Access to antibiotics for use in human medicine, veterinary medicine and food animal production should be viewed as a privilege and not a right. However, for much of the world’s population, antibiotics are accessible without restrictions, and are often used with no or little professional oversight. In developed countries with stricter regulatory oversight, the prescribing professions have enjoyed substantial leeway to exercise professional judgment, with little scrutiny, regarding practices of antibiotic use. For several decades, antibiotics have been widely used in food animals for ‘production purposes’ (growth promotion, feed efficiency), as well as for therapeutic purposes, often without veterinary oversight. Efforts to tighten control of antibiotic use in veterinary medicine (and other professions) are relatively recent and remain limited to the more developed nations. There can be little question that the historically laissez-faire attitude to antibiotic use, together with relatively low cost of antibiotics, has generated a less than critical mindset about antibiotic use. Studies indicate that some 50% of antibiotic use in US hospitals may be ‘inappropriate’, and the situation in outpatient and other settings (including companion and food animals) is unlikely to be better. At least in developed countries, we are now entering an era demanding more transparency and accountability in the food industry, including our practices of raising animals and approaches to preventing and treating disease.

The evolving global resistance crisis in medicine is bringing scrutiny of antibiotic use practices in all settings. The term stewardship has come to supplant “prudent” and “judicious” among others in the antibiotic use lexicon. These previous terms largely deferred to professional judgment and oversight as the means to avoid inappropriate antibiotic use. In contrast, emerging stewardship programs embody a more evidence-based approach with greater structure and accountability, including metrics of use, and evaluation of specific prescribing practices. The Society for Healthcare Epidemiology of America defines antibiotic stewardship as a ‘set of coordinated strategies to improve the use of antimicrobial medications with the goal of enhancing patient health outcomes, reducing resistance to antibiotics, and decreasing unnecessary costs’. Under any label, many basic principles and goals being promoted are relatively self-evident, e.g., minimising unnecessary antibiotic use; need for an accurate diagnosis and use of susceptibility testing; use of the ‘right drug, right dose, right time, right duration’, appropriate prevention strategies, etc. Formal antibiotic stewardship programs (ASP) are to date mostly limited to hospital settings, and in the USA, the CDC has recommended that all acute care hospitals should implement an ASP (http://www.cdc.gov/getsmart/healthcare/implementation/core-elements.html) although this goal is yet to be achieved. However, it is recognized that due to the complexity of health care and importance of local factors, for ASPs one size does not fit all. Similarly, as stewardship principles expand into veterinary medicine, we should expect that the clinical context (university hospital, vs. large geographically dispersed practices vs. small rural practices vs. population health management on farms) will significantly shape ASP efforts. It is important to note that even in the relatively narrow confines of human medicine in hospital settings, consensus of what
constitutes appropriate antibiotic use is yet to be achieved, and may not be achievable. A study comparing 4 criteria for defining ‘appropriateness’ found significant lack of agreement in classification of appropriate use among these criteria, pointing out that defining what appropriate actually means is not without challenges.(DePestel et al., 2014) Another question that remains to be resolved is who should be charged with determining appropriateness of use.

Guidelines for antibiotic stewardship in veterinary medicine are emerging, and a ‘5 Rs’ approach has been suggested incorporating elements of responsibility, reduction, refinement, replacement, and review’. (Weese et al., 2013) Again, the principles promoted are laudable, but there are some substantial gaps between the stated aspirations and current standards of practice. For example, with respect to ‘Responsibility” it is stated that ‘The prescriber acknowledges that an explicit risk assessment of the particular circumstances has found the benefits of such use together with any risk management measures recommended will minimise the likelihood of any immediate or longer term adverse impacts on the individual patient, other patients or public health.’ Therapeutic decisions in swine medicine that could invoke this standard for responsibility, particularly regarding ‘explicit risk assessments’ would certainly be the exception. One legacy of decades of antibiotic use being at the discretion of prescribers is that there is a paucity of published studies of the efficacy of treatment regimens beyond those conducted for product registration and promotion, many of which are very dated. This is changing as tightening pressures on antibiotic use in Europe have stimulated research into optimizing antibiotic use (Larsen et al., 2016), at least from the animal health perspective, and further studies are needed for the swine veterinary profession to be able to understand, document and communicate (ie., defend) benefits to animal health and welfare that are achieved with specific treatment regimens. Other important research directions relate to understanding veterinary attitudes to antibiotic use and resistance (Speksnijder et al 2015a, Postma et al., 2016) which are likely to govern current practices and must be understood to inform professional education on stewardship.

