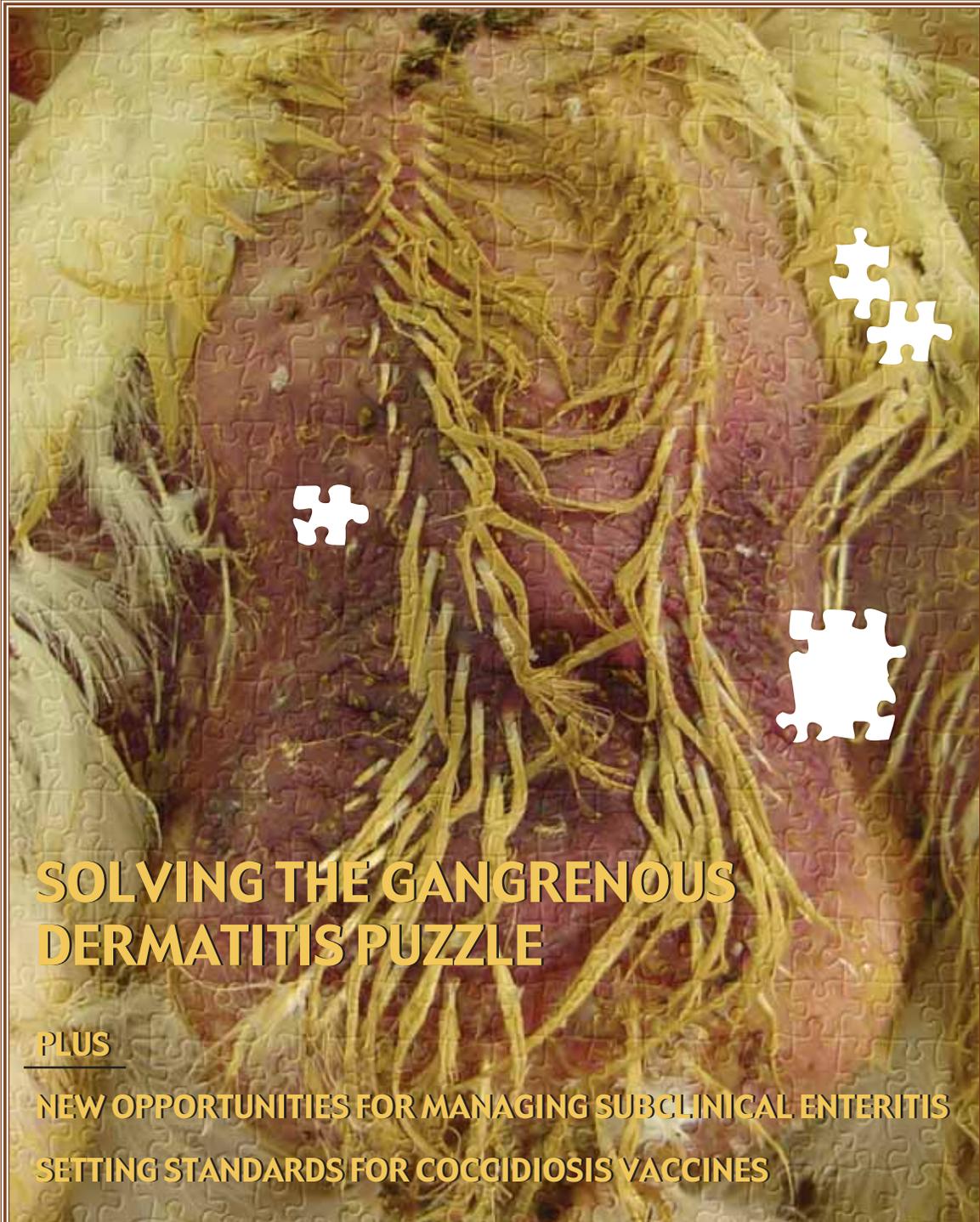

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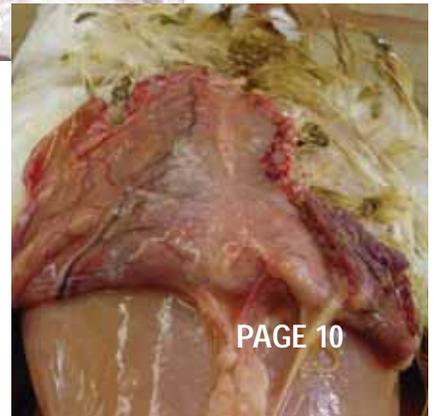


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Cover: Mortality, carcass condemnations and trimmed parts can result from gangrenous dermatitis, a costly disease in broilers. Now, new evidence suggests that vaccinating for coccidiosis may be the missing piece of the control puzzle. For more information see the article beginning on page 10.

Photo courtesy of Dr. Charles Broussard



WORKING UNDERCOVER

Subclinical necrotic enteritis often goes undetected, slowly erodes profits

A gut disease that often goes unrecognized and prevents broilers from achieving optimal performance is more common than thought and is certain to increase as poultry operations reduce their dependence on in-feed antibiotics.

The disease is subclinical necrotic enteritis (NE), caused by the pathogen *Clostridium perfringens*. Poultry veterinarians familiar with subclinical NE say the industry needs to intensify efforts to detect and manage the disease before it erodes performance and profits.

“It’s a big problem,” even though no one really knows the actual incidence because it is not easily detected or diagnosed, says Dr. Steve Davis, president and chief executive officer of Colorado Quality Research, Wellington.

“The effect is subtle and additive. Performance deteriorates from flock to flock, especially if you aren’t cleaning out your houses. The clostridium in the environment increases over time,” he says.

Conventional flocks at risk

Subclinical NE is most likely to be seen in standard broilers that are receiving ionophores for coccidiosis control but not antibiotic growth promoters (AGPs), a pattern becoming more typical in the US poultry industry, Davis says.

“Here at Colorado Quality Research, we saw the direction the industry was heading about 4 years ago and knew that necrotic enteritis was going to be a hot research topic,” he adds. “That’s why we developed and fine-tuned a live NE challenge model and, to date, have conducted over 30 NE studies.”

AGPs, Davis explains, have an inadvertent side benefit. They not only promote growth, they control clostridium. Overuse of ionophore anticoccidials, coupled with extended withdrawal periods, has resulted in resistant coccidia and late cycling of the coccidial challenge, which results in poor gut health, setting the stage for development of NE.

In contrast to subclinical NE, full-blown clinical outbreaks of NE are easily recognized and usually treated due to high mortality. They are more likely to occur in antibiotic-free birds and in birds receiving chemical anticoccidials or coccidiosis vaccines, which can do an excellent job controlling coccidiosis but have no secondary antibiotic effect against NE, says Davis, who has experience as a live production poultry veterinarian.

