Cancer in Men

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NOTE: There will be inadequate time in lecture to present renal cell carcinoma. This information is presented to the reviewer in the hope of assisting in preparation for the board examination.

Introduction

Renal cell carcinoma affects about 28,000 people per year and causes 11,000 deaths. The male: female ratio is 1.5:1. Most cases occur in patients between 50 and 70 years of age.

Both hereditary and non-hereditary forms have been reported. The non-hereditary form is by far the most common. The hereditary form presents frequently with bilateral disease and it occurs in younger patients. Histologically, clear cell carcinoma and papillary carcinomas are seen. There is also an increased incidence in vonHippel-Lindau disease, tuberous sclerosis, and autosomal dominant polycystic kidney disease in patients with the hereditary form.

Etiology

Smoking and obesity have been directly linked to renal cell carcinoma. Analgesic nephropathy, especially with phenacetin analgesics has also been implicated as an important cause of the disease. There is a direct correlation with occupational exposure, particularly with leather tanners and shoe workers, oil refinery and petrochemical workers, and in those with asbestos exposure.

Balkan nephropathy is an important consideration as well. The disorder is a familial nephropathy of unknown cause that results in progressive inflammation of the renal parenchyma leading to renal failure and multifocal low grade cancers. Many patients with Balkan nephropathy develop transitional cell carcinomas of the renal pelvis and ureters as well.

Thorotrast exposure (an old contrast agent for radiology that produces α particles and γ rays) is a rare cause in the present era, but an important cause historically.

Patients with end stage renal disease who develop acquired polycystic disease of the kidney have an increased risk as well.

Clinical Presentation

The classic triad for renal cell carcinoma is pain, hematuria, and flank mass, but most patients are without signs or symptoms until the disease is advanced. An interesting presentation is Stauffer’s syndrome which represents nonmetastatic renal cell carcinoma with ele-
vated liver enzymes; the laboratory abnormalities resolve with removal of the affected kidney.

Secondary erythrocytosis (DaSilva’s syndrome) from ectopic erythropoietin production represents a paraneoplastic phenomenon and a consideration in any patient with erythrocytosis. Most patients are asymptomatic early in course of their disease with coincidental finding on studies done for other reasons. Many are found with metastatic disease.

**Pathology**

Most tumors arise from the proximal renal tubular epithelium. Clear cell carcinoma and granular cell carcinoma are the most common types. Sarcomatoid carcinoma is the least common and clearly is not a sarcoma but a variant that appears to have morphologic features of sarcoma (spindle cells) microscopically. Sarcomatoid carcinoma of the kidney is very aggressive.

**Clinical Evaluation**

An initial evaluation of the patient with known or suspected renal cell carcinoma includes baseline hematologic and biochemical studies as well as radiographic studies to determine the extent of disease.

Computed tomography of the abdomen is the most common initial radiographic test, and it allows for evaluation of resectability. Renal ultrasound helps assist with staging and often may complement CT evaluation. In some cases renal arteriography is performed.

**Staging**

Staging for renal cell carcinoma follows the traditional TNM classification:

<table>
<thead>
<tr>
<th>Tumor size</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>T1</td>
<td>Small tumor, minimal renal and calyceal distortion or deformity; circumscribed neovasculature surrounded by normal parenchyma</td>
</tr>
<tr>
<td>T2</td>
<td>Large tumor with deformity or enlargement of kidney or collecting system (there are subcategorizations)</td>
</tr>
<tr>
<td>T3</td>
<td>Tumor involving perinephric tissues, renal vein, or infradiaphragmatic vena cava</td>
</tr>
<tr>
<td>T4</td>
<td>Direct invasion of contiguous structures or supradiaphragmatic vena cava</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Nodal status</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>N0</td>
<td>No involvement of lymph nodes</td>
</tr>
<tr>
<td>N1</td>
<td>Nodal involvement</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Metastasis</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>M0</td>
<td>No distant metastasis</td>
</tr>
<tr>
<td>M1</td>
<td>Distant metastasis (specify organs involved)</td>
</tr>
</tbody>
</table>

**Treatment**

For localized disease, nephrectomy is the treatment of choice. This involves removal of the kidney along with an en bloc resection of adjacent connective tissue and vascular supply. If there is disease present in the inferior vena cava it is resected as well. Lymph node dissection is favored by some in patients with nodal disease at the time of surgery.

