

## 2 Descriptive Terms in Anatomic Pathology

The ability to speak the language is essential to effective learning in pathology. This chapter covers the approach to defining and describing an unknown tumor or lesion and defines histologic terms commonly used in pathology.

### Common Prefixes and Suffixes and Their Definitions (a Very Short List)

Prefix or suffix	Definition	Example
angio-	Vessels (usually blood vessels)	Angiosarcoma
-blast	A precursor	Lipoblast
chol-	Bile	Cholangitis
chondro-	Cartilage	Chondroma
-cyte	Cell	Erythrocyte
dys-	Bad or improper	Dysplasia
ecto-	Outside	Ectocervix
-ectomy	Resection	Appendectomy
endo-	Inside	Endobronchial
epi-	Upon or in addition	Epidermis
exo-	Outside	Exogenous
extra-	Outside of, beyond	Extravasated
hist-	Tissue	Histology
hyper-	Above, beyond	Hyperchromatic
hypo-	Under, below	Hypopharynx
-iform	Resembling, but not the same as	Kaposiform
inter-	Between	Intercellular
intra-	Within, inside	Intrathoracic
-itis	Inflammation	Meningitis
leiomyo-	Smooth muscle	Leiomyoma
lipo-	Adipose tissue	Lipoblast
macro-	Large	Macroscopic
mega-	Very large	Megakaryocyte
meso-	Middle	Mesothelium
meta-	After, beyond, or accompanying	Metaphysis
micro-	Small	Microscope

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Prefix or suffix	Definition	Example
myxo-	Mucus	Myxoid
neo-	New	Neoplasia
-oid	Resembling, but not the same as	Sarcomatoid
-oma	Tumor or mass	Hemangioma
olig-	Few, small	Oligodendrocyte
-osis	Indicating a pathologic state	Diverticulosis
osteo-	Bone	Osteophyte
-otomy	To cut into	Laparotomy
-ous	Forming an adjective	Mucinous
para-	Next to	Paravertebral
-plasia	Growth	Hyperplasia
pseudo-	False	Pseudocyst
rhabdomyo-	Skeletal muscle	Rhabdomyosarcoma
trich-	Hair	Trichobezoar

## Interface with the Surrounding Normal Tissue

Term and definition	Appearance	Example
Circumscribed: well-delineated lesion	Well-defined border between normal tissue and the lesion	Fibroadenoma
Encapsulated: surrounded by a fibrous capsule	Thick pink border surrounding the lesion	Follicular adenoma, thyroid
Infiltrative: invading into and among the surrounding normal cells	No clear border between tumor and normal tissue	Prostate carcinoma
Lobular: in architecture, refers to a generally circumscribed or anatomic distribution	Circumscribed, rounded nodules of cells; simulates a normal anatomic unit	Lobular capillary hemangioma
Pushing border: expanding into and compressing the surrounding tissue	Can create the appearance of a capsule	Medullary carcinoma, breast

## Cellularity (Low to High) and Mitotic Rate

Note the cellularity (by *cellularity* we often mean how blue it is or how densely packed the nuclei are). Cellularity ranges from *hypercellular*, also called *cellular*, to *hypocellular* or *paucicellular*. Also look for mitoses on high power. High mitotic rate may be an indicator of malignancy. Atypical mitoses (tripolar or worse) are strongly suggestive of malignancy. Estimate how many mitoses are seen per high-power field (40× objective).

