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Disorders of the Urinary and Reproductive Systems in Ferrets

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OUTLINE

DISORDERS OF THE URINARY SYSTEM

The ferret has a classic bean-shaped kidney that sits in the retroperitoneal space; its dorsal surface lies in direct contact with the sublumbar musculature.[22] Paired ureters transport urine from renal calices to a pear-shaped urinary bladder. The urethra is compressed by the os penis in the male. Urinary pathologies—especially renal ones—are a common necropsy finding in ferrets.[26,38] Renal failure, urolithiasis, and ureteral disorders are seen with varying frequency in clinical practice.[15,62]

Renal Disease and Renal Failure

Variable degrees of chronic interstitial nephritis are commonly found at necropsy in geriatric ferrets.[41] Advanced interstitial nephritis, as well as pyelonephritis, glomerulonephritis, and immune complex–mediated glomerulonephropathy, can cause renal failure.[63] In one author's experience (N.D.), multiple cases of chronic kidney disease have been diagnosed in a group of young ferrets fed raw meat (e.g., as part of what is termed a biologically appropriate raw foods diet), which may suggest a dietary or familial cause. Although uncommon, renal tumors are another potential cause of chronic kidney disease in ferrets.[8] Chronic kidney disease may result in nephrotic syndrome, in which proteinuria and hypoalbuminemia lead to peripheral edema, ascites, or both.

Common causes of acute kidney injury (AKI) in the ferret are postrenal and intrinsic renal insults. In addition, postoperative renal failure can be seen in cases of severe anesthetic

hypotension. Ureteral stenosis, prostatic enlargement, and urolithiasis may result in obstruction of urine flow. Infectious disease and toxin exposure may result in acute disruption of the renal parenchyma (Fig. 4.1). Toxin exposure is especially relevant because of the small size of ferrets and their inquisitive habits.[18] For example, the minimum lethal dose of ibuprofen is 220 mg/kg, which means that ingestion of one tablet could be fatal in a small ferret. Clinical signs appear within 48 hours and as rapidly as 4 hours after ibuprofen ingestion in 40% of ferrets. The most common clinical signs are neurologic, and more than half of ferrets also have gastrointestinal (GI) signs. In rare instances, acetaminophen ingestion can also cause AKI.[18] Renal failure has also been reported as a result of an epinephrine overdose administered to a ferret during a vaccine reaction.[17]

Clinical signs of renal failure may be nonspecific (e.g., anorexia, weight loss, and lethargy) but may also include ulcers, signs of GI abnormalities (including melena and, in rare instances, vomiting), ataxia, ascites, and peripheral edema. Physical examination findings can include dehydration, pallor, irregularities or asymmetry in the size and shape of the kidneys, and increased blood pressure. Polyuria and polydipsia may be seen with chronic kidney disease, whereas AKI is usually characterized by oliguria or anuria.

Abnormal serum biochemical results typically include increased blood urea nitrogen (BUN) and creatinine levels and may also include hyperphosphatemia, hyperkalemia, or hypokalemia and reduced total carbon dioxide levels. Azotemia must be interpreted with care, because gastric ulcerations and meat-based diet consumption may artificially increase BUN levels. Reference levels for creatinine in ferrets (0.2–0.8 mg/dL) are lower than those in dogs and cats,[34] and increases in creatinine levels with renal disease are usually moderate (generally <1.5 mg/dL). In two ferrets with severe renal disease confirmed by histologic examination, both ferrets had a creatinine level of 1.1 mg/dL in conjunction with BUN values of 140 and 320 mg/dL.[41]

Decreased urine specific gravity can suggest proteinuria, as well as the inability of the kidney to concentrate urine. Reference ranges for urinalysis in young healthy ferrets have been published.[20] Mean endogenous creatinine, exogenous creatinine, and inulin clearance rates have been established in ferrets to help evaluate glomerular filtration.[21] Although reference values for urine protein/creatinine ratios (UP:C) have not been established for ferrets, results of a systematic review of literature in humans indicate that a UP:C value of a random urine sample may help rule out the presence of proteinuria as judged by measurement of protein in a 24-hour urine sample.[66] Canine reference values for UP:C are generally <1.0 and cats are <0.6.[86] Symmetric dimethylarginine (SDMA), a novel marker of renal function in small animals,[32] could be an interesting tool for early diagnosis of renal disease in ferrets.[54] In a recent study performed in a clinical setting, SDMA was measured in healthy ferrets and ferrets with renal disease.[54] The SDMA values in control ferrets ranged from 1.2 to 18.8 µg/dL, whereas, in ferrets with confirmed renal disease values ranged from 15.2 to 80.8 µg/dL,[54] resulting in a cutoff value similar to that in dogs and cats (14 µg/dL).

If renal disease is suspected based on urinalysis and biochemical results, attempt to identify the underlying cause with ultrasound examination. Loss of corticomedullary distinction, focal and multifocal alterations in the parenchyma, renal pelvic dilation, and hydronephrosis are sonographic abnormalities that may be detected in ferrets with nephropathies. Ultimately, chronic renal disease may lead to renal atrophy. Sonographically, healthy ferret kidneys show a resistive index (RI) of 0.54 ± 0.04 and a pulsatility index (PI) of 0.83 ± 0.10.[31] Even with severe renal parenchymal changes, no significant alterations in blood flow parameters are seen; however, these indices do increase with age.[31] If necessary, ultrasound-guided renal aspiration or biopsy may be performed. At necropsy, kidneys with significant disease are often grossly pitted with large, focal depressions in the outer cortex secondary to scarring (Fig. 4.1).

Although treatment should be aimed at the underlying cause, nonspecific therapy of renal failure includes supportive care, such as fluid therapy, vitamin and iron supplementation, omega-3 fatty acid supplementation, and nutritional support. Additional therapy may include dietary phosphorus restriction, intestinal phosphate binders, antioxidant supplementation, antihypertensive drugs, angiotensin-converting enzyme inhibitors, and erythropoietin in case of anemia. Begin antibiotics if clinically indicated and use culture and sensitivity results when

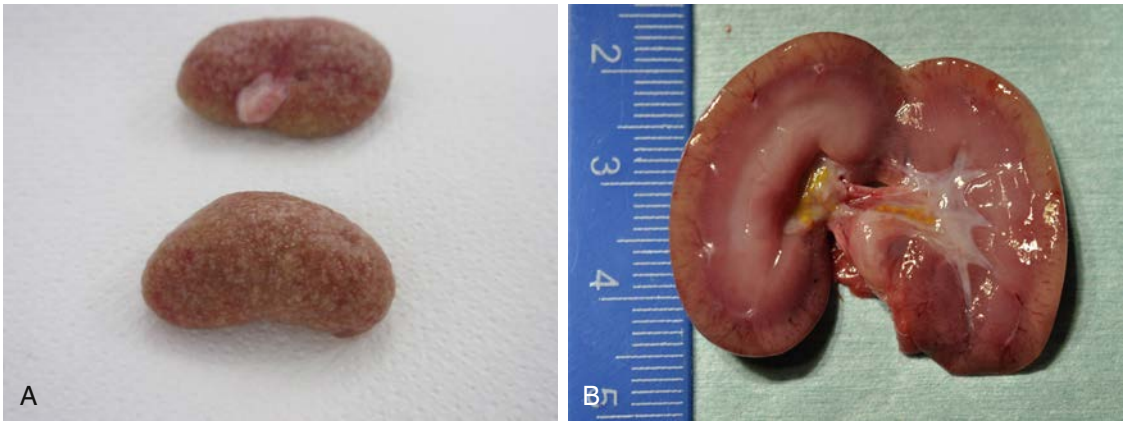

Fig. 4.1 (A) External surface of kidneys in a ferret with chronic kidney disease. (B) Hyperemia of the renal cortex in a ferret with canine distemper virus infection. (Courtesy Dr. Minh Huynh [A] and Dr. Nicola Di Girolamo [B].)

available. Discontinue any potentially nephrotoxic drugs and administer diuretics as needed. The use of small animal renal diets is difficult because these products are not palatable to most ferrets. Furthermore, the effects of long-term protein restriction in ferrets requires study. The prognosis for ferrets with renal failure depends on the cause and severity of the primary disease and response to therapy.

Renal Cysts and Polycystic Kidney Disease

Renal cysts of various sizes are a common incidental finding in ferrets (Fig. 4.2). The incidence of renal cysts ranges greatly in different studies, from 32% to 63% of ferrets affected.[31,38,68,69] Cysts are usually present singly or in small numbers; they are unilateral in most cases but can be present in both kidneys.[78] Cysts are commonly found in the cortices, in close relationship to the pelvic recesses.[68] Rarely, multiple cysts are present in the form of polycystic kidney disease (Fig. 4.3).[69] The causes of renal cysts and polycystic kidney disease in ferrets are uncertain.[38]

Renal cysts may be detected during physical examination as one or more smooth masses on the renal surface. Polycystic kidneys are palpable as slightly irregular, enlarged, firm, oval masses.[38] Ultrasonographic examination is the ideal diagnostic tool for confirmation of renal cysts (Fig. 4.2). If extensive renal architecture is disrupted, cysts will lead to renal failure. Pyelography with an intravenous contrast medium or nuclear scintigraphy may be used to evaluate renal function in clinically affected ferrets.

