14 Testis

The testis is not a common specimen. Resections in children or young adults may be due to a nonneoplastic condition such as torsion, which produces the relatively nonspecific picture of hemorrhage and/or ischemic necrosis. Uncommonly in young children, undescended (cryptorchid) testes are removed because of an increased risk of developing germ cell tumors. There are also a few tumors that typically only occur in children. Most testicular tumors occur in men in their twenties to forties, although they also occur in the elderly.

Normal Histology

The testis is composed of a tightly packed collection of tubules. In the prepubertal testis, the tubules are lined with spindly, radially arranged Sertoli cells and rare spermatogonia. After puberty, spermatogenesis begins, and the tubules are dominated by the developing spermatocytes. Maturation is completed near the lumen of the tubules, where you can see tiny sesame seed–like spermatids (which grow tails to become spermatozoa). Polygonal pink Leydig cells in the interstitium produce testosterone (Figure 14.1).

Sperm leave the testis via the rete testis (Figure 14.2), a collection of epithelial-lined slit-like channels at the hilum of the testis, which lead into the epididymis, which eventually feeds into the vas deferens. The epididymis is lined by a pseudostratified and ciliated epithelium (Figure 14.3).

Orchiectomy in Infants and Children

In the setting of an undescended testis, the testis may be removed to prevent the development of a germ cell neoplasm. The typical *cryptorchid testis* shows small atrophic seminiferous tubules, fibrosis, and widened interstitial spaces (Figure 14.4). A related finding is the "vanishing testis syndrome" in which, upon surgical retrieval of the undescended testis, there is nothing but a nub of fibrosis and dystrophic calcification attached to an epididymal remnant. These conditions are generally signed out descriptively.

Infertility

A testis biopsy may be indicated in the workup of a persistent low sperm count (male infertility). From the pathologists' perspective, the options are the following:

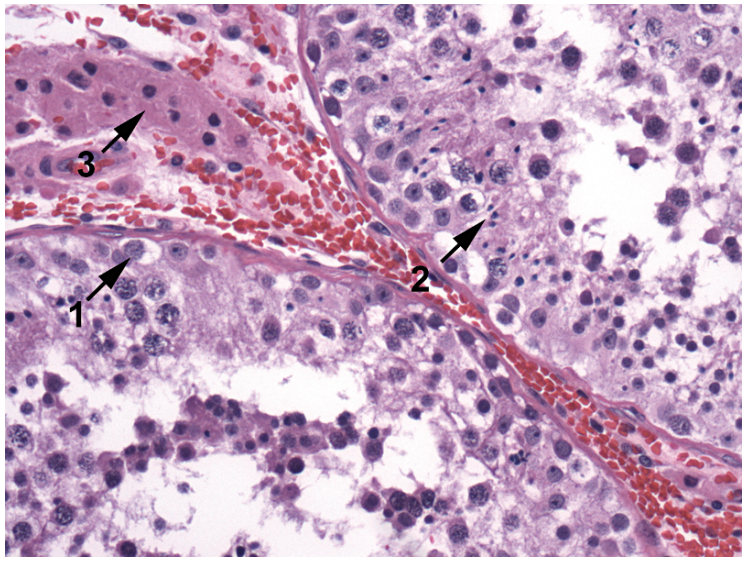

Figure 14.1. Normal seminiferous tubules. Large spermatogonia with clear cytoplasm are present at the tubule periphery (1). The developing spermatocytes have a wide range of morphologies, ending with the tiny spermatids (2), a marker of successful spermatogenesis. Plump pink Leydig cells are seen in the interstitium (3).

