ZOONOTIC DISEASES FROM PIGS

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INTRODUCTION

General Overview of Zoonoses

Zoonotic disease (zoonosis) is most commonly defined as any disease and/or infection which is naturally transmissible from vertebrate animals to man (WHO). The number of zoonosis is estimated to be at least 200, although this number could be much higher, depending how we classify agents. Although already high, this number is expected to increase further, in part due to changes in agricultural practices, human population growth, pathogen evolution, and international trade (Woolhouse and Gowtage-Sequeria, 2005).

The first key point in the above definition is that animals could show clinical signs (disease), or just transmit the agent (infection) to humans. In swine populations, a typical example of the former zoonosis would be a clinical disease in pigs caused by *Streptococcus suis*, whereas a typical example of the latter one would be infection with *Yersinia enterocolitica* which could have high prevalence on swine farms; but without any apparent clinical problems in pigs.

The second key point of the definition is "naturally transmissible". For infection to transmit between an animal and a person, contact between the two is needed and some probability of transmission during this contact. Along the swine and pork production chain, people have variety of contacts with pigs, their products and byproducts. During each stage, opportunities for contacts occur, but frequency and type of contacts differ along that chain. With this variability, high exposure and high risk demographic groups will vary.

As a food animal species, pigs are raised globally but under a variety of production systems. Distribution and occurrence of specific zoonosis in swine is directly linked with this environment. Perhaps the best illustration of this is occurrence of *Taenia solium*, parasite of high public health importance in many undeveloped countries, but not existent in modern swine production.

The objective of this article is to give an overview of selected endemic and emerging zoonotic agents in the modern swine production systems, and to show data about several zoonotic pathogens pertaining to Ontario. For the purpose of this overview, infections will be classified into the following, mutually non-exclusive, categories: foodborne zoonoses, and occupational zoonoses.

FOODBORNE ZOONOSES

Salmonella

Infection with *Salmonella* is one of the most frequent reported causes of enteric illnesses in humans in industrialized countries. Between 1996 and 2001 in Ontario, the incidence of sporadic cases of enteric disease due to *Salmonella* was 22.6 per 100,000 people, which was the second highest incidence among the eight reportable pathogens (Lee and Middleton, 2003).
Between 4.5% and 23% of human salmonellosis worldwide have been attributed to pork (Lee and Middleton, 2003; Hald et al, 2004; Hald and Wegener, 1999). Although proportionally not as significant as poultry and eggs, these statistics place pork as an important animal food-source contributor to salmonellosis, and *Salmonella* as the most important foodborne pathogen of the swine industry in industrialized countries.

While pigs can be infected with many different serovars, clinical disease is caused mainly by *S.* Choleraesuis, *S.* Typhisuis, and *S.* Typhimurium (Fedorka-Cray et al, 2000). Consequently, meat from pigs showing no clinical signs or lesions may be contaminated with *Salmonella*, and quality assurance throughout the production chain is required to lower the contamination level of the final product (Blaha, 1999). Due to public health implications, *Salmonella* surveillance programs may also have a potential to be used for commercial or trade purposes (Davies and Hueston, 2004). Interestingly, *S.* Cholereasuis has not been detected in Ontario recently, whereas *S.* Typhimurium is the most common *Salmonella* serotype in Ontario pigs.

On-farm management procedures have been evaluated as part of the overall effort to decrease *Salmonellae* in the preharvest portion of the production chain. Many of these studies evaluated farm-level management procedures (Beloeil et al, 2004; Lo Fo Wong et al, 2004; Nollet et al, 2004; van der Wolf et al, 2001). Although several management factors that could lower the risk of *Salmonella* shedding are identified, eradicating *Salmonella* from swine farms is unrealistic at this point. A realistic objective is disease control, which should be implemented using combination of measures along the pork production chain.

