Antimicrobial resistance and the food chain

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Outline of presentation

• What is antimicrobial resistance?
• The UK and international dimension
• Role of the food chain
• Systematic review
• Surveillance
• Looking ahead
Antimicrobials and resistance

• A compound which, at low concentrations, exerts an action against microorganisms and exhibits selective toxicity towards them

• Any substance of natural, synthetic or semisynthetic origin which is used to kill or inhibit the growth or microorganisms - bacteria, fungi, protozoa, viruses

• Antimicrobials include antibiotics, disinfectants, preservatives, other substances (e.g. copper, zinc)

• Antimicrobial resistance is the ability of a microorganism to withstand an antimicrobial.

Source: ACMSF (1999)
What is antimicrobial resistance?

- Can arise randomly - mutation in any gene occurs in ~1 cell per 10 million
- Mutants which give rise to resistance are selected - sensitive cells are killed

How does resistance transfer?

**Chromosomal** - only to daughter Cells - vertical

**Transferable** – between bacteria

Elements within plasmids - transposons and integrons

**Pathogen** ↔ **Commensal**
Pathogen or commensal?

• Impact can be direct or indirect (silent)

• Pathogens such as *Salmonella*, *Campylobacter* and *E.coli* O157 cause infectious intestinal disease (IID) and some strains will carry antimicrobial resistance genes which may be transferable to other bacteria.

• IID is usually self-limiting with antibiotics only being required if the infection becomes more serious.

• Other bacteria (e.g. commensal *E.coli* and *Klebsiella*) may or may not cause infection but can carry antimicrobial resistance genes transferable to other bacteria some of which may cause disease at some point.

• More work is needed to understand the role of the human gut microbiome as a reservoir for drug resistance genes.
PHE data - English surveillance Programme for antimicrobial utilisation and resistance (ESPAUR) 2010 to 2014*

Human use of antibiotics has selected for the escape of genes from the soil ‘resistome’ into human pathogens, as demonstrated by the presence of the same genes in soil bacteria and human bacteria” Blair et al. (2015)

What does this mean?
Without urgent action we are heading for a post-antibiotic era, in which common infections and minor injuries can once again kill

O’Neill Review - tackling drug-resistant infections globally; final report and recommendations

- 2016 – 700,000 deaths per year
- 2050 - 10,000,000 deaths per year

Cost $100 trillion on global world GDP

Critically Important Antimicrobials (CIAs)

- Quinolones / fluoroquinolones
- 3rd / 4th generation cephalosporins
- Carbapenems
OIE List of Antimicrobials of Veterinary Importance

Defines:

- **Veterinary Critically Important Antimicrobials**
- **Veterinary Highly Important Antimicrobials**
- **Veterinary Important Antimicrobials**:

‘Critically Important’ include:

- Aminoglycosides
- Cephalosporins
- Macrolides
- Quinolones/fluoroquinolones
The overall goal of the cross-government UK strategy is to slow the development and spread of antimicrobial resistance by focusing activities around 3 strategic aims:

- improve the knowledge and understanding of antimicrobial resistance
- conserve and steward the effectiveness of existing treatments
- stimulate the development of new antibiotics, diagnostics and novel therapies

FSA involved with the strategy and delivery of the action plan
FSA STRATEGIC OUTCOMES

- Food is safe
- Food is what it says it is
- Consumers can make informed choices about what to eat
- Consumers have access to an affordable healthy diet, now and in the future
FSA Online Omnibus survey 1263 adults
May 2016
74% had heard of “superbugs” (highest among those aged 55+);
61% had heard of antibiotic resistance;
16% had heard of antimicrobial resistance.

Of those aware of any of those terms 62% were concerned about AM/AB resistance within the food chain.
Washing hands regularly
Cooking food properly

4 Cs

Avoiding cross contamination

Chilling food properly

Antimicrobial resistant bacteria are no more heat resistant
Potential pathways for antimicrobial resistance

Source: ACMSF (1999) Microbial Antibiotic Resistance in Relation to Food Safety, HMSO
Some evidence of transmission via the food chain - *Salmonella*, *Campylobacter*

Paucity of food data and collected for different purposes

Difficult to compare–sampling and methodology

Need for more screening of *E.coli* isolates from foodstuffs
Growth in the literature on antimicrobial resistance - selected traits -1995-2015

Growth in the scientific literature on antimicrobial resistance to June 2016- all aspects and selected resistance traits

<table>
<thead>
<tr>
<th>Resistance trait</th>
<th>Antimicrobial Resistance</th>
<th>Antimicrobial resistance + food</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>All aspects</td>
<td>185,772</td>
<td>9,399</td>
<td>5.1%</td>
</tr>
<tr>
<td>Carbapenem</td>
<td>6,888</td>
<td>105</td>
<td>1.5%</td>
</tr>
<tr>
<td>ESBL</td>
<td>3,619</td>
<td>255</td>
<td>7.0%</td>
</tr>
<tr>
<td>Colistin</td>
<td>2,243</td>
<td>102</td>
<td>4.5%</td>
</tr>
<tr>
<td>Fluoroquinolone</td>
<td>11,725</td>
<td>637</td>
<td>5.4%</td>
</tr>
<tr>
<td>Vancomycin</td>
<td>11,756</td>
<td>713</td>
<td>6.1%</td>
</tr>
<tr>
<td>Tetracycline</td>
<td>10,827</td>
<td>1,492</td>
<td>13.8%</td>
</tr>
</tbody>
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Evidence gathering – Royal Veterinary College Systematic Review on AMR