There is no specific treatment for renal cysts. Ultrasound-guided paracentesis may be used as a palliative treatment, but fluid reaccumulates rapidly. In dogs and cats, renal cysts have been chemoablated by injection of ethanol after drainage.[88] Monitor affected ferrets with periodic ultrasound examination, biochemical analysis, and urinalysis. In people, simple cysts are usually clinically silent, although they occasionally hemorrhage and cause acute pain.[9]

Aleutian Disease

Many ferrets infected with the parvovirus that causes Aleutian disease are asymptomatic carriers. Clinical signs are usually consistent with chronic wasting and ataxia. Additional clinical signs may be attributed to immune complex deposition. Deposits in the kidney may cause membranous glomerulonephritis and tubular interstitial nephritis and possibly renal failure.[63] Aleutian disease virus may also cause liver failure,

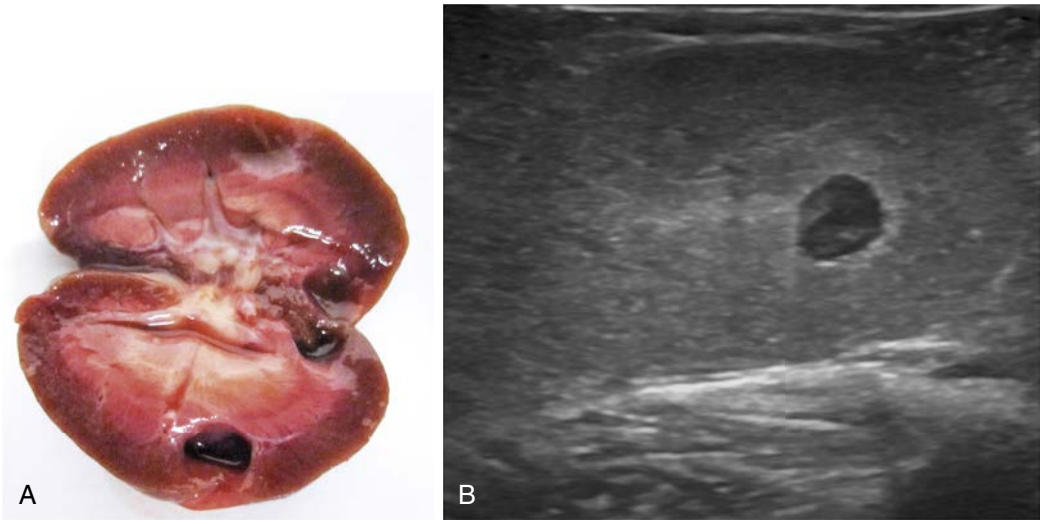

Fig. 4.2 (A) Cross-section of a kidney with two cortical cysts. (B) Sonogram showing a small renal parenchymal cyst of little clinical significance. (Courtesy Dr. Minh Huynh [A] and Dr. Nicola Di Girolamo [B].)

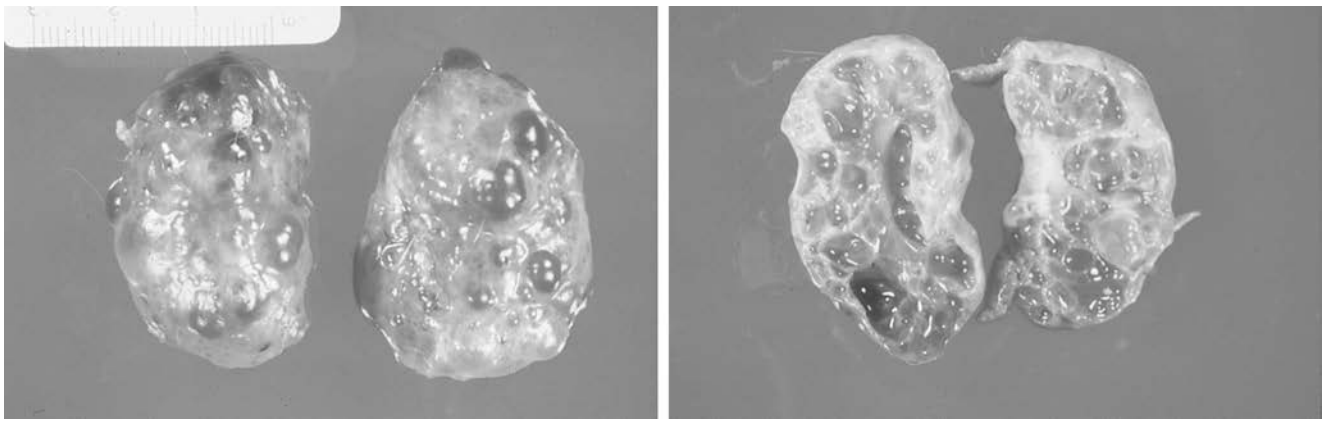

Fig. 4.3 Polycystic kidney in a 3-year-old female ferret in acute renal failure.

intestinal disease (including melena), and central nervous system disease.[63] See Chapter 5 for diagnosis and treatment of Aleutian disease.

Coronavirus

Pyogranulomatous inflammation of the kidney and green-tinged urine have been seen in ferrets with ferret systemic coronavirus (FSCV).[28] One study of ultrasonographic changes in ferrets with FSCV identified nephromegaly and changes in renal cortex echogenicity in most ferrets.[16] Immune complex–mediated glomerulonephritis was seen in an 18-month-old male ferret diagnosed with feline coronavirus.[27] See Chapter 3 for further discussion of FSCV.

Nephrocalcinosis

In three separate sonographic surveys in Europe, hyperechogenicity of the renal medulla was seen in 40% to 58% of pet ferrets.[31,68,69] This sonographic finding was not identified in laboratory ferrets. Histologic evaluation revealed calcium deposits in the renal tubules consistent with renal calcification. Crystalline structures within the renal parenchyma that could not be found sonographically were believed to be urates. Dietary analyses suggested that the presumptive nephrocalcinosis was related to excess dietary calcium and phosphorus.[69]

Pyelonephritis

Pyelonephritis is an uncommon finding in ferrets, usually associated with an ascending bacterial urinary tract infection or sepsis. Hemolytic *Escherichia coli* and *Staphylococcus aureus* are the most common causative agents. Clinical signs are anorexia, lethargy, fever, and pain on palpation of the kidneys. Severe suppurative pyelonephritis progressing to end-stage chronic renal failure was reported in a ferret treated for lymphoma.[71] In that case, immunosuppression from long-term corticosteroid administration may have led to cystitis and secondary pyelonephritis.[71]

To differentiate pyelonephritis from lower urinary tract disease, perform urinalysis and abdominal ultrasound and consider pyelocentesis. In cases of pyelonephritis, urinalysis would be expected to show hematuria, pyuria, renal tubular cells, and cellular casts. Provide supportive care and administer antibiotics based on urine culture and sensitivity results for 3 to 6 weeks.

Renal Neoplasia

Renal tumors are uncommon in ferrets (see Chapter 8).[8,44]

Hydronephrosis

Hydronephrosis and hydroureter in ferrets may develop as a consequence of ureteral obstruction, neoplasia involving the renal pelvis, cystitis, herniation of the bladder, and ligation of the ureter during ovariohysterectomy.[8,15,57] In severe cases, hydronephrosis may lead to renomegaly, and the affected kidney may be palpable as an abdominal mass. On survey radiographs, the hydronephrotic kidney appears as a radiopaque, midabdominal mass with a large fluid density. Normal length of the kidneys, expressed as a ratio to the body length of lumbar vertebra 2 (L2), are between 2.21 to 2.31 vertebrae for the right kidney and 2.15 to 2.25 vertebrae for the left kidney.[19]

If hydronephrosis is suspected, obtain samples for a complete blood count (CBC), biochemical analysis, and urinalysis. Use ultrasonography to confirm the diagnosis. In certain instances, excretory urography or retrograde pyelography may be required to establish the exact location of the obstruction and to distinguish between the different causes (Fig. 4.4). Note that when retrograde pyelography is performed, a certain degree of calicectasis is expected (Fig. 4.5).

Treatment of hydronephrosis depends on the causes and severity of the disease. If diagnosed early, resolution of the obstruction is curative. If diagnosis is delayed, unilateral nephrectomy carries a good prognosis if function of the remaining kidney is normal.

Ureteral Disorders

Ureteral Rupture

Traumatic avulsion of the ureter was reported in a ferret with blunt trauma severe enough to also create a diaphragmatic hernia. No specific urinary tract signs or abnormal clinical pathologic findings were observed. Excretory urography was used to detect ureteral leakage, and treatment included ureteronephrectomy.[85]

Retrocaval Ureter

Retrocaval ureter (also known as circumcaval ureter) was diagnosed in a ferret that presented with clinical signs of AKI.[14] Depending on the degree of ureteral compression, retrocaval ureters may be incidental findings or may result in hydroureteronephrosis.[11] Ureteroneocystostomy (i.e., reimplantation of the ureter into the bladder) should be considered in symptomatic cases or in cases with evidence of hydronephrosis.

