



food annualagenda

Superbugs in our Food: Should We be Worried?

Livestock Associated Methicillin Resistant *Staphylococcus aureus* ST398 (LA MRSA ST398) and other apparently livestock associated *Staphylococcus aureus* in the UK

Rhiannon Wood BBSRC PhD Candidate, supervisor Mark Holmes, advisor Milorad Radakovic





Overview

- Background
 - Foodborne illness
 - Foodborne bacteria
 - Resistant bacteria
 - Staphylococcus aureus
 - Resistant *Staphylococcus aureus*
 - Livestock associated *Staphylococcus aureus*
- Outline of work
- Aims of work
- Preliminary findings
- Summary
- Conclusions





Background: Foodborne illnesses

- c. 600 million people (about one in 10 world population) fall ill each year due to contaminated food
- Approx. 420, 000 die every year across the world.
- Usually caused by bacteria, viruses, parasites or chemicals entering body through contaminated food or water
- Global trade increases risk of dissemination of foodborne contamination making drivers and risks an international concern.

Information from WHO, 2020 (https://www.who.int/NEWS-ROOM/FACT-SHEETS/DETAIL/FOOD-SAFETY





Salmonella, Campylobacter and enterohaemorrhagic E. coli are among the most common foodborne pathogens affecting millions of people annually sometimes with severe and fatal outcomes.

Listeria and *Vibrio Cholerae* are also significant foodborne organisms.

Information from WHO (https://www.who.int/NEWS-ROOM/FACT-SHEETS/DETAIL/FOOD-SAFETY





Antimicrobial resistance thought to be one of the most significant global threats, making previously treatable diseases and conditions untreatable.

The finding of AMR in food products is therefore of concern.

Resistance is usually brought about by selection for pre-existing resistance genes. This may be due to overuse or misuse of antimicrobials in human and veterinary medicine and in agriculture.





However in order to assess the significance of a "superbug" (aka a resistant organism) in your food it is necessary to know:

Is it a pathogen?

- If so, how is it pathogenic? Eg ingestion? Colonisation of skin?
- How severe is the disease which it can cause?
- How easily is it spread? In environment, food, host-host
- Can it survive in the fridge/freezer/storing process?
- How easily is it destroyed by normal procedures likely to be carried out in the domestic environment?
- Can it acquire new genes or transfer its genes to other bacteria (on or off host)?

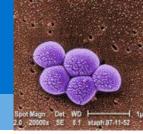


Read all about it?









Common commensal of the skin and upper airways (nose and throat) of many species including humans.

Commensal organisms are normally carried **asymptomatically**, as part of your normal flora.

Estimates of carriage rates vary around the world but it is thought that nasal carriage in healthy UK people are around **25-30%**

There are **many sequence types** of *S.aureus*, **differing characteristics**.

WHO information mentioned earlier does not mention Staphylococcus aureus and it is **not thought to be a major foodborne pathogen.**

Nevertheless, *S.aureus* does possess enterotoxins and is capable of causing foodborne illness, although it is more commonly associated with other disease such as skin and wound infections, toxic shock syndrome, septicaemia, mengingitis, osteomyelitis, endocarditis and pneumonia.

You would therefore probably be somewhat alarmed by the finding of this bacteria in your food!





What is MRSA?

- Methicillin Resistant Staphylococcus Aureus emerged in humans in the **1960s** shortly after the introduction of the antibiotic methicillin.
- Name has persisted although methicillin has now been replaced with other antibiotics and MRSA is typically **multidrug resistant**.
- Studies have shown approx. **1-3% nasal carriage rate** of MRSA in healthy UK humans.
- As with non-resistant strains, most of these people will be carrying it **asymptomatically**.
- It is usually only when they go to hospital for surgery or they have another condition or become immunocompromised that it causes a problem.
- In these cases the **consequences can be extremely serious**.
- As a result people being admitted to hospital in the UK now routinely swabbed for MRSA so treatment can be planned accordingly.





What is livestock associated MRSA?