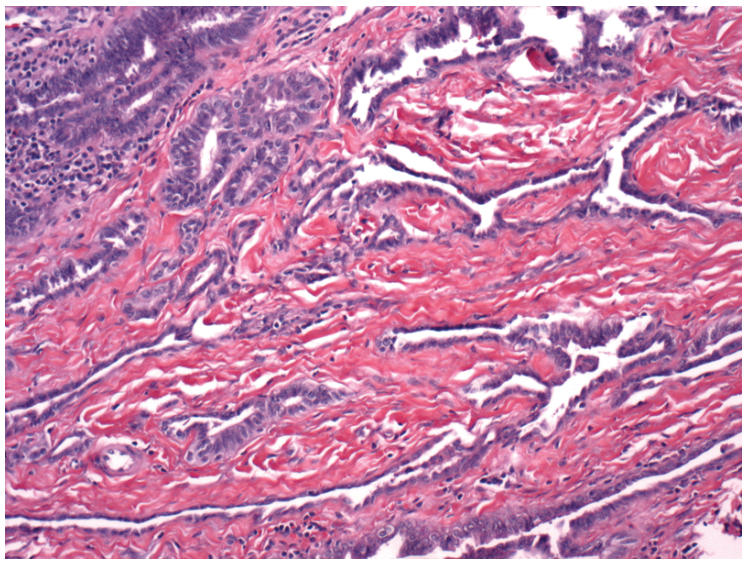

Figure 14.2. Normal rete testis. Slit-like spaces with cuboidal epithelium.

- Aplasia (or Sertoli-only syndrome, a total lack of germ cells; Figure 14.5)
- Hypospermatogenesis (decreased spermatogenesis in most tubules)
- Maturation arrest (when there is partial maturation but no spermatids produced)
- "End-stage testis" (global sclerosis and atrophy, no functioning tubules)
- Normal spermatogenesis (implying a distal obstruction)

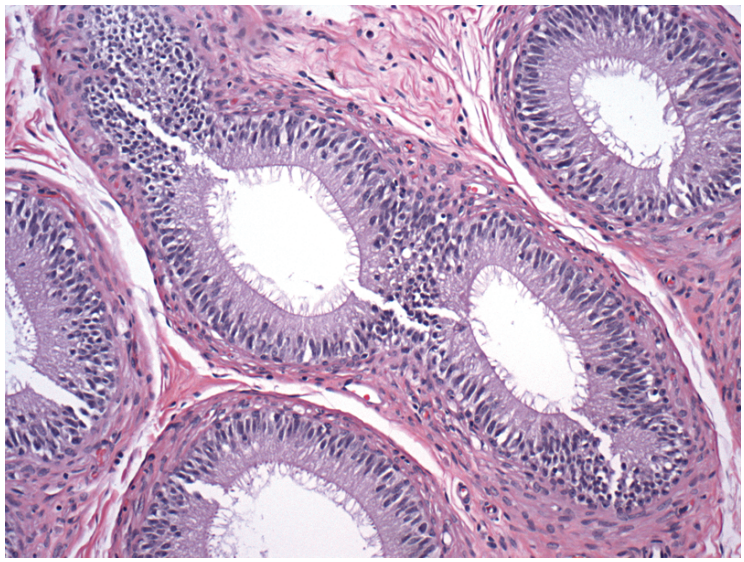

Figure 14.3. Normal epididymis. Columnar epithelium with cilia.

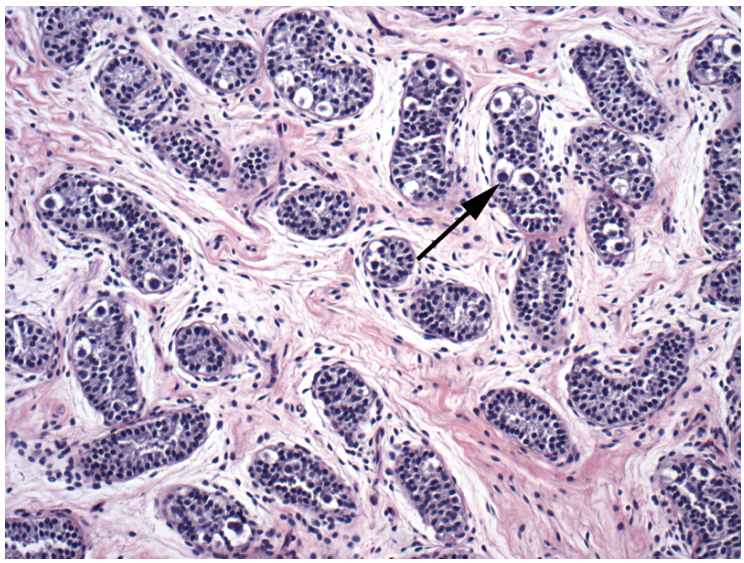

Figure 14.4. Cryptorchidism. In the infant testis, large dark spermatogonia are visible (arrow).

