AVIAN ADENOVIRAL INFECTIONS

DEFINITION

Adenoviral infections are very common in poultry and other avian populations. Although some infections such as those described in this section can be defined in terms of clinical and pathologic characteristics, most are either subclinical or associated with nondescript clinical syndromes.

OCURRENCE

Serologic surveys indicate that nearly all poultry flocks experience infections with one or more adenoviral serotypes. Because most adenoviruses are egg transmitted, they can be present in developing embryos. The frequent presence of these viruses even in healthy birds means that their role in disease must be very critically examined. Adenoviruses must also be carefully excluded from chicken, duck, or turkey embryo-propagated vaccines as well as cellular and blood products used in diagnostic or research reagents.

HISTORICAL INFORMATION

1. Adenoviruses have long been recognized in humans and animals but they serve as primary pathogens in only a few instances. More often they accompany other more pathogenic agents or initiate pathologic effects in immunologically deficient animals.

2. The first recognized adenoviral infections of birds were quail bronchitis, a severe respiratory disease of quail; and an infection causing spontaneous mortality in chick embryos caused by an adenovirus known as chick embryo lethal orphan (CELO) virus. These two infections, described in 1949 and 1952, respectively, were later discovered to be caused by the same adenovirus serotype.

3. The exact role that adenoviruses play in avian diseases is unclear. Adenoviruses are suspected of playing a primary or secondary role in a variety of syndromes including inclusion body hepatitis in chickens; marble spleen disease of pheasants; hemorrhagic enteritis of turkeys; splenomegaly in chickens; egg production declines in laying chickens (egg drop syndrome—1976); and miscellaneous respiratory, arthritic, encephalitic, and enteric syndromes.

ETIOLOGY

1. Adenoviruses are DNA viruses that replicate and frequently produce inclusion bodies in the nuclei of infected cells. The viruses are unenveloped and range in size from 70 to 80 nm. They tend to be host specific.

2. The avian adenoviruses have been divided into three major groups or types. Although members of each type may share group antigens, there is no common antigen shared between types and there is no antigenic relationship between avian and mammalian adenoviruses. Type I avian adenoviruses include the CELO virus and numerous other serotypes among which are viruses associated with inclusion body hepatitis of chickens; type II avian adenoviruses encompass the viruses causing marble spleen disease in pheasants and hemorrhagic enteritis in turkeys; type III adenovirus is the hemagglutinating agent responsible for egg drop syndrome—1976.
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EPIZOOTIOLOGY

1. Egg-transmitted adenoviruses may remain inactive in infected chickens or poults until maternal antibody wanes. Virus replication and shedding, especially in feces, occurs from 2 to 3 weeks of age onward.

2. In exposed birds the virus enters via the alimentary tract (and, in some cases, by the conjunctiva and nasal passages) and primary replication occurs in the nasopharynx and intestine. Frequently there is a viremic stage in the infection with widespread dissemination of virus to secondary sites of replication. As active antibody is produced viral activity wanes but the virus may persist in a latent state in some organs. There may be periods of virus reactivation throughout life especially during episodes of immunosuppression or stress.

3. Exposure to one serotype of type I avian adenovirus confers no immunity to other serotypes within this group. Similarly infections with type I will not protect against infection with types II or III. Thus, birds can and do suffer repeated infections with antigenically unrelated adenoviruses.

4. Adenoviruses tend to persist in a contaminated environment because they are relatively resistant to physical and chemical environmental factors. This group of viruses is susceptible to formaldehyde and iodine disinfectants.

CLINICAL AND PATHOLOGIC FEATURES

Diseases with reasonably well-established adenoviral etiologies, namely inclusion body hepatitis in chickens, quail bronchitis, hemorrhagic enteritis, and egg drop syndrome—1976 are presented in detail in this section. Reports of other diseases attributed to adenoviral causation should be scrutinized closely for solid evidence of a definitive etiologic role.

I. QUAIL BRONCHITIS

(QB)

DEFINITION

Quail bronchitis (QB) is an acute, contagious and sometimes highly lethal respiratory disease of bobwhite quail (Colinus virginianus) caused by an adenovirus (type I, serotype 1) and characterized by catarrhal tracheitis and airsacculitis.

