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EVOLUTION OF LIVE VACCINE ADMINISTRATION

New-Generation Advances

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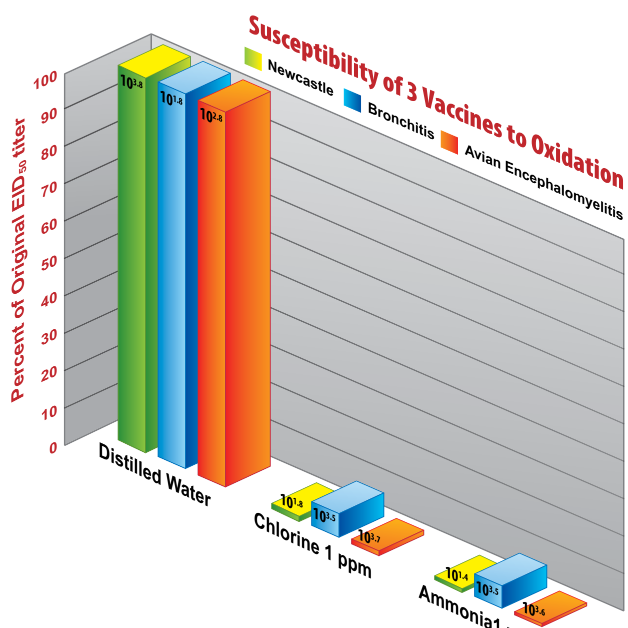
"HIT ME WITH YOUR BEST SHOT"

The industry is at a roadblock. The year is 1955, and live respiratory vaccines are being given logically…in the nose. After all, where else would you put a live respiratory virus like ND and IB? Flock sizes are increasing, confined houses are growing, and fledgling integrators are feeling more and more outbreaks. More outbreaks naturally require more vaccinations, and consequently more individual bird handling. Labor costs are climbing and something has to be done.

Historical perspective on mass respiratory vaccinations

Re-routing intranasal live vaccines to deliver them through the drinking water was not a guaranteed fix. It was a technique envisioned by Luginbuhl et al (1955), after they noticed significant amounts of intranasal vaccine were being swallowed during administration. Creatively they tested their idea by inserting capsules filled with ND and IB vaccine into the crops of chickens. It risked failure because it bypassed the respiratory tract target entirely; but the reward, as we know now, was successful protection with much-needed labor savings. Of course it seems nothing comes for free. Labor was reduced significantly but vaccine stability had to be managed with more finesse. After all, the key to success with a live vaccine is, well… it must be alive.

Worried that water quality posed unmeasured risks to vaccines, Gentry and Braun (1971) and Jordan and Nassar (1973) experimented to quantify the hazards. Among the risks first recognized by these workers was vaccine inactivation from oxidizing sanitizers. Using chlorine as an oxidizer to purify drinking water was widely accepted as a good management practice. Consequently, neutralizing chlorine's negative impact on vaccine virus by pre-treating the drinking water with powdered skim milk emerged as a key recommendation. The amount of powdered skim milk required to neutralize 5 ppm free chlorine is determined to be approximately 5.3 lb in 256 gallons (Gentry and Braune 1971). In practice adding this much insoluble milk powder via a concentrated vaccine stock solution proved infeasible. Vaccinators continued to add skim milk, but typically at suboptimal concentrations, about 20% of this amount, giving us the commonly adopted pound per 256 gallons.

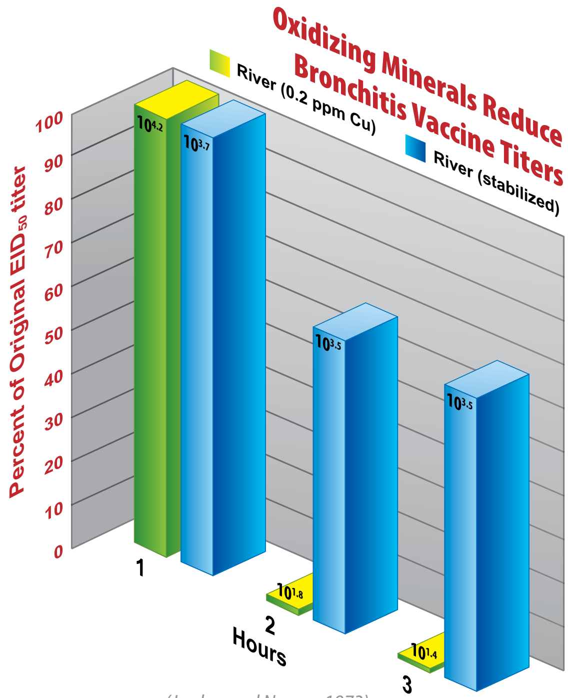


(Gentry and Braun, 1971)

Although water sanitizers were seen as the chief impediment to vaccine stability, these workers also studied other risks including pro-oxidant trace elements, temperature, pH, hardness and electrolyte concentrations. A later case study reported by Heins-Miller (1993) highlighted the positive impact that cleaning and purging water lines can have on vaccine efficacy. Constant chlorination retards some biofilm growth, but cannot eliminate the organic debris or reduce the accumulation of mineral scale. To this end, frequent acid purges should not be neglected. Using acidifiers to dissolve mineral scale and dislodge organic debris is an important management tool that helps avoid vaccine inactivation.

