Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

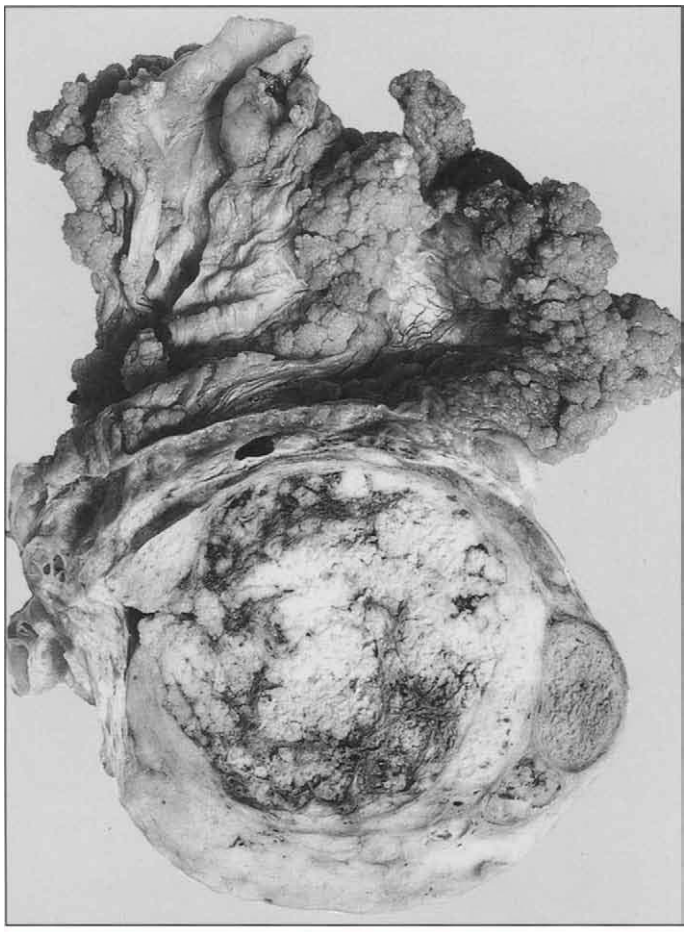

Figure 5.8 Papillary mesothelioma of the tunica vaginalis that covers the scrotal contents of a dog.

bull (Fig. 5.8). Extension of the tumor into the peritoneal cavity has been observed in the dog. Ultrastructural or immunohistologic study may be necessary to differentiate such mesotheliomas from adenocarcinoma. Origin of intrascrotal mesothelioma from the paramesonephric duct remnant has been suggested. There is a report of a lipoma occupying the right scrotal cavity in a ram, causing compression of, but apparently not directly involving, the testis.

Bibliography

Abbitt B, et al. Scrotal hydrocele secondary to ascites in 28 bulls. J Am Vet Med Assoc 1995;207:753–756.

Holyoak GR, et al. Pathological changes associated with equine arteritis virus infection of the reproductive tract in prepubertal and peripubertal colts. J Comp Pathol 1993;109:281–293.

Ladds PW, Crane CK. Scrotal mesothelioma in a bull. Aust Vet J 1976;52:534–535.

Shore MD, et al. Outcome of scrotal hydrocele in 26 bulls. J Am Vet Med Assoc 1995;207:757–760.

Welles EG, et al. *Eperythrozoon* infection in young bulls with scrotal and hindlimb edema, a herd outbreak. Theriogenol 1995;43:557–567.

TESTIS AND EPIDIDYMIS

Spermatozoa develop in the *seminiferous tubules* and pass through the *straight tubules* into the *intratesticular rete* within the mediastinum testis. They then leave the testis via the *rete testis* and enter the *efferent ductules*. The efferent ductules number between 13 and 20, depending on the species. Most join the single duct of the *epididymis*, but it is common in most species for one or more to end blindly. The epididymis is long and tortuous, and divided into many distinct areas. For this discussion, three main areas will be referred to: the *head, body, and tail*. The tail terminates in the *deferent duct*. Disease of one area has effects on other regions, and some diseases affect all areas.

Pathologists often examine individual testes or small biopsies rather than whole groups of animals. Gross and histological assessment of reproductive tissues is a valuable tool if used appropriately. Assessment of a problem often requires collaboration of the cytogeneticist, endocrinologist, theriogenologist and pathologist, who, alone, may not be able to determine the complete pathogenesis. For the pathologist to function optimally, appropriate samples must be collected and processed. For many of the diseases and the tissues, routine fixation with 10% formalin is adequate, but for a detailed assessment of spermatogenesis, or the histological appearance of seminiferous tubules, rapid fixation after death or collection (within minutes in many species) in Bouin's fluid or Zenker's fluid, with paraffin embedding, is necessary. Plastic embedding is the method of choice for a detailed assessment of the spermatogenic cycle. Inadequate fixation or suboptimal processing of testicular tissues will cause artifacts that cannot be distinguished from degeneration.

Normal spermatogenesis requires a normal scrotal testis in domestic mammals. The testis varies in its gross and microscopic appearance among the species, mostly in the extent to which the testis is divided into regions by fibrous tissue septa. This division is marked in the stallion, less so in the dog and boar, and mostly absent in ruminants. The basic microscopic appearance is similar – the testis is divided into the *interstitial or intertubular compartment* and the *seminiferous tubular compartment*. The interstitial endocrine cells are the major resident of the intertubular compartment; macrophages are another important cell type.

The interstitial compartment is a unique immunological environment. Nonspecific immunity is normal, but humoral and cell-mediated immunity is altered such that allogeneic and xenogeneic tissue transplants are maintained for a prolonged period. This state is dependent on the presence of testosterone, and is related in part to Fas ligand expression by Sertoli cells that induces apoptosis of Fas-expressing T cells. This environment is thought to provide protection to the germinal cells, and prevent autoimmune reactions or recognition of germinal cells by the immune system.

The peritubular cells and the basement membrane of the seminiferous tubule delineate the tubular compartment. Sertoli cells and germinal cells make up the intratubular compartment. The normal tubular diameter is 146 μm in the stallion, 180 μm in the dog, and 236 μm in the boar.

The normal testis is pale pink or even almost white. This is presumably because of the large quantity of chromatin material. Abnormalities that result in a lowering of spermatogenesis result in the dominance of other pigments – especially lipochrome pigments. The testes of boars become progressively brown with age, and are brown if degenerate.

A frequent misdiagnosis is made in equine fetal and neonatal gonads. Fetal testes undergo hypertrophy because of hyperplasia of the interstitial endocrine cells. These cells contain lipochrome pigments that are especially noticeable during the atrophic stage that

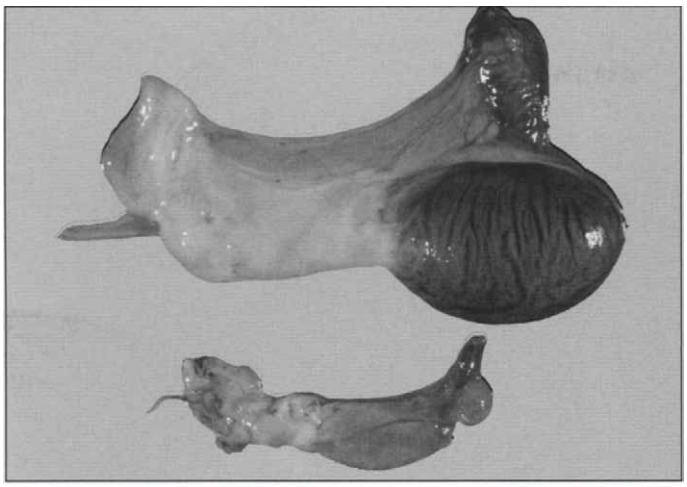

Figure 5.9 Equine **fetal** testis and epididymis (upper) with **physiological gonadal hypertrophy**: testis is dark brown. Testis undergoes atrophy to become the size of the **normal neonatal testis** (lower) before it passes through the inguinal canal.

occurs prior to birth. Many a practitioner and pathologist have been fooled by the apparent brown discoloration of the testicular parenchyma of the neonatal testis (Fig. 5.9).

Bibliography

Hemeida NA, et al. Ductuli efferentes in the epididymis of the boar, goat, ram, bull and stallion. Am J Vet Res 1987;39:1892–1900.

Riccioli A, et al. TNF-α and IFN-γ regulate expression and function of the Fas system in the seminiferous epithelium. J Immunol 2000;165:743–749.

Setchell BP. Male reproductive organs and semen. In: Cupps PT, ed. Reproduction in Domestic Animals, 4th ed. New York: Academic Press, 1991:221–250.

Anomalies of development

Cryptorchidism

Incomplete descent of the testes and associated structures (cryptorchidism) is one of the most common abnormalities of the male reproductive system, and is the most common genital abnormality of the male cat and horse. Descent of the testes, epididymides, and spermatic cord (including the testicular artery and vein and the deferent duct) is a complex series of events that requires hormonal, constitutive, and nervous control. Individual cases of cryptorchidism may be due to genotypic or environmental causes. Complete testicular descent usually occurs prior to birth in most species, with the exception of the dog.

Maldescent creates several problems. Most cases are presumed to be inherited, and, as such, breeding from affected individuals is not recommended. *Retained testes lack spermatogenesis*, and *fertility may be compromised. Increased rates of testicular neoplasia* are associated with cryptorchidism in several species, most notably the dog. Finally, *testicular torsion* is found almost exclusively in maldescended testes, although the stallion may be an exception.

Testicular (and therefore epididymal) descent occurs in three main stages: *the relative transabdominal migration phase, the intra-inguinal phase, and extra-inguinal migration*. The first phase may be partially controlled by Müllerian inhibitory substance, the second phase requires increased intra-abdominal pressure, and the third involves interaction of androgen, calcitonin gene-related protein, the genitofemoral nerve, and perhaps other factors. The exact mechanisms are yet to be elucidated in domestic mammals, but they no doubt are complex and involve an interrelationship of systemic and local factors. The effects of endocrine disruptors on male development are increasingly important, as multiple anomalies such as reduced anal–genital distance, delayed preputial separation, hypospadias, and ectopic and maldescended testes can all be induced by antiandrogenic and estrogenic chemicals.

In early fetal life, a cranial gonadal suspensory ligament supports the testis. It is retained when there is a lack of exposure to androgen, in which case subsequent development of the *gubernaculum testis* also is impaired. The gubernaculum testis is a gelatinous cord of tissue that extends from the caudal pole of the testis to the inguinal area and it exerts traction on the testis. A mutation in the *GREAT* gene, which is highly expressed in the gubernaculum and may mediate response to hormones, has been associated with intra-abdominal cryptorchidism in humans and, experimentally, in mice.

Diagnostic pathologists are frequently asked to ensure that the tissue removed during cryptorchidectomy was testis. Where the tissue resembles normal testis, there is little challenge, but, all too often, the retained testis has degenerated or is twisted and only a small remnant remains. The most difficult cases are those where necrosis of the testis presumably has occurred and all that remains is scar tissue and hemosiderin- and lipofuscin-containing macrophages. *Anorchia* is very rare and, where possible, should be separated from degeneration or death of a retained testis.

The structural anomalies associated with the failure of the testis to migrate to the scrotum include splenogonadal fusion, retention of the cranial gonadal suspensory ligament, and abnormalities of the gubernaculum and vaginal process.

A *hereditary basis* for cryptorchidism has been established or suggested in all species. Chromosomal abnormalities are implicated in many species including rams, bulls, and stallions. Chromosomal anomalies were detected in humans in 4% of a group of 160. However, a hereditary basis is unlikely in outbreaks of cryptorchidism, and *hormonal and environmental factors* are more likely.

Retained testes in pubescent animals are smaller than their normal counterparts (Fig. 5.10). This is because of the deleterious effect of body temperature on spermatogenesis. The seminiferous tubules are smaller than normal and often present with the "Sertoli cell only" pattern. Germ cells may be recognized in young animals, but in older animals, degenerative changes such as interstitial fibrosis and thickening of basement membranes superimpose on the hypoplastic appearance. In extreme forms, the outlines of distorted basement membranes are seen in a sclerotic tissue. Hyperplastic foci of Sertoli cells occur in some retained testes and these may be sites of development of Sertoli cell tumors. In unilateral testicular maldescent, which is typical, the contralateral testis is hypertrophied.

Cryptorchidism is the most common disease of the reproductive tract in male **cats**, and Persians are over-represented. The failure of testicular descent in cats tends to be unilateral without a bias to one side or the other. The testis can be anywhere along the migration path, although inguinal cryptorchidism predominated in one study.

In **dogs**, cryptorchidism may be an inherited disease (autosomal recessive) in some breeds, although there is some doubt that this is the main cause. Although it is a frequent clinical finding, little is known of the mechanism and features of the condition. There are

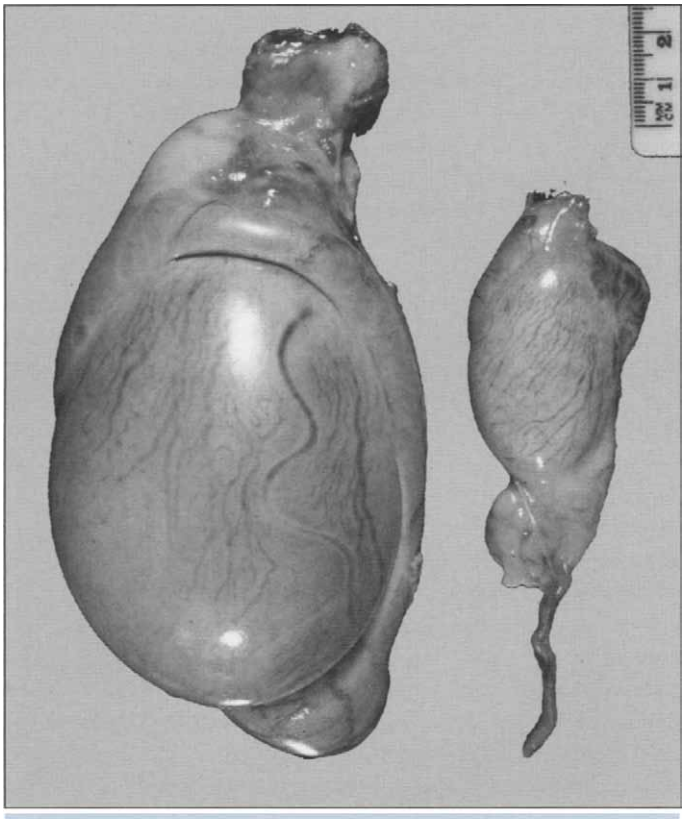

Figure 5.10 Unilateral **abdominally retained testis** (right) from a ram. The contralateral testis (left) was within the scrotum and is more bulbous than normal because of compensatory hypertrophy.

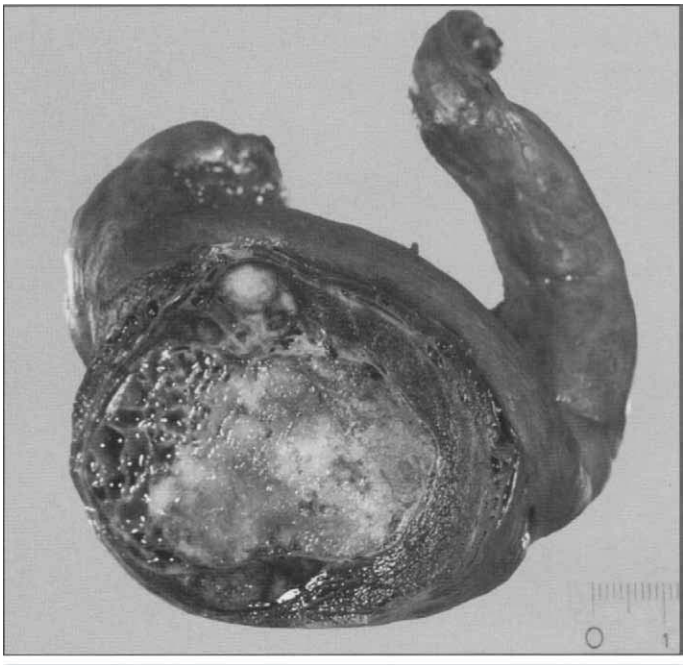

Figure 5.11 Intra-abdominal testis of a dog that developed a Sertoli cell tumor. The testis subsequently underwent torsion and venous infarction.

associations of cryptorchidism with several other diseases in dogs. *The association between testicular neoplasia and testicular maldescent is well recognized*. Sertoli cell tumors are the most common, especially in abdominally retained testes. Seminomas are the second most common neoplasm, and they are mostly in inguinally retained testes. Persistent Müllerian duct syndrome in Miniature Schnauzers is associated with unilateral or bilateral testicular maldescent. Testicular torsion usually involves cryptorchid testes – especially if there is a concomitant testicular neoplasm (Fig. 5.11). Other diseases associated with ectopic testes are patellar subluxation, hip dysplasia, penile and preputial defects, and umbilical and inguinal hernias.

Dogs are more likely to have retention of the right testis – perhaps because of a longer pathway for descent of the testis, or a less well-defined gubernaculum on the right. Inguinal testes predominate over intra-abdominal. Testicular neoplasms – Sertoli cell tumor and seminoma – are more prevalent in the right side also. Descent is usually complete by 3 months of age in the dog. Hormonal studies suggest that LH is lower in cryptorchid dogs, and the cryptorchid testis mediates the inhibition of LH secretion.

Cryptorchidism is common in **boars**. There is a hereditary basis, with the trait being recessive, and in the Duroc breed there may be involvement of recessive genes at more than one locus. Abnormal development of the gubernaculum including underdevelopment, excessive growth, and an abnormal location is the main cause of cryptorchidism in pigs.

Cryptorchidism is infrequently reported in **bulls**, but this does not necessarily indicate a low prevalence – because it is easily recognized by laypersons who do not report its occurrence. Retention of the testis and epididymis is mostly in the inguinal region, and occurs about twice as often on the left as compared to the right side. Polled Hereford and Shorthorn cattle are more at risk than other breeds. Little is known of the pathogenesis of cryptorchidism in bulls, although it is believed to be hereditary. The appearance of the cryptorchid testis is similar to that of hypoplastic testes and epididymides. Neoplasia is very rare, with an interstitial cell tumor being reported in a cryptorchid calf.

In **rams**, cryptorchidism is most likely the result of an autosomal recessive mode of inheritance, but it may also be due to a dominant gene with incomplete penetrance. Unilateral maldescent is more common than bilateral involvement, and the right testis is most often retained. Castration of ram lambs in many parts of the world is done by laypersons, and hemicastration is likely in unilateral cryptorchid animals. Some castrated animals have only their scrotum removed, leaving the testes in an "induced cryptorchid" state. Cryptorchidism in sheep has an increased prevalence in polled animals.

Cryptorchidism occurs sporadically in **goats**, mainly involving the right testis. It is a regular feature of the goat polled/intersex syndrome.

There are many reports of cryptorchidism in **stallions**, and the condition is particularly noted because of the aggressive tendencies of stallions as compared to geldings. Testicular retention is usually unilateral, with about equal frequency as to side affected. Abdominal retention of left testes is more common than inguinal; the reverse is the case on the right side. Neoplasia of the retained testis is occasionally seen, with teratomas, seminomas, and Sertoli cell tumors being reported.

Bibliography

Claxton JH, Yeates NTM. The inheritance of cryptorchidism in a small crossbred flock of sheep. J Hered 1972;63:141-144.

Dolling CHS, Brooker MG. Cryptorchidism in Australian Merino sheep. Nature 1964;203:49–50.
Gorlov IP, et al. Mutations of the GREAT gene cause cryptorchidism. Hum Mol Genet 2002;11:2309–2318.
Hayes HM. Epidemiological features of 5009 cases of equine cryptorchidism. Equine Vet J 1986;18:467–471.
Hayes HM, et al. Canine cryptorchidism and subsequent testicular neoplasia: case control study with epidemiological update. Teratol 1985;32:51–56.
Humphrey JD, Ladds PW. Pathology of the bovine testis and epididymis. Vet Bull 1975;45:787–797.
Kawakami E, et al. Peripheral plasma levels of LH, testosterone, and estradiol-17 β before and after orchiopexy in unilaterally cryptorchid dogs. Nippon Juigaku Asshi 1990;52:179–181.
Kersten W, et al. Bilateral cryptorchidism in a dog with persistent cranial testis suspensory ligaments and inverted gubernacula: report of a case with implications for understanding normal and aberrant testis descent. J Anat 1996;189:171–176.
Ladds PW. Congenital abnormalities of the genitalia of cattle, sheep, goats and pigs. Vet Clin North Am Food Anim Pract 1993;9:127–144.
Marshall LS, et al. Persistent Müllerian duct syndrome in miniature Schnauzers. J Am Vet Med Assoc 1982;181:798–801.
Millis DL, et al. Cryptorchidism and monorchidism in cats: 25 cases (1980–1989). J Am Vet Med Assoc 1992;200:1128–1130.
Romagnoli SE. Canine cryptorchidism. Vet Clin North Am Small Anim Pract 1991;21:533–544.
Rothschild MF, et al. Evidence for multigene control of cryptorchidism in swine. J Hered 1988;79:313–314.
Searle D, et al. Equine castration: review of anatomy, approaches, techniques and complications in normal, cryptorchid and monorchid horses. Aust Vet J 1999;77:428–434.
Soller M, et al. Cytogenetics of Saanen goats showing abnormal development of the reproductive tract associated with the dominant gene for polledness. Cytogenetics 1969;8:51–67.
St. Jean G, et al. Cryptorchidism in North American cattle: breed predisposition and clinical findings. Theriogenol 1992;38:951–958.
Tarigan S, et al. Genital pathology of feral male goats. Aust Vet J 1990;67:286–290.
Watt DA. Testicular pathology of Merino rams. Aust Vet J 1978;54:473–478.
Yates D. Incidence of cryptorchidism in dogs and cats. Vet Rec 2003;152:502–504.

Other testicular anomalies

Monorchia is the presence of only one testis. As a general term, monorchism is the result of cryptorchidism, severe unilateral testicular degeneration or agenesis. *True agenesis* occurs when there is a failure of one testis to develop. The differentiation between true agenesis and a cryptorchid with total testicular degeneration is impossible, but true agenesis is considered to be very rare. The presence of *supernumerary testes* or *fusion of abdominal testes* is also very rare.

The presence of testicular tissue outside the testis is reported in pigs, where nodules of tissue are found throughout the peritoneal cavity. In the cat, heterotopic interstitial endocrine cells are reported in the epididymis, and neoplasia of this tissue is reported.

Fusion of the testes to abdominal organs such as the spleen is reported, and is a cause of cryptorchidism.

Accessory or ectopic adrenal tissue is occasionally found in horses and rarely in other species. Most are located in the region of the head of the epididymis and distal spermatic cord (Fig. 5.12).