How *C. perfringens* affects a flock might also differ with the isolate. Some *C. perfringens* isolates tend to cause rapid illness and mortality with less impact on the performance of surviving broilers, while others rarely cause mortality but significantly decrease growth and feed conversion, he says.

Missed diagnosis

“Producers tend to miss subclinical NE in part because they haven’t had it before,” he says. In other cases, there’s a gradual drop in feed efficiency and poor weight gain that goes unnoticed. The problems may have gone on for so long that producers think it’s normal. There may be liver lesions that result in condemnation at processing. Sometimes, subclinical NE isn’t recognized until a change is made in the health



Davis: ‘Producers tend to miss subclinical NE.’

program and they see improved performance.

Davis' work has led him to believe that subclinical NE affects not only the gut, but also the joints in the form of synovitis and femoral head necrosis. "Generally, this problem is chalked up to an *Escherichia coli* infection, but if you culture the lesions anaerobically, I think you'd find clostridium is a much bigger issue because it allows bacteria to become systemic and it ends up in the joints," he says, noting that he presented the research supporting this theory at the 2006 American Veterinary Medical Association annual meeting in July.

Dr. Scott Gustin, director of veterinary services for North America and Asia at Cobb-Vantress, the Arkansas-based poultry research and development company that sells broiler breeders, has similar comments about subclinical NE. "Unless you're looking for it during routine posting sessions, you'll miss it," he says.

Does he believe that subclinical NE will increase as less AGPs are used? "Absolutely." There is still a lot unknown about subclinical NE, Gustin says. "With the declining use of in-feed antibiotics and rise in intestinal disease, we are realizing that gut health is an incredibly complex science. Diseases or syndromes such as 'dysbacteriosis' and subclinical NE are perfect examples of newly evolving diseases we don't understand and control optimally."

He's seen enough subclinical NE, however, to conclude that "it's probably much more of a significant issue than we realize and is probably much more widespread than clinical NE."

Cost of subclinical NE

An oft-quoted figure on the cost of subclinical NE is 5 cents per bird. Gustin says that "Subclinical necrotic enteritis can result in a 5- to 10-point increase in

feed conversion in controlled trials we have funded. It can be very damaging to economic returns across an operation due to that lost feed conversion ratio."

Dr. Charles Hofacre, a professor at the University of Georgia, Athens who is considered in the poultry industry to be a guru on the subject of NE, says, "Subclinical necrotic enteritis is probably *more* expensive to the industry than clinical NE because the acute form is obvious and gets treated while the subclinical form often goes unnoticed.

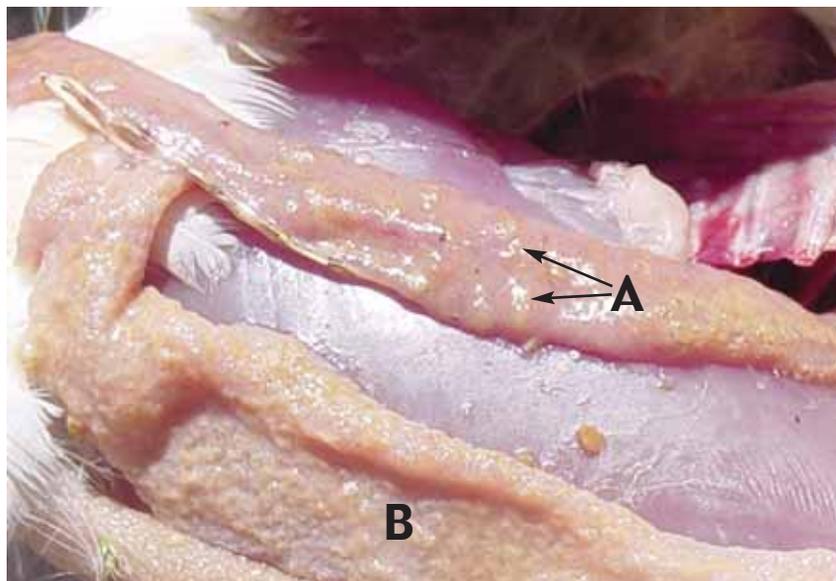
"You may have a large number of flocks affected before you realize you are losing feed efficiency and growth unless you conduct regular weekly posting sessions, which most producers do not," he says.

Hofacre likewise expects to see more acute and subclinical NE as the industry backs off the use of in-feed antibiotics. He cites the experience in Europe, where the poultry industry has seen a huge surge of NE in broilers since AGPs were banned by regulators.

"In the US, the reduction in AGPs is being driven by consumers, not by regulators as it is in Europe. I don't know



Gustin: 'Gut health is an incredibly complex science'



Multifocal yellowish necrotic plaques (A) may progress to complete necrosis of the intestinal mucosa (B), which has a "Turkish towel" appearance.

that we'll go to zero AGPs, but I think the US poultry industry will go pretty low. Consumers don't want AGPs used," he says.

Causes of NE

C. perfringens is a gram-positive, anaerobic bacterium that is normally found in the environment and gut of healthy birds. Although NE is caused by *C. perfringens*, not all *C. perfringens* causes NE, Hofacre points out. A toxic strain of the pathogen must be present. Most occurrences of NE are thought to be caused by the alpha (α -toxin) produced by *C. perfringens*.

A toxic strain of *C. perfringens* takes hold when the bird's intestines are damaged by other diseases, particularly coccidiosis, he says.

"With intestinal damage, the normal balance of bacteria is disrupted and mucus production increases. That's how the intestines respond, by coating their surface. But mucus also provides a food source for *C. perfringens*. The toxin utilizes mucus and further damages the intestines, and you get a damaging cycle," Hofacre says.

Recent evidence about the impact of coccidiosis on the development of NE comes from a study that was presented in July 2006 at the annual conference of the American Association of Avian Pathologists. It demonstrates that both coccidial pathogens *Eimeria acervulina* and *Eimeria maxima* cause enough intestinal damage to allow *C. perfringens* to proliferate.

In the study, conducted by Dr. Greg Mathis of Southern Poultry Research, Athens, Georgia with co-investigator Hofacre, birds were inoculated with the *Eimeria* species then challenged with *C. perfringens*. Those with *Eimeria* infections were more susceptible to the development of NE compared to birds without coccidial infections. Both *Eimeria* species were associated with an increased risk for NE, but the risk was greatest with *E. maxima*.

Davis says that another contributor to NE is animal byproducts. "We have conducted research showing there are literally tens of thousands of clostridium spores per gram in some animal byproducts found in blends. In one study we did, fish meal in the feed was heavily contaminated with *C. perfringens*. We've also found the pathogen in bone meal. So, in some cases, flocks are getting clostridium from their food."

