Hemangiomas and Other Vascular Lesions

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AAP Instructional Course
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Faculty Disclosure Information

In the past 12 months, I have had no relevant financial relationships with the manufacturer(s) of any commercial product(s) and/or provider(s) of commercial service(s) discussed in this CME activity.

I do not intend to discuss an unapproved/investigative use of a commercial product/device in my presentation.
Outline

• Introduction

• Classification

• Diagnosis and Treatment of Tumors

• Diagnosis and Treatment of Malformations

• Emerging Genetic Framework

• Case Examples

• Summary/Conclusions
Learning Objectives

(1) Comprehend biological classification and terminology

(2) Accurately diagnose major types of vascular anomalies

(3) Understand basic management
Vascular Anomalies

- ~4-5% population
- Psychosocial/functional morbidity
- Plastic surgeons (integument)
- Interdisciplinary centers
- Confusing field
  - Similar appearance
  - Imprecise terminology
- 71% papers “hemangioma” incorrect*

*Hassanein, et al. PRS 2011
Introduction
Confusing Appearance
## Introduction

Confusing Terminology

<table>
<thead>
<tr>
<th>19th Century Term</th>
<th>Vascular Anomaly</th>
</tr>
</thead>
<tbody>
<tr>
<td>“Hemangioma”</td>
<td>All Types</td>
</tr>
<tr>
<td>“Capillary Hemangioma”</td>
<td>Kaposiform hemangioendothelioma, capillary malformation</td>
</tr>
<tr>
<td>“Strawberry Hemangioma”</td>
<td>Superficial hemangioma pyogenic granuloma,</td>
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<tr>
<td>“Cavernous Hemangioma”</td>
<td>Deep hemangioma, venous malformation</td>
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<tr>
<td>“Port-Wine Stain”</td>
<td>Capillary malformation</td>
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<tr>
<td>“Lymphangioma”</td>
<td>Microcystic lymphatic malformation</td>
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<tr>
<td>“Cystic Hygroma”</td>
<td>Macrocystic lymphatic malformation</td>
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</tbody>
</table>
Introduction
Confusing Appearance and Terminology

### Vascular Anomalies Center
Incorrect Referral Diagnosis (n=3937)

<table>
<thead>
<tr>
<th>Tumors</th>
<th>Malformations</th>
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</thead>
<tbody>
<tr>
<td>29.6% (345/1167)</td>
<td>54.4% (1507/2770)</td>
</tr>
<tr>
<td>IH</td>
<td>VM</td>
</tr>
<tr>
<td>22.5%</td>
<td>69.0%</td>
</tr>
<tr>
<td>KHE</td>
<td>LM</td>
</tr>
<tr>
<td>48.8%</td>
<td>30.7%</td>
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<tr>
<td>CH</td>
<td>AVM</td>
</tr>
<tr>
<td>91.0%</td>
<td>40.6%</td>
</tr>
<tr>
<td>PG</td>
<td>CM</td>
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<tr>
<td>0.0%</td>
<td>67.2%</td>
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</table>

### 2009 Literature
Incorrect use of ‘Hemangioma’ (n=320)

<table>
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<tr>
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<th>Correct Management</th>
<th>Incorrect Management</th>
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<tbody>
<tr>
<td>Correct Nomenclature</td>
<td>100.0%</td>
<td>0.0%</td>
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<tr>
<td>Incorrect Nomenclature</td>
<td>79.4%</td>
<td>20.6%</td>
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</table>

n=105; *p=0.001 (Fisher’s Exact Test)

Hassanein, et al PRS 2011
## Biological Classification

Clinical & Endothelial Characteristics

<table>
<thead>
<tr>
<th>Hemangiomas</th>
<th>Malformations</th>
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<tr>
<td>Proliferating phase</td>
<td>Capillary</td>
</tr>
<tr>
<td>Involuting phase</td>
<td>Venous</td>
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<tr>
<td></td>
<td>Arterial</td>
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<tr>
<td></td>
<td>Lymphatic</td>
</tr>
<tr>
<td></td>
<td>Fistulae</td>
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</table>
Biological Classification

