In the child, differentiated mature teratomas usually follow a benign course. **In the postpubertal male all teratomas are regarded as malignant**, capable of metastatic behavior whether the elements are mature or immature. Consequently, it is not critical to detect immaturity in a testicular teratoma of a postpubertal male.

Mixed Tumors

About 60% of testicular tumors are composed of more than one of the "pure" patterns. Common mixtures include: teratoma, embryonal carcinoma, and yolk sac tumor; seminoma with embryonal carcinoma; and embryonal carcinoma with teratoma *(teratocarcinoma)*. In most instances the prognosis is worsened by the presence of the more aggressive element.

Clinical Features of Testicular Germ Cell Tumors. Although painless enlargement of the testis is a characteristic feature of germ cell neoplasms, any solid testicular mass should be considered neoplastic until proven otherwise. Biopsy of a testicular neoplasm is associated with a risk of tumor spillage, which would necessitate excision of the scrotal skin in addition to orchiectomy. Consequently, the standard management of a solid testicular mass is radical orchiectomy based on the presumption of malignancy.

Testicular tumors have a characteristic mode of spread. *Lymphatic spread* is common to all forms of testicular tumors. In general, retroperitoneal para-aortic nodes are the first to be involved. Subsequent spread may occur to mediastinal and supraclavicular nodes. *Hematogenous spread* is primarily to the lungs, but liver, brain, and bones may also be involved. The histology of metastases may differ from that of the testicular lesion. For example, an embryonal carcinoma may present a teratomatous picture in the secondary deposits. As discussed earlier, because all these tumors are derived from pluripotent germ cells, the apparent "forward" and "backward" differentiation seen in different locations is not entirely surprising. Another explanation for the differing morphologic patterns in the primary and metastatic site is that minor components in the primary tumor that were unresponsive to chemotherapy survive and subsequently become the dominant metastatic pattern.

Because of differing behaviors, tumors of the testis are segregated clinically into two broad categories: seminoma and nonseminomatous germ cell tumors (NSGCTs).

- Seminomas tend to remain localized to the testis for a long time, and hence approximately 70% present in clinical stage I (see later). In contrast, approximately 60% of males with NSGCTs present with advanced clinical disease (stages II and III).
- Metastases from seminomas typically involve lymph nodes. Hematogenous spread occurs later in the course of dissemination. NSGCTs not only metastasize earlier but also use the hematogenous route more frequently.
- The rare pure choriocarcinoma is the most aggressive NSGCT. It may not cause any testicular enlargement but instead spreads predominantly and rapidly by the bloodstream. Therefore, lungs and liver are involved early in virtually every case.

To summarize, as compared with seminomas, NSGCTs are biologically more aggressive and in general have a poorer prognosis.

In the United States, three clinical stages of testicular tumors are defined:

- Stage I: tumor confined to the testis, epididymis, or spermatic cord
- Stage II: distant spread confined to retroperitoneal nodes below the diaphragm
- Stage III: metastases outside the retroperitoneal nodes or above the diaphragm

Biomarkers. Germ cell tumors of the testis often secrete polypeptide hormones and certain enzymes that can be detected in blood by sensitive assays. Such biologic markers include HCG, AFP, and lactate dehydrogenase, which are valuable in the diagnosis and management of testicular cancer. The elevation of lactate dehydrogenase correlates with the mass of tumor cells, and provides a tool to assess tumor burden. Marked elevation of serum AFP or HCG levels are produced by yolk sac tumor and choriocarcinoma elements, respectively. Both of these markers are elevated in more than 80% of individuals with NSGCT at the time of diagnosis. As stated earlier, approximately 15% of seminomas have syncytiotrophoblastic giant cells and minimal elevation of HCG levels, which does not affect prognosis. In the context of testicular tumors, the value of serum markers is fourfold:

- In the evaluation of testicular masses
- In the staging of testicular germ cell tumors. For example, after orchiectomy, persistent elevation of HCG or AFP concentrations indicates stage II disease even if the lymph nodes appear of normal size by imaging studies.
- In assessing tumor burden
- In monitoring the response to therapy. After eradication of tumors there is a rapid fall in serum AFP and HCG. With serial measurements it is often possible to predict recurrence before the patients become symptomatic or develop any other clinical signs of relapse.

The therapy and prognosis of testicular tumors depend largely on clinical stage and on the histologic type. Seminoma, which is radiosensitive and tends to remain localized for long periods, has the best prognosis. More than 95% of patients with stage I and II disease can be cured. Among NSGCTs, the histologic subtype does not influence the prognosis significantly, and hence these are treated as a group. Approximately 90% of patients with NSGCTs can achieve complete remission with aggressive chemotherapy, and most can be cured. Pure choriocarcinoma has a poor prognosis. However, when it is a minor component of a mixed germ cell tumor, the prognosis is less adversely affected. With all testicular tumors, distant metastases, if present, usually occur within the first 2 years after treatment.

Tumors of Sex Cord-Gonadal Stroma

As indicated in Table 21-5, sex cord-gonadal stroma tumors are subclassified based on their presumed histogenesis and differentiation. The two most important members of this