TUMORS OF BLOOD VESSELS & LYMPHATICS

🩸❤️‍🩹

Overview

Tumors arising from blood vessels and lymphatics range from:

- Common benign lesions (e.g., hemangiomas)
- Intermediate-grade tumors (locally aggressive, rare metastasis)
- Rare but highly malignant tumors (angiosarcomas)

📌 Key Robbins idea: These tumors show a *spectrum of malignancy*, not just benign vs malignant.

Origin of Vascular Neoplasms

Vascular tumors may arise from:

1️⃣ Endothelial cells (ECs)

- Hemangioma
- Lymphangioma
- Angiosarcoma

2️⃣ Perivascular / supporting cells

- Glomus tumor

📍 Primary tumors of large vessels (aorta, pulmonary artery, vena cava):

- Rare
- Mostly sarcomas

Diagnostic Challenge ⚠️

- Benign hemangiomas ≠ anaplastic angiosarcomas (easy distinction)
- 🚨 Gray-zone lesions exist → tumors of *uncertain malignant potential*
- Tumor-like mimics:

- Congenital/developmental malformations
- Reactive proliferations (e.g., bacillary angiomatosis)

Benign vs Malignant Vascular Tumors 🎯

Feature	Benign	Malignant
Vascular channels	Well-formed	Poorly formed / absent
Lining cells	Single layer of bland ECs	Cytologic atypia
Cellularity	Low	High
Proliferation	Minimal	Marked
Vessel organization	Preserved	Disorganized

IHC needed?	Usually no	Often yes (EC markers)

📌 MCQ tip: Poor vessel formation + atypia → think angiosarcoma

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Classification of Vascular Tumors 📊

🟢 Benign Neoplasms

Developmental & Acquired

- Hemangioma
  - Capillary hemangioma
  - Cavernous hemangioma
  - Pyogenic granuloma
- Lymphangioma
  - Simple (capillary)
  - Cavernous (cystic hygroma)
- Glomus tumor

🔄 Reactive Vascular Proliferations

- Bacillary angiomatosis

🟡 Intermediate-Grade Neoplasms

- Kaposi sarcoma
- Hemangioendothelioma

🔴 Malignant Neoplasms

- Angiosarcoma

BENIGN TUMORS & TUMOR-LIKE CONDITIONS

Vascular Ectasias (NOT TRUE NEOPLASMS) ❌

Definitions

- Ectasia: Local dilation of any structure
- Telangiectasia: Permanent dilation of preexisting small vessels
    - Capillaries
    - Venules
    - Arterioles

📌 Occur mainly in:

- Skin
- Mucous membranes

Types of Vascular Ectasias

❑ Nevus Flammeus ("Birthmark") 🎨

- Most common vascular ectasia
- Appearance:
  - Light pink → deep purple
  - Flat lesion
- Location:
  - Head & neck
- Pathology:
  - Dilated vessels
- Course:
  - ⚠️ Most regress spontaneously

2️⃣ Port-Wine Stain 🍷

- A variant of nevus flammeus
- Key differences:
  - Do NOT regress
  - Enlarge with age
  - Cause skin thickening

Association: Sturge-Weber Syndrome 🧠

(Encephalotrigeminal angiomatosis)

Occurs when lesion is in trigeminal nerve distribution

Features:

- Facial port-wine nevus
- Ipsilateral leptomeningeal venous angiomas
- Mental disability
- Seizures
- Hemiplegia
- Skull radiologic opacities

📌 Exam pearl:

Large facial telangiectasia + seizures in child → think Sturge-Weber

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3️⃣ Spider Telangiectasia 🕷️

- Non-neoplastic lesion
- Structure:
  - Central arteriole ("body")
  - Radiating vessels ("legs")
- Blanches with pressure
- Often pulsatile

Common sites:

- Face
- Neck
- Upper chest

Associated with hyperestrogenic states:

- Pregnancy

- Liver cirrhosis

📌 One-liner: Spider nevi = estrogen excess

4️⃣ Hereditary Hemorrhagic Telangiectasia

(Osler-Weber-Rendu disease) 🧬

Feature	Details
Inheritance	Autosomal dominant
Molecular defect	TGF-β signaling pathway in ECs
Lesion type	Dilated capillaries & veins
Onset	Present at birth
Distribution	Skin, oral mucosa, GI, respiratory, urinary tracts

Clinical significance 🚨:

- Fragile lesions → spontaneous rupture
- Causes:
  - Epistaxis
  - GI bleeding
  - Hematuria

📌 Exam trap: Bleeding telangiectasias + AD inheritance = Osler-Weber-Rendu

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Quick Flowchart: Vascular Lesion Approach 🧩

Dilated vessel lesion

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True neoplasm?