Yersinia enterocolitica

On the basis of biochemical properties, *Y. enterocolitica* is frequently classified into six biotypes, one of which (1A) is considered non-pathogenic for people, whereas others are considered to be human pathogens (1B, 2, 3, 4, and 5) (Nesbakken, 2005). Based on serological properties associated with another group of antigens, *Y. entercolitica* is additionally classified into approximately 60 serotypes, 11 of which are reported to be associated with clinical illness in people (Bottone, 1999). Sources of *Y. enterocolitica* include the intestinal tract of mammalian, avian, and cold-blooded species (Bottone, 1997), and the environment, including water and soil (Bottone, 1997; Nesbakken, 2005). Environmental isolates are commonly classified as non-pathogenic, whereas animal isolates are typically classified as pathogenic (Bottone, 1997). In particular, porcine sources are frequently associated with pathogenic serotypes (O:3, O:9, and O:5,27) (Bottone, 1997; Nesbakken, 2005), and sometimes with the highly virulent serotype O:8 (Bottone, 1997).

Infection with *Y. enterocolitica* in humans may cause clinical disease affecting the gastrointestinal tract. Clinical signs may include watery, occasionally bloody, diarrhea; signs suggestive of appendicitis; necrotizing enterocolitis; and septicemia (Bottone, 1997). Infection with *Y. enterocolitica* in people may have a greater economic and public health burden than what is suggested by the incidence of reported cases (Nesbakken, 2005). Changes in farming, as well as the food processing industry might have contributed to the occurrence of this pathogen. A feature that likely has an impact on this emergence is the ability of *Y. entercolitica* to multiply at temperatures near 0º C (Nesbakken, 2005).

The annual incidence of reported cases of *Y. enterocolitica* was 3 cases per 100,000 people in Ontario in the period between 1997 and 2001 (Lee and Middleton, 2003). Of the eight reportable and laboratory confirmed enteric pathogens, this was the fourth highest incidence, accounting for a 3.9% of total cases. Approximately 90% of clinical yersiniosis cases are considered to be of foodborne origin (Mead et al, 1999), and pork is an important source (Bottone, 1997; Jones, 2003; Nesbakken, 2005). In Ontario, 72.7% of people with yersiniosis were epidemiologically linked with pork (Lee and Middleton, 2003). In Denmark, the incidence of pork-related human yersiniosis and salmonellosis in 1996 was equal, at an estimated 9 cases per 100,000 people (Nielsen and Wegener, 1997).

Infection with *Y. enterocolitica* in pigs does not cause clinical disease. As such, it does not present a production problem, which disqualifies this pathogen as a subject of passive monitoring through clinical signs followed by diagnostic testing. Results collected during Ontario Swine Sentinel Project confirmed that finishing pigs shed *Y. enterocolitica* (Table 1). The most frequently identified *Y. enterocolitica* in all three years was phenotyped 4, O:3, a bioserotype frequently associated with clinical disease in people. Our data also demonstrated that herds tended to be repeatedly positive with the same bioserotype suggesting the presence of farm environmental contaminants, or alternatively, a cycle of repeated infections in pigs.

Interestingly, association between type of feed and *Yersinia* positivity was detected, but was opposite to common findings for *Salmonella*. For *Yersinia*, liquid feeding was found to be a factor that increases positivity, but this needs to be interpreted cautiously until we have more evidence to support or refute this finding.

Table 1. Pig and herd seroprevalence or prevalence of shedding of selected zoonotic pathogens.