Tumors

Infants and children	Young adults and adults	Older adults
Yolk sac tumor	Seminoma	Spermatocytic seminoma
Teratoma	Embryonal carcinoma	Lymphoma
	Choriocarcinoma	Sex cord stromal tumors
	Teratoma	

Germ Cell Tumors

Germ cell tumors, which include seminoma, teratoma, yolk sac tumor, choriocarcinoma, and embryonal carcinoma, can all occur as pure tumors in and of themselves, but they do have a tendency to collide in adults, with the resulting mixture called a *mixed germ cell tumor*

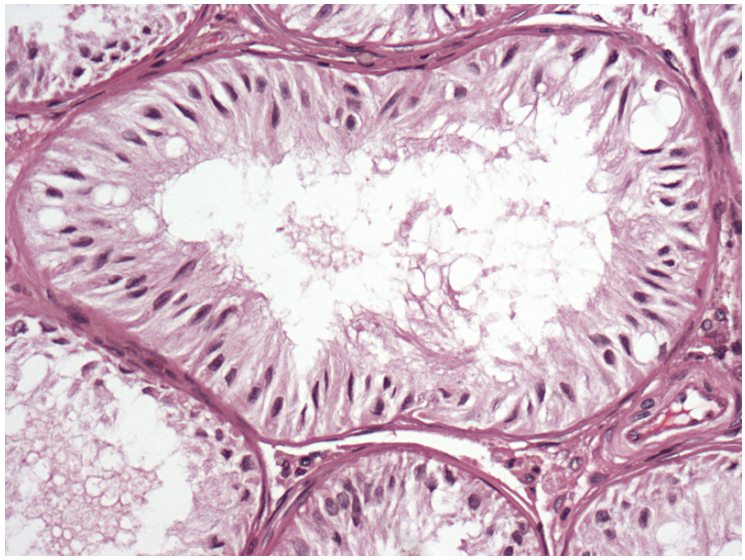

Figure 14.5. Sertoli-only syndrome in an adult. The tubules are lined with spindly Sertoli cells, and no germ cells are visible.

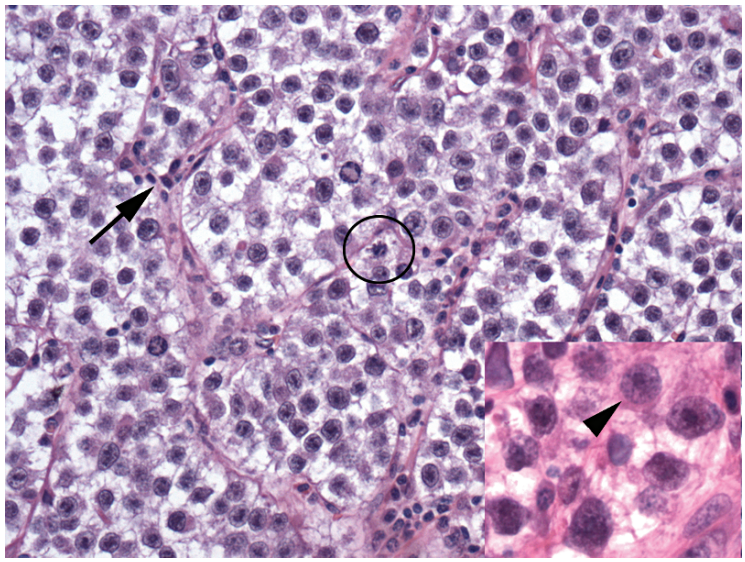

Figure 14.6. Seminoma, classic type. Delicate fibrovascular septae divide the cells into packets (arrow); collections of lymphocytes can be seen along the septae. The nuclei are widely spaced, with clear cytoplasm. Mitoses are common (circle). Nuclei have distinct nuclear membranes and prominent nucleoli (arrowhead).

(MGCT). Here, they will be described individually, but remember that for any adult neoplasm you are trying to identify every component present.