OCCURRENCE

QB, originally recognized in 1950, has been documented sporadically in captive quail throughout the United States. There is evidence suggesting occurrence in wild quail as well.

ETIOLOGY

The adenovirus causing QB is closely related to the prototype CELO (chick embryo lethal orphan) virus, which is widespread in chickens. This suggests a potential hazard to quail in situations where there is direct or indirect contact with chickens and perhaps other avian carriers.
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EPIZOOTIOLOGY

1. As with other birds, the probable sources of the causative adenovirus for susceptible bobwhite quail are infected breeders (via transovarial passage), carrier birds, or contaminated feces, or mucus mechanically carried from infected premises.

2. Once established in a flock the QB virus spreads rapidly primarily by the fecal-oral route. Morbidity usually reaches 100% in susceptible birds.

3. The disease frequently occurs in succeeding broods of quail reared on contaminated premises owing in great part to the resistance and persistence of the causative adenovirus.

CLINICAL SIGNS

1. QB occurs with sudden onset of severe respiratory signs including tracheal rales, coughing, and sneezing. Lacrimation, conjunctivitis, and neurologic disorders may also be seen but are less consistent signs.

2. The disease is most severe in young quail (under 4 weeks of age). Infections are milder or subclinical in birds over 8 weeks of age.

3. The incubation period of QB is 2-7 days, which explains the explosive spread of the disease in susceptible flocks. Morbidity and mortality can be substantial, ranging from 10 to 100% in young birds and the course of the disease in affected flocks varies from 1 to 3 weeks.

LESIONS

1. Excess mucus with thickening and roughening of the mucosa are the major lesions in the trachea [Fig. 1; Quail bronchitis; Cornell U] and bronchi. Air sacs may be mildly thickened and cloudy.

2. Clouding of corneas, conjunctivitis, and mucosal congestion in the nasal passages and infraorbital sinuses are occasionally noted.

3. Microscopically, the major lesions include mild to moderate epithelial deciliation and hyperplasia of respiratory epithelium and variable lymphocytic/plasmacytic infiltration in the tracheal or bronchial propria. Intranuclear inclusion bodies may be present in respiratory epithelium in early stages of infection.

DIAGNOSIS

1. Acute respiratory disease with high mortality in young quail chicks is highly suggestive of QB.

2. Confirmation of severe catarrhal tracheitis and bronchitis on histopathologic examination and demonstration of intranuclear inclusion bodies in respiratory epithelium establish a strong tentative diagnosis.

3. Isolation and identification of the causative adenovirus confirms the diagnosis of QB. Isolation is accomplished by inoculation of 9-11-day-old specific-pathogen-free embryonating eggs via the allantoic sac with triturates of trachea, air sacs, lungs, etc. Virus isolation may also be accomplished using cell cultures (chick embryo kidney or chicken kidney).

4. Serologic tests are of limited value unless flock sampling is done on both an acute and convalescent basis to demonstrate definitive seroconversion. Agar-gel precipitin and virus neutralization for type I serotype 1 avian adenovirus are applicable tests.
CONTROL

Little can be recommended except frequent monitoring to assure QB virus-free breeding stock and strict isolation of young growing birds to avoid introduction of the virus. No federally licensed vaccines are available.

TREATMENT

There is no effective treatment but increasing brooding house temperature, elimination of drafts, and expanding floor space may be helpful as supportive measures in the face of an outbreak.

II. INCLUSION BODY HEPATITIS
(IBH; Adenoviral Infection)

DEFINITION

Inclusion body hepatitis (IBH) is an adenoviral infection of young chickens characterized by sudden onset and sharply increased mortality, short course, anemia, and hepatitis, often accompanied by intranuclear inclusion bodies.