More recently, data have demonstrated value for nephron-sparing nephrectomy, a procedure that removes an extended portion of the cancer but leaves unaffected kidney intact. Long-term studies have suggested locore-
gional control rates for selected patients approaching those with total nephrectomy. Patient selection is an important consideration. Adjuvant therapy (radiation, systemic therapy) is not of value in patients resected for cure. Patients with metastatic disease are treated with palliative intent. Sorafenib (Nexavar®) and sunitinib (Sutent®) are new agents with tyrosine kinase inhibitory and vascular endothelial growth factor (VEGF) inhibitory properties. Toxicity can be significant, with asthenia and arthralgias representing the dose limiting toxicities. Additionally, sunitinib can cause myelosuppression.

Inhibitors of the mammalian target of rapamycin (mTOR) have been under development as second line agents in treatment of patients with metastatic disease. Their side effects are generally mild and control or reduction of disease after progression with sunitinib or sorafenib is approximately 25%. Commercially available mTOR inhibitors include temsirolimus (Torisel®) and everolimus (Affinitor®), and additional agents are currently under development.

**Bladder Cancer**

**Introduction**

Transitional cell carcinoma of the bladder is the most frequent uroepithelial tumor seen in this country. There are about 69,000 cases per year and 14,000 deaths. The Male:Female ratio is 2:1. Most cases occur in patients between 50 and 80 years of age. The most common focus for the cancer is on the posterior and lateral walls of the urinary bladder.

The concept of field cancerization is essential to the modern understanding of the disease. Field cancerization denotes the fact that the entire bladder is susceptible to toxin exposure and second primary malignancies are frequent. The risk of bladder cancer is 2-3 times as high in urbanites.

**Carcinogens and Bladder Cancer**

Workers in rubber, leather, chemical materials, paint, metal, textile, and laboratory industries are at increased risk. There is a significantly increased incidence in smokers. Dietary sweeteners such as tryptophan metabolites, cyclamates, and saccharin had been implicated in the past as being causative agents for bladder carcinomas. However, large population studies have failed to support laboratory evidence of these as carcinogens. There is a long history of association with *Schistosoma hematothium* and the incidence of squamous carcinoma of the bladder.

**Pathology of Bladder Cancers**

Transitional cell carcinomas account for 90-95% of all bladder cancers diagnosed in North America. Squamous carcinomas and adenocarcinomas account for the bulk of the remainder. Leiomyosarcoma is rare, but does occur. The current thinking is that all carcinomas begin in situ and progress to either papillary or sessile tumors if untreated.

**Clinical Presentation**

Hematuria (often painless) is the presenting symptom in 70% of patients with bladder cancer. Bladder irritability occurs in 25% of patients. At the time they are diagnosed 70% are confined to the bladder and only 7% of patients have clinical evidence of metastases. Urinary obstructive symptoms may occur when tumors occur near the urethral ostium.
**Diagnosis**

The diagnosis is most often established by cystoscopic biopsy. In high risk patients, urinary cytology may be an effective screening tool and is helpful for evaluating high grade in situ lesions. Due to the high incidence of second primaries, visualization of the upper urothelial tract (by contrast urography) is required.

**Staging**

Required studies include cystoscopic examination of the bladder and biopsy with rectal (vaginal) examination under anesthesia, contrast urography of the upper urinary tract, chest radiograph, and baseline biochemical and hematologic studies. Additionally, computed tomography of the abdomen and pelvis to exclude local spread and nodal metastases may be helpful.

**Tumor size**

- **TX**-Primary tumor cannot be assessed
- **T0**-No evidence of primary tumor
- **Ta**-Noninvasive papillary carcinoma (confined to the urothelial layer)
- **Tis**-Transitional cell carcinoma in situ (“flat tumor”)
- **T1**-Lamina propria invasion
- **T2a**-Superficial muscle invasion (inner half)
- **T2b**-Deep muscle invasion (outer half)
- **T3a**-Perivesical fat invasion – microscopic
- **T3b**-Perivesical fat invasion – macroscopic (mass)
- **T4a**-Invasion of adjacent pelvic organs (prostate, uterus, vagina)
- **T4b**-Invasion of abdominal or pelvic walls

