

Review

Antimicrobial-resistant Bacteria: An Unrecognized Work-related Risk in Food Animal Production

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The occupations involved in food animal production have long been recognized to carry significant health risks for workers, with special attention to injuries. However, risk of pathogen exposure in these occupations has been less extensively considered. Pathogens are a food safety issue and are known to be present throughout the food animal production chain. Workers employed at farms and slaughterhouses are at risk of pathogen exposure and bacterial infections. The industrialization of animal farming and the use of antimicrobials in animal feed to promote growth have increased the development of antimicrobial resistance. The changed nature of these pathogens exposes workers in this industry to new strains, thus modifying the risks and health consequences for these workers. These risks are not yet recognized by any work-related health and safety agency in the world.

Key Words: Occupational diseases, Agricultural workers, Methicillin-resistant *Staphylococcus aureus*, *Campylobacter jejuni*, Anti-microbial drug resistance

Introduction

The occupations involved in food animal production include farming, animal transport, animal slaughter, and the processing and production of consumer products derived from animals, including poultry, cattle, sheep, pigs, and fish. These occupations have long been recognized to involve significant safety and health risks, particularly injury, ergonomic impacts, and exposures to dusts and bioaerosols [1-3]. However, work-related exposures to pathogens have been less extensively considered

except in cases of zoonotic disease outbreaks such as avian and swine influenzas [4]. This paper presents the case that work-related exposure to pathogenic agents occurs routinely in many sectors of food animal production, and the occurrence of antimicrobial-resistant bacterial exposures presents an especially concerning disease risk for workers and, indirectly, for their families and communities.

Bacteria and other pathogens are known to be present throughout the production of food animals, from farm to fork [5]. The risk they represent has been most often considered in the context of food safety, but not in the context of occupational risk for workers who raise, transport, slaughter, and process animals into consumer food products. Yet, infection and carriage of pathogens are prevalent among animals raised for food, and pathogen contamination has been widely reported in consumer products on the wholesale and retail markets [5]. This knowledge has not been translated into recognition of

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work-related risks from these pathogens.

The relatively recent transformation of food animal production into an intensive and highly controlled process has altered the nature of these risks. Livestock in industrial agricultural systems frequently are fed antimicrobials at non-therapeutic concentrations, purportedly for economic reasons that include growth promotion [6]. Use of one antimicrobial may select for pathogen genes resistant to an entire class of antimicrobials, or even to multiple classes at once, including drugs used in human medicine [6]. These selected antimicrobial-resistant genes can also be passed horizontally within and between bacterial species. Such was the case in the *Escherichia coli* (*E. coli*) O104 : H4 outbreak in 2010 in Germany where mobile genetic elements were passed from proteobacteria to *E. coli*, conferring antibiotic resistance to this pathogenic strain [7]. While the European Union has passed legislation to phase out the use of growth-promoting antimicrobials, use continues to be approved in other countries [8]. In the US, such non-prescription, non-therapeutic agricultural use accounts for 80% of drug production, far exceeding the amount (in kg) of all antimicrobials prescribed for human therapeutic use [6].

Numerous studies have demonstrated associations between the use of antimicrobials in animal feed and negative health outcomes [9-11]. These associations have been both temporal and spatial, and include the presence of drug-resistant pathogens in food animals and their wastes, as well as the likelihood of contamination of consumer-ready poultry and meat products by drug-resistant pathogens. Currently, the consequences of pathogen exposure for workers involved in food animal production are not recognized by any work-related health and safety agency in the world. Such occupational hazards must become a general public health priority, and be examined and reduced.

Work-Related Risks on the Animal Farm & Industrial Food Animal Production Environment

Farm working conditions internationally, including in the US, have changed dramatically in recent decades, partially in response to pressures to increase animal based protein in global food production. Driven by an industrial model of production, modern industrial animal farms are typified by large numbers of animals confined to small areas, resulting in a high animal density and elevated concentrations of airborne hazards as well as animal wastes.

Globally, farm environments, regardless of their scale, contribute to work-related pathogen exposures for farmers,

ranchers, and other animal industry workers, including approximately 1.2 million US workers [12]. Additional occupations with exposure to farm environments include veterinarians and other animal health workers, transportation drivers, temporary, transient and seasonal laborers hired to assist with specific on-farm tasks, and others with business on a farm [13]. Workplace protections for these workers may vary among countries. In the US, agricultural workplaces are exempt from many of the protections extended to larger workforces or industries, and most regulation of farm worker exposure focuses on reducing exposure to pesticides [14]. In countries with similar regulatory policies, little information is reported to authorities on the nature and frequency of farm worker exposures to pathogens.