There is a wrongful perception that chemical anticoccidials and coccidiosis vaccination cause NE, he says. "In fact, the opposite is true. These products in no way cause NE. They just don't have direct efficacy against bacterium. There's no secondary antibiotic effect," he says.

A clinical impression

No tests for *C. perfringens* are currently available, but researchers are hoping to change that. Investigators in Europe, for instance, have been working on a blood test that would show antibodies to toxic *C. perfringens*.

Hofacre cautions that there is also no way to predict which farms are at increased risk for NE based on litter samples. "Culturing *C. perfringens* from the litter is an exercise in futility," he explains, because there is no way to tell if any clostridium that is isolated has the gene needed to produce the toxin that results in NE.

In other words, "You can have a high level of clostridium in the environment, but that doesn't prove it is causing disease," he says.

The lack of tests for identification of toxic *C. perfringens* means that diagnosis of subclinical NE depends on an astute clinician.

"It's a clinical impression among those experienced with the disease," says Hofacre. "There's a certain amount of enteritis, but it never gets severe enough to call it clinical NE. The term subclinical enteritis really reflects the severity of NE."

continued on page 7



Hofacre: 'You are losing feed efficiency and growth.'

Understanding acute NE

Acute or clinical necrotic enteritis (NE), caused by the pathogen *Clostridium perfringens*, results in necrosis or death of the intestinal lining and remains one of the most common and costly diseases of modern broiler flocks around the world.

In commercial flocks, acute NE has been relatively well controlled — though inadvertently — with antibiotic growth promoters (AGPs). However, with the use of in-feed antibiotics on the decline, the incidence of NE is certain to be on the rise.

Dr. Steve Davis, president and chief executive officer of Colorado Quality Research, Wellington, says that flocks most at risk for acute NE are antibiotic-free birds such as those not receiving AGPs and birds receiving coccidiosis vaccines or chemical anticoccidials, which have no antibiotic effects.

Dr. Scott Gustin, director of veterinary services for North America and Asia at the Arkansas-based Cobb-Vantress, agrees that “For niche markets such as organic or antibiotic-free flocks, acute NE is a significant problem.” In large-scale broiler production, “acute NE is a nagging problem that is sporadic in nature.”

Earlier onset noted

Davis has noted that among some flocks, acute NE seems to occur earlier than before. “It used to be at 3 to 4 weeks of age and now it’s between 2 and 3 weeks of age,” he adds. “I think it may have to do with coccidiosis control; ionophore anticoccidials and the chemicals used are allowing more leakage faster than they used to.”

The earlier occurrence of acute NE may also be linked to bird genetics that allow for faster growth, says Davis, adding that “We have also found in our studies that acute NE is more prevalent in males, which are more likely to die from the disease than females.”

Mortality

When clinical NE strikes, it can cause mortality ranging anywhere from 5% to 50%; 10% mortality is a frequently cited figure. Comments Davis, “We keep mortality from clinical NE at around 10% because we recognize and treat.”

Mortality is usually the first sign of the disease. In less severely affected flocks, birds may exhibit depression,

poor appetite, ruffled feathers and diarrhea.

Hofacre says an official diagnosis of clinical NE is made upon necropsy of affected birds. “Once you see it, you won’t forget it. The liver is firm and a dark mahogany color. The surface of the small intestines is thick and rough.”

Sometimes, warns Davis, “I’ve seen cases so acute that the gut starts to deteriorate rapidly and you may not see the classic ‘Turkish towel’ lesions characteristic of NE, which could lead to a missed diagnosis.”



Irritation in the gut can help C. perfringens produce toxins that cause necrotic enteritis.

Conversely, a heavy growth of clostridium does not always mean NE because after a bird dies, clostridium in the gut balloons in great numbers since there are perfect anaerobic conditions with a lot of protein and mucus. Therefore, “in a full outbreak, you may need to necropsy quite a few birds before you see classic NE gut lesions,” he says.

Prevention

The risk factors that lead to acute NE are same as for subclinical NE, since both are simply different degrees of the same disease, Hofacre says. The primary factors are damaged intestines that can occur due to other diseases, such as coccidiosis, and a toxic strain of *C. perfringens*. Other factors linked to NE range from the level of litter moisture to certain feed ingredients.

Preventing acute or subclinical NE, say these veterinarians, requires good coccidiosis control and other methods of promoting a healthy gut. In the future, NE control may include vaccination against the disease as well as general management measures that promote good gut health and reduce the clostridium challenge. (See sidebar on management).

Management strategies for preventing NE in broilers

Necrotic enteritis (NE) is the same disease whether it has an acute or subclinical presentation. Measures to prevent NE, therefore, are similar for both forms of the disease, though the specifics may vary depending on the type of broiler production system in place.

One of the first steps that can be taken to control NE is sound cleaning and disinfection of the environment between flocks to decrease the bacterial load in the broiler environment, especially in facilities with a history of NE, says Dr. Steve Davis, president and chief executive officer of Colorado Quality Research, Wellington. "More attention to the efficacy of disinfectants and litter treatments against *Clostridium perfringens* will become important factors in controlling NE."

Litter moisture should not be too high or low. Oat or rice hull may increase the risk for NE because it is less absorptive, he says.

Dr. Scott Gustin, director of veterinary services for North America and Asia at Arkansas-based Cobb-Vantress, notes that some of his colleagues would disagree, but "I have found that reusing litter if possible helps stabilize the environmental and coccidial make-up of the house in organic operations that continually struggle with NE."

Dietary influences

Gustin and Davis both emphasize that diet can influence the development of NE. Grains that contain a lot of indigestible soluble fiber, such as wheat, barley, oats and rye, have been linked to intestinal disease in poultry. The use of some feed ingredients associated with NE, Gustin says, is unavoidable due to cost constraints, but producers may be able to at least limit their inclusion rate, especially during times of heavy coccidia cycling when there is more stress on the gut.

Davis' research has shown that broilers receiving high protein diets are easier to challenge with *C. perfringens*, as are broilers receiving higher density diets, which may be because nutrients remain available to the bacteria in

the intestine if they are fed at higher levels than the broiler can utilize. "Integrators raising broilers without feed grade antibiotics may be able to decrease the incidence of NE by using lower density formulations or concentrating on amino acid fortification and balance over feeding diets with higher protein levels," he says.

However, dramatic changes in diet, which are linked to development of NE, should be avoided, Davis cautions.

Other factors

Overeating is yet another factor he has linked to NE. "If you slow down feed consumption with measures such as decreased lighting, you can decrease the incidence of NE, which is the opposite of what most people think," Davis says.

Cooler temperatures that chill birds and increase feed consumption are linked to NE mortality, he continues. "It appears that increasing the environmental temperature also decreases feed intake in a broiler flock breaking with NE and will help curtail the severity of an outbreak."