Congenital Ureteral Stenosis

A ferret with bilateral ureterovesical junction stenosis developed bilateral hydroureteronephrosis.[82] A subcutaneous ureteral bypass was placed in one of the kidneys and was removed after 3 months because of obstruction and persistent urinary tract infection. At that time, bilateral ureteroneocystostomy was successfully performed.

Congenital Hydroureter

Two ferrets with suspected congenital hydroureter have been described.[15] In both ferrets, hydroureter was an incidental finding. The ferrets were periodically monitored by ultrasound scanning and did not develop hydronephrosis. No treatment was deemed necessary in either ferret.

Urolithiasis

Urolithiasis is characterized by solitary or multiple calculi found anywhere throughout the urinary tract or by the presence of sandy material within the bladder and urethra.

The most common calculus composition reported in ferrets in both the United States and the United Kingdom used to be magnesium ammonium phosphate $6H_2O$, or struvite.[62,70] Dietary factors are believed to play an important role in struvite crystal formation. Urine pH is greatly influenced by diet,

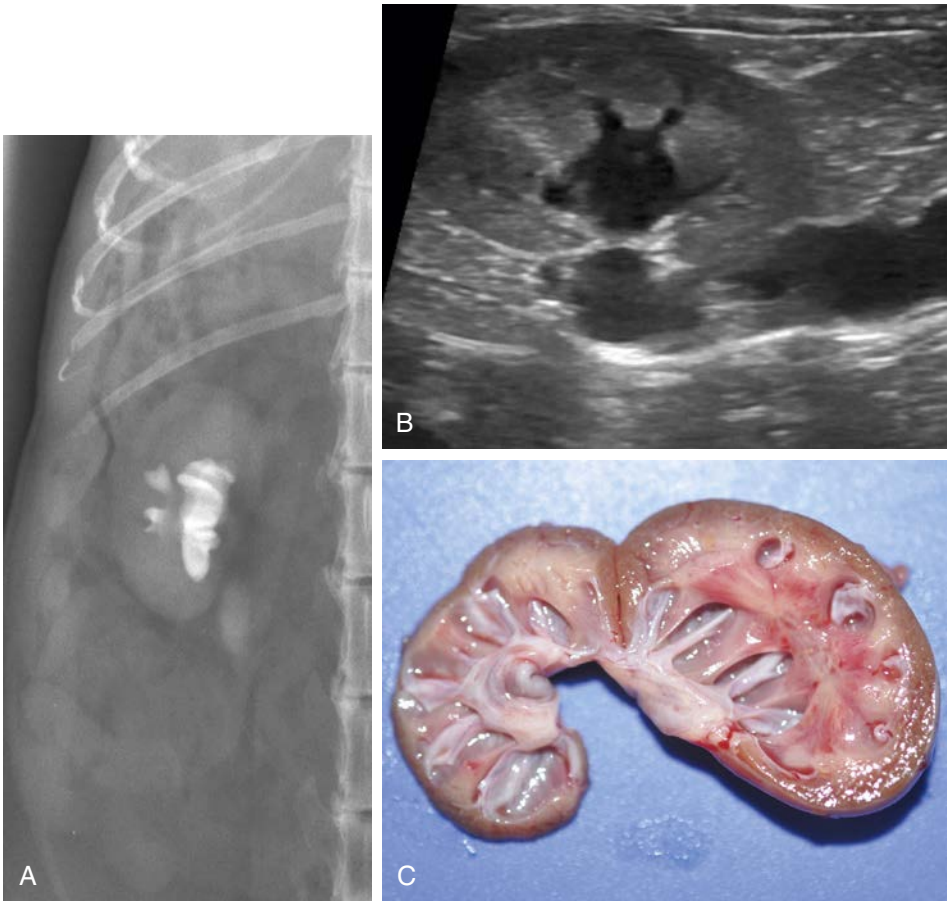

Fig. 4.4 Severe hydronephrosis and hydroureter in a ferret. (A) Excretory urogram shows accumulation of contrast material in the renal pelvis consistent with decreased renal outflow. (B) Sonogram shows distention of the renal pelvis and the proximal ureter. (C) Cross-section of the kidney after surgical removal. (Courtesy Dr. Nicola Di Girolamo.)

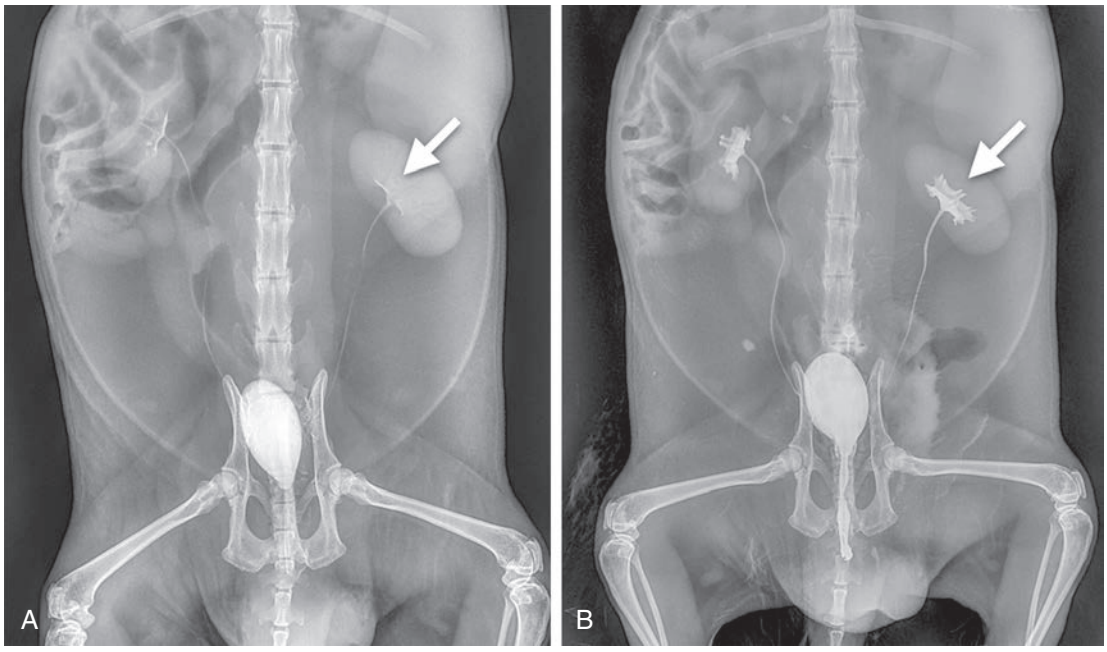

Fig. 4.5 Representative comparison of excretory urogram (A) and retrograde pyelogram (B) in the same renal-healthy ferret. Notice the increased dilation of the calix in the retrograde pyelography image, caused by the pressure required to make the contrast media reach the kidneys. (Courtesy Dr. Nicola Di Girolamo.)

specifically by the source of dietary protein. Metabolism of animal protein tends to produce acidic urine, whereas plant-based protein diets, such as dog food or inexpensive cat foods, produce alkaline urine. Struvite crystals commonly form at a urine pH exceeding 6.6. Significant crystalluria leads to the development of calculi or sandy material in the bladder and urethra. In one report, 6 of 43 ferrets (14%) fed dog food had renal or cystic calculi at necropsy.[59] In ferrets, struvite uroliths appear to be uncommonly associated with urease-producing microbial urinary tract infections.[62]

However, in the last decade, cystine has become the most prevalent ferret calculus component in the United States.[53] Based on data from the Minnesota Urolith Center, which included 1108 ferret uroliths, cystine uroliths shifted from 15% of the total uroliths in 1981–2007 to 89% in 2010–2017.[53,62] In the same time frame, in Europe only 27% of the uroliths submitted to commercial laboratories were cystine.[53] A familial pattern due to inbreeding, similar to what is described in other carnivores, may explain such a dramatic increase in cystine prevalence in North America.[53,62].

Urolithiasis is seen most commonly in adult neutered males.[61] A small percentage of uroliths are voided.[62] However, most struvite uroliths are retrieved in the urinary bladder, whereas most cystine uroliths are retrieved from the urethra.[61,62]

Clinical signs of urolithiasis are stranguria, dysuria, pollakiuria, hematuria, urine dribbling, and frequent licking of the prepuce. If not corrected, urinary obstruction can result in severe metabolic disturbances, coma, and death. Affected jills may be asymptomatic or show intermittent straining for days or weeks. Although urethral obstruction is most common in male ferrets, females can also become obstructed, sometimes straining hard enough to cause rectal or vaginal prolapse and potentially fatal hemorrhage.[7]

Cystic calculi or sand is often palpable in ferrets without obstruction, and a distended bladder is readily palpable in obstructed ferrets. Abdominal radiographs allow evaluation of the entire urinary tract for radiodense uroliths and other abnormalities. Calculi lodged at the os penis can be difficult to detect. Abdominal ultrasound scanning provides additional information regarding the urinary tract, including visualization of radiotransparent uroliths, and can be used to concurrently screen the adrenal glands and prostate. In affected ferrets, submit samples for a CBC, biochemical analysis, urinalysis, and, ideally, urine bacterial culture and sensitivity testing.

