# CLOSTRIDIAL DISEASES

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- The genus Clostridium consists of a diverse group of Gram-positive spore-forming anaerobic rods which are distributed worldwide.
- Most of the species are harmless nonpathogenic bacteria living in a wide range of environments including wetlands and soils, marine and freshwater sediments, on plants, on the skin, and in the gastrointestinal tract of humans and animals.
- One of these commensals, C. butyricum, produces butyric acid, and is used as a probiotic in humans. It has even shown potential as an alternative to antibiotics in broilers exposed to pathogens such as Salmonella Enteritidis and Escherichia coli.
- However, some of these species contaminate and cause food spoilage, and others are pathogenic for both humans and animals.

Pathogenic clostridia species produce several toxins responsible for lesions and clinical signs hence the categorization of clostridial diseases into 3 major groups based on toxin activity:

(1) Those interfering with neurotransmitters, such as C. botulinum and C. tetani.

(2) clostridial strains proliferating in the intestines and causing enteritis and toxemic shock such as C. perfringens type A.

(3) clostridium localized in liver and muscle – the histotoxic clostridia: C. chauvoei, C. septicum, C. novyi type A, C. perfringens type A, C.

- **Most commonly encountered clostridial-caused diseases in poultry are**: ulcerative enteritis, necrotic enteritis, botulism, and gangrenous dermatitis respectively caused by C. colinum, C. perfringens, C. botulinum, and C. septicum (in association or not with C. perfringens and/or Staphylococcus aureus).

- Quail and chickens are often predisposed to infection by prior infection with coccidia. Chickens are also predisposed by immunosuppressive infections such as infectious bursal disease or infectious anemia

# Ulcerative Enteritis

Ulcerative enteritis (UE), a bacterial infection, was first described in quail, hence the name “quail disease.” UE also occurs in chickens, turkeys, and other birds.

## Etiology

Clostridium colinum was initially classified as Corynebacterium perdicum.

## Morphology and Staining

Clostridium colinum is a Gram-positive rod, occurring singly as straight or slightly-curved rods.

## Growth Requirements

Clostridium colinum is fastidious in its growth requirements. It needs an enriched medium and anaerobic environment. The best isolation medium is tryptosephosphate agar (Difco) with 0.2% glucose, 0.5% yeast extract, and 8% horse plasma. Pre-reduced plates are inoculated with material from liver, intestinal, or splenic lesions and incubated anaerobically for 24–48 hours at 35 °C–42°C.

## Transmission

- Clostridium colinum is transmitted by ingestion of feed, water, litter or other materials contaminated with feces. When cases of UE occur, the spores of C. colinum contaminate the premises which, after an outbreak of the disease, are assumed to remain contaminated for many months.
- Suggested that flies feeding on contaminated feces may introduce infection in the premises

## Incubation Period

After experimental inoculation, the acute disease develops, accompanied by death of quail, in 1–3 days. The course of the disease in a flock is generally about 3 weeks, with peak mortality occurring 5–14 days after the initial case

## Pathogenesis

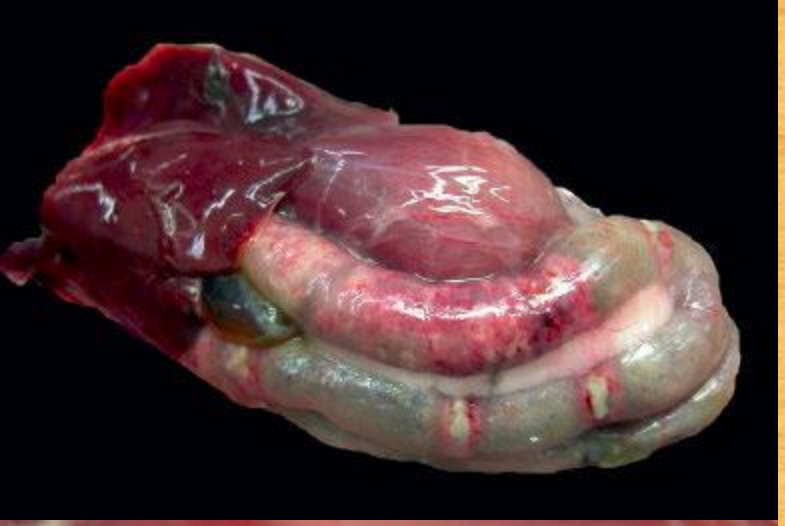
After oral infection, C. colinum adheres to the intestinal epithelium, producing the characteristic lesions in the small intestine and, occasionally, proximal colon. The organism then may migrate to the liver via portal circulation, producing the foci of hepatic necrosis frequently seen in cases of UE.