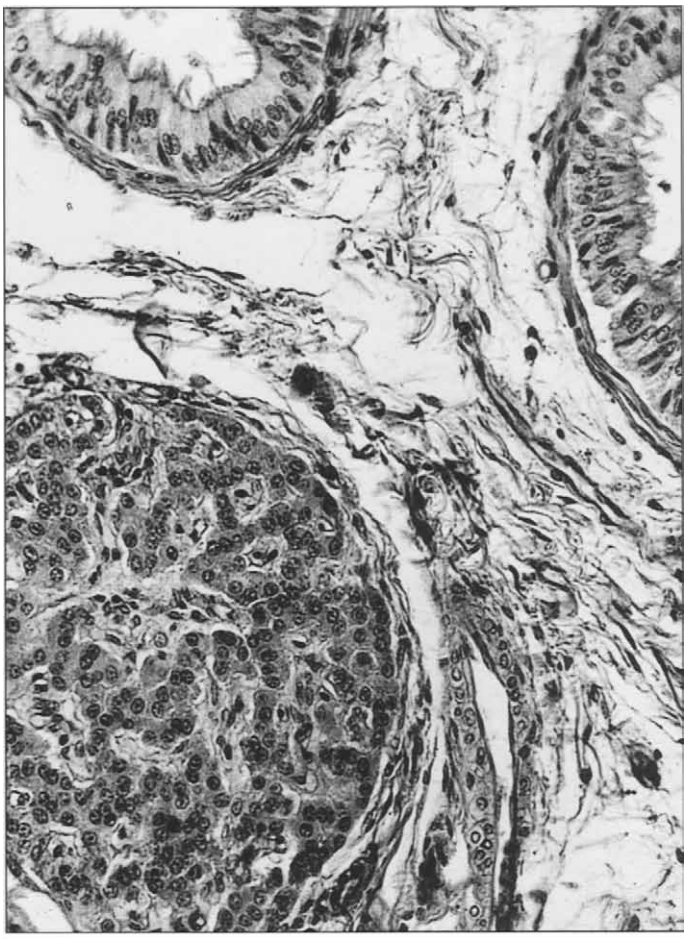

Figure 5.12 Microscopic **ectopic nodule of adrenal cortex** in the epididymis of a ram.

Variations in the shape of testes are described. "Hour-glass" shaped, round, and horizontally placed testes are all reported.

A variety of cystic structures have been described in and around the testis and epididymis. Some arise from the rete testis and others are remnants of mesonephric ducts or ductules, or paramesonephric ducts.

Bibliography

McEntee K. Reproductive Pathology of Domestic Mammals. London: Academic Press, 1990:230–231.
Parks AH, et al. Monorchidism in the horse. Equine Vet J 1989;21:215–217.

Ductular anomalies

The ducts that transport spermatozoa and fluid from the testis join the intratesticular rete testis to the pelvic urethra. Maturation and storage of spermatozoa occurs in this conduction system. There is a single duct from the efferent ductules to the urethra, and any interruption has potentially catastrophic effects to the fertility of that side. The eventual effect of continuous spermatozoal production and disruption of one of the efferent ductules has a similar outcome.

Many ductular anomalies have minor significance. Melanosis of the epididymis occurs in rams and bulls. Adrenal ectopia, various cystic remnants of the mesonephric and paramesonephric ducts

Figure 5.13 Miniature Schnauzer dog with **persistent Müllerian duct syndrome**. This dog is phenotypically male with retained testes (sectioned) and well-developed uterine horns and body.

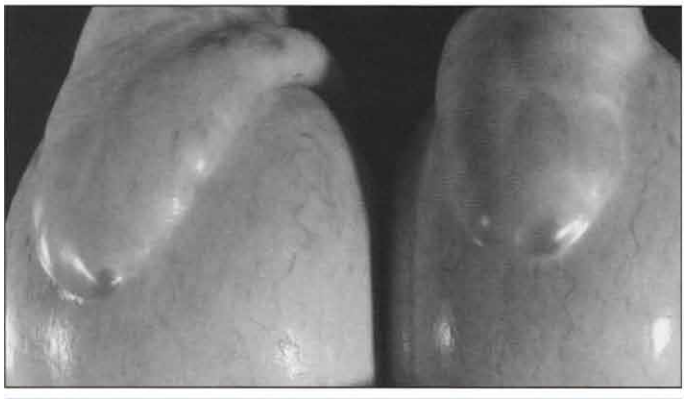

Figure 5.14 Bilateral congenital **retention cysts** at the junction of the head of the epididymis and testis of a ram.

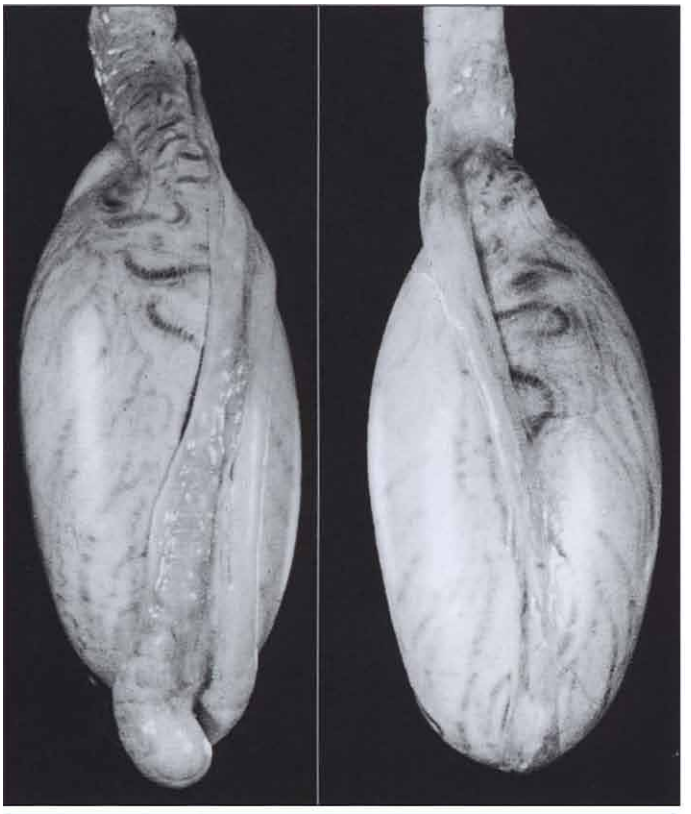

Figure 5.15 Unilateral aplasia of the tail of the epididymis (right) in a bull.

Figure 5.16 Sperm granuloma of the **epididymal head** in a dog.

(Figs 5.13, 5.14), and inclusion cysts also are reported in the epididymis. Most are incidental findings and are important as differential diagnoses for epididymitis.

Segmental aplasia of the mesonephric duct is an important condition because it has a profound effect on fertility of the affected side (Fig. 5.15). Segmental aplasia is rare, but further examination of species (such as the cat) in which it has not been reported would no doubt complete the list of species in which it is known to occur. Unilateral aplasia may be an inherited condition. The lack of one part of the epididymis or deferent duct is most likely to be identified if the tail of the epididymis is missing, so it is not surprising that this is the most frequently recognized anomaly. Apart from an absence of the structure, continuous production of spermatozoa results in the complications of spermiostasis, tubular dilation, formation of sperm granulomas, dilation of the mediastinum testis, and testicular atrophy. Examination of the accessory genital glands will usually reveal a smaller vesicular gland on the affected side – presumably because of a lack of trophic stimuli. Hypertrophy of the contralateral testis is also likely.

Sperm granuloma of the epididymal head (Fig. 5.16) is often mistaken for infectious epididymitis. Failure of one or more of the 12–25

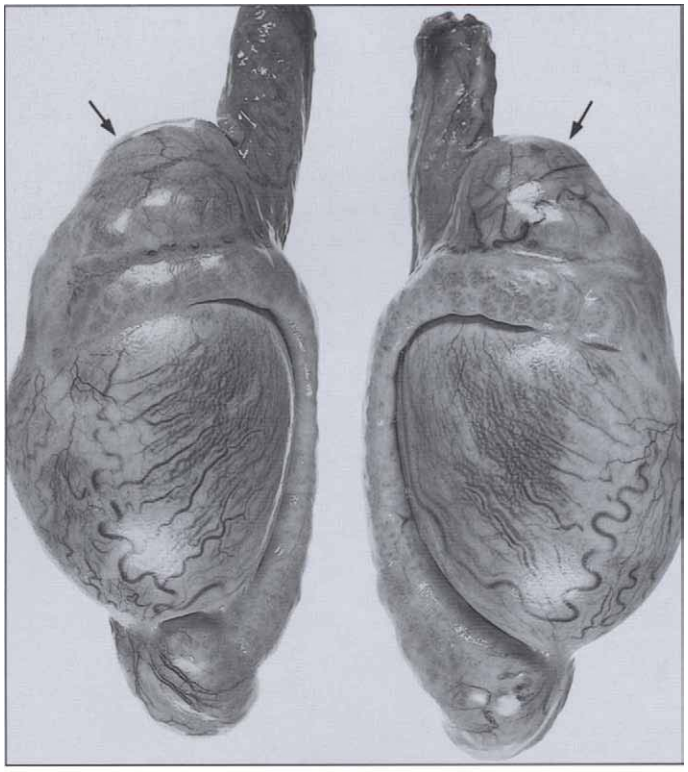

Figure 5.17 Bilateral **sperm granulomas** of the **epididymal head** (arrows) in a goat. Each efferent ductular region, and the head of the epididymis are large and contain sperm granulomas.

efferent ductules to join with the epididymal duct is believed to be the underlying defect. After puberty, the blind-ended ductule(s) fill with spermatozoa and, with spermiostasis, may rupture and/or form a sperm granuloma. The associated inflammation and fibrosis will eventually cause obstruction of other efferent ductules or the epididymal duct. The result will be complete obstruction to flow of spermatozoal-rich fluid and progressive formation of more sperm granulomas. The distal epididymal tissues are reduced in size, the mediastinum testis dilates, and the testis undergoes pressure atrophy. This condition is often misdiagnosed as epididymitis and the potential congenital or hereditary basis for the problem is missed. Sperm granuloma of the epididymal head is a common finding in polled Saanen goats, where they may be bilateral (Fig. 5.17).

Ectopic interstitial endocrine cells and *ectopic interstitial cell tumors* have been reported in the tunica albuginea, mediastinum testis, or spermatic cord of cats.

Many *cystic lesions* have been reported in the tunica albuginea, epididymis, spermatic cord, and adjacent to the accessory genital glands. These are presumed to be remnants or duplications of the paramesonephric and mesonephric duct systems. Remnants of the mesonephric duct include the paradidymis (interna and externa), epididymal cysts, and appendix epididymis. So-called *retention cysts* are very common in the region of the head of the epididymis, especially in rams (see Fig. 5.14). They are usually up to 3 mm in diameter, contain clear fluid, and are lined by epithelium similar to that of the epididymis. The paradidymis is seen proximal to the epididymis in the spermatic cord as one or several small cysts, particularly in neonates. Other cysts, seen particularly in the epididymis, can be microscopic or up to 4 cm in diameter.

Remnants of the paramesonephric ducts include the appendix testis, the uterus masculinus near the accessory genital glands, and, in some cases a completely retained duct that runs beside the testis. Histologically these may have the appearance of a juvenile uterus with prominent musculature and uterine glands.

Bibliography

Estrada A. et al. Azoospermia associated with bilateral segmental aplasia of the ductus deferens in a stallion. J Am Vet Med Assoc 2003;222:1740–1742.

Humphrey JD, Ladds PW. Pathology of the bovine testis and epididymis. Vet Bull 1975;45:787–797.

Foster RA, et al. Pathology of reproductive tracts of merino rams in northwestern Queensland. Aust Vet J 1989;66:263–264.

Ladds PW, et al. Epididymal aplasia in two rams. Aust Vet J 1990;67:457–458.

Wrobel KH, Hees H. Heterotopic Leydig cells in the cat. Anat Histol Embryol 1987;16:289–292.

Variation in testicular and epididymal size

The daily spermatozoa output of the testes is directly and highly correlated to testicular volume, most commonly evaluated using scrotal circumference, for which reference ranges have been established by species or breed. Testes above this range are hypertrophied; those below the range are too small because of atrophy or hypoplasia. *Even experienced pathologists have difficulty in differentiating hypoplastic from atrophic testes in adults.* This is because there are variations in the degree of hypoplasia and, over time, hypoplastic testes may undergo degeneration. The dogma is that in atrophic testes, the ratio of testicular to epididymal weight is reduced since the reduction in size of the testis is greater than the reduction in size of the epididymis. The basement membrane of appropriately fixed atrophic testes is buckled or has a "wavy" outline. In hypoplastic testes, the ratio of the weight of the testis to epididymis is similar to that of normal testes. The size of both is smaller that normal and there are histological features of spermatogenic arrest in tubules that are smaller than age- and breed-matched controls. The best method to be sure that degeneration has occurred is to demonstrate a decrease from normal testicular weight or size over time. In contrast, hypoplastic testes are smaller than normal and remain so. Since pathologists usually must make an assessment based on a single observation, a diagnosis of "small testes" is not necessarily an indication of ignorance; rather, it is an indication of appropriate caution.

Testicular hypertrophy

Enlargement of an otherwise normal testis is rarely a primary disorder. *Secondary or compensatory hypertrophy* is a unilateral condition that indicates an underlying disease such as orchitis or neoplasia in the contralateral testis. It is a well-recognized phenomenon in hemicastrates, and in hypoplasia, cryptorchidism, or atrophy of the contralateral testis (see Fig. 5.10). Hemicastration of prepubertal boars, especially in those younger than 3–4 months, results in dramatic hypertrophy of the contralateral testis. In rams and bulls, hypertrophy appears to occur mostly when the unilateral condition is present during the peripubertal period and is associated with increased FSH production. The increase in size can be up to 100%,

Figure 5.18 Testes and epididymides of four rams of the same age. There is a gradation of **testicular hypoplasia** from severe (upper left) to normal (lower right).

and is due to an increase in the size of Sertoli cells and in the number of germinal cells per Sertoli cell. In some instances there may be an increase in the number of Sertoli cells and spermatogonia, and an increase in diameter and length of seminiferous tubules.

The presence of *dilated cystic remnants and pseudocysts* can also cause, or be confused with, enlargement of a testis. Occlusion of the efferent ductules can lead to dilation of the rete and mediastinum testis and appear as testicular enlargement, although the thickness and fibrous nature of the tunica albuginea makes sudden enlargement of the testis less likely. Adhesions and thickenings of the tunica vaginalis can also appear clinically as testicular enlargements. To the unsuspecting, lesions of the scrotum or its contents are frequently mistaken as testicular enlargement; hydrocele, epididymitis, or the presence of sperm granulomas are examples.

Bibliography

Boockfor FR, et al. Effects of unilateral castration and unilateral cryptorchidism of the Holstein bull on plasma gonadotropins, testosterone and testis anatomy. J Anim Sci 1983;56:1376–1385.

Cox JE. Factors affecting testis weight in normal and cryptorchid horses. J Reprod Fertil Suppl 1982;32:129–134.

Lunstra DD, et al. Sertoli cells in the boar testis: changes during development and compensatory hypertrophy after hemicastration at different ages. Biol Reprod 2003;68:140–150.

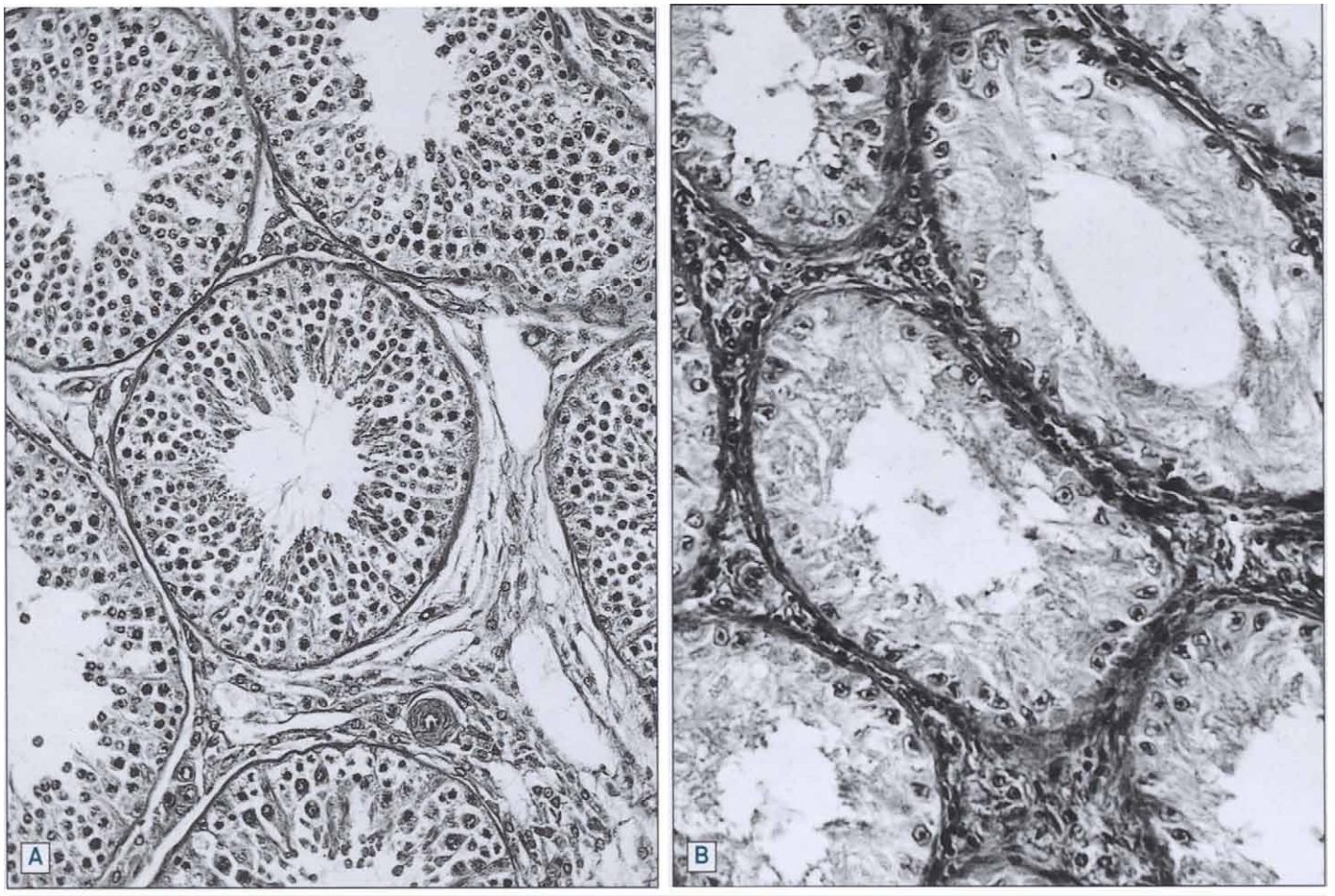

Figure 5.19 A. Normal seminiferous tubules of an adult bull. **B.** Severe **testicular hypoplasia** in a bull, with the Sertoli cell only pattern and a complete lack of germ cells.

Putra DKH, Blackshaw AW. Quantitative studies of compensatory testicular hypertrophy following unilateral castration in the boar. Aust J Biol Sci 1985;38:429–434.
Schanbacher BD, et al. Testicular compensatory hypertrophy in the hemicastrated calf: effects of exogenous estradiol. Biol Reprod 1987;36:1142–1148.

Testicular hypoplasia

Hypoplastic testes have failed to grow to a normal size. *Testicular hypoplasia occurs in cryptorchidism, some intersex conditions, and as an "uncomplicated" disease.* It can be unilateral or bilateral, and the small size is because of a reduction in the amount of the seminiferous epithelium. An affected testis is grossly similar to a normal testis in almost every way, except size (Fig. 5.18).

Hypoplasia is the potential outcome of a large number of different abnormalities that may operate at a systemic or local level, as perhaps occurs in the case of unilateral disease. The small size is theoretically because of an abnormally small number, length, or diameter of tubules, or one or more combinations of these (Figs 5.19A, B and 5.20). Germ cells may be absent, or be present but fail to produce enough spermatozoa. Germ cells may have failed to migrate to the genital ridge in utero, failed to migrate in sufficient numbers, failed to survive, or they may have arrested development, undergo excessive apoptosis, or undergo degeneration at some stage of spermatogenesis (Fig. 5.21).

Studies of hypoplasia have been mostly observational, at the clinical, gross, or microscopic level. Microscopic abnormalities include a total lack of germ cells, arrested spermatogenesis in all tubules, or arrested spermatogenesis that varies from tubule to tubule (low germ cell resistance). Hypoplastic testes with a total lack of germ cells are very small and fail to enlarge from their size at birth. Those testes with arrested development of all tubules fail to progress beyond a certain stage of spermatogenesis.

A deficiency of gonadotrophins is associated with hypoplasia (hypogonadotrophic hypogonadism) in men and mice, but studies in domesticated mammals indicate a normal or raised serum concentration of FSH and LH. Testosterone concentration was lower than normal in some bulls with hypoplasia; in sheep, testosterone and inhibin concentration may be normal.

At the chromosomal level, testicular hypoplasia in animals with a condition resembling Klinefelter's syndrome is recognized. Affected cats, bulls, dogs, pigs, horses, and sheep have an XXY genotype or a mosaicism with XXY chromosomes. The best known of these is the male tortoiseshell or calico cat. In goats of the Saanen breed with the gene for polledness, testicular hypoplasia is seen in genetically female pseudohermaphrodites. A variety of other chromosomal abnormalities have been identified as being associated with hypoplasia.

At the genetic level, hypoplasia is known or suspected to be *hereditary* in the bull, ram, and buck. The exact genetic abnormality

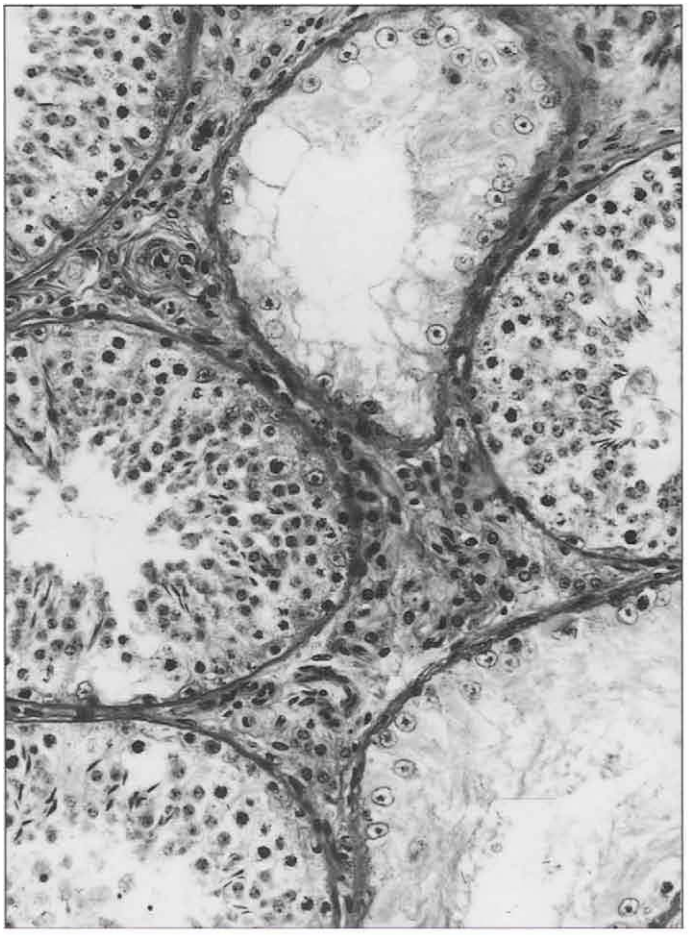

Figure 5.20 Hypoplastic seminiferous tubules adjacent to normal tubules of a bull.

