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A fatal disease associated with progressive weight loss despite a ravenous appetite was first described in macaws in the late 1970s in the United States. Because of the clinical changes and the affected species of bird, the syndrome was initially called macaw wasting syndrome. The disease is associated with damage to the nerves that supply the gastrointestinal tract, causing a partial or generalized ileus. Names used in the literature to describe this syndrome include neuropathic gastric dilatation (NGD), proventricular dilatation syndrome (PDS), proventricular dilatation disease (PDD), myenteric ganglioneuritis, psittacine wasting syndrome, proventricular hypertrophy and infiltrative splanchnic neuropathy. The most recent name suggested for the disease is lymphoplasmacytic gangglioneuritis and encephalomyelitis, a comprehensive term which most accurately describes the microscopic changes in affected birds.\textsuperscript{7,10,13} In this chapter proventricular dilatation disease (PDD) is being used to describe a group of changes recognized by dysfunction and distention of the ventriculus and proventriculus, and the accumulation of lymphocytes and plasma cells adjacent to the nerves that infiltrate these organs.

Histologic changes in affected birds and epizootiologic evidence suggests that PDD has a viral etiology; however, a direct association between a virus and the disease has not been confirmed. Some evidence indicates that the disease is caused by a highly infectious organism; other data suggest that the disease occurs randomly and is not caused by a readily transmissible agent. Multiple cases of PDD can occur in the same flock, and mates or siblings can develop the disease following the death of an affected bird — facts that support the theory that this disease is caused by an infectious agent. However, many birds exposed to affected individuals remain asymptomatic, suggesting that the etiologic agent may be of low transmissibility or that some infected birds survive. It has been suggested that the clinical changes associated with the disease occur after a virus that causes the disease has been eliminated, making the detection of the etiologic agent difficult.\textsuperscript{8} However, the microscopic changes that occur with the disease suggest that an active inflammatory response is occurring.

Adenovirus-like particles have been demonstrated within intranuclear inclusion bodies in the cells lining the kidneys of one affected bird.\textsuperscript{15} Paramyxovirus-like viral particles have been demonstrated within inclusion bodies located in the neural cells of the spinal cord and in visceral nerve ganglia.\textsuperscript{2,11,22} Similar inclusion bodies have been described in the nerves of pigeons with paramyxovirus infections.\textsuperscript{10} Birds
with PDD have been shown to lack detectable levels of antibodies to paramyxovirus (serotypes 1, 2, 3, 4, 6 and 7), Pacheco’s disease virus, avian polyomavirus and avian encephalitis virus. An eastern equine encephalitis (EEE) virus was recovered from neonates with abdominal distention from an aviary with a history of PDD. However, EEE virus occurs primarily in the eastern portion of the United States, and PDD has been shown to occur throughout North America and Europe. Additionally, only 2 of 17 birds from a California aviary with a history of PDD had antibodies to EEE virus, and serologic surveys indicate EEE antibodies are detected with a similar prevalence in birds with and without PDD. These findings suggest that PDD is not caused by currently known strains of EEE virus.

Because an infectious agent has not been recovered from affected birds, it has been suggested that the observed changes in the nerves may be a result of an autoimmune process. However, most autoimmune diseases that affect nerves cause demyelination, which has not been reported in birds with PDD.

**Clinical Features**

Clinical changes suggestive of PDD in mature birds include depression, sustained regurgitation, passage of undigested food, impaction of the crop, abdominal distention, progressive weight loss (weeks to months), and central nervous system signs Figure 17.1. Diarrhea or scant feces has been reported in rare cases. Some birds develop only gastrointestinal or central nervous system signs; others develop a combination of both. Of 89 birds described in the literature with confirmed PDD, 86.5% had one or more of the most common clinical signs including depression, weight loss, regurgitation or passage of undigested food. In one affected Goffin’s Cockatoo, the only clinical sign was progressive seizures. A mature, wild-caught Nanday Conure with PDD developed difficulty in walking, and progressively lost control of both legs over a three-month period. Clinical changes suggestive of the syndrome in young birds include frequent regurgitation, failure to properly gain weight and a reversion of weaned birds to begging behavior.

