

Diminishing control of avian mycoplasmas

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Abstract

A large number of commercial laying operations in Asia are multi-age facilities which create a degree of difficulty in control of mycoplasmas including, *Mycoplasma gallisepticum* (MG) and *Mycoplasma synoviae* (MS). As a result, many facilities maintain a continuous mycoplasma positive status and utilize commercially available vaccines as part of their control programs. The current approaches to mycoplasma control include continuous surveillance and quarantine, medication, vaccination and/or elimination of infected breeding flocks. With worldwide increase in the use of live attenuated vaccines as a control method, molecular techniques that allow the differentiation of live attenuated and killed mycoplasma vaccine strains are increasingly important for diagnostics and applied research.

Antibiotics have been used around the world since the 1960's for control and prevention of MG and MS problems in chicken production systems. Indeed, anti-mycoplasmal antibiotics are the only intervention to salvage flocks after they become infected and they have been used extensively for prophylaxis especially in lay in layers and broiler breeders and to prevent CRD in vertically contaminated broiler stock. They are not the complete solution to mycoplasma infections (or these problems would have been solved in the sixties) but they have been a pragmatic solution. Now their use is generating problems.

When an antibiotic is used extensively there can be rapid development of resistance. Examples of tylosin resistance in Indonesia and Malaysia and, Tiamulin resistance in India have been suspected because of the observation of clinical disease in birds despite being routinely treated with these drugs. MS is innately resistant to erythromycin and closely related macrolides and we have seen cases of therapeutic failure in the treatment of mycoplasma disease in India that makes one suspect MS as the main mycoplasma involved. A further problem is that live mycoplasma vaccines need to colonize the chicken to maintain effective long-term immunity. All live mycoplasma vaccines are sensitive to all antibiotics (this is preferred by regulators) and the administration of antibiotics every 4-6 weeks will see mucosal immunity wane. This is not a problem if the field challenge is sensitive to the antibiotic but is a problem if it is resistant. Salmonella infections (carriage and then excretion) may be increased by antibiotics by destabilisation of the gut microflora. Although antibiotics are chosen for their effects on a target pathogen they put pressure on all sensitive organisms.

This phenomenon might be further aggravated by some other practises in Asia. Some people only use antibiotics in lay when the humoral serology increases to MG or MS (India, Indonesia and Thailand). These responses in vaccinated flocks may be normal vaccine responses. Other people

worldwide has misinterpreted increasing serology in vaccinated flocks as vaccine failure. Certainly, they are sacrificing the vaccine component of protection by giving antibiotic treatments for serological increases.

Antibiotic stewardship is a worldwide effort to decrease antibiotic usage in animals and humans to maintain the usefulness of antibiotics in human medicine (and hopefully this will also maintain their effectiveness in animals). This is predicated on the idea that antibiotic use leads to higher levels of resistance (and the development of multi-resistance). So far, this effort has lacked focus, just pressuring for decreased use rather than looking at why antibiotics are used and finding alternative solutions (focused antimicrobial stewardship). In terms of quantity of antibiotic used, the routine application of antibiotics every 4 to 8 weeks during lay is the major use in Asia but because it is one step from the food (the production of fertile eggs) it has had little attention to date. Hopefully Asia will focus on eliminating antimicrobial prophylaxis rather than being excessively worried about ionophore usage (a current issue in the Americas and Europe). Thailand has recently banned antibiotics for prophylaxis because of needs of its export market and is leading the way. Also the idea of antibiotic testing mycoplasmas before starting treatment is not practical (6 weeks before treating) but knowing the sensitivity profiles of strains bouncing around in an area and chasing therapeutic failures and PCR at end of treatment to see that the numbers are reduced on a yearly basis is probably more practical.

Mycoplasmas are very difficult to culture in Asia (and becoming more so as resistance in coliforms and other contaminating bacteria increases in resistance). Contamination of samples with fungi and bacteria that are resistant to traditional selective inhibitors sees overgrowth. This means that PCR based systems are favoured but antimicrobial resistance testing needs isolates from animals. This can be counteracted by filtering samples (0.45 µm) at the time of sampling. Then resistance testing in mycoplasma is technically very demanding and not routine in many labs. The WHO recommendation that some antibiotics not be used in humans unless a culture and sensitivity is done first. In animals in Asia some of these important antibiotics are being used extensively and resistance levels are poorly understood.

In general, the more effective a treatment is the faster resistance will develop. These resistance determinants are making our traditional responses to these organisms ineffective and may be continuing pressure on the selection for multi-resistance. Our initial response is more control, but this may need reassessing and reorientation. Establishment of normal flora and its protection may be more important.