OCCURRENCE

IBH occurs in 3-15-week-old chickens but more frequently in 4-8-week-old chickens. IBH appears to be a secondary invader when there is immunosuppression caused by other diseases (infectious bursal disease or chicken infectious anemia). Many flocks of older chickens are solidly immune and serologic testing indicates that they carry antibody to the disease. IBH has been described in Canada, the United States, the United Kingdom, Italy, Iraq, and Australia. With the advent of breeder vaccination for infectious bursal disease (IBD), the incidence of IBH has been reduced substantially.

HISTORICAL INFORMATION

1. In 1963 hepatitis with inclusion bodies was described in chickens but the causative agent was not identified. That outbreak probably was the disease we now call inclusion body hepatitis (IBH). In the early 1970s a similar disease occurred in many flocks in Canada and the United States. Adenovirus was isolated from an Indiana outbreak and, eventually, from flocks in many other locations.

2. Hemorrhagic syndrome (aplastic anemia), a syndrome diagnosed frequently in the 1950s, is now suspected of being caused by adenoviral infection. However, there may be more than one cause of hemorrhagic syndrome. A virus designated “chicken infectious anemia (CIA) virus” is strongly suspect as an important causative factor.

ETIOLOGY

1. At least three serotypes of adenovirus have been isolated from chickens with IBH. In several IBH adenovirus isolates there is an accompanying adenovirus-associated parvovirus.

2. Although many features of IBH can be reproduced using adenovirus isolates in specific-pathogen-free chicks, many investigators conclude that the natural disease does not occur without the immunosuppressive effects of early infectious bursal disease.
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EPIZOOTIOLOGY

1. Infected chickens shed adenovirus in their feces for at least a few weeks and infection is suspected of spreading slowly through a flock. The virus is resistant to many environmental influences and could be spread readily on fomites or mechanically. Farm-to-farm spread has been observed.

2. Circumstantial evidence suggests that the IBH adenovirus can be transmitted through the egg. The virus spreads laterally from infected to susceptible chickens, presumably through contaminated feed, water, and the environment.

CLINICAL SIGNS

1. A sudden marked increase in mortality often is the first indication of the disease. Mortality increases for 3-5 days, levels off for 3-5 days, and then decreases to normal levels over another 3-5 days. Total mortality may approach 10% but is usually considerably lower.

2. The morbidity in an outbreak is less than would be expected considering the mortality. Affected birds often show clinical signs for only a few hours and then die.

3. There are few specific signs. There may be pallor of the comb, wattles, and facial skin. The affected birds are depressed and listless. In some outbreaks the clinical signs are masked by other diseases in the flock.

LESIONS

1. The skin is pale and may be icteric and contain hemorrhages, particularly over the legs and breast. Internally, hemorrhages often are present in skeletal muscles and under serous membranes.

2. The liver is swollen, yellow to tan, and there may be mottling with focal soft areas [Fig. 1; Inclusion body hepatitis; Cornell U]. There are petechial and ecchymotic hemorrhages under the capsule and in the parenchyma.

3. The kidneys frequently are swollen and pale and may contain cortical hemorrhages.

4. The bone marrow is often pale yellow and the blood is thin and watery. The bursa of Fabricius and spleen are usually small. Pericardial fluid is often increased and there may be gray to white patches on the heart.

5. Microscopically there is extensive degeneration and necrosis in the liver and there may be intranuclear inclusions in parenchymatous cells [Fig. 2; Inclusion body hepatitis; Cornell U] during the early stages of the disease. There is hypoplasia of the bone marrow.

DIAGNOSIS

1. In young, growing flocks a sudden increase in mortality accompanied by low morbidity is suggestive of IBH. Typical gross lesions and a history of prior outbreaks in the area or on the premises are helpful.

2. Demonstration of typical microscopic lesions in the liver, including intranuclear inclusions, is often used as a basis for a diagnosis. The adenovirus often can be isolated from the respiratory or digestive tract.

3. Isolation of an adenovirus or the demonstration of a titer to adenoviral group antigen do not prove infection in ailing flocks; adenoviruses and antibody to them are widely distributed in poultry. Nevertheless, an agar-gel precipitin test is widely used to demonstrate antibody. It may be useful if the reactor rate can be shown to increase between onset and convalescence.

