congestion and edema of the head and arm, and, ultimately, circulatory compromise—the **superior vena cava syndrome.** Extension to the pericardial or pleural sacs may cause **pericarditis** (Chapter 11) or **pleuritis** with significant effusions.

Staging. A uniform TNM system for staging cancer according to its anatomic extent at the time of diagnosis is useful, particularly for comparing treatment results from different centers (Table 15-10).

Clinical Course. Lung cancer is one of the most insidious and aggressive neoplasms in the realm of oncology. In the usual case it is discovered in patients in their 50s or older whose symptoms are of several months' duration. The major presenting complaints are cough (75%), weight loss (40%), chest pain (40%), and dyspnea (20%). Some of the more common local manifestations of lung cancer and their pathologic bases are listed in Table 15-11. Not infrequently the tumor is discovered by its secondary spread during the course of investigation of an apparent primary or metastatic neoplasm elsewhere. Symptoms of metastases depend on the site, for example, back pain in bone metastases, headache, hemiparesis, cranial nerve damage, and seizures in brain metastases.

Table 15-10 International Staging System for Lung Cancer

TNM Staging			
Tis	Carcinoma in Situ		
T1	Tumor ≤ 3 cm without pleural or mainstem bronchus involvement (T1a, <2 cm; T1b, 2-3 cm)		
T2	Tumor 3-7 cm or involvement of mainstem bronchus 2 cm from carina, visceral pleural involvement, or lobar atelectasis (T2a, 3-5 cm; T2b, 5-7 cm)		
T3	Tumor >7 cm or one with involvement of parietal pleura, chest wall (including superior sulcus tumors), diaphragm, phrenic nerve, mediastinal pleura, parietal pericardium, mainstem bronchus < 2 cm from carina but without involvement of carina, or entire lung atelectasis, or separate tumor nodules in the same lobe		
T4	Any tumor with invasion of mediastinum, heart, great vessels, trachea, recurrent laryngeal nerve, esophagus, vertebral body, or carina or separate tumor nodules in a different ipsilateral lobe		
N0	No metastasis to regional lymph nodes		
N1	Ipsilateral hilar or peribronchial nodal involvement		
N2	Metastasis to ipsilateral mediastinal or subcarinal lymph nodes		
N3	Metastasis to contralateral mediastinal or hilar lymph nodes, ipsilateral or contralateral scalene, or supraclavicular lymph nodes		
M0	No distant metastasis		
M1	Distant metastasis (M1a, separate tumor nodule in contralateral lobe or pleural nodules or malignant pleural effusion; M1b, distant metastasis)		
Stage Grouping			
Stage IA	T1a, T1b	N0	M0
Stage IB	T2a	N0	M0
Stage IIA	T2b	N0	M0
	T1a, T1b, T2a	N1	M0
Stage IIB	T2b	N1	M0
	T3	N0	M0
Stage IIIA	T1, T2	N2	M0
	T3	N1, N2	M0
	T4	N0, N1	M0
Stage IIIB	Any T	N3	M0
	T4	N2, N3	M0
Stage IV	Any T	Any N	M1a, M1b

Table 15-11 Local Effects of Lung Tumor Spread

Clinical Feature	Pathologic Basis
Cough (50%-75%)	Involvement of central airways
Hemoptysis (25%-50%)	Hemorrhage from tumor in airway
Chest pain (20%)	Extension of tumor into mediastinum, pleura or chest wall
Pneumonia, abscess, lobar collapse	Airway obstruction by tumor
Lipoid pneumonia	Tumor obstruction; accumulation of cellular lipid in foamy macrophages
Pleural effusion	Tumor spread into pleura
Hoarseness	Recurrent laryngeal nerve invasion
Dysphagia	Esophageal invasion
Diaphragm paralysis	Phrenic nerve invasion
Rib destruction	Chest wall invasion
SVC syndrome	SVC compression by tumor
Horner syndrome	Sympathetic ganglia invasion
Pericarditis, tamponade	Pericardial involvement

SVC, Superior vena cava.

Despite some earlier studies that did not show any benefit, the first large-scale early detection trial produced a 20% reduction in lung cancer-related mortality by screening high-risk individuals with low-dose computed tomography. However, the outlook is still poor for most patients with lung carcinoma. Even with many incremental improvements in thoracic surgery, radiation therapy, and chemotherapy, the overall 5-year survival rate is only 16%. The 5-year survival rate is 52% for cases detected when the disease is still localized, 22% when there is regional metastasis and only 4% with distant metastases. In general, adenocarcinoma and squamous cell carcinoma tend to remain localized longer and have a slightly better prognosis than do the undifferentiated cancers, which are usually advanced by the time they are discovered.

Targeted treatment of patients with adenocarcinoma and activating mutations in EGFR (present in about 15% of all patients) or in other tyrosine kinases with specific inhibitors of the mutated kinases prolongs survival. Many tumors that recur carry new mutations that generate resistance to these inhibitors, proving that these drugs are "hitting" their target. In contrast, activating KRAS mutations (present in 30%) appear to be associated with a worse prognosis, regardless of treatment, in an already grim disease. New therapeutic targets are clearly needed.

Untreated, the survival time for patients with small-cell carcinoma is 6 to 17 weeks. This cancer is particularly sensitive to radiation therapy and chemotherapy, and cure rates of 15% to 25% for limited disease have been reported in some centers. However, most patients with small cell carcinoma have distant metastases at diagnosis. Thus, even with treatment, the mean survival after diagnosis is only about 1 year.

Paraneoplastic Syndromes. Lung carcinoma can be associated with several paraneoplastic syndromes (Chapter 7),