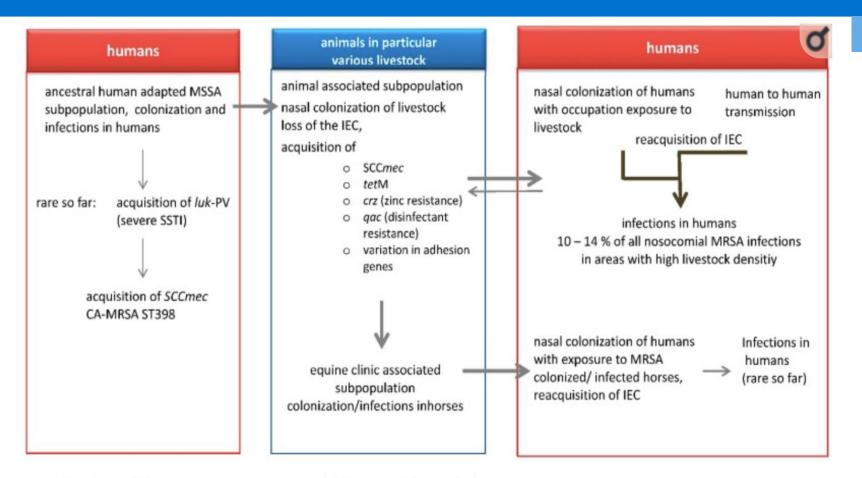
- *S.aureus* is roadly categorised as Healthcare acquired (HA), Community acquired (CA) and Livestock associated (LA).
- Boundaries becoming increasingly blurred.
- Livestock associated MRSA was first identified in the early 2000s
- Sequence type 398 being the most dominant LA MRSA ST in Europe, north America and some other parts of the world, while ST9 is the dominant LA MRSA ST in Asia.
- LA MRSA ST9 has been associated with significant disease and mortality but for the purposes of this talk I will be focusing on LA MRSA ST398 as my work looks primarily at samples from the UK.





Staphylococcus aureus CC398 in humans and animals

Figure 1 from "Livestock-Associated MRSA: The Impact on Humans", Cuny, Wieler and Witte, 2015



Abbreviations: IEC = immune evasion gene cluster; SSTI: skin soft tissue infection

Staphylococcus aureus CC398 in humans and in animals.





euobserver

SECTION / OPINION

OPINION

Danish pigs are bacteria 'time bomb'



article MRSA cases in Denmark doubled in just one year

AFP/The Local news.denmark@thelocal.com

@thelocaldenmark 15 November 2014 12:28 CET+01:00

mrsa

in



Photo: V. Meadu/CCAFS/CGIAR/Flickr

The Local news.denmark@thelocal.com @thelocaldenmark

12 February 2015 08:16 CET+01:00

The variant of MRSA that can be transmitted from livestock to humans used to account for just two percent of all MRSA cases but in 2014 the pig-borne bacteria accounted for 43 percent - "an epidemic that is out control", an expert warned.

Second Danish death attributed to MRSA



Neither of the individuals who have died from MRSA this year were in direct contact with pigs. Photo Claus Fisker/Scanpix

A second person has died in Denmark from swine MRSA, the latest report from the Danish State Serum Institute (SSI) has revealed.

According to SSI's third quarter report, a patient was hospitalised with a hardening of the arteries and underwent several procedures before dying within 30 days of being infected with MRSA CC398, a variant that can be transmitted from livestock to humans.

"There were three new incidences [of MRSA] in the third quarter, one of which ended in death. Throughout all of 2014 there have been six cases of toxaemia in total, two of which ended in death with 30 days," SSI spokesman Robert Skov told DR.

Two leading experts said in August that between 6,000 and 12,000 people are currently infected with MRSA CC398 in Denmark. It has also been found that at least 13 babies whose parents work in the swine industry have been infected with MRSA.





Key features of LA MRSA ST398

- Present in wide range of animals and the environment
- In food products of animal origin
- More common in **intensively farmed** species
- Transmissible to humans
- Less able to transfer human to human than some other sequence types
- Many resistance genes, fewer virulence genes, lack enterotoxins
- **Potentially dangerous and occasionally fatal** to humans, especially to vulnerable patients
- Like other *S.aureus*, can live between 4 and 65°C





UK situation

- Been found here in **several species** including humans, pigs, cattle, horses, poultry
- **Sporadic reporting** of human cases to PHE and counterparts in Wales, Scotland and NI
- Been isolated from milk and meat
- Media scare stories
- Lack of engagement by some sectors of UK livestock industry (notably pork industry)
- Not much UK data





OF BBSRC Doctoral Training Partnerships

Does LA MRSA matter?

