REVIEW 10.1111/1469-0691.12262

Socio-economic, industrial and cultural parameters of pig-borne infections

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Abstract

The pork-processing industry has been possibly the fastest growing sector of the food industry in recent years. Specialization, genetic homogenization of the pig population, high density of the breeding population, reduced human–animal interactions, slaughter at a lower age and increased international trade of live animals and pork are parameters that affect, positively or negatively, the emergence of novel pig-borne pathogens, many of which are pig-specific, and many of which have significant zoonotic potential, as observed in recent outbreaks of Nipah virus and *Streptococcus suis* in Southeast Asia and China, respectively. Numerous other pathogens are transmitted to humans through direct contact with or consumption of pig products, and globalization trends in trade and human population movements have resulted in outbreaks of pig-borne diseases even in Muslim countries and in Israel, where pork consumption is religiously prohibited. The role of pigs as potential reservoirs of antibiotic-resistant pathogens or genes encoding resistance, and the role of feral pigs as a reservoir of zoonotic disease, are scientific fields in direct need of further research.

Keywords: Industrialization, Nipah virus, pig-borne infections, religion, *Streptococcus suis*, wild boar, zoonoses
Article published online: 7 May 2013
Clin Microbiol Infect 2013; **19:** 605–610

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Introduction

And also the pig, because even though its hoof is divided, it does not chew the cud. It is therefore unclean for you. You must not eat their meat or even touch their carcasses [1].

He has only forbidden to you dead animals, blood, the flesh of swine, and that which has been dedicated to other than Allah [2].

We observed 112 positions where the porcine protein has the same amino acid that is implicated in a human disease … Most of these changes in humans have been shown to increase risk in multifactorial traits such as obesity … and diabetes … or shown to result in relatively mild phenotypes (for example, dyslexia …) or late-onset diseases such as Parkinson's disease … and Alzheimer's disease [3].

In the 2011 film *When Pigs Have Wings* (original title *Le cochon de Gaza*) directed by Sylvain Estibal and achieving moderate success in cinephile circles, a lacklustre Palestinian fisherman surprisingly finds in his nets a huge Vietnamese pig that fell off a cargo ship. He is a Muslim, so the pig is of little use to him—he is ashamed to possess a filthy animal, even attempting to disguise it as a sheep. He cannot slaughter and eat it, he cannot offer it as a gift to any of his compatriots (it would be considered an insult), he cannot sell it to anyone of Jewish origin, as it is a filthy animal for them too, he has to be extremely careful, as both fundamentalists and the Israeli soldiers present on his roof would be highly critical of his possession, and he fails to persuade a United Nations official (his only Christian acquaintance) into buying it ('who in their right mind would buy a pig?'). Of course, this being cinema, through various misadventures he succeeds in collaborating with a young Russian immigrant in using the pig for breeding purposes. But until then, and even

then, the pig wanders in a politically fragile ground as a loner, wanted by no one. And this is just a recent, brilliant example of the way in which pigs are viewed in popular culture.

Why is it that an animal that shares an impressive percentage of its genetic material with humans (although this genetic homology is less pronounced than the widely circulated proprotion of 98% implies) is perceived in such a notorious manner? Nobody would use the word 'sheep' for swearing, religions consider it filthy, and there are few sympathetic pigs that have entered popular culture: in George Orwell's classic *Animal Farm*, pigs were the bad guys in the end. In Pier Paolo Pasolini's *Porcile* (known as *Pigsty* among English-speaking cinephiles), pigs are directly used as a metaphor for any suppressive social forces that torture the young protagonist, and they finally cause his death by devouring him while he is befriending them. Even the most memorable fictional pig, the Muppets' Miss Piggy, is probably the least sympathetic character in the show (on the other hand, it took a medically trained producer, George Miller, to create culture's most famous heroic pig, Babe, in a surprisingly, budget-wise, successful 1995 film that garnered numerous awards and led to an also successful sequel).