If the ferret is not obstructed, provide supportive care, including parenteral fluids, and then schedule cystotomy to remove cystic calculi and flush the bladder. Submit calculi for mineral analysis and send crushed calculi and a sample of the bladder mucosa for bacterial culture and sensitivity testing. However, most calculi in ferrets are sterile.[61] Renal calculi may be managed by medical and dietary therapy unless clinical signs warrant immediate surgical removal.

Begin antibiotics before surgery if you suspect infection. Select a broad-spectrum antibiotic that reaches high levels in the urinary tract until culture and sensitivity results are available. Administer antibiotics for a minimum of 10 to 14 days, but use urinalysis and urine culture results to guide the duration of therapy. Continue antimicrobials several days past resolution of clinical signs. In male ferrets with urethral calculi, retrograde urohydropulsion can be attempted by placing a urinary catheter (see Chapter 2) and then flushing the urolith into the urinary bladder for future removal via cystotomy. If this procedure is unsuccessful, a perineal urethrostomy should be performed. As a part of the long-term management of urolithiasis, convert the ferret to an animal protein–based diet.

The prognosis is good for urethral or cystic calculi with aggressive treatment. As in other species, the prognosis for bilateral renal calculi is guarded.

Urethral Obstruction

Urethral obstruction is an important reason for emergency treatment of male ferrets. In the United States, urethral obstruction is most frequently caused by adrenal-associated prostatic disease or, less commonly, urolithiasis. Neoplasia and iatrogenic trauma are also considered. On physical examination, the urinary bladder is distended and painful. Results of biochemical analysis may include azotemia, hyperkalemia, hyperphosphatemia, and metabolic acidosis.

Urethral catheter placement is described in Chapter 2. Relief of obstruction and forced diuresis are usually sufficient to manage hyperkalemia. Medical treatment is indicated if an arrhythmia is present in addition to poor perfusion or altered mentation. To provide additional relief for acute urethral obstruction, some clinicians use smooth muscle relaxants, such as diazepam or midazolam.

Monitor urine production in catheterized ferrets by using a closed line attached to a 150- to 250-mL intravenous bag. Urinary output should be at least 1 to 2 mL/kg per hour, and with diuresis, urine production may be as high as 140 mL per ferret per day. Maintain the urinary catheter for 1 to 3 days while providing aggressive supportive care: correct metabolic and acid–base disturbances and administer fluids to correct perfusion abnormalities and rehydrate the patient. Monitor the ferret carefully for signs of overhydration.

If attempts at urinary catheterization are unsuccessful, consider cystocentesis to help stabilize the patient before surgery,[6] although there is some risk of urinary bladder rupture and subsequent uroabdomen. Temporary tube cystostomy has been described in cases of prostatic or paraurethral cysts (Fig. 4.6).[60] A 5- or 8-Fr Foley catheter is placed through the abdominal wall into the bladder during laparotomy. The catheter is left in place for 1 to 5 days.[60] Particular care must be taken to avoid self-removal by the ferret.[60]

In case of permanent damage (penile amputation or bladder atony), a long-term cystostomy tube can be placed. Two case reports describe using a silicon low-profile gastrotomy tube as a cystostomy tube.[36,77] Before tube placement, a Foley catheter must be in place for 1 to 2 weeks to create a continuous ostium between the abdominal wall and the bladder. The low-profile tube is inserted in the ostium and secured with a purse string suture (Fig. 4.6). Daily care of the tube is required to maintain a clean environment, and regular urinary culture must be performed to screen for urinary tract infection. One ferret reportedly tolerated the tube for more than 1 year.[36] Complications include removal and leakage of the device, mechanical cystitis, urinary tract infection, and septicemia. A urethrostomy may be needed in male ferrets with preputial neoplasia or recurrent urethral obstruction.[24,80]

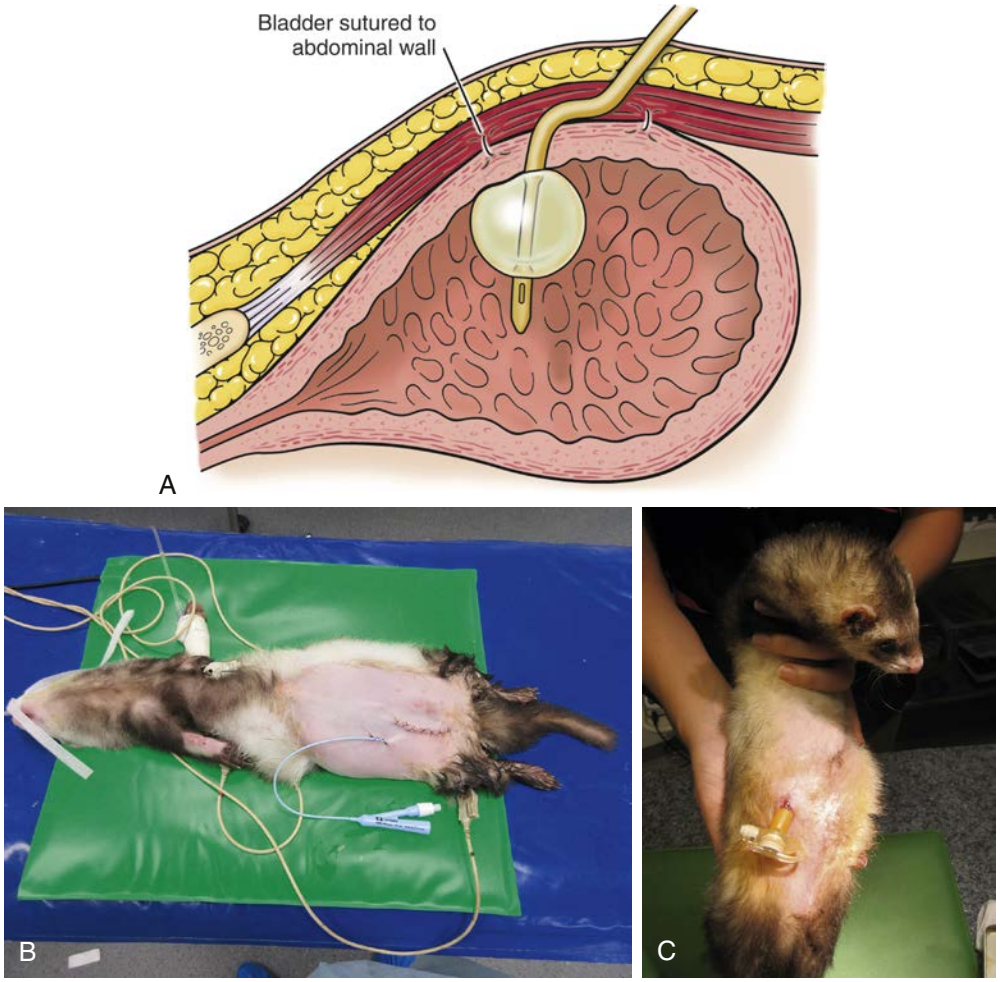

Fig. 4.6 Percutaneous cystostomy in ferrets. (A) A Foley catheter is placed within the bladder, and the bladder wall is sutured to the abdominal wall. (B) Ferret with a temporary cystostomy tube (Foley catheter) in place. (C) Ferret with a low-profile cystostomy tube in place. (Courtesy Dr. Marla Lichtenberger [A] and Dr. Minh Huynh [B, C].)

Cystitis

Spontaneous bacterial cystitis is rare in ferrets. If cystitis is identified, screen the ferret for underlying disease, such as adrenal-associated prostatomegaly or urolithiasis. Long-term corticosteroid use for concurrent disease (e.g., insulinoma, lymphoma) may predispose to urinary tract infection. A possible adverse effect of cyclophosphamide chemotherapy is hemorrhagic cystitis induced by the metabolite of the drug.

Infection may initially be asymptomatic; however, by the time of treatment, most ferrets demonstrate pollakiuria, dysuria, hematuria, and urine staining of the perineum. Ferrets with severe cystitis may have anorexia, lethargy, weakness, or even collapse. The abdomen may be painful, and the bladder wall may feel thickened.

Obtain a urine sample, ideally via cystocentesis, for urinalysis and bacterial culture and sensitivity testing. Urinalysis may reveal hematuria, pyuria, bacteriuria, and tubular casts. The CBC and biochemical results are often unremarkable, although an inflammatory leukogram may be observed with an ascending bacterial infection. Because primary cystitis is rare, consider survey abdominal radiography and abdominal ultrasound scanning to help identify the underlying cause of infection.

Administer a broad-spectrum antibiotic until culture results are available, and then adjust antibiotic therapy accordingly. Continue treatment for a minimum of 10 days and for at least 4 weeks in complicated cases. Provide fluids and supportive care as needed and ensure that the ferret is fed a high-quality diet with a meat-based protein source.

