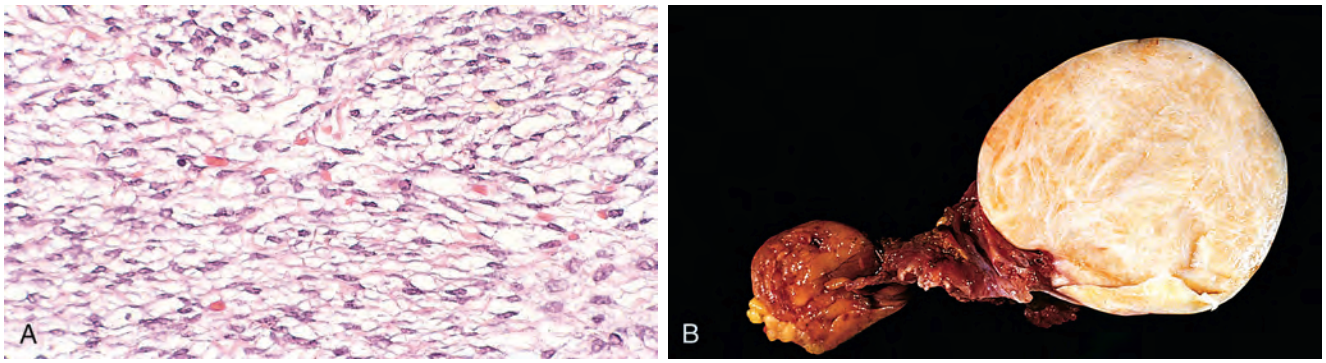

Figure 22-44 Ovarian fibromas **A,** Thecoma-fibroma composed of plump, differentiated stromal cells with thecal appearance. **B,** Large bisected fibroma of the ovary apparent as a white, firm mass *(right)*. The fallopian tube is attached.

factor that is important in granulosa cell development, which presumably explains its strong association with this tumor type. Interestingly, mutations in *FOXL2*, in one small study, were uncommon in juvenile granulosa tumor, suggesting that it is genetically distinct from the adult type.

Fibromas, Thecomas, and Fibrothecomas

Tumors arising in the ovarian stroma that are composed of either fibroblasts (fibromas) or plump spindle cells with lipid droplets (thecomas) are relatively common and account for about 4% of all ovarian tumors (Fig. 22-44*A*). Many tumors contain a mixture of these cells and are termed *fibrothecomas*. Pure thecomas are rare, but tumors in which these cells predominate may be hormonally active. By contrast, fibromas as a rule are hormonally inactive.

Fibromas of the ovary are unilateral in about 90% of cases and are usually solid, spherical or slightly lobulated, encapsulated, hard, gray-white masses covered by glistening, intact ovarian serosa (Fig. 22-44*B*). On histologic examination, they are composed of well-differentiated fibroblasts and a scant interspersed collagenous stroma. Focal areas of thecal differentiation may be identified.

Most of these tumors come to attention as a pelvic mass, sometimes accompanied by pain and two decidedly curious associations. The first is ascites, found in about 40% of cases in which the tumors measure more than 6 cm in diameter. Uncommonly there is also a hydrothorax, usually only on the right side. This combination of findings (ovarian tumor, hydrothorax, and ascites) is designated *Meigs syndrome.* Its genesis is unknown. The second association is with the basal cell nevus syndrome, described in Chapter 25. The vast majority of fibromas, fibrothecomas, and thecomas are benign. Rarely, cellular fibromas with mitotic activity and increased nuclear-to-cytoplasmic ratio are identified; because they may pursue a malignant course, they are termed *fibrosarcomas*.

Sertoli-Leydig Cell Tumors

These tumors are often functional and commonly produce masculinization or defeminization, but a few have estrogenic effects. The tumor cells recapitulate, to a certain extent, testicular sertoli or Leydig cells at various stages of development. They occur in women of all ages, although the peak incidence is in the second and third decades. In over half of cases, the tumor cells have mutations in *DICER1*, a gene that you will recall encodes an endonuclease that is essential for proper processing of micro-RNAs (Chapter 1). The presence of *DICER1* mutations suggests the genesis of male-directed stromal cells may involve abnormalities of gene expression related to dysregulation of micro-RNAs.

MORPHOLOGY

These tumors are unilateral and may resemble granulosa cell tumors grossly. The cut surface is usually solid and varies from gray to golden brown in appearance (Fig. 22-45A). Microscopically, a range of differentiation is seen. Well-differentiated tumors show tubules composed of Sertoli cells or Leydig cells interspersed with stroma (Fig. 22-45*B*). The intermediate forms show only outlines of immature tubules and large eosinophilic Leydig cells. The poorly differentiated tumors have a sarcomatous pattern with a disorderly disposition of epithelial cell cords. Leydig cells may be absent. Heterologous elements, such as mucinous glands, bone, and cartilage, may be present in some tumors.

The incidence of recurrence or metastasis by Sertoli-Leydig cell tumors is less than 5%. These neoplasms may block normal female sexual development in children and may cause defeminization of women, manifested by atrophy of the breasts, amenorrhea, sterility, and loss of hair. The syndrome may progress to striking virilization (hirsutism) associated with male distribution of hair, hypertrophy of the clitoris, and voice changes.

Other Sex Cord-Stromal Tumors

There are several other uncommon but distinctive ovarian tumors of sex cord or stromal origin that often produce steroid hormones.

- *Hilus cell tumors (pure Leydig cell tumors)* are usually derived from clusters of polygonal cells arranged around hilar vessels. These rare, unilateral tumors are comprised of large lipid-laden Leydig cells with distinct borders and characteristic cytoplasmic structures called Reinke crystalloids. Women with hilus cell tumors usually present with evidence of masculinization in the form of