- A systematic literature review of the occurrence of antimicrobial resistance in pathogens and commensals in retail food
- Focus on *Salmonella*, *Campylobacter*, *E.coli* and Enterococci
- Critically important antimicrobial groups and multi-drug resistance
- Follows Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)
- PROSPERO an international database of prospectively registered systematic reviews
- Studies published between 1999-2015 (since the last ACMSF report)
- Peer reviewed literature and some “grey literature”
- Publication expected September 2016
- Gaps in review will help to guide future research

The evolving threat of antimicrobial resistance

WHO report (2012) Chapter 4: Reducing the use of antibiotics in animal husbandry

“More information is needed on the prevalence of AMR in bacteria of animal origin and its impact on human health, on the quantity of antibiotics used for different indications and on the classes of antibiotics used”.

“Risk assessments and risk management are impeded by a lack of data and/or inability to access available data”

CODEX has produced guidelines for risk analysis of foodborne antimicrobial resistance CAC/GL77-2011

http://whqlibdoc.who.int/publications/2012/9789241503181_eng.pdf
JIACRA - Joint Inter-agency Antimicrobial Consumption and Resistance Analysis

- First integrated report by the European Centre for Disease Prevention and Control (ECDC), the European Food Safety Authority (EFSA) and the European Medicines Agency (EMA)

- “The epidemiology of resistance is complex, and several factors aside from the amount of antimicrobial consumption influence the level of resistance”

- “No associations were observed between the consumption of fluoroquinolones in food-producing animals and the occurrence of resistance in *Salmonella* spp. and *Campylobacter* spp. from cases of human infection”.

Report published January 2015
Comparison of biomass-corrected consumption of antimicrobials (mg per kg estimated biomass) in humans and animals in 26 EU/EEA countries in 2012

Asterisk (*) denotes that only community consumption data were available for human medicine. Figures of human sales from these countries probably represent a considerable underestimate.
Comparison of consumption of selected antimicrobial classes for humans and food-producing animals in 26 EU/EEA countries in 2012

Highest selling AMs classes:
- **Human medicine**: penicillins, macrolides, fluoroquinolones
- **Food-producing animals**: tetracyclines, penicillins, sulphonamides

Source: JIACRA
Levels of AMR in the Food Chain

Based on “European Union Summary Report on antimicrobial resistance in zoonotic and indicator bacteria from humans, animals and food in 2013”.

Source: EFSA

Variability in percentage of bacteria presenting microbiological resistance reported by Member States

Need for better alignment of AMR data

- EU surveillance (Decision 2013/652/EC)
- Lays down specific technical requirements for AMR testing and reporting in representative isolates from randomised sampling of food animals at farm and/or slaughter, and retail meat
- Testing stated in 2015-2020 for retail meat in all 28 Member States
- Testing retail meats (beef/pork/chicken) in the UK for: ESBL-/ AmpC-/ Carbapenemase-producing E. coli
- FSA included testing for colistin resistance and the mcr-1 colistin resistance gene
- EU results for 2015 expected in early 2017
Antimicrobial resistance and fresh produce?

- Global sourcing of a diverse range of fresh produce - minimal processing

- Shiga toxin producing *E. coli* O104:H4 outbreak in 2011 - ~4000 EHEC cases, >900 HUS cases, 54 deaths. Linked to Fenugreek seeds from Egypt. Strain resistant to a wide range of β-lactamase antibiotics (ESBL), streptomycin, nalidixic acid, tetracyclines, trimethoprim sulphonamides (Bielaszewska et al., 2011)

- EFSA reports some information - need for more studies

- FSA are supporting a collaborative study with DH to quantify ESBL-producing *E. coli* in raw meats and fresh produce
Plasmid-mediated colistin resistance reported from *E. coli* in pigs, raw meat and human infections in China*.

Resistance previously thought to be chromosomal.

Now becoming an antibiotic of last resort for certain infections in human medicine.

Animal and Plant Health Agency find *mcr-1* gene in *E. coli* in UK pigs.

Public Health England screened WGS archive of 24,000 bacterial isolates for *mcr-1* gene (24 hours) – found 12 *Salmonella* and 3 *E. coli* isolates with *mcr-1*.

Denmark (DTU) reported 6 positives from screening ~3000 WGS.

AMR - Plasmid-mediated colistin resistance (mcr-1 gene)

• In China 0.7-1.4% of inpatient isolates of *E.coli* and *Klebsiella pneumoniae* with the *mcr-1* gene - much lower than in animals (21%) or pork, chicken (15%).

• Frequency of *mcr-1* gene in UK clinical isolates ~10 fold lower

• UK direct and indirect risk was very low - medium to high uncertainty - supported by ACMSF

• Jan 16 - screening of *E.coli* from retail meat for the *mcr-1* gene as an add on to EU antimicrobial resistance monitoring  - more data needed!

• *mcr-1* gene now reported from many countries

• EU AMEG re-looked at colistin – report May 16
Looking ahead

• FSA Board – paper on antimicrobial resistance

• RVC systematic review

• Risk assessment for Meticillin-resistant *Staphylococcus aureus* (MRSA) in the food chain

• Antimicrobial resistance in *Campylobacter* from retail chicken

• 2015 findings from EU surveillance of animals and retail meats

• Joint EFSA-EMA opinion on measures to reduce the need to use antimicrobials in animal husbandry (RONAFA)
THANK YOU

Acknowledgement: John Threelfall