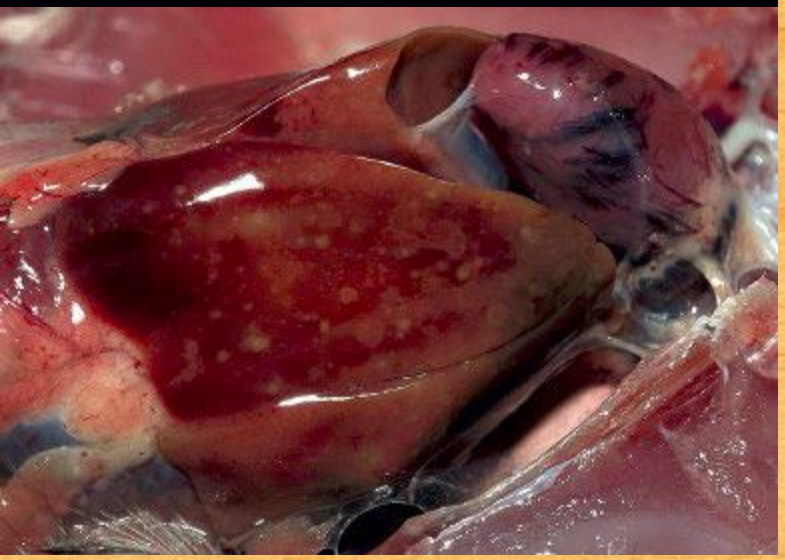
# Clinical Signs

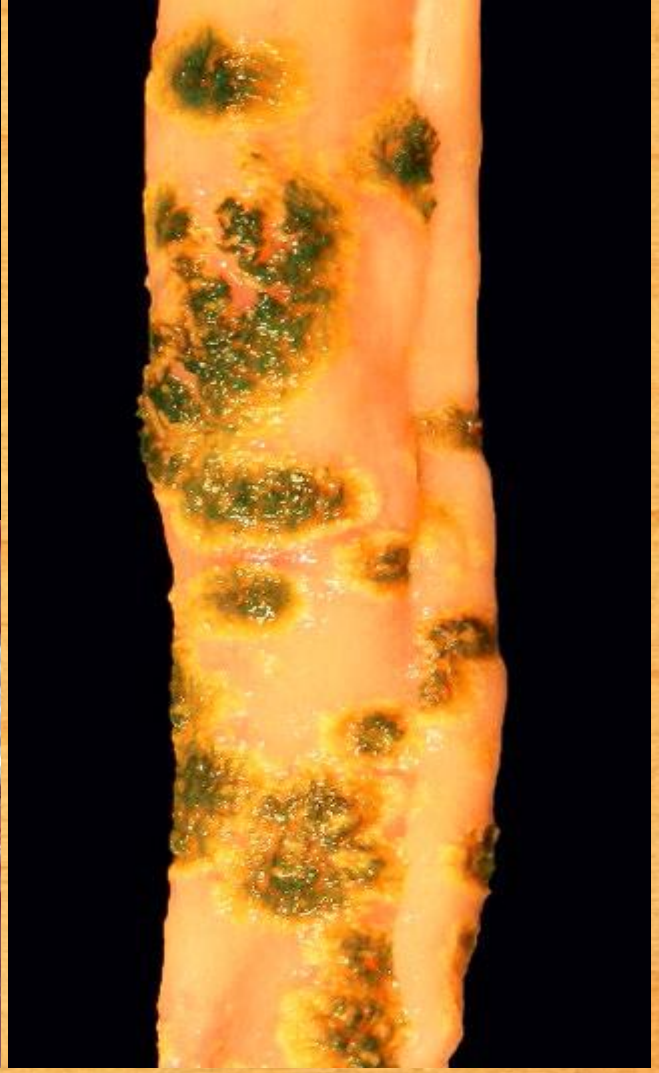
- The hallmark of UE is diarrhea, which is initially watery but may become hemorrhagic.
- As UE progresses, infected birds become listless and humped up, with eyes partly closed and feathers dull and ruffled.
- Notable emaciation, with atrophy of pectoral muscles, is seen in birds affected for a week or longer.
- Birds may die from acute disease with no premonitory signs.
- Young quail may be subject to 100% mortality in a few days. The mortality rate in chickens typically ranges from 2% to 10%.