## Architectural Pattern

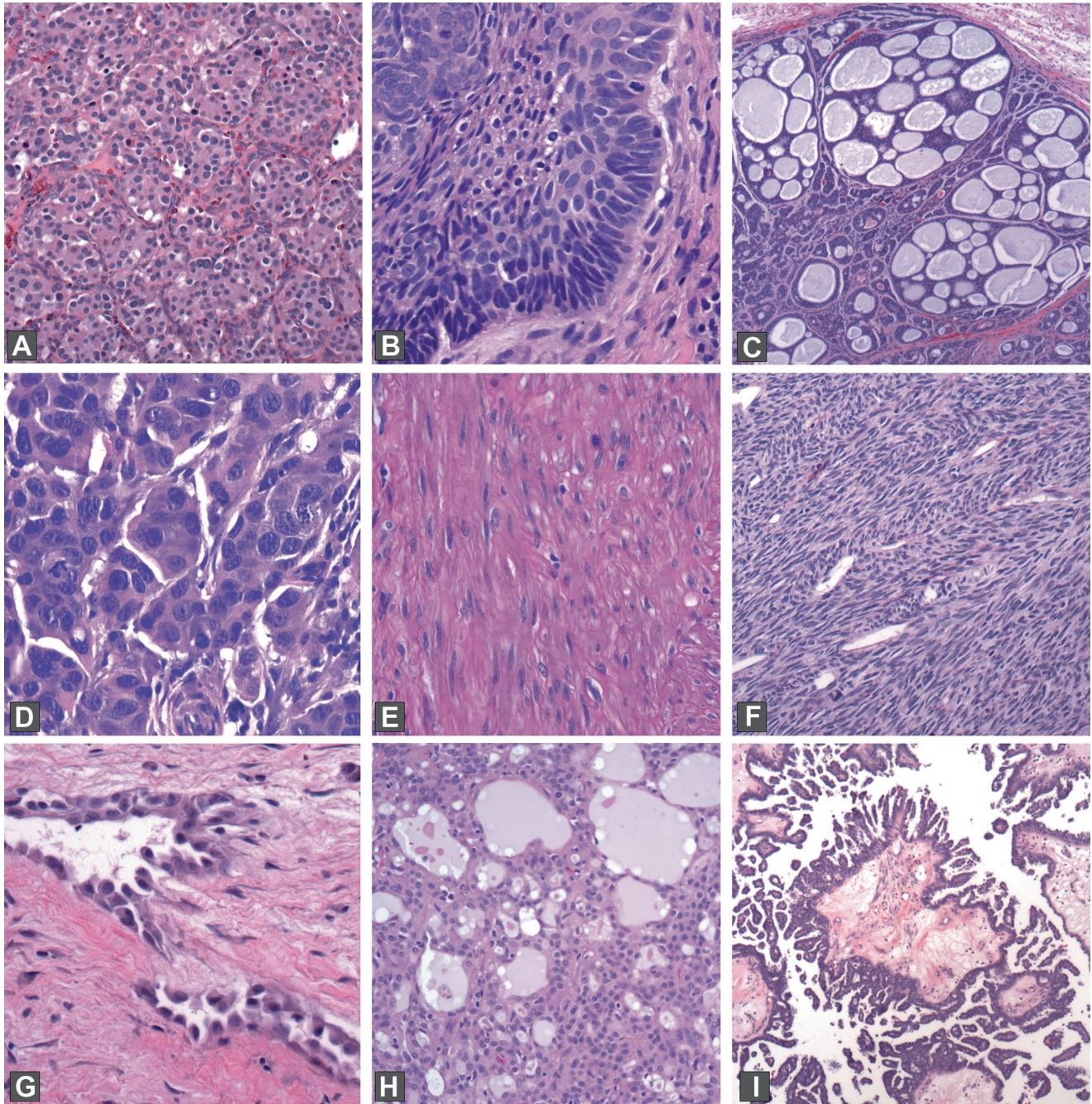
Term and definition	Appearance	Example
Alveolar: resembling alveoli or little cells, sacs, or nests	Nested—there is structure to the lesion but no glands or ducts	Paraganglioma (Figure 2.1a)
Basaloid: resembling basal cell carcinoma	A blue, nested tumor (often poorly differentiated squamous) with tightly packed nuclei and palisading around the edge of the nest	Basal cell carcinoma (Figure 2.1b)
Biphasic: having components of two cell lineages	Spindled cells with islands of epithelial cells or glands	Synovial sarcoma
Cribriform: perforated, like a colander	Crisp round holes within a glandular structure	Adenoid cystic carcinoma (Figure 2.1c)
Discohesive: falling apart into single cells	No common borders among cells	Lobular carcinoma in situ