The ‘Guidelines of Judicious Therapeutic Use of Antimicrobials in Pork Production’ of the American Association of Swine Veterinarians (https://www.aasv.org/documents/2014_JUG.pdf) articulates many of the accepted principles in relation to the legal and practical aspects of therapeutic decision making in swine. However, as always the devil is in the details, and the challenge lies in how these general principles get translated into practice via the knowledge, skills and attitudes of prescribers and the compliance of their clients. While such guidelines provide a good base of principles, in developed countries there are several avenues by which the professional judgment of the clinician will be increasingly directed with respect to antibiotic use

1. Regulation of drug approval and veterinary oversight

In any environment where antibiotics are available over the counter or for production purposes, stewardship programs will likely amount to window dressing. EU countries have charted the course of regulatory changes by phasing out use of growth promotion in 2006 (earlier in some countries), requiring prescriptions (of shorter duration) for all antibiotic use, and stipulating more rigorous standards for veterinary oversight. In the USA, implementation of FDA guidance #213 from January 1, 2017, will phase out the use of medically important antibiotics for growth promotion and bring most other uses under veterinary oversight. There is little expectation for new antibiotics to become available for animal use, and greater restrictions or outright removal
of some product classes (e.g., fluoroquinolones, cephalosporins) have already occurred or are anticipated. In Denmark, the swine industry has voluntarily ceased use of cephalosporins, and the industry faces further pressure with respect to tetracycline use, despite having one of the lowest rates of antibiotic use among EU countries. Legislation to ban ‘preventive’ uses has also been established in some countries, with some inherent challenges in defining exactly what this means and how it can be enforced in the farm environment.

2. Formularies

The use of formularies is another mechanism to direct prescribing behaviours and is promoted by the WHO to indicate specific antibiotics to be used to treat common conditions. For example, The Netherlands reclassified veterinary antimicrobials into first, second and third choice for use veterinary practice. They have also introduced other measures restricting the availability of antibiotics for administration by farmers, even under veterinary supervision. (Speksnijder et al 2015b)

3. Measurement and benchmarking

Optimization of antibiotic use requires measurement, but systematic efforts to measure antibiotic use in animals at a national scale are a relatively recent undertaking. Data on gross sales of antibiotics by country are reported in several countries including the USA, but generally lack sufficient granularity to allow meaningful assessment of usage or to inform antibiotic stewardship efforts. Calls for more detailed quantification of antibiotic use in animals (and particularly food animals) come from multiple sources:

- World Health Organisation policy to standardize protocols to facilitate global harmonization in surveillance of antibiotic use in humans and animals, and of antibiotic resistance (http://www.who.int/world-health-day/2011/presskit/whd2011_fs4d_subanimal.pdf?ua=1)
- European Union directive to harmonize antibiotic use surveillance across countries as part of the an action plan against the rising threats from antibiotic resistance (http://ec.europa.eu/dgs/health_food-safety/docs/communication_amr_2011_748_en.pdf)
- Calls for better surveillance of antibiotic use in food animals as part of the National Action Plan for Combating Antibiotic Resistant Bacteria in the USA (https://www.whitehouse.gov/sites/default/files/docs/national_action_plan_for_combating_antibiotic-resistant_bacteria.pdf)
- US Government agencies seeking to gauge the impact of regulatory changes to antibiotic use, specifically FDA guidance 209/213
- Consumer groups/ politicians seeking stricter regulation and monitoring of antibiotic use in food animals to underpin stewardship (e.g., the Delivering Antibiotic Transparency in Animals Act in the USA)
- Specific initiatives in some EU countries (Denmark, Netherlands, Belgium, Germany) to monitor and benchmark antibiotic use at the end user (farm, veterinarian) level
- Growing demands from downstream customers for assurances related to judicious antibiotic use in the supply chain
- Scientists advocating the need for reliable data to enable meaningful risk assessment of the impact of antibiotic use in food animals on human health.
The question of defining metrics is challenging, and is inherently tied to the specific purpose of measurement. If the purpose is to estimate industry level use for benchmarking and tracking trends over time, sample based approaches are likely to be adequate. However, several EU countries have implemented very detailed systems on a census basis to quantify antibiotic use by individual producers and veterinarians, with interventions targeting individuals that are high users. However, a recent summary from ESVAC (European Surveillance of Veterinary Antimicrobial Consumption, 2016) stated that ‘the highly resource demanding ‘manual’ collection of data on consumption per species at national level suggests that it would not be a sustainable approach in the long term’, and less comprehensive approaches will be required for most countries.

4. Arbitrary targets for reducing antibiotic use

A number of European countries have announced specific targets for reduction of antibiotic use in food animals. (Speksnijder et al., 2015b; Daeseleire et al., 2016) Notably, reduction per se is the stated goal, without being linked to other outcomes such as animal health and welfare, or to specific goals in reducing resistance in animal or human pathogens. However, the a 54% reduction in antibiotic use in swine in the Netherlands has been associated with 22% reduction in resistance in E. coli (http://cdn.ipulse.nl/imail2u/Userfiles/def-engl-s-rapport-abgebruik-en-resistentie-0516.pdf), and apparently without measurable impact on animal health. It is probable that in most industries there is considerable scope for ‘judicious’ reduction in antibiotic use. However arbitrary targets for reduction, whether they emerge from the socio-political arena or from downstream sectors of the food supply chain, themselves need to be treated judiciously.

References