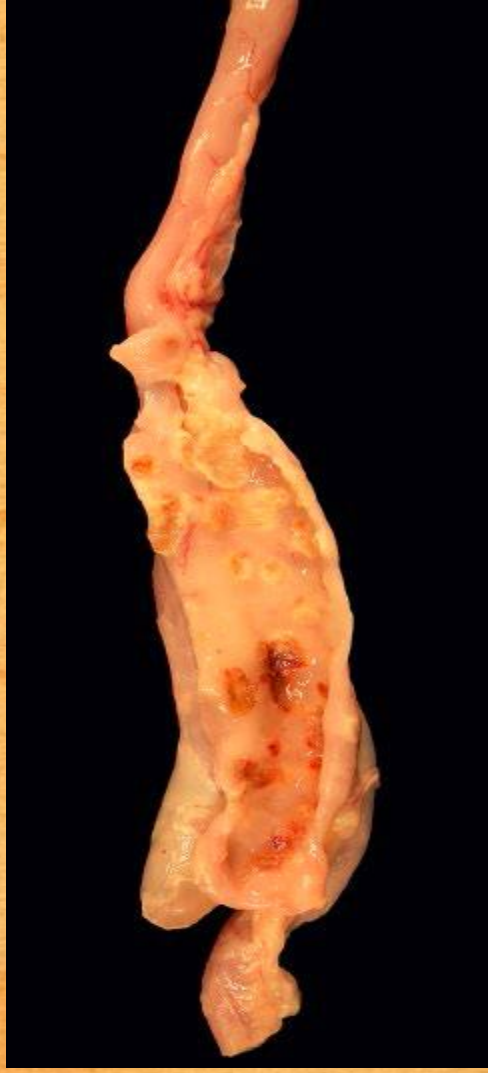
# Pathology

- Acute lesions in quail are characterized by severe ulcerative and hemorrhagic enteritis. Variable size mucosal ulcers surrounded by a hemorrhagic halo may be visible from the mucosal and serosal side of the intestine. Ulcers may be deep and involve the whole thickness of the intestinal wall, causing perforation and subsequent peritonitis.
- These ulcers later coalesce to form larger lesions and may be covered by diphtheritic membranes.
- Ulcers in ceca may have a central depression filled with firmly attached, dark staining, soft material.
- light yellow mottling to multiple large, irregular, gray, or yellow circumscribed foci in liver.
- congested, enlarged, and hemorrhagic, with or without multifocal necrotic areas in spleen.





