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## **Antibiotic dry cow therapy: where next?**

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Responsible use of antibiotics and concerns surrounding antimicrobial resistance (AMR) are pervading all areas of both veterinary and human medicine. It is the prescribing clinician's responsibility to ensure that the use of antimicrobials is justified in all situations.

Increasingly, the assurances justifying the prescription and use of antibiotics are under scrutiny and may in the future be subject to challenge on a number of fronts. The routine use of antibiotics at drying off in dairy cows is one such area of reappraisal and challenge.

In order to validate and uphold the principles of responsible use of antimicrobials, analysis of past prescribing practices and outcomes must be combined with robust clinical research evidence. Even a cursory analysis of on-farm and within-practice data has the potential to influence future prescribing; challenging and reappraising the necessity for antibiotic prescribing in certain clinical situations has been known to lead to a marked reduction in antibiotic use.

When critically appraising the current approach to drying off dairy cows, it is worth looking not only at current and future drivers for change but also at how we got to where we are today. Many factors have influenced the approach to managing dairy cows at the end of lactation: the social environment (attitudes to antibiotic use), pharmacological environment (products available) and physical environment that cows occupy have all seen significant change.

Antibiotic dry cow therapy (aDCT) was introduced in the 1950s as part of a structured mastitis control plan (Five-Point Mastitis Control Plan) developed at the National Institute for Research in Dairying at the University of Reading. Slow release antibiotic preparations infused into each quarter of a cow at drying off not only improved the chance of elimination of existing intramammary infections (IMI) but also afforded the cow some protection from new IMI during the dry period. Hence, this practice became an important component in the management of dry cows. Over time, the prevalence of persistent contagious pathogens has

declined, and the need for blanket antibiotic therapy in every cow at drying off to improve cure rates over the dry period has diminished and can therefore no longer be justified on most UK dairy farms.

Since the dry period is a particularly high risk for the establishment of new IMI in the dairy cow, various attempts have been made to impart protection, including the application of Stockholm Tar and external teat sealants ('plastic skin') to teats; these were not particularly effective, nor were they easy to apply. The development of bismuth subnitrate-based internal teat seals (iTS) in Ireland and their subsequent introduction to the UK in 2002 heralded a significant improvement in protection from new IMI during the dry period. Initially used as an alternative to aDCT, iTS soon became used in combination with aDCT, a practice that is common throughout the dairy industry in the UK today.

It can be argued that all cows, whether uninfected or infected (and then cured), are susceptible to new infection in the dry period and therefore justify the protection afforded by iTS administered at drying off. However, the same cannot be said about administration of aDCT to all cows at drying off. There needs to be a paradigm shift from the decades of blanket aDCT irrespective of udder infection status to rational prescription and administration of aDCT based on the risk of an intramammary infection being present. In other situations when faced with infectious diseases, such as calf pneumonia, decisions are around identifying which calves to treat with antibiotic, not which calves not to treat. Rather than thinking about the problem of deciding which cows should not receive aDCT, we believe decisions should instead be based around which cows justify aDCT, so that antimicrobial products can be targeted towards cows likely to have major pathogen IMI at drying off. The approach to dairy cows at drying off can therefore be summed up as: 'Underwrite the whole herd with iTS and target aDCT to those cows that justify it', while maintaining the responsible approach of using 'as little antibiotic as possible but as much as necessary'.

#### Identifying cows that justify antibiotic therapy at drying off

Methods to assess the risk of the presence of an IMI include direct methods, such as detection of bacteria by culture or PCR, or indirect methods, such as California Milk Test (CMT) or individual cow somatic cell count (ICSCC). Assessment of the relative risk of a cow having an IMI at drying off may also be influenced by clinical mastitis history from farm records or observation of teat lesions at the time of drying off. All methods of diagnosis will have inherent false-negative and false-positive rates that depend on the sensitivity ( $S_n$ ) and specificity ( $S_p$ ) of each test and the predictive positive and predictive negative values, respectively, within the population in which they are being used.