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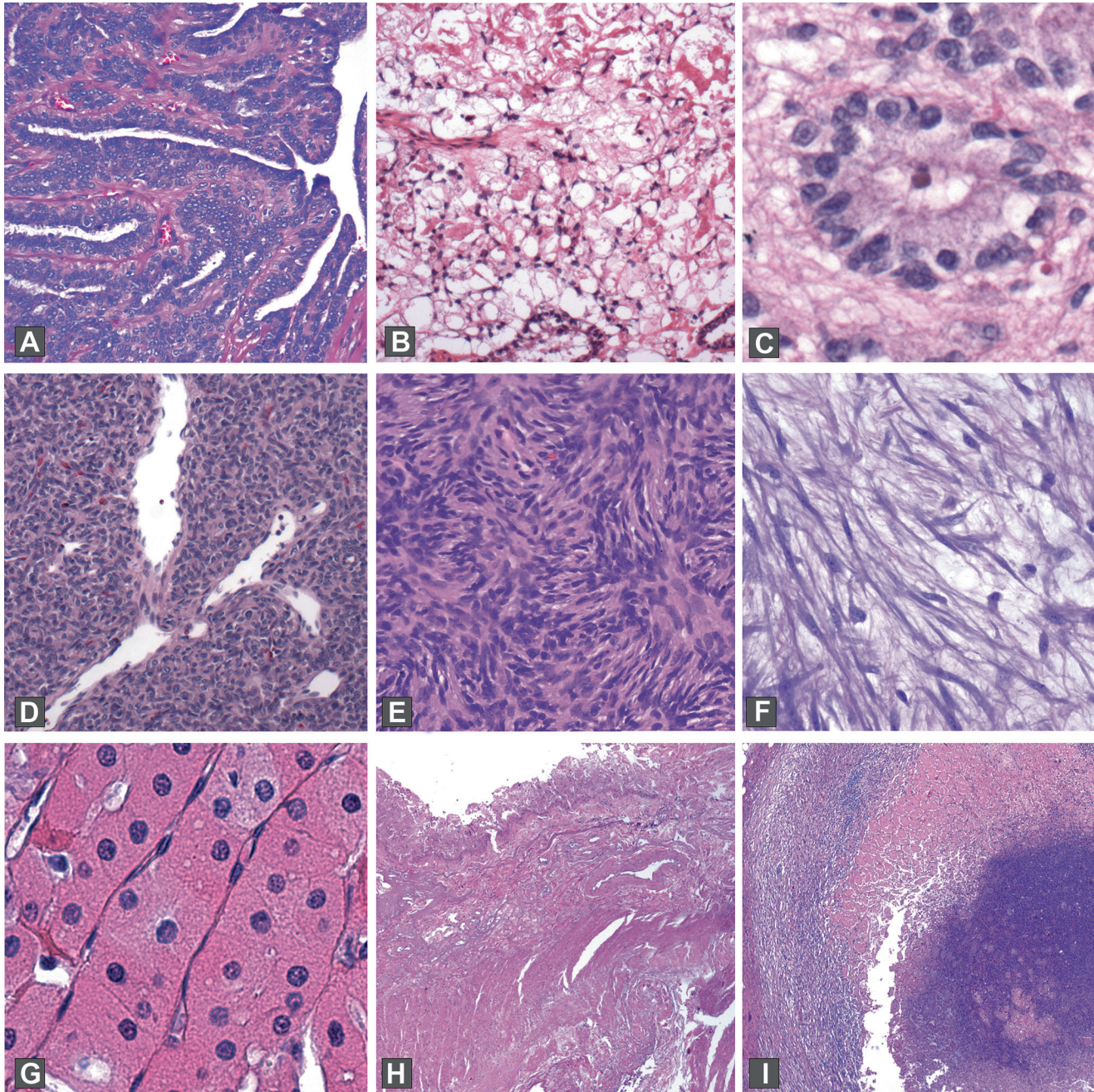
Term and definition	Appearance	Example
Epithelioid: composed of round to oval cells with abundant cytoplasm	Cells look plump and have clear cell borders; the opposite of sarcomatoid	Ductal carcinoma, breast (Figure 2.1d)
Fascicular: composed of fascicles	Bundles of elongated, spindly cells streaming in parallel arrays	Leiomyoma (Figure 2.1e)
Glandular: forming gland structures with lumens	True glands should have polarized cells radiating around a lumen	Adenocarcinoma
Glomeruloid: resembling the glomerulus	A coiled tangle of vessels, capillaries, or glands	Vascular proliferations in glioblastoma (GBM)
Herringbone: resembling a pattern of tweed fabric	A variant of fascicular that shows bundles alternating in a zigzag array	Fibrosarcoma (Figure 2.1f)
Hobnailed: resembling a large-headed nail once used in shoes	Epithelial or endothelial cells that round up and protrude into the lumen as little humps	Angiosarcoma (Figure 2.1g)
“Indian file”: cells infiltrating through the tissue in single-file lines	Lines may be only three to four cells long and run parallel to stromal planes	Lobular breast carcinoma
Microcystic: scattered small cystic spaces that are not ducts, tubules, or glands	Microcysts lack polarized epithelial linings and are haphazard; nuclei touch the lumen	Mammary analogue secretory carcinoma (Figure 2.1h)
Micropapillary: papillary-shaped epithelial projections without true fibrovascular cores	Can have a medusa-head appearance (serous carcinoma) or lollipop projections into a duct (micropapillary DCIS)	Micropapillary serous carcinoma, ovary (Figure 2.1i)
Nested: see <i>alveolar</i>		
Pagetoid spread: single malignant cells scattered throughout a benign epidermis	Cells standing out at low power as not belonging in the epithelium	Paget's disease
Palisading: resembling a fence made of sharp stakes	Parallel arrays of nuclei catching your eye at low power as a dark border	Basal cell carcinoma (see Figure 2.1b)
Papillary: an exophytic growth pattern with fibrovascular cores supporting proliferative epithelium	Cauliflower- or coral-shaped structures with branching fibrovascular cores	Papilloma, breast (Figure 2.2a)