**Nodal status**

- **NX**-Regional nodes cannot be assessed
- **N0**-No regional lymph node metastasis
- **N1**-Metastasis to a single node in primary drainage region
- **N2**-Metastasis to multiple nodes in primary drainage region
- **N3**-Common iliac nodal involvement

**Metastasis**

- **M0**-No distant metastasis
- **M1**-Distant metastasis is present

**Grouping**

Stage 0a  
Stage 0is  
Stage I  
Stage II  
Stage III  
Stage IV

**Treatment**

**Carcinoma in situ**

Transitional cell carcinoma in situ is frequently a multifocal disease characterized as severe dysplasia without a discrete mass or lesion. Treatment is tailored to the individual needs of the patient. Initially, many lesions may be managed by surgical fulguration or intravesical chemotherapy. If voiding symptoms occur or invasiveness occurs (adverse prognostic
signs) the patient is urged to undergo total cystectomy. Close follow-up is required as 80% of patients ultimately develop invasion.

**High grade high stage tumors**

Simple transurethral resection of the bladder (TURB) is seldom adequate. Resection of the involved bladder (segmental cystectomy) is an option to total cystectomy in patients who refuse radical surgery. The five year survival rate of Stages B and C carcinoma is about 25% with surgery alone. Radiation is not of benefit in an adjuvant setting for this disease. Some recommend adjuvant chemotherapy as for advanced disease. There are clinical trials demonstrating an improvement in long term survival of about 20% compared to no additional therapy.

**Advanced disease**

Surgical fulguration and resection are utilized for palliative benefit. Radiation may be of use for local control and relief of urinary irritability in patients who are poor candidates for surgery. Most patients are managed by combination chemotherapy for palliative intent.

**Chemotherapy for Bladder Cancer**

Effective single agents include cisplatin, carboplatin, pemetrexed, methotrexate, paclitaxel, adriamycin, cyclophosphamide, ifosfamide, vinca alkaloids, and gemcitabine. A newer taxane-like agent, ixabepilone, has been recently approved as well; it is utilized primarily in a palliative setting. Combinations are preferred over single agents due to their higher response rates (at the risk of added toxicity). One of the more popular regimens is MVAC (Methotrexate, Vinblastine, Adriamycin, Cisplatin). It is given on a 28 day cycle. Its response rate is 65% and duration of response averages 8 months. It is a fairly toxic regimen.

As a result of the toxicity associated with MVAC, some oncologists prefer the combination of gemcitabine and cisplatin. The regimen is safer and better tolerated, but has not yet demonstrated superiority over MVAC in clinical trials.

**Prostate Cancer**

**Introduction**

Adenocarcinoma of the prostate is the most common cancer in men. Over 240,000 cases and 28,000 deaths occur each year. The median age at onset is 70 years and the incidence increases exponentially after age 40. 98% of all prostate cancers are adenocarcinomas, the remainder are sarcomas, transitional carcinomas, and small cell carcinomas. Prostate cancer is more common in blacks than whites.

**Etiology**

The cause of prostate cancer is unknown. It is suspected that environmental factors play a role as the incidence is higher in Westernized society. Familial clustering can be found in some cases. Autopsy studies have found occult prostate cancer in as much as 40% of males over 75 years of age.

**Clinical Presentation**

The disease is most often asymptomatic, with a mass found on routine rectal exam. Many present with obstructive uropathy, with carcinoma found on transurethral resection of the prostate (TURP) specimen. If the disease is widespread, patients may complain of leg edema, leg pain and pelvic fullness from me-
tastases to presacral and iliac lymph nodes. Additionally, metastases to bone and lung may occur. Liver metastases are infrequent.

**Diagnosis**

A biopsy of every suspicious prostate mass is essential. Most biopsies are done as a transrectal approach with either direct palpation or guidance by ultrasound with an 80-90% success rate. Complications (bleeding, abscess formation) are rare.

**Tumor Markers and Prostate Cancer**

**Prostate specific antigen (PSA)**

The PSA may be elevated in BPH and prostate cancer. Serum levels may be increased slightly with manipulation of prostate. It was initially hoped to be more specific for prostate cancer than other markers but subsequent studies show this is not the case. In an effort to obtain more accurate information, some have recommended measurement of free serum PSA and correlating with bound levels. Others have advocated evaluation of PSA velocity with time. There is no clear consensus on the validity of these additional tools. Progressive increases in serum levels of prostatectomized males appear to correlate with amount of tumor present.