Bladder Neoplasia

There are rare reports of transitional cell carcinoma of the urinary bladder in ferrets (see Chapter 8).[87]

Urinary Incontinence

True urinary incontinence is rare in ferrets. More commonly, ferrets are treated for dribbling due to overfill of the urinary bladder as a result of partial urethral obstruction secondary to urolithiasis or prostatomegaly. True incontinence may be associated with bladder neoplasia, severe cystitis, or Aleutian disease virus. Additionally, although rabies virus is extremely rare in domestic ferrets, bladder atony and incontinence were reported in 65% of experimentally infected ferrets.[58] Bladder atony can also be seen with long-term paresis in ferrets with lumbar trauma or neoplasia.[36,37]

Paraurethral Cysts or Paraurethral Disease

Paraurethral cysts rarely affect both female and male adult ferrets.[43] Cysts may be single or multiple and of various sizes, with variable communication between the cysts and the bladder, urethra, or both. Paraurethral cysts appear to be most common on the dorsal aspect of the urinary bladder trigone and the proximal urethra. Clinical signs may include dysuria, hematuria, and alopecia, as well as vulvar swelling in females. On physical examination, cysts may be palpable as fluctuant masses caudodorsal to the bladder. In a study of six ferrets (four males and two females) with paraurethral cysts, adrenal hyperplasia or neoplasia was detected in five ferrets, and the adrenal gland was not evaluated in the sixth animal.[43] Initial therapy involves relief of the urethral obstruction, hydration, and treatment of secondary bacterial infection. Definitive therapy is surgical.

DISORDERS OF THE REPRODUCTIVE SYSTEM

Primary reproductive tract disease is uncommon in ferrets in the United States, where animals historically have been routinely spayed and neutered at 6 weeks of age. Outside the United States, most ferrets are either not gonadectomized or are gonadectomized at 5 to 6 months of age. A recent randomized trial has confirmed the association between surgical gonadectomy and adrenocortical disease.[73] Therefore other preventive measures, such as chemical sterilization, may be considered in favor of surgical neutering.[30,72,81]

Refer to Chapter 1 for normal reproductive parameters in ferrets. The ferret's breeding season occurs from September to December in the Southern Hemisphere and from March to August in the Northern Hemisphere.[1] Ferrets are "long-day" breeders, and providing more than 12 hours of light promotes reproductive activity.[1]

The Male Ferret

Plasma testosterone levels increase at the end of January in the Northern Hemisphere, and a peak plateau is maintained from the end of February until late July. Increases in testicular size begin in late January and peak in April. The stages and cycle duration of ferret spermatogenesis are similar to those reported in other carnivores.[56]

Cryptorchidism

Ferret testes usually descend into the scrotum during fetal development, but complete descent may take several months after birth. Cryptorchidism is uncommon and was reported in less than 1% of 1597 male ferrets.[10] Cryptorchid testes may become neoplastic and should be surgically removed or closely monitored.

Tumors of the Male Reproductive Tract

Testicular tumors are not uncommon in middle-aged to older ferrets and are considered more common in cryptorchid testes.[40,87]

Prostatic Cysts

Prostatic disease is the leading cause of urinary tract disease and urethral obstruction in middle-aged and older male castrated ferrets in the United States, where it is associated with adrenal disease.[12] Adrenocortical disease in the ferret has been correlated with gonadectomy,[73,76] which is routinely performed at 6 weeks of age in the United States. Outside of the United States, most ferrets are not gonadectomized but are instead chemically neutered with long-term 4.7-mg deslorelin acetate implants (Suprelorin, Virbac, https://virbac.com). In these cases, adrenal disease and prostatic cysts are relatively uncommon.

Adrenocortical disease in the male ferret is associated with the development of sterile prostatic cysts. Although the exact pathogenesis is unclear, high levels of circulating sex steroid hormones appear to stimulate proliferation of prostatic tissue (see Chapter 7).[12] Prostatic cysts can become very large and compress the urethra, leading to urethral obstruction.[12]

Although prostatic disease may be seen at any age, it is most common in neutered ferrets at least 3 years of age. Signs of lower urinary tract disease caused by prostatomegaly are pollakiuria, hematuria, stranguria, dysuria, or anuria. Ferrets may lick excessively, creating an inflamed prepuce. Because of straining, some ferrets may be presented with diarrhea or, in rare instances, rectal prolapse. Signs of adrenal disease, such as alopecia, pruritus, or behavioral changes, may be present.[2,60] Ferrets with urethral obstruction may have a history of anorexia, lethargy, weakness, or collapse.

The enlarged prostate may be palpable as a variably-sized fluctuant mass dorsal to and near the base of the urinary bladder (Fig. 4.7), although not all ferrets with prostatic disease demonstrate prostatomegaly. Perform a full medical workup in affected ferrets. On radiographs, prostatomegaly may appear as a mass lesion caudodorsal to the urinary bladder, displacing the bladder cranioventrally. Use ultrasound scanning to evaluate the adrenal glands, kidneys, urinary bladder, and prostate. Computed tomography allows identification of contact of the prostate with the surrounding structures. Prostatic cysts

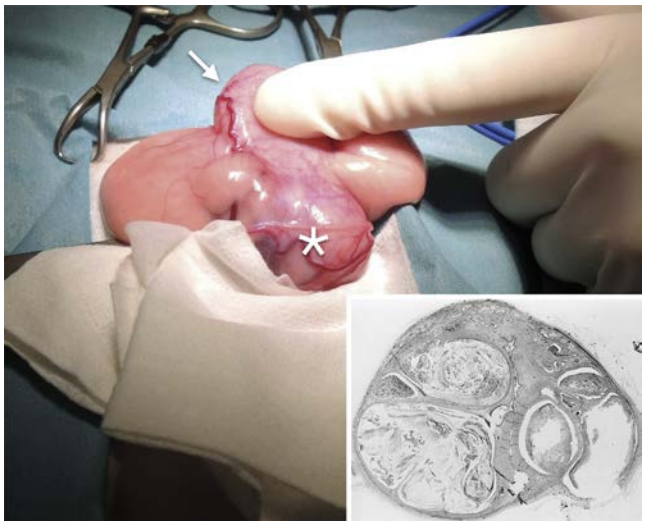

Fig. 4.7 Gross aspect of paraprostatic cyst (asterisk) in a ferret. The urinary bladder is manually retracted (arrow). (Inset) The prostate is expanded by cysts of various sizes filled with keratin and proteinaceous debris. (Courtesy Dr. Minh Huynh; [Inset] From Coleman GD, Chavez MA, Williams BH. Cystic prostatic disease associated with adrenocortical lesions in the ferret. Vet Pathol 1998;35:547-549.)

contain hypoechoic to anechoic fluid. Collect cyst fluid via ultrasound-guided fine-needle aspiration for cytologic examination and aerobic and anaerobic culture. Contrast cystography may show an irregular blockage around the bladder neck (Fig. 4.8). Submit blood samples for a ferret adrenal panel available through the University of Tennessee College of Veterinary Medicine Endocrinology Lab (www.vet.utk.edu/diagnostic/endocrinology/index.php) to confirm the presence of adrenocortical disease, particularly if ultrasound results are equivocal.

Medical therapy is generally attempted as first-line treatment. This involves managing urethral obstruction, if present, and adrenocortical disease (see Chapter 7). Medical therapy includes placing a 4.7-mg deslorelin acetate implant (Suprelorin, Virbac,).[42,84] Another alternative is to administer the depot formulation of the synthetic gonadotropin-releasing hormone (GnRH) agonist, leuprolide acetate (100 to 250 µg/kg/month intramuscularly [IM]).[83] Administration of high-dose leuprolide acetate can cause prostatic tissue to shrink within 12 to 48 hours, and the ferret may even begin to urinate around the urethral catheter. Oral melatonin (0.5 by mouth every 24 hours) may also be administered.[67] Surgical therapy involves adrenalectomy, and large prostatic cysts may require surgical debulking. Cystic prostatic hypertrophy usually begins to resolve within 2 to 3 days after surgery.[2]

In addition to standard treatment for adrenal disease, the use of antiandrogen agents, such as flutamide, bicalutamide, and finasteride, has been suggested. Effects may be seen within days in some ferrets; however, use caution in patients with liver disease. Because research findings on the use of these drugs are lacking, their effectiveness and safety are still unclear.

If left untreated, prostatic disease can lead to urethral blockage, acute renal failure, and death. Fortunately, the prognosis for prostatic cysts is generally good in ferrets that undergo aggressive therapy for underlying adrenocortical disease. Ensure that prostatic cysts resolve completely by monitoring their sonographic appearance. Long-term persistence of cysts may promote the development of bacterial prostatitis and abscessation.

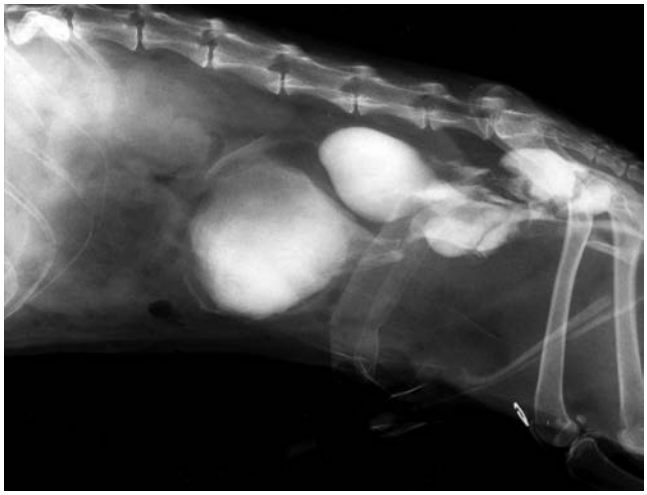

Fig. 4.8 Contrast cystography illustrating irregular mass lesions near the bladder neck caused by prostatitis. Note the caudal extension of the inflamed prostate gland.

