tumor cells. The peritoneal pattern of spread is distinctive: all serosal surfaces are diffusely seeded with 0.1- to 0.5-cm nodules of tumor that only rarely invade deeply into the underlying parenchyma. The regional nodes are often involved, and metastases may be found in the liver, lungs, gastrointestinal tract, and elsewhere. Metastasis across the midline to the opposite ovary is discovered in about half the cases at surgery and heralds a progressive downhill course and death within a few months or years.

Most women with ovarian carcinoma present with high stage disease. This is the primary reason for the relatively poor 5- and 10-year survival rates of patients with these tumors, compared with rates for patients with cervical or endometrial carcinoma. For these reasons, development of new assays that permit early diagnosis is a top priority. Biochemical tests for tumor antigens or tumor products in the plasma of these patients are being sought vigorously, but none proposed to date has sufficient sensitivity and specificity to be useful. The serum marker CA-125 is used in patients with known disease to monitor disease recurrence/progression.

Prevention of ovarian cancer also remains an elusive goal. Screening to identify women at risk (positive for *BRCA* mutations or with strong family histories) and treatment with prophylactic salpingo-oophorectomy are currently standard, but the long-term impact of these approaches remains to be determined.

KEY CONCEPTS

- Epithelial ovarian tumors are classified into benign, borderline or malignant.
- About 80% of all ovarian epithelial tumors are benign and occur in young women. The malignant tumors occur most commonly in older women and account for approximately 3% of all cancers in women in the United States.
- The majority of the malignant epithelial tumors are high-grade serous carcinomas, which have a poor prognosis in large part due to the fact that they are detected after they have spread beyond the ovary.
- There are three major histologic types of epithelial ovarian tumors: serous, mucinous and endometrioid, all of which have a benign, borderline and malignant category.
- Benign tumors are composed of well-differentiated epithelial cells with minimal proliferation. Borderline tumors show increased cell proliferation, but lack stromal invasion. Malignant tumors show increased epithelial atypia and are defined by the presence of stromal invasion.
- Ovarian carcinomas are currently divided into Type I (low grade) and Type II (high-grade) tumors.
- The origin of ovarian tumors is still under investigation, but it is clear that *BRCA1*- and *BRCA2*-related tumors as well as a subset of sporadic, ovarian serous tumors are likely to arise from fallopian tube epithelium instead of ovarian epithelium.

Germ Cell Tumors

Germ cell tumors constitute 15% to 20% of all ovarian tumors. *Most are benign cystic teratomas*, but others, found principally in children and young adults, may show malignant behavior and pose problems in histologic diagnosis and in therapy. They bear a remarkable similarity to germ cell tumors in the male testis (Chapter 21) and arise in a similar manner (Fig. 22-37).

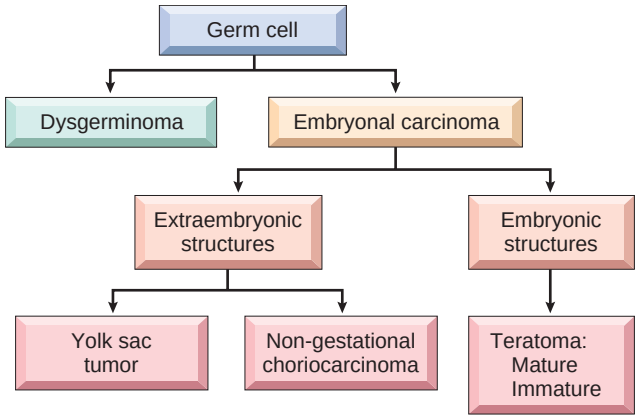

Figure 22-37 Histogenesis and interrelationships of tumors of germ cell origin.

Teratomas

Teratomas are divided into three categories: (1) mature (benign), (2) immature (malignant), and (3) monodermal or highly specialized.

Mature (Benign) Teratomas. Most benign teratomas are cystic and are often referred to as *dermoid cysts*, because they are almost always lined by skin-like structures. Cystic teratomas are usually found in young women during the active reproductive years. They may be discovered incidentally, but are occasionally associated with clinically important paraneoplastic syndromes, such as inflammatory limbic encephalitis, which may remit upon removal of the tumor.

MORPHOLOGY

Benign teratomas are bilateral in 10% to 15% of cases. Characteristically they are unilocular cysts containing hair and sebaceous material (Fig. 22-38). Sectioning reveals a thin wall lined by an opaque, gray-white, wrinkled epidermis, frequently with protruding hair shafts. Within the wall, it is common to find grossly evident tooth structures and areas of calcification.

Microscopically, the cyst wall is composed of stratified squamous epithelium with underlying sebaceous glands, hair shafts, and other skin adnexal structures (Fig. 22-39). In most cases tissues from other germ layers can be identified, such as cartilage, bone, thyroid, and neural tissue. Dermoid cysts are sometimes incorporated within the wall of a mucinous cystadenoma. **About 1% of the dermoids undergo malignant transformation, most commonly to squamous cell carcinoma, but also to other cancers as well (e.g., thyroid carcinoma, melanoma).**

In rare instances a benign teratoma is solid and composed entirely of benign-looking heterogeneous collections of tissues and organized structures derived from all three germ layers. These tumors presumably have the same histogenetic origin as dermoid cysts but lack preponderant differentiation into ectodermal derivatives. These neoplasms may be difficult to distinguish, on gross inspection, from malignant immature teratomas.