4. IBH should be differentiated from aplastic anemias caused by toxic agents.

5. One should attempt to determine if the birds were previously infected with IBD or CIA virus. Inclusion
body hepatitis is now suspected of occurring in immunologically deficient flocks as a consequence of earlier infection with IBD or CIA virus.

**CONTROL**

1. Because IBH virus is suspected of being transmitted through the egg, eggs from primary breeding flocks whose progeny have consistently had IBH should not be used for hatching.

2. Application of quarantine and good sanitary practices appears to be the best defense against infection. Wild birds should be kept out of poultry houses because they possibly may serve as disseminators of virus.

3. No vaccine is available. It appears that only polyvalent vaccines would be of value because at least three serotypes of adenovirus have been isolated from birds with IBH.

4. Prevention must begin with the control of IBD and CIA. Vaccination of breeders for IBD virus and natural or controlled exposure of breeder pullets for CIA virus is the most practical method for preventing IBH.

**TREATMENT**

There is no effective treatment for chickens with IBH. Good husbandry and care usually suppress mortality.

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**III. HEMORRHAGIC ENTERITIS OF TURKEYS**

(HE; Bloody Gut)

**DEFINITION**

Hemorrhagic enteritis (HE) is a viral disease of young turkeys characterized by sudden onset, depression, bloody droppings, and variable but often high mortality. A subclinical form characterized by an enlarged, mottled spleen occurs and is more common than the acute form.

**OCCURRENCE**

HE typically occurs in 6-12-week-old turkeys but has been seen in pouls as young as 2 weeks and in older turkeys. It is rare in turkeys less than 4 weeks of age, presumably because of maternal antibody. The disease is more prevalent in the summer and in turkeys on range. HE has been reported from most turkey-raising areas of the United States and appears to be increasing in incidence. The disease has a worldwide distribution.

**HISTORICAL INFORMATION**

HE was first reported in 1937 but the cause was unknown. Only a few reports of the disease were published during the next 30 years. In 1972 the disease clearly was demonstrated to be caused by a viral infection. Since 1970 there have been numerous reports on research and field aspects of the disease. HE now is recognized as a common and important disease of turkeys.

**ETIOLOGY**

1. The etiologic agent is a type II adenovirus. Thus far it has not been possible to propagate the agent in embryos but recently it has been propagated in tissue culture.

2. Marble spleen disease (MSD) in pheasants and splenomegaly in chickens are caused by the same or similar viruses. The latter has been confused with Marek's disease and resulted in high condemnations of affected flocks.
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EPIZOOTIOLOGY

The epizootiology of HE is not known. The virus possibly is transmitted by chickens or other birds, rodents, or on contaminated equipment, shoes, boots, etc. Once introduced, the virus spreads laterally, presumably through ingestion of feces from infected turkeys. Infection frequently reoccurs on the same farm in successive flocks. There is no evidence of egg transmission. Infection of turkeys with HE virus results in a transient immunosuppression, often involving secondary colibacillosis.

CLINICAL SIGNS

1. Sudden deaths are often the first sign of HE in a flock. A concurrent drop in feed and water consumption may be noted. Droppings containing fresh blood or melena can be seen, especially around waterers.

2. A few birds exhibit signs of depression and have bloody feces. Blood may be seen oozing from the vent of dead or moribund birds or may be adhered to feathers around the vent. Blood may be expelled from the vent if the abdomen is squeezed. Most birds with bloody feces die.

3. The disease usually runs its course in a flock in 10-14 days. Most mortality occurs over a 10-day period. Mortality may exceed 60% but averages 5-10%.

4. Outbreaks of colisepticemia often follow clinical and subclinical infections with hemorrhagic enteritis virus 12-14 days later. Colisepticemia may be the only indication of prior subclinical infection.

LESSONS

1. Skin of dead poults often exhibits pallor. The birds are well fleshed.

2. The intestinal tract, especially the small intestine, is distended, dark purple, and filled with bloody material [Fig. 1; Hemorrhagic enteritis; Cornell U]. The mucosa is congested, especially in the duodenum, and may be covered with a yellowish layer of fibrinous debris. An intact spleen and bursa of Fabricius have been shown to be necessary for development of intestinal hemorrhage.