These neoplasms are notorious for their rare ability to nearly completely regress in the testis, leaving behind mainly a fibrotic scar. This does not, however, mean that they have not already metastasized.

Seminoma (Classic Type)

The seminoma is the most common germ cell neoplasm in adults. In typical form it is a large nodular mass in the testis. Microscopically, it is poorly circumscribed and infiltrates in between tubules at the periphery. The histologic features (Figure 14.6) include the following:

- An array of large, round, coarse nuclei, nonoverlapping and nonmolding, suspended in a network of delicate cell membranes
- One to two prominent central nucleoli
- Associated inflammation, especially lymphocytes, granulomas, and fibrosis
- Delicate branching fibrovascular septa
- Surrounding intratubular germ cell neoplasia (see below)

The classic type of seminoma has fairly monomorphic cells; at low power this uniformity can be deceptively bland. It may occur in pure form, but all tumors should be carefully sampled for other germ cell components (in which case it becomes an MGCT).

Intratubular Germ Cell Neoplasia

Think of intratubular germ cell neoplasia (IGCN) as the carcinoma in situ of the testis. It is actually very hard to spot, as normal spermatogenesis creates some strange looking cells. The easiest way to find IGCN is to slowly scan the tubules at 4×, looking for areas that stand out as having scattered dark, or large, or fried egg–type cells. Another approach is to study the seminomatous cells in the main tumor and look for similar cells in the adjacent tubules. An IGCN may be as subtle as a few big cells in the tubule, spreading in pagetoid fashion, or as obvious as a lumen packed with malignant cells (Figure 14.7). An IGCN is often seen next to seminomas (classic type), embryonal carcinomas, or choriocarcinomas. It is helpful because it confirms that you have a germ cell neoplasm (as opposed to a carcinoma or lymphoma). The following features help distinguish spermatogonia from IGCN:

Spermatogonia	Intratubular germ cell neoplasia
Clear cytoplasm	More abundant clear cytoplasm
Condensed chromosomes	Coarse chunky chromatin
Smooth nuclear membrane, if any	Irregular nuclear membrane
No nucleolus	Prominent nucleolus
Mature into spermatids	Little to no maturation
Placental alkaline phosphatase (PLAP) negative	c-kit, OCT3/4, and (often) PLAP positive

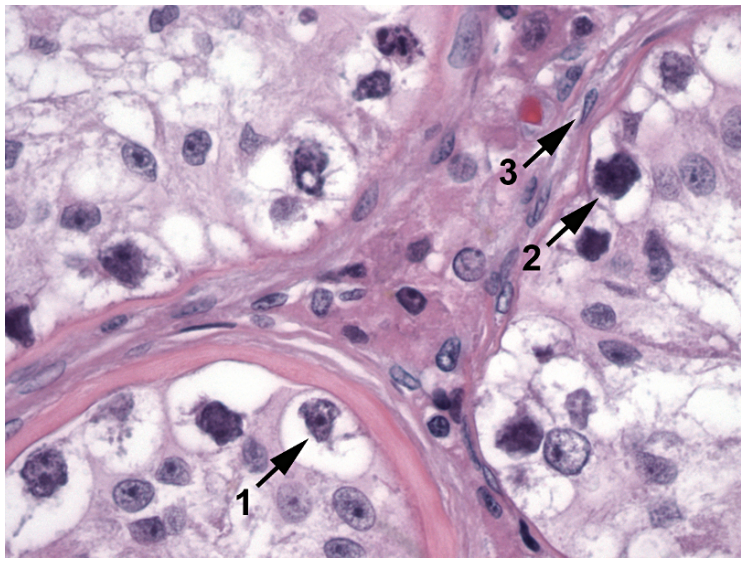

Figure 14.7. Intratubular germ cell neoplasia. Large cells with clear halos of cytoplasm and prominent nucleoli are seen at the tubule perimeter (1). Other malignant nuclei appear hyperchromatic and solid (2). Compare the malignant cells to the euchromatin of nearby endothelial cells (3).

