Is an antibiotic-free future likely?

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in the third of six reports, discusses the reality of whether a world without antibiotics could exist and reasons behind explosive rates of their resistance

ANTIBIOTICS can be defined as substances that kill or inhibit bacterial growth.

Frequently used in the prevention and treatment of bacterial disease today, their use in modern medicine began in the early 1940s. However, both antibiotics and resistance strategies developed simultaneously with bacteria around 3.5 billion years ago.

Many of us fall into the trap of considering antibiotic resistance a recent phenomenon, yet research from D'Costa et al (2011) described 30,000-year-old bacteria with genes coding for resistance to penicillins, tetracycline and glycopeptides – proving antibiotic resistance is simply another evolutionary survival tactic, predating modern selection pressures of clinical use.

It is likely this represents natural resistance – that is, the innate ability to withstand specific antibiotic activity through inherent structural or functional characteristics. Genes conferring such resistance are passed on to bacterial progeny (vertical transmission), while high bacterial reproductive rates result in significant resistance effect within a population.

Panel 1. The five rights of drug administration

- the **R**ight drug
- the **R**ight patient
- the **R**ight dose
- the **R**ight route
- the **R**ight time

Resistance reasons

So, why are we seeing such an explosive rate of resistance? The application of antibiotics for medical use dramatically increased selection pressures exerted on bacterial populations.

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*VT*46.30 – Richard Meers

Bacteria were being deliberately exposed to multiple antibiotics: easy access, perceived effectiveness and poor knowledge resulted in widespread misuse and resistant colonies formed rapidly. Ongoing misuse of antibiotics worldwide – for example, as growth promoters in livestock and mis-prescription in the face of viral disease – create further selection pressures.

In the face of widespread drug use, bacteria developed mechanisms for acquiring resistance at a much faster rate than vertical transmission allowed, to secure their long-term survival.

Resistant strains of bacteria pass resistance genes to naive, non-resistant populations in three ways: conjugation, transduction and transformation, which are all forms of horizontal transmission. This enables bacteria to acquire multiple resistance traits rapidly, even prior to drug exposure.

Careful examination and consideration of the likely aetiology is essential prior to dispensing antibiotics. This wound resulted from extensive periapical abscessation and healed fully following extraction of tooth 208 with perioperative antibiotic use only.

Consequences

Consequences of drug resistance are serious and far-reaching; consider ramifications for immunosuppressed patients, or those facing severe infections or major surgery. While reversal of resistance is possible, the rate at which this may be achieved is far slower than is useful.

Vigilance in preserving existing antibiotics is critical and we should all adhere firmly to the five rights of drug administration (**Panel 1**).

Veterinary practice presents several specific prescription challenges with economical, logistical and practical hurdles. Many clients are financially mindful; insisting on culture and sensitivity prior to treatment in every patient is not sustainable.

Careful consideration of the expected causal organism, along with testing treatment failures, is essential.

It is not uncommon to find the best practice drug choice precluded due to patient non-compliance, the cascade, costs, logistics prohibiting appropriate dosing intervals – the list goes on.

Restrictions on drug availability (for example, crystalline penicillin, cephalosporins and oxytetracycline) is just the latest challenge for the equine practitioner.

Mindset changes

Despite this, we must hold ourselves accountable and make fundamental changes in our mindset of how we use antibiotics. Restricting dispensing to essential use, employing an evidence-based approach, treating topically where possible, promoting preventive health care and auditing our practice to highlight clinic weaknesses are all achievable goals.

While the destiny for our antibiotics may be grim, new technologies are being developed to combat this battle and give us hope for a new future in bacterial warfare:

- Inspirational research into methods to bypass resistance.
- Nanotechnology to achieve new delivery techniques (magnetic nanoparticles/nanobiotics) or bacterial gene targeting (small interfering ribonucleic acids; Hussein-Al-Ali et al, 2014).
- Chemically programmable immunity to tag pathogens, instantly identifying them as foreign.
- Other ideas, such as pathogen nutrient chelation.

References

D'Costa VM, King CE, Kalan L et al (2011). Antibiotic resistance is ancient, *Nature* **477**(7,365): 457-461.

Hussein-Al-Ali SH, El Zowalaty ME, Hussein MZ et al (2014). Synthesis, characterization, and antimicrobial activity of an ampicillin-conjugated magnetic nanoantibiotic for medical applications, *Int J Nanomedicine* **9**: 3,801-3,814.

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