Agent	Year	Pig prevalence (%)	Herd prevalence (%)
SIV H1N1	2001	61.1	87.7
SIV H1N1	2001	24.3	47.2
SIV H3N2 (TX	2003	0.7	9.2
SIV H3N2 (CO)	2003	0.6	7.9
Toxoplasma gondii	2001/03/04	1.4/0.06/0.25	13.7/1.3/3.8
Salmonella enterica	2004	11.4	46.3
Yersinia enterocolitica	2004	12.5	37.5

Toxoplasma gondii

Toxoplasma gondii (*T. gondii*) is a parasite with worldwide distribution. It is able to infect all warm-blooded animals and invade multiple cell types within these animals (Tenter et al, 2000). The life cycle of this parasite is divided into two parts. The sexual cycle occurs in the intestines of cats, which are the definitive hosts. This cycle results in the production of environmentally-resistant oocysts, each containing 4 sporozoites. The asexual cycle occurs in tissues of various mammalian and avian species which are the intermediate hosts. Tissue cysts may have lifelong persistence (Tenter et al, 2000). Tissue cysts stimulate the immune system, so that infected hosts become serologically positive and immune to new infections (Tenter et al, 2000). Seropositivity correlates with potential infectivity of the meat in food-producing animals (Dubey et al, 1995). *Toxoplasma gondii* may infect definitive and intermediate hosts through different routes. For example, orally through the ingestion of: meat containing tissue cysts and tachyzoites (foodborne; horizontal transmission); food and water contaminated with oocysts (foodborne; horizontal transmission); or transplacentary with tachyzoites (congenital; vertical transmission).

Seroprevalence vary between countries and geographical regions, but overall seroprevalence in the global human population is high (Tenter et al, 2000). In a recent serological survey of the human population of the United States, 22.5% tested positive (Jones et al, 2001). Acute infection with *T. gondii* (toxoplasmosis) in healthy people most frequently is asymptomatic or manifests with non-specific symptoms, although outbreaks of clinical disease have been recorded (Ho-Yen, 1992). Similarly, chronic toxoplasmosis in healthy people is most frequently a dormant, asymptomatic, but persistent infection.

In contrast, during acute toxoplasmosis in pregnant women, tachyzoites may transplacentally infect the unborn fetus and cause conditions that range from asymptomatic infection to death or serious disability of children (Gagne, 2001). Moreover, toxoplasmosis in immunocompromised people may manifest as a serious clinical disease with lesions located in the central nervous system (Skiest, 2002) or other organs (Gagne, 2001). Foodborne toxoplasmosis has been reported as the third leading cause of mortality due to foodborne illness in the American population (Mead et al, 1999).

Toxoplasmosis in pigs is not a production problem (Lindsay et al, 1999). However, pork is considered as one of possible sources of foodborne toxoplasmosis in people (Evans, 1992). Changes in the pig farming systems over time have decreased the contact of swine with the outside environment, thus decreasing the *T. gondii* prevalence to a low level (Tenter et al, 2000). This low prevalence is also reflected in the way researchers currently look at swine toxoplasmosis. For example, Van Knapen et al (1995) recommended the use of within-herd seroprevalence of *T. gondii* infection as an indicator of pig contact with the outside environment, and Blaha (1999) considered the production of pork free of *T. gondii* as one of the objectives of quality assurance programs.

In early 1990s the apparent seroprevalence of 6.6 % in finisher pigs and 16.2% in sows was determined (Gajadhar et al, 1998; Smith, 1991) in these studies. In three Ontario studies, based on Ontario Swine Sentinel Project, in 2001, one herd had an apparent prevalence close to 50%, and 6% of herds had an apparent prevalence of ≥10%. In contrast, only one herd in 2004 had an

apparent prevalence of 10% (2 out of 20 tested), while other apparently positive herds in 2003 and 2004 each had only one positive pig (Table 1).

Campylobacter

Incidence of campylobacteriosis in the last several years regularly ranks highest among reported foodborne pathogens. It has been reported that it infects an estimated 1% of the population of Western Europe each year (Humphrey et al, 2007). *Campylobacter* species are particularly important for food safety, *C. jejuni* and *C. coli*, with the former causing the majority of human disease. Poultry is considered as a primary source of *Campylobacter jejuni*, whereas potential importance of swine, measured by prevalence of this type in swine, varies among regions. While in some regions *C jejuni* is frequently found in swine, in others it is almost an accidental finding. In a study of 1200 samples from 80 Ontario swine farms, Varela et al (2007) found Campylobacter in all but 6 samples. However, most isolates were typed as *C. coli* (99.2%) whereas only 2 isolates were classified as *C. jejuni*.

