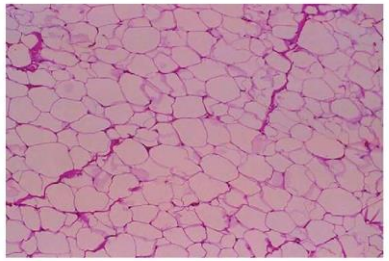
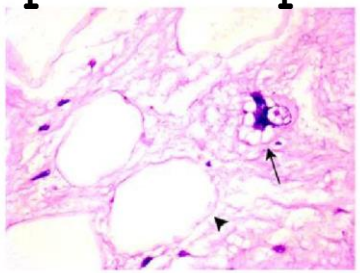
Miscellaneous tumors

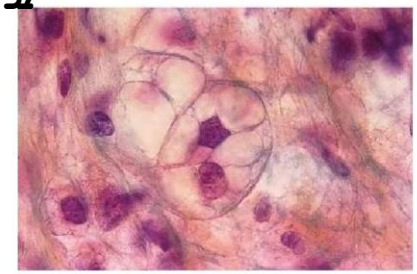
Lipoma


Lipoma

- MC soft tissue tumor
- Painless except_____
- Cytogenetics: Chr 6p, 12q and 13q
- Usually cured by simple excision

Liposarcoma: Morphology





- Lipocytes with supernumerary rings & giant rod chromosomes – 12q (MDM2 oncogene)
- Lipoblasts: scalloping of nucleus

Liposarcoma

- Most common sarcomas of adulthood
- MC: proximal extremities & retroperitoneum
- t(12;16) : Myxoid/round cell variant of liposarcoma

Tumors & Tumor-like lesions of fibrous origin

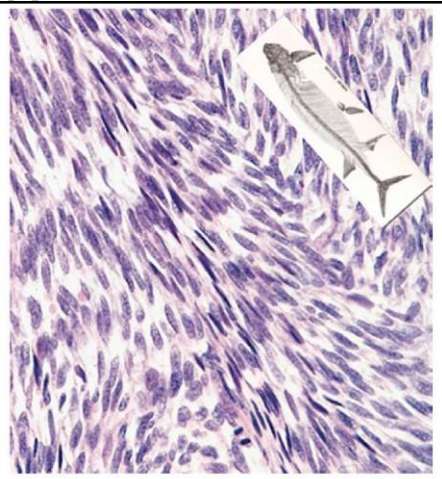
Fibromatoses:

Superficial	Deep

• Palmar- Dupuytren contracture
• Plantar
• Penile: Peyronie disese
	• Desmoid tumors-
	  • Locally aggressive
	  • Associated with Gardner syndrome (APC)
	  • Recurs
	  • Rx- wide Excision

Fibrosarcoma

- MC in extremities
- Herringbone pattern
- Aggressive
- Recurs
- Metastasises



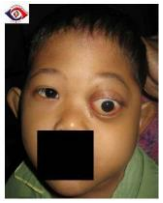
Herring bone pattern

Inflammatory myofibroblastic tumor

- Benign spindle cell tumor along with scattered inflammatory cells (lymphocyte and plasma cells)
- Occurs in viscera (lungs) and soft tissue of children and young adults
  - ALK (2p23) gene mutation (hereditary hemorrhagic telangiectasia-1, Adenocarcinoma lung, Neuroblastoma, Large, anaplastic large B cell lymphoma

Tumors of skeletal muscles

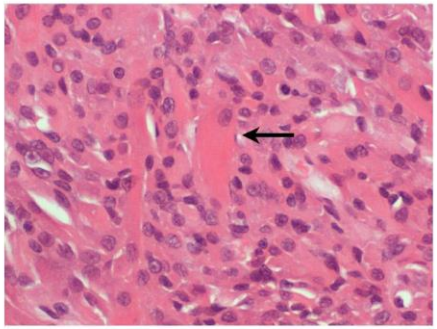
Rhabdomyosarcoma (RMS)



- Primitive mesodermal origin
- MC soft-tissue sarcoma of childhood & adolescence
- Most common—head/neck; 2nd Mc—genitourinary tract

Histology of RMS

- Rhabdomyoblast
- Stains--
  desmin, MYOD1 & myogenin.
- Histologically sub-classified into:
  - embryonal
  - alveolar
  - pleomorphic



Tadpole or strap cells

Embryonal RMS (MC, 60%)

- It includes sarcoma botryoides
- Occurs in children < 10 yrs of age
- Chr 11p involved
- A submucosal zone of hypercellularity -> cambium layer.