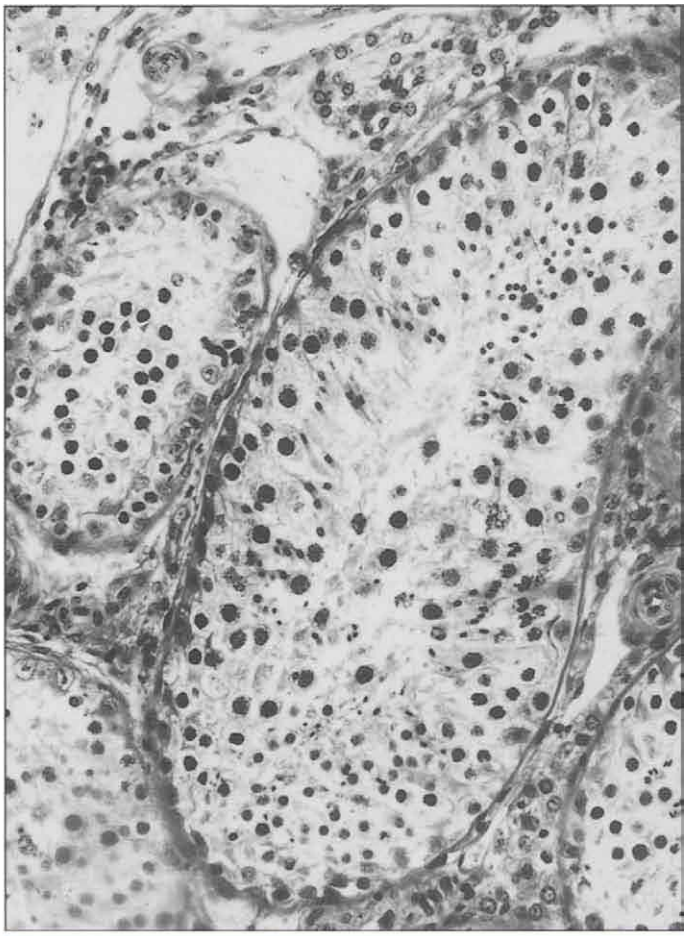

Figure 5.21 Seminiferous tubules of a bull with **testicular hypoplasia**. Tubules have arrested spermatogenesis.

is often not established. There are few studies of hypoplasia in domesticated animals, but there are some special features of the disease in selected species discussed below.

Hypoplasia in bucks

There are several types of hypoplasia recorded in bucks. It is a common abnormality in the polled/intersex (XX sex reversal) syndrome of polled Saanen goats, where the animals are genotypically female but phenotypically male. The testes of affected animals have rudimentary seminiferous tubules. Other sporadic forms of hypoplasia occur, and the cause is not known.

Hypoplasia in bulls

As with other species, testicular hypoplasia in bulls probably is a multifactorial condition. Studies suggest it is hereditary, particularly in the Swedish highland breed, where it has a recessive inheritance with incomplete penetrance. Animals with white body and ears are particularly likely to have hypoplasia. The majority of unilateral hypoplastic testes are on the left side.

The defect in hypoplasia varies from case to case. Some are regarded as a "germ cell weakness," whereby germ cells are present in most seminiferous tubules but there is marked pyknosis of primary spermatocytes. Some are described as having "sticky chromosomes" with the presence of multipolar spindles in primary spermatocytes, or having germinal epithelium that does not progress to spermatogenesis. Other cases of hypoplasia have a Sertoli cell-only pattern or they have some normal and abnormal tubules intermixed, often with affected tubules being in the more dorsal parts of the testis. Despite the various abnormalities observed, there generally appears to be a cessation of spermatogenesis at some stage, with either degeneration or excessive apoptosis of the germinal epithelium.

Hypoplasia in cats

Testicular hypoplasia is a sporadic disease of cats. It is most frequently seen on cryptorchid animals and in cats with a tricolor or calico coloration. Males with tricolor or calico coloration often have an XXY genotype. Affected cats may have no germ cells and markedly hypoplastic testes with small diameter tubules. Chimeric animals may be fertile.

Hypoplasia in dogs

A diagnosis of testicular hypoplasia in dogs is usually made only after azoospermia is found during an investigation of infertility. Hypoplasia cannot be implicated as a cause of azoospermia if the dog has been previously fertile, and can only be considered if acquired azoospermia can be ruled out with certainty. Confirmation of congenital azoospermia because of testicular hypoplasia requires historical information or testicular biopsy after the expected date of puberty.

Congenital azoospermia occurs in some lines of dogs. This suggests a familial or hereditary basis, implicating inbreeding.

Hypoplasia is commonly seen in animals with failure of testicular descent, and in chromosomal abnormalities such as XX sex reversal and XXY syndrome. Offspring of bitches treated with diethylstilbestrol may have hypoplastic testes.

Hypoplasia in rams

Testicular hypoplasia of rams usually is a sporadic disease that may be either bilateral or unilateral. The disease is not well studied. A condition resembling Klinefelter's syndrome, with an XXY genotype is reported. Zinc deficiency has been implicated in some cases.

Various degrees of hypoplasia are recognized, and affected testes may have tubules that, at the extreme are about 90 μm in diameter (normal 160 μm) and are lined by mostly fetal Sertoli cells. An outbreak of gonadal hypoplasia that affected rams born within a short time frame is reported. The affected testes were uniformly small and had a "Sertoli cell-only" pattern histologically. An environmental cause was suspected.

Bibliography

Centerwall WR, Benirschke K. An animal model for the XXY Klinefelter's syndrome in man: tortoiseshell and calico male cats. Am J Vet Res 1975;36:1275–1280.

Galloway DB, et al. An outbreak of gonadal hypoplasia in a sheep flock: clinical, pathological and endocrinological features, and aetiological studies. Vet Rec 1992;131:506–512.

Gimbo A, et al. Ram testicular hypoplasia: anatomical and histopathological observations. Schweiz Arch Tierheilk 1987;129:481–491.

Kay GW, et al. Heritable testicular hypoplasia in Nguni (*Bos indicus*) bulls: vascular characteristics and testosterone production. J Reprod Fertil 1992;96:537–547.

Olson PN, et al. Clinical and laboratory findings associated with actual or suspected azoospermia in dogs: 18 cases (1979–1990). J Am Vet Med Assoc 1992;201:478–482.

Table 5.1 Causes of testicular degeneration

- Advancing age
- Chemicals
  1. Chemotherapy
  2. Chlorinated naphthalenes
  3. Halogenated compounds, including hexachlorophene
  4. Nitrogen-containing compounds, including benzimidazoles, nitrofurans
  5. Metal compound toxicity
- Epididymitis
- Heat
- Hormones
  1. Dexamethasone
  2. Estrogen
  3. Testosterone
  4. Zearalenone
- Neoplasia
  1. Pituitary tumors
- Nutritional disorders
  1. Negative energy balance
  2. Fatty acid deficiency
  3. Hypovitaminosis A
  4. Hypervitaminosis A
  5. Hypovitaminosis B
  6. Hypovitaminosis C
  7. Hypovitaminosis E
  8. Protein and amino acid deficiency
  9. Zinc deficiency
- Plants
  1. Locoweed (*Astragalus*)
  2. Lysine seeds (gossypol)
- Radiation
- Stress/corticosteroid therapy
- Trauma
- Ultrasound
- Viral infection
  1. *Porcine reproductive and respiratory syndrome virus*
  2. *Canine distemper virus*

Olson PN. Clinical approach for evaluation dogs with azoospermia or aspermia. Vet Clin North Am Small Anim Pract 1991;21:591–607.

Settergren I, McEntee K. Germ cell weakness as a cause of testicular hypoplasia in bulls. Acta Vet Scand 1992;33:273–282.

Sponenberg DP, et al. Unilateral testicular hypoplasia in a goat. Vet Pathol 1983;20:503–506.

Veeramachaneni D, et al. Pathophysiology of small testes in beef bulls: relationship between scrotal circumference, histopathologic features of testes and epididymides, seminal characteristics, and endocrine profiles. Am J Vet Res. 1986;47:1988–1999.

Testicular degeneration

Testicular degeneration is manifested clinically and grossly as atrophy, mineralization, and fibrosis. It usually occurs because of influences external to the testis (see Testicular hypoplasia). There is a seemingly endless list of potential causes, as outlined in Table 5.1. The close interrelationship of the Sertoli cells, interstitial endocrine cells, and germ cells means that insults to any one or several of them eventually affect them all. Even though the insult is external to the testis, the manifestation in the testis is not always bilateral or uniform. The testes of aged bulls frequently degenerate from the ventrum, and those from rams appear to degenerate from the dorsum.

Testes undergoing degeneration are usually reduced in size. In early or rapidly progressing degeneration, the testis is soft and flabby, lacks turgor, and the cut surface does not bulge. Wrinkling of the tunica albuginea may be apparent. With ongoing loss of fluid and reduction in the germinal epithelium relative to the stroma, the result is a small testis of firm consistency. The substance of the testis takes on a darker color that is often brown. Since the epididymis usually is less affected than the testis, it ultimately will appear to be disproportionately large (Fig. 5.22A, B). With continued degeneration and fibrosis, the testis becomes increasingly hard and variable mineralization may occur (Fig. 5.23).

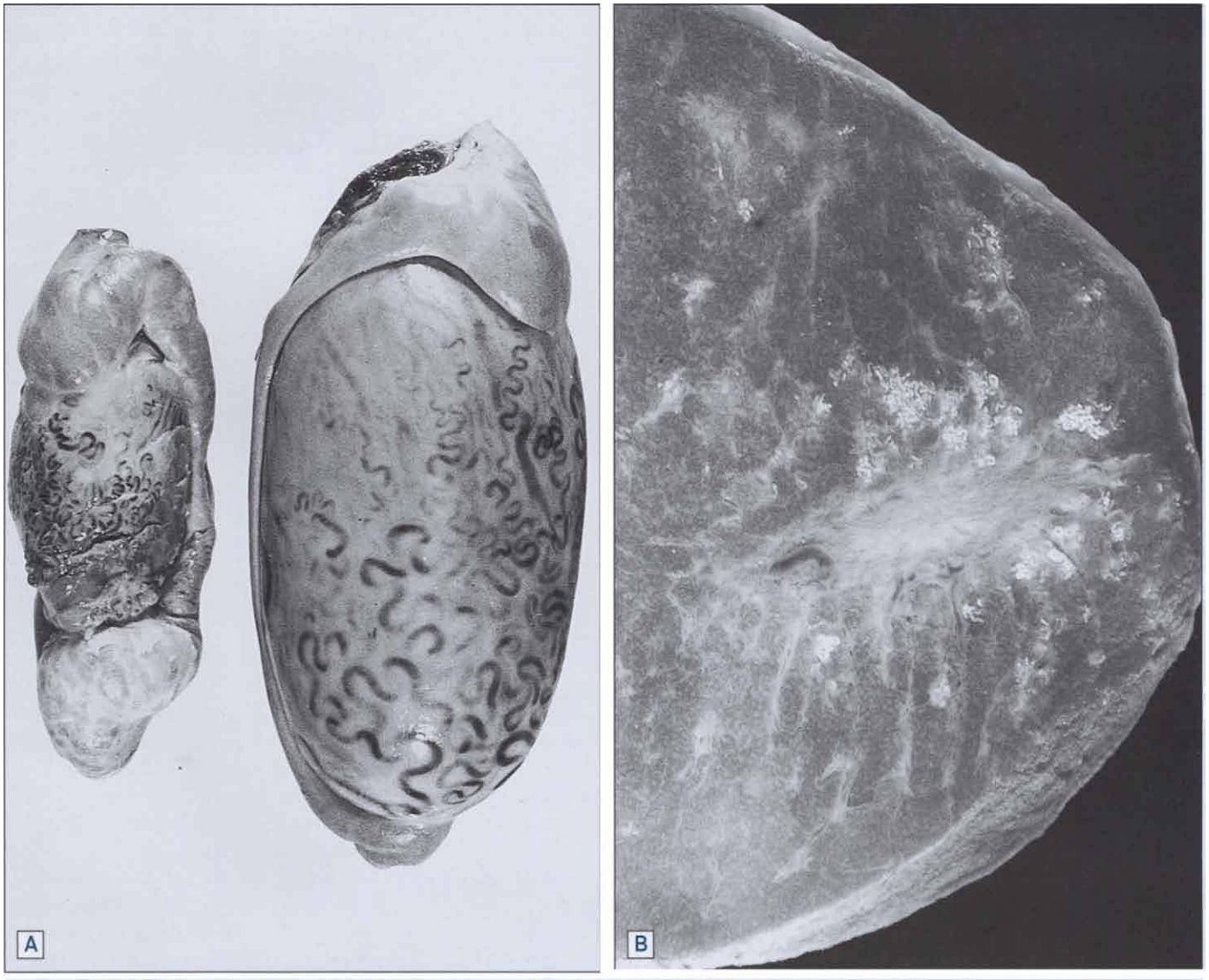

Figure 5.22 A. Unilateral **testicular degeneration** in a bull. The epididymis of the atrophic testis appears disproportionately large. **B.** Discoloration (brown) of the testis and mineralization of seminiferous tubules in a bull with testicular degeneration/atrophy.

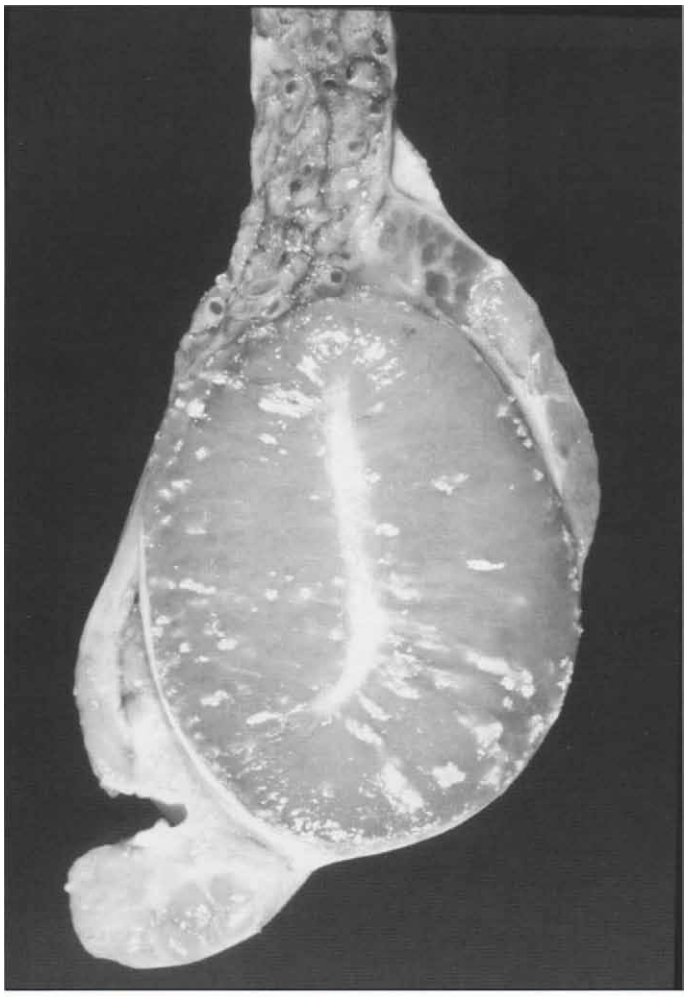

Figure 5.23 Testicular atrophy and resultant darker testicular color, and multifocal mineralization in a buck.

Testicular degeneration may be uni- or bilateral, and *it is assumed that unilateral degeneration is the result of a local event, while bilateral degeneration usually is the result of a systemic problem.*

Histological changes in degeneration (Fig. 5.24A, B) vary in degree, but are relatively stereotypic. In the early stages, Sertoli cells develop either a fine basal vacuolation or a more dramatic vacuolation of the apical cytoplasm. There also is disorganization and exfoliation of germ cells. In some cases there may be failure of release of germ cells from Sertoli cells (spermiation) and spermatozoa are phagocytized by Sertoli cells.

Early changes in the germ cells include failure of maturation of spermatozoa and degeneration of spermatids; many spermatids are necrotic and others produce characteristic spermatidic multinuclear giant cells. When the degeneration is more advanced, the affected areas are more extensive and degenerative changes appear in the precursors of spermatids. Depending on the insult, there may be cytoplasmic vacuolation and nuclear pyknosis, or apoptotic bodies are seen. Progression of the changes results in loss of germinal cells, and eventually, loss of even the resistant Sertoli cells. Basement membrane thickening is a frequent finding, and as a result of shrinkage and collapse of tubules, it becomes wavy and buckled. The PAS stain clearly accentuates the basement membrane change. In ultrastructural studies of the testes of normal bulls and bulls with atrophy or hypoplasia, mean thicknesses of the actual basal lamina were approximately 0.7, 1.5, and 1.0 μm, respectively.

Once-only scrotal heating can cause the appearance of giant cells in degenerate testes and perhaps in the semen. Two types of giant cells, mononuclear giant cells probably derived from pachytene spermatocytes that fail to differentiate further, and multinucleate cells considered to be derived from coalescence of identical spermatids, are observed histologically. Even extremely brief heating, of several minutes only, induces giant cell formation. Such giant cells are seen as early as 6 hours and as late as 7 weeks post-heating, but they seem to be most prevalent at about 1 week. The fate of these cells is unclear. They may disintegrate or pass out of the testis. In addition to giant cell formation, minor increases in testicular temperature in sheep produce a marked accumulation of B-type spermatogonia; histologically this can be demonstrated by the presence of many cells in which mitosis is incomplete.

Granulomas can form in degenerate testes (Fig. 5.25A, B). This and the presence of lymphocytes and plasma cells indicates an immune response to spermatozoa, but complicates the differentiation of simple degeneration from interstitial orchitis. *Osseous metaplasia* sometimes occurs in tubules affected by spermiostasis for a long time.

Mineralization is a common sign of degeneration, and it may involve all or part of one seminiferous tubule, or whole regions (Fig. 5.26). This latter pattern of change is only significant if the testes are to be biopsied, wherein the section may not be representative of the whole.

The basic mechanism of degeneration of the cells that make up the germinal epithelium is presumed to be via *apoptosis*.

The testis is very susceptible to the effects of increased scrotal temperature. Both testicular and epididymal function are altered when intrascrotal temperatures increase. In the epididymis, an increase in temperature reduces mRNA expression of a spermatozoal membrane glycoprotein (CD52) in a testosterone-independent manner. An inability to maintain the testes at a temperature lower than normal body temperatures can occur with pyrexia, increased environmental temperatures, scrotal thickening and hair and wool cover, and by the presence of intrascrotal inflammation or scrotal dermatitis. Varicocele is also implicated in the failure to maintain testicular thermoregulation. The progressive degeneration of maldescended testes is believed to be the result of abnormally high testicular temperature.

Degeneration of the testes with advancing age is a recognized phenomenon. The cause is not fully known but it may be secondary to degenerative vascular lesions within the testis. Old bulls and rams have a diffuse increase in intertubular stroma and a decreased proportion of tubular mass. Other changes include increased thickness of tunics and tubular basement membrane, increased proportion of degenerate tubules, and an apparent increased number of interstitial endocrine cells, which contain increased lipofuscin.

Gonadotrophins are essential for the normal development and function of the reproductive tract. The pathology of *disruptors of endocrine function* is a major focus because of the effects of antiandrogenic and estrogenic substances on male reproduction. Substances that reduce androgen concentrations, such as lead and ethanol, adversely affect spermatogenesis and cause degeneration. Sometimes the degeneration is subtle – such as reducing the number of

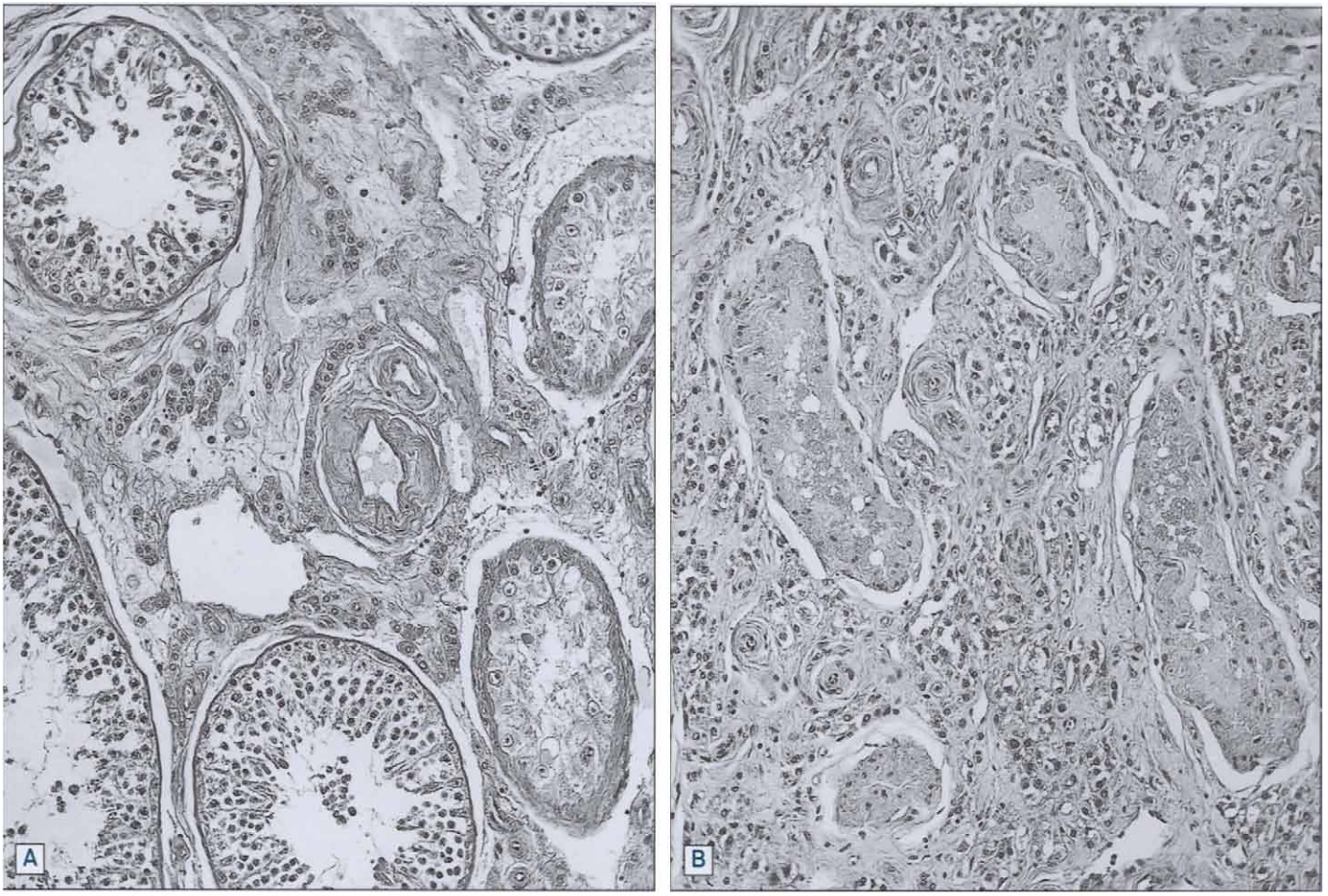

Figure 5.24 Testicular degeneration in a bull. **A.** Tubules are at various stages with changes that include a Sertoli cell only pattern, reduced spermatogenesis, and buckling of basement membranes. Hyalinized blood vessels are in the interstitium. **B.** More advanced degeneration with hyalinized tubules and depletion of both germinal and Sertoli cells.

spermatids. Drugs and chemicals (phenobarbital, DDT) that stimulate the hydroxylases that reduce testosterone activity also can create antiandrogenic effects.