↓ ↓

Yes No

Hemangioma / Angiosarcoma ↲ ↳ Vascular ectasia (nevus flammeus, spider telangiectasia, HHT)

HEMANGIOMAS 🩸

Definition

Hemangiomas are common benign vascular tumors composed of blood-filled vessels.

📌 Referenced earlier in Robbins (Ch. 4) as well.

Epidemiology & Natural History 📊

- Account for ~7% of all benign tumors of infancy & childhood
- Most present at birth
- Typical course: Present at birth → rapid growth → spontaneous regression
- Malignant transformation: 🚫 *Extremely rare*

Distribution & Extent

- Commonly localized lesions
  - Head & neck (most frequent)
- May be:
  - Extensive → *Angiomatosis*
  - Internal
    - ~⅓ of internal hemangiomas occur in the liver 🧠➡️🫀

Classification of Hemangiomas 🧩

Several histologic & clinical variants exist:

❑ Capillary Hemangioma (MOST COMMON) ⭐

Sites

- Skin
- Subcutaneous tissue
- Oral cavity & lips
- Internal organs:

- Liver
- Spleen
- Kidneys

Histology 🔬

- Thin-walled capillary-sized vessels
- Scant connective tissue stroma

📌 Exam phrase: *Well-formed capillaries with minimal stroma*

2️⃣ Infantile Hemangioma (Clinical Variant of Capillary Type) 👶

Key Features

- Extremely common
- Often multiple
- Cutaneous (skin)

Growth Pattern (VERY EXAM-FRIENDLY) 🎯

Rapid growth (first few months)

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Involution begins: 1–3 years

↓

Complete regression by ~7 years (majority)

📌 One-liner: Infantile hemangiomas grow fast, then disappear.

3️⃣ Pyogenic Granuloma 🩹

Definition

- Capillary proliferation of uncertain etiology
- Not actually pyogenic ❌
- Not a granuloma ❌

Clinical Features

- Rapidly growing
- Red, pedunculated lesion
- Common locations:
    - Skin
    - Gingiva
    - Oral mucosa

Histology 🔬

- Resembles exuberant granulation tissue

Behavior

- Bleeds easily
- Frequently ulcerates

Special Points (HIGH-YIELD) ⚠️

- ~25% follow trauma
- Size:
    - Reaches 1–2 cm within weeks
- Treatment:

    - Curettage + cautery → curative
- Age:
    - All ages
    - Peak: 2nd–3rd decades
- Pregnancy association 🤰:
    - Gingival pyogenic granulomas
    - May regress after pregnancy
    - Some undergo fibrosis
    - Occasional surgical excision needed

📌 MCQ trap: Rapidly growing, bleeding oral lesion after trauma → Pyogenic granuloma

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4️⃣ Cavernous Hemangioma 🕳️

Structural Features

- Large, dilated vascular channels
- More infiltrative than capillary hemangiomas
- Often involve deep structures
- ❌ Do NOT regress spontaneously

Common Sites

- Liver (very common)
- Can occur in any tissue
- Brain (clinically important)

Clinical Features

- Usually asymptomatic
- Often discovered incidentally on imaging

Histology 🔬

Feature	Description
Borders	Sharply defined
Capsule	Absent

Vascular spaces	Large, blood-filled
Stroma	Connective tissue
Complications	Thrombosis, dystrophic calcification

Special Clinical Associations 🧠

Brain Cavernous Hemangiomas

- Cause:
  - Compression symptoms
  - Risk of rupture → hemorrhage

Genetic Associations 🧬

☐ von Hippel-Lindau Disease

- Cavernous hemangiomas are a component
- Common sites:

- Cerebellum
- Brain stem
- Retina
- Pancreas
- Liver

2️⃣ Familial Cerebral Cavernous Hemangiomas

- Caused by mutations in:
  - CCM1
  - CCM2
  - CCM3
- Tumor suppressor genes

📌 Clinical rule:

Multiple cerebral cavernous hemangiomas → do genetic testing

Capillary vs Cavernous Hemangioma (EXAM TABLE) 📊

Feature	Capillary	Cavernous
Vessel size	Small	Large, dilated
Stroma	Scant	Abundant
Depth	Superficial	Deep
Regression	Yes	No
Infiltration	Minimal	More infiltrative
Brain involvement	Rare	Common

Quick Flowchart: Hemangioma Types 🧠

Hemangioma

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Capillary type

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- Infantile hemangioma
- Pyogenic granuloma

Cavernous type

↓

- Deep structures
- Liver
- Brain
- VHL association

LYMPHANGIOMAS 🫧

Definition

Lymphangiomas are benign tumors of lymphatic vessels, considered the lymphatic counterpart of hemangiomas.