What is constantly feeding this public perception? Admittedly, pigs are not beautiful, like to lie down in mud and dirt, and are not eclectic in their dietary habits; they do not look innocent like sheep, are not faithful like dogs, and do not produce milk or look as reassuringly silly as cows. However, one other factor that, possibly aggravated by the previously mentioned ones, may influence public perception is the magnitude of pig-related infections: just remembering recent history, the latest pandemic, in its beginnings, was colloquially described as swine flu, a name that remains in the minds of the public and media. Ordinary people were not surprised that pigs might be the source of a human infection with major morbidity and significant mortality. Initial reports on the whereabouts of the 2009 H1N1 influenza pandemic stressed the perception of the pig as pulling the pandemic trigger, leading to outrageous responses worldwide, including the culling of all pigs in Egypt: approximately 300 000 pigs were slaughtered, an action that was widely criticized and even viewed by some as an actual political issue, as the majority of the pigs belonged to the Christian minority of Egypt [4]. The public worldwide was less informed about the potential of the novel H1N1 influenza virus to cause a reverse zoonosis, i.e. to be transmitted from animals to humans, and the numerous reports of such small outbreaks in pig farms went unnoticed by the media, although pork product professionals seemed to be better informed at that time, and, in surveys, the pork industry was even considered to be a more reliable source of scientific information than health authorities [5].

The Expansion and Intensification of the pork Industry and its Effect on Human Zoonotic Disease

The pork industry has grown into the most rapidly and geometrically expanding sector of the food industry in recent decades, with the global increase in pork production reaching 80% [6], and the predicted increase in annual pork demands reaching 7% [7]. This increase in pork production has been disproportionate, being observed mainly in certain central and eastern provinces of China, which today produce more than half (51.7 million tons of meat annually) [6] of the total global pork for consumption. This increase could not have been achieved without intensification and industrialization of the production systems, but the exceptional rise in production has dramatically entered in the epicentre of environmental, food chain and industrial interest in recent days.

Rivers of blood: dead pigs floating in the river

Thousands of dead pigs were found floating on the waters of the Huangpu river (a river crossing through Shanghai) in China in early March 2013, the officials tracing the source to pig carcasses in Zhejiang Province [8], where intense pig farming has developed to be the main employment of the population since the 1980s, with the Zheijang province environmental protection bureau estimating that 7.7 million pigs are raised in the province; there are seven pig-processing plants that can host thousands of carcasses [9]. For the inhabitants of this area, the pig industry, even at a family-run, small-farm level, is an extremely profitable employment; for example, the village Zhulin is also called 'to Hong Kong', owing to its constant export of pork to Hong Kong territory. Chinese officials estimate that the Chinese pig population is 700 million, with an annual mortality rate of 2.5% [10]; this extrapolates to Zhejiang province needing to process approximately 200 000 carcasses annually, and this is a number that might not be contained by the state's processing pits. Furthermore, a recent official report revealed the existence of an extensive, extremely profitable black market network of trade in dead animals (which have died from natural causes or disease)—the strict sentences may have driven many participants to abandon this trade, and thus conveniently get rid of the dead pigs by disposing of them in the river. [9] A few days later, dead pigs were found floating on the Liuyang river in Hunan province [10]. Porcine circovirus, which is not pathogenic for humans, was considered to be the cause of death in both cases, and officials have provided assurance that there are no problems regarding the water supply for cities on river banks. However, the dramatic images of thousands of pig carcasses being pulled

from a river crossing one of the world's largest cities outlines how this explosive industrialization of the pork market will raise environmental and public health issues: one needs to remember that waste products from small farms and even larger units may not be disposed of hygienically, particularly when the promise of rapid profit is at stake for previously impoverished populations.