Also, monitor patient progress by following sex steroid hormone levels and size of the adrenal glands.

Prostatitis and Prostatic Abscesses

The pathogenesis of bacterial prostatitis and prostatic abscessation in ferrets is poorly understood. Urine stasis secondary to adrenal-associated prostatomegaly may promote bacteriuria and regional migration of bacteria into prostatic tissue. Bacteria may also enter the prostate hematogenously. Prostatitis has been described in a ferret with a Sertoli cell tumor associated with a retained testicle, and there are rare reports of prostatic abscesses associated with transitional cell tumors of the bladder.[87] Prostatitis has been associated with heavy growth of *E. coli*, as well as *Staphylococcus*, nonhemolytic *Streptococcus*, *Proteus*, and *Pseudomonas* species.

A thick, white to yellow, opaque penile discharge may be seen with prostatitis, and a purulent discharge may be associated with urination. Round structures may be palpable near the urinary bladder, and the abdomen may be swollen, tense, and painful.[65]

An inflammatory leukogram may be observed, although results of biochemical analysis are frequently unremarkable.[65] Urinalysis and urine culture results are variable. Abdominal ultrasound of the prostate shows hypoechoic to anechoic fluid-filled cysts with hyperechoic sediment. Perform ultrasound-guided fine-needle aspiration of prostatic cysts with the ferret sedated. Aspirated fluid may be turbid or flocculent and appear yellow to green,[65] and results of cytologic examination will reveal suppurative exudate. Submit the sample for aerobic and anaerobic bacterial culture and sensitivity.

Select a lipid-soluble antibiotic known to penetrate the prostatic capsule, such as a potentiated sulfa or fluoroquinolone. Use culture and sensitivity results to adjust therapy, and administer antibiotics for at least 4 to 6 weeks.[2,3,6] Although antimicrobials are an important ancillary treatment, antibiotics generally fail to achieve effective tissue levels throughout the prostate. Therefore, surgical management of prostatitis or prostatic abscess is recommended.

If prostatitis is secondary to adrenal gland disease, treatment is the same as for prostatic cysts. In cases of primary prostatitis, ultrasound-guided chemoablation or surgical treatment, including marsupialization and omentalization, can be considered (see Chapter 11).[2,3,6] In marsupialization, the infected prostate is flushed and marsupialized to the abdominal wall. Marsupialization allows for repeated lavage. Because drainage is external to the abdominal cavity, the risk of peritonitis may be reduced.[2] Omentalization of prostatic abscess can be performed in ferrets by using a technique similar to that described in dogs.[2,3,6,65] The prostatic abscess is opened and flushed, and as much of the cranial capsule is excised as possible. The caudal aspect of the abscess may extend deep into the pelvic canal.[65] The remaining abscess cavity is irrigated, then a portion of greater omentum is inserted into the abscess and sutured into place. Omentum is believed to promote tissue adhesion, angiogenesis, hemostasis, peritoneal lymphatic drainage, fibrinolysis, and immune system function.[35]

Regardless of the surgical technique selected, potential complications are recurrent cystitis and peritonitis.[3] Prostatic cysts

may extend into bladder or urethral tissue, increasing the risk of urinary incontinence, uroabdomen, or urethrocutaneous fistula formation.[3]

Culture prostatic fluid and urine 2 to 4 weeks after completing antibiotic therapy, and use serial abdominal ultrasound scanning to monitor the prostatic abscess. Follow underlying adrenal disease by measuring serial sex steroid hormone levels.

Penile Lesions

Penile lesions are occasionally seen in male ferrets kept on hay bedding when grass awns catch in the prepuce. Breeding males may also incur injury as they move along the ground pressing their groin down to mark their territory. Anesthetize ferrets to remove foreign bodies in the prepuce, then apply a topical antibiotic-corticosteroid ointment.

Preputial gland neoplasia is relatively common in ferrets. Lesions are frequently malignant and require aggressive treatment. Surgical resection, including penile amputation, with margins of at least 1 cm is indicated.[80]

The Female Ferret

Proestrus usually occurs in January or February and is signaled by increasing vulvar tumescence.[45] The advent of estrus is variable and can be seen from late January to early August. The jill may eat and sleep less, and she may become irritable. Superficial epithelial cells make up 90% or more of epithelial cells in vaginal cytology, and, after several days, cells are fully keratinized. Neutrophils are common during all stages of the estrous cycle. Until mated, jills may exhibit constant estrus for up to 5 months, and hyperestrogenism may occur.[45]

Ferrets are induced ovulators, and coital stimulation is required to trigger ovulation.[1,49] Once ovulation is induced, either pregnancy or pseudopregnancy occurs. Several days after induced ovulation, numbers of superficial vaginal cells decline to anestrus levels and the vulva decreases in size and turgidity.[45] Transfer of embryos has been described in mustelids and could be potentially feasible in ferrets.[46] See Chapter 1 for additional information on reproductive parameters in ferrets.

Hyperestrogenism

Hyperestrogenism is extremely common in female ferrets that are not bred or artificially stimulated to ovulate.[45] Estrus lasting more than 1 month is associated with hyperestrogenism, which leads to bone marrow depression and hypoplasia of all cell lines.[33] Other potential causes of estrogen toxicosis are cystic ovaries, an estrogen-secreting ovarian remnant, and ovarian neoplasia.[50,64] Untreated adrenocortical disease may also lead to hyperestrogenism.

Clinical signs may include bilaterally symmetric dorsal alopecia, vulvar swelling, vulvar discharge, pallor, and a systolic murmur. Extended hyperestrogenism may cause melena and petechial or ecchymotic hemorrhages. Metritis, pyometra, or vaginitis may also be involved.

Results of a CBC generally reveal nonregenerative anemia with a hematocrit less than 25%, nucleated red blood cells, neutropenia, and thrombocytopenia.[33,75] Hemorrhage may occur when platelet counts fall below 20,000 cells/μL.[75] Confirm nonregenerative anemia with a reticulocyte count. In intact female ferrets, recent estrus and consistent clinical signs are usually sufficient for a preliminary diagnosis. In spayed ferrets, abdominal ultrasound scanning may help to discriminate between an ovarian remnant and adrenal disease.

Treatment of hyperestrogenism includes stabilizing the ferret and reducing estrogen levels. Ferrets do not have blood groups; therefore, if necessary, multiple transfusions from multiple donor ferrets are possible.[48] Less commonly, bone marrow transfusions have also been described. Additional supportive care measures may include anabolic steroids, corticosteroids, and iron dextran.

In the United States, the widespread practice of routinely spaying female ferrets not intended for breeding by 6 months of age has drastically reduced the prevalence of hyperestrogenism. However, early gonadectomy in ferrets is currently discouraged, given its proven association with later development of adrenal disease.[73,76] As an alternative to surgical sterilization, hyperestrogenism is prevented by injecting a long-term GnRH-agonist (4.7 mg deslorelin acetate [Suprelorin, Virbac]) implant, every 1 or 2 years.[81] If the ferret is presented after the onset of estrus, a long-term GnRH-agonist, a short-acting GnRH agonist (e.g., buserelin [0.25 mg IM per ferret, repeated in 14 days] or leuprolide acetate [100 to 250 ug/kg IM]), human chorionic gonadotropin (hCG, 100 IU IM per ferret), or a second-generation progestogen (proligestone, 40-50 mg SC per ferret) can be used to induce ovulation.[26] Give hCG at least 10 days after the onset of estrus and repeat in 7 days if vulvar swelling has not resolved.[52] Monitor the reproductive tract with serial ultrasound scans to identify changes in the uterine structure or content (e.g., development of pyometra).

Tumors of the Female Reproductive Tract and Mammary Glands

Both neoplasia of the ovaries and uterus occur in ferrets.[44] Mammary gland tumors are a rare differential diagnosis for severely swollen, firm glands in domestic ferrets (see Chapter 8).[26,87]

Pyometra and Mucometra

Pyometra is often documented in intact females, particularly jills with estrogen toxicosis or in older, pseudopregnant jills. Stump pyometra is occasionally seen in spayed females because of elevated sex steroid hormone levels secondary to adrenocortical disease.[23] Bacteria that have been cultured from pyometras include *E. coli*, as well as *Staphylococcus*, *Streptococcus*, and *Corynebacterium* species.[26]

Clinical signs of pyometra are similar to those in dogs and cats. In a case seen by one author (N.D.), pyometra developed approximately 1 week after administration of 4.7-mg deslorelin acetate (Suprelorin, Virbac) to a ferret in estrus. This was presumed to be a consequence of a reversed estrogen/progesterone ratio after a long period of estrogenic stimulation. Therefore, when administering a GnRH agonist to suppress estrus, perform serial abdominal ultrasound scans to monitor the status of the uterus.

