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Veterinarians + Live vaccines = One Health

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Vaccination, a historical triumph in public health, has been instrumental in safeguarding the health and well-being of both humans and animals. The pioneering efforts of Edward Jenner and Louis Pasteur in the 18th and 19th centuries paved the way for significant advancements in this field. By the 20th century, these advancements led to the eradication of rinderpest in bovine and smallpox in human populations, marking crucial milestones in the history of public health.

While antibiotics are undoubtedly crucial in managing bacterial infections in poultry production, it is important to stress that they are not a substitute for the fundamental pillars of prevention: good hygiene, husbandry, breeding, genetics, and biosecurity measures. When implemented by poultry health professionals, these measures serve as the first line of defence in preventing infections and safeguarding animal health, making them the primary focus. Additionally, acute nutrition management, stocking densities, implementation of all-in/all-out systems that allow for complete shed cleaning and proper disinfection, and maintaining high housing standards also play a significant role in disease prevention, underscoring the importance of a comprehensive approach. When executed effectively, this comprehensive approach, which outlines the multifaceted nature of poultry health management, yields One Health benefits.

The Australian poultry industry, driven by a commitment to health and welfare, was pivotal in developing live Mycoplasma vaccines to bolster poultry's immune resilience. In the 1980s, a report revealed a concerning trend: a progressive buildup of resistance to Erythromycin, a macrolide class of antibiotic used to treat respiratory complex diseases in poultry caused by Mycoplasma spp. This prompted the industry to take action, leading to the introduction of the live *Mycoplasma gallisepticum* (MG) Vaxsafe®MGts-11 vaccine in 1990, followed by the live *Mycoplasma synoviae* (MS) Vaxsafe®MSH vaccine five years later. These vaccines provide life-long immunity (Morrow et al., 2022; Achari et al., 2023b). This turning point inspired a new era in Australia's poultry health management and human health protection.

Since their introduction and use in Australia to control avian mycoplasmosis, there has been a significant reversion in Erythromycin sensitivity in non-target *Enterococcus faecium* isolated from chickens in Australia (Barton & Wilkins, 2001; O'Dea et al., 2019; ACMF report, 2022). These Australian vaccines, now distributed globally, are not just making a positive impact locally but also on an international scale. The success stories of these live vaccines in controlling respiratory diseases caused by MG and MS are a powerful testament to their efficacy and the global impact of Australian contributions to One Health (Veen et al., 2021 & 2024). Breeders vaccinated at 21 days to 6 weeks of age did not require routine antibiotic programs, nor did their progeny for their entire productive life (Morrow & Achari, 2020a; Yadav et al., 2022). The ultimate goal is to effectively control Mycoplasma infections by bolstering life-long immunity using safe vaccines

that prevent vertical transmission, eliminating the need for routine antibiotic administration (Achari et al., 2018; Condello et al., 2020; Ramasamy et al., 2021). This experience was mirrored by using the live Vaxsafe®ST vaccine in chickens, which reduced human *Salmonella* infections in Australia (McLure et al., 2022). These are clear examples of how live vaccines have contributed to the judicious and targeted use of antibiotics for AMR and reduced potential public health risks associated with food production.

According to the 8th annual report published by the World Organization for Animal Health (WOAH), the global use of antimicrobials in food-producing animals increased from 107.3 milligrams per kilogram (mg/kg) to 107.9 mg/kg (2%) from 2019 to 2021. In 2021, the total amount of antimicrobial agents intended for use in animals ranged between 81,084 and 88,927 tonnes. Tetracyclines were reported to be the most used antimicrobial agent globally, accounting for 35.6% of the total amount, followed by penicillins and polypeptides. Poultry accounted for 18% of the total animal antimicrobials coverage. This increase comes after several years of decline. However, the report also reveals concerning trends. Nearly 20% of WOAH member states reported using antimicrobials as growth promoters, a practice discouraged by WOAH and other global health agencies (https://www.woah.org/en/document/eighth-annual-report-on-antimicrobial-agents-intended-for-use-in-animals/). This report underscores the need for continued education and importance of structured monitoring and surveillance to address antimicrobial resistance.

The issue of AMR in *Mycoplasma* is significant in Southeast Asia (Tian et al., 2021; Malik et al., 2023; Morrow et al., 2020b). In India, the use of antibiotics in chickens is expected to triple by 2030 compared to 2015 due to increasing consumer demands and poor intensive farming practices (Mathur et al., 2024). The upward adjustments of dosages and testing of new combinations are being increasingly observed in Asia (Morrow, 2024; pers obs.). In a recent study conducted in Vietnam, Taiwan, and India, the minimum inhibitory concentrations (MICs) of the most commonly used antimycoplasmal antibiotics, including Ciprofloxacin, required to effectively control the two most important strains of avian mycoplasma, MG and MS, have drastically increased, potentially rendering them ineffective for the future (Morrow et al., 2020b; Achari et al., 2023a). This problem demands urgent attention and action.

Some argue that veterinary vaccines may offer only up to 70% protection (Westman et al., 2016; Aida et al., 2021). However, even at this level, such vaccines are crucial in mitigating human health risks while minimising animal health issues by reducing disease outbreaks and decreasing the reliance on medications such as antibiotics and other antimicrobials. Consequently, this reduces the pressure for resistance development and maintains the efficacy of existing chemicals for longer. This effect was also observed in the case of acaricides used for tick control in cattle (Johann Schroder, pers comm). A key challenge lies in convincing producers thatconsistent and dedicated use of vaccines over a prolonged period leads to a sharp decrease in the occurrence of respective diseases, as supported by Veen et al., 2024. Today, approximately 93% of the Australian long-lived bird population continuously uses the mycoplasma vaccine, making it an established

vaccine in the vaccination programs. Another risk is that as diseases become less prevalent, producers may become more complacent (because they do not see the disease) and, therefore, discontinue interventions for those diseases, leading to re-emergence problems later.

One of the veterinarians' most important preventative responsibilities is managing the immunocompetence of the birds under our care (Sorci, 2013; Achari & Morrow, 2019). This includes using available vaccines against immunosuppressive agents and understanding what is causing the immunosuppression, which could include mycotoxins, infections, management practices and nutrition, etc. (Prezotto et al., 2016; Bao et al., 2020; Achari & Achari, 2024). Infectious Bursal Disease Virus (IBDV) and Chicken Anaemia Virus (CAV) infections have been shown to impact the immunity generation to a live *Mycoplasma* vaccine (Arachchige et al., 2021). Therefore, it becomes the responsibility of the veterinarian to consider the vaccination program holistically when designing and selecting the most appropriate live vaccines, especially for *Mycoplasma*

control. Combating AMR requires a multifaceted approach, including prudent use of antimicrobials, robust infection control measures, investment in research for alternatives such as vaccines, and global collaboration. By advocating for the use of live vaccines and implementing improved hygiene, nutrition, and biosecurity measures, we can significantly contribute to One Health and address this silent pandemic. As professionals in the poultry industry, we play a pivotal role in mitigating long-term unintended consequences to animal health from our decisions and preventing risks to human health resulting from our animal health management practices. This means it is crucial to stop the use of antibiotics as growth promoters or for any reason not justified by the health needs of the animals. Doing so is essential to safeguard global animal and human health from the severe threat of AMR. Encouragingly, there are promising trends indicating that farmers and veterinarians are increasingly accepting the idea that not every visit requires a prescription. Determining appropriate interventions involves identifying the root cause of disease and then engineering solutions accordingly .This is particularly crucial in poultry, especially for controlling *Mycoplasma* in layer hens.

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