Polarized: epithelial cells that have a uniform nuclear position, either apical (lumen side) or basal (basement membrane side)	Polarized cells surrounding a true lumen should show a distinct ring of cytoplasm surrounding the lumen, if the nuclei are basal	Cribiform DCIS
Pseudopapillary: a papillary pattern caused by cell die-off in between fibrovascular septa	Looks papillary but there is evidence of solid or nested growth in some areas	Solid pseudopapillary neoplasm, pancreas
Reticular: resembling a network or netlike array	Microcystic or honeycomb appearance	Yolk sac tumor, testes (Figure 2.2b)
Rosettes: a group of non-epithelial cells that are clustered around a common center	Pseudorosettes are rosettes around a vessel; true rosettes surround a lumen or a fibrillary core	Ependymoma (Figure 2.2c) and other neuroglial and neuroendocrine lesions
Sarcomatoid: resembling a sarcoma, but not one	Sheets or bundles of tumor cells without epithelial structures or clear cell borders	Sarcomatoid carcinoma
Spindled: composed of elongated cells with fusiform nuclei	Sheets or fascicles of fusiform cells; suggests a lesion is either a soft tissue neoplasm or a sarcomatoid variant of something else	Leiomyoma
Staghorn vessels: gaping, branching vessels with thin walls, scattered throughout a lesion	Vessels should strike you as prominent at low power; the shape is unusual, and the walls are disproportionately thin for the diameter	Hemangiopericytoma (Figure 2.2d)
Storiform: having a cartwheel pattern—spindle cells with elongated nuclei radiating from a center point	A cellular spindled lesion with short whorls of cells as opposed to long parallel fascicles	Dermatofibrosarcoma protuberans (Figure 2.2e)
Syncytial: having apparent cytoplasmic continuity between adjacent cells	Looks like a collection of nuclei without recognizable cell borders	Meningioma
Tissue culture pattern: a loose aggregate of stellate (star-shaped) cells	Cells have delicate tentacles of cytoplasm	Nodular fasciitis (Figure 2.2f)
Trabecular: cord-like arrays separated by fibrous septa	Long nests and cords of cell groups	Oncocytoma (Figure 2.2g)





