What can dairy farmers do to help reduce the risk of antibiotic resistance?

In this article, Finola McCoy, senior programme manager CellCheck, with the support of the Cellcheck Technical Working Group, explores some key questions around antibiotic resistance and why it is cause for concern

What role does antibiotic use on the farm play in the development of antibiotic resistance (AMR), and how can those of us working in the dairy sector positively influence this? When drying off cows, has a selective dry-cow strategy a role to play in reducing the use of antibiotics on farm? What science is available to help choose which herds are suitable for selective dry-cow strategies, and how do we best identify the cows in these herds that may not need antibiotics at drying off, while still protecting the udder health of the herd? This article draws on national and international research to answer some of these questions, while also highlighting that there are still some questions to which we don't have all the answers.

RECAP – WHAT IS ANTIBIOTIC RESISTANCE?

Antibiotic resistance, also antimicrobial resistance (AMR), arises when the bacteria, which cause infection, survive exposure to an antibiotic that would normally kill them or stop their growth. AMR allows strains of bacteria that are capable of surviving exposure to a particular antibiotic, to grow and spread. Resistance to one or more antibiotics may occur and this is a real threat to our planet especially when we only have a limited number of antibiotic groups to treat infections in humans and animals. We can grow bacteria on an 'agar plate' and use different antibiotic discs to check which antibiotic works best. Where there is a zone of 'no growth' around the disc, we know the antibiotic works. Where there is bacterial growth around the disc, then the bacteria are resistant to that antibiotic. See Figure 1.

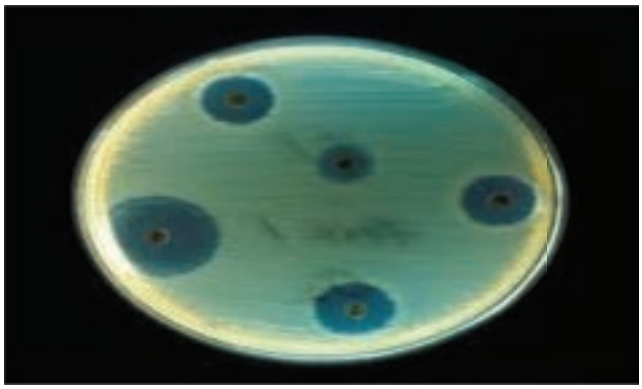


Figure 1.

Not only do we see bacterial infections on farms that are difficult to treat because of resistance, but we also encounter human infections resistant to antibiotic treatment. Worse still, bacteria that are resistant may spread and share these traits with other bacteria including those in the environment, eventually tracking back to the bacteria that cause infections in humans. The pace at which AMR has been developing in more recent years has increased, and it is now recognised as being a significant threat to human health. See Figure 2.

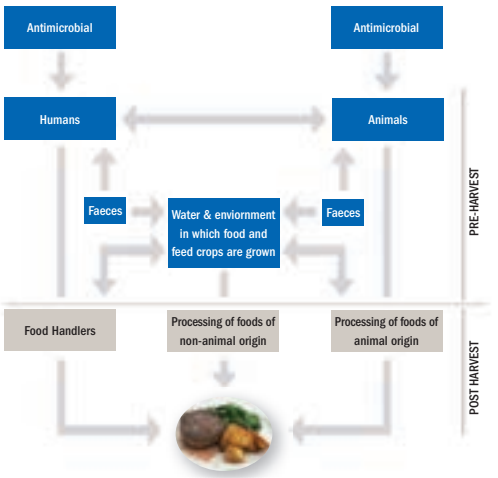


Figure 2. Potential routes of transmission of antimicrobial-resistant bacteria via the food chain (EFSA, 2008).

THE IMPORTANCE OF ANTIBIOTICS IN HUMAN AND ANIMAL HEALTH

AMR is responsible for an estimated 25,000 deaths and €1.5 billion in extra healthcare costs every year in the EU alone. Hence, the sense of urgency about addressing this issue and doing so at a global level. AMR is linked to antibiotic use – increased antibiotic use in both humans and animals is associated with an increase in AMR. In relation to mastitis-causing pathogens, there is evidence to show that different bacterial species develop resistance to different antibiotic groups at different rates.

Currently, antibiotics are used by doctors to treat sick people and used in the agricultural sector to treat animals. In recent years, there has been increasing recognition of the linkage between AMR in people and antibiotic use in animals. For these reasons, there is increasing scrutiny of the use of antibiotics in the agricultural sector. There is agreement on the importance of antibiotics to treat sick animals. However, it is no longer considered acceptable that antibiotics should be used to prevent disease, particularly when there are other proven strategies. The type of antibiotic used for treatment of animals is also an important consideration. 'Highest Priority Critically Important Antibiotics' (HP-CIAs) need to be preserved for human use. The Department of Agriculture, Food and the Marine (DAFM) recently published guidelines on the use of CIAs in animals (Table 1). Disease prevention and improved

herd health certainly help reduce the need for antibiotic on farm. Vets and farmers need to be mindful to avoid using those antibiotics that are classified as HP-CIAs.