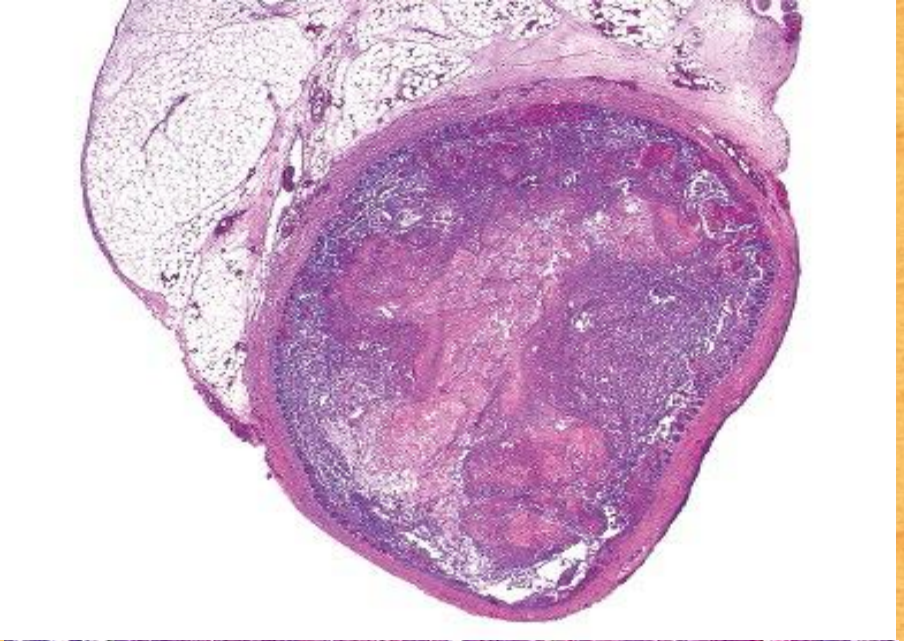


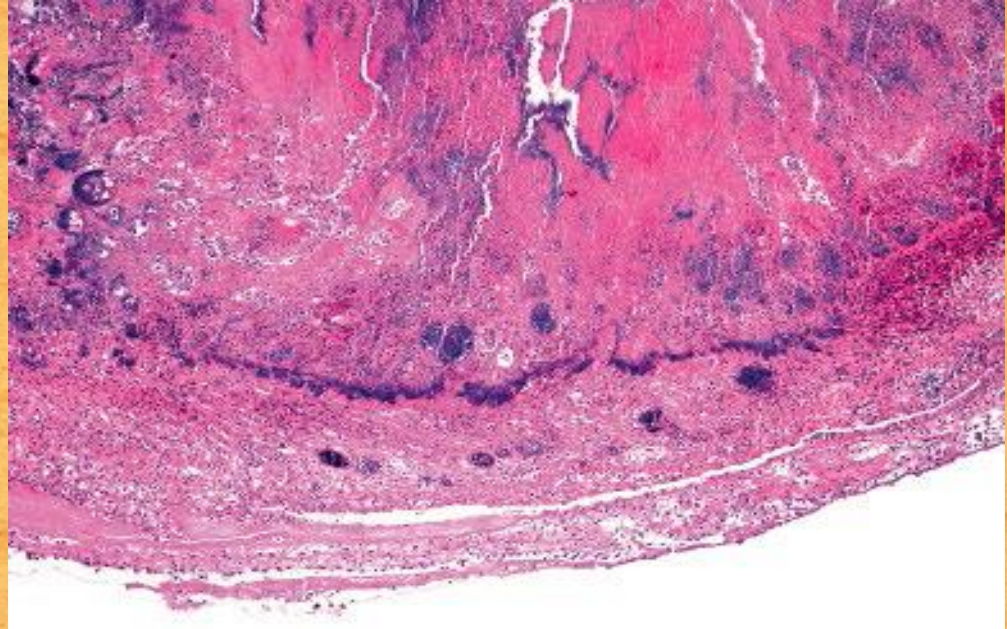


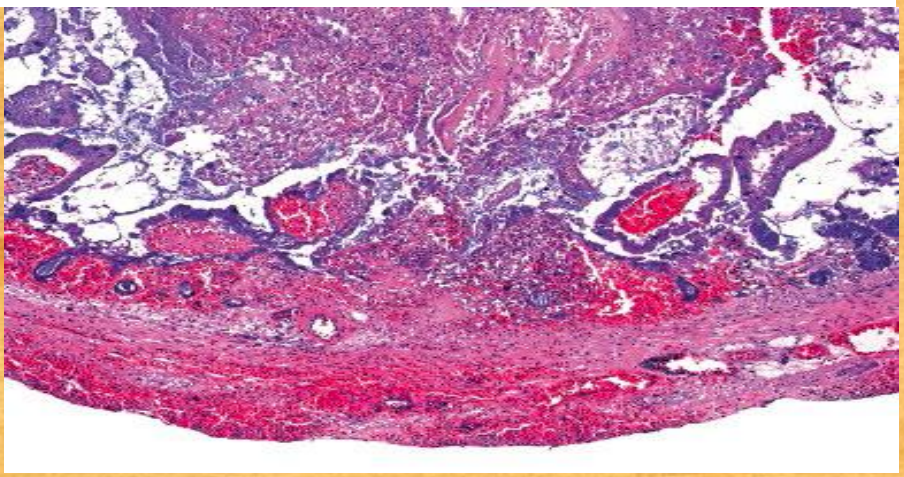
**A**. Note hyperemia and hemorrhage around ulcers. A few pin point lesions are also visible on the surface of the liver. **B**. Acute ulcers on the mucosal surface of the small intestine some of them hemorrhagic and/or surrounded by a hemorrhagic rim. **C.** Chronic ulcers seen on the mucosal surface of the small intestine; notice diphtheritic membranes covering the ulcers. **D.** Multifocal areas of necrosis in the liver.