Proventricular dilatation disease is invariably fatal; some reports describe the disease as having a protracted course that can persist for months, while others document death within five days of developing clinical signs. In one study, affected birds died over a period that ranged from six weeks to four months after diagnosis. Birds with the more chronic form of the syndrome will gradually lose weight and pass increasing quantities of poorly digested food. The excrement from these birds is frequently odoriferous and of increased volume because of poor absorption of nutrients. Intact seeds may be noted in the excrement of birds on a seed-based diet. Affected birds that are fed formulated diets may have only voluminous stools, and it is more difficult to discern that the food is being poorly digested. It should be noted that weight loss and regurgitation
can be induced by any extra-luminal or intraluminal mass that restricts passage of ingesta through the upper alimentary tract. Weight loss, regurgitation and passage of undigested food may occur in birds with enteritis or pancreatitis.

Changes in the complete blood count or serum chemistries of affected birds are inconsistent, possibly due to the effects of concomitant bacterial or fungal infections in the damaged gastrointestinal tract. Hypoproteinemia was the only consistent change in three birds with PDD. In other reports, affected birds had heterophilia, monocytosis, hypoglycemia and anemia.

It has been suggested that increased creatinine kinase (CPK) activity may be an indication of PDD. However, not all birds with microscopic changes consistent with PDD have elevated CPK activity. In mammals, CPK activity transiently increases when active damage is occurring to skeletal muscle or to the central nervous system. Because the skeletal muscle change associated with PDD is atrophy and not necrosis, it is likely that any increased CPK activity associated with this disease is caused by continuing damage to the central nervous system.

FIG 17.1
Clinical changes suggestive of PDD in mature birds include:
A depression (also note the prominent keel indicating severe weight loss); and B sustained regurgitation.

C Progressive weight loss may occur over several weeks to months. This can be detected by a loss of pectoral muscle mass making the keel more prominent. Here, the bird is lying on its back and the view is from the neck toward the tail.

D Central nervous system signs that include ataxia, tremors and seizures may occur in some birds, particularly during the end stages of the disease.

E Intact seeds may be noted in the excrement of birds on a seed-based diet.
F Affected birds fed formulated diets may have only voluminous stool, which is difficult to discern.
Throughout the late 1970s and mid-1980s, PDD was considered a disease of psittacine birds. However, microscopic lesions suggestive of the disease have been reported in geese, toucans and spoonbills, indicating that many avian species may be susceptible to the disease.

### TABLE 17.1

<table>
<thead>
<tr>
<th>Birds in which microscopic changes suggestive of PDD have been described</th>
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<tbody>
<tr>
<td>African Grey Parrots</td>
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<tr>
<td>Brotogeris spp.</td>
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<tr>
<td>Buffalo Weaver</td>
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<td>Cockatiels</td>
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<td>Conures</td>
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<td>Hawk-headed Parrots</td>
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<td>Lovebirds</td>
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<tr>
<td>Meyer’s Parrots</td>
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<td>Pionus Parrots</td>
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<td>Quaker Parakeets</td>
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<tr>
<td>Rock Pebbler</td>
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<td>Spoonbills</td>
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<td>Toucans</td>
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### EPIZOOTIOLOGY

Proventricular dilatation disease was first discussed in the late 1970s in imported psittacine birds in the United States and Germany. Subsequently, an epornitic of PDD has been occurring in imported and captive bred psittacine birds in North America and Europe, probably as a result of the widespread shipment of companion birds. Clinical or microscopic changes characteristic of the disease have been described in over 50 species of psittacine birds, as well as toucans, spoonbills, a Buffalo Weaver and free-ranging Canada Geese Table 17.1. The description of PDD in multiple families of birds would suggest that its cause is not restricted to distinct hosts Figure 17.2. There is no reference to spontaneous disease in free-ranging psittacine birds; however, there is every reason to assume that these birds would be susceptible. Given the severe nature of PDD and its apparent ability to affect a wide range of bird species, the importation of psittacine birds or their eggs into any region with indigenous Psittaci-formes must be considered extremely dangerous.