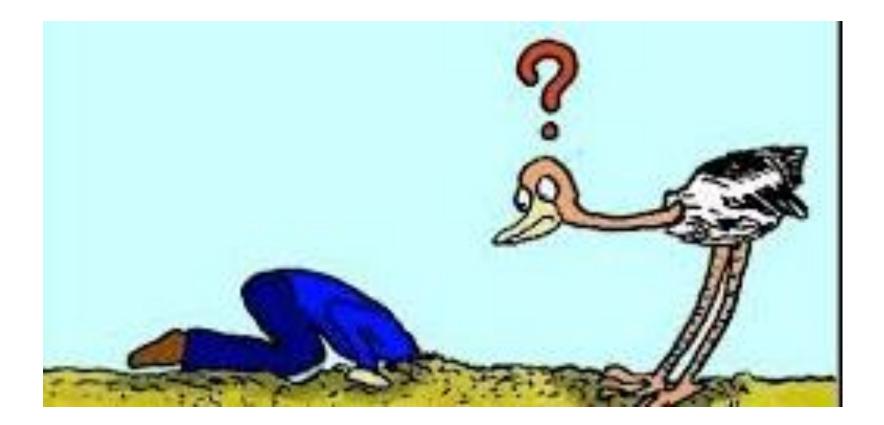
- Not a common cause of disease in pigs
- Less commonly implicated in infections in humans than other sequence types (eg HA and CA strains)
- Few enterotoxins and elimination by adequate hygiene make presence in meat less important than might otherwise be

BUT

- Can cause illnesses and fatalities in people
- **Prevalence increasing** more chance of problems and more chance of getting into more **vulnerable population.**
- Readily able to exchange genes with other bacteria current virulence and resistance profiles not necessarily going to stay that way already evidence its **profile is changing**













Three strands:-

Meat – A study replicating the one done a few years ago looking at pork and chicken bought from supermarkets (also raw pet food)

Pig farms

- 3 "whole farm" studies sampling pigs and their environment at all production stages, along with farm workers
- 12 "poo and people" studies using pig poo and human nasal swabs

People, in addition to workers on pig farms (see above);-

- Vet students on EMS placements
- In conjunction with PHE and PHW. Official Veterinarians (OVs), Meat Hygiene Inspectors (MHIs) and Plant Inspection Assistants (PIAs) working in abattoirs and packing plants





Aims of work

- Provide information regarding population structure of LA-MRSA ST398 in the UK by looking at new isolates from farms, humans, meat
- Assess data from sensitive and resistant *Staphylococcus aureus* isolates within the context of other UK *S.aureus* isolates and findings in other countries (both published and unpublished data)
- Look for evidence of any dominant pig-associated *S.aureus* lineages in samples obtained from farms and for on-farm changes and mixing of bacterial genomes
- Provide some basic information on prevalence and relative risk of LA-MRSA ST398 carriage in certain sectors of the UK human population
- Assess prevalence of LA-MRSA ST398 in pig farms and of factors which may appear to be associated with the MRSA status of a herd by looking for differences between farms which may contribute to positive or negative status





1. Meat – *S.aureus* isolated from a large number of samples. 4 MRSA were isolated, all from pork sausages or mince, as with Hadjirin et al 2015. MRSA are ST398. Various MSSA found in pork and chicken,

2. Farms – *S.aureus* was found on 12/15 (80%) farms and MRSA in 5/15 (33.3%). Sequencing data shows MRSA to be ST398.

3. People -

- Students found to be carrying MSSA and MRSA at beginning and end of placements, slight increases seen by end of placements. S.aureus carriage similar to general population. MRSA higher than general population. MRSA ST398 found including from students working with pigs.
- OV/MHI/PIA MRSA and MSSA found both at beginning and end of day, fewer positive swabs by the end of the day. Carriage rates higher than general population. ST398 found including (but not exclusively) in those working with pigs. However all but one ST398 were actually MSSA. It is not yet clear whether the other mrsa sts found are livestock or human strains.
- Farm workers MSSA and MRSA found in farm workers. Carriage rates higher than general population. MRSA ST398 found where farm positive ie livestock contact relevant.