**Pathology and staging**

Histologic evaluation of tumor differentiation is important in overall prognosis and in determining the aggressivity of disease. The most favored histologic grading is that described by Gleason. Tumors are graded 1 (most like normal tissue) to 5 (anaplastic) in each of two features—nuclear differentiation and cellular composition. The two scores are added together to arrive at a final score:

- 2-4—well differentiated, closely resemble normal glands
- 5-6—moderately well differentiated, some glandular appearance
- 7—moderately poorly differentiated
- 8-10—poorly differentiated

More recently, the AJCC rephrased tumor grading:

- GX—Grade cannot be assessed
- G1—Well differentiated (slight anaplasia)
- G2—Moderately differentiated (moderate anaplasia)
- G3-4—Poorly differentiated or undifferentiated (marked anaplasia)

**Tumor size**

- TX-Primary tumor cannot be assessed
- T0-No evidence of primary tumor
- T1-Clinically inapparent tumor not palpable nor visible by imaging
- T1a-Tumor incidental histologic finding in 5% or less of tissue resected
- **T1b-Tumor incidental histologic finding in more than 5% of tissue resected**

- **T1c-Tumor identified by needle biopsy (e.g., because of elevated PSA)**

- **T2-Tumor confined within prostate**

  *Note: Tumor found in one or both lobes by needle biopsy, but not palpable or reliably visible by imaging, is classified as T1c*

  - **T2a-Tumor involves one lobe**
  - **T2b-Tumor involves both lobes**

- **T3-Tumor extends through the prostate capsule**

  **Note: Invasion into the prostatic apex or into (but not beyond) the prostatic capsule is not classified as T3, but as T2.**

  - **T3a-Extracapsular extension (unilateral or bilateral)**
  - **T3b-Tumor invades seminal vesicle(s)**

- **T4-Tumor is fixed or invades adjacent structures other than seminal vesicles: bladder neck, external sphincter, rectum, levator muscles, and/or pelvic wall**

**Pathologic tumor staging**

- **pT2***Organ confined**
  - **pT2a-Unilateral**
  - **pT2b-Bilateral**

  ***Note: There is no pathologic T1 classification***

- **pT3-Extraprostatic extension**
  - **pT3a-Extraprostatic extension**

- **pT3b-Seminal vesicle invasion**

- **pT4-Invasion of bladder, rectum**

**Nodal status**

- **NX-Regional lymph nodes cannot be assessed**
  - **N0-No regional lymph node metastasis**
  - **N1-Metastasis in regional lymph node or nodes**

**Metastasis**

- **MX-Distant metastasis cannot be assessed**
  - **M0-No distant metastasis**
  - **M1-Distant metastasis**
    - **M1a-Nonregional lymph node(s)**
    - **M1b-Bone(s)**
    - **M1c-Other site(s)**

  ****Note: When more than one site of metastasis is present, the most advanced category is used. M1c is most advanced***

**Grouping**

<table>
<thead>
<tr>
<th>Stage</th>
<th>T1aN0M0</th>
<th>G1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage II</td>
<td>T1aN0M0</td>
<td>G2, 3–4</td>
</tr>
<tr>
<td></td>
<td>T1bN0M0</td>
<td>Any G</td>
</tr>
<tr>
<td></td>
<td>T1cN0M0</td>
<td>Any G</td>
</tr>
<tr>
<td></td>
<td>T1N0M0</td>
<td>Any G</td>
</tr>
<tr>
<td></td>
<td>T2N0M0</td>
<td>Any G</td>
</tr>
<tr>
<td>Stage III</td>
<td>T3N0M0</td>
<td>Any G</td>
</tr>
</tbody>
</table>
Stage IV  T4N0M0  Any G
Any TN1M0  Any G
Any TAny NM1  Any G

Treatment

General principles

The roles of surgery and radiation are still not clearly defined. Significant overlap in treatment exists, and treatment for most men can be tailored to meet the needs of the individual. Treatment to maintain urinary patency is required, but with current surgical practice, urinary continence is maintained in over 90% of patients.