Cure rates of IMI will vary for a number of reasons (including the causal pathogen); however, during the dry period, cure rates are significantly higher than during lactation so, arguably, tests used to identify IMI at drying off should be optimised for the detection of infected cows ( $S_n$ ) to avoid missing that opportunity for cure. When availability, practicality,  $S_n$ ,  $S_p$  and

cost of data are taken into account, the use of regular routine ICSCC (most commonly performed monthly) in combination with clinical mastitis case records is often the most appropriate approach. ICSCC has the advantage that changing the threshold used to determine the risk of infection can alter Sn and Sp, albeit with a trade-off that lower thresholds will improve Sn to the detriment of Sp, while higher thresholds will improve Sp to the detriment of Sn. The internationally accepted individual cow threshold of 200,000 cells/ml is optimised for balanced Sn and Sp. However, primiparous cows (heifers) generally have lower ICSCC, and therefore thresholds should be set appropriately lower than for multiparous cows.

Although decisions to use aDCT are made at an individual cow level, the herd characteristics will influence those decisions. The prevalence of IMI in a herd – broadly indicated by the bulk milk somatic cell count (BMSCC) – will influence the positive predictive value for any given threshold (the probability that cows above the threshold have an infection). Therefore, herds with low BMSCC should use a higher ICSCC threshold to justify aDCT, while herds with a higher BMSCC should use a lower ICSCC threshold to justify aDCT (Table 1). In our view, the criteria to justify aDCT should be bespoke for each dairy farm, and should be expected to change over time, based on farmer and veterinary knowledge of predominant pathogens, BMSCC, mastitis management and risk to the cow. Targeting aDCT towards cows likely to have a major pathogen IMI at drying off should be influenced by the available data indicating likely infection status at drying off. Cows with an IMI in early lactation (either a clinical case or elevated ICSCC above threshold), where data towards the end of lactation indicate that an IMI with a major pathogen is unlikely, do not justify aDCT at drying off; for example, a cow with a self-limiting *E coli* clinical case within one month of calving with no further clinical cases and an ICSCC that remains below threshold for the rest of the lactation would not need aDCT.

Consequently, criteria such as no clinical mastitis or ICSCC above the threshold within, for example, the past three months of lactation rather than within the whole lactation should be set to evaluate the likelihood of an IMI with a major pathogen at drying off. In some herds it may be appropriate to use quarter level tests at drying off (such as the CMT) to improve Sn.

Although a ‘one size fits all’ ICSCC threshold (eg, 200,000 cells/ml for all herds) might seem a simple solution, we feel that this approach will put many herds, particularly those with a low BMSCC, at risk of treating too many uninfected cows with aDCT, while herds struggling with a higher BMSCC may find they miss that golden opportunity to cure many unidentified infected cows during the dry period, with a resultant increase in BMSCC over time. Indeed, since the BMSCC and pathogen profile of a herd is likely to change over time, there is a need to continually refresh and re-evaluate the thresholds needed to apply targeted aDCT.

The authors of this article have been working with farmers to implement a selective approach to the use of aDCT for many years. However, we feel there is now a golden opportunity for

all practitioners to engage in advising dairy farmers on selective or targeted aDCT. Increased, continuous veterinary involvement in these on-farm decisions can make a meaningful contribution to responsible prescribing of antibiotics to dairy cows without compromising the many years of hard work that have gone into achieving the current laudable UK BMSCC national average.

**TABLE 1:**

An example of how a sliding scale of thresholds for making decisions to use targeted antimicrobial dry cow therapy (aDCT) might be applied

|                              | <b>ICSCC threshold x 1000 cells/ml</b>   |                         |
|------------------------------|--|-------------------------|
| <b>BMSCC x 1000 cells/ml</b> | <b>Multiparous cows</b>  | <b>Primiparous cows</b> |
| <100                         | 250  | 200                     |
| 100 - 150                    | 200  | 150                     |
| 150 - 200                    | 150  | 100                     |
| 200 - 250                    | 100  | 50                      |
| >250                         | A low threshold could be used (eg, 50) otherwise selective/targeted aDCT may not be appropriate until the BMSCC is reduced |                         |

BMSCC The prevalence of intramammary infections in a herd, broadly indicated by the bulk milk somatic cell count; ICSCC Individual cow somatic cell count