It is likely that this disease can occur in any psittacine bird of any age; however, adult birds appear to be more commonly affected Figure 17.3. In a group of 127 birds that had histologic lesions suggestive of PDD, 43.3% were macaws, 21.3% were cockatoos, 12.6% were conures, 18.1% were African Grey Parrots, and 4.7% were other psittacines (Eclectus Parrots, Thick-billed Parrot, Blue-fronted Amazon Parrot). In a large survey of over 10,000 companion and free-ranging birds evaluated histologically over a ten-year period, 1.2% of the birds had lesions suggestive of PDD. In one study, PDD was diagnosed in birds ranging from 10 weeks to 17 years of age, with a mean age of 3.8 years. The average age of a group of 44 affected psittacine birds was 4.6 years.

Proventricular dilatation disease can occur in any aviary despite excellent hygiene, valid quarantine procedures and the absence of new additions to the flock. In some aviaries, numerous cases of PDD will occur simultaneously. In others, several affected birds may die and the problem seemingly resolves, only to reappear one to two years later. In a group of mixed species, wild-caught psittacine birds exposed to a bird confirmed by histopathology to have PDD, signs of disease in the other
Birds were not noted for up to a year following exposure. In other cases, a single bird in a breeding pair may die, with no subsequent losses in the aviary even four to five years later. It is common for many birds exposed directly or indirectly to an affected bird to remain asymptomatic. These variances in the occurrence of clinical changes in exposed birds would suggest that some are resistant to the disease or are able to mount an effective defense.

**INCUBATION AND TRANSMISSION**

Because the etiology of PDD has not been confirmed, the incubation period or potential routes by which a bird may be exposed to the reputed infectious agent have not been confirmed. It has been proposed that the incubation period for PDD may be as long as four years; however, the occurrence of acute outbreaks in multiple birds at the same time suggests a much shorter incubation period. Microscopic lesions suggestive of the disease have been detected in birds as young as ten weeks of age. Young birds may die within a week of developing suggestive clinical changes, while older birds can slowly deteriorate over a period of months to years.

During one outbreak, there was a two-week interval between the time that the first bird developed clinical signs and the occurrence of additional cases. Five of ten exposed psittacine birds (macaws and cockatoos) developed clinical signs that included acute depression, weight loss, regurgitation or abnormal digestion over a three-week period. An exposed Green-winged Macaw remained clinically normal, as did two Red-lored Amazon Parrots and two Senegal Parrots.

Proventricular dilatation disease was diagnosed in a mature, wild-caught, Nanday Conure that developed neurologic signs after being isolated from direct contact with other birds for seven months. An affected hand-raised African Grey Parrot had no direct contact with other birds for four years. A captive-raised male Moluccan Cockatoo with a one-year history of passing undigested food was found by biopsy of the ventriculus to have histologic lesions suggestive of PDD. Radiographically, this bird’s parents and a clutchmate had an enlarged proventriculus and ventriculus; however, proventricular biopsies of these birds were normal. The random occurrence of this disease in established aviaries or single bird households could indicate that PDD is...
not caused by an infectious agent, or that it is a slow progressive disease, has a long incubation period, can be transmitted by a mechanical or biologic vector or can occur following activation of a latent infection. The repeated occurrence of PDD in neonates from the same pair of adults suggests that a carrier state may exist.\(^8\)

**Pathology**

Gross changes associated with PDD include emaciation, ventricular ulcers, proventricular dilatation, ventricular dilatation, flaccid crop and undigested food in the dilated lower gastrointestinal tract *Figure 17.4*.\(^{16}\) The proventriculi in emaciated Canada Geese with lesions suggestive of PDD were described as being five times the normal size.\(^4\) These lesions are suggestive of PDD, but confirming the diagnosis requires the histologic detection of an accumulation of lymphocytes and plasma cells in the nerves of the gastrointestinal tract, brain or spinal cord.\(^9,13,23\)

