causing detectable illness (Webster 1992, Fouchier et al, 2004). Influenza A virus is a constantly changing RNA virus, and is known to jump species frequently. Influenza A viruses are also common in pigs and cause an economically important respiratory disease (Easterday BC et al, 1992). Pigs can become infected with swine influenza viruses from other pigs, with avian viruses from birds, and with human viruses from people. Likewise, swine influenza viruses are known to infect humans. The proclivity for influenza viruses to jump species, has led to concern that at any time, avian or swine viruses could adapt to people and spread person-to-person, leading to the next pandemic. Pigs play a particularly important role in the ecology of these viruses, in that they are susceptible to both avian and human viruses, and therefore can serve as a mixing vessel that increases the likelihood of producing a virus with pathogenic avian components that can be spread person to person.

Before 1997, avian influenza A virus (H5N1) was known to only infect birds. This changed in 1997, when an influenza outbreak caused by avian influenza A H5N1 virus occurred in humans in Hong Kong. These human infections had occurred as a consequence of contact with infected birds (CDC, 1998). In January 2004, new human cases of influenza A H5N1, resulting in significant mortality, had been reported to WHO (WHO, 2004). As of August 1, 2005, 109 confirmed human cases of avian influenza A (H5N1), of whom 55 have died, have been reported to WHO by Vietnam, Thailand, Cambodia and most recently, Indonesia (WHO, 2005). Additionally, unprecedented and widespread large scale outbreaks of influenza A H5N1 have occurred in poultry flocks of 9 countries in SE Asia during this same time period. These outbreaks have caused major mortality in flocks, either from the disease directly or from depopulation of flocks in efforts to control the disease, and adverse economic consequences from loss of trade. Of great concern is that during the widespread outbreaks of avian influenza H5N1 in poultry in Asia, infections have been detected in pigs in both China (WHO 2004) and most recently in Indonesia (although clinical illness was not observed) (Cyranoski, 2005). Infections of avian influenza H5N1 in swine continue to raise global concern over the potential for the virus to become better adapted to humans, such that it could spread easily and directly from person to person.

Nipah virus

During March 13-19, 1997, nine cases of encephalitis (one fatal) and two cases of respiratory illness occurred among slaughterhouse workers in Singapore. Because specimens from some patients were positive for infection with Japanese encephalitis (JE) virus, a virus endemic to the region, JE originally was considered the probable cause of the outbreak. Authorities implemented a fogging program to eliminate the mosquito host, and a mass vaccination program. However, the accuracy of the JE diagnosis was soon called into question. First, cerebrospinal fluid collected from patients was negative for JE; second, all case-patients were related to pig farming or pork selling and this would be unusual with a vector-borne disease; third, case-patients were predominantly adult men with close contact with swine, while JE largely affects children; fourth, despite vector control measures, cases of disease continued to occur and the disease spread to other regions through the sale and movement of pigs; fifth, people vaccinated for JE fell ill with the disease; and sixth, clinical features of the illness differed from those traditionally associated with JE. From Sept. 29, 1998 to May 31, 1999, 265 cases were reported to Malaysian Ministry of Health, and of these, 105 (39.6%) died. A new paramyxovirus, named Nipah virus after the village where it was first detected, was identified from tissue culture isolation of specimens collected from ill patients. The virus was related to Hendra virus, and caused a 3-14 day illness of fever, headache followed by drowsiness, and disorientation that progressed to coma within 24-48 hours (Chua et al 2000).