Industrialization parameters

The evolution of the pork industry in recent decades is similar to Henry Ford's mass production line: all aspects of industrialization are aimed at more rapid, more profitable and safer production; the herds are larger (and, even in smaller farms, production tends to be specialized; that is, the farmers breed only pigs and no other domestic animals) and live in high-density areas; feeding is intensive, in order to allow slaughter time to be reduced to approximately 6 months of age; the human–animal interface is minimized; the pig population is largely genetically homogeneous, partly through selection of more productive breeds [9]; and the live animal and meat trades have also grown rapidly (by 260% and 170% since 1985, respectively [10]). These production modifications affect the potential of a zoonotic pathogen to cause human disease: a larger herd in a contained area results in increased potential for intraspecies transmission, but herd specialization and a reduction in animal–human contact minimize the potential of interspecies transmission of a zoonotic pathogen. Genetic homogenization of the pig population may allow for the breeding of herds that are less susceptible to certain pathogens, but we do not know how this homogeneous population might respond immunologically to a novel pathogen.

The Burden of Pig-borne Zoonotic Infections

Pig-related infections are numerous and cause varying human disease burdens. Table 1 summarizes the most important infectious agents that may be transmitted directly or indirectly from pigs to humans, and the extensive list shows that there are two broad categories: pig-specific pathogens, and zoonotic agents that have other animal reservoirs (this categorization may be more complex as we move from genus to species, but is extremely useful in understanding the religious, social and cultural dynamics that may influence the national and international incidence of the infections caused by certain of these pathogens).

A recent review of emerging pig pathogens [6] showed that at least 77 novel emerging species have been characterized since 1985, 30 of which were zoonotic. Thirty-five of these novel species were pig-specific, usually tending to be DNA viruses, whereas RNA viruses were multi-host pathogens. These novel emerging pig-borne pathogens may have resulted from the growth in the pig food industry, as 20 of the 29 top pork-producing countries that have demonstrated increased production in recent decades have also reported a new pig pathogen variant. On the other hand, this correlation may be symptomatic and attributed to enhanced surveillance in an environment of intensified pig breeding and the availability of novel molecular techniques that can relatively easily characterize novel species, particularly viruses.

TABLE 1. Zoonotic pathogens that can be transmitted from pigs to humans

Pathogens	Zoonotic significance[a]
Bacterial	
Bacillus anthracis	±
Brucella suis	*_**
Campylobacter	**
Coxiella burnetii	*
Enterococcus faecalis	*_**
Escherichia coli	*_**
Salmonella	**_***
Staphylococcus aureus	*
Streptococcus suis	****
Yersinia enterocolitica	***
Viral	
Hepatitis E virus	***
Influenza virus	**
Nipah virus	***_****
Norovirus	*
Rabies	±
Rotavirus	*
Parasites	
Cryptosporidium	***
Taenia solium	****
Toxoplasma gondii	*
Trichinella spiralis	***

The higher the number of stars, the greater the significance, while ± denotes doubtful significance.
[a]Author estimates, based on overall disease burden, pig-specific status of the pathogen, and mortality patterns of the human infection induced.

On behalf of the Food and Agricultural Organization, Fournie *et al*. [6] attempted to quantify the potential public health impact of pig-borne zoonotic pathogens by using a complex risk model. Most of the pathogens in Table 1 have a moderate to high theoretical public health impact, although the fact that most of these agents are multi-host pathogens means that the actual public health effect specifically related to pig-breeding and pork consumption cannot be quantified easily. An example is *Toxoplasma gondii*, a parasite with abundant animal reservoirs that can be transmitted through consumption of raw or undercooked pork, but is mainly associated with contact with feline species, lamb consumption, and eating of inadequately washed fresh vegetables [11]: this means that, even if pork consumption was not incriminated in toxoplasmosis, the global burden of the disease would not change drastically. Similarly, it has been demonstrated that <1% of zoonotic human salmonellosis can be attributed to pork consumption in the USA [12]. The same is true of *Bacillus anthracis*, the only agent to achieve a very-high-impact categorization in this

ranking system, but anthrax is not a disease that has entered scientific and public perception as being related to pigs.