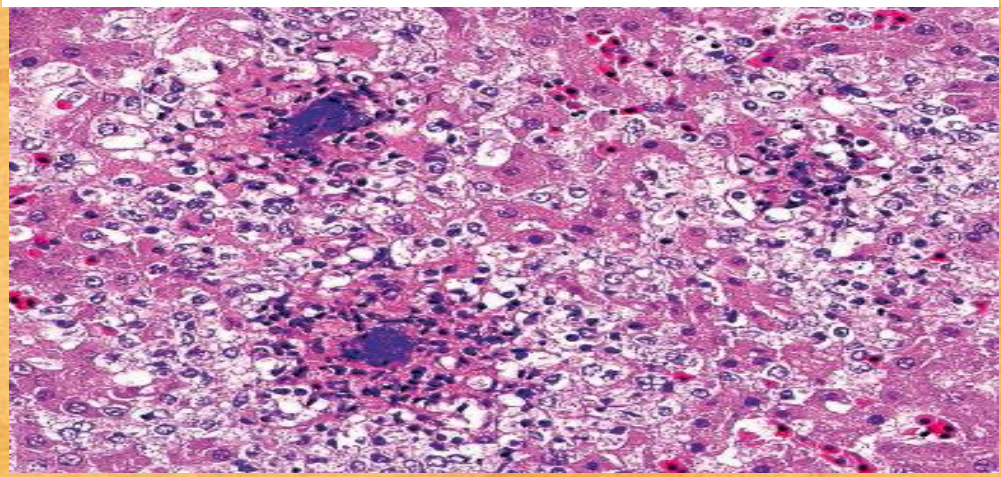
## Microscopic Pathology

- Variable size clumps of Gram-positive rods are often present deep in the mucosa, and in necrotic tissue and the lumen. At later stages, transmural necrosis and inflammation can be observed.
- Liver lesions, when present, are poorly demarcated foci of coagulative necrosis, with minimal inflammatory reaction and occasional intra lesional clumps of Gram positive rods, randomly scattered throughout the parenchyma.









**E.** Acute lesions affecting mostly the mucosa of the small intestine. **F.** Mucosal and submucosal ulcers showing numerous bacterial colonies typical of Clostridium colinum. **G.** Deep lesions affecting all layers of the small intestine. **H.** Microscopic appearance of liver lesion. Note the multifocal areas of necrosis without distinct separation from normal tissue, minimal inflammatory response and bacterial colonies.

## Diagnosis

- A presumptive diagnosis of UE can be made based on gross and microscopic lesions. The observation of large, Gram-positive rods usually with sub terminal spores.
- Final diagnosis, however, should be based on detection of C. colinum by culture or PCR in intestine, liver, or spleen.

## Differential diagnosis:

coccidiosis, necrotic enteritis by C. perfringens and histomoniasis.

## Intervention Strategies

Clostridium colinum is shed in feces and remains viable indefinitely in litter. Thus, on problem farms, contaminated litter should be removed and clean litter introduced for each brood after thorough disinfection. Coccidiosis control, prevention of stress and immunosuppression, in-feed enzymes, and prophylactic antibiotics are the most important management procedures to prevent UE.

## Treatment

Clinically, affected flocks can be treated successfully with bacitracin, lincomycin or penicillin where legal. Streptomycin administered by injection or in feed or water has prophylactic and therapeutic value against the disease in quail. Streptomycin at a level of 60 g/ton of feed or 1 g/gal of water gives complete protection when administered prophylactically.

# Necrotic Enteritis

- Clinical NE can be defined as a disease of primarily young chickens, caused by infection with, and toxin production by, Clostridium perfringens type A, type C and type G. The clinical infection is characterized by sudden onset, high mortality, and necrosis of the small intestine mucosa.
- The disease is also known as **clostridial enteritis**, **enterotoxemia**, and **rot gut**.

## Economic Significance

- Necrotic enteritis is a major cause of loss of efficiency of growth and increased mortality in poultry, both of which significantly negatively impact profitability.

## Public Health Significance

Clostridium perfringens type A and type C, in addition to producing toxins which can induce NE in poultry, also produce enterotoxins at the moment of sporulation which can produce foodborne illness in humans. Two distinct diseases are induced by these subtypes: type A C. perfringens produces diarrhea and type C C. perfringens produces necrotic enteritis in humans.

## Etiology:

Clostridium perfringens produces 17 or more toxic exo-proteins. NE is commonly caused by C. perfringens types A.

## Clinical Signs

Birds with NE are depressed, with ruffled feathers, diarrhea, anorexia, and dehydration. Clinical illness is very short; birds can be found dead without clinical signs of disease. Mortality rates may be as high as 50%.

## Pathology

The small intestine is distended and friable. Confluent necrotic ulcers progress to a pseudomembrane covering the intestinal mucosa.

