

## Highly antibiotic-resistant strain of MRSA that arose in pigs can jump to humans

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A highly antibiotic-resistant strain of the superbug MRSA has emerged in livestock in the last 50 years, probably due to widespread antibiotic use in pig farming. Credit: Dan Tucker

A new study has found that a highly antibiotic-resistant strain of the superbug MRSA—methicillin resistant *Staphylococcus aureus*—has



emerged in livestock in the last 50 years, probably due to widespread antibiotic use in pig farming.

The strain, called CC398, has become the dominant type of MRSA in European livestock in the past fifty years. It is also a growing cause of human MRSA infections.

The study found that CC398 has maintained its antibiotic resistance over decades in pigs and other livestock. And it is capable of rapidly adapting to human hosts while maintaining this antibiotic resistance.

The results highlight the <u>potential threat</u> that this strain of MRSA poses to public health. It has been associated with increasing numbers of human infections, in people who have and have not had direct contact with livestock.

"Historically high levels of antibiotic use may have led to the evolution of this highly antibiotic resistant strain of MRSA on pig farms," said Dr. Gemma Murray, a lead author of the study, previously in the University of Cambridge's Department of Veterinary Medicine and now at the Wellcome Sanger Institute.

She added: "We found that the antibiotic resistance in this livestock-associated MRSA is extremely stable—it has persisted over several decades, and also as the bacteria has spread across different livestock species."

Antibiotic use in European livestock is much lower than it has been in the past. But the researchers say that ongoing reductions in antibiotic use on pig farms—due to recent policy changes—are likely to have a limited impact on the presence of this strain of MRSA in pigs because it is so stable.



While livestock-associated CC398 is found across a broad range of livestock species, it is most commonly associated with pigs. Its rise has been particularly evident in Danish pig farms where the proportion of MRSA-positive herds has increased from less than 5% in 2008 to 90% in 2018. MRSA doesn't cause disease in pigs.



Intensification of farming, combined with high levels of antibiotic use in livestock, has led to particular concerns about livestock as reservoirs of antibiotic-resistant human infections. Credit: Mark Holmes

"Understanding the emergence and success of CC398 in European livestock—and its capacity to infect humans—is vitally important in managing the risk it poses to <u>public health</u>," said Dr. Lucy Weinert in the



University of Cambridge's Department of Veterinary Medicine, senior author of the paper.

The success of CC398 in livestock and its ability to infect humans is linked to three mobile genetic elements in the MRSA genome. These are chunks of genetic material that give the MRSA certain characteristics, including its resistance to antibiotics and its ability to evade the human immune system.

The researchers reconstructed the <u>evolutionary history</u> of two particular mobile genetic elements called Tn916 and SCCmec that confer antibiotic resistance in MRSA, and found they have persisted in a stable way in CC398 in pigs over decades. They also persist when CC398 jumps to humans—carrying with them high levels of resistance to antibiotics commonly used in farming.

In contrast, a third mobile genetic element called  $\phi$ Sa3—which enables the CC398 strain of MRSA to evade the <u>human immune system</u>—was found to have frequently disappeared and reappeared over time, in both human-associated and livestock-associated CC398. This suggests that CC398 can rapidly adapt to human hosts.

"Cases of livestock-associated MRSA in humans are still only a small fraction of all MRSA cases in <u>human populations</u>, but the fact that they're increasing is a worrying sign," said Weinert.

Intensification of farming, combined with high levels of antibiotic use in livestock, has led to particular concerns about livestock as reservoirs of antibiotic-resistant human infections.

Zinc oxide has been used for many years on pig farms to prevent diarrhea in piglets. Due to concerns about its environmental impact and its potential promotion of antibiotic resistance in <a href="https://livestock.nih.gov/livestock">livestock</a>, the European



Union will ban its use from this month. But the authors say this ban may not help reduce the prevalence of CC398 because the genes conferring <u>antibiotic resistance</u> are not always linked to the genes that confer resistance to zinc treatment.

MRSA was first identified in human patients in 1960. Due to its resistance to antibiotics it is much harder to treat than other bacterial infections. The World Health Organization now considers MRSA one of the world's greatest threats to human health.

The findings are published today in the journal *eLife*.

**More information:** Marta Matuszewska et al, Stable antibiotic resistance and rapid human adaptation in livestock-associated MRSA, *eLife* (2022). DOI: 10.7554/eLife.74819

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