Mostly ST398,

those which are not are: ST1, ST80 or novel/unknown ST

st1 and 80 are from **humans in the OV study**. They had fewer other resistance genes than the ST398 but more virulence including enterotoxin and one with pvl

ST398 was found in all settings apart from chicken meat and showed greater diversity of resistance genes than other sequence types, but fewer virulence genes with no enterotoxins, PVL (skin/soft tissue) or TSST.





Summary of preliminary meat findings

- Various strains of S.aureus were found in chicken meat, pork and raw pet food
- Some of these were MRSA. Ie "Superbugs"
 - These had multiple resistance genes but fewer virulence genes and no enterotoxins, TSST or PVL
- MSSA found had resistance genes along with virulence genes including enterotoxins, TSST and PVL in some cases
- Some of these may be from human contamination at abattoir/cutting/processing rather than from farm level – need to look at this in more detail to establish if they appear to be human or livestock adapted strains.



Summary of overall preliminary findings

- So, "superbugs" have been found on farms, in people working with livestock and in meat.
- These bacteria ARE carrying multiple resistance genes, particularly those associated with livestock
- They do possess virulence genes HOWEVER the livestock associated ST398 seem to have fewer and lack enterotoxins
- These findings are in line with current literature
- BUT not all bacteria found were livestock associated MRSA ST398 and the other sequence types are also capable of causing disease
- Carriage rates of *S.aureus* were higher than general population BUT this needs to be looked at in comparison with other sectors eg. healthcare workers.



Is LA MRSA st398 a pathogen? Yes it can be but carriers can also be asymptomatic

If so, how is it pathogenic? Eg ingestion? Colonisation of skin? It can be either although none of the st398 I found possess enterotoxins (in line with current literature) so gi disease less likely from this

How severe is the disease which it can cause? It can be fatal but generally it is less likely to cause severe disease than other S aureus sts.

How easily is it spread? In environment, food, host-host – all of this possible although not readily human to human

Can it survive in the fridge/freezer/storing process? Can survive freezing. Lives happily in wide temp range 4-65°C.

How easily is it destroyed by normal procedures likely to be carried out in the domestic environment? **Killed** by adequate cooking and hand hygiene helps enormously, as will cleaning of work surfaces etc. – ie normal raw meat prep hygiene

Can it acquire new genes or transfer its genes to other bacteria (on or off host)? Yes absolutely



Final thoughts

- *S aureus* may be in your meat but so are lots of other things! Adequate cooking and washing of work surfaces, hands etc (ie hygienic food preparation) should help.
- •
- Clearly **situation needs monitoring**, with most immediate risk seeming to be that posed by risk of transfer of genes within and between bacterial species and spread of the bacteria to those working with livestock (and subsequently spreading more widely), along with spread off livestock establishments in air and water, into soil etc.
- It isn't just the food, but the **whole food chain** which needs looking at.
- British pork industry has made huge reductions in ab usage
- Consumer education regarding risk and choice. They will drive change.
- Global population increasing, as is demand for food. Need to balance this with safety and sustainability, and not just blame agriculture!





ACKNOWLEDGEMENTS



Supervisor: Mark Holmes Advisor: Milorad Radakovic Dan Tucker BIG lab group, especially: Ibrahim Ba Harriet Bartlett Liz Lay Juan Hernandez Garçia Nazreen Hadjirin **Claire Raisen David Seilly** lain Kean Tom Wileman Daniel Buhl

Desirée Corander

All participants (anonymous) for the samples
Daisy Morgan
David Chennells
Eville and Jones - Jason Aldiss, Duncan Garfield
Food Standards Agency - Collin Wilson
Coilin Nunan, Emma Rush, Katherine Button, Suzi Shingler - Alliance to Save out Antibiotics (Compassion in World Farming, Soil Association, Sustain)
Angela Kearns, Lesley Larkin, Bruno Pichon, Colin Brown - Public Health England Robert Smith - Public Health Wales
Robert Muir, David Wilson, Graham Cooper - Health Protection Scotland
Emma Deans and my mum for help with all the swab packs

BBSRC and MRC for the money