Farm workers' tasks include direct contact with animals and their wastes, working in an enclosed environment with high animal density, operation of heavy machinery, and performance of veterinary procedures on animals, such as vaccination or minor surgeries, involving needles, blades and other sharps [15]. Such duties expose farm workers to infectious agents, many of them transmittable from animals to humans. On farms, humans (including farmers, family members, or hired assistants) may be at higher risk of contact with microbes [16]. For example, *Staphylococcus aureus* (*S. aureus*) has been found in air inside and downwind of poultry facilities [17]. Some evidence points to occupational exposure to microbes [4,18-20], including antimicrobial-resistant pathogens [21], for farmers and other animal workers. Infections associated with some of these exposures may be exacerbated if the work environment carries a high risk of penetrating injury [18]. In a review study, not only were veterinarians at risk for contracting a disease agent from working with animals, but also they were 42% more likely to do so after they had sustained an accident or injury [18].

Work-related Risks in Meatpacking Plants – Injury and Pathogen Exposure

Animal slaughtering and processing plants are establishments primarily engaged in the slaughtering, dressing, and packing of animal meat for sale or for further processing into other products for human or pet consumption. Although some facilities engage in all of these functions, some plants are uniquely slaughter facilities, and others are uniquely processing operations. This industry employs approximately 500,000 workers in the US [22] and historically has been considered one of the most hazardous, with the highest incidence rates of occupational injuries and illnesses in recent years of all occupations in the US [22].

The tasks within the production line of slaughter and processing plants include handling livestock, slaughtering animals, cleaning carcasses, and the cutting, dressing, and packing of meat. Support tasks include cleaning floors and equipment and sharpening knives. Many of these tasks carry high risks of cuts and lacerating injuries [22]. Moreover, these tasks can expose workers to bacterial infections, which have been documented frequently in these industries, including infections by *Staphylococci*, *Streptococci*, *Mycobacterium spp.* and *Bacillus anthracis* [19]. Risk of exposure to these pathogens within the workplace can be inferred by the fact that live animals are transported to slaughter carrying a range of zoonotic pathogens, and meat products that are sold to consumers have also been found to be contaminated by these pathogens, indicating a failure to reduce or control pathogen contamination or cross contamination during slaughter and processing [23].

The speed of the production line has been reported as one of the main factors for cuts and lacerations [24], and this speed is especially high in the industrial plants where tens of thousands of animals are processed in a day. Animals raised on industrial farms with antimicrobial growth promoters are sent to these industrial plants. The concomitant presence of antimicrobial-resistant pathogens in the animals and the high prevalence of open skin wounds on the staff at these facilities may result in a dramatic increase in the risk of infection and illness. This was observed in a British study of skin infections in slaughterhouses which found high rates of beta-haemolytic group L *Streptococci* and *S. aureus* in poultry-meat handlers and in red-meat handlers [25]. Since lacerating injuries are of considerable concern in poultry processing and meatpacking, the coincidence of these risks with the presence of antimicrobial resistant pathogens, particularly methicillin-resistant *S. aureus* (MRSA), is of concern.

Health Impacts of Antimicrobial-resistant Bacteria in Food Animal Production Occupations

Work-related exposures to antimicrobial-resistant pathogens can have important health implications for food animal industry workers. They can be exposed to antimicrobial-resistant bacteria through different routes of transmission including inhalation, dermal contact, and ingestion. The risk of work-related injury in conjunction with pathogen exposure may increase the severity of health consequences in food animal production workers. Workers may be exposed to pathogens that can cause both acute illness and long-term sequelae [26,27]. Drug-resistance can increase the difficulty and expense of treat-

ment. Pathogens may also spread from workers to their family members, including children and the elderly, as well as to the community.

Workers in close contact with large numbers of animals are exposed to zoonotic pathogens, including *Campylobacter jejuni* (*C. jejuni*), *E. coli*, and *Salmonella*, which are associated with acute gastrointestinal illnesses that can cause severe symptoms, such as bloody diarrhea [27]. Infections that are multidrug-resistant, such as multidrug-resistant *S. aureus*, pose a particular challenge and can be extremely difficult to treat.