Radical prostatectomy

Radical prostatectomy is the only curative surgical approach available. Candidates for surgery include those patients with clinical stage T1c or T2 disease, serum PSA < 10 ng/ml, and a Gleason score < 8 on biopsy specimen. Patients who present with clinical T3 disease and low grade disease and only focal capsular extension may still be surgically curable; generally, however, these patients are not ideal candidates for prostatectomy.

Patient age is also a strong predictor of curability, with the likelihood of findings at surgery consistent with curable disease declining with advancing age.

Stage I disease

Patients with Stage I disease may be managed by watchful waiting, though prostatectomy is reasonable if the patient is relatively young.

Stage II disease

In most cases, it is possible to tailor treatment to the age and overall performance status of patient. Standard therapy is radical prostatectomy, but there are some studies demonstrating that external beam radiation therapy and brachytherapy are effective; some studies show equivalent results to radical prostatectomy.

 Patients with T2 disease or with microscopically diffuse disease are at increased risk for metastases and lymphadenectomy is considered in this population.

Stage III disease

Radical prostatectomy with lymphadenectomy and XRT have virtually identical outcomes. The reason is that the relapse rate is high in this group, thus making any treatment of benefit difficult to demonstrate. Though it has been carefully studied, adjuvant chemotherapy not of proven value in this patient population. In some studies, hormonal therapy may improve the disease free interval with questionable benefit to overall survival.

Stage IV disease

Patients in this group are treated for palliative benefit, as the disease is incurable by definition. In some cases, the long term benefit to therapy can be substantial. Prostate cancer tissue is hormonally sensitive and hormonal manipulation is usually the systemic treatment of first choice. This can be accomplished by castration or my medical means using lutenizing hormone releasing hormone agonists (LHRA-a). These agents lower serum testosterone levels to castrate levels within 3 weeks of administration. Efficacy can be further in-
creased by the addition of testosterone receptor blocking agents such as flutamide (Eulexin®) or bicalutamide (Casodex®). The length of benefit with hormonal agents is inversely proportional to the grade of tumor, with higher grade lesions having shorter times to progression.

Cytotoxic chemotherapy is reserved for patients with progressive disease on hormonal therapy. There is no standard therapy for prostate cancer. Active agents include Adriamycin, vinca alkaloids, ketoconazole, aminogluthethamide, estramustine, mitoxantrone, abiraterone, cabazitaxel, and etoposide. Recent taxotere-based clinical trials have demonstrated improved response rates and time to progression over mitoxantrone-based regimens, and represent the current standard of care for initial chemotherapeutic intervention.

On progression, patients previously treated with taxotere are offered abiraterone or the new taxane cabazitaxel. Satriplatin is a new platinum-based agent with additional promise for palliative control of disease. Sipuleucel-T (Provenge®) therapy is available for asymptomatic or minimally symptomatic patients with hormone refractory disease; this approach offers adoptive immunotherapy for selected patients, although its high cost and requirement for special handling limits availability. Intravenous radiopharmaceuticals, such as strontium-89, are effective for palliative relief of bone pain. Radiotherapy can be used for focal pain as well.

**Germ Cell Tumors**

**Introduction**

Germ cell tumors represent only about 1% of all male cancers, but it is the most common solid tumor in males between ages 29 and 40. There are three peak age groups...

- Infants—embryonal carcinoma and yolk sac tumors most common
- Young adults—all types
- Older adults—seminoma

There is a strong association with cryptorchidism and testicular tumors. The cause of germ cell tumors is unknown.

**Clinical Presentation**

Most complain of scrotal swelling, discomfort, or heaviness. Pain is reported less than 20% of the time; when present, it usually occurs in the scrotum, but back pain from paraaortic node metastases can occur. Gynecomastia occurs 10-15% of the time. Constitutional symptoms include fatigue, malaise, weight loss, and fever.

**Pathology of Germ Cell Tumors**

For general purposes, germ cell tumors can be divided into two broad categories: seminomas and nonseminomatous germ cell tumors (NGCT). Additionally, germ cell tumors can occur in the testis (over 90%) or in primordial germ cell nests in the mediastinum or retroperitoneum which fail to regress in embryonic life (about 5%).

**Seminoma subtypes**

The most common variety is classic seminoma. On occasion, anaplastic seminomas are
seen and they present with a higher stage when diagnosed. Often, 3 mitoses per high power field can be identified, an indication of a very aggressive tumor. They are treated just like classic seminoma. A variant of seminoma called spermatocytic seminoma occurs universally in elderly men. It is slow growing with an excellent prognosis. It tends not to metastasize.