3. Small hemorrhages have been reported at various sites including: subcutaneous tissues, breast and thigh muscles, on the epicardium of the heart or surface of the liver, the gizzard, the proventricular-ventricular junction, at the pyloric opening, and on the kidneys.

4. The spleen is strikingly mottled and enlarged [Fig. 2; Hemorrhagic enteritis; NCSU]. Experimentally infected birds have splenic enlargement only during the first 4 days of illness. Afterwards the spleen is shrunk and silver-gray. Similar splenic lesions are seen in affected chickens and pheasants.

5. Microscopically, white pulp of the spleen is hyperplastic and there may be small, necrotic foci. Large acidophilic to basophilic intranuclear inclusions bodies are present in reticuloendothelial cells. The condensed nuclear chromatin around inclusions often resembles a signet ring. Similar inclusions can occur in cells in the lamina propria of the intestine and in many other organs but are less numerous.

6. The only lesion of MSD in pheasants not seen in turkey poults is marked congestion and edema of lungs. In affected pheasants this lesion often appears to be the probable cause of death. Pheasant lungs may also have focal areas of necrosis and reticular cell hyperplasia and the intranuclear inclusions may be found in reticular cells.

DIAGNOSIS

1. Typical history and gross lesions strongly suggest the diagnosis. Demonstration of intranuclear inclusions in reticuloendothelial cells in the spleen or intestine confirms the diagnosis.
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2. The disease can be reproduced in 6-week-old or older, susceptible pouls by giving minced splenic tissue or its supernate intravenously, orally, or intracloacally. Typical intestinal content also will reproduce the disease when given orally or cloacally.

3. If known-positive antiserum and known-infectious splenic tissue are available, it is possible to use the agar-gel diffusion test to demonstrate antigen in the spleen of an infected turkey or to demonstrate antibody in the convalescent sera of recovered birds.

4. HE must be differentiated from other causes of severe enteritis, from acute coliform septicemia, and, rarely, from reticuloendotheliosis viral infection in turkeys. Occasionally septicemic diseases including streptococcosis, colisepticemia, and fowl cholera produce an enlarged, mottled spleen. Adenoviral splenomegaly in broilers must be differentiated from Marek's disease.

CONTROL

1. Use a live tissue culture vaccine by water administration to prevent HE in turkeys. This vaccine can also be used to prevent MSD of pheasants.

2. Good biosecurity is helpful in preventing spread of infection from flock to flock.

3. Good care and management will reduce mortality and economic loss. Radical changes in feed or management should be avoided.

4. Antibiotic therapy should be started within 1 week after onset of the disease to prevent secondary colisepticemia.

TREATMENT

1. There is no practical satisfactory treatment of HE in turkeys.

2. The subcutaneous inoculation of 0.5-1.0 ml of immune antiserum from recovered turkeys may decrease the severity of a flock outbreak. Inoculation is done as soon as possible after onset of the disease.

3. Antibiotic therapy should be started within 1 week after onset of the disease to prevent secondary colisepticemia.

IV. EGG DROP SYNDROME—1976 (EDS76)

DEFINITION

Egg drop syndrome (EDS76) is an infectious disease of laying hens caused by a hemagglutinating adenovirus and characterized by loss of color in pigmented eggs and failure to achieve production targets or by production of thin-shelled or shell-less eggs in otherwise healthy birds.

OCCURRENCE

EDS76 is known to affect only laying hens although the causative virus has been recovered from ducks, geese, and a variety of other waterfowl. It appears that the EDS76 virus is a well-adapted duck or goose adenovirus and the chicken is not a natural host. Reproductive disorders are not associated with infection in waterfowl. EDS76 has been documented in numerous countries throughout the world, but not in the United States.
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HISTORICAL INFORMATION

This syndrome was first described as a unique problem in laying hens in Holland in 1976. Isolation of a hemagglutinating adenovirus and much of the research defining the disease and the circumstances accounting for establishment of the virus in chickens were reported from Northern Ireland in the 1970s. Reports documenting the infection in other locations around the world are numerous.