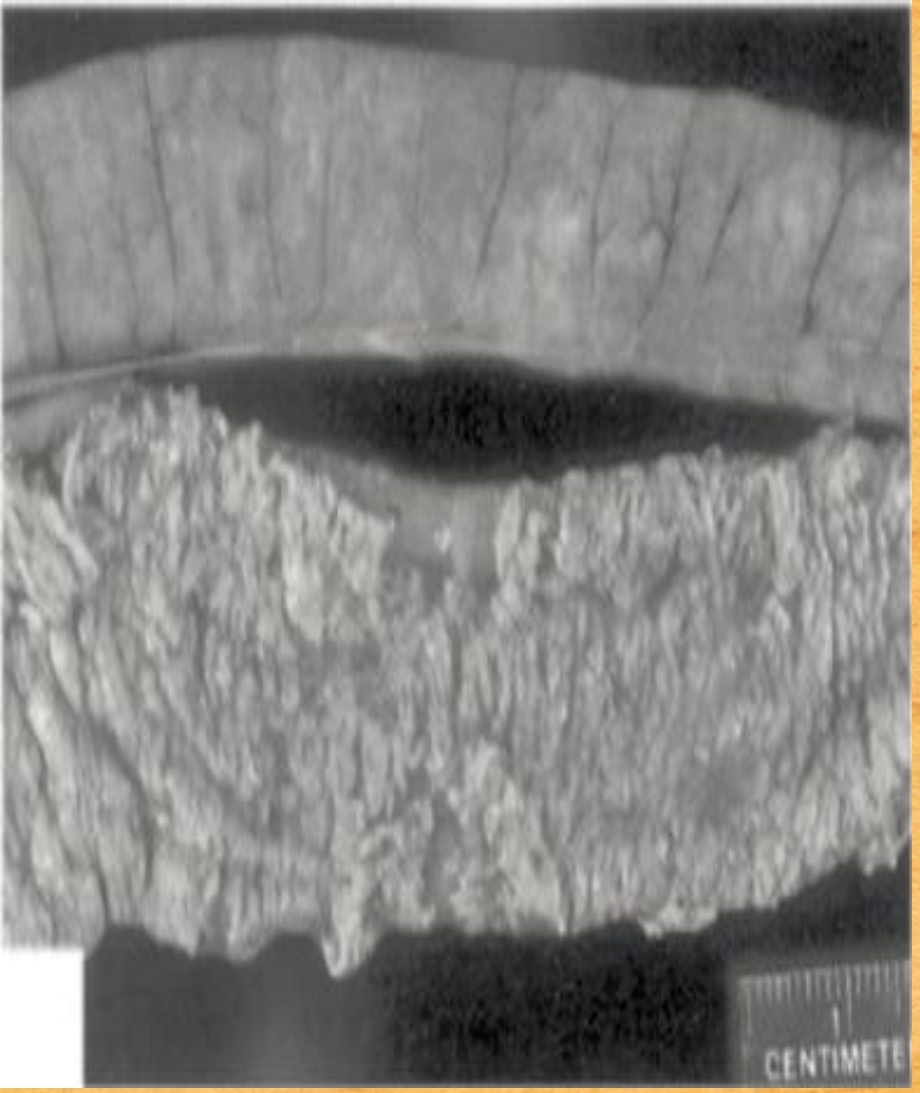
## Microscopically

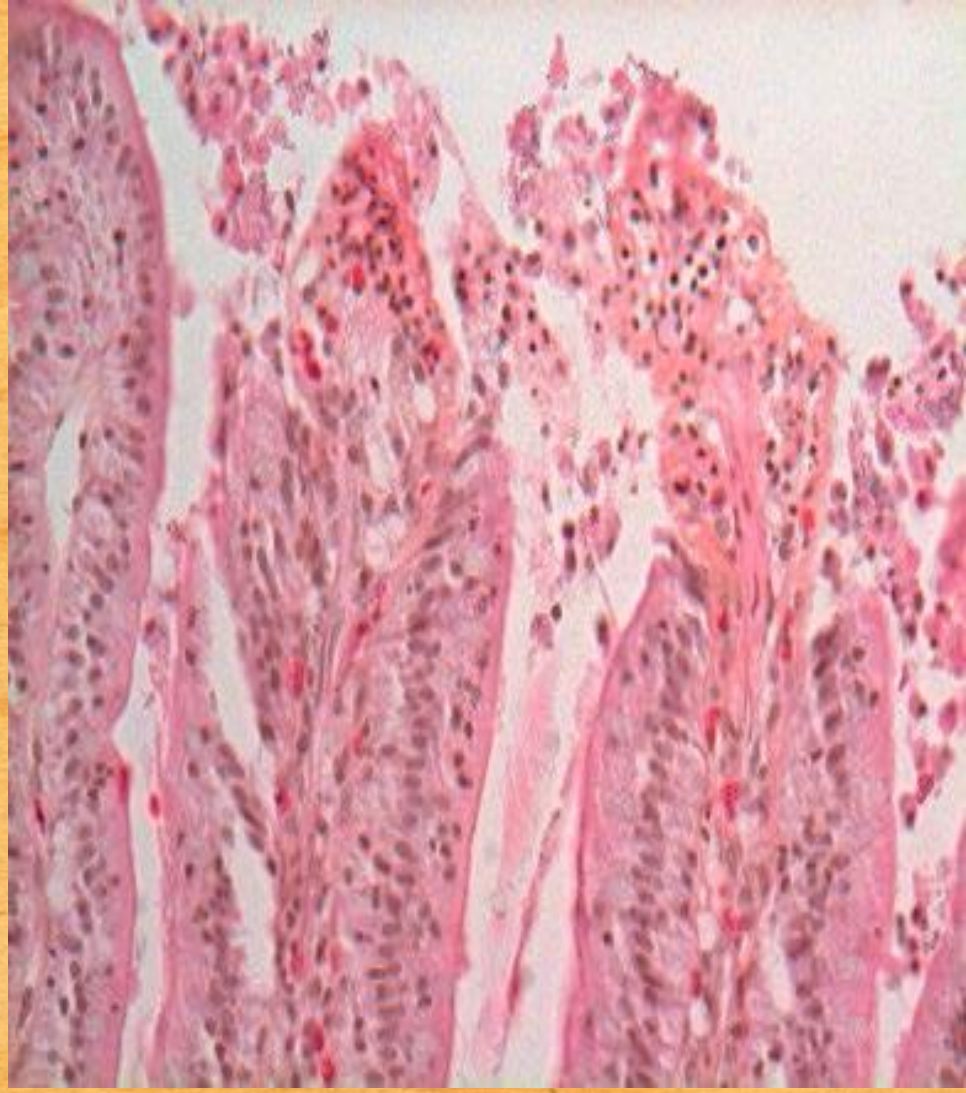
There is extensive villous necrosis, and cellular degeneration may reach the submucosa or even the muscularis mucosa. Coagulation necrosis is common at villous and the demarcation between necrotic and normal tissue is defined by accumulation of mononuclear cells at the junction. Large, Gram-positive rods will attach to the villi tips early in the infectious process and are later associated with areas of necrosis.