**FIGURE 2.1.** (a) Alveolar pattern, paraganglioma; (b) basaloid pattern and palisading, basal cell carcinoma; (c) cribriform pattern, adenoid cystic carcinoma; (d) epithelioid cells, breast carcinoma; (e) fascicular pattern, leiomyoma; (f) herringbone pattern, fibrosarcoma; (g) hobnail cells, angiosarcoma; (h) microcystic pattern, mammary analogue secretory carcinoma; (i) micropapillary architecture, serous carcinoma of the ovary.





**FIGURE 2.2.** (a) Papillary architecture, papilloma of breast; (b) reticular pattern, yolk sac tumor of the testis; (c) rosette, ependymoma; (d) staghorn vessels, hemangiopericytoma; (e) storiform pattern, dermatofibrosarcoma protuberans; (f) tissue culture cells, nodular fasciitis; (g) trabecular pattern and oncocytes, oncocytoma; (h) coagulative necrosis, ischemic bowel; (i) caseating necrosis in a granuloma, tuberculosis.

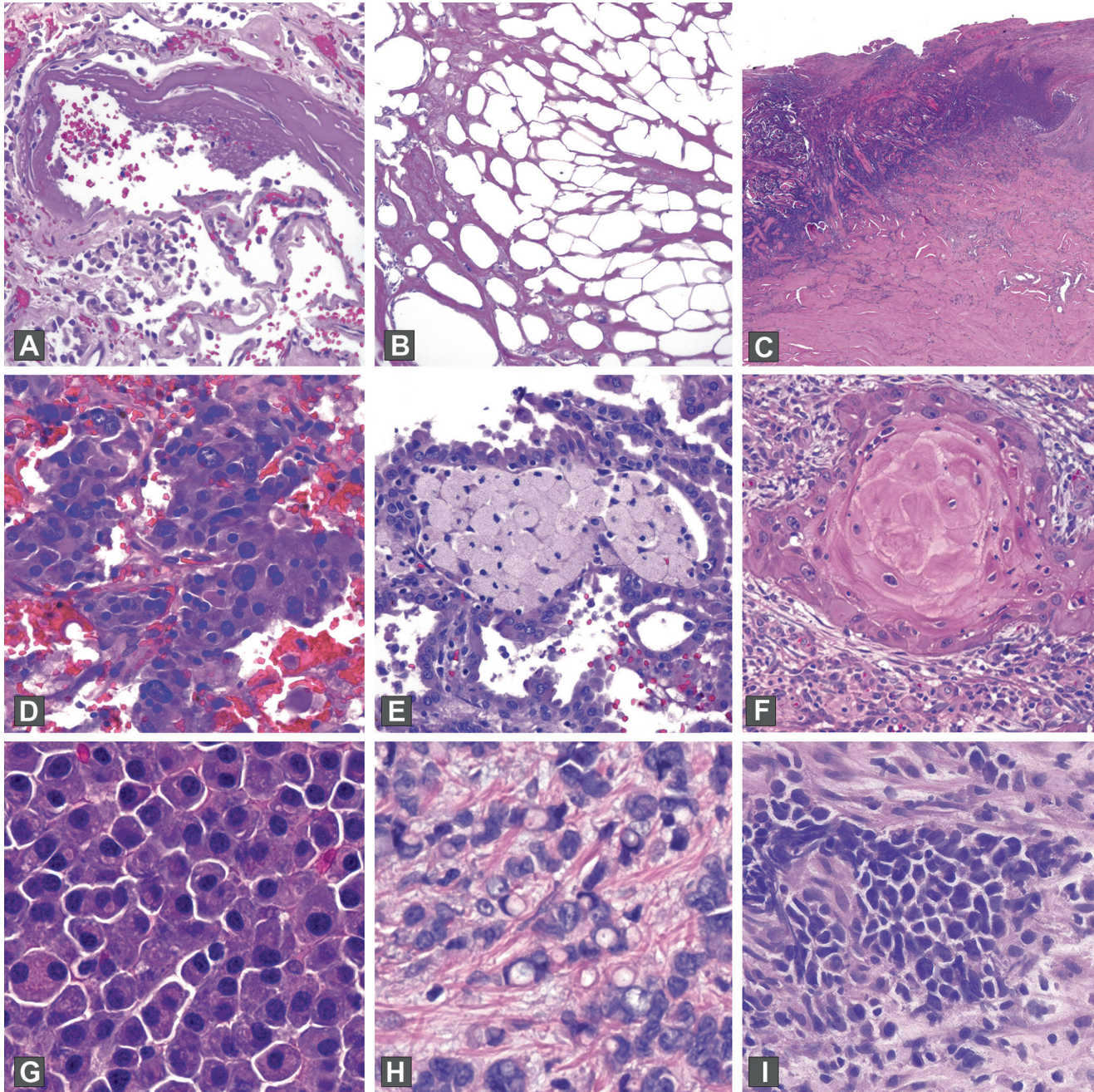
## Presence or Absence of Necrosis

Term and definition	Appearance	Example
Coagulative necrosis	Cells appear mummified; architecture is preserved, but there is no basophilia or cell detail	Ischemia (Figure 2.2h)
Caseating necrosis	Total loss of cellular structure and architecture; basically degenerates into pink soup	Tuberculosis (Figure 2.2i)
Fibrinoid necrosis	Vessels with replacement of wall by pink amorphous material	Vascular necrosis (Figure 2.3a)
Fat necrosis	Grossly hard and chalky white; microscopically the fat cells are disrupted and collapsed, with foamy macrophages and giant cells	Biopsy site changes in breast (Figure 2.3b)
Geographic necrosis	Describes large confluent “continent-shaped” patches of necrosis	Kikuchi’s disease
Necrobiosis or gangrenous necrosis	Has a granular and blue look, with lots of fibrin deposition; loss of cellular and architectural detail	Gangrene (Figure 2.3c)