Determine whether the ferret with pyometra is suffering from estrogen-induced bone marrow suppression.[75] Definitive treatment of pyometra or mucometra involves ovariohysterectomy or surgical excision of the infected stump and adrenalectomy. Provide systemic antibiotics and supportive care such as fluids, analgesia, and nonsteroidal antiinflammatory drugs. Medical management of pyometra has also been described, but it should be reserved for cases where surgery is not an option. In these cases, administer prostaglandin F2-α (dinoprost tromethamine) (0.1 to 0.5 mg IM; Lutalyse, Zooetis, Parsippany, NJ), followed in 1 hour by oxytocin (0.2–3 IU SC, IM) to stimulate myometrial contraction and expulsion of exudate.[55]

Hydrometra

Hydrometra is the accumulation of aseptic fluid within the uterus in the presence of persistent corpora lutea and is typically associated with ovarian disease (Fig. 4.9).[39,64] Segmental atresia of the uterus associated with hydrometra has also been reported in a 2-year-old ferret.[5] Definitive treatment relies on ovariohysterectomy.

Vaginitis/Vulvar Swelling

Primary vaginitis is uncommon in ferrets. More frequently, vaginitis is associated with chronic vulvar swelling subsequent to hyperestrogenism caused by persistent estrus, an ovarian remnant, adrenal disease, or estrogen-secreting neoplasia. Less commonly, vulvar swelling develops with cystitis, crystalluria, or even aggressive hob mating behavior. Poor husbandry and inadequate sanitation may also promote vaginitis in breeding jills kept on particulate bedding when hay, straw, or shavings adhere to the swollen vulva during estrus. Vaginitis is associated with overgrowth of bacteria such as *E. coli, Staphylococcus, Streptococcus, Proteus,* or *Klebsiella* species.[26] Vaginitis may be differentiated from the swelling associated with estrus by history, results of vaginal cytology, presence of mucopurulent vaginal discharge, and ultrasound of the reproductive tract. Administer systemic antibiotics and treat the underlying problem, including reducing estrogen levels as necessary.

PERIPARTURIENT DISEASE

Normal Parturition

Parturition normally lasts approximately 2 to 3 hours. Approximately five kits are born per hour, although some jills take longer. Progress should be steady, and no signs of distress should be seen. Domestic ferrets average 8 or 9 kits (range 7–15) per litter.[1,45] Newborn kits are altricial and weigh 6 to 12 g at birth.[7]

Females will return to estrus within 2 weeks after weaning if exposed to the appropriate photoperiod. If kits are removed at birth, the jill will return to estrus 8 weeks after mating, as will pseudopregnant females and females with resorbed fetuses. If a jill gives birth to a small number of kits (five or fewer), she may return to estrus while nursing.[25]

Management of Breeding Ferrets

Successful breeding requires constant supervision during gestation, parturition, and lactation. Breeders should monitor jills closely for any change in appetite or body condition, particularly late in gestation.[4,7]

Place the pregnant jill's cage in a quiet area well before parturition. Minimizing stress is particularly important in young primiparous jills. Avoid environmental stressors such as excessive heat. Room temperature should not exceed 70°F (21°C). Place a heat lamp over only part of the nesting box so that the jill and kits can select warmth as necessary. The risk of poor mothering also increases with crowding or unusual noise and nearby activity. Jills become excited and may bury the kits in bedding or place them in a pile in a corner or in food or water containers. Some jills will cannibalize the first few or all of their kits as they are born. Handling kits does not appear to cause rejection of the litter.[7]

The jill must also be able to easily enter and exit the nesting box without traumatizing her mammary glands. Shredded aspen shavings, recycled paper bedding, or small cloth towels are practical choices for whelping nest substrate. Do not use large towels because kits can get lost in them.[7]

Feed jills proper nutrition containing 36% to 40% animal-based protein and 18% to 20% fat.[26] Make food and fresh water available at all times.

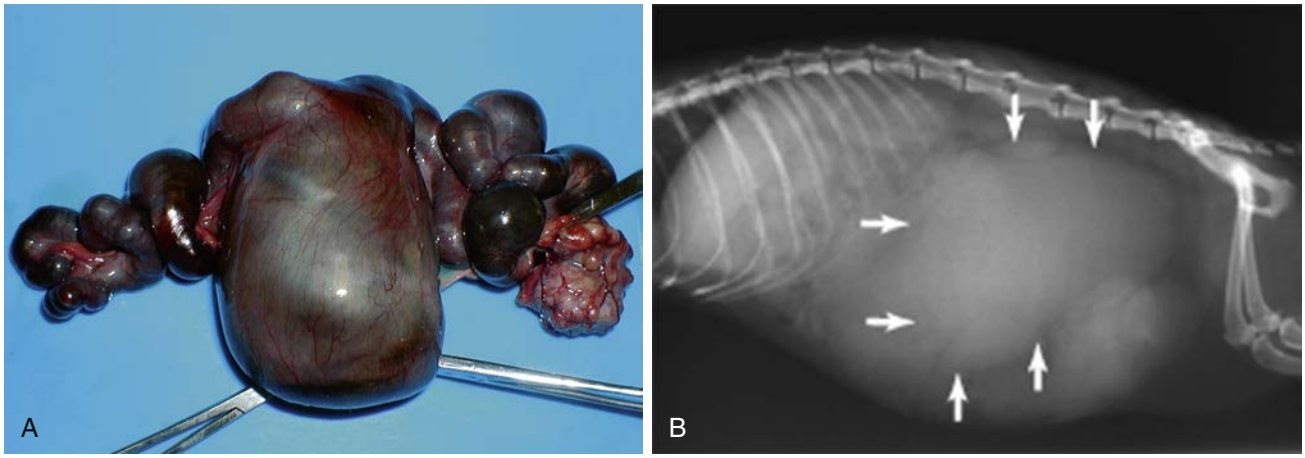

Fig. 4.9 Hydrometra in a ferret. (A) Gross image of hydrometra in association with an ovarian tumor (far right). (B) Lateral radiograph shows a soft tissue opacity (arrows), creating a mass effect in the ventrocaudal aspect of the abdomen. (Courtesy Dr. Vladimir Jekl.)

Diseases of the Jill

Pregnancy Toxemia

Pregnancy toxemia is a life-threatening disease seen sporadically in jills, especially young primiparous females, during late gestation.[4] Negative energy balance promotes abnormal energy metabolism and subsequent hyperlipidemia, hypoglycemia, ketosis, and hepatic lipidosis during the 10 days before parturition. This energy deficiency is caused by either inadequate dietary intake or excess demand for nutrients due to an exceptionally large litter (e.g., 15 or even 20 kits).[4,7]

Common clinical signs include acute onset of severe lethargy, anorexia, dehydration, weight loss, and excess shedding.[4,13,26] There may also be diarrhea with or without melena. In some cases, sudden death occurs.[4,7,26]

Hematologic and biochemical abnormalities may include anemia, hypoproteinemia, azotemia, hypocalcemia, hyperbilirubinemia, increased liver enzyme activities, and hypoglycemia.[4,26] Urinalysis may reveal ketonuria. In a survey of 10 jills with pregnancy toxemia, hepatic lipidosis was observed grossly in the 7 jills that died.[4]

Provide aggressive treatment in the form of cesarean section and intensive supportive care. Correct fluid and electrolyte imbalances and provide nutritional support. Gastroprotectants are commonly indicated because of the high incidence of concurrent gastrointestinal ulcers. After surgery, surviving jills frequently produce no milk for at least several days, and cross-fostering of kits is often required.[7]

Because of the guarded prognosis, prevention through client education is much more effective than treatment. Advise breeders to provide consistent proper nutrition, avoid stressors, and be vigilant for any changes in the jill's appetite or body condition.[4] Make palatable food available at all times and provide several small food dishes so that accidental spillage or contamination does not restrict the jill's intake. During the last week of gestation, even one overnight fast can induce toxemia in a jill with a large litter. Provide plenty of fresh water because jills will also stop eating without adequate water.

Dystocia

Dystocia is defined as labor exceeding 12 to 24 hours or whenever there are signs of difficulty. Potential causes of dystocia are pregnancy in an older jill or an elevated environmental temperature (above 70°F [21°C]). Kits of very large size (more likely with small litter size), posterior or sideways presentation, and deformed or anasarcous fetuses may also increase the risk of dystocia.[7] In one case of dystocia, a "single ferret kitten" syndrome was suspected,[29] where a young jill with only one kit may not exhibit expulsive efforts because of lack of cortisol stimulation from the fetus. Depending on the underlying cause of dystocia, jills may be managed medically with oxytocin (5–10 IU IM) or surgically via cesarean section. Follow current standards for management of dystocia in other domestic carnivores.