OCCUPATIONAL ZOONOSES

Influenza virus

In the late 1990's, after the emergence of a triple reassortant H3N2 strain of swine influenza virus, the epidemiology of swine influenza virus (SIV) in North America has changed (Olsen, 2002). The triple-reassortant H3N2 viruses (containing genes related to corresponding genes of human, swine and avian influenza viruses) were documented on swine premises from different regions of North America (Karasin et al, 2000c; Zhou et al, 1999). As expected, multiple reassortant SIV variants between the classical swine H1N1 and the triple-reassortant H3N2 virus (and other influenza viruses) emerged as a result of recombination. First, a reassortant H1N2 was detected in multiple herds and regions of North America (Karasin et al, 2000b; Karasin et al, 2002), followed by reassortant H3N1 (Lekcharoensuk et al, 2006; Ma et al, 2006). Although the antigenic drift in the classical swine H1N1 was documented in the early 2000's (Olsen et al, 2000); more recently, a reassortant swine H1N1 (containing PA and PB2 genes corresponding to genes of avian influenza viruses) has been found to be the predominant H1N1 strain isolated from the US swine population (Janke, 2004; Ma et al, 2006). Reassortant swine H1N1 (containing human influenza virus PB1 gene) have also been identified in Ontario swine (Karasin et al, 2000a). In addition, different influenza virus subtypes of wholly avian (H1N1, H3N3, H4N6) and human lineages (H3N2, H1N2) were identified from clinical cases in pigs in Canada (Karasin et al, 2000a; Karasin et al, 2004; Karasin et al, 2006).

Although the spatial distribution of all aforementioned subtypes and variants does not necessarily overlap, and different variants are not necessarily effectively transmitted; the intensive trade between regions in North America provides opportunity for mixing pigs from different sources. Consequently, the number of possible recombinations is high which could represent challenges from diagnostic and clinical perspectives, and concern for public health. Currently swine influenza virus is considered to be an occupational hazard. Although being of clinical importance in swine and in human population, direct transmission of swine influenza viruses to people is

reported at a surprisingly low level. Despite this apparently low occurrence, cases of human influenza due to exposure to swine influenza viruses are always concerning. This is because swine harbor receptors that could interact with human and avian influenza viruses. Thus, the concern is that a virulent virus, such as highly pathogenic H5N1 could emerge in avian population, infect swine and experience changes that could lead to more efficient transmission in people.

From surveys of Ontario herds prior to 2005 we concluded that the sow population was likely free from the selected H3N2 strains (Table 1). In early 2005, an outbreak of triple-reassortant H3N2 SIV in Ontario swine herds was documented (Carman and Ojkic, 2005).

Using sera collected in 2004, based on Ontario Swine Sentinel Project, 919 sera from 46 finisher herds were tested for H1N1 and 920 sera from 46 herds for H3N2. In 2005, 978 sera from 49 herds were tested for both SIV subtypes. At the pig-level, prevalence of antibodies against H1N1 SIV was 13.4% and 14.9% in 2004, respectively. Prevalence of antibodies against H3N2 SIV varied between 2.7% and 25.9% in 2004 and 2005, respectively.

Streptococcus suis

Streptococcus suis is a causative agent of septicemia, neurological signs, endocarditis and arthritis in swine. There are 35 serotypes reported so far, but clinical disease as well as illness in people is associated with serotype 2 (Gottschalk et al, 2007). This disease has been considered primarily as an occupational hazard in people who work in close contact with live pigs and during processing. Recently, two outbreaks were reported in China and atypical characteristics of this infection caused concerns in public health circles. Based on molecular typing, it seems that North American serotype is not molecularly similar to the variant that caused the disease in Asia.

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