Spermatocytic Seminoma

Many organ systems have low-grade, indolent, better differentiated versions of their neoplasms. Spermatocytic seminoma is the indolent seminoma in that it does not metastasize. It occurs in older men and has seminoma-like cells, except in three cell sizes: small, medium, and large. This tumor also lacks inflammation and PLAP positivity. It is the one tumor type not found in mixed germ cell tumors, nor is it associated with IGCN.

Embryonal Tumor

Rare as a pure tumor, embryonal tumors are a common component of MGCT. Remember embryonal as the ugly one. The cells are very pleomorphic, with hyperchromatic, angular, overlapping, or molding nuclei and large nucleoli (Figure 14.8). It looks epithelioid, like a carcinoma, and is in fact keratin positive. The architecture is solid, glandular, or papillary.

Yolk Sac Tumor (Endodermal Sinus Tumor)

Yolk sac tumor is the most common testicular neoplasm in children (in pure form), but it is also a common component of MGCT. It is famous for its many forms, especially microcystic and reticular (net-like). The pathognomonic finding is the Schiller-Duval body, a little glomeruloid form, but these are not always seen. The nuclei tend to be somewhat smaller and a little more regular than embryonal carcinoma, yet more atypical than seminoma (Figure 14.9). When found next to embryonal carcinoma, these areas look hypocellular and myxoid in comparison to the large epithelioid embryonal cells.

Choriocarcinoma

Choriocarcinoma is a rare tumor, especially in pure form. Like the placental tumor, it is characterized by two cell types (cytotrophoblast and syncytiotrophoblast), lots of blood, and human chorionic gonadotropin production. Also like the placenta, this tumor is very good at invading blood vessels, and widespread metastases are common. Syncytiotrophoblasts, the multinucleated giant cells that stain for human chorionic gonadotropin, can show up in other germ cell tumors; this does not make them choriocarcinomas. The cytotrophoblasts resemble

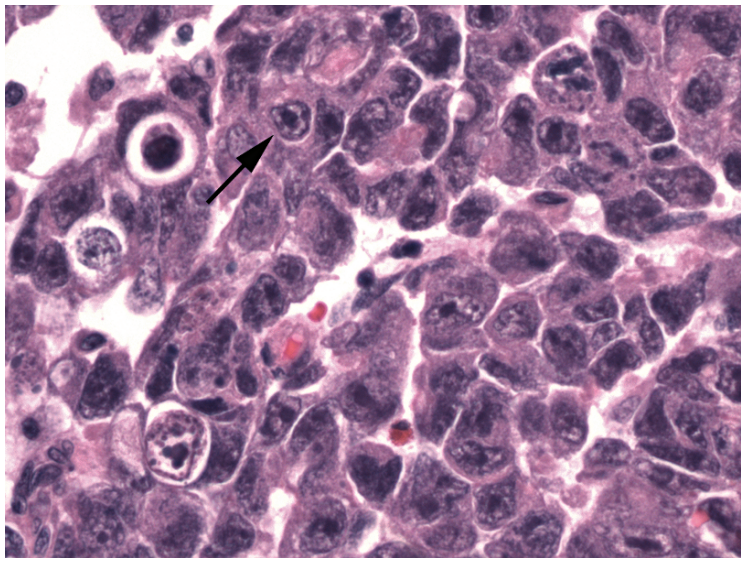

Figure 14.8. Embryonal carcinoma. Large epithelioid cells with pleomorphic nuclei grow in sheets. Unlike in seminoma, the cytoplasm is dense, and the nuclei have irregular shapes and sizes, some showing nuclear molding. Many have coarse chromatin with dark nuclear membranes and prominent nucleoli (arrow).