## Pathogenesis of NE

Scientists strictly focused on the role of toxins. CPA toxin, a phospholipase C/sphingomyelinase was thought to be mainly responsible for the observed intestinal damage, causing hydrolysis of the phospholipids, damaging the enterocyte wall and hence leading to cell death.

**A**. Mild to moderate necrotic enteritis in a 5-week-old broiler chicken with concurrent coccidiosis. Note the hyperemia and diffuse necrosis of the mucosa with multifocal ulcerations.



**C.** Severe necrotic enteritis in a commercial broiler. Note the “Turkish towel” appearance to the necrotic pseudomembrane covering the intestinal mucosa. **D.** Large, Gram-positive rods will attach to the villi tips early in the infectious process and are later associated with areas of necrosis.

# Intervention Strategies

- Necrotic enteritis can be controlled or prevented by reducing exposure to risk factors.
- The use of organic acids and formaldehyde has been shown to reduce levels of clostridial contamination in plant and animal feed ingredients.
- Coccidiostatic drugs have been the method of choice for the prevention of coccidiosis in broiler chickens for the past 50 years.
- Ionophores have been most popular and these drugs are serendipitously anticlostridial
- Prebiotics: the use of prebiotics such as yeast wall extracts, which stimulate growth of beneficial intestinal flora, have produced inconsistent results.
- Probiotics have been shown to lessen the impact of NE in laboratory challenge. Competitive exclusion products have been shown to decrease the incidence and severity of NE in experimental challenge.
- Phytogenic compounds have been evaluated for their efficacy in reducing the incidence and severity of NE. Anise oil, citral and essential oil blends.

# Botulism

Botulism is a flaccid paralytic disease caused by intoxication with botulinum neurotoxins (BoNTs) produced mainly by Clostridium botulinum.

## Economic Significance

Avian botulism is a significant cause of morbidity and mortality in free-living wild waterfowl, game birds, and poultry. Worldwide, avian botulism probably represents the most important cause of death in migratory birds, with a single outbreak killing tens of thousands of birds. Botulism occurs sporadically in commercial poultry flocks.

## Public Health Significance

The public health significance of avian type C outbreaks is considered minimal.

There are no recorded occurrences of poisoning of people caused by type.

## Etiology:

most commonly reported neurotoxin is secreted by C. botulinum, a strictly anaerobic, spore-forming Gram positive bacterium commonly found in the soil and feces of many animals.

## Incubation Period

The incubation period of avian botulism is usually short, varying from a few hours to 13 days, depending on the amount of preformed toxin or type C spores Ingested.

## Clinical Signs

flaccid paralysis of legs, wings, neck, and eyelids are predominant features of the disease. Initially, affected birds are found sitting and are reluctant to move. If coaxed to walk, they appear lame. Paralysis progresses cranially from the legs, affecting wings, inner eyelid or nictitating membrane, and neck muscles; the latter resulting in inability to hold. the head erect. Gasping can be observed in some birds shortly before death, which results from cardiac and respiratory failure.