**Nonseminoma subtypes**

Embryonal carcinoma is a highly malignant, anaplastic tumor whose presence indicates the need for aggressive therapy.

Various forms of teratoma are often present; the mature variety is slow growing and is the least aggressive of the nonseminomass, the immature form of teratoma is more aggressive.

Choriocarcinoma is rare. In order to establish the diagnosis there must be both cytotrophoblastic and syncytiotrophoblastic tissue present. Choriocarcinoma is fairly aggressive.

Yolk sac tumor is a very rare but very aggressive tumor.

**Clinical Course**

The natural history of germ cell tumors is metastases via the retroperitoneal lymph nodes. Occasionally, hematogenous spread can occur. These are highly treatable, mostly curable tumors.

**Embyronic origin of the various germ cell cancers.**

**Diagnosis and Staging**

The diagnosis depends on biopsy of suspicious testicular mass. The correct procedure for testicular biopsy is delivery of the testis out of the scrotum into the inguinal canal followed by removal of the testis and cord (radical orchiectomy). Transscrotal biopsies are to be discouraged, as such a procedure changes the lymphatic drainage of the tumor and, hence, the natural course of the disease.

Tumor markers (AFP, βHCG) are often elevated in NGCT but are normal in seminoma. Levels directly reflect tumor bulk and are valuable in detecting disease recurrence. The lactate dehydrogenase isoenzyme LDH-1 may be elevated in seminomas.

Additional staging examinations include chest x-ray, computed tomography of the abdomen and pelvis for adenopathy, and ultrasound of both testes in view of the 15% risk for bilateral disease.

**Treatment of Seminomas**

**Stage A**

Treatment of Stage A seminoma includes radical orchietomy followed by active surveillance or retroperitoneal radiation if the patient is not trustworthy.
**Stage B1 and B2**

In the case of more advanced disease, radical orchiectomy is followed by radiation. Chemotherapy as for advanced disease can be utilized if radiation is not appropriate.

**Stage B3 and C**

With extremely advanced disease, radical orchiectomy is followed by chemotherapy.

**Treatment of Nonseminomas**

**Stage A**

In patients with minimal disease, radical orchiectomy is followed by retroperitoneal node dissection in view of the increased rate of occult retroperitoneal nodal metastases. Retroperitoneal lymph node dissection is an aggressive surgery, however, and observation of conscientious patients is an option. Those patients being observed who relapse in the retroperitoneum can still be cured in the majority of cases with retroperitoneal lymph node dissection.

**Stage B1 and B2**

For more advanced disease, radical orchiectomy is performed with retroperitoneal lymph node dissection in patients with nodes larger than 3 cm on CT. Patients with lymph node positive disease receive two cycles of chemotherapy.

**Stage B3 and C**

With advanced disease, radical orchiectomy and chemotherapy are the mainstays of treatment. Surgery is effective for debulking residual tumor after chemotherapy.

**Surgery for Germ Cell Tumors**

As previously discussed, radical orchiectomy involves removal of the affected testis and cord. It allows for determination of adverse prognostic factors such as capsule invasion, direct extension to the spermatic cord or vascular structures, and it permits precise pathologic diagnosis.

Retroperitoneal lymph node dissection involves gross exoneration of all paraaortic, iliac, and presacral lymph nodes. The morbidity of the procedure is significant, with lymphedema, ileus, and a lengthy postoperative recovery period the norm.

**Radiation for Germ Cell Tumors**

Radiation is usually delivered to the retroperitoneum. There are three circumstances where radiation is of value:

- Retroperitoneal treatment in patients who are not surgical candidates.
- Residual masses after treatment for seminoma.
- As part of multimodality therapy.

**Chemotherapy for Germ Cell Tumors**

The cornerstone of chemotherapy is a platinum-containing combination regimen. Etoposide and bleomycin are usually added to improve efficacy (the BEP regimen). Both seminomas and NGCT are responsive, usually curable diseases. Treatment is aggressive and some morbidity occurs in about 75% of cases, but mortality from treatment is rare. Complications include alopecia, pancytopenia, nausea and vomiting, pulmonary fibrosis (bleomycin), and cardiomyopathy (Adriamycin).
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