Some birds with histologic lesions consistent with PDD die acutely with or without neurologic signs, and the only gross lesions in these birds may be congestion of the blood vessels to the proventriculus. Gross lesions in one Umbrella Cockatoo were limited to dilatation of the duodenum and proximal jejunum.\(^18\)

As an example of the importance of microscopic examination of the proventriculus, ventriculus and brain to confirm PDD, only 34 of 55 (62%) of the birds suspected to have PDD based on gross findings were confirmed to have the disease microscopically.\(^{10}\) In another study, 16 of 421 (3.8%) psittacine birds examined had dilatation of the proventriculus, and only 4 of these 16 suspect birds had microscopic changes consistent with PDD.\(^3\) Of 89 birds in the literature with lymphoplasmacytic infiltrates in the proventriculus, 80 (90%) had dilatation of the proventriculus.\(^{13}\) In a group of 15 birds with lymphoplasmacytic infiltrates in the proventriculus, only 10 (67%) had proventricular dilatation. The distribution and prevalence of lymphoplasmacytic infiltrates in birds diagnosed with PDD are listed Table 17.2.

Accumulation of lymphoplasmacytic infiltrates in nerves is characteristic of the disease. Other histologic changes that have been reported in some birds include myocarditis, serositis, ventriculitis, degeneration of the lining of the ventriculus, smooth muscle degeneration and accumulation of lymphocytes in affected tissues.\(^9,16,23\) Intranuclear and intracytoplasmic eosinophilic inclu-
sion bodies have been identified in nerve cells of intestinal ganglia; however, their importance in the disease remains unconfirmed.9,16,19,23

**Pathogenesis**
Whatever its etiology, PDD clearly is associated with damage to the nerves supplying the proventriculus, ventriculus and, in some cases, the duodenum. This impedes an affected bird’s ability to properly digest food. The tremors and incoordination associated with PDD are caused by damage that occurs in the brain and spinal cord. The progression of PDD varies widely among affected individuals, probably as a result of differences in the speed with which damage to the nerves occurs.

As food is swallowed by a psittacine bird, it goes down the upper portion of the esophagus and into the crop. Food then exits the crop, enters the lower portion of the esophagus and travels into the proventriculus, where the food is mixed with stomach acids and digestive enzymes. The food then passes from the proventriculus to the thick-walled, muscular ventriculus where the food is crushed, allowing further mixing with digestive secretions. The food passes from the ventriculus into the intestinal tract where further digestion takes place and nutrients are absorbed into the body. If food is not passing correctly from the ventriculus into the intestines, it accumulates in the proventriculus, esophagus and crop, causing them to dilate. Accumulated food may be expelled by vomiting. If the ventriculus does not properly crush ingested food, whole portions of the diet may be passed in the feces. Thus, the primary clinical changes noted with PDD (regurgitation, weight loss, passing undigested food) can be attributed to failure of the proventriculus and ventriculus to properly contract. Affected birds continue to have ravenous appetites but the food that passes through the gastrointestinal tract is improperly digested, nutrients are poorly absorbed and the bird slowly starves due to insufficient consumption of energy.

The passage of food and water through the gastrointestinal tract ensures that bacteria, fungi and other microorganisms found in the lumen are constantly being removed. This ongoing “flushing” of the gastrointestinal tract helps prevent infectious agents from accumulating in the lumen and colonizing the intestines in large numbers see Figure 3.16. When the gastrointestinal tract is not emptying properly, bacteria and other organisms accumulate and are afforded a greater opportunity to colonize the gastrointestinal tract and cause disease. In some birds with PDD, the severely dilated, thin-walled proventriculus may rupture, resulting in the movement of impacted food into the abdominal cavity causing peritonitis.