## Cell Shape and Size and Cytoplasm

Term and definition	Appearance	Example
Amphophilic: having an affinity for both acid and basic dyes	Has a unique color character, almost an iridescent purple that is hard to capture on film	Pheochromocytoma (Figure 2.3d)
Foamy macrophages: macrophages (histiocytes) stuffed with lipid	Macrophages have a small dark eccentric nucleus; the lipid vacuoles give a glittery granular appearance	Papillary renal cell carcinoma (Figure 2.3e)
Granular: containing granules or tiny vacuoles	Color may vary, but granular texture is visible especially with lowered condenser	Granular cell tumor
Hof: a perinuclear clear zone corresponding to the Golgi apparatus	Looks like a pale spot hugging the nucleus	Plasma cells
Keratinized: keratin-producing	Keratin has a very pink and dense appearance on H&E stain	Squamous cell carcinoma (Figure 2.3f)
Mucous (adj.): mucinous or producing mucus (n.); also called <i>colloid</i>	Mucin (mucus) appears clear after processing but can be stained with mucicarmine or PAS-AB	Adenocarcinoma
Oncocytic: large cells with cytoplasm that is granular and eosinophilic due to the presence of abundant mitochondria	Oncocytes are usually cytologically bland (uniform small dense nuclei) and look pink on H&E, mahogany on gross examination	Oncocytoma (see Figure 2.2g)
Plasmacytoid: like plasma cells	Round cells with abundant cytoplasm and an eccentric round nucleus	Plasmacytoma (Figure 2.3g)
Rhabdoid: refers to a specific malignant tumor that resembles rhabdomyosarcoma or used to describe a tumor with similar histology	Large tumor cells with eccentric nuclei, prominent nucleoli, and globules of pink cytoplasm	Rhabdoid tumor of the kidney
Signet ring: having the shape of a jeweled ring, with a flattened nucleus compressed by a cytoplasm stuffed with mucin	Can be very hard to see on low power; on high power, the cell is a droplet of mucin with a faint cell wall and a nucleus pushed to one side	Signet-ring cell carcinoma (Figure 2.3h)





**FIGURE 2.3.** (a) Fibrinoid necrosis, pulmonary vessel; (b) fat necrosis, breast; (c) gangrenous necrosis, toe wound; (d) amphophilic cytoplasm, pheochromocytoma; (e) foamy macrophages, papillary renal cell carcinoma; (f) keratin, squamous cell carcinoma; (g) plasmacytoid morphology, plasmacytoma; (h) signet-ring cells, breast carcinoma; (i) nuclear molding, small cell carcinoma.

## Nucleus

Let's take a moment to talk about the nucleus. If you are beginning your pathology residency, you will spend the next 4 years learning to read nuclei. The H in H&E stands for hematoxylin, which stains nucleic acids, and therefore nuclei, purple; the eosin highlights everything else.



A large chunk of pathology can be boiled down to recognizing nuclear changes that suggest malignancy. The nucleus is the genetic center of the cell, and surprisingly, molecular changes that disconnect the cell from normal feedback mechanisms (i.e., cancer) can often be detected by actual physical changes in the nucleus. For example, changes in the nuclear membrane, changes or irregularities in the nuclear size and shape, alterations in the chromatin pattern and density, or abnormally prominent nucleoli all prompt the pathologist to look more closely. Part of what makes pathology so challenging is that different organs play by different rules, so that what is a “normal” nucleus in one organ represents dysplasia in another. As you learn pathology, above all you must get a feel for which nuclei should make you worry, and the way to do this is to ask your mentors to describe exactly what they are seeing when they use the single most overused and least specific word in our field: atypical.

*Atypical: literally, not typical or outside the norm of a certain class of cells* When a pathologist uses the term, however, it means “nuclear changes which concern me.” The exact nuclear alterations which warrant the *atypical* label vary by tissue type. On the clinical side, *atypical* is read to mean “the differential diagnosis includes benign and malignant,” and it often ends up punting the question the biopsy was intended to answer. Although it is sometimes unavoidable, try to minimize the use of “atypical” in your diagnoses.

Variants:

*Reactive atypia:* nuclear changes which might concern me if it weren’t for this blazing inflammation.

*Degenerative atypia:* nuclear changes which would concern me if I wasn’t 100% sure this was a benign tumor.

*Marked atypia:* nuclear changes which are so pronounced I’m almost certain this is cancer, but if it turns out to be reactive atypia instead, you can’t sue me.

*Mild atypia:* nuclear changes which are so trivial I’m almost certain this is benign, but if it turns out to be dysplasia instead, you can’t sue me.

