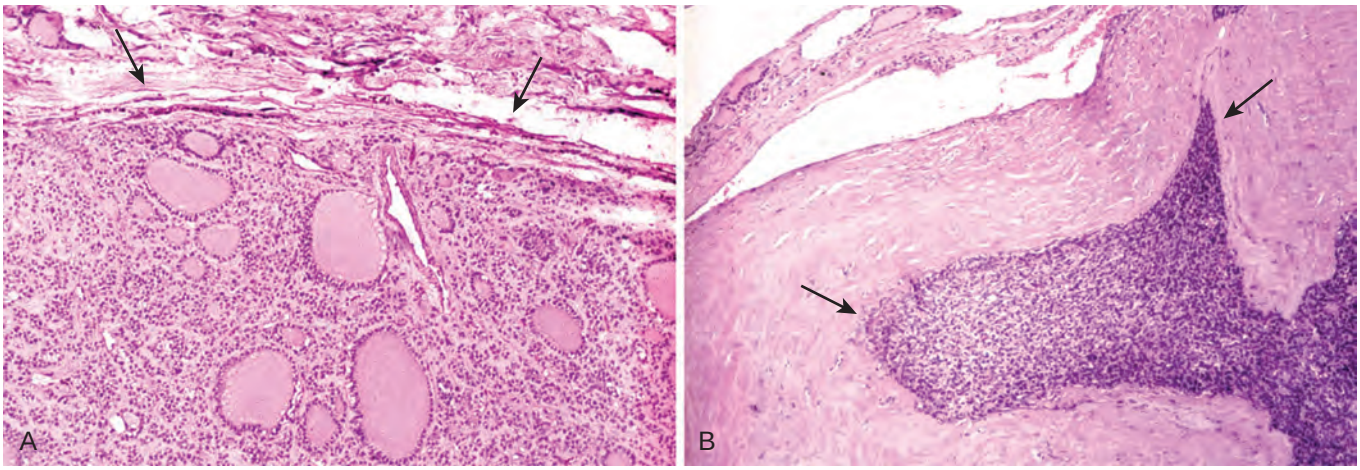

Figure 24-21 Capsular integrity in follicular neoplasms. In adenomas (**A**), a fibrous capsule, usually thin but occasionally more prominent, circumferentially surrounds the neoplastic follicles and no capsular invasion is seen *(arrows)*; compressed normal thyroid parenchyma is usually present external to the capsule *(top of the panel)*. In contrast, follicular carcinomas demonstrate capsular invasion (**B,** *arrows*) that may be minimal, as in this case, or widespread. The presence of vascular invasion is another feature of follicular carcinomas.

Microscopically, most follicular carcinomas are composed of fairly uniform cells forming small follicles containing colloid, quite reminiscent of normal thyroid (Fig. 24-20*B*). In other cases follicular differentiation may be less apparent, and there may be nests or sheets of cells without colloid. Occasional tumors are dominated by cells with abundant granular, eosinophilic cytoplasm **(Hürthle cell or oncocytic variant of follicular carcinoma)**. Whatever the pattern, the nuclei lack the features typical of papillary carcinoma, and psammoma bodies are not present. While nuclear features (optically clear nuclei, nuclear grooves) are helpful in distinguishing papillary from follicular neoplasms, **there is no reliable cytologic difference between follicular adenomas and minimally invasive follicular carcinomas**. Making this distinction requires extensive histologic sampling of the tumor-capsule-thyroid interface to exclude capsular and/or vascular invasion (Fig. 24-21). The criterion for vascular invasion is applicable only to capsular vessels and vascular spaces beyond the capsule; the presence of tumor plugs within intra-tumoral blood vessels has little prognostic significance. Unlike in papillary cancers, lymphatic spread is uncommon in follicular cancers.

In contrast to minimally invasive follicular cancers, the diagnosis of carcinoma is obvious in **widely invasive follicular carcinomas,** which infiltrate the thyroid parenchyma and extrathyroidal soft tissues**.** Histologically, these cancers tend to have a greater proportion of solid or trabecular growth pattern, less evidence of follicular differentiation, and increased mitotic activity.

Clinical Course. Follicular carcinomas present as slowly enlarging painless nodules. Most frequently they are *cold nodules* on scintigrams, although rare, better-differentiated lesions may be hyperfunctional, take up radioactive iodine and appear *warm* on scintiscan. Because follicular carcinomas have little propensity for invading lymphatics, regional lymph nodes are rarely involved, but vascular (hematogenous) dissemination is common, with metastases to bone, lungs, liver, and elsewhere.

The prognosis depends largely on the extent of invasion and stage at presentation. Widely invasive follicular carcinoma often presents with systemic metastases, and as many as half of affected patients succumb to their disease within 10 years. This is in sharp contrast to minimally invasive follicular carcinomas, which have a 10-year survival rate of greater than 90%. Most follicular carcinomas are treated with total thyroidectomy followed by the administration of radioactive iodine, which can be used to identify metastases and to ablate such lesions. In addition, because any residual follicular carcinoma may respond to TSH stimulation, patients are usually treated with thyroid hormone after surgery to suppress endogenous TSH levels. Serum thyroglobulin levels are used for monitoring tumor recurrence, because this thyroid protein should be barely detectable in a patient who is free of disease.

Anaplastic (Undifferentiated) Carcinoma

Anaplastic carcinomas are undifferentiated tumors of the thyroid follicular epithelium, accounting for less than 5% of thyroid tumors. They are aggressive, with a mortality rate approaching 100%. Patients with anaplastic carcinoma are older than those with other types of thyroid cancer, with a mean age of 65 years. Approximately a quarter of patients with anaplastic thyroid carcinomas have a past history of a well-differentiated thyroid carcinoma, and another quarter harbors a concurrent well-differentiated tumor in the resected specimen.

MORPHOLOGY

Microscopically, these neoplasms are composed of highly anaplastic cells, with variable morphology, including (1) large, pleomorphic **giant** cells, including occasional osteoclast-like multinucleate giant cells; (2) **spindle** cells with a sarcomatous appearance; and (3) **mixed** spindle and giant cells. Foci of papillary or follicular differentiation may be present in some tumors, suggesting an origin from a better-differentiated carcinoma. The neoplastic cells express epithelial markers like cytokeratin, but are usually negative for markers of thyroid differentiation, like thyroglobulin.