(A) and (B) Botulism in chickens showing paralysis of wing and lower eyelid, difficulty breathing caused by partial paralysis of respiratory muscles, and ruffled hackle feathers.

## Pathology

Gross, Microscopic, and Ultrastructural Birds with type C botulism lack characteristic gross, microscopic, and ultrastructural lesions.

## Differential Diagnosis

- mild intoxications.
- transient paralysis syndrome of Marek’s disease.
- Newcastle disease, avian encephalomyelitis,
- fowl cholera, drug and chemical toxicity, and appendicular skeletal problems.
- Lead poisoning of waterfowl is commonly confused with botulism.

# Intervention Strategies

Management Procedures

- Management practices should emphasize removal of potential sources of the organism and its toxin from the environment.
- Prompt disposal of dead birds and culling of sick birds is very important in prevention and control.
- Fly control may be another means of reducing the risk of toxic maggots in the environment.
- Removal of contaminated litter and thorough disinfection using calcium hypochlorite or formalin may help reduce spore numbers in the environment in problem areas.
- Disinfection of areas around poultry houses has been recommended because spores may be located in the soil outside of the poultry facility and can be transported back into houses.

# Intervention Strategies

**Vaccination**

Active immunization with inactivated toxin has been successfully used in pheasant operations and to protect chickens and ducks from experimental botulism. However, the practical usefulness of vaccination of large numbers of birds has so far not been evaluated.

# Treatment

- Many sick birds, if isolated and provided with water and feed, will recover.
- Treatment of large numbers of morbid birds is difficult and various protocols have been used but not verified experimentally.
- Commercial broiler chickens in outbreaks of botulism have been successfully treated with several antibiotics including bacitracin, streptomycin, tylosin, amoxicillin, penicillin, and chlortetracycline.
- Inoculation with specific antitoxin neutralizes only free and extracellular bound toxin and might be considered for treating valuable birds in zoologic collections.

# Gangrenous Dermatitis

Clostridium septicum, C. perfringens type A, and Staphylococcus aureus are the primary causative agents of GD, a disease of chickens and turkeys. Characteristic serosanguinous lesions may occur on the wing, thigh, breast, and abdomen and will appear as dark reddishpurple to green, weepy areas of the skin. Subcutaneous emphysema may or may not be present. GD is also characterized by a sudden onset of acute mortality within a flock.

## Economic Significance

The primary economic impact of GD is associated with the mortality that accompanies the disease. Losses are associated with any lost investment in production costs (chick/ poult cost and feed consumed) and the resulting loss of income related to the reduction in marketable pounds.

## Public Health Significance

The public health significance of this disease is thought to be minimal.

## Etiology:

*Clostridium septicum* produces 4 exotoxins (alpha, beta, delta, and gamma). Clostridia are short, thick, Gram-positive, anaerobic, spore-forming bacillus. Clostridial spores, when present, are oval.

## Etiology:

## Names and Synonyms

Gangrenous dermatitis is also referred to as clostridial dermatitis, necrotic dermatitis, gangrenous dermatomyositis, gangrenous cellulitis, gas edema disease, avian malignant edema, wing rot, and, in some instances, blue wing disease – a component of chicken infectious anemia virus infection

## Transmission:

Clostridia are normal inhabitants of the avian intestinal tract and are ubiquitous in the poultry house environment. They can be easily isolated from feces, soil, contaminated litter, dust or feed, and intestinal contents.

## Incubation Period

Relatively short (12–24 hours).

## Clinical Signs

The clinical signs associated with GD include depression, inappetence, leg weakness, ataxia, and pyrexia.

## Pathology

### Gross

Gross lesions of GD in turkeys and chickens appear as dark reddish-purple to green, weepy areas of the skin. Affected areas usually include breast, abdomen, wings, thighs and legs. Extensive serosanguinous edema, with or without gas (emphysema), is present in the subcutaneous tissue below the affected skin lesions.

## Microscopic

Microscopic changes are characterized by edema and emphysema with numerous large, basophilic bacilli or small cocci within subcutaneous tissues. Severe congestion, hemorrhage, and necrosis of underlying skeletal muscle are often present. Liver, if affected, contains small, randomly scattered, discrete areas of coagulation necrosis with intralesional bacteria

## Treatment

- Historically, antibiotic therapy in either the feed or drinking water has been used to effectively manage GD.
- Water treatment with copper sulfate or drinking water acidification with citric or propionic acid have been used to reduce, but not eliminate.