ETIOLOGY

EDS76 virus is classified as an adenovirus on the basis of its morphology, replication, chemical composition, and resistance to chemical and physical agents. However, the virus appears not to be related to 11 fowl and 2 turkey prototype adenoviruses based on serum neutralization or hemagglutination inhibition tests. Only one serotype of EDS76 virus is known. The virus is readily propagated in cell cultures derived from ducks and duck embryos but grows poorly in turkey cells and not at all in a wide range of mammalian cells. The virus replicates to very high titers in embryonated duck and goose eggs but no growth has been detected in embryonated chicken eggs.

EPIZOOTIOLOGY

It appears that the EDS76 virus was first introduced to chickens through a contaminated vaccine. Initially, major transmission was vertical from breeders to progeny chicks and the virus often remained latent until birds approached peak production. In many cases infected chicks do not excrete the virus or develop detectable antibodies until the flock is between 50% and peak production. At this stage the virus is excreted and spread of the virus occurs. Lateral spread to susceptible contacts is slow in cage houses but faster in birds on litter. Infected chickens develop a viremia and the virus is distributed in various internal organs including the alimentary canal, respiratory tract, spleen, liver, and oviduct. Virus is shed primarily from the pharynx and in feces but spread seems to depend on contact with feces. Virus can also be spread by contaminated needles when infected birds are in the viremic phase. Although ducks and other waterfowl are the natural hosts of the EDS76 virus, natural transmission from waterfowl to chickens either does not happen or is extremely rare. There appears to be no age or breed predilection in chickens and effects of infection are not apparent until pullets achieve peak production.

CLINICAL SIGNS

There are no reliable clinical signs other than effects on the ovary and oviduct. Alterations in egg production vary depending on the serologic status of the infected flock. In flocks with a low rate of serologic reactors the first sign is loss of color in pigmented eggs followed rapidly by production of thin-shelled or shell-less eggs. Other than shell quality there are few other problems with eggs; internal quality, fertility, or hatchability are not frequently affected. In flocks with a substantial level of antibody before the virus is unmasked the major reproductive effects are failure to achieve projected egg production or delay in the onset of lay. The drop in production associated with EDS76 may be rapid or extended. Depressed production lasts 4-10 weeks and production is reduced up to 40%.

 LESIONS

Gross lesions other than inactive ovaries and atrophied oviducts are not seen in natural infections. Edema and swelling of the mucosal folds of the uterus have been described in experimentally infected hens. Histologically, oviductal changes include proprial edema, infiltration of mononuclear leukocytes (lymphofollicular aggregates in some cases), atrophy of tubular glands, and degeneration/desquamation of uterine epithelium. Intranuclear inclusion bodies may be seen in epithelial cells of the uterus, isthmus, and vagina.
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DIAGNOSIS

Reduction in production with the occurrence of depigmented, soft-shelled eggs in the absence of other clinical signs should trigger consideration of EDS76. Isolation and identification of the virus is best achieved using EDS76-free embryonated duck or goose eggs or cell culture of duck or goose origin. Harvested allantoic fluid or cell culture supernatant can be checked for hemagglutinating activity, which is inhibited by specific EDS76 antiserum. Use of immunofluorescence with labeled EDS antiserum is perhaps the most direct means of identifying the virus in cell cultures. Application of serology in suspect flocks is most helpful immediately after egg changes are observed because many infected flocks do not have demonstrable antibody during the growing period. The hemagglutination inhibition test or the serum neutralization tests are the most helpful in serodiagnosis.

CONTROL

An oil-adjuvant inactivated vaccine is widely used at 14-16 weeks of age in replacement pullets. Although the vaccine confers good protection against clinical disease, vaccine-induced antibody titers may not be high or uniform. As with other diseases, avoidance of infection is the best prevention. Knowledge of the infection status of breeder flock sources of replacement chicks is essential. If chicks are reliably determined to be free of EDS76 virus, traffic control to avoid introduction is critical as is avoidance of contact with waterfowl.