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Pigs and MRSA: What are the human health risks and to whom?

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Summary of Findings:

- MRSA (methicillin resistant *Staphylococcus aureus*) has been a major cause of human infections for over 50 years, particularly in hospitals. MRSA is among the foremost bacteria of concern regarding antimicrobial resistance.
- From the mid 1990s, MRSA epidemiology changed globally as new MRSA variants caused infections in otherwise healthy people having no exposure to hospitals.
- Since 2004, the discovery of novel MRSA variants in livestock has raised concerns about potential public health impacts of animal reservoirs of MRSA.
- A specific MRSA lineage (ST398) is the focus of concern in livestock. ST398 was unknown before being found in patients in the Netherlands who had exposure to pig farms. ST398 MRSA is now known to occur in many countries and species (cattle, poultry, and horses).
- Exposure to MRSA from livestock is a concern for people working with live animals (farmers, veterinarians). Risk to the general public via other routes appears minimal.
- MRSA of livestock origin are less likely to persist and spread in people than MRSA of human origin. No community outbreak of ST398 MRSA infection has been reported anywhere, nor has a single case of clinical infection been reported in the United States of America (USA).
- The impact of ST398 MRSA on human illness has been very low. Policy strategies to reduce ST398 should be assessed with respect to feasibility and cost prior to implementation.

How prevalent are MRSA in pig populations and farmers?

S. aureus are normal inhabitants of pigs, and occur in all herds. The prevalence of MRSA in pig herds varies widely (0 to 50%) among European countries. The pig herd prevalence of MRSA in North America is uncertain, but appears lower than in many European countries. MRSA prevalence (>50%) in pigs in positive herds, but has minimal effect on swine health. *S. aureus* is found in dust and air on pig farms, and healthy people working in barns often harbor the swine *S. aureus* variants in their noses. MRSA can be detected in 20 – 80% of healthy workers on MRSA positive herds, much more than in the general public (1.5% in the USA; <0.11% in the Netherlands). The risk of exposure to MRSA from livestock is mostly limited to people with direct animal contact and their immediate families.

Do people get permanently colonized by MRSA acquired from livestock?

The capacity of *S. aureus*/MRSA strains of livestock origin to colonize, spread, and cause disease in humans remains uncertain. It appears that ST398 persist only briefly (hours to days) in most people, but some may be colonized for months to years and not necessarily develop an infection. Studies in Dutch hospitals found ST398 spread between people was some fourfold less likely than for human MRSA strains. No community outbreak of ST398 MRSA infection has been reported to date. Other MRSA lineages also occur in pigs (e.g., ST9 in Asia, ST5 in North America), but their public health implications are not known.

Do MRSA acquired from livestock cause significant disease in humans?

A study of a pig dense region of Denmark concluded there is ‘an infectious occupational exposure of huge quantitative dimensions but of unknown clinical importance’. ST398 MRSA have been found in both superficial and systemic infections of humans, confirming a *non-zero* risk. The common statement that ST398 cause a large proportion of MRSA cases in countries like the Netherlands is misleading as it is based on studies that include people who are colonized (e.g., positive nasal swabs), but not infected. Analyses of actual infections show ST398 MRSA are much less prevalent, particularly among serious MRSA infections such as bacteremia.

Globally, there has been only one ST398 MRSA fatality reported over 9 years (compared to an estimated 18,000 annual MRSA fatalities in the USA alone). Population-based estimates (cases per 100,000 people per year) of the incidence of ST398 MRSA infections in pig dense areas where ST398 MRSA are prevalent are: 2 clinical infections, 0.38 invasive infections, and 0.04 bacteremia cases in the Netherlands; and 0.25 clinical infections in Denmark (none invasive). In contrast, the CDC estimates 31.8 invasive cases and 6.3 fatalities from MRSA per 100,000 people per year in the USA. Although ST398 MRSA have been found in nasal swabs of USA livestock, farmers, and veterinarians, there has yet to be a case of infection with ST398 MRSA reported in the USA. Future reports of ST398 MRSA infections, particularly minor skin infections, are certain to occur and will need to be assessed in the context of the substantial burden of MRSA infections due to human adapted strains in the USA.

How are livestock-associated MRSA different from MRSA that cause infections in hospitals?

Reports of medically significant ST398 MRSA infections in healthy livestock workers are few despite high exposure to MRSA. Overall, *S. aureus* are remarkably versatile and virulent bacteria that can survive and multiply in many environments. However, ST398 MRSA from pigs appear to contain few of the known *S. aureus* virulence factors (genetic components that enable them to cause severe infection), which may explain the rarity of serious clinical infections. Recently, ST398 variants were found in urban populations in the USA, China, and Europe without livestock contact. These strains are genetically distinct from animal variants, indicating that not all ST398 infections can be attributed to livestock.

How or why did livestock-associated MRSA come to be?

The reasons for the emergence of ST398 in pigs are not understood and are likely complex. Although use of antimicrobials for growth promotion has been suggested, this simplistic hypothesis conflicts with the emergence of ST398 MRSA after growth promotion use was phased out in Europe. More plausible candidates are increased feeding of zinc to pigs consequent to removal of growth promotion antimicrobials, and use of long-acting injectable cephalosporins for livestock. Ongoing research indicates that pigs harbor diverse populations of methicillin-susceptible *S. aureus* (MSSA). In the USA, the predominant lineages of MSSA in pigs correspond with MRSA variants found in pigs around the world (ST398, ST9, ST5). This suggests that preexisting variants of *S. aureus* that are normal inhabitants of pigs have acquired resistance to methicillin, rather than the recent emergence of novel organisms in livestock.

What policy options should be considered?

Other than increasing surveillance, only the Netherlands (where people carrying MRSA are isolated and treated before admission to hospitals), has changed health policy in response to ST398 MRSA. Hospitals now screen all livestock workers (who are commonly positive for ST398 MRSA) and this policy markedly increased health care costs. However, due to the rarity of severe ST398 MRSA infections and lower transmissibility, it is argued that less stringent containment measures are warranted in hospitals for ST398 than human MRSA to reduce costs. The theoretical case for reducing MRSA in livestock is self-evident, but no strategies to do so have been defined yet alone assessed with respect to feasibility or cost.

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