In addition to acute illness, certain pathogens prevalent in the food production environment have also been found to be associated with long-term or chronic health sequelae, including hemolytic uremic syndrome, reactive arthritis, inflammatory bowel disease, and septicemia [27]. Inflammatory peripheral neuropathies, particularly Guillain-Barré Syndrome, can occur after *C. jejuni* infection [28]. Antimicrobial resistance may be relevant to the severity of illnesses and sequelae. Infection with antimicrobial-resistant *Salmonella* has been associated with increased risk of hospitalization, longer duration of illness, and invasive infection [27].

Infections and sequelae from exposure to pathogens that may be ubiquitous in animal production environments are of increasing concern [28]; however, failure to collect data on exposures and illness makes it difficult to determine the attributable risk of these exposures to the overall burden of disease.

In the next sections, we examine occupational risks for pathogen exposure through two specific examples; multidrug-resistant *S. aureus* and antimicrobial-resistant *C. jejuni*.

Work-related Exposure to Multidrug-resistant *S. aureus* in Livestock Production

S. aureus exposure is of growing concern in the food animal industry. This gram-positive bacterium can cause a wide array of infections ranging from relatively benign skin and soft tissue infections to fatal sepsis and endocarditis [29]. *S. aureus* colonization is common among humans and typically asymptomatic, but carriers are at excess risk for infection as compared to non carriers [30]. Methicillin, oxacillin and other related beta lactam antimicrobials historically have been the most successful antimicrobial therapeutics for *S. aureus* infection, but the emergence and proliferation of MRSA has led to rampant treatment failures, increased morbidity, and death. Much of what we know about the epidemiology of *S. aureus* has been garnered from studying MRSA infections, which are typically grouped in: 1) those that are found in humans with healthcare contact, called hospital-associated MRSA (HA-MRSA); or 2) those that are

unrelated to hospital exposures, called community-associated MRSA (CA-MRSA). Recently, a third group of MRSA related to livestock exposure has gained recognition, called livestock-associated MRSA (LA-MRSA) [29].

Most of what we know regarding current occupational exposure to *S. aureus* in livestock production is based on one particular *S. aureus* sequence type, MRSA ST398. Studies conducted in Europe and Canada reveal that veterinarians and livestock workers are more likely to test positive for MRSA ST398 than those employed in other fields [29,31]. Epidemiological investigations suggest that MRSA ST398 may not be transmitted person-to-person as readily as other sequence types more commonly associated with human infection [29], but those in direct contact with livestock are at higher risk for colonization [29]. A number of serious infections related to livestock-exposure to MRSA ST398 have been reported [29].

The risks of livestock exposure to *S. aureus* include the families of those employed in the industry. For example, the index case of MRSA ST398 was an infection in a young Dutch girl whose family owned a hog farm [29]. Epidemiologists investigating the case tracked the girl's infection back to her farm, finding that her parents and the pig herd also tested positive for the same MRSA ST398 [29]. Other studies also suggest that farmers and livestock workers can transmit *S. aureus* to their families [29]. Further studies are required to determine risk factors for these events in terms of contact with contaminated environmental media, direct skin-to-skin contact with workers, secondary exposure to contaminated clothing, or consumption of food from the farms.

Work-related health risks extend beyond MRSA. Livestock-associated methicillin-susceptible *S. aureus* (MSSA) isolates are frequently resistant to tetracycline, clindamycin, and erythromycin (intermediate resistance), which are common alternatives to beta lactams [31]. Likewise, resistance to two other alternatives, ciprofloxacin and quinupristin-dalphopristin, are disproportionately prevalent among chicken- and turkey-associated *S. aureus*, respectively [32]. Resistance to all five of these antimicrobials limits therapeutic options for livestock-associated *S. aureus* infections, particularly among the 10 % of the human population who are allergic to beta lactams. The work-related risks related to *S. aureus* exposure in livestock production are not well studied. While substantial research has been conducted on MRSA ST398, future research must include other sequence types as well as both MRSA and MSSA.

Recent data may suggest a shift in MRSA ST398 epidemiology and virulence, as it is now one of the most rapidly emerging MRSA sequence types in Denmark and the Netherlands. *S. aureus* can evolve rapidly through the acquisition

of sporadic genetic mutations and horizontal acquisition of mobile genetic elements. The massive flocks and herds of food animals that exist globally provide ample opportunity for the emergence of novel virulence types. Livestock workers constantly contact animals, and hence may be exposed to a variety of *S. aureus* strains testing their ability to colonize and infect humans.