Some *directly acting toxicants* are known in domesticated mammals. These may be derived from plants, or from other environmental or therapeutic sources. Biotransformation of such compounds can occur in the testis, as those formed elsewhere may not attain significant concentrations in the testis. The toxicant may affect any one or several of the cell types, including the Leydig cells, Sertoli cells, spermatogonia, spermatocytes, spermatids, spermatozoa, or the epididymal tissues.

Interstitial endocrine cell toxicants, as expected, affect testosterone production. Ketoconazole, ethanol, acetaldehyde, and cannabinoids are examples. Their effects include alteration of Sertoli cell function and maturation of germ cells, especially pachytene spermatocytes and spermatids.

Direct Sertoli cell toxicants will have detrimental effects on the blood–testis barrier, orientation and translocation of germ cells, hormonal and nutritional support of germ cells, and phagocytosis of residual bodies. The targets for toxicants include the actin filaments, intermediate filaments, and microtubules. Cytochalasin disrupts actin filaments, acrylamide disrupts intermediate filaments, and colchicine, vinblastine, and vincristine affect microtubules. Fortunately, many of these drugs, when used at therapeutic doses, have a temporary effect that is reversed when therapy ceases.

Effects seen microscopically include vacuolation or swelling and germ cell changes. Failure of spermiation can occur.

Toxicants that affect the germ cells are those that are used to prevent rapid mitotic division, and the spermatogonia are the major targets. Adriamycin and cyclophosphamide are examples. Damage by these compounds to the genetic composition of stem cells will also have effects on the later stages of development, up to spermatozoa. Toxicants of the other germ cells are little recognized in domestic species, although in rodents, ethyl glycol alkyl ethers affect spermatocytes, nitroimidazoles affect spermatids, and compounds that impinge on energy metabolism affect spermatozoa. Damage to various stages causes apoptosis, with a rapid uptake of the detritus by Sertoli cells. Within 48 hours, there may no longer be evidence of apoptosis – just the appearance of "maturation arrest."

Toxicants can also affect the efferent ductules and epididymis and/or the spermatozoa in transit. The difficulty with investigating efferent ductular toxicosis is separating the effect due to alteration in testosterone concentration, and direct toxic effects. Substances that affect the efferent ductules include cyclophosphamide, methyl chloride, and reserpine. Such toxicants decrease spermatozoal concentration and cause spermiostasis, sperm granuloma formation,

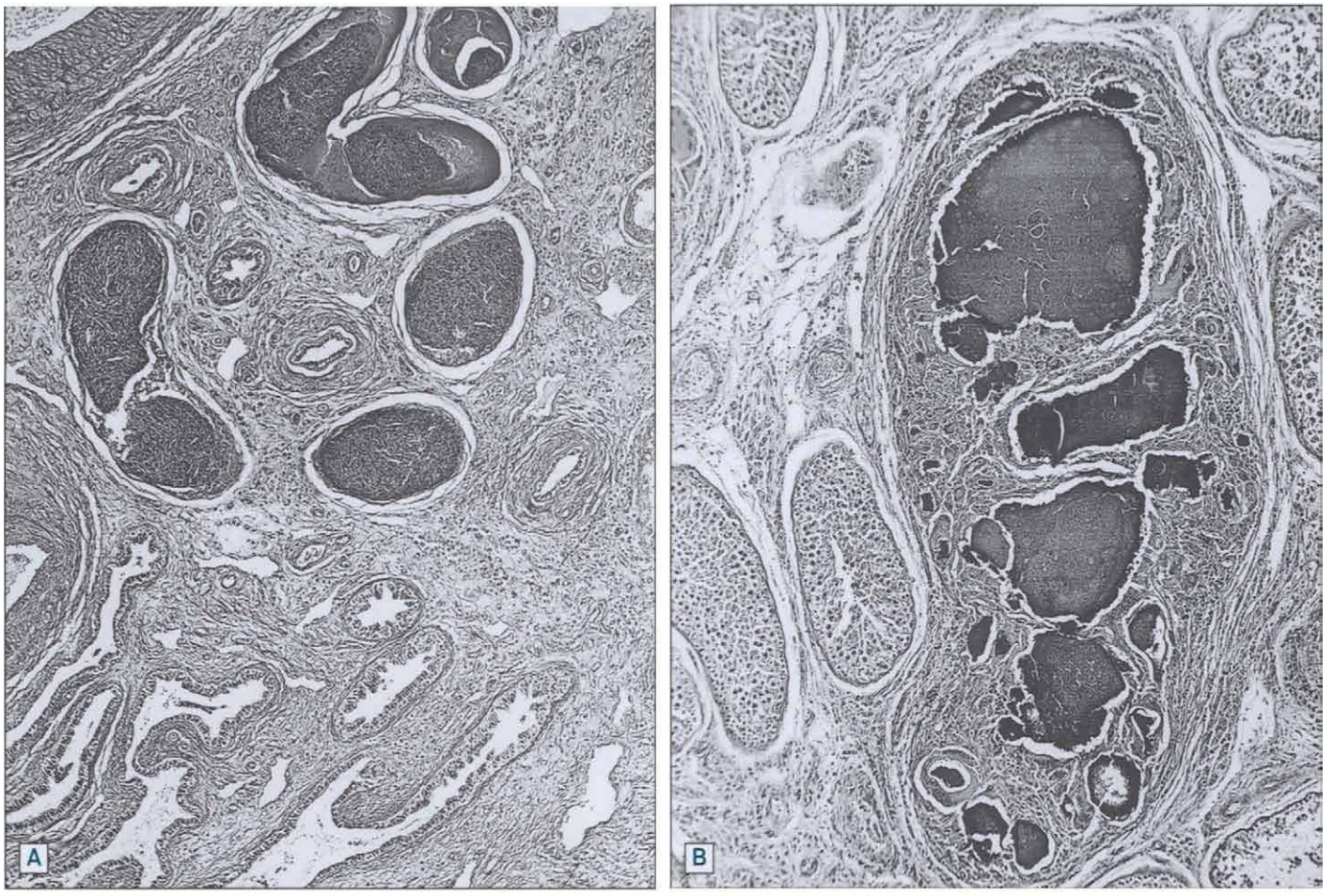

Figure 5.25 A. Spermatozoal stasis in remnants of seminiferous or straight tubules near the mediastinum testis. **B.** Sperm granuloma in a focus of spermatozoal stasis in the testis of a bull.

and necrotic and degenerative changes to the epithelium. Several have direct effects on spermatozoa in the ducts.

There are few reports of *direct viral infection* and their effects on spermatogenesis. However, *Porcine reproductive and respiratory syndrome virus* replicates in germ cells, alters spermatogenesis, and induces apoptosis. *Canine distemper virus* infection of dogs can cause testicular degeneration.

Bibliography

Boekelheide K, et al. The Sertoli cell cytoskeleton: a target for toxicant-induced germ cell loss. Toxicol Appl Pharmacol 1989;101:373–389.

Chapin RE, Williams J. Mechanistic approaches in the study of testicular toxicity: toxicants that affect the endocrine regulation of the testis. Toxicol Pathol 1989;17:446–451.

Creasy DM. Pathogenesis of male reproductive toxicology. Toxicol Pathol 2001;29:64–76.

Creasy DM, Foster PMD. The male reproductive system. In: Haschek WM, Rousseaux CG, eds. Handbook of Toxicologic Pathology. San Diego, CA: Academic Press, 1991:860–874.

Hess RA. Effects of environmental toxicants on the efferent ducts, epididymis and fertility. J Reprod Fertil Suppl 1998;53:247–259.

Pera I, et al. Body temperature (37 C) specifically down-regulates the messenger ribonucleic acid for the major sperm surface antigen CD52 in epididymal cell culture. Endocrinol 1996;137:4451–4459.

Settergren I, McEntee K. Germ cell weakness as a cause of testicular hypoplasia in bulls. Acta Vet Scand 1992;33:273–282.

Sur JH, et al. Evidence for the localization of porcine reproductive and respiratory syndrome virus (PRRSV) antigen and RNA in ovarian follicles in gilts. Vet Pathol 2001;38:58–66.

Inflammation of the testis and epididymis

Orchitis

Apart from bulls in areas endemic for *Brucella abortus* or tuberculosis, orchitis is a rare and sporadic disease in domesticated animals. *The vast majority of cases diagnosed clinically as orchitis are actually epididymitis* (see below). Focal accumulations of lymphocytes are occasionally seen in the testes of most species as incidental findings (Fig. 5.27). Lymphocytic (or nonsuppurative) inflammation is seen in some infertile animals; an immunological pathogenesis is invoked after it was demonstrated that immunization of guinea pigs and bulls with spermatozoa induced inflammation of the rete testes. Efferent ductules are also involved experimentally.

Orchitis as the primary and severe disease has historically been attributed to brucellosis or tuberculosis. Tuberculous orchitis is a multifocal granulomatous disease that is much less common now because of eradication in many countries. Brucellosis is similarly reduced in

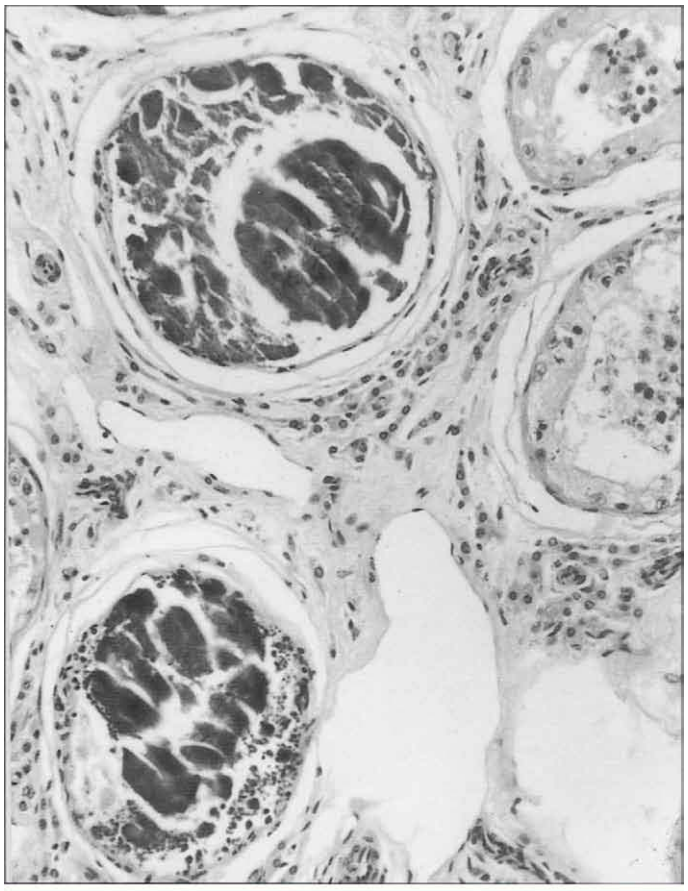

Figure 5.26 Mineralization of seminiferous tubules in the testis of a bull with testicular degeneration.

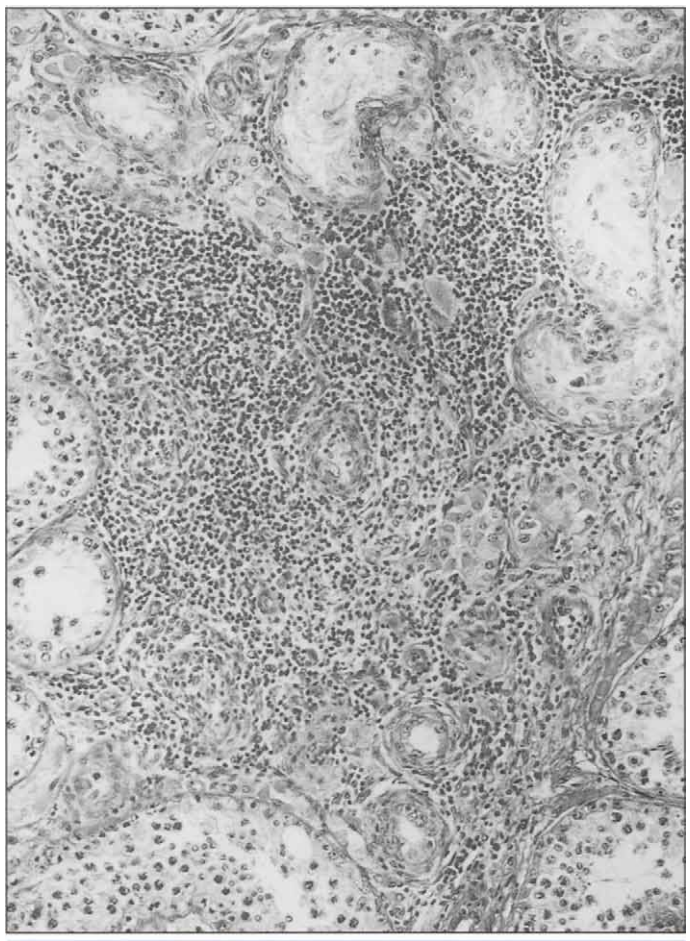

Figure 5.27 Focal interstitial accumulation of lymphocytes with seminiferous tubular degeneration in a stallion.

prevalence. *Brucella abortus* (bulls), *Brucella suis* (pigs), *Brucella canis* (dogs), and *Brucella melitensis* (goats) can cause orchitis as a dominant change. However, epididymitis is often the primary manifestation.

Orchitis occurs sporadically in cats with feline infectious peritonitis, in rams and bucks with *Corynebacterium pseudotuberculosis*, in pigs with *Burkholderia pseudomallei*, and in stallions with migrating larvae of *Strongylus* spp. nematodes. Sporadic infection with other bacteria will no doubt occur from time to time. The relative isolation of the testis suggests that infection with the various agents is mostly hematogenously derived, or occurs by direct penetration.

Orchitis has been divided into three major categories: interstitial orchitis, intratubular or granulomatous orchitis, and necrotizing orchitis.

Interstitial orchitis

Interstitial orchitis may not be recognized macroscopically, but histologically it is characterized by *lymphocytic infiltration of intertubular stroma, with concurrent or subsequent fibrosis* (Fig. 5.28). In bulls, small mononuclear infiltrates are frequently observed adjacent to seminiferous or rete tubules or efferent ductules of otherwise normal testes. Such foci may be of infectious or immune origin, the latter being in response to antigen leaking from a damaged tubule. In stallions, interstitial lymphocytic foci, often perivascular, are particularly common and occur in areas of tubule degeneration and vasculitis. Foci of lymphocytes in cats are considered an age-associated change.

Intratubular orchitis

Intratubular orchitis probably results from *ascending infection*. Macroscopically, solitary or multiple white–yellow foci of up to ~1 cm in diameter are seen. Histologically, the tubule outline is retained in the affected area, but the seminiferous epithelium is obliterated and replaced by numerous macrophages and multinucleated giant cells that surround neutrophils and debris (Fig. 5.29A, B). The pathogenesis of this granulomatous orchitis is comparable to sperm granuloma formation in the epididymis. Sertoli cell hyperplasia and mineralization may accompany these changes.

Necrotic orchitis

Necrotizing orchitis is characteristic of *brucellosis* but may result from other infections, or conditions causing severe trauma or ischemia of the testis. Severe periorchitis may reduce blood supply to the testis so that it dies and becomes a necrotic mass encased within the markedly thickened tunics. Necrotic areas are dry, yellow, often laminated, and slightly mineralized. The histological picture is ultimately one of coagulative necrosis bordered by fibrosis and inflammatory cells. Abscessation and fistulation through the scrotum may accompany necrotizing or other forms of orchitis.

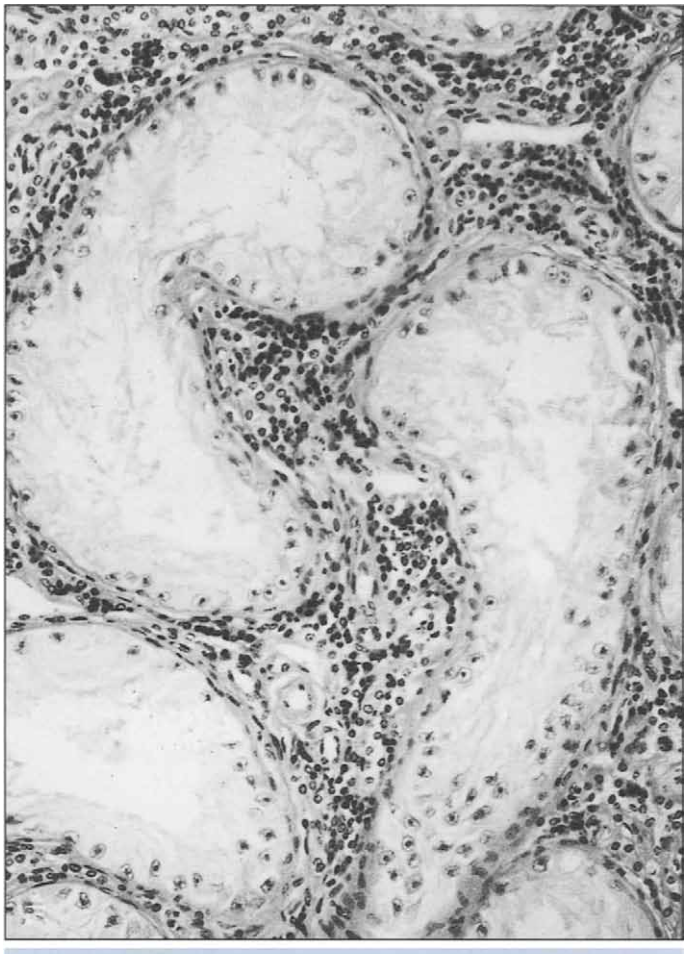

Figure 5.28 Lymphocytic infiltrates in the interstitium of a bull with **interstitial orchitis** and degeneration of seminiferous tubules.

Many infectious agents have been isolated from testes or semen of animals with orchitis, but the significance of many and perhaps most isolates is unclear.

Orchitis in bulls

In bulls, viruses have been isolated from testes or semen, but changes in the testes are observed in association with only some of them. Persistent infection with *Bovine viral diarrhea virus* causes spermatozoal defects, but no distinct histologic lesions in the testis. Severe interstitial orchitis and testicular degeneration associated with inflammation of spermatic arteries occurs in malignant catarrhal fever. In experimental bluetongue virus infection in bulls, interstitial orchitis is also associated with arteritis. Clinical orchitis and aspermatogenesis have been observed in association with enteroviral infection, but lesions are not described. A focal nodular orchitis may be observed in lumpy skin disease of bulls.

Orchitis caused by *Brucella abortus* occurs in regions of endemic **bovine brucellosis**. The live vaccine strain (strain 19) is also capable of producing the lesion. In most instances, the orchitis is acute and the lesion is irreversible. It may be unilateral but affected animals are sterile. The scrotum swells and is hot and doughy due largely to inflammatory changes in the tunics and to a lesser extent in the epididymis (Fig. 5.30). Swelling of the testis is limited by the inability of the tunica albuginea to stretch, and any swelling constricts venous and then arterial flow causing infarction. The cavity of the tunica vaginalis is distended with fibrinopurulent exudate. Scattered yellow foci of necrosis coalesce to produce total testicular necrosis. Sequestration by inflammation and thickening of the tunica soon follows. Sometimes the necrotic parenchyma liquefies and the organ then is a pus-filled cavity surrounded by a thick connective-tissue capsule. Rupture may occur but is unusual. Occasionally, the necrotic foci may not expand and coalesce but rather remain as dry areas of necrosis surrounded by a thick layer of fibrous tissue.

Microscopically, the inflammatory involvement of the tunics is similar to any serous membrane with organization resulting in adhesions between the parietal and visceral layers. These adhesions may be extremely dense. Within the testes, the infection appears to progress along the lumen of the seminiferous tubules. The seminal epithelium becomes necrotic and desquamates. Large numbers of the organisms are visible in the lumen, especially when stained by the modified Ziehl–Neelsen method. At the early stage, a variety of leukocytes invade the interstitial tissues and form cuffs about the tubules. The tubules and the interstitial tissues then become necrotic. There is often focal necrotizing epididymitis complicated by the development of sperm granulomas.

Tuberculous orchitis in bulls is an uncommon lesion, even in areas of endemic infection. The testis is less frequently involved than the epididymis or tunics. The granulomatous response to the tubercle bacilli is similar to the granulomas that occur to spermatozoa. Involvement of the testis may be either miliary or regional. In the miliary form, small or large caseous and mineralized foci are irregularly scattered throughout the testes but may spare the epididymis entirely. Broad bands of caseous necrosis radiate out from the rete testis in the more regional or diffuse form, and the epididymis is usually involved. This distribution is due to the extension of the chronic tuberculous process within the seminiferous tubules. The path of infection in such cases is probably intratubular from a primary epididymal lesion.

Other bacteria causing orchitis in bulls, sometimes in association with overt abscessation, include streptococci, staphylococci, *Arcanobacterium pyogenes*, *Escherichia coli*, *Histophilus* spp., and *Salmonella* spp. *Actinomyces bovis*, *Actinobacillus* sp., and *Nocardia farcinica* may also cause bovine orchitis. In nocardiosis, the lesions are at first nodular but ultimately transform the whole testis into an abscess, the capsule of which is the tunica vaginalis.

Infection of bulls with *Chlamydophila* spp. causes orchitis, and in field cases focal granulomatous lesions have been observed. The spontaneous occurrence of orchitis and epididymitis has been described in a bull with *Mycoplasma* sp. infection.