Another factor that can affect the severity of NE is the source of chicks and their quality, Davis says. Flocks with excellent chick quality and uniformity require a greater challenge to create disease, so continued improvements in chick quality should improve control of NE. It could be that different breeds have varying levels of maternal antibody against *C. perfringens*, indicating that vaccinating breeders or broilers may be useful in preventing NE.

Gustin agrees that the broiler breed should be considered and that some breeds seem to be more or less likely to develop NE. "As a primary breeder, you try and stay ahead by breeding a bird that can withstand these industry changes. As a producer, you need as many options and tools as possible to keep the feed conversion ratio and live performance competitive," he says.

Last but not least, bird density is a critical factor in preventing NE, because density affects many of the other variables involved, he says.

Recently he visited a farm with enteritis and liver lesions that appeared to be caused by NE. "This farm is on the tip of flipping over into acute NE, but I won't allow birds to go untreated just to prove I'm right. I think this happens a lot."

It was a conventional flock and he suspects that their anticoccidial was beginning to lose efficacy and that too much coccidia was leaking through, Hofacre says.

Says Gustin, "The diagnosis of sub-clinical NE relies heavily on the quality and frequency of technical service by those with the ability to diagnosis sub-clinical NE. Routine posting sessions conducted by individuals with special training in diagnosis of the disease are needed, and performance data must be correlated to necropsy findings, especially during times that coccidiosis programs are transitioning."

Davis adds, "To accurately diagnosis subclinical NE, I think it's very important to get anaerobic cultures of very fresh, dead birds by euthanizing if necessary."

Once familiar with the disease and the intestinal lesions that characterize NE, says Hofacre, subclinical NE can be diagnosed upon necropsy. The small intestinal surface is covered with mucus and may be thick and rough. The liver may be firm and is a dark, mahogany color.

Hofacre uses a scoring system with a range of zero to three for assessing necrotic enteritis, he says. Zero would be no intestinal lesions, one would be a mucus-covered intestine, characteristic of subclinical NE, while scores of two to three would indicate clinical NE because the intestines would be obviously diseased with bloody exudate in birds about to die or that died.

NE control strategies

To best control both clinical and sub-clinical NE in flocks, especially for pro-

Checklist for necrotic enteritis control

- ✓ Implement a good coccidiosis control program, which may consist of a properly administered vaccine or efficacious in-feed products.
- ✓ Maintain good hygiene. Clean out and sanitize houses between flocks.
- ✓ Maintain appropriate flock density.
- ✓ Use absorbent litter to help maintain proper litter moisture.
- ✓ Avoid food sources contaminated with toxic *C. perfringens* and consider monitoring ingredients for *C. perfringens* spores.
- ✓ Eliminate or reduce food ingredients associated with an increased risk for NE, such as wheat, barley, rye and other grains with a high level of indigestible soluble fiber, and animal byproducts.
- ✓ Avoid dramatic dietary changes.
- ✓ Feed a low density, high-quality diet fortified with amino acids; avoid high protein diets.
- ✓ Vaccinate against NE when a vaccine becomes widely available.
- ✓ Consider administration of competitive exclusion and organic acid products to promote good gut health.
- ✓ Consider bird breed and the source of chicks, since some may be more or less prone to development of NE.

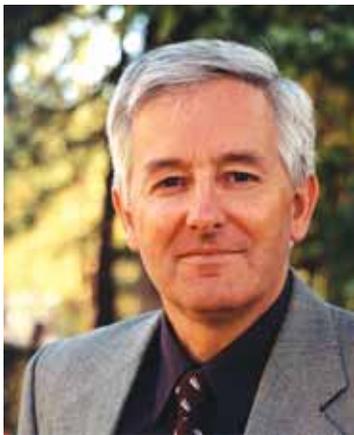
ducers backing off antibiotic use, a combination approach will most likely be needed, starting with good coccidiosis control, say these experts.

"One combination might be coccidiosis vaccination, natural products such as organic acids and NE vaccination," says Davis, who believes that a key to any successful combination will involve immunity.

"Consider dermatitis, which is a
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ESSENTIAL ELEMENTS

Independent project group develops guidelines for coccidiosis vaccines



By H.D. Chapman, Ph.D.
Department of Poultry Science,
University of Arkansas, USA

Increased recognition that live vaccines provide a valuable alternative to chemotherapy for coccidiosis control has encouraged researchers around the world to consider development of coccidiosis vaccines for local use. As with all products developed for the poultry industry, it is essential that vaccine development be carried out using rigorous procedures and high professional standards that also comply with any official regulations that may be applicable.

Guidelines have long been available to help researchers satisfy standards for drugs and many viral and bacterial vaccines — but none have been produced for vaccines against coccidiosis. Consequently, the author recently assembled a group of experts to participate in a joint project aimed at finding a remedy to this deficiency. The team included myself and the following esteemed experts:

- **Professor Martin Shirley**, deputy director of the Institute for Animal Health, United Kingdom, lead the

research team in the 1980s that developed the world's first attenuated coccidiosis vaccine. More recently, he was instrumental in organizing a successful project to sequence the entire genome of *Eimeria tenella*, the most widespread, pathogenic species of *Eimeria* that infects the chicken.

- **Dr. Ray Williams**, of the UK, is one of the world's leading coccidiosis researchers with vast experience in the poultry industry. Dr. Williams has published numerous papers about avian coccidiosis and vaccination.

- **Dr. Brian Roberts**, also of the UK, is an international authority with detailed knowledge of the registration requirements necessary for obtaining marketing authorization for poultry vaccines.

The project group's goal was to develop guidelines to assist scientists and others in the design, implementation and interpretation of studies for assessing the efficacy and safety of live coccidiosis vaccines and to suggest standards for manufacture and quality control. The resulting guidelines are intended to help researchers obtain specific information for those involved in the decision making process and to facilitate the worldwide adoption of consistent, standard procedures.

The team received advice from veterinarians, researchers and those with practical knowledge of poultry production. Scientists working in government, academia and industry around the world were consulted, but the sometimes controversial opinions expressed in the guidelines are the group's own. A leading poultry veterinary journal, *Avian Pathology*, published the guidelines¹, which are shown on the following page.

KEY POINTS

- Rigorous procedures and high professional standards are necessary to ensure safe and effective poultry products.
- Standards for evaluating coccidiosis vaccines have been lacking.
- To remedy the deficiency, several top coccidiosis experts recently developed guidelines to facilitate the worldwide adoption of consistent standards for evaluating the efficacy, safety, manufacture and quality control of coccidiosis vaccines for poultry.

Procedures

Birds in vaccine development studies should be vaccinated under conditions that duplicate as closely as possible the manner in which vaccination will be carried out in the field. Subsequently, birds should be intentionally challenged with the parasite to see whether they have acquired protective immunity.

