Antimicrobial resistance and antimicrobial use in veterinary medicine

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Public health

• Resistance influenced by both human and non-human antimicrobial usage and exposure

• Antimicrobial resistance in various commensals in animals and/or zoonotic pathogens
  – Food borne, direct contact or environmental transmission
    – MRSA: livestock and workers, dogs and owners
    – Extended spectrum β-lactamase (ESBL) producing *E. coli*
    – *Campylobacter*
    – *Salmonella*
    – *Pseudomonas*
    – *Colistin (plasmid borne)*
Ecology of AMR
Correlation between veterinary antimicrobial use and antimicrobial resistance in food-producing animals: a report on seven countries. Chantziaras et al., 2013
Animal health

- Resistant infections in animals
  - ESBL *E. coli* - emerging threat?
    - *Infections in dogs and cats* - urinary tract etc.
  - Multidrug resistant *Enterotoxigenic E. coli lambs*
  - Multidrug resistance *E. coli* pigs
  - Multidrug swine dysentery
  - MRSA infections (hospitalised animals)
Reducing/optimising antimicrobial use in animals

- Restriction or banning use of the critically important antimicrobials (fluoroquinolones etc)
- Threat of separating prescribing and dispensing
- Restriction of prophylactic antimicrobials
  - In feed
  - Dry cow therapy
- Banning use as growth promoter (outside EU)
- Data collection
  - How much antimicrobials should be used?
  - Benchmarking – farms, countries!
- Economics of food production
- Animal welfare
- Internationally - lack of data, legislation. AM use crossover between human-animal.
Collection of antimicrobial sales data across EU/EEA Countries

• The European Surveillance of Veterinary Antimicrobial Consumption (ESVAC)
  – data on the sales of veterinary antimicrobials from 26 EU/EEA countries

• Data limitations
  – Sales data only
  – Many antimicrobial products authorised for use in multiple species
  – Major species differences in usages
  – Not actual on farm use
Sales of antimicrobials for food-producing animals in mg/PCU, 2013

Source – ESVAC, 2015
NB – Food producing animals includes horses
Sales of critically important antimicrobials for food-producing animals in mg/PCU, by country, for 2013

Source – ESVAC, 2015
Global consumption of antimicrobials in food animal production

• Estimated at 63,151 tons in 2010
• Projected rise by 67%, to 105,596 tons, by 2030.
  – Two thirds of increase due to the growing number of animals raised for food production.
  – third is imputable to a shift in farming practices, to be intensive farming

Global trends in antimicrobial use in food animals
Van Boeckel et al 2015.PNAS
7. Highest Priority Critically Important Antimicrobials

These are the classes of drugs that met all three priorities (1.1, 1.2 and 2.1): Fluoroquinolones, 3rd and 4th generation cephalosporins, Macrolides, and Glycopeptides.

**Fluoroquinolones** are known to select for fluoroquinolone-resistant Salmonella spp. and E. coli in animals. At the same time, fluoroquinolones are one of few available therapies for serious Salmonella spp. and E. coli infections. Given the high incidence of human disease due to Salmonella spp. and E. coli, the absolute number of serious cases is substantial.

**3rd and 4th generation cephalosporins** are known to select for cephalosporin-resistant Salmonella spp. and E. coli in animals. At the same time, 3rd and 4th generation cephalosporins are one of few available therapies for serious Salmonella and E. coli infections, particularly in children. Given the high incidence of human disease due to Salmonella spp. and E. coli, the absolute number of serious cases is substantial.

**Macrolides** are known to select for macrolide-resistant Campylobacter spp. in animals, especially Campylobacter jejuni in poultry. At the same time, macrolides are one of few available therapies for serious campylobacter infections, particularly in children, in whom quinolones are not recommended for treatment. Given the high incidence of human disease due to Campylobacter spp., especially Campylobacter jejuni, the absolute number of serious cases is substantial.

**Glycopeptides** are known to select for glycopeptides-resistant Enterococcus spp. in food animals (e.g., when avoparcin was used as a growth promoter, vancomycin resistant enterococcus (VRE) developed in food animals and were transmitted to people). At the same time, glycopeptides are one of the few available therapies for serious enterococcal infections. Given the high number of cases, the previously documented occurrence of transmission of VRE to people from food animals and the very serious consequences of treatment failures in such cases, this class was re-classified as being of highest priority in the 3rd revision of the List.
International and national responsible use initiatives
What is happening in reality?