Orchitis in boars

Pigs experimentally infected with *Porcine rubulavirus*, a paramyxovirus that causes "blue eye," may develop orchitis and epididymitis. The virus targets the head of the epididymis where it causes interstitial inflammation and sperm granulomas. Interstitial fibrosis is seen in animals that recover. Viral antigen is seen in the epithelial cells. Seminiferous tubular degeneration and interstitial orchitis occur in some animals. *Suid herpesvirus 1* infection (pseudorabies, Aujeszky's disease) may cause edema of the scrotal region, but

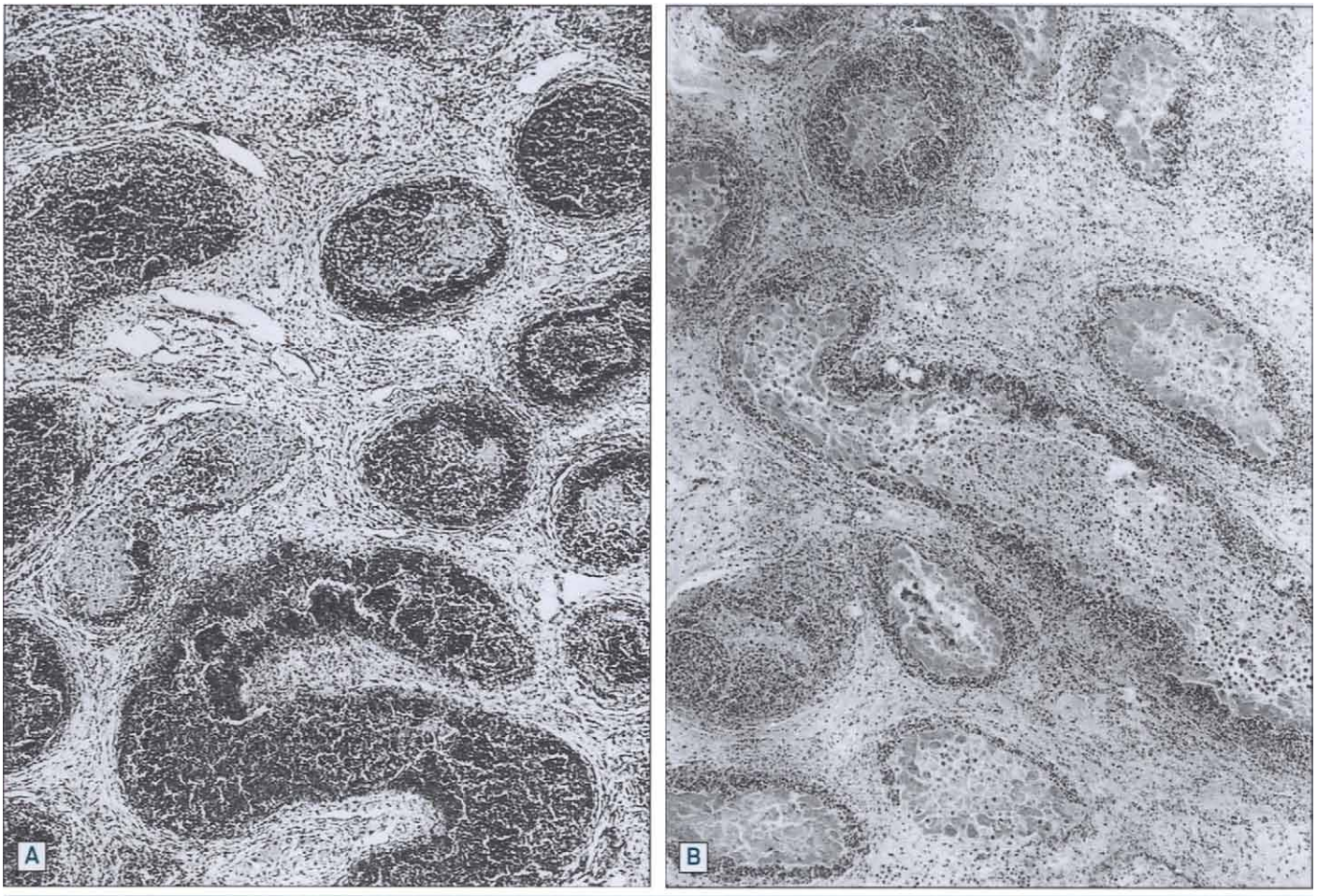

Figure 5.29 Orchitis in a bull, caused by *Brucella abortus*. **A.** The inflammatory reaction is predominantly intratubular. **B.** Necrosis of tubules and inflammatory infiltrates of leukocytes, fibrin, and edema.

results of experimental infection have varied. Viral replication occurs in the serosa after intratesticular inoculation; exudative periorchitis results. Intratesticular inoculation of boars with porcine parvovirus caused testicular degeneration. Enteroviruses and parvovirus have been isolated from semen.

Orchitis caused by *Brucella suis* results in multiple abscesses rather than confluent necrosis. Some cases have fibrinopurulent and hemorrhagic periorchitis. Abscessation develops in the epididymis as well as in the testis; there is central caseation surrounded by a zone of epithelioid macrophages, and these in turn by a broad connective-tissue capsule infiltrated by leukocytes.

In some tropical countries, orchitis caused by infection with *Burkholderia pseudomallei* occurs in boars and other small domestic animals. Lesions may also be found in the vesicular glands (seminal vesicles), prostate, and other organs. Extreme enlargement of the testis due to accumulation of purulent exudate may occur. The main histological lesion is multifocal caseous necrosis with marked mononuclear cell infiltration and encapsulation by much fibrous connective tissue. Severe testicular degeneration accompanies orchitis. Other organisms isolated from boars with orchitis include *Arcanobacterium pyogenes*, *Streptococcus zooepidemicus*, and *Streptococcus equisimilis*.

Orchitis in stallions

In stallions, mild interstitial orchitis is common. Similar lesions may be part of generalized vascular involvement in equine viral arteritis. Infarcts may also occur in equine infectious anemia. Orchitis can occur as part of systemic disease, and is reported in glanders (*Burkholderia mallei*), and as an acute suppurative, sometimes abscess-forming orchitis in infection with *Salmonella abortus-equi*, *Streptococcus equi*, and *Streptococcus zooepidemicus*. Focal lesions due to the larvae of *Strongylus edentatus* may be seen in the testis, tunics, and epididymis, especially of young horses. Cryptorchid testes are more commonly affected. Hemorrhagic 2 mm wide tracts containing the migrating larvae are seen. The histological lesions are initially hemorrhagic and then eosinophils infiltrate. *Halicephalobus gingivalis* can cause granulomatous orchitis as a consequence of systemic spread. A pseudocyst, or fluid-filled cavities that have no epithelial lining, is reported in a horse as a sequel to fibrinonecrotic orchitis. The lesion was associated with trauma and secondary infection with *Streptococcus zooepidemicus* occurred.

Periorchitis in horses occurs as part of generalized septic disease, and as a complication of trauma, penetrating injury, or surgery.

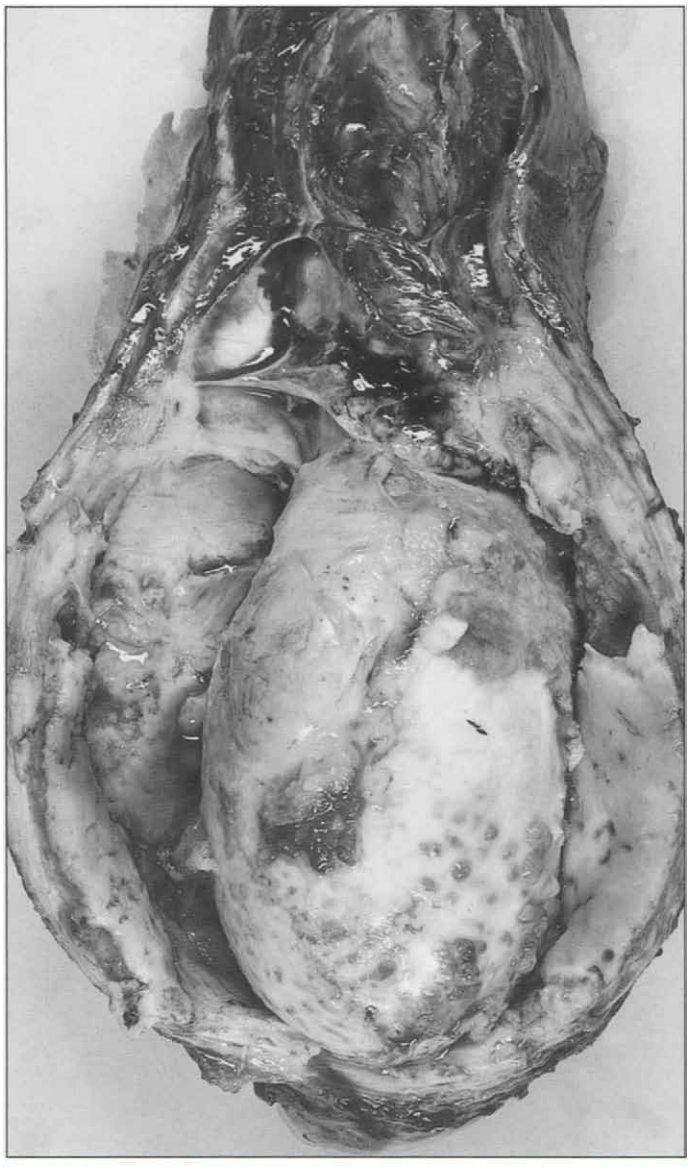

Figure 5.30 Orchitis and periorchitis in a bull, caused by *Brucella abortus*. Fibrin is adherent to tunica vaginalis, epididymis, and testis.

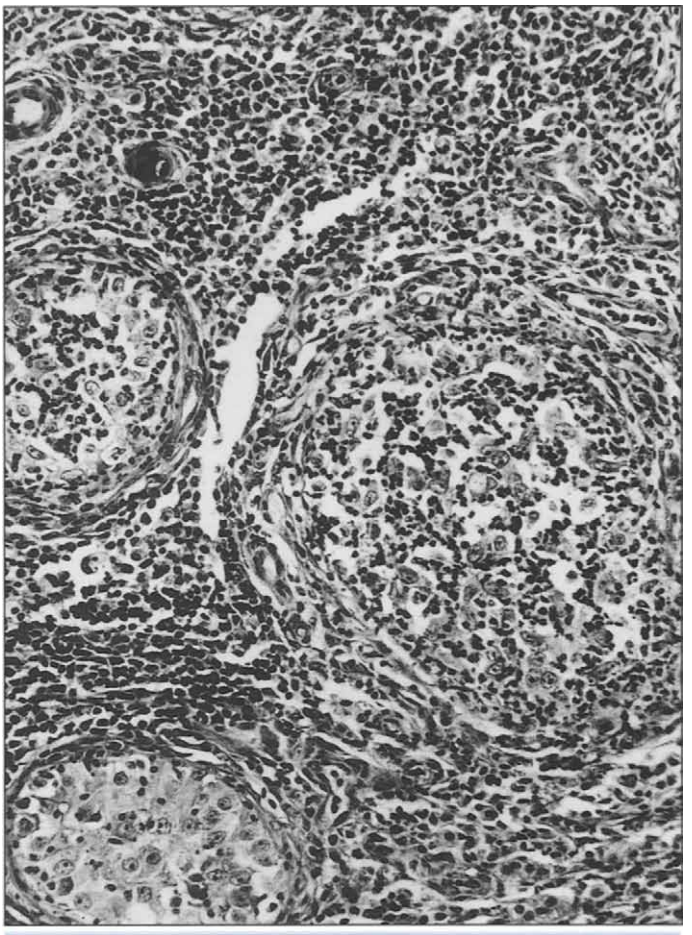

Figure 5.31 Orchitis in a dog, caused by *Escherichia coli*. There are interstitial and intratubular infiltrates of macrophages, neutrophils, and lymphocytes.

Orchitis in small ruminants

Nodular orchitis occurs in sheep pox, and chronic interstitial orchitis, but not epididymitis, has been observed in rams infected with the *Visna/maedi virus*. Sporadic testicular abscesses result from infection with *Arcanobacterium pyogenes* and *Corynebacterium pseudotuberculosis*. In bucks, orchitis, which in many respects resembles brucellosis in bulls, may result from infection with *Brucella melitensis*. Orchitis also occurs in breeding goats as a component of besnoitiosis. Orchitis in rams occurs mostly in association with epididymitis.

Orchitis in dogs and cats

In dogs, orchitis is usually accompanied by epididymitis. Intranuclear and cytoplasmic inclusions are found in the Sertoli cells in mature dogs with distemper. The majority of seminiferous tubules degenerate, and inflammation occurs in a few tubules. Penetrating wounds of the scrotum may occasionally be implicated in the pathogenesis of epididymoorchitis in the dog, but the commonest route is by reflux along the deferent duct from the bladder, urethra, or prostate of infection, chiefly by *Escherichia coli*, *Proteus vulgaris*, and other miscellaneous organisms. An acute inflammatory response in either the epididymis or testis is usually suppurative, with the formation of one or more abscesses (Fig. 5.31). The tunica vaginalis may be involved by extension of the inflammatory process, and fistulation through the scrotal skin to the exterior may occur. Alternatively, dogs will self-traumatize the scrotum and cause a fistula to develop. Acute inflammation usually is centered on the ducts, with degeneration and desquamation of the epithelium, and edema and mononuclear cell infiltrates in the surrounding stroma. Healing occurs with dense scarring, which in the epididymis will cause some tubular obstruction with spermatocele formation. Subacute and chronic inflammatory lesions present no special features. The affected testis is usually firm, small, and irregular, although the epididymis may be enlarged and woody. Lymphocytes and plasma cells now predominate and fibrosis is well developed. Neutrophils predominate in the lumen of the epididymal tubules.

Other bacterial causes of orchitis in dogs are *Brucella canis* and *Burkholderia pseudomallei*, both of which are associated with epididymitis (see below). A familial occurrence of interstitial, lymphocytic orchitis, associated with testicular atrophy and reduced fertility, has

been observed in inbred Beagle dogs with lymphocytic thyroiditis; immune factors have been implicated.

Orchitis in **cats** is very rare and may be a manifestation of feline infectious peritonitis. Periorchitis is also a presenting complaint in feline infectious peritonitis and in traumatic injury to the scrotum; orchitis can be a sequel to these conditions.

Bibliography

Foster RA, et al. Chronic fibrinous and necrotic orchitis in a cat. Can Vet J 1997;37:681–682.

Holyoak GR, et al. Pathological changes associated with equine arteritis virus infection of the reproductive tract in prepubertal and peripubertal colts. J Comp Pathol 1993;109:281–293.

McEntee K. Reproductive Pathology of Domestic Mammals. London: Academic Press, 1990:224–358.

Njenga MJ, et al. Semen characteristics of goats with subacute, acute and chronic besnoitiosis. J S Afr Vet Assoc 1999;70:18–20.

Ramirez-Mendoza H, et al. Lesions in the reproductive tract of boars experimentally infected with porcine rubulavirus. J Comp Pathol 1997;117:237–252.

Sigurdardottir OG, et al. Orchitis in a cat associated with coronavirus infection. J Comp Pathol 2001;124:219–222.

Van Camp SD. Common causes of infertility in the bull. Vet Clin North Am Food Anim Pract 1997;13:203–231.

Epididymitis

Inflammation of the epididymis is one of the more common inflammatory diseases of the genitalia, but frequently it is diagnosed clinically as "orchitis." Regardless of cause, damage to the epididymal duct is complicated by the formation of sperm granulomas and subsequent development of epididymitis. The exception is in prepubertal animals where there are no spermatozoa; in these cases, true abscesses occur. Epididymitis in the absence of sperm granulomas is possible in adults, but it usually is a subclinical or early event.

Epididymitis is often *infectious*, and infectious disease frequently causes a spectrum of lesions, including inflammation of the accessory genital glands. The effects of epididymitis are so much more dramatic than prostatitis, vesicular adenitis, or ampullitis that these latter manifestations are often overlooked. *Sterile epididymitis* does occur, and is caused by congenital ductal anomalies, adenomyosis, trauma, and the reflux of urine.

Bacteria cause most infections of the epididymis, although viruses such as *Equine arteritis virus* and others are reported to induce epididymitis.

Primary infection with *Brucella* spp. in each species results in epididymitis. *Brucella ovis*, *B. canis*, *B. melitensis*, and *B. suis* are especially virulent for the epididymis. It is assumed that the infection is systemic and the bacterium localizes in the epididymis.

Direct infection of the epididymis by penetrating injury is a rare event. Secondary infection from periorchitis, or peritonitis is an occasional possibility.

Almost all species develop infection of the epididymis by the ascending route. This has been studied in the ram where *Actinobacillus seminis* and *Histophilus somni* (*Haemophilus somnus*/*Histophilus ovis*) are common isolates. While the exact mechanism is not known, it seems that preputial organisms migrate to the accessory genital glands and infect the epididymis by retrograde movement. The privileged environment of the lumen of the epididymal duct allows the organisms to infect the organ and incite damage. The formation of sperm granulomas means that the reproductive potential of the affected side is lost. Complete return to normal is rare. In the dog, the sequel of self-trauma of the scrotum, and systemic affects of infection with endotoxin-producing bacteria such as *Escherichia coli* further complicate epididymitis by causing systemic illness.

Local immunity to prevent epididymitis is not likely to be achieved in the short term. The epididymis has no natural local immune system of antigen receptors, nor known recirculation of immunocytes, and no local plasma cell population. Some aggregates of lymphocytes are occasionally seen in otherwise normal animals. After infection, the epididymis must develop a local immune system, but unfortunately, the damage is usually so extensive, and the sequel so severe, that the response is too late. Even so, the epithelial cells do have the ability to express MHC I and II, and lymphocytes and plasma cells can be recruited after challenge.

Once initiated, the course of epididymitis is variable. The acute stage with edematous enlargement may be followed by abscess and sperm granuloma formation, sometimes with perforation, periorchitis and peritonitis, and increasing fibrosis.

Macroscopically, an increased epididymal size and dissymmetry in shape is apparent especially in unilateral cases in comparison with the contralateral side. Fibrinous and then fibrous adhesions may be present between affected epididymis and adjacent tunics. Consistency will depend on duration of inflammation and the development of sperm granulomas. In chronic epididymitis, the marked increase in fibrous tissue both within the epididymis and between the epididymis and tunics results in atrophy of epithelial elements and the recognizable epididymis becomes hard and nodular, perhaps enclosing dilated remnants of epididymal duct (Fig. 5.32). Distinct hard "sperm stones," the end products of spermiostasis, may be present within such ducts. Concurrent testicular atrophy will also result in the epididymis appearing disproportionately large in relation to the testis.

Histologically, affected epididymal ducts contain fibrin, neutrophils, and spermatozoa in various stages of disintegration, damaged epithelium, macrophages, and multinucleate giant cells, many of which contain spermatozoa. Other features of sperm granuloma, with prominent interstitial accumulation of lymphocytes and plasma cells, become apparent (Fig. 5.33). Epithelial hyperplasia, with the development of intra-epithelial lumina has been observed in most domestic species in association with epididymitis, but such lumina also occur in noninflammatory lesions. In chronic epididymitis, squamous metaplasia of epithelium may also occur in affected ducts in association with progressive fibrosis, and there may be hypertrophy of smooth muscle surrounding ducts.

Epididymitis may also be caused by sperm granulomas resulting from congenital ductal anomalies, adenomyosis, trauma, and infections.

Epididymitis in bulls

Infectious and immunologic causes of epididymitis in bulls are largely the same as those for orchitis, but bulls develop a specific infectious epididymitis, so-called epididymitis-vaginitis ("epivag"), first described in Kenya and later in South Africa. Lesions in the bull consist of initial soft swelling of the epididymis with subsequent enlargement and fibrosis. Associated lesions are "abscess" formation, tunic adhesions, ampullitis and vesicular adenitis, and testicular degeneration. Sometimes, however, the vesicular glands only are

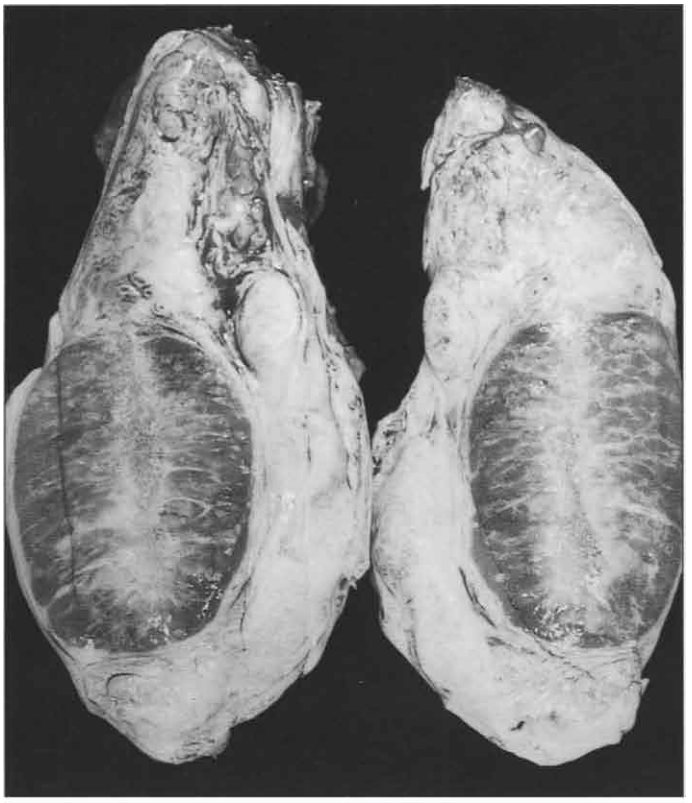

Figure 5.32 Chronic epididymitis in a bull, with marked epididymal fibrosis, adhesion of the tunica vaginalis, and marked testicular atrophy.

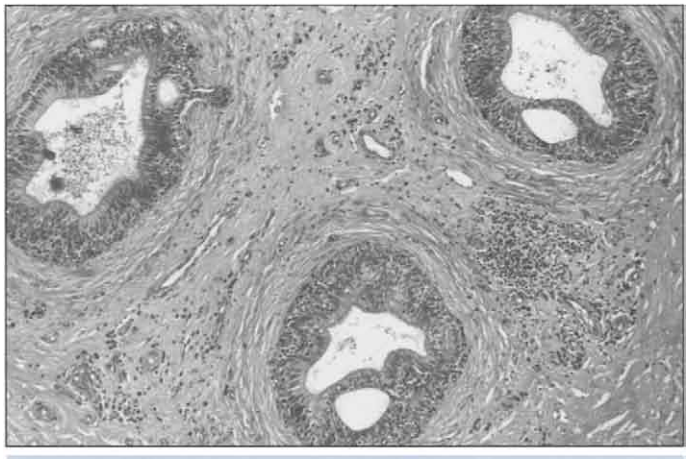

Figure 5.33 Chronic epididymitis in a ram, with interstitial fibrosis and epididymal epithelial hyperplasia and intraepithelial lumina formation.

affected. The possible role of a herpesvirus in the pathogenesis of "epivag" is discussed in Vol. 3, Female genital system.

Brucella abortus rarely causes epididymitis in the absence of orchitis. *Actinobacillus seminis*, a frequent cause of epididymitis in rams, has been isolated from the semen of a bull with bilateral epididymitis. Epididymitis has been observed in bulls with vesicular adenitis induced by inoculation of *Mycoplasma bovigenitalium*, but the roles of mycoplasmas and chlamydias in causing epididymitis await clarification. Epididymitis may accompany orchitis, periorchitis, and testicular degeneration in cattle, sheep, goats, horses, and dogs infected with *Trypanosoma brucei*.

Epididymitis in small ruminants

Epididymitis is of particular importance in rams, in which it is a frequent and serious cause of reduced fertility. Although one of two organisms *Brucella ovis* or *Actinobacillus seminis* are usually associated with the condition, many other bacteria, such as *Histophilus somni*, *Mannheimia haemolytica*, *Escherichia coli*, and *Arcanobacterium pyogenes* have been isolated from cases of epididymitis. Whereas *Brucella ovis* is a cause of epididymitis in mature rams, other gram-negative pleomorphic organisms are found more commonly in epididymitis in virgin rams, suggesting the existence of two separate disease entities, dependent upon sexual experience of the animal.

Ovine epididymitis caused by *Brucella ovis* is an important cause of reduced fertility in many countries and has been extensively studied. Progression of the disease is very slow, from a local infection persisting in the exposed mucous surface for 1 month, to a regional one involving adjacent lymph nodes, leading to bacteremia. The bacteremic stage appears to subside after about 2 months, but organisms localize in the genital tract, spleen, kidney, and liver where they persist for an indefinite period. Following experimental infection, neither gross nor microscopic lesions are seen in organs other than genitalia.