Pseudopregnancy

False pregnancy is caused by failure of implantation, which is associated with reduced light intensity 1 month before the start of breeding, or failure to conceive.[26] For instance, jills may be bred with infertile hobs, particularly males less than 6 months of age. Pseudopregnancy has also been associated with termination of estrus through hCG use or mating with vasectomized hobs. In pseudopregnancy, the physical and behavioral changes normally associated with pregnancy may be seen, such as weight gain, mammary gland enlargement, and nesting behavior. Jills may also mother inanimate objects. One important difference is that pseudopregnant jills develop a full hair coat approximately 1.5 weeks before "whelping," whereas pregnant jills lose their coat and develop hairless rings around their teats. After "whelping," pseudopregnant jills return to estrus if it is early in the breeding season, or they become quiescent if it is late in the breeding season.[7] Minimize the risk of pseudopregnancy by ensuring that jills are exposed to maximum light intensity during the spring, and artificially extend light hours in late summer.

Agalactia

Agalactia is defined as failure of the jill to lactate enough milk for a normal litter of eight or nine kits. Agalactia may be seen when the jill is stressed because of environmental factors such as overcrowding, noise, visits from strangers, or overheating (temperature exceeding 70°F [21°C]). Agalactia may be inherited, and some ferret breeds (e.g., Angoras) are known to have little to no production of milk. Agalactia is also more common in litters with fewer than five kits and in jills on a poor diet or suffering from systemic disease or chronic mastitis.[7] Agalactia leads to thin kits that cry and move around restlessly. Determine the underlying cause while offering the best-quality diet available to lactating jills.[7]

Mastitis

Mastitis is occasionally seen in pet ferrets and frequently in laboratory ferrets.[26] Acute mastitis develops soon after whelping or after the third week of nursing when milk production peaks and kits become more aggressive feeders. Because kits demand greater quantities of milk, this may stress the jill, or the kits' teeth can damage the nipples. Potential etiologic agents may include *Staphylococcus* species and coliforms such as hemolytic *E. coli*.[7,26]

A firm, painful swelling in one or more glands and red or purple discoloration of the overlying skin may be evident. Milk may be discolored and clotted. If not recognized and treated early, infection will spread rapidly to nearby glands.[26] In severe cases, abscesses may form. The affected jill may present with signs of systemic illness such as depression, fever, anorexia, and dehydration.[26] Chronic mastitis may develop as a result of acute mastitis.

Begin systemic antibiotics, such as clavulanic acid–amoxicillin, for both acute and chronic mastitis.[7] For acute mastitis, culture a milk sample before starting antibiotics, and apply warm compresses to affected glands. More aggressive treatment is indicated for gangrenous mastitis. Perform wide surgical resection of the involved gland and adjacent tissue in combination with analgesia, fluid therapy, nutritional support, and systemic antibiotics.[7]

The kits will require nutritional support. One option is to remove and hand-feed kits, although neonates are very difficult

to hand-raise. If kits must be left with the dam, provide supplemental feedings at least three or four times daily. Kits may also spread bacteria to unaffected glands.[7] Kits may also be fostered, but there is significant risk of infecting the foster dam. Some clinicians also routinely treat the kits and foster mother with oral antibiotics.[7]

Postparturient Hypocalcemia

Postparturient hypocalcemia, or "milk fever," was reported in primiparous jills that exhibited posterior paresis, hyperesthesia, and seizure activity 3 to 4 weeks postpartum. Jills responded to treatment with parenteral calcium borogluconate injections.[26] Prevent hypocalcemia by providing a balanced diet and calcium supplementation if needed.

Metritis

Metritis develops in the immediate postpartum period and occasionally after abortion or breeding. Metritis may also be associated with retained fetuses or placenta. On physical examination, the uterus is distended, and a red vaginal discharge may be seen. Definitive treatment is ovariohysterectomy. Medical management of metritis includes analgesics, systemic antibiotics, and prostaglandin F_2-α (Lutalyse, 0.5 mg IM) to evacuate the uterus. Select an antimicrobial that reaches high urinary levels to reduce the risk of ascending cystitis and secondary urolithiasis.[7]

Diseases of the Kit

The Normal Kit

Ferret kits have little ability to maintain a normal body temperature for the first 2 weeks of life. A healthy litter normally lies quietly close to the jill, nursing and sleeping except when the jill leaves the nest. When kits reach 3 weeks of age, they begin to explore and nibble on soft food, even though their eyes are still closed. Eyes usually open by day 30 to 35 and as early as day 25. Kits generally weigh 8 to 10 g at birth, 30 g at 1 week, 60 to 70 g at 2 weeks, and 100 g at 3 weeks. Kits are weaned at 6 to 8 weeks.[7]

Caring for Ill Kits

Provide supplemental heat, offering kits a temperature gradient of 85°F to 104°F (30°C–40°C).[47] Hypothermic kits do not nurse, so it is prudent to also administer a few drops of 50% dextrose solution by mouth or to rub sugar syrup on the gums.[7] Then administer warmed fluids (50–100 mL/kg) subcutaneously. Feed kits only once they are normothermic and hydrated.

Neonatal ferrets have voracious appetites and are difficult to hand-rear. Kits require ferret milk for the first 7 to 10 days of life.[7,47] The composition of ferret milk varies over the course of lactation (Table 4.1).[74] Some success has been described feeding neonates with pipettes every 1 to 1.5 hours. By day 10 to 21, kits may be offered puppy or kitten milk replacer 4 to 6 times daily.[25] Some authors recommend enriching milk replacer with cream until the fat content is 20%, and additional hand-feeding recipes are available.[7,47] At week 4 to 5, offer a slurry of milk replacer and kibble mixed with solid food.[7]

Because hand-rearing is so challenging, consider supplemental hand-feedings when the jill's milk production is reduced because of illness. The stimulus of nursing may promote lactation as the jill improves. Cross-fostering is an alternative. In fact, it is best to breed jills in pairs so one may serve as a foster mother if problems arise. Most jills accept kits of any size or age at any stage of lactation. Merely remove kits from both litters for a short time, mix the two litters together, and then replace all kits with the foster mother.[7]

TABLE 4.1 Composition of Ferret Milk

Postpartum (Days)	Mean % Fat	Mean % Protein	Mean % Lactose
5	7.8–8.5	7.2–8.8	2.7–4.2
11	9.3–10.5	6.3–7.9	2.8–4.4
19	8.9–10.8	6.0–8.3	3.8–4.2
25	8.8–9.5	5.0–7.9	3.3–4.2
33	9.2–10.3	8.6–9.8	3.0–4.1
39	9.0–13.0	8.4–10.6	1.5–3.2

Data from Schoknecht PA, Cranford JA, Akers RM. Variability in milk composition of the domestic ferret *(Mustela putorius). Comp Biochem Physiol A Comp Physiol* 1985;81:589-591.

Entangled Umbilical Cords

Kits in large litters are occasionally born so rapidly the dam is unable to chew the placenta off each individual, creating a mass of kits bound together by their umbilical cords. The entanglement may be exacerbated if kits are born on coarse, sharp-edged shavings. The mass of entangled kits cannot nurse, so they quickly become hypoglycemic. In addition, the jill cannot curl around them and they also become hypothermic. If this occurs, carefully dissect placentas from each kit's umbilicus with blunt scissors as far as possible from the kit's abdomen.[25] If the placenta has become dry, soften tissue with water. Minimize the risk of entangled cords by closely supervising whelping. If necessary, pick up kits as they are born and separate the placenta.[7,25,51]

Diarrhea

Diarrhea in kits may be caused by ferret rotavirus alone, concurrent rotaviral and bacterial infections (e.g., *Campylobacter jejuni, E. coli, Proteus* species, *S. aureus,* and *Enterobacter cloacae*), or bacterial infection alone. Ferret rotavirus is carried by adults and may cause diarrhea in stressed kits or even unstressed kits if they have no passive immunity.[7,79] The jill typically grooms away all evidence of diarrhea, but the kits will appear wet and dehydrated. Disease may be mild and self-limiting in older kits but is potentially life-threatening during the first week of life. The prognosis is good if kits receive aggressive supportive care. Provide fluids and oral broad-spectrum antibiotics for 5 to 7 days. Monitor the jill closely because anorexia in the kits may promote mastitis, agalactia, or both.[7,25]

Neonatal Conjunctivitis

In neonatal conjunctivitis, or ophthalmia neonatorum, purulent discharge collects in the conjunctival sac behind the unopened eyelids of the kit. A variety of pathogens have been cultured. Unilateral or bilateral conjunctivitis is typically seen

in kits between a few days to 3 weeks of age. Kits typically stop nursing because of the pain associated with pressing their eyes against the dam. Open the eyelids by cutting along the natural suture line with a small scalpel blade or 25-gauge needle bevel. Flush debris and apply a broad-spectrum ophthalmic ointment. Littermates are often affected; therefore carefully examine the entire litter regularly. The prognosis is good in 3-week-old kits because the eyelids will stay open. In younger kits, the eyelids may reseal, and infection may recur.[7]

Splay-Legged Kits

Splay-legged kits, or "swimmers," are tetraparetic. Affected kits must lie on their sternum leading to rib compression and death secondary to anoxia by 8 weeks of age. Although the cause is unknown, "splay leg" has been theorized to be either hereditary or husbandry-related when a rapidly growing kit housed on smooth flooring places excessive weight on its immature limbs.

ACKNOWLEDGMENTS

We thank Christal G. Pollock, Elizabeth V. Hillyer, and Judith Bell for authoring previous editions of this chapter. Their outstanding work was the basis of this chapter.

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