HIGHEST PRIORITY CRITICALLY IMPORTANT ANTIMOCROBIALS LICENCED AND SOLD IN 2016 IN IRELAND FOR USE IN ANIMALS

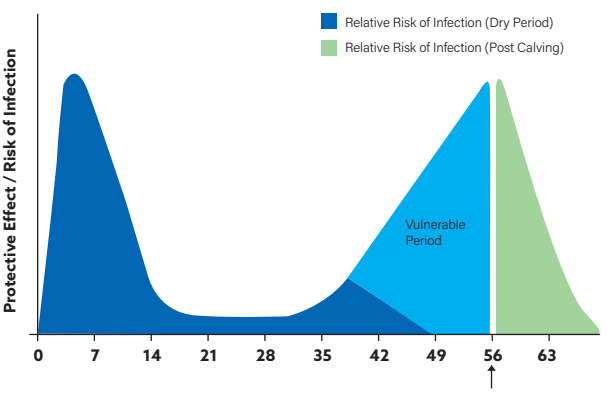
ANTIMICROBIAL CLASS	HP-CIA CATEGORY	ACTIVE SUBSTANCE	EXAMPLES OF PRODUCTS
3rd & 4th generation cephalosporins	Category 2	cefovecin ceftiofur cefquinome	Convenia Alfacef, Cefavex, Cefinil, Cefokal, Ceftiocyl, Cemay, Cevaxel, Curacef, Eficur, Excenel, Naxcel Ceffect, Cefinam, Cefquinome, Cephaguard, Cobactan, Flenix, Qivitan
Fluoroquinolones	Category 2	enrofloxacin marbofloxacin pradofloxacin	Baytril, Doraflox, Enrobactin, Enrocare, Enrodexil, Enrofloxacin Kirka, Enro-K Aurizon, Boflox, Efex, Forcyl, Kelacyl, Marbon, Marbocare, Marbocyl Veraflox
Polymyxin	Category 2	colistin	Colifree, Coliscour, Colistin APSA, Hydrocol, Sogecoli
Macrolides	Category 1	erythromycin gamithromycin kitasamycin tilmicosin tulathromycin tylosin tylvalosin	Erythrocin Zactran Zuprevo Hymatil, Micotil, Milbotyl, Pulmotil, Pulmovet, Tilmodil, Tilmovet Draxxin Bilosin, Bilovet, Pharmasin, Tylan, Tylo, Tylosin, Tylovet, Tylucyl Aivlosin

List updated June 2018, based on 2016 sales
List due for review annually
Product names sourced from Health Products Regulatory Authority website

Table 1: Highest Priority Critically Important Antibiotics licensed and sold in Ireland in 2016.

WHAT CAN CELLCHECK AND THE DAIRY FARMER DO TO REDUCE AMR?

The focus of the CellCheck programme is on improving herd and udder health, thereby minimising clinical and subclinical disease. This also reduces the need for mastitis treatments, both injectable and intramammary.



THE ROLE OF ANTIBIOTIC DRY COW THERAPY

The practice of dry cow therapy is being questioned in many countries by farmers, consumers and society in general. Antibiotic dry cow therapy undoubtedly has an important role to play in treating infections that persist at the end of lactation and maximising cure rates. It has also traditionally been used to prevent new infections occurring over the dry period. While the dry period is a high-risk period for udder infections both clinical and subclinical, the consumer at home and abroad is becoming intolerant of using antibiotics on a 'just-in-case' basis. Considering our changing attitude and approach towards the use of antibiotics in a 'preventative' fashion, do we also need to rethink how and why we use dry cow therapy? And in fact, how do we define dry cow 'therapy'?

Recent analysis of sales data in Ireland (More et al., 2017) indicated that sales of dry cow intramammary antibiotics were sufficient to treat 100% of the national milking herd, ie. all quarters of all cows are being treated at the end of lactation. This is what is referred to as 'blanket dry cow therapy,' which until recently was recognised as best practice in mastitis control and has made a very positive contribution to udder health in many countries. However, as we learn more about AMR and what drives it, we need to review what is considered best practice, as well as the implications of modifying those 'traditional' recommendations. Change is not without risk.

WHAT ARE THE RISKS AND BENEFITS OF MOVING AWAY FROM BLANKET DRY COW THERAPY?

An alternative to blanket dry cow therapy is a 'selective' dry cow strategy. A selective dry cow strategy involves administering internal teat sealant only to a selected proportion of suitable cows at drying off, with the remainder of the cows receiving both an antibiotic tube and an internal treat sealant. While this is considered a more prudent use of antibiotics and would reduce antibiotic use on many farms, we need to bear in mind that this practice is not without risk. So how can we manage this risk? The CellCheck Technical Working Group recently reviewed all of the science and research on dry cow therapy published since the early 2000s, and have identified the following key risks:

1. The first risk is of introducing bacteria when we infuse any intramammary tube into a quarter. When we use internal teat seal only, there is no antibiotic present as 'backup' and so the potential consequences are even greater. These 'introduced' bacteria can cause severe cases of mastitis, sometimes resulting in death, early in the dry period. In addition, many of the cases of mastitis in early lactation have been shown to have a dry period origin. Hygiene standards and practices at drying off – as outlined in detail in the CellCheck Farm Guidelines (pages 117-119) – are essential to protect the udder health of the uninfected cow. Hygiene and management of the dry cow environment is also crucial.
2. The second risk is of missing the opportunity to cure quarters that were infected at the point of drying off in order to maximise cure rates before the next lactation starts. A very common question is 'how do I know which ones are the infected animals?' There are many criteria that need to be considered when making these decisions, including milk-recording results and milk-culture results. Even with all this information on hand, further questions remain such as 'how many milk-recording results do I need to have and how close to drying off do they need to be?'