An important aspect of experimental design is that vaccinated birds must be reared in floor-pens to allow adequate exposure to infection following vaccination; the challenge phase of experiments can be carried out in wire-floored cages or pens. The guidelines as published in *Avian Pathology* provide detailed information about conducting these studies.

Once satisfactory results have been obtained from experimental studies, large-scale field tests can then be carried out; this is important to establish that a vaccine is safe for use in the field. Preferably, such trials should be carried out in all geographical regions where a vaccine is intended for use.

Criteria for efficacy

The criteria conventionally used to evaluate drug efficacy, such as weight gain, mortality, feed conversion and the presence of intestinal lesions, may similarly be used to determine the extent of immunity development following vaccination and subsequent challenge. However, in the opinion of the project group, lesion scores are of questionable value. Lesion scoring requires considerable expertise. It is inherently subjective and, unfortunately, does not necessarily correlate with protection because lesions may be present in the gut of partially or completely immune birds, even though their weight gain is not depressed.

In some countries, guidelines for avian vaccines have been produced by registration authorities, but specific standards for anticoccidial vaccines in

Guidelines for coccidiosis vaccines

Ideally, any live anticoccidial vaccine should have the following 13 characteristics:

- ❑ Induce protective immunity against economically important species of *Eimeria*
- ❑ Be safe for the target host, non-target animals and humans
- ❑ Not represent an environmental hazard
- ❑ Comprise parasites of normal or low virulence
- ❑ Comprise parasites that remain viable during storage for a reasonable period of time
- ❑ Protect against field strains in geographical areas where the vaccine is used
- ❑ Be administered by a commercially practical method to ensure that as many birds as possible receive an immunizing dose
- ❑ Have no adverse effects on final performance or other production criteria
- ❑ Be compatible with other poultry vaccines
- ❑ Be free from viral, bacterial, mycoplasmal, fungal and chemical contaminants
- ❑ Be cost effective compared with other methods of coccidiosis control
- ❑ Include drug-sensitive lines that may reduce drug resistance in field populations
- ❑ Raise no problems with residues or impose a need for mandatory withdrawal periods



Good biosecurity helps ensure that coccidiosis vaccines are free from contaminants.

poultry apparently have not been published so far. Detailed knowledge of any local requirements is essential to obtain product approval.

The guidelines drafted by the project group provide information on the general requirements of regulatory authorities based on regulations currently applicable in the EU and the US. Topics covered in the guidelines include efficacy requirements, safety and environmental considerations, quality control in terms of purity, phar-

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SOLVING THE GANGRENOUS DERMATITIS PUZZLE

Preventing late coccidiosis cycling with vaccination may halt this costly bacterial disease

If you're like many other modern poultry operations, you probably vaccinate at least a portion of your broiler chicks for coccidiosis. Maybe you do it to improve the performance of broiler flocks when traditional in-

feed anticoccidials don't seem to hold up to the challenge. Or maybe you do it to meet the growing consumer demand for birds raised without drugs.

Now, early field trials and experience indicate there's one more reason to vaccinate for coccidiosis: It can help control or eliminate the growing problem of gangrenous dermatitis.

The coccidiosis vaccine itself is not effective against the disease. However, vaccination prevents late coccidiosis cycling, an event that some veterinarians and production managers now believe is the trigger for costly outbreaks of gangrenous dermatitis.

The consequences of gangrenous dermatitis include high mortality, carcass condemnations and trimmed parts. Economic losses are an estimated \$0.80 to \$1.31 per affected bird, which is significant because the disease occurs late during grow-out, when a lot has already been invested in birds that can't be saved, investigators say.¹

Number one health problem

"We're hearing more people discuss this disease," says Dr. Charles Broussard, global technical services director for Schering-Plough Animal Health's Poultry Business Unit.

At some U.S. poultry companies, gangrenous dermatitis has become a very serious problem, with 10% to 25% of flocks affected and mortality running about 2% to 4% — and sometimes higher. The incidence seems severe enough that it's on the minds of veterinarians and has become a "number one" health problem for some producers, he says.

Broussard notes that when 17 U.S. broiler company veterinarians were asked in a survey to list their top disease concerns, 12 cited gangrenous



Mortality, carcass condemnations and trimmed parts can result from gangrenous dermatitis, a costly disease in broilers. In the second photo, note the gas bubbles formed by clostridium, one of the pathogens that causes gangrenous dermatitis.

dermatitis. It was, in fact, “the most consistent and serious problem in their operations,” according to a 2005 Report of the Committee on Transmissible Disease of Poultry and other Avian Species.

It has long been thought that gangrenous dermatitis starts with a scratch that gets infected with a bacterium, which rapidly proliferates when birds also happen to be immunosuppressed due to diseases such as infectious bursal disease (IBD) or chick anemia virus (CAV). The remedy was thought to be good control of IBD, CAV and other immunosuppressive diseases, as well as management changes ranging from low lighting to special diets that are primarily aimed at keeping birds calm to prevent scratching.

But control of IBD, CAV and the environment has not resolved the problem of gangrenous dermatitis, says Broussard. In addition, recent experience and trials indicate that an instigator of gangrenous dermatitis may be one not considered before, and that’s late coccidiosis cycling.

“The remedy may be coccidiosis control that prevents late coccidiosis

cycling — and there may be no need to make significant management changes,” he says.

Adds Broussard: “Coccidiosis might have been a cause of dermatitis all along, but we’re approaching coccidiosis control differently now. We aren’t using as many anticoccidials and resistance has developed to some of them, which may be allowing dermatitis to rear its head.”

Patterns of disease

Although high mortality is the most obvious sign of a gangrenous dermatitis outbreak, says Broussard, producers might also notice that affected birds have a poor appetite, poor coordination and leg weakness, skin lesions and edema. The pathogen most often associated with gangrenous dermatitis is clostridium of various species, but *Escherichia coli* and staph infections can also be the culprits. The pathogens act as an opportunistic infection, which is set off by coccidiosis.

“Even though spring is often associated with outbreaks of dermatitis, lately we’ve also seem problems with the disease occurring in winter. Cold

Table 1. Gangrenous dermatitis control on three farms with and without coccidiosis vaccination to promote late coccidiosis control.

Farm	Date Moved	Mortality (%)
A	05-Apr-05	10.29
	10-Jun-05	12.12
Coccivac-B Cycle 1	22-Mar-06	3.27
Coccivac-B Cycle 2	06-May-06	2.28
B	06-Apr-05	11.60
	10-Jun-05	8.91
Coccivac-B Cycle 1	21-Mar-06	3.37
Coccivac-B Cycle 2	06-May-06	3.31
C	05-Apr-05	11.94
	09-Jun-05	6.94
Coccivac-B Cycle 1	21-Mar-06	3.08
Coccivac-B Cycle 2	06-May-06	2.96

Table 2. Paired house performance comparing coccidiosis vaccination against nicarbazin/monensin and salinomycin.