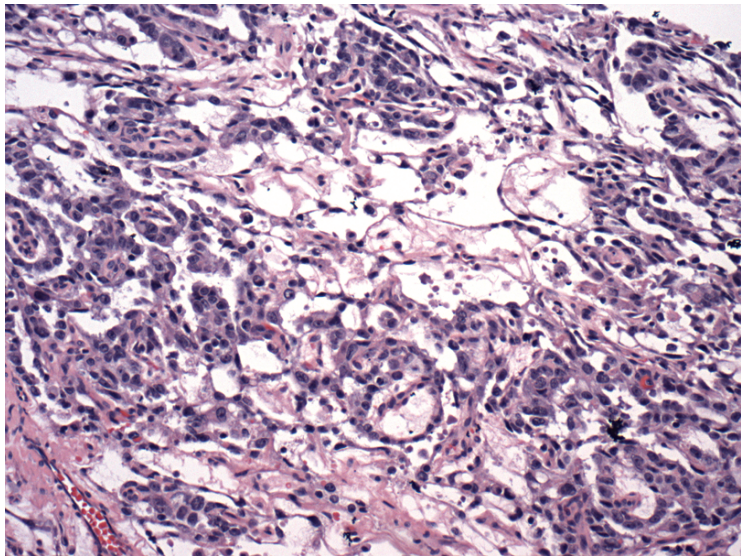

Figure 14.9. Yolk sac tumor. The cells of yolk sac tumor often appear more low grade than other germ cell tumor types. The cells are cuboidal, with pink cytoplasm, and have a tendency to pull apart into a microcystic pattern (shown here).

embryonal carcinoma, but the nuclei are smaller and not quite so pleomorphic, and the cytoplasm is pale.

Teratoma

A teratoma is a neoplasm composed of elements of the primitive germ layers: ectoderm (skin, central nervous system), mesoderm (cartilage, bone), and endoderm (gut, viscera), but not all layers have to be present in a tumor to call it a *teratoma*. Pure teratomas are found in prepubertal boys and are always considered benign in this population. In contrast, in postpubertal males, teratomas are malignant and are usually seen in the context of mixed germ cell tumors. A pure teratoma in an adult male is still malignant whether or not it contains immature elements (i.e., immature neural tissue), so there is no need to comment if a testicular teratoma is immature or mature (this is in contrast to teratomas in females). Rarely, teratomas can develop non–germ cell tumors, such as carcinomas, sarcomas, or "small blue cell tumors."

Sex Cord Stromal Tumors

The sex cord stromal tumors include the Sertoli cell and Leydig cell tumors. They are not germ cell neoplasms and are usually benign. They resemble their normal counterparts, so a tumor of oncocytic pink cells with very round nuclei is likely to be a Leydig cell tumor (Figure 14.10), and a collection of primitive tubules lined with spindly cells and oval nuclei is likely to be a Sertoli cell tumor (Figure 14.11). In both tumors, approximately 10% behave badly, but there are no hard criteria by which to predict malignancy. The usual rules apply (atypia, mitotic rate, necrosis, vascular invasion, and invasion beyond the testis all suggest poor prognosis).

Lymphoma

While uncommon in the testis, lymphoma is always in the differential diagnosis when sheets of discohesive malignant cells are present. Lymphoma can look like seminoma, yet the cells are not as homogeneous. The usual type is diffuse large B cell, which means CD20-positive cells with large nuclei, often with vesicular chromatin and large nucleoli (Figure 14.12). Lymphoma occurs in an older age group than seminoma and should not have any IGCN.

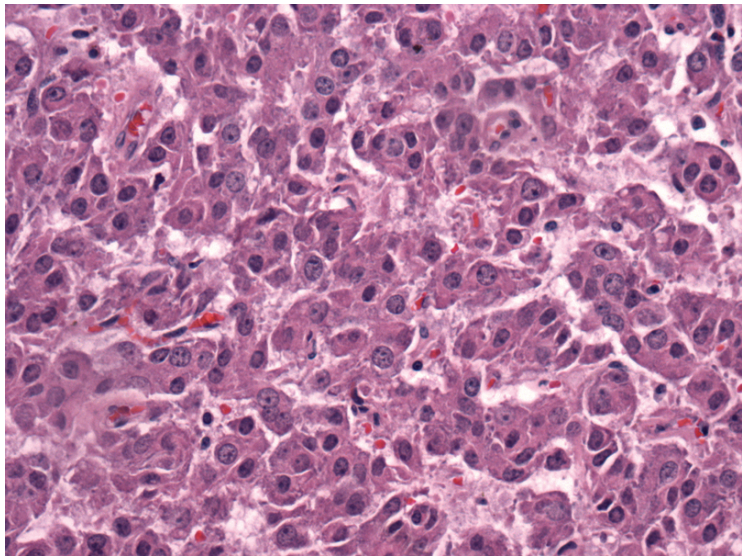

FIGURE 14.10. Leydig cell tumor. These neoplasms are reminiscent of oncocytomas in other sites. Most are benign.