During the outbreak in humans, illness and death were occurring in swine from the same regions. The disease in pigs was rapid, with labored breathing, an explosive nonproductive cough, and neurologic changes, including lethargy or aggressive behavior. Spread of the virus to different parts of Malaysia occurred from the transport of infected swine. In March, 1999, there was an associated outbreak of Nipah virus that occurred in Singapore, with

11 cases of respiratory and encephalitis illness in slaughterhouse workers who handled pigs from outbreak areas of Malaysia. The outbreak in Singapore ended when a ban was placed on importation of pigs from Malaysia. In Malaysia, the outbreak ended following the culling of over 1 million pigs from the outbreak and surrounding areas (Chua et al 2000). During the institution of culling and other control measures, protective equipment (gloves, masks, boots) worn by workers was observed to be effective in preventing people from becoming infected. Since those outbreaks, the Island Flying Fox (pteropus hypomelanus), a fruit bat, has been identified as the probable natural reservoir of the virus (Johara et al, 2001; Chua et al et al, 2002). A hypothesis has been put forward that these fruit bats were forced away from their natural habitat in 1998 because of forest fires prevalent in the region at that time, and attracted to the fruit trees surrounding pig farms, infecting pigs through infective urine and other secretions (Lam 2003). Nipah virus has been shown to infect dogs, cats, horses, and other animals. Since 1998, additional Nipah virus outbreaks have been reported from Bangladesh (Hsu et al., 2004). Investigations have suggested that human to human transmission can occur, or from exposure to a common source, and need not involve an intermediate host such as a pig.

Mystery disease in humans having close contact with ill or dead pigs, China, 2005

Streptococcus suis, a pathogen involving pigs, is endemic in many pig-rearing countries of the world. Infection in pigs can be asymptomatic, with transmission between pigs occurring by nose-to-nose contact or by aerosol over short distances. The bacteria can infect humans, causing meningitis, septicemia, endocarditis, and deafness. People in direct contact with pigs or pig products are at increased risk of infection, mainly through cuts or abrasions when handling infected animals or carcasses. The first human case of *S. suis* was reported in Denmark in 1968 (Perch et al., 1968). Until late June 2005, human cases of this disease occurring sporadically were described, with between 100-200 cases reported in the world literature. Beginning in late June 2005, and continuing until the time of this writing (August 5, 2005), Sichuan Province in southwest China, had reported 206 people from 11 cities in the province were ill from *S. suis*. Of the 206 human cases, 38 had died, and 18 were reported to be in critical condition (WHO, 2005). Only 19 cases had been reported as laboratory-confirmed (WHO/WPRO 2005) at the time of this writing. Several clinical characteristics were different from those described for *S. suis* infections in humans previously, and so questions remained in the scientific community outside China as to whether this outbreak was a consequence of *S. suis* alone, *S. suis* as a coinfection with another pathogen, or another disease. The majority of ill people were described as male farmers, and all case-patients were reported as having direct contact with ill or dead pigs. One informal account described a long tradition of farmers in the area eating sick pigs due to poverty and associated shortage of food. The account went on further "Farmers called over their relatives and neighbors to help them slaughter the sick pigs, even though the animals were foaming at the mouth.".”Entire families and neighbors pitched in to shave the hair off the killed swine, wash the internal organs and chop the meat to distribute. The victims had open wounds which allowed the bacteria to get into their body." (Promed-mail 28 July 2005). The Ministry of Health issued national guidelines on July 27, 2005, ordering farmers to bury their infected pigs deep in the ground or to burn them, to prevent dogs and other animals from coming into contact with infected carcasses, although as of August 2nd, Chinese farmers were reported to be non compliant with the guidelines (Promed-mail, 2 August 2005). In addition, the Chinese CDC (2005) reported that at least 50,000 health workers had been sent to approximately 1.4 million farming households to register every pig in the region, that more than 2 million posters urging farmers not to slaughter or eat sick pigs have been issued, and that 39 temporary roadside quarantine stations have been set up to stop dead swine from being transported to markets. The production of a vaccine to protect pigs against *S. suis* infection was being accelerated to produce vaccine for at least 10 million pigs could be sent to Sichuan province by August 3rd although it can take three weeks post vaccination for pigs to develop immunity (Gaia 2005). The disease outbreak remained under investigation as of 4 August 2005.