Pigs may also serve as amplifiers for zoonotic infections: the typical example is Nipah virus, an emerging paramyxovirus for which fruit bats serve as the natural animal vector. In Malaysia, the site of the initial outbreak, which resulted in 105 deaths, and the area in which there was an expansion of pig-breeding areas overlapped with the natural habitat of fruit bats: thus, secretions of the natural reservoirs infected fruits devoured by pigs, which subsequently infected humans—more than 1 million pigs were slaughtered after the initial outbreak [13], although subsequent minor outbreaks indicate that the lessons from Malaysia were not studied effectively in other Southeast Asian countries.

The *Streptococcus suis* Example

S. suis was considered to be rare pathogen until 2005; an agent known to induce sporadic severe disease manifesting as septicaemia, endocarditis, or, predominantly, meningitis, exclusively in patients in close/direct contact with pigs (butchers, abattoir workers, and pig and pork handlers) [14]. In pigs, *S. suis* can induce disease, particularly in newborn and neonatal pigs, but adult pigs may serve as nasopharyngeal carriers. In 2005, a human and pig outbreak (molecularly demonstrated as being caused by the same *S. suis* strain) in the Sichuan province of China resulted in 204 human cases and 38 deaths, a mortality rate that was higher than expected; the outbreak was characterized by the unexpectedly high percentage of patients developing streptococcal toxic shock syndrome (unexpected because *S. suis* was not considered to be cause of streptococcal toxic shock syndrome until then), the shorter incubation period, the rapid disease progression, and the high mortality rate [15,16]. Since then, scientific interest in *S. suis* has increased, but still there is not a definite answer on whether the 2005 outbreak was caused by a novel, more virulent strain, or whether previous smaller outbreaks were under-reported/underdiagnosed. A subsequent report from Thailand indicated that *S. suis* meningitis was far from being a rare sporadic disease in the area, with a series of 66 cases in the period 2005–2007 showing the traditional disease characteristics [17]. Even more surprisingly, *S. suis* was convincingly demonstrated to be the commonest cause of bacterial meningitis in humans >14 years of age in two different cohort studies from Vietnam in 2011 and 2012 [18,19], indicating that, at least for Southeast Asia, the disease is not as sporadic as was previously considered. Industrialization in the case of *S. suis* may actually limit human exposure, as the trend for rapid culling (at approximately 6 months of age) precludes the exposure of humans to the adult pig carriers. However, as with Nipah virus, the geometric rise in demands for pork processing may overwhelm any state's ability to impose public health regulation in pig farms, and thus may allow for further human exposure, either directly or through consumption of illegally marketed infected meat.

Commercial Pork Products as Mediators of Bacterial Resistance—Significance for Humans

An increasingly worrying trend, which has been the subject of numerous scientific publications in the last decade, is the evolution of antibiotic resistance through zoonotic transmission of genes. It has been shown that veterinarians can acquire methicillin-resistant *Staphylococcus aureus* (MRSA) from pigs, despite the use of traditional protective measures, and pig farmers and their families may also carry community-acquired MRSA of direct zoonotic origin [20,21]; furthermore pigs, can serve as reservoirs for extended-spectrum β-lactamase-producing *Enterobacteriaceae*, as has increasingly been demonstrated in various European countries in recent years [22–24]. In a Greek 2011 study [25], commercially sold pork products sampled from retail shops showed bacterial contamination with Gram-negative pathogens that were predominantly resistant to tetracycline (68.2%), whereas *Escherichia coli* isolates were rarely resistant to ciprofloxacin (15.7%). The majority of the *Staphylococcus aureus* isolates in this study were also ciprofloxacin-resistant, but no MRSA was detected.

The use of antibiotics as growth promoters in the animal-raising industry has been a subject of debate for years. Denmark has been a pioneer in the banning of the subtherapeutic use of antibiotics in the animal industry, and the effect of the prohibition of this use has been ambivalent [26,27]. On the one hand, researchers observed an increased need for the therapeutic use of antibiotics, particularly for pig diarrhoea, in a percentage of the sampled pig farms; on the other hand, the voluntary discontinuation of cephalosporin use resulted in a significant reduction in the occurrence of extended-spectrum cephalosporinase-producing *E. coli*.