Work-related Exposure to Antimicrobial-resistant *Campylobacter*

Campylobacter, an avian commensal, causes an acute gastrointestinal illness campylobacteriosis, which is the leading bacterial cause of diarrhea worldwide [33], and can be associated with both acute illness as well as long-term sequelae. *C. jejuni* infection is also the most commonly identified antecedent to Guillain-Barré Syndrome, an autoimmune peripheral neuropathy that is the most frequent cause of acute flaccid paralysis globally [34]. In addition to foodborne exposure, work-related exposure to *Campylobacter* may also be an important source of infection. Increased levels of anti-*C. jejuni* antibodies have been reported in poultry workers [35] and significant associations have been found between exposure to farm animals and *Campylobacter* infection [36]. Significant increases in self-reported symptoms of peripheral neuropathy among poultry house workers compared to community referents has been reported [35], and similar epidemiologic findings were documented in a large cohort of swine, poultry, and cattle farmers in the Agricultural Health Study [28].

Ciprofloxacin, a fluoroquinolone antibiotic, is an important treatment for human *Campylobacter* infection, as well for infections caused by other pathogens including anthrax. Fluoroquinolones have also been used in food animal production in several countries. In the US, fluoroquinolones were used in poultry production from 1995 until 2005, when they were banned due to increasing concerns about human health impacts [37]. In regions of the US where fluoroquinolones were used in poultry production, the prevalence of fluoroquinolone-resistant bacteria, particularly *Campylobacter*, in poultry, poultry products, and humans increased after the introduction of fluoroquinolones into agriculture [37]. Fluoroquinolone resistance has also increased in other pathogens including *Salmonella* [37].

While fluoroquinolone resistance has received attention in the context of foodborne *Campylobacter* infections, the potential risk for work-related exposure to and infection with fluoroquinolone-resistant pathogens should also be of concern. We have reported on the presence of drug-resistant *Campylobacter* within confinement houses for poultry and swine [38]. *Campylobacter*

resistant to fluoroquinolones as well as other antibiotics have also been reported on surfaces within slaughter and processing plants [39]. Given the evidence for the presence of antimicrobial-resistant *Campylobacter* in food production environments, and for the exposure of food-production workers to *Campylobacter* [28,35], work-related exposure to antimicrobial-resistant *Campylobacter* should be considered a potential occupational risk.

Conclusions and Recommendations

This paper briefly has reviewed evidence supporting the importance of evaluating pathogen exposures for workers in food animal production, including farm workers, veterinarians, and workers in slaughter and processing plants. Moreover, exposure to antimicrobial-resistant pathogens, such as MRSA, may represent an emerging health risk for workers in food animal production. In addition, in the case of MRSA (which is known to be carried by several species of livestock and poultry, and to be present in slaughterhouses), the coincident risks of pathogen exposure and lacerating injuries may result in heightened risks of serious infections among this workforce. Based on this evidence, there is an urgent need for work-related medicine and health care professionals, and worker organizations to recognize these exposures as work-related health risks in order to implement appropriate measures for risk reduction.

Recognition and response should include several steps. First, eliminating or restricting the use of antimicrobial drugs in animal feeds can reduce the development of antimicrobial-resistant pathogens. Second, disease can be prevented through targeted monitoring and surveillance of the presence of pathogens in work environments and exposures in workers. Third, contact with pathogens can be controlled at least partially by improving work conditions, specific work practices, and the industrial design to facilitate sterilization of equipment and reduction of lacerating injuries. Fourth, workers may be protected through provision and training in use of personal protective equipment as well as ensuring access to on-site facilities for hygiene.

At present, pathogen exposures are not considered work-related risks by any work-related health authority in these industries, except in the case of outbreaks such as highly pathogenic avian influenza (HPAI). The available evidence strongly indicates that antimicrobial-resistant pathogens are typically present in animal confinement houses as well as in slaughter and processing plants. Truck drivers and other workers involved in the transportation of livestock between farms and from farms to slaughterhouses are an important risk group since they are in contact with and connect several of these facilities [13].

Efforts to address work-related risks from exposure to infectious disease agents should consider the continuum of animal-related occupations, from farmers to slaughterhouse and processing-plant workers, veterinarians, and other professionals. Further, such efforts, while national or regional in scale, should account for the global nature of pathogen movement and transfer of antimicrobial resistance.

Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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