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and 'at what cow somatic cell count (SCC) level should I consider using antibiotic dry cow therapy?' The reality is that there are still many unknowns, and not all of these key questions can yet be answered. Everyone agrees about the key role of milk recording in helping with this decision. At this point however, different countries have adopted different herd and cow-level thresholds for deciding to treat with antibiotics at drying off. This highlights that there isn't one, simple answer to this question. Future research, both Irish and international, should help answer some of these questions, assist in making good and appropriate decisions, and help us to predict the outcomes and manage some of the risks involved.

IS A SELECTIVE DRY COW STRATEGY SUITABLE FOR MY HERD?

All decisions around dry cow therapy should be made in consultation with a veterinary practitioner who has knowledge of the herd, its history and environment. Antibiotics used at drying off are subject to Irish and EU regulatory and prescription control. Currently the CellCheck Farm Guidelines for Mastitis Control, including Management Note C, outline some of the essential herd- and cow-level information that must be available in order to safely consider adopting a selective dry cow strategy.

A selective dry cow strategy may be considered in herds:

1. Where there is good evidence of a low prevalence of infection, for example a bulk milk SCC consistently below 200,000 cells/mL, a dry period new infection rate of less than 10%, etc.;
2. Where good practices and high levels of hygiene can be achieved at drying off, throughout the dry period and at calving;
3. Where regular milk recording is carried out, with at least one recording in the last month prior to drying off; and
4. Where the herd keeper is willing to engage with their veterinary practitioner in decision-making around their dry cow treatment programme.

Within these herds:

- Cows with an SCC consistently below 100,000 cells/mL; throughout the lactation and with no history of clinical mastitis may be considered suitable for internal teat sealant only at drying off, provided high levels of hygiene can be achieved during administration; and
- In all other cows, the TWG recommends using an internal teat sealant as well as an antibiotic tube.

Who wins/loses from an effective, selective dry cow strategy?

- The farmer wins because fewer antibiotics are used on the farm. A selective strategy is likely to be cost-saving and economically beneficial. Also, there is less chance that antibiotic milk is fed to young calves and a reduced risk of a milk residues failure. The farmer also gets the opportunity to contribute to global AMR reduction.
- The consumer wins because of a reduced opportunity for AMR via food or in the environment.
- The processor wins because of higher quality milk and, therefore, key market access with high-value dairy products (baby milk formula, yoghurts, cheeses etc).
- The bacteria lose because when animal and human infections arise, antibiotics are more likely to be effective and kill the bacteria.

All decisions around dry cow therapy should be made in consultation with a veterinary practitioner who has knowledge of the herd, its history and environment. Over time, as more research and technologies become available, these decision-making thresholds and recommendations may change, reflecting changes in our ability to predict infection and treatment outcomes. However, the fundamental requirements of good quality information, excellent hygiene and risk management will never change.

REFERENCES:

- More SJ, Clegg T, McCoy F. The use of national-level data to describe trends in intramammary antimicrobial usage on Irish dairy farms from 2003 to 2015. J. Dairy Sci. 2017;100:6400-6413
- https://amr-review.org
- https://ecdc.europa.eu
- CellCheck Farm Guidelines for Mastitis Control

READER QUESTIONS AND ANSWERS

1. A SELECTIVE DRY COW STRATEGY IS SUITABLE FOR A HERD IF BULK MILK RECORDING IS BELOW

A. 200,000 cells per ml
B. 300,000 cells per ml
C. 350,000 cells per ml

2. WHICH OF THE FOLLOWING ARE NOT 'HIGH RISK CRITICALLY IMPORTANT ANTIBIOTICS?

A. Flouroquinolones
B. Tetracyclines
C. 3rd and 4th generation cephalasporins
D. Macrolides

3. IN A HERD WHERE A SELECTIVE DRY COW STRATEGY IS BEING USED, WHICH OF THE FOLLOWING COWS ARE NOT SUITABLE?

A. Cow with an SCC consistently below 200,000 cells/ml
B. Cow with an SCC consistently below 100,000 cells/ml
C. Cow with a history of only one clinical mastitis incident during the lactation
D. Cow with no history of clinical mastitis during the lactation

4. IN THE EU, EVERY YEAR AMR IS RESPONSIBLE FOR APPROXIMATELY

A 250 human deaths
B. 2,500 human deaths
C. 25,000 human deaths

ANSWERS: 1: A; 2: B; 3: A & C; 4: C