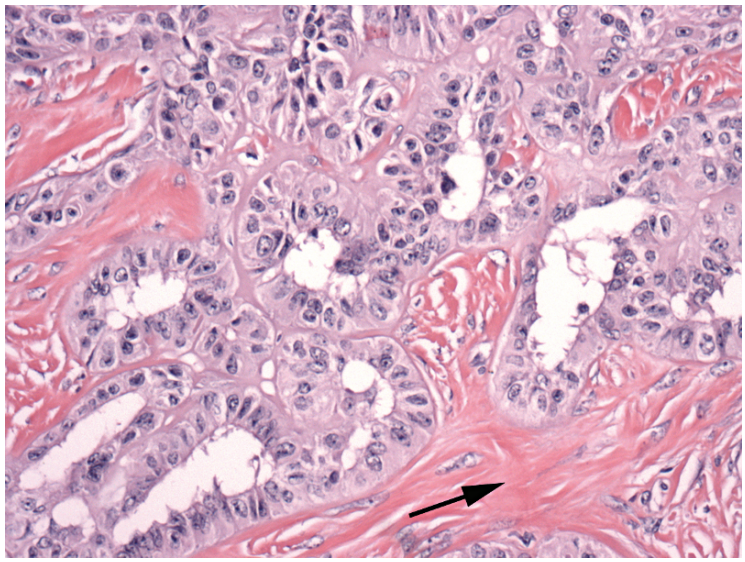

FIGURE 14.11. Sertoli cell tumor. This tumor attempts to recapitulate the seminiferous tubules. The stroma may become hyalinized (arrow).

Outside the Testis

All of the germ cell tumors can also occur in other body locations, mainly in the midline (e.g., sacrum, mediastinum, sella or pineal in brain). A germ cell tumor in the brain is called a *germinoma*. These neoplasms can also occur in the female ovary. A seminoma occurring in the ovary is called a *dysgerminoma*. Yolk sac tumors, embryonal carcinomas, and teratomas can occur in ovary. Choriocarcinoma is more commonly associated with placental tissue in women but can also arise in the ovary. Sex cord stromal tumors also arise in women, usually

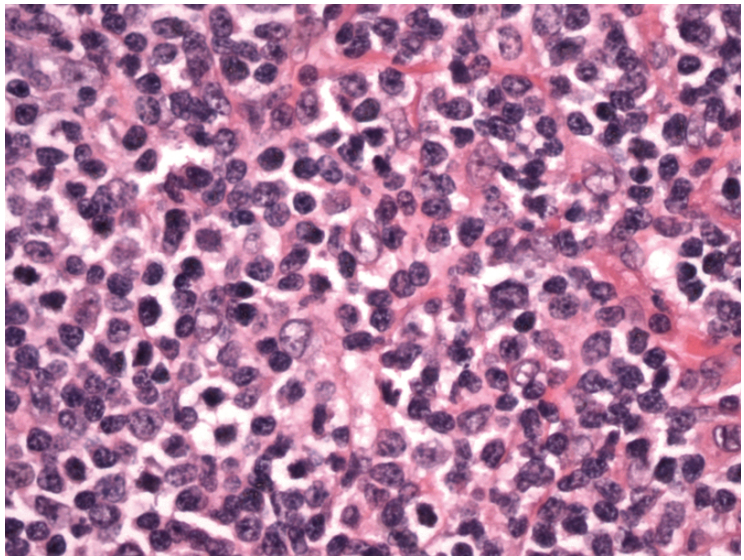

Figure 14.12. Diffuse large B-cell lymphoma. The main histologic feature is sheets of discohesive tumor cells. Nuclear chromatin is chunky.

of the thecoma and granulosa cell groups, but Sertoli and Leydig cell tumors can also develop. Strangely, you can also rarely see granulosa cell tumors in the testis. In fact, when presented with a tumor in the testis or ovary that looks like nothing you recognize, the sex cord stromal tumors are a good place to start.