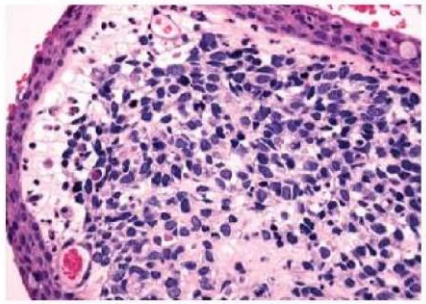
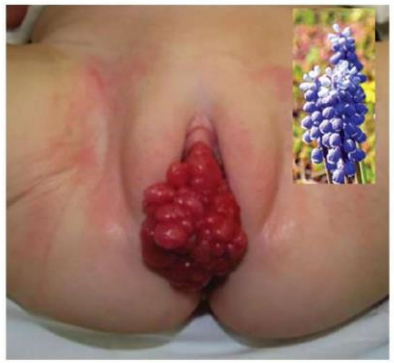


Figure 3. Cambium layer: tendence of the subepithelial cells to aggregate as a dense layer beneath the epithelium, leaving a free "band" zone. H&E.

Sarcoma Botryoides

- At age < 5 yrs
- Grape like clusters in vagina
- H/E: Tennis racket cells
- Rx: surgery + Chemotherapy



Botryoides tumor

Treatment and prognosis of RMS

- Rx: Surgery and chemotherapy with or without RT
- Histologic type and location of tumor influence survival

Best prognosis: Botryoid subtype

Intermediate prognosis: Embryonal NOS

Poor prognosis: pleomorphic and alveolar

Tumors of uncertain histogenesis

Synovial Cell Sarcoma

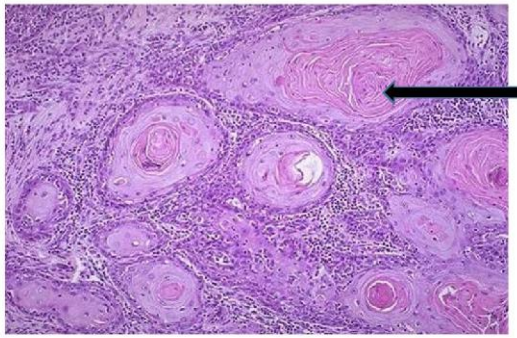
- Only 10% intra-articular!!!
- MC around knee
- H/E: Biphasic- epithelial & mesenchymal (spindle cells)
- Stains: Keratin, vimentin, S-100 & EMA
- Cytogenetics: t(X;18)

Tumors of Skin

Squamous Cell Carcinoma (SCC)

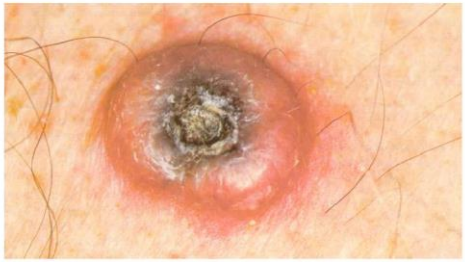
- 2nd most common tumor arising on sun-exposed sites
- Males>females (except on lower legs)
- Locally invasive; Metastasis uncommon
- Risk factors: UV light, immunosuppression, HPV (5 & 8), tobacco
- p53 mutation

Squamous cell carcinoma



Keratoacanthoma

- A variant of well-differentiated squamous cell carcinoma
- After a period of rapid growth, it usually regresses spontaneously

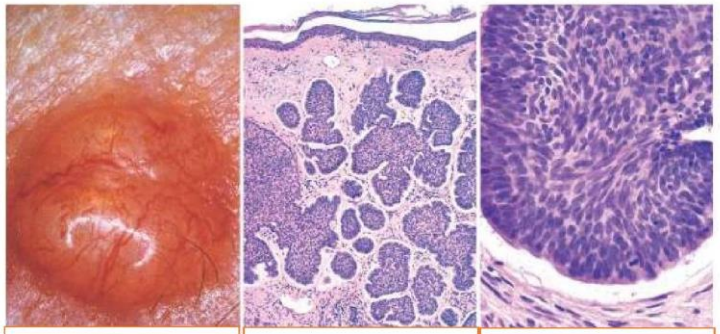


Basal Cell Carcinoma (Rodent ulcer)