Trichinellosis

Trichinellosis has been known as a foodborne disease for many years. The past several decades, efforts to eliminate it from the human food chain have been very successful. During the 1980s and 1990s, a resurgence of trichinellosis occurred in Eastern Europe—thought to be a consequence of political unrest and economic challenges posed to local and national economies. Due primarily to a lack of resources, a number of large intensive or industrial slaughterhouses were forced to close, and experienced veterinary inspectors were lost because of unacceptably low salaries. These and other factors, including a failure of veterinary quality control during slaughter, resulted in the re-emergence of the opportunistic *Trichinella spiralis* parasite (Djordjevic et al, 2003).

Bioterrorism

Several zoonotic infectious diseases associated with swine are considered important biological warfare agents or have been associated with biocrimes and bioterrorism. They include: *Brucella suis*, *Bacillus anthracis*, *Ascaris suum*, *Salmonella typhimurium*, *Yersinia enterocolitica*, and Nipah virus (Kortepeter and Parker, 1999).

Xenotransplantation

The pig is considered one of the most likely potential sources of animal cells, tissues, or organs for transplantation into humans. Substantial concerns have been raised over the potential for a number of different pathogens to be transferred from pigs to humans through xenotransplantation involving swine. That transplant recipient patients are often iatrogenically immunocompromised to minimize rejection of transplanted cells, tissues, or organs increases their susceptibility to infection. At least 33 bacteria, 11 fungi, 25 parasites and protozoa, prions, and 25 viruses, including many of those listed in **Table 1** are zoonotic pathogens capable of transmission to humans following xenotransplantation (Onions et al, 2000). In the event that xenotransplatation, the use of specific pathogen free animals raised over several generations, pre-transplant screening of animal herds and source animals, and prescreening xenotransplantation products, post transplant surveillance of recipients for previously unrecognized xenogeneic organisms have been recommended to minimize risk of pathogen transmission (DHHS, 2001).

Discussion and conclusions

There are many pathogens of swine that can be and are transmitted to humans, resulting in significant morbidity and mortality. Not only are individuals and communities at risk, but many of these pathogens present an occupational risk to those working in the swine food and by-product industries. The factors cited by the IOM as important for facilitating the transmission of infectious disease agents, have been shown to be important in the emergence and re-emergence of a number of different diseases in humans caused by viruses, bacteria, and parasites of swine.

Without question, however, the risks to human health from the zoonoses discussed in this paper, are offset by large and substantive benefits accrued from increased animal protein in the human diet, use of swine by-products medically, and increased household income for those working in the swine food and by-product industries, among others. Nonetheless, it is important to continually strive to minimize the risks to public health from swine zoonoses. Many of these risks are associated with foodborne or occupational transmission of pathogens. Veterinarians, swine farmers, operation managers, animal scientists, abbatoir workers, or others working with pigs are at risk for a number of zoonotic infections, and continual efforts must be taken, by individuals or through public health programs, to reduce risk via effective interventions, including hand washing, ensuring hygienic conditions are in place, utilizing appropriate and safe waste management, and using personal protective equipment when needed, among others.

There is much about the pathogenesis, transmission, prevention, and control of zoonoses associated with swine, factors involving the development of antibiotic resistance in humans in frequent contact with pigs, and the threat posed by the potential use of swine pathogens as agents of bioterrorism that is not understood. So the need for sound research to address these information gaps is great.

Veterinarians and other swine health experts are on the front line to protect human health. They are in key positions to detect new zoonoses that emerge or reemerge early, to communicate unusual events to animal and public health authorities as appropriate in a timely manner, and to institute effective response measures. They are essential in preventing zoonoses from infecting humans at the source by preventing and controlling these diseases in swine, and educating their clients and the communities in which they work and live on the risks and benefits of swine and what they can do to prevent becoming ill from these diseases (e.g., cooking their meat well; maintaining hygienic animal husbandry practices, etc).

Swine and human health have been linked for centuries. Globalization, changes in ecosystem health, and demographic, social, political, and economic factors are facilitating the transmission of pathogens across species. Swine practitioners and others involved with promoting and protecting swine health are also front line public health practitioners, protecting human health and well being as well as animal health in every aspect of their work. It is essential that they are well informed about the causes and challenges of emerging and re-emerging infectious zoonotic diseases as threats to human and animal health, and how most effectively to overcome them.

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