	Mortality (%)	Average Weight	Adj. FC
Coccivac-B	4.62	6.706	1.903
Control	3.95	6.709	1.894

Paired house performance comparing coccidiosis vaccination against salinomycin 60 Gr.			
	Mortality (%)	Average Weight	Adj. FC
Coccivac-B	4.14	4.909	1.804
Control	4.36	4.841	1.819

Note: Dermatitis was causing problems within the company during the trial period. Sister flocks to these farms had to be treated for dermatitis-related mortality.

weather is a stress in and of itself, but that's also the same time that a lot of flocks experience a late coccidiosis challenge due to the anticoccidial control program in use," he says.

"The disease is occurring in birds on chemical-to-ionophore programs and on straight ionophore programs," he adds.

Broussard points to research conducted by Dr. Steve Collett of the Poultry Diagnostic and Research Center, University of Georgia, Athens, which was presented at the Georgia Veterinary Medical Association 2006 annual meeting. The results diverge from standard gangrenous dermatitis dogma. Collett's challenge model consistently induces gangrenous dermatitis lesions in 100% of challenged birds and the degree of mortality is dose-responsive. Most immune-competent broilers are able to contain the infection — become culture negative 7 days after challenge — and recover.

Current dogma regarding the pathogenesis of gangrenous dermatitis is based on the premise that when the skin's barrier function is compromised by scratches, contamination with *Clostridium perfringens* commonly occurs and the progression of disease following wound contamination requires the bird to be immune-suppressed. Using his model, Collett

demonstrated that immunosuppression caused by IBD and CAV did not increase the severity of gangrenous dermatitis lesions. From this, he suggested that immunosuppression is more likely a predisposition to the process of infection (currently thought to be skin scratches) and not the consequence of infection (skin necrosis). This is important because it supports Collett's earlier hypothesis that the skin and scratches is not always the way that clostridial organisms enter the body and cause gangrenous dermatitis; an alternative route is mostly likely the gastrointestinal tract.

Collett went on to point out that, in the field, gangrenous dermatitis typically occurs in 4- to 6-week-old broilers. This coincides with the time between peak coccidiosis challenge — peak oocyst output is around 28 days of age — and the development of solid immunity against *Eimeria* spp. challenge at 6 weeks of age. Gut lesions caused by *Eimeria* parasites, particularly late cycling *Eimeria maxima*, could easily provide a portal of entry for the clostridial organisms responsible for gangrenous dermatitis, as evidenced by human research on the pathogenesis of gas gangrene.

Interestingly, the prevalence of gangrenous dermatitis in flocks vaccinated with Coccivac appears to be extremely

low when compared to vaccinated flocks. It would seem that reducing the severity of gut epithelial damage, or shifting the time at which it occurs, could be an important means of preventing or at least reducing the prevalence of gangrenous dermatitis.

Major producer's experience

Consider the experience at one large US broiler producer, where gangrenous dermatitis became a problem in several complexes, particularly among small birds that had received nicarbazin/monensin for coccidiosis control.

"We had dermatitis coming in at 32 to 35 days — toward the end of the anticoccidial control program cycle," says the producer's veterinarian, who spoke to *CocciForum* with the condition that his company not be revealed.

"Gangrenous dermatitis can be devastating and, for some operations, results in mortality as high as 8% per week. That's very costly to individual growers," the veterinarian says.

The producer followed the problem for a while and realized that "we had some late-breaking coccidiosis," he says. When the birds received the chemical anticoccidial Clinacox after

nicarbazin/monensin, the dermatitis stopped.

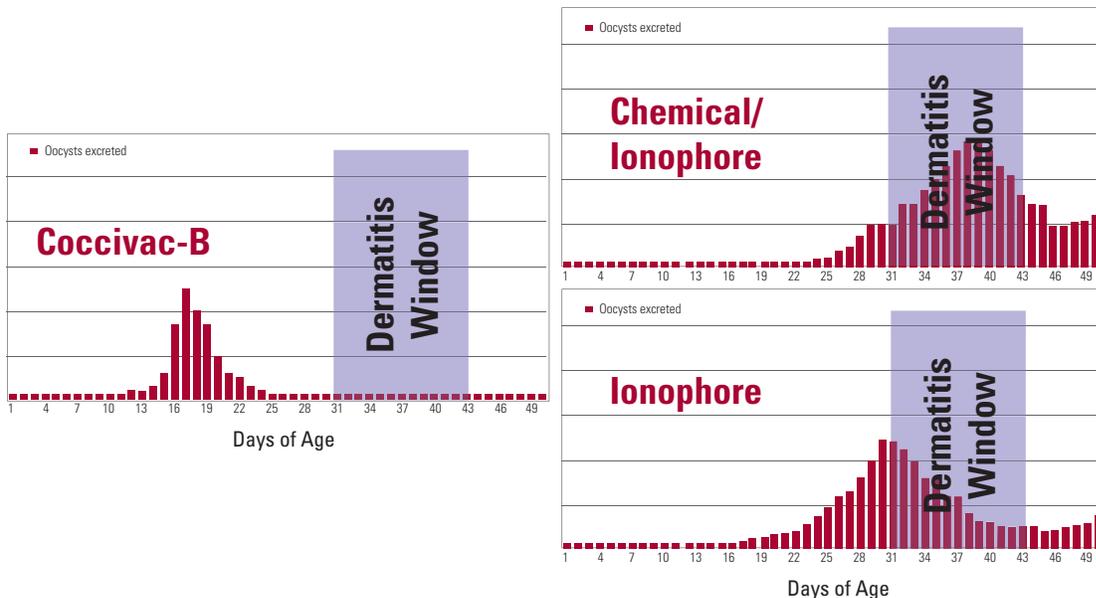
The veterinarian has not been able to link gangrenous dermatitis outbreaks with the traditional villains IBD nor CAV. "We've had dermatitis in areas with a good IBD program and in birds that I think are normal. We have also had dermatitis in chickens vaccinated against CAV. The only link I've seen is this late coccidiosis challenge."

Some complexes with larger birds on the same nicarbazin/monensin program also experienced gangrenous dermatitis, which ceased when coccidiosis control was managed with vaccination administered at the hatchery to initiate early immunity and prevent a late coccidiosis challenge.

"I don't want to sound too definitive about the association, but we see much less dermatitis when we control coccidiosis late in the production cycle," he says. "I think the vaccine helped with dermatitis because it did away with the late coccidiosis challenge."