In approximately 90% of epididymides with lesions caused by *Brucella ovis,* the epididymal tail is involved, and lesions in this location probably occur in all epididymides infected with this organism. Initial localization of the bacteria produces edema, and lymphocytic and macrophage infiltration. Later, neutrophils are added when spermatozoa enter the interstitium. Early epithelial changes include hyperplasia and hydropic degeneration, with the formation of intraepithelial lumina (Fig. 5.33). At the same time there is increasing fibrosis in interstitial areas. The combination of fibrosis and epithelial hyperplasia obstructs the lumen and causes spermiostasis. These changes develop over many months, and large numbers of organisms are excreted in the ejaculate. Subsequent events depend on the extravasation of spermatozoa and formation of sperm granulomas. The tail of the epididymis in these cases may be enlarged 4–5 times (Fig. 5.34), and the lesion is often bilateral. If the extravasated spermatozoa enter the cavity of the tunica vaginalis, adhesions will result and testicular degeneration increases. Unlike brucellosis in the bull, there is no primary orchitis. Lesions in the deferent duct similar to those in the epididymis may occur, but are not associated with sperm stasis or leakage. There is pronounced epithelial hyperplasia, with thickening and folding of the wall, and the lamina propria is densely infiltrated with lymphocytes, plasma cells, and histiocytes. Unfortunately for control purposes, many rams do not develop detectable gross lesions or they develop them only late in the course of the disease. Identification of *B. ovis* in histological sections is difficult, but can be aided by immunohistochemistry.

Actinobacillus seminis and related strains of the so-called gram-negative pleomorphic organisms also induce epididymitis (Fig. 5.35). These bacteria consist principally of *Histophilus somni* (*Histophilus ovis*) and *Actinobacillus seminis*. Both *H. somni* and *A. seminis* are temporarily resident in the prepuce and become opportunistic pathogens by ascending infection, under appropriate conditions, such as those resulting at puberty from elevated levels of LH and FSH releasing hormones. The pathogenesis of *E. coli* epididymitis in rams probably is similar. Typically, these are acute infections that occur mostly in young rams, and there may be severe and diffuse periorchitis. In epididymitis caused by *Actinobacillus seminis,* there is abscessation of one

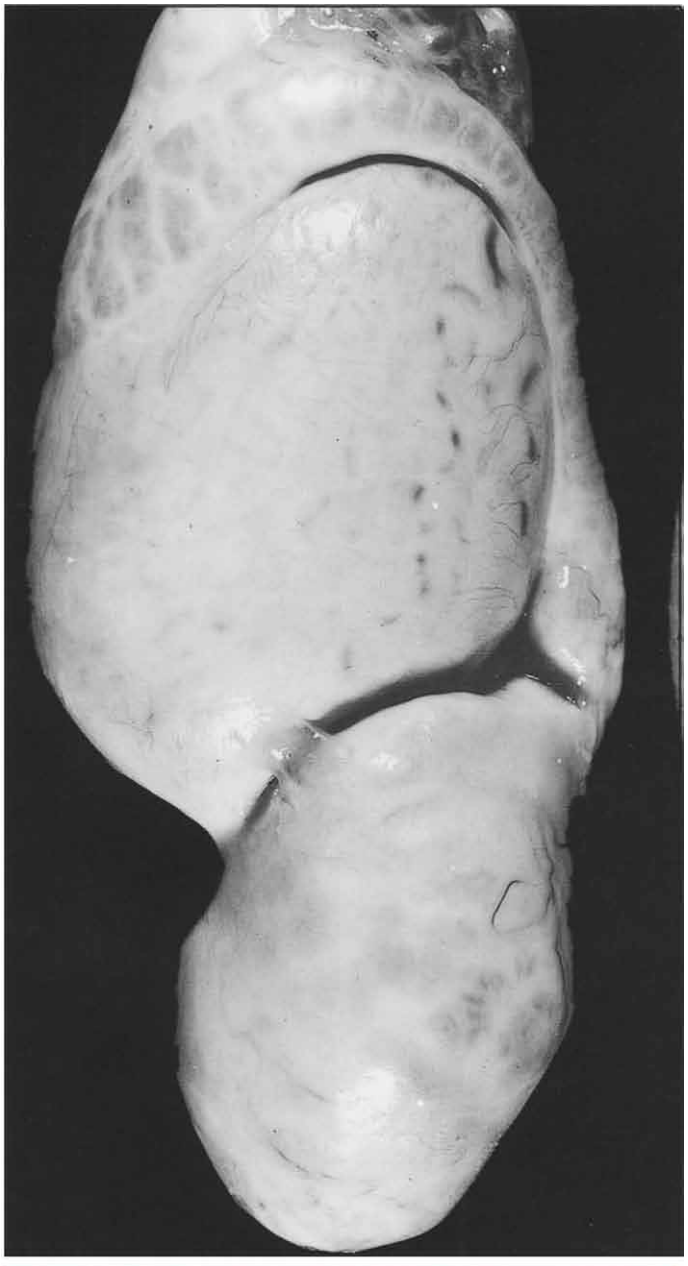

Figure 5.34 Chronic epididymitis in a ram, caused by *Brucella ovis*. The epididymal tail is enlarged with fibrosis and sperm granulomas (not visible). The testis is also atrophic.

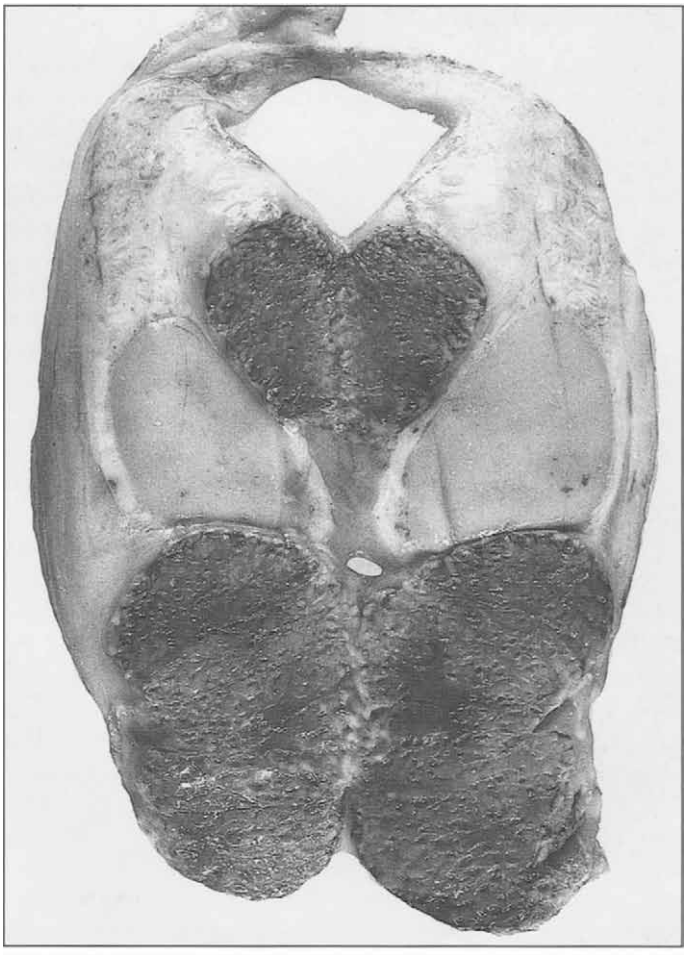

Figure 5.35 Acute epididymitis caused by *Actinobacillus seminis* in a ram. (Courtesy of KL Hughes.)

or both epididymides, and these may fistulate through the scrotal wall. Histologically, the initial epididymal lesion is similar to that of *Brucella ovis*, being characterized by intraepithelial lumina. In the chronic form of the disease seen in older rams, the epididymides are enlarged and fibrotic, and the testes are atrophic. The vesicular glands or prostate also may be affected. Experimental inoculation of rams by various routes with *Actinobacillus seminis* has shown that part of or the entire genital tract may become infected, but that the epididymis is most constantly involved.

Lesions in the epididymis caused by *Histophilus somni* are similar. The disease occurs sporadically, is sometimes accompanied by a febrile response, and the most frequent lesion is a large multilobulated abscess affecting one epididymis. The abscess cavities contain much fluid and green-yellow flocculent material, often with lumps of necrotic material. Fibrous adhesions of the tunics also occur. In early cases with epididymal abscessation, the deferent duct is usually patent and contains pus and spermatic fluid but in older cases that part of the epididymis adjacent to the deferent duct is usually empty and has grossly fibrosed walls. Microscopically, the early response is severe suppurative inflammation involving the walls of epididymal tubule. In appropriately stained sections, numerous bacteria can be demonstrated in intraluminal necrotic debris. Subsequently, infection may extend to the stroma, so that in chronic cases there is extensive interstitial epididymitis with much fibrosis. As with brucellosis, the testis is only involved secondarily.

Epididymitis is less studied in **bucks** than in rams. *Brucella melitensis*, *Actinobacillus seminis*, *Staphylococcus aureus*, *Escherichia coli*, or *Pseudomonas* spp. may be isolated from lesions, and there is a report of possible *Brucella ovis* epididymitis in an angora goat.

Epididymitis in boars

In boars, the macroscopic lesions caused by *Brucella suis* infection are quite variable. Single or multiple "abscesses" are frequent in the epididymis, but less so in the testes, which may be enlarged or atrophic. Enlargement of the vesicular glands due to localization of *B. suis* may also occur, and abscessation, perhaps seen only microscopically, occurs in the vesicular glands and prostate and bulbourethral glands.

Epididymitis in dogs and cats

In male dogs infected with *Brucella canis,* there is epididymitis, prostatitis, scrotal dermatitis, and testicular atrophy. These changes can be unilateral. Infected animals are bacteremic and the organism can persist in certain tissues, particularly the prostate, for many months, but recovery can eventually occur and recovered dogs are immune to reinfection. Venereal transmission to females by infected males can occur, although the organism is not consistently isolated from semen. Scrotal swelling is apparent 1–2 weeks after experimental intravenous inoculation, or 3–5 weeks after oral infection. Such swelling is caused by accumulation of fibrinopurulent exudate in the cavity of the tunica vaginalis. Scrotal ulceration is the result of persistent licking of the scrotum caused by the pain of epididymitis. Testicular abscesses are seldom if ever observed but testicular necrosis (as observed in the bull) may occur rarely, and is accompanied by marked fibrous thickening of tunics.

Microscopically in such cases, there is coagulative necrosis with a predominantly mononuclear, reparative response in peripheral areas where necrotizing vasculitis and associated thrombosis may also occur. More frequently, however, histological findings are those of interstitial epididymitis and prostatitis, and testicular atrophy. Lymphocytic infiltration of epididymal stroma is variable. Fibrosis may be extensive but, in contrast to brucellosis in other species, obliteration or stricture of ducts is unusual. Lymphocytes, neutrophils, and macrophages are present in the epididymal duct. In chronic cases, there is marked enlargement of the epididymis, especially the tail, with possible spread of inflammation to the deferent duct. As well as containing inflammatory cells and an increased percentage of abnormal spermatozoa, the ejaculate of male dogs with chronic brucellosis contains spermatozoa agglutinins, and the resulting infertility may, in part, be mediated by isoimmune reactions resulting from the heightened nonspecific phagocytic activity of inflammatory cells attracted to the sites of bacterial growth in the epididymis. *Brucella suis* also may cause spontaneous granulomatous epididymitis and prostatitis in the dog.

Escherichia coli or other gram-negative bacteria cause most sporadic cases of canine epididymitis (Fig. 5.36). The epididymitis caused by these agents is often seen as an acute disease and the dogs may be systemically ill with endotoxemia. Scrotal swelling and mutilation is relatively common. Following infection of dogs with *Burkholderia pseudomallei*, epididymitis, orchitis, and scrotal edema may occur in association with pyrexia, depression, swelling of one or more limbs, and lameness. Macroscopically, the epididymides are enlarged to perhaps 3–4 times normal size, are firm and hemorrhagic, and may contain small abscesses or necrotic foci. The testis and deferent duct may also be involved.

Mycoplasma canis can cause urinary tract infection in dogs, with subsequent purulent epididymitis and prostatitis.

Mycotic epididymitis caused by *Rhodotorula glutinis* or *Blastomyces dermatitidis* produces granulomatous epididymitis with a reaction pattern similar to disease in other tissues. The complication of sperm granulomas adds to the granulomatous nature of the disease.

Epididymitis occurs in sexually mature dogs with *canine distemper.* The histological appearance is similar to that seen in epididymitis of other causes, but, in addition, cytoplasmic and intranuclear inclusions are present in the epithelial cells. Some care is necessary to differentiate the specific inclusions from the eosinophilic cytoplasmic bodies normally present in the head of the epididymis and from the intranuclear bodies that are present in normal dogs; immunohistochemistry will differentiate inclusions in question.

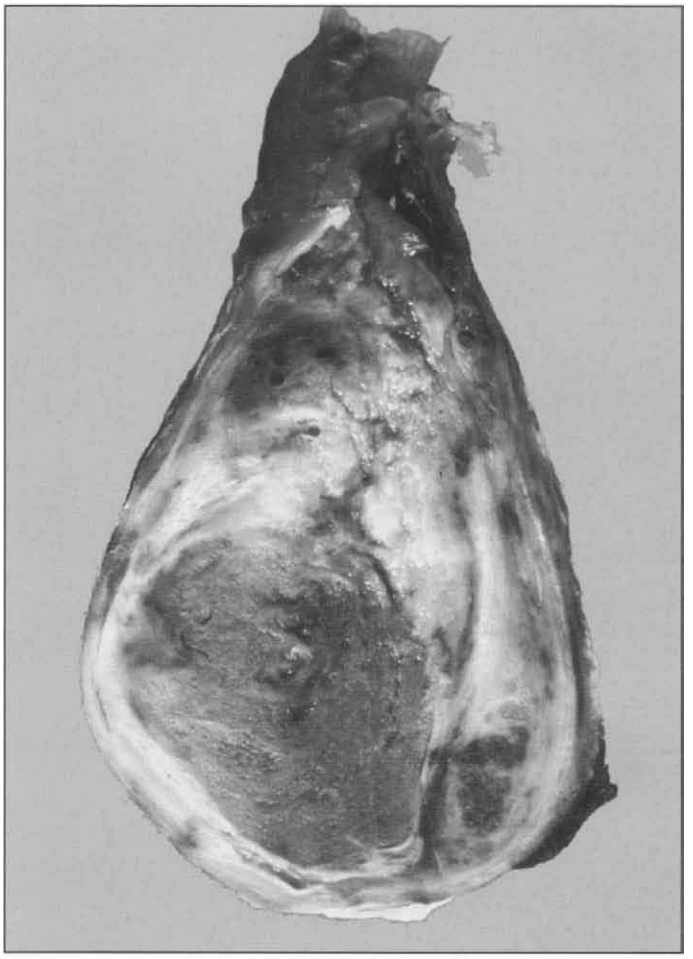

Figure 5.36 Severe **epididymitis and periorchitis** in a dog. The tail of the epididymis is large and edematous, and there is fibrin and exudate in the cavity of the tunica vaginalis.

Epididymitis is exceedingly rare in **cats**. It has been seen as fibrinonecrotic vasculitis and epididymitis in association with genital involvement in feline infectious peritonitis. Ascending epididymitis also occurs.

Epididymitis in stallions

In the stallion, migrating strongyle larvae are considered a likely cause of epididymitis and sperm granuloma of the epididymis; adenomyosis has been shown to be a further cause. Rare sporadic cases of bacterial epididymitis are also reported. *Streptococcus zooepidemicus* has been isolated from such cases.

Bibliography

Blue MG, McEntee K. Epididymal spermatic granuloma in a stallion. Eq Vet J 1985;17:246–251.

Cerri D, et al. Epididymitis by *Brucella ovis*: experimental infection in virgin ram lambs. New Microbiol 1999;22:227–231.

Constable PD, Webber JJ. *Escherichia coli* epididymitis in rams. Aust Vet J 1987;64:123.

Fodor L, et al. Purulent epididymitis in a sucking lamb caused by *Pasteurella haemolytica*. Acta Vet Hung 1987;35:427–431.

Foster RA, et al. Identification of *Brucello ovis* in formalin fixed paraffin embedded genital tissues of naturally infected rams by the indirect peroxidase antiperoxidase technique. Aust Vet J 1988;65:324–326.

Hajtos I, et al. Ovine suppurative epididymo-orchitis caused by *Histaphilus ovis*. J Vet Med B 1986;33:528–536.

Healy MC, et al. Comparison and partial characterization of the protein profiles and outer membrane antigens of *Actinobacillus* species isolated from ram lambs with epididymitis. Am J Vet Res 1988;49:1824–1831.

Held JP, et al. Bacterial epididymitis in two stallions. J Am Vet Med Assoc 1990;197:602–604.

Holzmann A, et al. Orchiepididymitis in a bull with *Mycaplasma* in its ejaculate. Zbl Vet Med A 1983;30:760–766.

Kadota K, et al. Granulomatous epididymitis related to *Rhodatorula glutinis* infection in a dog. Vet Pathol 1995;32:716–718.

L'Abee-Lund TM, et al. *Mycoplasma canis* and urogenital disease in dogs in Norway. Vet Rec 2003;153:231–235.

Metz AL, et al. Chronic suppurative orchiepididymitis associated with *Haemophilus somnus* in a calf. J Am Vet Med Assoc 1984;184:1507–1508.

Saravanamuthu V, et al. T and B lymphocyte subsets in spermatic granuloma in the ram. Vet Pathol 1991;28:482–491.

Vermeulen SO, et al. *Brucella ovis* as a possible cause of epididymitis in an Angora goat. J S Afr Vet Assoc 1988;54:177–179.

Wanke MM. Canine brucellosis. Anim Reprod Sci 2004;82–83:195–207.

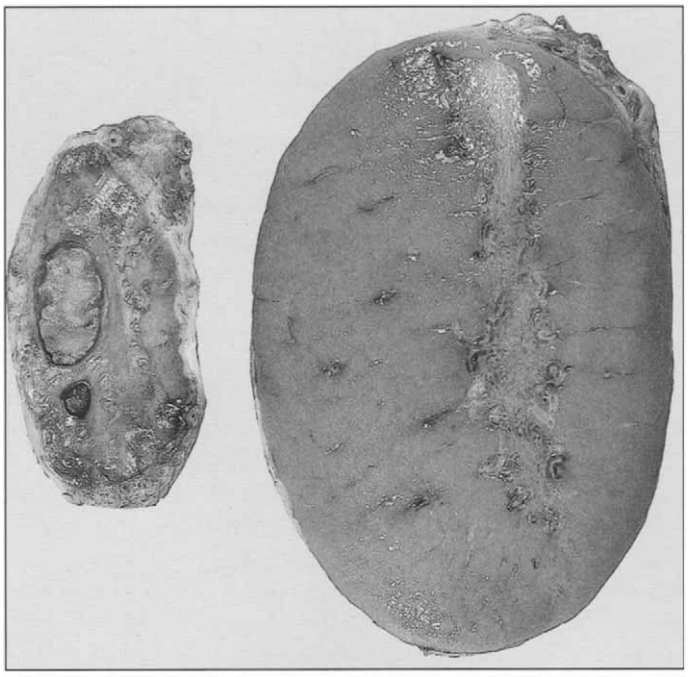

Figure 5.37 Atrophy and infarction of the left testis of a bull due to compression of the spermatic cord while removing tissue for biopsy. The right testis is normal.

Circulatory disturbances

The spermatic artery is very long because of the coiled portions proximal to the testis. The degree of coiling varies between species, being quite pronounced in ungulates, in which the spermatic artery is several meters long. Testicular blood flow is low in relation to metabolic needs, and hypoxia develops quickly if increasing testicular temperature increases metabolic demand or if blood flow is impaired. By the time the artery penetrates the tunica albuginea, pulsatile flow is almost eliminated and the structure of the vessel changes. The diameter enlarges, the wall becomes thinner, and the elastic fibers are reduced. Increased intratesticular pressure will have dramatic effects on circulation.

The interstitial tissue of the testis is richly supplied with *lymphatics*. In addition to the usual role in fluid exchange, they probably assist in transportation of hormones between interstitial endocrine cells and the tubules. Edema of the testis occurs after trauma and is a frequent early change in orchitis. Although the tunica albuginea is relatively indistensible, some enlargement can occur and serous fluid drips from the cut surface. There is distinct separation and dilation of tubules, diffuse vacuolation of germinal epithelium, and dilation of lymphatics.

Hyaline degeneration of the walls of arterioles is associated with wedge-shaped areas of fibrosis in the testes of old bulls, but the precise cause of this lesion is not clear. In old dogs, hyaline degeneration of both arterioles and arteries accompanies testicular degeneration. Initial lesions occur in the tunic and parenchyma, but larger vessels in the spermatic cord are subsequently involved. Focal areas of infarction may occur as a result of severe vascular lesions. Atheromatous lesions are rare; in dogs they may indicate hypothyroidism or diabetes mellitus.

Thrombosis of testicular arteries, usually of unknown cause, is seen occasionally in bulls. Such thrombi are present in both the parenchyma and tunics and may be partially mineralized and sometimes occluding. The mild degenerative changes in germinal epithelium in association with thrombi emphasize the good collateral circulation. In experimental *Trypanosoma vivax* infection in sheep, thrombosis of testicular vessels probably contributes to testicular degeneration. Subsequent infarction and necrosis may sometimes occur. Occluding venous thrombosis has been observed in the testes of rams. Some had a concurrent varicocele; testicular degeneration associated with such thrombi was mild.

Inflammation of the testicular artery occurs frequently in the horse. The known causes are migrating strongyle larvae and *Equine arteritis virus*, but the cause is not established in many cases. The usual morphologic manifestations in testicular tissue include focal infiltration of lymphocytes and degeneration of seminiferous tubules adjacent to the inflamed arteries and arterioles. The inflammatory reaction is rarely of such a severe degree as to cause thrombosis and infarction. Horses infected with *Equine arteritis virus* may have an acute lesion with a necrotic vasculitis, edema, and hemorrhage. Chronic cases will have lymphocytic vasculitis and perivasculitis.

A striking *vasculitis* with marked interstitial epididymitis, orchitis, and testicular degeneration occurs in malignant catarrhal fever in buffaloes and bulls in association with generalized vasculitis. Dogs may develop vasculitis as part of a localized or generalized polyarteritis, and it may occur in systemic necrotizing vasculitis ("Beagle pain syndrome").

Occlusion of the testicular artery with resulting ischemia of the testis may result from torsion, contusion of the spermatic cord, inappropriate placement and/or hypotension during surgery, or the use of an emasculatome for castrating young lambs and calves (Fig. 5.37). Experimentally, destruction of germinal epithelium can be

demonstrated after ischemia of more than 1 hour. Necrosis of testicular parenchyma follows after 4–6 hours, although spermatozoa are relatively resistant to lysis and may retain their staining characteristics for weeks or months. Following ligation of the spermatic artery in prepubertal rams, however, revascularization of the tunica albuginea occurs by penetration of capillaries from the epididymal arteries. Islets of seminiferous tubules associated with the tunic (Moskoff's islets) may thus survive, and considerable regeneration occurs during the ensuing months. As the regenerated tubules lack a normal drainage system, there is spermiostasis and ultimately degeneration.