- Are guidelines being followed?
- Are all vets prescribing responsibly?
- Are animal owners/farmers using responsibly?
- Is resistance a real or perceived issue in veterinary medicine?
- What are the main drivers of antibacterial use?
- What role do owners/farmers have?
- What are the barriers to changing behaviour?
- How do we sustain ‘good’ behaviour?
- What impact on animal health?
- What impact on animal productivity?
Antimicrobial Prescribing Practice by Vets in UK

- Farm animal veterinary surgeons (cattle)
  - 2.8% of practices had a written antimicrobial use policy document
  - 95.3% reported being able to dispense antimicrobials at their own discretion
  - Only 9.4% and 7.8% of vets respectively, reported that they had **not used** fluoroquinolones or cephalosporins in the last year
    - Bacterial culture and sensitivity testing
      - Only 4.7% reported frequently undertaking this

*Williams N, Pinchbeck G et. al. 2010*
What influences choice of antibiotic for treatment of dairy cattle.

(1= not important; 5 =very important)
Economic drivers

- Pen/strep €7.80 for a 3 day course for 600Kg cow
- Milk loss 4.5 days in total (3 days treatment)
- 40 litres per day x 4.5 = 180 litres = € 68.60

- 3rd gen cephalosporin 3 day course = € 16.51 course, or one injection € 23.50.
- Convenient
- Nil milk withdrawal.

- Milk price and withdrawal times are the drivers
- Evidence for best treatment?
Antimicrobial Prescribing Practice by Vets in UK (2010)

- Small animal veterinary surgeons (dogs)
  - 3.5% of practices had a written antimicrobial use policy document
  - Fluoroquinolones and 3rd generation cephalosporins.
    - 6.0% and 4.6% of all prescriptions
  - 25.9% dogs received antimicrobials

Hughes et. al.
Drivers and motivations associated with antimicrobial prescribing practices by UK pig veterinarians and farmers

Mixed methods approach – Qualitative and quantitative

Objectives
To develop an in-depth understanding of the key drivers of prescribing and use and to determine major barriers to behaviour change

– in depths interviews with veterinarians and farmers.
– focus groups with vets and farmers
– questionnaires to vets and farmers.
'I do believe in prophylactic treatments because there are too many times where you try and not use antibiotics and then you end up with a bad mortality…'

'I think the one [prescribing practice] that we as pig veterinarians are weak on are the habitual repeat users. It’s the repeated in feed prescription that’s the issue, isn’t it? I’m as guilty as the next man of that.’

*Tylan* is a growth promoter. It is used as a growth promoter. There are thousands and thousands of tons of *Tylan* going in at relatively low rates. Whether you say it’s against *lawsonia*, or whatever you call it, or whether you say it’s growth…’

*I think the hardest thing in pig production at the moment is obviously... antibiotics are used as a management tool. But there aren’t the financial rewards in pig production at the moment for people to actually go out and spend money on improving the use, improving the management to make that happen.’
‘human bacterial resistance, is from antibiotic use in humans, rather than transfer from animals’ (v)

‘...it’s [antimicrobial resistance] obviously an issue in human medicine, which I think they’re probably using us as the scape goats for. At the moment I think we’ve just got to be seen to conform or to reduce our usages to take the party line.’ (v)

‘My opinion, personally, is that if the doctors and the human health control was more under control, we would probably get less resistance.’ (F)

Should we be saying we shouldn’t be letting humans have antibiotic? In terms of why are we so hell bent on stopping animals when it’s the humans themselves in some respects that are causing all their own problems?’ (F)

‘I think there’s a greater danger when they’re dished out like Smarties in GP practices for somebody with a common cold.’
Stewardship

- Good stewardship requires a multi-faceted approach.
- ‘One size fits All’- not likely to work
  - Different sectors, different countries, different production systems
- Education?
  - Vets, farmers, owners, nurses, dispensers
- Regulation
  - Bans/restrictions on use?
  - Penalising non-compliance?
  - Targets for reduction?
  - May drive improper use
Acknowledgements

Nicola Williams, Lucy Coye, Sophia Latham, Susan Dawson, Gina Pinchbeck, and Rob Smith

All of the veterinary surgeons and farmers who gave their time.