- Most common invasive skin cancer
- Slow-growing tumors, rarely metastasize.
- Seen in immunosuppression & xeroderma pigmentosum
- NBCCS or Gorlin Syndrome – AD, multiple sites,

  Chr 9: PTCH gene receptor for product of SHH (Sonic Hedgehog) gene, p53 mutation

Basal Cell Carcinoma



Pearly, telangiectatic nodule | Tumor nests | Pallisading Separation artefact

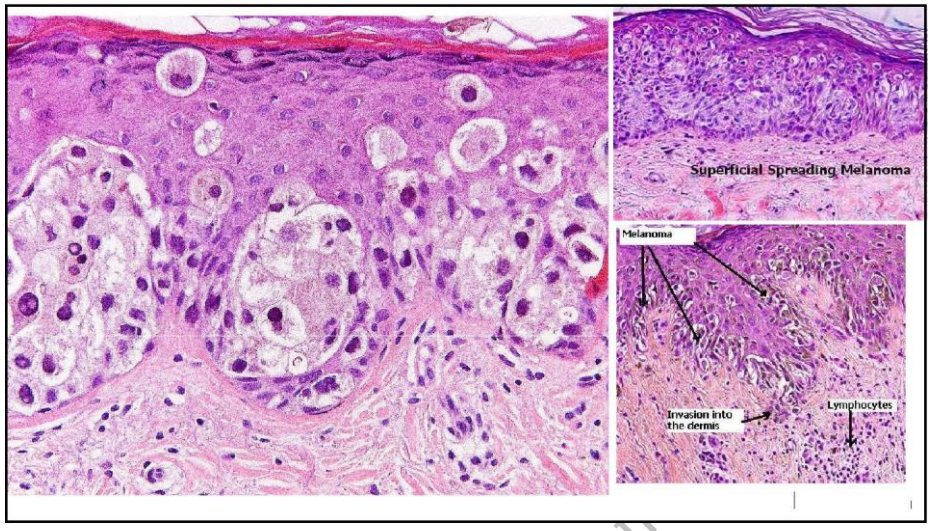
Melanoma

- Predisposing factors are inherited genes and sun exposure (induced mutations)

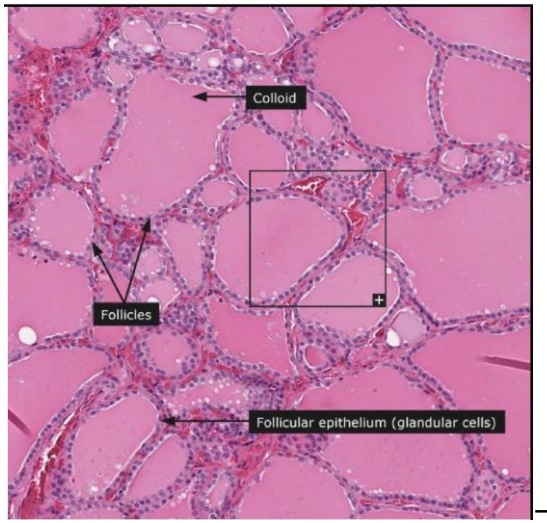
Growth patterns:

- Radial growth- horizontal spread within epidermis/superficial dermis
  - lentigo maligna: indolent lesion on the face of older men
  - Superficial spreading: (MC) sun-exposed skin
  - Acral/mucosal lentiginous melanoma: unrelated to sun exposure
- Vertical growth -appearance of a nodule & correlates with metastatic potential

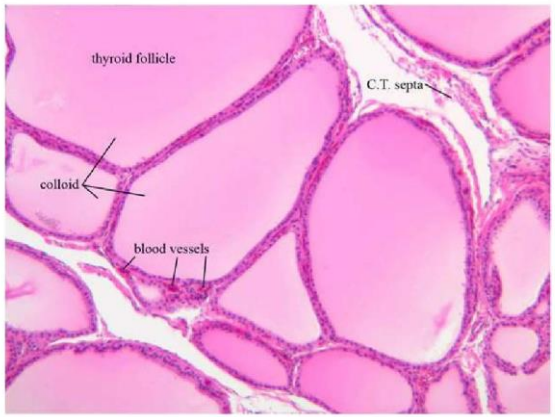
- 3 mutations:
  - Cell cycle regulators (p16/INK4a, CDK4),
  - Growth factor receptors e.g. BRAF, RAS,
  - TERT- activate telomerase
- Prognosis: metastasis correlates with the depth of invasion, which by convention is the distance from the superficial epidermal granular cell layer to the deepest intradermal tumor cells (Breslow thickness)
- Warning signs: ABCDE (1) asymmetry; (2) irregular borders; and (3) variegated color, (4) increasing diameter, and (5) evolution
- Marker- HMB-45 (Tendon clear cell sarcoma & Angiomyolipoma)