Based on his experience, this poultry veterinarian believes that the observed link between late coccidiosis cycling and gangrenous dermatitis represents a changing pattern. He also

Figure 1: Dermatitis outbreaks overlap with the late coccidiosis cycling that occurs when traditional coccidiosis control methods are used.



thinks there may be a breed predisposition. Gangrenous dermatitis has occurred in three different bird breeds, but there have also been breeds that seem highly resistant to dermatitis, he notes.

Integrator's trial

To test the theory that gangrenous dermatitis may be triggered by a gut insult created by the late coccidiosis cycling that results with traditional in-feed anticoccidial programs, another large broiler integrator conducted a trial.

In January 2006, four farms of straight run broilers were immunized with one dose of the coccidiosis vaccine Coccivac-B, which was sprayed on at one day of age in the hatchery before chicks were placed on farms with the strongest history of gangrenous dermatitis. All other management and vaccination procedures were identical to the standard company program. The trial was then replicated with the same format in April 2006 for the next sequential grow-out on the same farms and houses.

On three of the farms, two cycles of Coccivac-B vaccine were administered in the spring, a peak time for gangrenous dermatitis outbreaks. During the same time period in 2005 — when coccidiosis control comprised one cycle of nicarbazin/monensin then a cycle of salinomycin — average mortality exceeded 10%, but after coccidiosis vaccination in 2006, mortality was only about 3% (see Table 1). The “sister” farms of the trial houses had gangrenous dermatitis and a mortality of 3 to 6 birds/1,000 per day for at least 4 days.

At the fourth farm in the trial, paired house performance was studied; coccidiosis vaccination was compared against nicarbazin/monensin and against salinomycin (Table 2).

Performance in vaccinated birds was very similar or better to performance among birds receiving traditional anticoccidial control, according to the

results. For instance, the average weight in birds that received Coccivac-B vaccine was 4.9 lbs, compared to 4.8 in birds receiving salinomycin.

Says Broussard, “These trial results confirm our anecdotal observations that the prevailing trigger for dermatitis can be correlated to late coccidiosis cycling. Traditional anticoccidial programs that shift coccidiosis cycling into peak dermatitis periods may compound the effect or even create it.

“Coccidiosis vaccination shifts coccidiosis cycling out of the dermatitis ‘window’ to eliminate what now appears to be the predominant predisposing factor for dermatitis,” he says. (See Figure 1).

In addition, control of gangrenous dermatitis by preventing a late coccidiosis challenge has not required management changes traditionally necessary to rid an operation of this disease, Broussard says.

Vaccine is cost competitive

Economic data from the trial was also considered as well as data from other sources. Compared to other methods of anticoccidial control in the trial, Coccivac-B was less costly for controlling coccidiosis. This was the case even before other benefits of vaccination, such as reduced mortality and fewer medication costs, were considered, he says.

“Most exciting is the ability to reduce or eliminate dermatitis by shifting coccidiosis cycling, which gives coccidiosis vaccination added value,” Broussard says.

“We’re on to something here that could really help broiler producers get rid of the dermatitis problem, the staggering losses caused by this disease and, at the same time, provide good coccidiosis control,” he says.

Reference

¹ Norton, RA et al. Gangrenous dermatitis reemerges in broilers. *Watt Poultry USA*. March: 38.

clostridial disease that occurs later in the life of birds, unlike NE, which occurs early in the bird's life. I have never seen or met another poultry veterinarian who has seen a flock of broilers with NE that get dermatitis later, and the reason for that is immunity," he says. In short, birds that survive NE build immunity against dermatitis.

That observation indicates that vaccinating for NE could be helpful in flocks at risk. This would include not just antibiotic-free birds, but birds receiving chemicals or vaccines to prevent coccidiosis and birds on a rotation program during times they transition off ionophores, he says.

A *C. perfringens* type A toxoid vaccine for NE has been developed by Schering-Plough Animal Health and, at this writing, is being used in the US with a conditional license granted last year by the USDA. It is administered to breeders, which convey passive immunity against NE to their broiler progeny.

The vaccine has obvious benefits for antibiotic-free birds at risk for acute NE outbreaks and might also benefit producers still using AGPs by enabling them to lower the amount of antibiotic used, says Davis. When his firm vaccinated birds with the type A toxoid then challenged their progeny with clostridium, they performed just as well whether they received 25 grams/ton of bacitracin methylene disalicylate (BMD) or twice that amount. "There seemed to be some synergistic effect between the vaccine and BMD."

Gustin couldn't comment specifically on the new vaccine but says, "If you look at many of the diseases we vaccinate for in poultry, it is obvious that we take advantage of passive immunity. We should do so for other diseases if we can do so effectively.

"One would assume that if clinical necrotic enteritis can be prevented with a vaccine, the same mechanism could improve control of subclinical NE. Since



Severe necrosis of the intestinal lining (mucosa).

subclinical NE is much more widespread than clinical NE, the benefits to conventional sectors would be there," he says.

Hofacre says, "When anticoccidials start to fail, a vaccine may have a role" and it may also have a role in birds receiving AGPs, since antibiotics are not always 100% effective against NE. Producers, however, will have to weigh the cost of the vaccine against other factors."

To improve NE control, he advises that producers "look at ways to maintain good gut flora and overall intestinal health, perhaps by feeding competitive exclusion products and organic acids. If a coccidiosis vaccine is used, make sure it's managed well" and administered properly so that birds do not get overexposed to coccidia.

Control of NE also relies on good basic management, these experts emphasize. Litter moisture, house temperature, the diet fed to flocks as well as bird density and other factors must be considered and will play an increasingly important role in the control of NE (see article, page 6).

Late production *E. maxima* problems linked to anticoccidial resistance

Problems with *Eimeria maxima* infections late in the production cycle appear to be linked to extensive use of ionophore antibiotics and resulting ionophore-resistant *E. acervulina*, says Dr. Greg F. Mathis of Southern Poultry Research, Inc., Athens, Georgia.

An earlier study suggested that *E. acervulina* can interfere with *E. maxima* colonization. Consequently, Mathis designed a battery cage study to examine the relationship of *E. acervulina* sensitivity to the ionophore salinomycin and subsequent infection levels with *E. maxima*.

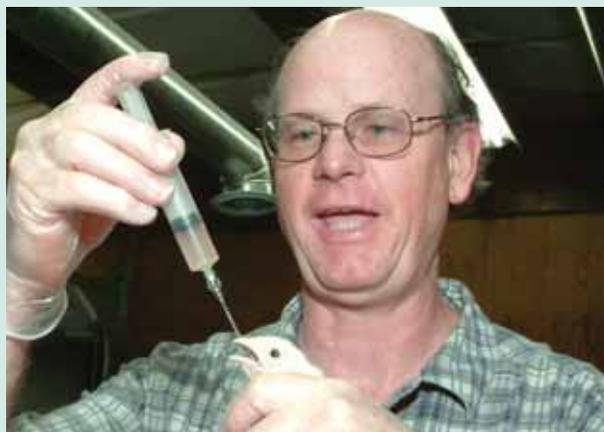
Birds were fed nonmedicated feed or salinomycin at the rate of 60 grams/ton and were then challenged with either a salinomycin sensitive strain of *E. acervulina*, a resistant strain of *E. acervulina* and/or an *E. maxima* field isolate.