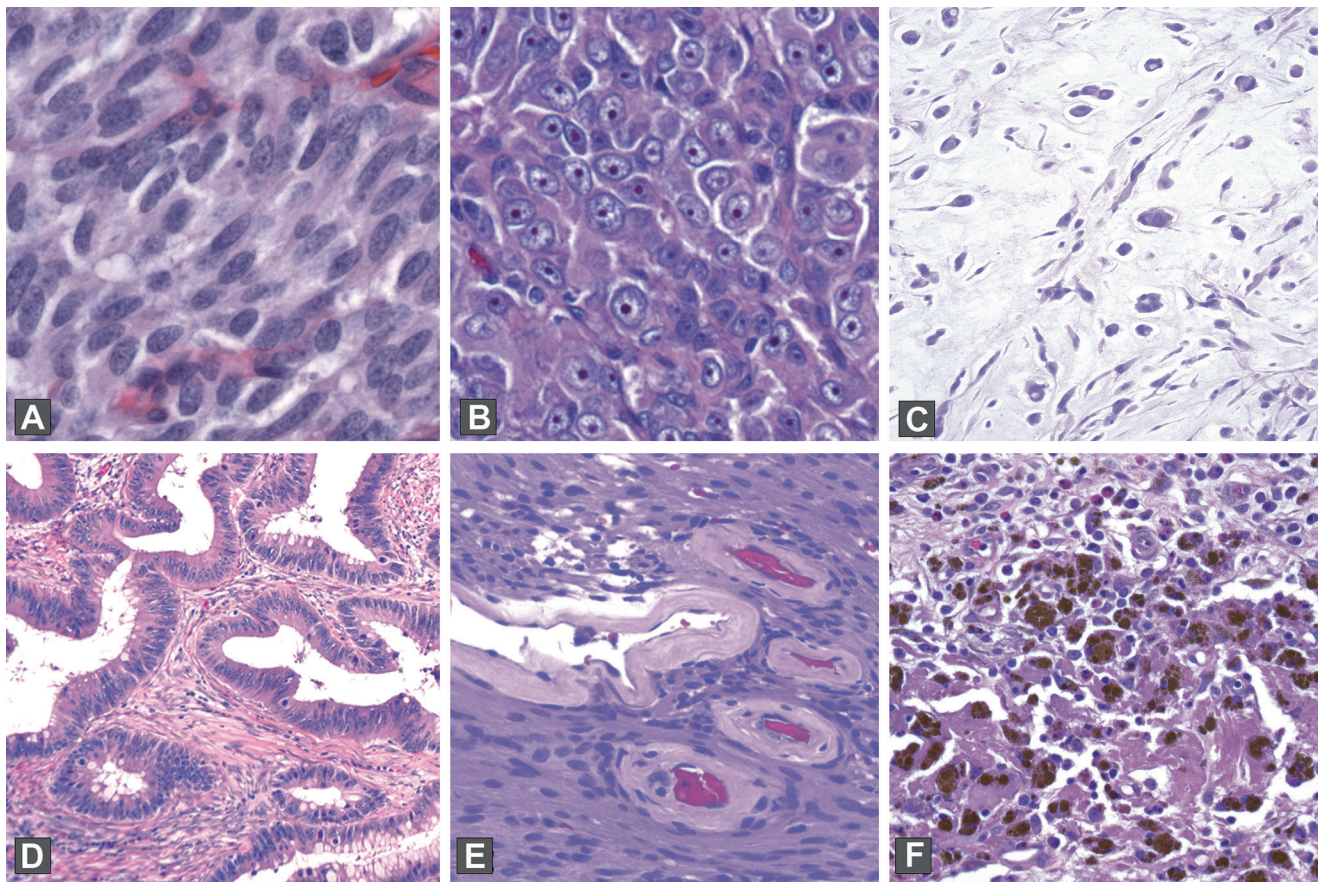
*We see this:* not atypical.

Making the interpretation of nuclei more complicated is the fact that changes in fixation, staining intensity, crush artifact, cautery, desiccation, and other variables can make the same tumor look very different. Part of the learning process is determining which nuclear features are truly part of the tumor and which are due to artifact. One way is to calibrate using the non-tumor nuclei in the tissue, such as normal epithelial or endothelial nuclei. This is similar to the process by which your brain learns to identify “blue” in all different lighting conditions, by comparing the actual color signal (which may not be blue at all) to the color signals of other known objects, like skin tone or white paper. Some nuclear artifacts become signatures of the tumor type, like the cleared-out chromatin of papillary thyroid carcinoma. Vesicular nuclei, however, while associated with malignancy, can also be a consequence of delayed fixation.

There are some general categories of nuclear changes that you should be able to recognize, which are listed below. Large and hyperchromatic nuclei often indicate an instability of karyotype (literally too much chromatin) that is seen in certain malignancies, whereas large but euchromatic nuclei are commonly seen in benign reactive cells. Irregular nuclear membranes (folds, crenations, corners, asymmetry) are usually not found in benign cells. A prominent nucleolus indicates an active nucleus, but does not equal malignancy. Normal myeloid blasts, for example, have prominent nucleoli, and reactive epithelial cells often have multiple small nucleoli. However, the presence of a large and reddish (protein-rich) nucleolus in a tumor is characteristic of certain tumor types, including carcinoma, melanoma, angiosarcoma, and some lymphomas (e.g., Hodgkin lymphoma). Very finely speckled chromatin is typical of neuroendocrine tumors, which generally do not show a nucleolus. Finally, primitive cells, such as small round blue cell tumors and fetal cells, have a characteristic homogeneous dispersed evenly blue chromatin, as though the undifferentiated cell has yet to sort out what genes are relevant and has all of them spread out in anticipation of starting the filing system. (As a pathologist, you will begin to anthropomorphize individual cells. This is not atypical.)