Swine-borne Zoonoses in Situations Where Pork Consumption is not Allowed

To study the effect of religious prohibitions on pork consumption on the incidence of pig-borne zoonotic infections, one has to focus on pig-selective pathogens. Toxoplasmosis, as discussed above, is not a suitable model; on the other hand, trichinosis is a proper model, as it is almost exclusively

transmitted through consumption of raw/undercooked pork (the cases attributed to horsemeat consumption are localized in certain countries, although the recent European food-chain scandal with the erroneous processing of horse meat may invert this localization). In 2004, a peculiar outbreak of trichinosis caused by *Trichinella britovi* was observed in Izmir, Turkey: the disease is practically unknown in Muslim countries such as Turkey, and the outbreak was traced to the illegal addition of infected pork in the preparation of beef raw meatballs—a local delicacy [28]. Typically, the incriminated butcher sold his preparations below the average price to local restaurants, which is reminiscent of a line from the 1984 British film *A Private Function*, which is set in early post-war rural Britain, suffering from meat rationing that makes the ownership of a single pig illegal and precious: 'It's not pork, Gilbert, it's power!' pronounces Dame Maggie Smith, similarly to the Turkish butcher. Similarly, in Israel, where the population avoids pork consumption, being either Jewish or Muslim, trichinosis was a very diagnosis until immigrant workers from Thailand moved there, along with their traditional feasts and dishes. Consumption of uninspected wild boar resulted in a trichinosis outbreak involving 26 of the 47 Thai workers [29], and wild boar was also the source of the limited outbreaks aobserved in Christian Arab populations in Lebanon. It cannot be overstated that, in such multi-religious environments, patient history-taking must include the clarification of religious beliefs.

Both outbreaks underline the fact that the modern epidemiology of infectious diseases has limited borders and is affected by changes in established patterns through extended population movements (for employment in the Israeli case) or illegal trade practices (as in the Turkish case).

In stark contrast is the situation in certain secluded communities, such as the small Polynesian islands of Wallis and Futuna, where ownership of pigs equates to social respect and power, despite the fact that these same pigs serve as a reservoir for *Brucella suis*, a pathogen that is now observed extremely rarely anywhere else in the world [30]. Eradication of *B. suis* would require testing and culling of the infected animals, but this practice would lead to social humiliation in these communities.

Feral Pigs as Infectious Sources

As already discussed, feral pigs may constitute the source of pig-borne infections, as with the trichinosis outbreak in Israel. However, the spectrum of zoonotic pathogens that can be transmitted to humans through wild boar is wide, and has actually only recently been recognized, either in the context of wild boar as a potential direct source of human zoonotic infection, particularly in hunters and slaughterhouse workers, or in the context of wild boar as a pathogen reservoir that can serve as a vector for pathogen spillover in domestic animals. Increasing reports of *T. gondii* seroprevalence in feral pigs highlight the latter scenario [31,32], and the same is true of hepatitis E virus, the subject of another review in the present issue, and to a lesser extent for *Trichinella spiralis* [33], but also for mediators of bacterial resistance such as extended-spectrum β-lactamases [34]. A typical example of the former scenario is provided by the increasing reports of brucellosis, Q-fever and leptospirosis in Australian hunters, with the pathogen being transmitted through direct contact with/consumption of feral pigs [35].

Conclusions

The pork industry will probably continue to grow geometrically, at rates that cannot be easily contained by veterinary authorities worldwide. This, along with the environmental alterations that follow, will allow for the constant emergence of novel pig-borne pathogens, many of which will be zoonotic, with varying morbidity and mortality potential [36,37]. Rigorous surveillance may be the only method to contain future outbreaks caused by emerging pig-borne pathogens, although the ideal scenario would be to prevent such emergence: the example of Nipah virus, where humans and pigs encountered an unknown lethal pathogen deep in the forests, should be thoroughly re-evaluated.

Transparency Declaration

The author declares that there is no conflict of interest.

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