The oocyst per bird challenge levels were as follows:

- None (control)
- *E. acervulina* (sensitive strain) 50,000
- *E. acervulina* (resistant strain) 50,000
- *E. acervulina* (sensitive strain) 50,000 plus *E. maxima* 5,000
- *E. acervulina* (resistant strain) 50,000 plus *E. maxima* 5,000
- *E. maxima* 5,000

E. maxima alone caused a 20% weight reduction and 2.70 lesion score, says Mathis.

Salinomycin controlled the sensitive strain with 5% weight reduction and 1.25 lesion score. It did not control the resistant strain, resulting in a 22% weight reduction and 2.75



Mathis: 'Increases the chance for late problems'

lesion score.

Birds infected with *E. maxima* and the sensitive *E. acervulina* strain had *E. maxima* lesion scores of 2.25. The birds infected with *E. maxima* and the resistant *E. acervulina* strain had *E. maxima* lesion scores of 1.30.

"From the results it can be inferred that *E. acervulina* interfered with development of *E. maxima*," Mathis says. "Higher anticoccidial resistance allows more *E. acervulina* colonization, which appears to interfere with colonization of *E. maxima*, and thus indirectly slows *E. maxima* immunity development."

This increases the chance for late problems with *E. maxima*, possibly explaining an increase in field reports of late *E. maxima* infections where salinomycin has been extensively used, Mathis adds.

ESSENTIAL ELEMENTS continued from page 9

macopoeial sterility, potency, quantification and stability etc., manufacturing practice and, last but not least, necessary documentation.

Purpose

In the foreseeable future, new vaccines are likely to be introduced for protecting poultry against coccidiosis. Some of these vaccines will be produced by companies with an established track record in providing high quality vaccines to the poultry industry but, as pointed out at the 2005 International Coccidiosis Conference held in Brazil, many smaller companies lacking such experience are also likely to be involved. It is important that all commercial vaccines, whatever their source, be produced to the same high standards. For example, in the US,

source flocks used to produce poultry vaccines must be serologically tested to ensure freedom from at least 11 kinds of virus, not to mention *Mycoplasma* and *Salmonella* species.

To reiterate, the purpose of the project group's guidelines is to facilitate the worldwide adoption of consistent, standard procedures for evaluating the efficacy, safety, manufacture and quality control of coccidiosis vaccines for poultry. The poultry industry deserves no less.

Reference

¹ Chapman, HD, Shirley, MW, Williams, RB. Guidelines for evaluating the efficacy and safety of live anticoccidial vaccines, and obtaining approval for their use in chickens and turkeys. *Avian Pathology* 2005;34: 279-290.

Water potential carrier of coccidia

Drinking water may be a potential carrier of coccidia to chickens, according to a French study.

The study focused on 24 farms that used forage or surface water and did not include farms supplied by treated water.

Fecal samples from the farms showed that 75% of the flocks were positive for coccidia. When filters were placed to capture oocysts where water entered the buildings, four of the samples were positive for coccidia.

The species of coccidia found in the water was *Eimeria acervulina*, which was also present in litter from farms in the study.

These preliminary results suggest that water can be a potential carrier of coccidia for chickens.

Study shows Coccivac antigens protect against recent field isolates

The antigens in Coccivac vaccines provide good protection against coccidia in the field, according to the results of a controlled study.

Chickens were orally immunized with one dose of either Coccivac-B, a coccidiosis vaccine for broilers, or Coccivac-D, a coccidiosis vaccine for breeders and layers.

There were 70 birds in each group and a third group, comprised of unimmunized hatch mates, served as positive controls for the study, which was designed to compare the antigenicity of coccidia in the field against the antigenicity of antigens in the vaccine.

After immunization, birds in the study were placed into floor pens on clean wood shavings and grown to about 35 days of age. They were then challenged with three predominant species of coccidial field isolates that were collected from 60 broiler and breeder pullet farms across the United States.

From 144 to 156 hours after challenge, the birds were euthanized and examined for gross coccidial lesions. In addition, mucosal scrapings from multiple intestinal sites were taken and examined microscopically with a compound light microscope and the severity of parasitic infection was scored.

The average level of protection provided by the vaccines was determined to be 97% for *Eimeria acervulina*, 86% for *Eimeria maxima* and 91% for *Eimeria tenella*.

Compared to the unimmunized birds, the birds vaccinated with Coccivac-B or Coccivac-D demonstrated substantial immunity as determined by the level of parasitism.



Fitz-Coy: Closing in on mivati

Lesser known *Eimeria* species underestimated

One of the lesser-known *Eimeria* species in poultry may be underestimated in importance.

Dr. Steve H. Fitz-Coy, of Schering-Plough Animal Health, explains that *E. mivati* is a coccidial species that some researchers have considered to be a variant of *E. acervulina* or a mixture of *E. acervulina* and *E. mitis*, but not a unique species.

To further determine whether *E. mivati* is unique, Fitz-Coy obtained several field isolates from Georgia

and the Delmarva Peninsula that fit descriptions of the species. He selected three of the isolates and sent them with 10 other *Eimeria* species samples to an independent lab for polymerase chain reaction (PCR) assay. The identity of each sample was not known by the lab.

"The only isolates that could not be identified by PCR assay were the *E. mivati* samples," he reports. The current primers for identification of *Eimeria* species include *E. acervulina* and virtually all the other *Eimeria* species known to affect chickens — except *E. mivati*.

The PCR test indicates that *E. mivati* is, in fact, a valid and unique *Eimeria* species, he said.

E. mivati is also "moderately pathogenic" in chickens and, on some occasions, can cause mortality, according to Fitz-Coy. In one study, mortality was 40% in naive chickens, but there was no pathology in hyper-immunized hatch-mates.

Sanderson: Organic going mainstream

The all-natural food trend is gaining momentum and attracting the attention of larger poultry producers, according to Joe Frank Sanderson, chairman and CEO of Sanderson Farms.

He says the trend is not only showing up in the company's research, it is in evidence elsewhere, according to a report in *Watt Poultry USA's* July 2006 issue. Sanderson points to the successful development of the Whole Foods grocery chain. In addition, most traditional grocery stores now offer organic products and promotion and even Arby's fast food chain is promoting all-natural chicken.

All-natural products were considered a small niche market that now appears to be burgeoning and "I predict this trend will continue," he says.

COCCI FORUM

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