Endocrine system



Colloid goitre



Thyroiditis: Inflammation of the thyroid gland

(1) Hashimoto thyroiditis: autoimmune disease that results in destruction of the thyroid gland and gradual and progressive thyroid failure

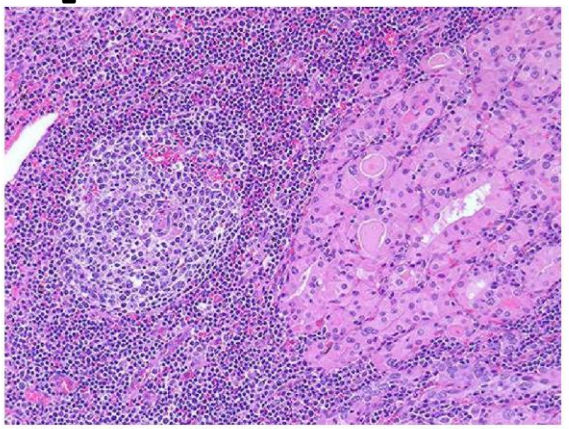
(2) Granulomatous (de Quervain) thyroiditis is a self-limited disease, probably secondary to a viral infection, and is characterized by pain and the presence of a granulomatous inflammation in the thyroid.

(3) Subacute lymphocytic thyroiditis often occurs after a pregnancy (postpartum thyroiditis), typically is painless, and is characterized by lymphocytic inflammation in the thyroid.

Hashimoto's thyroiditis

- Most common cause of hypothyroidism in Iodine-sufficient areas
- Most common clinically apparent cause of chronic thyroiditis
- M:F 1 : 10-20
- Genes involved: CTLA4 & PTPN22
- C/F: Painless enlargement of thyroid + hypothyroidism
- HPE: Lymphocytic infiltration of the gland, well-developed germinal centers, atrophic thyroid follicles, Hurthle cell metaplasia or oxyphil change (Hallmark)

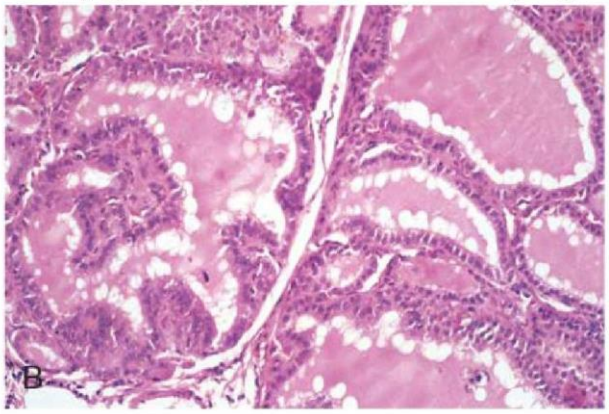
Hashimoto's thyroiditis



Grave's disease

Most common	**Most common cause of endogenous hyperthyroidism**[Q] **Most common cause of thyrotoxicosis**[Q]
Epidemiology	**Mean age**: **20–40** yrs of age[Q], **Female: Male = 10:1**[Q]
Genetic basis	Polymorphisms in immune-function genes like **CTLA4 and PTPN22 and the HLA-DR3**
Pathogenesis	**Autoimmune disorder** characterized by **autoantibodies against TSH receptor:**[Q] **Thyroid-stimulating immunoglobulin (TSI)**[Q] (90% cases)
Clinical features (Triad)	• **Hyperthyroidism**[Q] with diffuse enlargement of the gland • **Infiltrative ophthalmopathy**[Q] with resultant exophthalmos • **Localized, infiltrative dermopathy**[Q] (pretibial myxedema)
Morphology	**Symmetrically enlarged**[Q] gland due to **diffuse hypertrophy and hyperplasia**[Q] of **thyr**
Laboratory findings	**Elevated** free **T4 and T3 levels** and **depressed TSH levels**[Q]