📌 Much less common than hemangiomas.

Types of Lymphangiomas 🧩

❑ Simple (Capillary) Lymphangioma

Clinical Features

- Slightly elevated or pedunculated
- Size: 1–2 cm
- Common sites:
  - Head
  - Neck
  - Axillary subcutaneous tissue

Histology 🔬

- Network of endothelium-lined spaces
- Key distinguishing feature:

- ❌ No red blood cells
- (This differentiates them from capillary hemangiomas)

📌 Exam line: "Endothelium-lined channels without blood cells"

2️⃣ Cavernous Lymphangioma

(Cystic Hygroma) 🫧

Epidemiology & Sites

- Typically seen in children
- Common locations:
  - Neck
  - Axilla
- Rare sites:
  - Retroperitoneum

📌 Association:

- Common in Turner syndrome (45,X)

Gross Features

- Can be very large (up to 15 cm)
- Effects:
  - Fill axilla
  - Cause gross neck deformities

Histology 🔬

Feature	Description
Lymphatic spaces	Massively dilated
Lining	Endothelial cells
Stroma	Connective tissue

Additional finding	Lymphoid aggregates

Surgical Importance ⚠️

- Margins:
  - Indistinct
  - Unencapsulated
- Result:
  - Complete excision is difficult

📌 MCQ pearl: Neck mass in child + Turner syndrome → cystic hygroma

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Quick Comparison: Simple vs Cavernous Lymphangioma 📊

Feature	Simple	Cavernous (Cystic Hygroma)

Size	Small (1–2 cm)	Large (up to 15 cm)
Location	Head, neck, axilla	Neck, axilla
Age	Any	Mostly children
Blood cells	Absent	Absent
Margins	Better defined	Poorly defined
Surgery	Easy	Difficult

GLOMUS TUMORS (Glomangiomas) 🔥

Definition

Benign but exquisitely painful tumors arising from specialized smooth muscle cells of glomus bodies.

What are glomus bodies?

- Arteriovenous shunts
- Function: Thermoregulation

Clinical Features 🎯

- Severe pain (classic!)
- Often triggered by:
  - Cold
  - Pressure

Common Location

- Distal digits
- Especially subungual (under fingernails) 💅

Diagnosis

- Distinguished from hemangiomas by:
  - Clinical presentation (pain)
  - Immunohistochemistry:

- Positive for smooth muscle markers

Prognosis & Treatment

- Surgical excision → curative
- Malignant glomus tumors:
  - Very rare
  - Deeper
  - Locally invasive

📌 One-liner: Painful subungual tumor = glomus tumor

BACILLARY ANGIOMATOSIS 🦠

Definition

A reactive vascular proliferation occurring in immunocompromised patients, caused by Bartonella species.

At-Risk Populations ⚠️

- AIDS patients
- Solid organ transplant recipients
- CD4 count <100

Causative Organisms 🧬

1️⃣ *Bartonella henselae*

- Reservoir: Domestic cat 🐱
- In immunocompetent hosts:
  - Causes cat-scratch disease
  - Necrotizing granulomatous lymphadenitis

2️⃣ *Bartonella quintana*

- Transmission: Human body lice
- Historical disease:
  - Trench fever (World War I)

Clinical Features

- Skin, bone, brain, and other organs involved
- Skin lesions:
  - Red papules & nodules
  - Rounded subcutaneous masses
  - Bleed easily

📌 Clinical mimic: Kaposi sarcoma

Histology 🔬

- Capillary proliferation
- Lined by plump epithelioid endothelial cells
- ECs show:
  - Nuclear atypia
  - Mitoses
- Additional findings:
  - Neutrophilic infiltrate
  - Nuclear debris
  - Purplish granular bacterial clusters

