The emerging issue of antibiotic stewardship in Asia

Antibiotic stewardship is rapidly emerging as an important issue for animal production systems throughout the world, with the agenda being set largely by the first world.

In Asian agriculture the biggest impact to date has been in the area of prophylactic administration to food producing animals, especially in products that are going to be directly consumed (more so if these products are destined to be exported).

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Some clumsy regulatory interventions have been seen with nominal banning of administration of antibiotics to food producing animals and indeed there may still be big gaps between policy and practise in many countries but the future is less antibiotics.

Prophylactic programmes

Since the 1960s poultry and egg production have traditionally used antibiotics in prophylactic programmes with many interventions having their effects on controlling the impact of avian mycoplasma infections in birds.

Obviously, antibiotics are not the solution as the bacterial problems are still here. Only the routine prophylactic administration of antibiotics around hatch has a target bigger than mycoplasma, if we do not consider ionophore administration for coccidiosis control.

The administration of antibiotics at day 18-22 in broilers to control post vaccinal reactions or prevent CRD is only necessary in broilers derived from mycoplasma positive breeder flocks (or flocks vaccinated with F strain).

The administration of antibiotics in the laying period of breeders and layers every 4-8 weeks has been used for many years in Asia and is of particular concern.

WAM (week a month) programmes apply selection pressure on all bacteria in long lived birds generating and maintaining resistance elements. These programmes presumably destabilise the intestinal microbiota and probably facilitate the colonisation by salmonella.

Another feature that has not been extensively considered is where does this antibiotic end up? In the litter!

If the target of an antibiotic intervention is in the respiratory tract then using compounds like lincospectin seem to be at odds with antibiotic stewardship. The spectinomycin will not give any benefit in the case of a respiratory infection when given orally as it is not absorbed and will only apply selective pressure on the intestinal microbiota for resistance.

To remove antibiotic prophylactic programmes there needs to be an alternative solution for mycoplasma protection.

Practically throughout the world these solutions are:

- Mycoplasma freedom.
- Killed vaccines (now an anachronism and too expensive).
- Live vaccines.
- Combination of interventions.

Combinations especially with antibiotics may be antagonistic and not synergistic as was expected.

On top of this antibiotic resistance in avian mycoplasmas in Asia is an unquantified problem. Few studies have been done on isolates east of the Middle east and west of Japan.

Enrofloxacin therapeutic failures rapidly appeared in the 1980s in India, Thailand, China and elsewhere, probably associated with the massive use of this antibiotic to the point where this class of antibiotic is not considered anti-mycoplasmal by clinicians from their everyday experience.

Clinically we have seen tylosin resistance in Indonesia and tiamulin resistance in India and China.

Therapeutic failures in the treatment of clinical mycoplasmosis are common in Asia but when an antibiotic is used prophylactically you are not curing existing clinical effects and the resistance may be cryptic (although subclinical effects may be large and vertical transmission may give bigger problems in the next generation).

In general, the more you use antibiotics the more you lose effectiveness from a medium to long-term perspective; the rate may vary but resistance has been seen for every antibiotic.

Mycoplasma monitoring

There are many reasons why antibiotic resistance in mycoplasmas has not been monitored. Most importantly worldwide the results are not available in real time to allow the clinician to select a treatment in clinical cases. People are trying to develop PCR based tests to get results rapidly but this has some problems including missing novel resistance mechanisms and, to date, still needing pure cultures rather than swabs of clinical samples to get results. The result is that very little mycoplasma MIC testing has been done in Asia (Papinyo 2007 in MG is a rare exception). First is the problem of mycoplasma culture (bacterial and fungal overgrowth) and then the second problem is finding laboratories with expertise in testing MICs in mycoplasma.

The culture problem may have been solved. We have been using filtering of clinical samples in media within one hour of taking through a 0.45µm disposable filter.

The filtered media sample is then transported at room temperature to a competent laboratory within 10 days. The filter removes walled-bacteria and fungi and replaces inhibitory antibiotics in media (antibiotic resistance in commensals is a problem with traditional sampling nowadays). Isolations from these filtered samples has been particularly successful.

It has been suggested that PCR for detection before and at the end of therapy would also be a good way to monitor antibiotic effects.

If the Ct of tracheal samples does not significantly increase by the end of antibiotic therapy then antibiotic resistance or other causes of therapeutic failure should be considered. This has been seen in China with tiamulin therapy failure.

Sometimes antibiotic suppliers claim that antibiotic resistance has not been reported to a particular antibiotic in a particular organism. This claim is often wrong and surveys in Asia would give us a lot more relevant information to base therapy decisions on.

In contrast to antibiotics, the protection generated by live mycoplasma vaccines seems more sustainable. The ability to increase the resistance of flocks to infection with wild strains has been recently demonstrated.

MG and MS vaccines are nearly available throughout Asia and allow a massive decrease in antibiotic dependence in poultry production by replacing WAM programmes. Protection by vaccination is for the life of the flock if antibiotics are not used.

The monitoring of vaccinated flocks is not done by serology. Serological responses in vaccinated flocks are uninterpretable.

Troubleshooting vaccinated flocks is done by DIVA PCRs (for example MSH MAMA Kreizinger and others 2017). Australia has successfully weaned the poultry industries off antibiotics since the registration of these vaccines. These vaccines were originally developed in Australia because of the emergence of tylosin resistant MG strains. ■

References are available from the author on request