<table>
<thead>
<tr>
<th>TABLE 17.2</th>
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<tr>
<td>Prevalence of lymphoplasmacytic infiltrates in birds with PDD12,13,16</td>
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<td>Proventriculus</td>
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<td>Ventriculus</td>
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<td>Proventriculus/Ventriculus</td>
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<td>Small intestines</td>
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<td>Crop</td>
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<tr>
<td>Heart</td>
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<tr>
<td>Brain or spinal cord</td>
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<tr>
<td>Pons, Medulla, Midbrain</td>
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<tr>
<td>Cerebrum</td>
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<tr>
<td>Cerebellum</td>
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CHAPTER 17 PROVENTRICULAR DILATATION SYNDROME
Progressive weight loss, regurgitation and passing of undigested food, with or without neurologic signs, are suggestive of PDD. This disease should also be suspected in any bird with neurologic signs that include ataxia, head tremors or seizures. Contrast radiographs of affected adult birds may indicate a rapid gastrointestinal transit time early in the disease process, followed by a slowed transit time (chronic disease) and gaseous distention of the intestines as the ventriculus becomes increasingly dysfunctional and the proventriculus and intestines dilate Figure 17.5. However, any process that causes partial blockage of the intestinal tract or maldigestion — that prevents the passage of food — including fungal proventriculitis, megabacteriosis, parasitic enteritis, foreign bodies, neoplasia, heavy metal toxicosis, bacterial enteritis, papillomatosis of the stomach or any intraluminal or extraluminal mass can cause similar clinical, radiographic or gross changes. The proventriculus of neonates is normally dilated, a condition which should not be misinterpreted as PDD Figure 17.6. The proventriculus of a neonate attains its adult tone and size as the bird enters and completes the weaning period.

Currently, diagnosis of PDD requires the microscopic demonstration of accumulated lymphocytes and plasma cells in association with the nerves of the gastrointestinal tract or central nervous system. In most cases, a post mortem diagnosis is rendered when a complete set of tissues (including proventriculus, ventriculus, brain and spinal cord) are examined microscopically. It may be possible to obtain a diagnosis before death by submitting a biopsy of the crop or ventriculus for microscopic evaluation Figure 17.7. Biopsy of the crop is simple, relatively noninvasive and may have some diagnostic merit. In one study, PDD was reliably diagnosed in 66% of crop biopsies collected from positive birds. Other studies have indicated that a sample of the crop collected at necropsy was 76% accurate in detecting birds that died from PDD. Thus, a positive crop biopsy in a bird with suggestive clinical changes is of diagnostic value, but a negative crop biopsy in a bird with suggestive clinical changes does not rule-out PDD. When the etiology of PDD is confirmed, a screening test to determine whether exposed birds are...
infected may be of value in controlling the disease.

It should be noted that microscopic lesions suggestive of PDD have been described in birds that die from other causes and have absolutely no gross or clinical signs of the disease. This finding may indicate more than one cause for the accumulation of lymphoplasmacytic infiltrates in the nerves of the gastrointestinal tract. All clinical, necropsy and microscopic findings should be considered in diagnosing PDD.

**CONTROL**

Definitive control or prevention of PDD will require confirmation of the etiology. Mates, offspring or clutchmates of birds that are diagnosed histologically with PDD should be considered at extra risk of developing the disease; however, they should not be euthanized. Many of the birds that are directly exposed to those with PDD never develop the disease. Until the cause of PDD is confirmed, and an appropriate screening test is developed, it would be prudent to place exposed birds in single-bird households where they have no direct or indirect exposure to other birds.

Provided with an easily digested, high-energy diet, a stress-free environment and treatment for secondary bacterial or fungal infections, affected companion birds can survive for months or years. Any bird with the disease that is being treated should be placed in strict isolation with no direct or indirect contact with other birds. Some birds with clinical changes suggestive of PDD have been reported to recover when provided supportive care. However, a
positive diagnosis of this disease requires the demonstration of microscopic lesions in the nerves, and none of the reported recoveries have been in birds confirmed to have PDD.21

Some clinicians believe that birds with clinical and radiographic signs consistent with the disease respond favorably to treatment with interferon. While there are no scientific data to support these clinical observations, the treatment regime that has been loosely discussed is 30 units of interferon daily for five days, followed by 30 units twice a week for two weeks, then 30 units once a week for an additional two weeks.24b

REFERENCES