Pathogenesis Flowchart 🩸

Bartonella infection

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↑ HIF-1α production

↓

↑ VEGF expression

↓

Marked vascular proliferation

📌 Key mechanism: HIF-1α–mediated VEGF induction

Treatment & Outcome 💊

- Antibiotic therapy
- Infection eradication → lesion regression

High-Yield Summary Table 📊

Condition	Nature	Key Feature
Lymphangioma	Benign tumor	No RBCs in channels
Cystic hygroma	Cavernous lymphangioma	Turner syndrome
Glomus tumor	Benign SMC tumor	Severe pain, subungual
Bacillary angiomatosis	Reactive proliferation	AIDS + Bartonella

KAPOSI SARCOMA (KS) 🩸

Definition

- Kaposi sarcoma (KS) is a vascular neoplasm caused by Kaposi sarcoma herpesvirus (KSHV / HHV-8)

- Occurs in several clinical contexts, most commonly AIDS
- Not caused by HIV, but AIDS-associated KS is more common due to immunosuppression

📌 Exam pearl: KS = HHV-8 driven vascular tumor; AIDS increases susceptibility, but HIV ≠ cause

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Forms of KS 🧩

Type	Population / Location	Key Features
Classic KS	Older men, Central/Eastern Europe, Mediterranean	Red-purple skin plaques/nodules, distal lower limbs, slowly progressive, usually asymptomatic, localized
Endemic African KS	Sub-Saharan Africa, HIV-negative, <40 yrs	Can be indolent or aggressive; lymph node involvement common; severe in prepubertal children → poor prognosis

Transplant-associated KS	Solid organ transplant, T-cell immunosuppressed	Aggressive; may involve nodes, mucosa, viscera; cutaneous lesions may be absent; may regress if immunosuppression reduced
AIDS-associated KS	HIV-positive patients	AIDS-defining illness; often disseminated to lymph nodes & viscera early; mortality usually from opportunistic infections

📌 Tip: Always relate type to immune status & geography

Pathogenesis 🔬

Key Points

- Virus: KSHV (gamma-herpesvirus)
- Transmission:
  - Sexual contact
  - Oral secretions
  - Cutaneous exposure
- Host factor: Altered T-cell immunity required

- Genetic susceptibility: Variants in IL-8 receptor β (IL8Rb) and IL-13 may contribute

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Mechanism of Tumor Formation

1. Lytic infection of endothelial cells → local inflammatory milieu
    - Virally encoded G-protein → ↑ VEGF → endothelial proliferation
    - Cytokines from recruited inflammatory cells → growth stimulation
2. Latent infection of endothelial cells
    - Viral cyclin D homologue → bypass normal cell cycle control
    - Inhibition of p53 → reduced apoptosis
3. Clonality
    - Early: Poly/oligoclonal
    - Late: Mostly monoclonal

📌 MCQ tip: KS spindle cells + HHV-8 = hallmark

Morphology & Histology 🩸

Progression of Skin Lesions

Classic KS (and sometimes other variants) progresses through 3 stages:

Stage	Clinical Appearance	Histology / Microscopy
Patch	Pink, red, purple macules; distal lower extremities	Dilated, irregular, angulated vessels lined by ECs; chronic inflammatory infiltrate; may contain hemosiderin
Plaque	Violaceous, raised, larger; spreads proximally	Jagged dermal vascular channels; plump spindle cells; extravasated RBCs; hemosiderin-laden macrophages; mononuclear infiltrates
Nodule	Raised nodular lesions; dermis/subcutis	Proliferating spindle cells; slit-like vascular spaces; hemorrhage & hemosiderin deposition; mitoses common; nodal/visceral involvement possible

📌 Visual clue: Violaceous skin nodules + spindle cells + slit-like vessels → KS

Clinical Features & Prognosis 🌡️

- Primary infection: Usually asymptomatic
- Classic KS: Localized; surgical excision usually curative
- Radiation therapy: For multiple lesions in limited area
- Chemotherapy: Disseminated disease / nodal involvement
- Iatrogenic (transplant) KS: Often regresses if immunosuppression reduced
- AIDS-associated KS: Antiretroviral therapy ± chemotherapy depending on extent
- Mortality: AIDS-KS patients often die from opportunistic infections rather than KS itself

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Pathogenesis Flowchart 🧩

KSHV infection of ECs

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Lytic infection → VEGF ↑ → endothelial proliferation