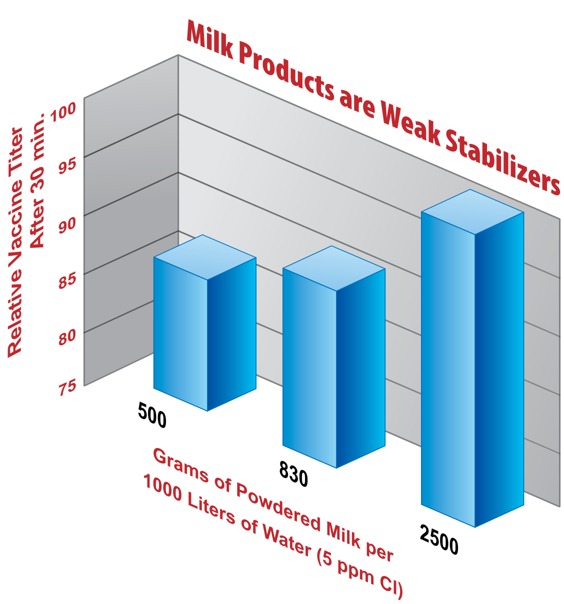
New-generation… beyond chlorine

The propensity for organic material, such as milk powder, to neutralize free chlorine was promising for vaccine stability. However the powder's notoriously poor solubility and slow reaction time created management headaches in the form of plugged drinkers, prolonged mixing times, and occasional use of detrimentally-hot water to hasten dissolving. Poultry managers also came to find that the protein and sugar present in milk powder could contribute to biofilm blooms. In recent years regulatory authorities and others focusing on biosecurity have also taken an increasingly negative view of products of animal origin. Avoiding animal proteins and their associated handling problems in water spurred a drive toward more ideal solutions than milk powder, although milk powder is still used in many parts of the world.



(Jordan and Nassar, 1973)

Davis and Lasher (2000) collaborated in testing a new-generation stabilizer, with derivatives ultimately being developed and tuned for the circumstances specific to each delivery method, such as drinking water or spray. Their initial work resulted in significant improvements in IBV vaccine stability using smaller additions of a more concentrated stabilizer that was completely soluble and rescued the vaccine from higher oxidizer concentrations. This antioxidant protection also helps reduce other pro-oxidizing inorganic mineral elements, such as iron, and nitrates, peroxides and ozone. Continued research at Lasher Associates, USDA laboratories, and private institutions confirmed the stabilizer's antioxidant protection extends broadly to other important respiratory antigens for poultry and swine, including NDV, Mycoplasma, Salmonella, and Erysipelas.



(Adapted from Gentry and Braun, 1971)

In the case of the bacterial vaccine antigens, particularly Mycoplasma, inappropriate osmotic balance can also decrease vaccine effectiveness. Whole-cell bacterial vaccines survive best in an environment where osmolarity is properly balanced. At USDA laboratories, Leigh et al (2006) demonstrated that distilled water, which is commonly recommended as a spray diluent, is hypotonic enough to inactivate Mycoplasma vaccine before the vaccine can be sprayed. The vaccine cells quickly pull in hypotonic water and ultimately burst, leaving ruptured cell debris instead of effective vaccine. A similar hypotonic condition exists for ground water supplies. In one important aspect, ground water can be deemed superior to bottled water or water from above ground storage. Jordan and Nassar (1973) also documented the thermal instability of IB vaccine, showing significant losses with temperature increases from their experimental low of 20 C. Delivering vaccine in cooler ground water is supportive for sprayed vaccines, provided the stabilizer addresses the risk of hypotonic conditions to bacterial antigens. Among the side benefits of using more concentrated new-generation stabilizers is the ability to incorporate electrolytes and other functional components into the formulation. Leigh et al (2006) confirmed that the stabilizer, when formulated for proper osmotic balance, shielded the Mycoplasma bacterial vaccine from inactivation.

In addition to osmotic balance, new-generation stabilizers also impart buffering capacity to concentrated vaccine solutions. For a stabilizer to be trusted globally, it must universally address water quality problems in disparate regions. The stabilizer must be able to overcome pH excursions both above and below the vaccine's optimum range. Multiple buffering systems allow a single stabilizer to increase the pH of a vaccine concentrate in acidic farm water and decrease it in alkaline conditions, ensuring the different water sources are more consistently ideal. Even distilled water, which has an acidic average pH at 5.2, is not necessarily ideal for vaccines. Additionally, acidifiers used to support bird digestive health can harm vaccines, and should be discontinued before vaccinating. The stabilizer's buffering action can be important in helping protect against traces of residual acids.

The sensitivity of vaccines to acidic pH must also be considered when using stabilizers or dyes produced as effervescent compressed tablets or granules. The effervescence that speeds up slow-dissolving tablets or granules is a byproduct of acid and carbonate chemistry. Many effervescent additives release excess acid that drops the pH in the vaccine solution well below the optimum within 15 seconds of being added to water (Izard, unpublished).

Other functional properties have been added to new-generation stabilizers to facilitate vaccination management. Examples are traditional food dyes that mark individual animals to visually assess uniformity in both drinking water and spray vaccination, ultra-violet and infrared colorants with amplified wavelengths to stimulate the birds' visual cues and preening of sprayed vaccine, and ocular-nasal additives with strong surface tension to increase the vaccine's residence in the eye. More recently gel sprays have also been developed to create positionally stable suspensions that hold the vaccine uniformly in solution, useful for preserving the vaccine and at the same time delivering less-soluble edible active ingredients like live probiotics. Early-adopting hatcheries have even used these stabilized gel suspensions to combine coccidiosis vaccines (which are preserved with oxidizers) with live organisms in a single-pass spray, something unthinkable until now.

Summary

The trade off between individual bird inoculation and mass vaccination is this… individual inoculation requires more labor, while successful mass application requires more management. Failing to manage the numerous risks that exist among all water supplies can reduce vaccine effectiveness and leave holes in the flock's immunity. New-generation stabilizers for drinking water, spray and eye-drop seek to protect vaccines from as many risks as possible. In the end, safe food comes from companies with healthy birds, healthy birds come from farms with strong vaccination management, and strong vaccination management includes new-generation stabilizers.