### Other Nuclear Adjectives

Term and definition	Appearance	Example
Clock face: evenly distributed clumped chromatin	Looks like a soccer ball	Plasma cells
Eccentric: displaced to one side	Nucleus on one side, cytoplasm on the other	Plasma cells, rhabdoid cells
Molding: nuclei that press together and indent each other due to the near absence of cytoplasm	Has a mosaic appearance and usually seen in conjunction with small dense blue nuclei	Small cell carcinoma (Figure 2.3i)
Neuroendocrine: having finely speckled or salt-and-pepper chromatin	Nuclei should be round, pale, and smooth, without nucleoli, but with occasional chromatin “chunks” or speckles	Carcinoid (Figure 2.4a)
Pleomorphic: multiple sizes and shapes	Usually refers to nuclei and implies a very irregular mix of sizes and shapes	Embryonal carcinoma, testis
Vesicular: a nucleus in open phase, in which the chromatin is expanded (as opposed to compact and condensed)	A nucleus that is swollen and distorted by apparent bubbles in the chromatin	Various malignant neoplasms



**FIGURE 2.4.** (a) Neuroendocrine nuclei, carcinoid tumor; (b) cherry-red nucleolus, melanoma; (c) myxoid stroma, myxofibrosarcoma; (d) desmoplastic stroma, colon cancer; (e) hyaline deposits, vessels in schwannoma; (f) hemosiderin, nasal polyp.

## Nucleolus

Cherry red: implies a malignant-looking nucleolus	An enlarged, solid nucleolus with a refractile red tinge due to increased protein content	Melanoma (Figure 2.4b)
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## Cell Membrane

Ciliated: having cilia	If the cilia are not visible, sometimes the terminal bar is enough	Respiratory mucosa
Intercellular bridges: desmosomes	The prickles or spines between squamous cells	Normal skin, especially visible if edematous

## Stroma of Lesion, If Present

Term and definition	Appearance	Example
Chondroid: resembling, or made of, cartilage	Bluish-gray stroma with small cells suspended in lacunae (open spaces)	Normal cartilage
Desmoplastic: causing edema and fibrosis in the stroma next to a neoplasm	Alternating layers of pink fibrosis and clear edema surrounding malignant glands; overall appears pale at low power	Adenocarcinoma, pancreas or colon (Figure 2.4d)
Edematous: waterlogged	Water is clear on H&E so appears as lots of cleared-out space	Granulation tissue
Fibrotic/sclerotic: replaced by collagen (fibrosis)	Collagen is pink and opaque on H&E and usually streams in parallel fibers	Sclerosed intraductal papilloma
Hyaline: clear, transparent, homogeneous	Glassy-pink appearance	Characteristic vessel walls in schwannoma (Figure 2.4e)
Myxoid: resembling mucus, but usually associated with a soft tissue lesion and hyaluronic acid	Appears as a faint pink to bluish-gray background, with a stringy mucous look	Myxofibrosarcoma (Figure 2.4c)

## Other Noncellular Entities

Term and definition	Appearance	Example
Amyloid: protein deposited in a $\beta$ -pleated sheet molecular structure	Appears glassy pink, stains salmon-pink with Congo red, and fluoresces apple green	Medullary carcinoma, thyroid
Anthraxotic pigment	Very black, very dense fine granules	Pulmonary lymph nodes
Calcium and psammoma bodies	Purple and granular, with hard edges; psammoma bodies are concentrically laminated	Papillary thyroid carcinoma
Colloid: refers to a mucin-producing neoplasm <i>or</i> the pink substance in thyroid follicles	Thyroidal colloid is a thin homogeneous pink	Thyroid tissue
Hemosiderin	Has a glittery golden-brown refractile appearance with the poor man's polarizer (waving your finger above the light source)	Old blood in any lesion (Figure 2.4f)
Lipofuscin	Appears yellowish brown and globular	Seminal vesicle
Melanin	Unlike hemosiderin, is <i>not</i> refractile; may be brown to gray	Melanoma
Tattoo pigment	Similar to anthracotic pigment, may be multicolored	Skin with tattoos



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