Torsion *of the testis is rare unless there is incomplete descent.* The stallion appears to be the exception, as spontaneous torsion is a recognized cause of "colic." In dogs especially, testicular neoplasia is often also present, to provide sufficient weight to maintain the torsion. The usual clinical presentation is acute abdominal pain, and the testis is blackened due to venous infarction, and is sometimes unidentifiable as testis. Spontaneous torsion of the cryptorchid testis of boars is seen commonly at slaughter. Torsion with complete ischemia and infarction will cause complete loss of spermatogenesis of the affected testis. Correction of torsion in laboratory animals and humans can save the testis, but some continue to be aspermatogenic even if infarction does not occur. Interstitial endocrine cells and Sertoli cells retain their ability to function, but reactive oxygen species may induce germ cell apoptosis and loss.

Bibliography

Holyoak GR, et al. Pathological changes associated with equine arteritis virus infection of the reproductive tract in prepubertal and peripubertal colts. J Comp Pathol 1993;109:281–293.

Parker JE, Rakestraw PC. Intra-abdominal testicular torsion in a horse without signs of colic. J Am Vet Med Assoc 1997;210:375–357.

Turner TT, et al. Acute testicular ischemia results in germ cell specific apoptosis in the rat. Biol Reprod 1997;57:1267–1274.

Neoplasms of the testis and epididymis

Testicular neoplasms are most commonly found in the dog. There is no satisfactory explanation for this, but intact dogs are allowed to live as long as they are able, and they tend to be watched closely. Male cats tend to be castrated early and fewer of those that are intact live to old age. Neoplasms arise in all species sporadically, and with the exception of the dog, it is possible to predict the histologic type of neoplasm based on species and age. Seminoma is the common tumor of the aged horse, and teratoma is more common in the young. Cats, boars, rams, and bucks rarely get testicular neoplasms, and both seminoma and Sertoli cell tumor are reported. Bulls are more likely to have interstitial cell tumors, but Sertoli cell tumors are also reported.

The three main testicular neoplasms of dogs are the Sertoli cell tumor, the interstitial (endocrine) cell tumor, and the seminoma. The fourth most common, but still rare, is a mixed germ cell and stromal cell neoplasm. Multiple types of neoplasia may be found in one testis. *Most primary testicular neoplasms in dogs are benign.* Exceptions are rare, but malignant Sertoli cell tumors and seminomas are reported. Identification of metastasis in lymphatics, spermatic cord, lymph node, or distant sites is the only way to determine that the neoplasm is malignant; there are no good cytological or histologic markers of malignancy.

Most neoplasms cause enlargement of the testis. In general, seminomas are white, soft, and usually bulge on cut section. Sertoli cell tumors induce fibrous tissue so they are white and are tough. The interstitial cell tumor is yellow, often contains areas of hemorrhage, and is soft. *Sertoli cell tumors, and rarely interstitial cell tumors, may produce a hyperestrogenism syndrome and feminization.* In dogs, this is usually manifested by attractiveness to other male dogs, gynecomastia, and alopecia. Prostatomegaly and squamous metaplasia of the prostate also occur. Affected animals return to normal after removal of the neoplasm. The signs are not always associated with estrogen production and not all dogs will have a raised serum estrogen concentration. In these instances, inhibin secretion by the neoplastic Sertoli cells inhibits the secretion of FSH and LH by the pituitary, which, in turn, inhibits testosterone production and presumably alters the ratio of estrogen to testosterone. Some animals will develop bone marrow suppression, and poorly responsive pancytopenia. Feminization is much more common when the neoplasm is larger, and therefore is more common in cryptorchid dogs. It is also in these dogs that the unfortunate sequel of testicular torsion can occur.

Testicular tumors are seen mostly in mature and old animals; the occurrence of interstitial cell tumors in dogs is especially age associated. Canine testicular tumors are found more frequently in the right than in the left testis, and this is also true for the cryptorchid testis.

Other neoplasms of the testis include the *mixed germ cell–sex cord–stromal neoplasms* that have been reported in the horse and dog, *rete adenoma and adenocarcinoma*, and *embryonal carcinoma* in the horse.

Metastasis of neoplasms to the testis is rare. Lymphoma in the horse, dog, and bull, and hemangiosarcoma in the boar and dog are reported. The list will no doubt increase in length if pathologists routinely examine the testes at all necropsies.

Epididymal neoplasms are exceedingly rare. Ectopic interstitial cell tumors have been described in the cat. Lymphoma or any other systemically metastatic neoplasm may affect the testis and epididymis.

Gonadal stromal tumors

Interstitial (Leydig) cell tumor

Interstitial cell tumors are derived from the endocrine cells of the testicular interstitium. They are grouped with Sertoli cell tumors in being derived from tissue of the sex cords or stroma. Lesions that are less than 1 cm in diameter may be hyperplasia, although this distinction may have little biologic significance.

In the dog, interstitial cell tumors are found chiefly in older animals. It also occurs in the bovine testis, is found in the older age groups, and mainly in Guernseys. In horses, the tumor develops almost exclusively in cryptorchid testis. There are very few reports of testicular neoplasia in boars, but interstitial endocrine cell hyperplasia and tumor are more common than the others.

Normal interstitial endocrine cells produce androgens, and some interstitial cell tumors of dogs have been shown to produce excess androgen, but *most tumors do not cause signs of hyperandrogenism.* Signs of hyperestrogenism have been observed in a few dogs with interstitial cell tumors and estradiol concentration in testicular venous blood of affected dogs may be elevated. The condition has been corrected by removal of the neoplasm. However, in dogs,

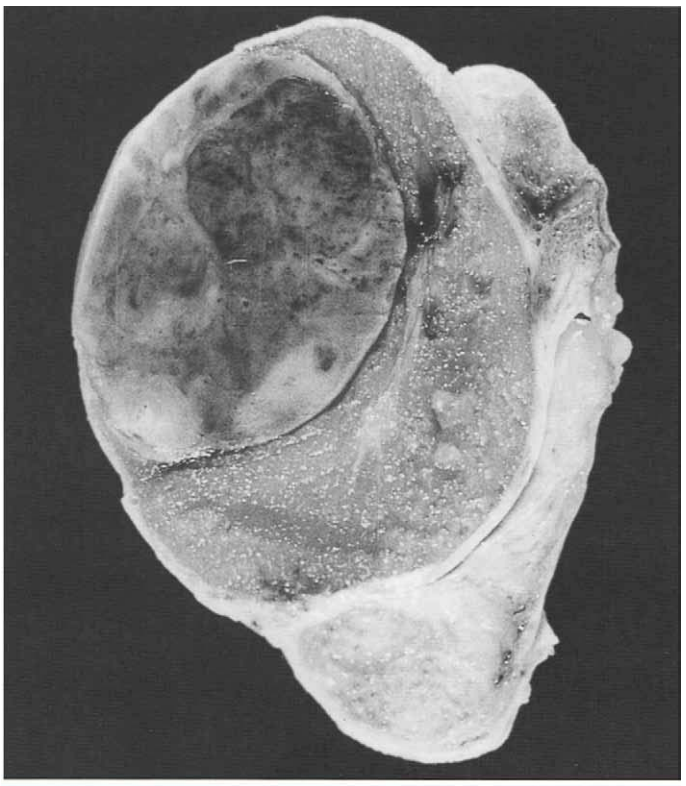

Figure 5.38 Intratesticular **interstitial cell tumor** in a dog. These are soft and tan, with regions of hemorrhage.

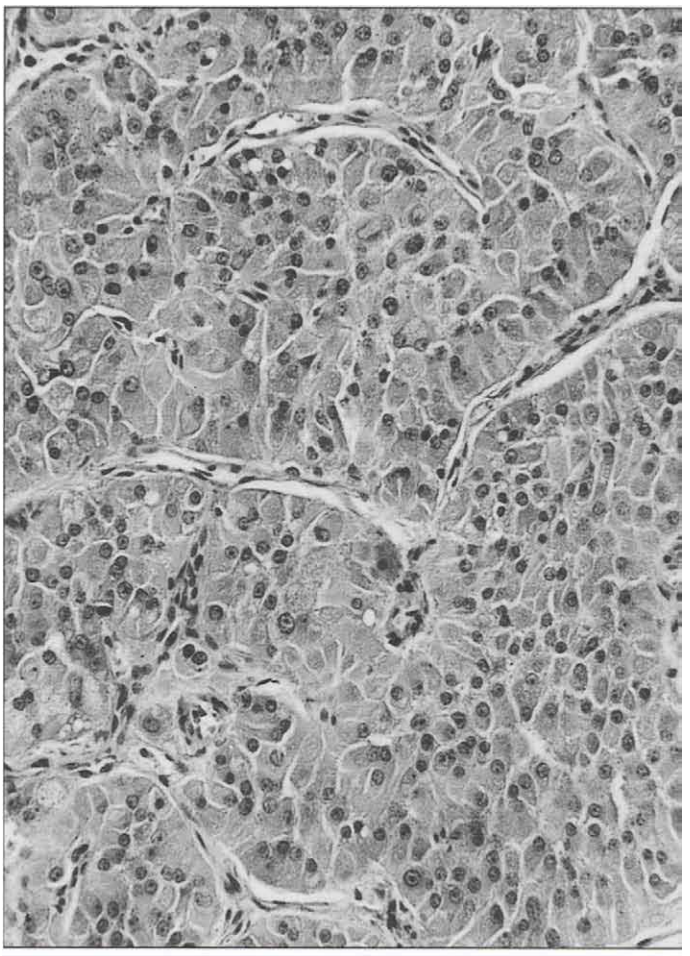

Figure 5.39 Endocrine pattern, with large polygonal cells packed into groups by a fine fibrous stroma, of an **interstitial cell tumor** in a dog.

a common association is with perianal gland neoplasia, tail gland hyperplasia, and prostatic enlargement, which suggests that secretion of excess androgens also occurs.

Interstitial cell tumors in stallions have been seen most often in undescended testes. They contain two cell types; the first is essentially a hypertrophic interstitial endocrine cell but the other is a pleomorphic fusiform cell with fibrillar, vacuolated cytoplasm and indistinct borders. Hormone determinations have not been reported on horses with these tumors, but viciousness, which was corrected by castration, has been observed.

A high incidence of telangiectasis of the liver, thyroid C (parafollicular) cell tumors, and infertility has been observed in Guernsey bulls with interstitial cell tumors, but it is not known whether the lesions are in any way interdependent or possess a common denominator.

Nodular hyperplasia is probably a preneoplastic change in some instances of interstitial cell tumor of the dog. The hyperplastic nodules occur principally in testes that have undergone senile atrophy and, although they may be macroscopically visible, the nodules are small, nonencapsulated, and consist of an increased number of interstitial endocrine cells in the intertubular stroma. The apparent diffuse hyperplasia of interstitial endocrine cells in cryptorchid and hypoplastic testes does not predispose to the development of tumors. In both nodular and diffuse hyperplasia, the hyperplastic cells are regular in form and size with increased acidophilia of the cytoplasm and without mitoses.

Interstitial cell tumors in the dog are often multiple, but may be solitary and unilateral or bilateral (Fig. 5.38). Commonly they are from 1 mm to 2 cm or more; only exceptionally are they large enough to increase the size of the organ, but they may lend the organ an irregularity in contour, the rounded bulge of the tumor being visible in an otherwise small, soft, atrophic testis. On cut surface, the tumors are well demarcated but only lightly encapsulated, spheroidal, and yellow. The tumor is predisposed to hemorrhage which causes dark discoloration, and to cyst formation in areas. Even a large tumor may be obviously composed of confluent nodules indicating multicentricity of origin, and this is readily apparent in the form of discrete tumors when they are small. The consistency is soft, there being little stroma, and the cut surface is slightly greasy.

Interstitial cell tumors grow slowly and expansively with surrounding compression atrophy, and often with a thin condensed capsule. They are not notably invasive. In bulls with interstitial cell tumors, semen production and fertility may be reduced.

Typically, the component cells in the dog are rather respectable interstitial endocrine cells, being round or polyhedral, with abundant cytoplasm that may be granular or vacuolar and that often contains yellow lipochrome pigment (Fig. 5.39). The neoplastic cells in the bull are not vacuolated and contain very little lipid. Sometimes and in some tumors, the cells have a more mesenchymal appearance, being spindle-shaped with indistinct cytoplasmic outline and a streaming arrangement. It is in such tumors especially that necrosis and cyst formation occur. The nuclei are regular in size and staining affinity, and mitoses are rare. The stroma is scant, supporting a capillary network, but occasionally suffices to give the tumor an endocrine appearance.

Intranuclear cytoplasmic invaginations or inclusions have been observed consistently in up to 15% of neoplastic cells in canine interstitial cell tumors. The inclusions, which are strongly PAS-positive and which are composed of smooth and rough endoplasmic reticulum, vesicles and lipid vacuoles, myelin figures, and disrupted membranous profiles, have not been demonstrated in other testicular tumors. Nuclei containing these invaginations are enlarged. Except where invaginations are present, the ultrastructural appearances of neoplastic and normal interstitial endocrine cells in the dog are similar.

Sertoli cell tumor

The Sertoli cell tumor is rare in domestic species other than the dog, but has been observed in the bull, horse, ram, and cat. These tumors often cause enlargement of the affected testis, and there is, sometimes, the development of a *feminization syndrome* in the host. The feminizing effect of these tumors is due to either their high content of estrogen or to secretion of inhibin. The degree of differentiation of the neoplastic cells will influence the content of hormone but, usually, it is larger tumors that are responsible for feminizing syndromes, which suggests that the mass of the tumor is related to the quantity of hormone elaborated. The attractiveness of affected dogs to other male dogs is well known, but a hyperestrogenism syndrome also is manifest as reduction of libido, female distribution of body fat, cutaneous and pilosebaceous atrophy leading to symmetrical alopecia, atrophy of testes and penis, an estrogenic form of mammary development, swelling of the prepuce, and hyperplasia or squamous metaplasia of the prostate, which may be accompanied by perineal hernia. Prostatic metaplasia can progress to the stage where quite large keratin accumulations fill glandular lumina. Enlargement of the seminal colliculus with partial obstruction of the urethral lumen may also accompany prostatic changes in these dogs.

As well as feminization, there may be *depression of bone marrow activity* with resultant clinical signs of hemorrhage caused by thrombocytopenia, anemia caused by blood loss and/or diminished erythrocyte production, and infection and fever associated with granulocytopenia. Recovery may follow castration and supportive therapy.

The gross appearance of a Sertoli cell tumor can be quite distinctive. The larger tumors are somewhat irregularly ovoid, lobulated and enclosed in a tense tunica albuginea (Fig. 5.40). The cut surface bulges and usually is white and quite firm or even hard, although sometimes it may be discolored or cystic. *The firmness of the tumor is due to the abundance of its stroma*, something the other two common types of tumor have in small amounts only.

Although metastasis of Sertoli cell tumor to the regional lymph node is unusual, local extension of neoplastic tissue into the testicular vein and associated lymphatics may result in hydrocele with massive swelling of the scrotum.

Histologically, Sertoli cell tumors may be of two types, either intratubular (with or without invasion as determined by penetration of the basement membrane) or diffuse. *There seems to be little correlation, however, between histologic type and metastasis.* Stroma is always plentiful, and it may be hyalinized. The stromal tissues are commonly arranged to provide a tubular pattern in which the neoplastic cells tend to palisade. Such arrangements to some degree can be found in most Sertoli cell tumors (Fig. 5.41A, B). In the early and well-differentiated tumors, the cells resemble normal Sertoli cells, being rather elongate

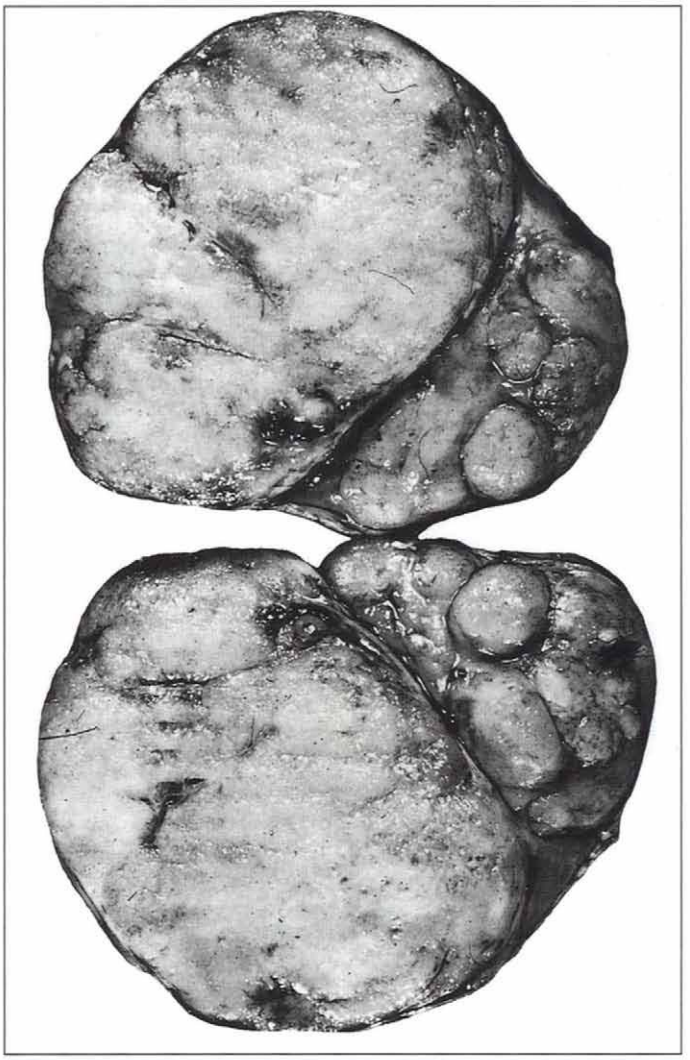

Figure 5.40 Malignant **Sertoli cell tumor** in a dog. Presence of metastasis is the only criterion to differentiate malignant from benign neoplasia.

with foamy acidophilic cytoplasm and small, basally situated, dark-staining nuclei. In less differentiated varieties, the cells are still elongate and possess eosinophilic cytoplasm, but the nuclei are elongate and pleomorphic and no longer basally located against the trabecular pole (Fig. 5.41A, B). In the less common form of the tumor, the cells show little or no tendency to palisade but are discrete and spherical with well-defined eosinophilic cytoplasm and some nuclear irregularity. Mitoses are sparse. Lipids are demonstrable in the neoplastic cells as large droplets and globules in more differentiated tumors and as fine droplets in the least differentiated tumors.

Sertoli cells are reported to be the only cells of the testis that stain immunohistochemically with antibody to neuron-specific enolase, wherein the stain is intracytoplasmic. They stain diffusely intracytoplasmically with vimentin (as do interstitial endocrine cells). Cytokeratin stains are negative. There are varied reports of staining with other antibodies, including S100, melan A, and inhibin. Because of the conflicting results from different laboratories, it is not possible to generalize about their staining characteristics.

Ultrastructural examination of canine Sertoli cell tumors reveals that the characteristic specific intercellular junctions and crystals of

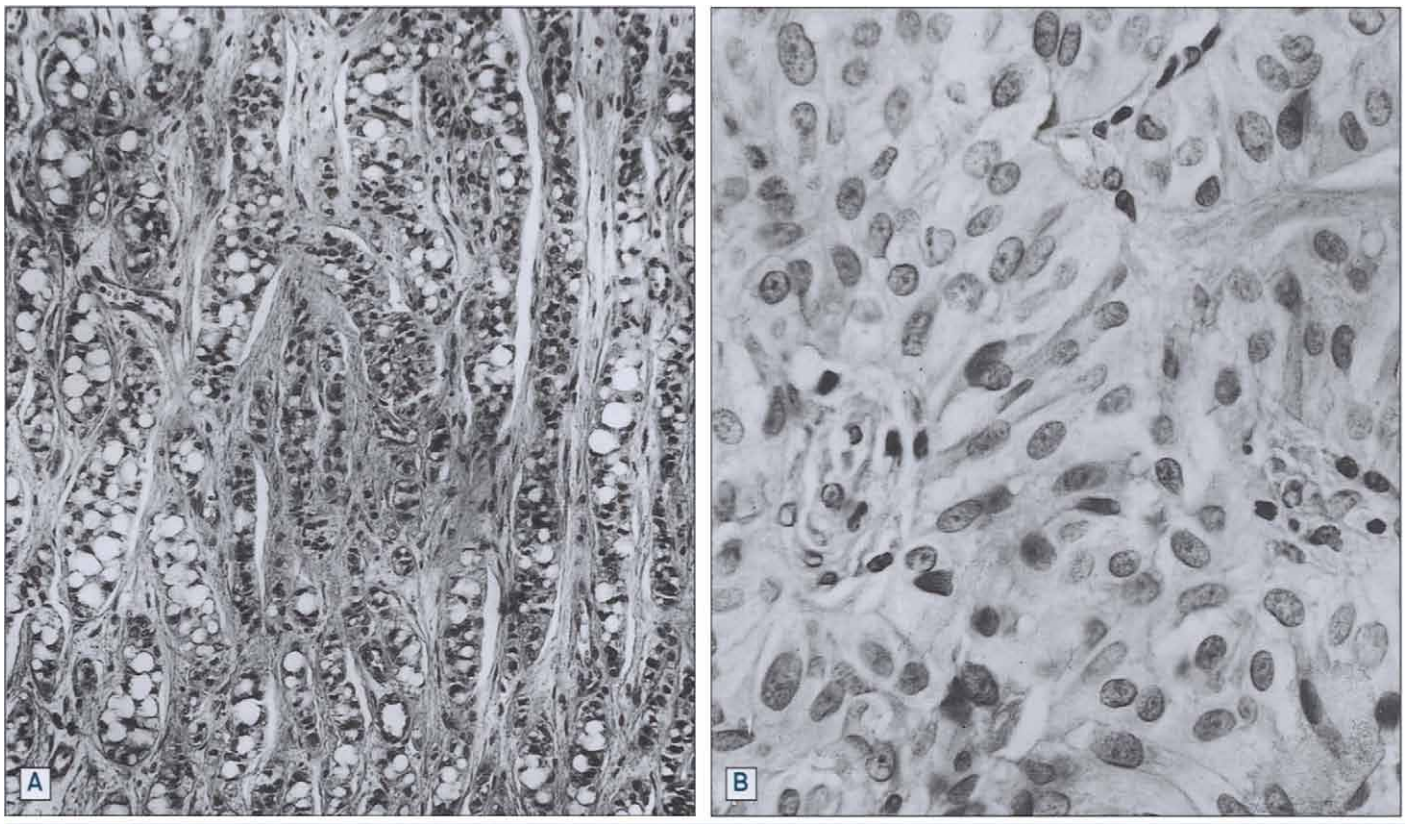

Figure 5.41 A. Histological appearance of **Sertoli cell tumor** in a dog showing tubular structures separated by abundant fibrous tissue. **B.** On higher magnification, the cells tend to bridge from one side of the tubular structure to the other.

Charcot–Bottcher do not occur in neoplastic cells. Nevertheless, a number of common features do persist so that these and the abundant intracytoplasmic organelles permit differentiation from interstitial cell tumors and seminomas. Prominent intercellular gap junctions have been observed in a Sertoli cell tumor in the dog and it is possible that these were induced by the hormonal activity of the tumor.