Crowded tall columnar follicular cells
w/ papillary infolding +/- Scalloping



Thyroid Ca

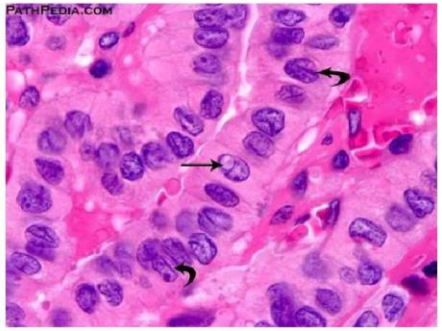
Thyroid Ca	%	Route of Metastasis	Genes Mc mutated
Papillary	MC 85%	Lymphatic	RET, BRAF
Follicular	5–15%	Hematogenous	RAS/P13K
Medullary	<5%	Regional : Lymphatic Distant : Hematogenous	MEN-2 RET
Anaplastic	<5%	Direct & hematogenous	RAS, P53

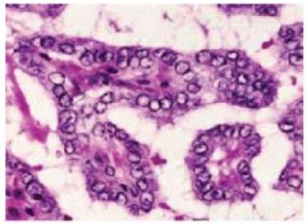
Mc: Most common

Papillary Ca

Microscopic hallmarks

- Branching papillae with a fibrovascular stalk
- Nuclear features: Hallmark of diagnosis
  - Orphan Annie eye nuclei (clear or empty appearing ground-glass appearance),
  - Pseudo-inclusions" – invaginations in cytoplasm- appearance of intranuclear inclusions or intranuclear grooves.
- Psammoma bodies (Absent in follicular and medullary Ca)
- Lymphatic invasion is common



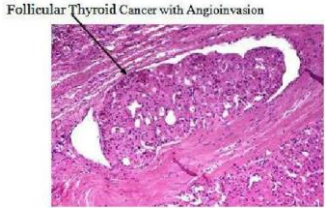


Follicular Ca Thyroid

Gross: Single well circumscribed or widely infiltrative nodule

Microscopically:

- Small follicles containing colloid, Hurthle cell or oncocytic variant: cells with abundant eosinophilic cytoplasm,
- Capsular &/or vascular invasion is the sign of carcinoma & differentiates follicular adenoma ,
- Lymphatic spread is uncommon

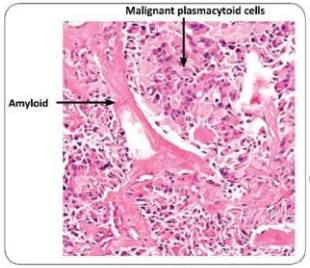


Medullary Ca Thyroid

- Neuroendocrine neoplasm derived from the parafollicular cells, or C cells, of thyroid
- MEN syndrome 2A or 2B or familial medullary thyroid carcinoma,

Microscopy

- Polygonal spindle-shaped cells form nests, trabeculae and follicles
- Acellular amyloid deposits (Acal)
- Tumor Markers: Calcitonin, serotonin, ACTH, and vasoactive intestinal peptide (VIP)



Medullary carcinoma thyroid

Pheochromocytoma

Gross Morphology	• **Small**, circumscribed lesions to **large hemorrhagic** masses • **Richly vascularized fibrous trabeculae** producing **lobular pattern**. • Incubation of **fresh tissue** with a **potassium dichromate** solution turns the tumor a **dark brown color (hence the name "chromaffin")**[Q].
Microscopy	• Tumors made of **clusters of polygonal to spindle-shaped chromaffin cells** surrounded by **sustentacular cells**, creating **small nests (zellballen)**[Q], with rich vascularity. • **"Salt and pepper"**[Q] nuclear chromatin: **characteristic** of neuroendocrine tumors. • **Electron microscopy:** Membrane-bound, **electron-dense secretory**[Q] granules.
Markers	• **Chromogranin**[Q] **and Synaptophysin**[Q] in the chief cells • **S-100** in peripheral **sustentacular** cells[Q]
Definitive diagnosis of malignancy	• Based on the **presence of metastases (vascular invasion)** & **not on histology.** • **Metastasis:** Involve regional **lymph nodes**[Q], **liver**[Q], **lung**[Q], **and bone**[Q]

Pheochromocytoma