Latent infection → Viral cyclin D + pS3 inhibition → apoptosis ↓

↓

Spindle cell proliferation → Patch → Plaque → Nodule

↓

Local or disseminated disease (nodes, viscera)

High-Yield Exam Tips 📌

- Spindle cells + slit-like vascular spaces → KS histology hallmark
- HHV-8 positive → diagnostic
- AIDS patient with violaceous skin lesions → think KS

- Classic KS → distal lower extremities, older men
- Endemic African KS → lymph nodes, children, poor prognosis
- Transplant KS → immunosuppressed, regression possible if therapy reduced

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ANGIOSARCOMAS 🩸

Definition

- Angiosarcomas are malignant neoplasms of endothelial cells
- Spectrum:
  - Well-differentiated → resemble hemangiomas
  - Anaplastic / poorly differentiated → aggressive, hard to recognize

📌 MCQ tip: Any malignant tumor of blood vessels = think angiosarcoma

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Epidemiology

- Age: Older adults (most common)
- Gender: No predilection
- Sites: Any site, but commonly:
  - Skin
  - Soft tissue
  - Breast
  - Liver

Clinical Features 🌡️

- Aggressive tumors
- Locally invasive
- Metastasize frequently
- Prognosis: Poor survival

Special Clinical Settings ⚠️

❑ Lymphedema-Associated (Stewart-Treves Syndrome)

- Setting: Upper extremity after lymph node dissection for breast cancer
- Tumor arises from lymphatic vessels → lymphangiosarcoma

2️⃣ Post-Radiation Angiosarcoma

- Can occur in breast/skin after radiotherapy
- Does not require lymphedema

3️⃣ Hepatic Angiosarcoma

- Caused by chemical carcinogens:
  - Arsenical pesticides
  - Polyvinyl chloride (PVC)
- Latency: Often several years after exposure

📌 Exam pearl: Hepatic angiosarcoma + PVC exposure → classic occupational hazard

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Morphology 🔬

Gross Features

- Skin lesions:
  - Early: Small, sharply demarcated, red nodules
  - Advanced: Large, fleshy red-tan → gray-white masses
  - Margins: Blend with surrounding tissue
  - Necrosis & hemorrhage common

Microscopic Features

Differentiation	Histology
Well-differentiated	Plump atypical endothelial cells forming vascular channels
Poorly differentiated	Spindled or epithelioid cells; vessels may be absent

Immunohistochemistry (IHC)

- Used to confirm endothelial origin in poorly differentiated tumors
- Common markers:
  - CD31 ✅ (most sensitive & specific)
  - ERG ✅

Summary Table: Vascular Tumor Spectrum 📊

Tumor Type	Nature	Key Features	Sites / Associations
Hemangioma	Benign	Blood-filled channels; regress (capillary); can be large (cavernous)	Skin, liver, spleen, kidney
Lymphangioma	Benign	Lymph-filled channels; no RBCs; may be cystic	Neck, axilla; Turner syndrome for cystic type
Glomus tumor	Benign	Painful, distal digits, subungual; smooth muscle origin	Fingers, toes

Bacillary angiomatosis	Reactive	Immunocompromised; Bartonella-induced; mimics KS	Skin, bone, viscera
Kaposi sarcoma	Intermediate	HHV-8; spindle cells, slit-like vessels; patch → plaque → nodule	Skin, mucosa, nodes; AIDS / transplant / endemic / classic
Angiosarcoma	Malignant	Highly aggressive; variable differentiation; poor prognosis; IHC: CD31, ERG	Skin, soft tissue, breast, liver; Stewart-Treves, radiation, chemical exposure

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High-Yield Exam Tips 📌

- Stewart-Treves = post-mastectomy lymphedema + angiosarcoma
- Hepatic angiosarcoma → PVC / arsenical pesticide exposure
- IHC markers for EC origin = CD31, ERG

- Aggressive local invasion + early metastasis → hallmark of angiosarcoma
- Malignant vascular tumor with spindle cells → always consider angiosarcoma

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Flowchart: Vascular Tumors by Grade 🧠

Benign

- ├── Hemangioma (capillary / cavernous)
- ├── Lymphangioma (simple / cystic)
- └── Glomus tumor

Intermediate

- └── Kaposi sarcoma

Malignant

- └── Angiosarcoma

├── Stewart-Treves (lymphedema)

├── Post-radiation

└── Hepatic (PVC, arsenic)

-> The End <-