Early age of slaughter of most food animals precludes studies on true tumor occurrence with increasing age. However, in one study, in which **bulls** and buffaloes were kept until 9–14 years for draft purposes, 20 of 161 testes examined contained neoplasms; all but one were Sertoli cell tumors. Seven tumors were in undescended testes. In contrast to Sertoli cell tumors in the dog, those in cattle have been observed in newborn or young calves with sufficient frequency to suggest that impaired embryogenesis, possibly of genetic origin, might have some role in causation. In support of this suggestion is the presence, in some bovine Sertoli cell tumors, of laminated intratubular concretions resembling those seen in bovine testicular hypoplasia and cryptorchidism. Moreover the simultaneous occurrence of Sertoli cell tumor and epididymal aplasia has been observed. One described bovine Sertoli cell tumor was in a testis of an animal in which castration by the burdizzo method had been attempted 5 years previously. In general, the gross and microscopic appearance of Sertoli cell tumors in the bull resembles those in the dog (Fig. 5.42A, B). Metastasis of Sertoli cell tumor in the bull has not been observed, and there is no clear evidence of hyperestrogenism.

In **rams**, occasional Sertoli cell tumors, comparable to those in the bull, have been observed. Hyperplastic Sertoli cells occur in cryptorchid rams (Fig. 5.43), but whether these could potentially develop into neoplasms seems unlikely, given the rarity of the tumors.

One case of Sertoli cell tumor in a **stallion** involved the single descended testis; a ductal pattern of neoplastic Sertoli cells, which contained clusters of distinct hyaline bodies, was evident.

Germ cell tumors

Seminoma

Seminomas are common in canine testes and have also been observed in the stallion (and mule), ram, buck, and bull. They occur in *older animals* and are disproportionately common in cryptorchid testes. They arise from cells of the spermatogenic series, presumably from basal spermatogonia, and they are usually multifocal of origin in the affected testes. These tumors do not produce hormones. They are not often malignant, but are probably more so than either of the other two types. However, *they tend to be locally invasive* and there are no known factors to predict the metastatic potential of seminomas.

Seminomas often attain a size of 6 cm or more before removal, and by then the stretched tunica albuginea encloses neoplastic tissues only. Sudden enlargement of the testis, and pain caused by hemorrhage and necrosis in the tumor, are often the presenting signs in dogs. In all species, the sectional surface is coarsely lobulated by a few fine trabeculae, the color is usually white or gray-white, and the texture is soft to moderately firm (Fig. 5.44). If lightly squeezed, a milky fluid may exude from the cut surface. The texture and color closely resemble that of neoplastic lymphoid tissue.

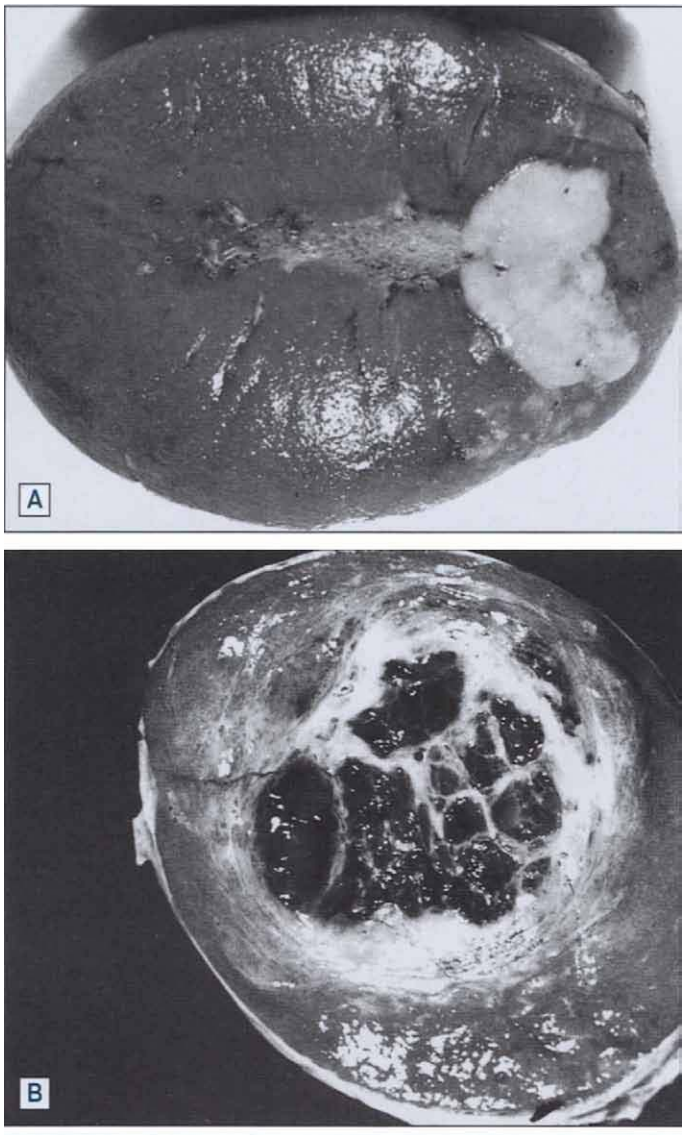

Figure 5.42 Sertoli cell tumor in a bull. Macroscopic appearance varies from (**A**) a solid to (**B**) a cystic type. (Both courtesy of J Comp Pathol.)

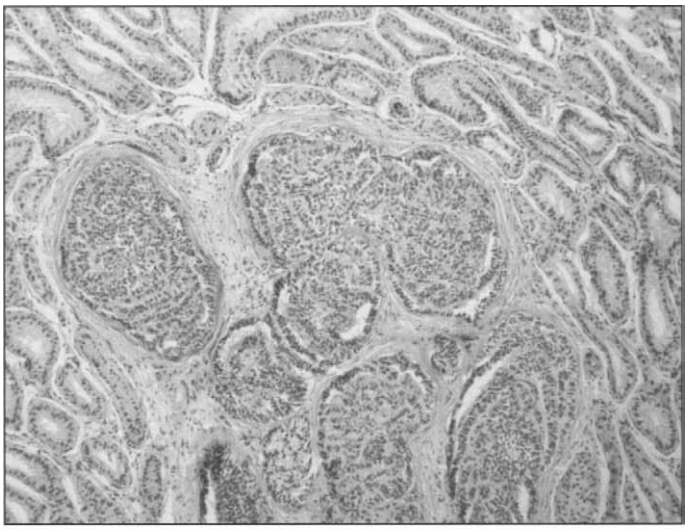

Figure 5.43 Focal **Sertoli cell hyperplasia** in the cryptorchid testis of a ram.

Microscopically, intratubular, and diffuse types are recognized. The earliest development of the tumor is intratubular and even in some large specimens intratubular growth is still evident and undoubtedly comprises one method of spread (Fig. 5.45A). Rupture of the tubules soon occurs and the growth becomes confluent, forming broad sheets of closely packed cells with scant supporting stroma. There is only slight cytological variation from tumor to tumor. The cells are large and polyhedral and fairly discrete, with a rim of visible cytoplasm that may be basophilic or eosinophilic (Fig. 5.45B). The nuclei are large and rounded and usually strongly chromatic with one or more large acidophilic nucleoli. In some tumors, the nuclei are larger and vesicular but still regular in shape, and the cells are closely packed with scant or invisible cytoplasm. In many seminomas, it is possible to find scattered mono- or multinucleate giant cells with abundant granular acidophilic cytoplasm. *Focal or diffuse accumulations of CD8+ lymphocytes occur in most seminomas and are a useful distinguishing feature.* Whereas atrophy of tubules at the edge of the tumor is normally evident, occasional foci of marked intratubular spermatogonial proliferation and early seminoma formation in this location are sometimes seen.

Germ cells stain by immunohistochemistry with *vimentin* in a perinuclear pattern, but they are negative for neuron-specific enolase and cytokeratin.

When examined by electron microscopy, tumor cells in canine seminoma resemble normal germinal epithelium and are characterized by a relative scarcity of cytoplasmic organelles, oval nuclei, straight cell borders, and distinct Golgi complex. Intercellular bridges, as seen in normal germinal cells, are present in seminomas. In all cases, the cells are markedly distinct from cells of interstitial or Sertoli cell tumors.

Presumably because abdominal location of seminomas in retained testes precludes their early clinical recognition, they may become quite large and metastasize widely. In the stallion, seminomas up to 9 kg have been found, and metastasis to most parts of the abdominal cavity and also the thoracic cavity, has been observed.

Intratubular seminomas have been reported in mature and aged rams with testicular degeneration. The proliferating spermatogonia are confined to the seminiferous tubules and do not attain sufficient size to be recognized on gross examination. It appears that this may be a dysplastic rather than a neoplastic process. A similar dysplastic process in otherwise degenerate testes is also observed in dogs. Several such foci occur in the organ, the affected tubules being slightly dilated and the abnormal cells distinctively large, rounded or polyhedral, usually multinucleate, and with pigments in the cytoplasm. Rarely, a highly malignant form of seminoma occurs in the ram, producing overall enlargement of the testis, and hemorrhage, necrosis, and massive neoplastic infiltration of the entire testis.

Seminomas are exceedingly rare in boars and cats.

Teratoma

Teratoma of the testis is a neoplasm that is virtually unknown in domesticated mammals other than the horse, in which it is the most frequently reported testicular tumor in the young animal. Equine teratoma is a benign tumor found in the scrotal, or more often, cryptorchid testis of young animals. It is probable that its presence in a fetal testis would prevent normal descent. There is a report of testicular teratoma that caused partial obstruction of the colon in a neonatal foal.

Macroscopically, teratomas are single or multiple and quite varied in color and texture. They are usually less than 10 cm in diameter

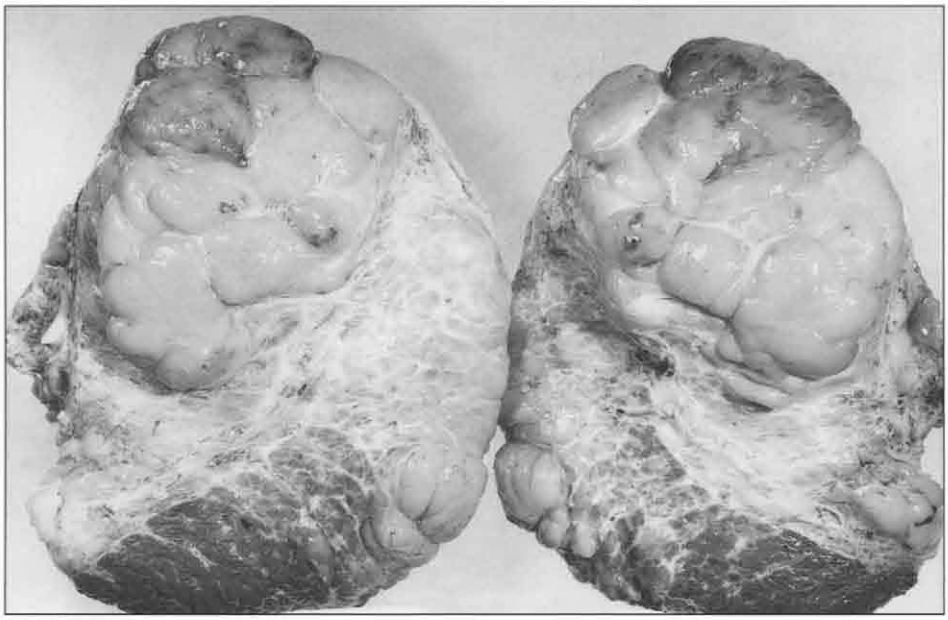

Figure 5.44 Multinodular appearance of a **seminoma** in a horse. The neoplastic tissue varies from white to tan, and can be firm. The adjacent testis is atrophic.

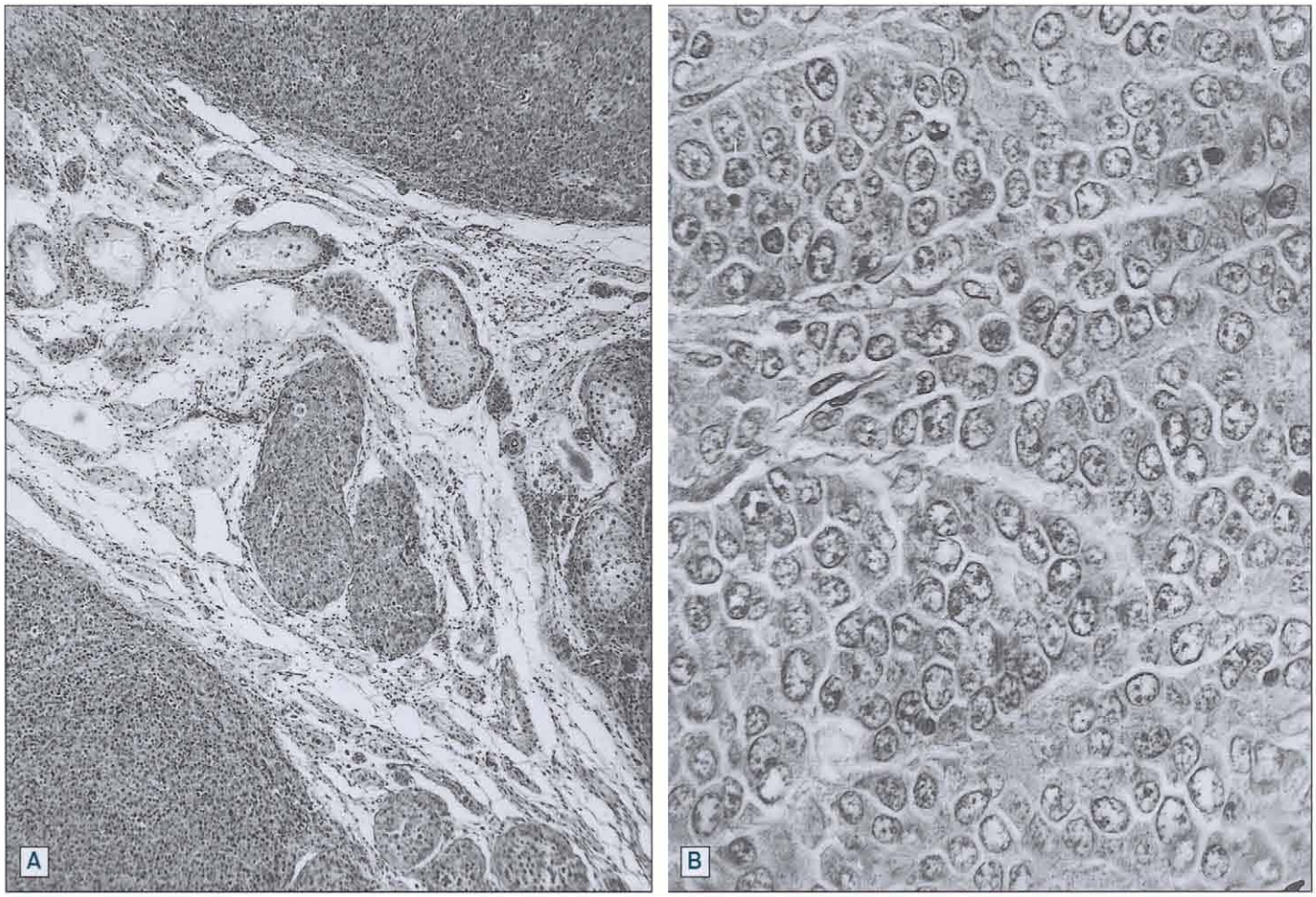

Figure 5.45 A. Seminomas usually have a combination of diffuse and intratubular growth. The adjacent testis may be atrophic as was the case in this horse. **B.** Histologically, the cells are large round cells with scant cytoplasm and large nuclei with prominent nucleoli. Mitoses are frequent.

but may be greater than 25 cm. A cystic and/or multilocular structure is common and, on section, hair and mucoid or sebaceous-like secretions are often seen, hence frequent use of the term "dermoid cyst." Yellow-white solid masses with fibrous, adipose, cartilaginous, and bony tissue are also frequent.

Histologically, *structures derived from all embryonic germ layers may be present*, including ectodermal (dermoid cysts, hair, teeth), neuroectodermal (nervous tissue, melanoblasts), entodermal (salivary gland, respiratory), or mesodermal (fibrous or adipose tissue, bone, muscle). Nervous tissue is almost always present, and adipose tissue is also very common. Testis adjacent to a teratoma may show reduced spermatogenesis, with various degrees of tubular atrophy. The histogenesis of gonadal teratoma is discussed in Vol. 3, Female genital system.

Embryonal carcinoma

Embryonal carcinoma is rare in animals but is of significant frequency among the germinal tumors of humans in which it is highly malignant. It is probably best regarded as belonging, histogenetically, with the teratomas but not displaying the tissue differentiations that identify the teratoma. The cells are of indifferent embryonic types. Trophoblastic differentiation and demonstrable α-fetoprotein in the epithelial cells supports the diagnosis.

Teratocarcinoma, a neoplasm with features of teratoma and embryonal carcinoma, is reported in the horse.

Mixed germ cell–sex cord stromal tumor

These neoplasms are a combination of germ cells and cells derived from either the primitive sex cords or the stroma of the gonad. *Gonadoblastoma* is another name for this neoplasm. There is a suggestion that these have been missed and, hence, underreported. The lesions grossly are firm, white to tan, and expansile. Larger neoplasms may be hemorrhagic. *The histological features are a combination of seminoma and Sertoli-like cells with tubular structures intimately associated with germ cells.* Immunohistochemical staining with neuron-specific enolase for Sertoli cells and with vimentin for germ cells may confirm the dual nature of this neoplasm.

Other primary tumors

Adenomas and adenocarcinomas presumably originating from the rete testis are described in dogs and horses. These are tubulopapillary structures with scant supporting stroma. The papillae and anastomosing tubules are lined by small closely packed cells with scant cytoplasm either in single or multiple layers. Evidence of transformation from normal to neoplastic rete epithelium is a useful criterion for diagnosis, and it is desirable to exclude other teratomatous structures or distant primary tumor elsewhere. Immunohistochemically, cytokeratin is stainable in epithelium of the rete testis.

Reports of *mesenchymal tumors* of the testis are mostly of individual cases. They include leiomyoma and leiomyosarcoma, hemangioma and hemangiosarcoma, mast cell tumor, peripheral nerve sheath tumor, and histiocytic sarcoma, to name a few.

Neoplasia of the epididymis is a very rare event. Any tissue may transform, and metastatic neoplasia or involvement of systemic neoplastic conditions such as lymphoma may occur. Interstitial cell tumor of the epididymis of the cat is a recognized disease and arises from ectopic interstitial endocrine cells.

Bibliography

Bazzo R, et al. Sertoli cell tumour with Call-Exner-like bodies in a dog. J Vet Med A Physiol Pathol Clin Med 2002;49:535–537.

Brinsko SP. Neoplasia of the male reproductive tract. Vet Clin North Am Equine Pract 1998;14:517–533.

Kennedy PC, et al. Histological classification of tumors of the genital system of domestic animals. WHO International Histological Classification of Tumors of Domestic Animals, Series 2, vol III. Washington, DC: AFIP, ARP, 1998.

McEntee K. Reproductive Pathology of Domestic Mammals. London: Academic Press, 1990:230–231.

McEntee MC. Reproductive oncology. Clin Tech Small Anim Pract 2002;17:133–149.

Mischke R, et al. Blood plasma concentrations of oestradiol-17β, testosterone and testosterone/oestradiol ratio in dogs with neoplastic and degenerative testicular diseases. Res Vet Sci 2002;73:267–272.

Patnaik AK, Mostofi FK. A clinicopathologic, histologic and immunohistochemical study of mixed germ cell-stromal tumors of the testis in 16 dogs. Vet Pathol 1993;30:287–295.

Peters MA, et al. Ageing, testicular tumours and the pituitary-testis axis in dogs. J Endocrinol 2000;166:153–161.

Peters MA, et al. Use of antibodies against LH receptor, 3β-hydroxysteroid dehydrogenase and vimentin to characterize different types of testicular tumour in dogs. Reproduction 2001;121:287–296.

Radi ZA, et al. Rete testis mucinous adenocarcinoma in a dog. Vet Pathol 2004;41:75–78.

Reis-Filho JS, et al. Bilateral gonadoblastomas in a dog with mixed gonadal dysgenesis. J Comp Pathol 2004;130:229–233.

Taniyama H, et al. Immunohistochemical detection of inhibin-α, -βB, and -βA chains and 3β-hydroxysteroid dehydrogenase in canine testicular tumors and normal testes. Vet Pathol 2001;38:661–666.

Weaver DM, et al. Bilateral testicular interstitial cell tumour in an aged boar. Vet Rec 2000;146:224.

Miscellaneous diseases of the testis and epididymis

Sperm granulomas occur at any location that spermatozoa may be found. The most recognized syndrome is *sperm granuloma of the epididymal head*, a condition believed to be associated with blind-ending efferent ductules (see Ductular anomalies). It has been seen in virtually every species, except perhaps the cat.

Adenomyosis of the mesonephric ducts is a histological finding where *diverticula of the epithelium of the efferent ductule, epididymis, or deferent duct protrude through the muscular wall.* Spermatozoa may become entrapped and ultimately incite an inflammatory reaction. Hyperestrogenism may be an inciting cause. Adenomyosis is the suspected underlying defect when a sperm granuloma is found in a location apart from where blind-ending efferent ductules would be expected. Virtually every species has been reported to develop adenomyosis of the mesonephric duct.

The **rete testis** is a series of interconnected channels that join the seminiferous tubules to the efferent ductules. It has intratesticular and extratesticular segments. Spermatophagia occurs in this area, and immune reactions to spermatozoa may be manifested by inflammation in this region. There are two main primary diseases of the rete: *neoplasia and cyst formation.* The epithelial cells are the origin of adenomas and adenocarcinomas in horses, dogs, and other species. Cysts of this region are reported in the stallion, cats, and

Figure 5.46 Dilation of rete tubules and the mediastinum testis secondary to obstruction and increased pressure caused by sperm granuloma of the epididymal head in a ram.

Figure 5.47 Varicocele with thrombosis in a stallion. The grossly dilated and thrombosed pampiniform plexus causes a large multilobular mass above the testis in the spermatic cord.

dogs. Secondary dilation of the rete testis occurs with obstruction of the efferent ductules or epididymis (Fig. 5.46).

SPERMATIC CORD

The spermatic cord is made up of the testicular artery, vein, and nerves, and the deferent duct. They are critical structures for the function of the testis and epididymis. Scrotal hernia and varices of the pampiniform plexus are probably the most commonly recognized disease of the spermatic cord. Most of the other diseases become differential diagnoses for these.

Varicocele

A varicocele is a dilation and tortuosity of the veins of the pampiniform plexus and the cremasteric veins. Varices of the spermatic veins are most commonly seen in old rams. They occur sporadically in other species, such as the stallion (Fig. 5.47), as an incidental finding or secondarily to conditions where there is constriction of the veins of the spermatic cord. Varices are seldom recognized unless they are thrombosed, and inexperienced persons may miss them. There is no concrete evidence that small varicoceles are detrimental, but the very large ones are, by virtue of their size and the reduced ability of the animal to raise the testis to maintain thermoregulation. The pathogenesis of varices in animals is not well understood. In humans, the left unilateral location is regarded as the result of altered hemodynamics from insertion of the testicular vein to the renal vein rather than directly to the vena cava. Evidence in humans with varicose veins of the legs suggests that the elastic properties of the walls of the veins and arterial flow are major factors and varicoceles in rams may be similar. Many rams and bucks have intimal sclerosis of the spermatic vessels but no varicocele.