90% Diagnosed by History and Physical Examination

Infantile Hemangioma

Venous Malformation
"Cavernous Hemangioma"
<table>
<thead>
<tr>
<th>Tumors</th>
<th>Malformations</th>
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<tr>
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<tr>
<td>Hemangioma</td>
<td>Capillary</td>
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<tr>
<td>Hemangioendotheliomas</td>
<td>Lymphatic</td>
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<tr>
<td>Angiosarcoma</td>
<td>Venous</td>
</tr>
<tr>
<td>Miscellaneous</td>
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</table>

International Society for Study of Vascular Anomalies (ISSVA) 1996
<table>
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<th>TUMORS</th>
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<td>CLM</td>
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<td>CMTC</td>
<td>LVM</td>
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<td>Fading stain</td>
<td>CLVM</td>
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<td>Epithelioid hemangioma</td>
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<td>CAVM</td>
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<td>Pyogenic granuloma</td>
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<td>CLAVM</td>
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<td>Locally Aggressive</td>
<td>Lymphatic</td>
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<tr>
<td>KHE</td>
<td>Macrocystic</td>
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<tr>
<td>Kaposi sarcoma</td>
<td>Microcystic</td>
<td></td>
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<tr>
<td></td>
<td>Mixed</td>
<td></td>
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<tr>
<td></td>
<td>GLA, Gorham</td>
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<tr>
<td></td>
<td>Lymphedema</td>
<td></td>
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<tr>
<td>Malignant</td>
<td>Venous</td>
<td></td>
</tr>
<tr>
<td>Angiosarcoma</td>
<td>CMVM</td>
<td></td>
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<tr>
<td>Epithelioid hemangioendothelioma</td>
<td>Blue rubber bleb</td>
<td></td>
</tr>
<tr>
<td></td>
<td>GVM</td>
<td></td>
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<td></td>
<td>CCM</td>
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<tr>
<td></td>
<td>Arteriovenous</td>
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</tr>
<tr>
<td></td>
<td>HHT</td>
<td></td>
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<tr>
<td></td>
<td>CM-AVM</td>
<td></td>
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<td></td>
<td>AV Fistula</td>
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</table>
Vascular Anomalies Simplified
8 Types Comprise \( \sim 95\% \) of Lesions

<table>
<thead>
<tr>
<th>TUMORS ((n=4))</th>
<th>MALFORMATIONS ((n=4))</th>
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<tbody>
<tr>
<td>Infantile Hemangioma</td>
<td>Capillary</td>
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<tr>
<td>Congenital Hemangioma</td>
<td>Lymphatic</td>
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<tr>
<td>Kaposiform Hemangioendothelioma</td>
<td>Venous</td>
</tr>
<tr>
<td>Pyogenic Granuloma</td>
<td>Arteriovenous</td>
</tr>
</tbody>
</table>
Epidemiology of Referrals

General Population

- Hemangioma (~5.0%)
- Malformations (~0.5%)

Vascular Anomalies Center (n=5621)

<table>
<thead>
<tr>
<th>Tumors</th>
<th>Malformations</th>
</tr>
</thead>
<tbody>
<tr>
<td>35.2% (n=1976)</td>
<td>64.8% (n=3645)</td>
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<tr>
<td>Infantile Hemangioma</td>
<td>85.9%</td>
</tr>
<tr>
<td>Hemangioendotheliomas</td>
<td>7.8%</td>
</tr>
<tr>
<td>Congenital Hemangioma</td>
<td>5.4%</td>
</tr>
<tr>
<td>Pyogenic Granuloma</td>
<td>0.9%</td>
</tr>
<tr>
<td></td>
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</tr>
</tbody>
</table>

Vascular Tumors

- Infantile Hemangioma
- Congenital Hemangioma
- Kaposiform Hemangioendothelioma
- Pyogenic Granuloma
Infantile Hemangioma

- 4-5% Caucasians
- 2/3 head/neck, 30% multiple
- Female: male = 3:1
- Noted ~ 2 weeks of age
- *Proliferating phase*: birth-9 months (80% complete 5mo)
- *Involuting phase*: 1-4 years
Phenotypes of Infantile Hemangioma

- **Superficial**
- **Deep**
- **Multiple**
- **Midline**
- **Reticular**
- **PHACES**

### Multiple (≥5)
- Small, < 5mm, dome-shaped
- 16% hepatic lesions (92% asymptomatic)
- US

### Lumbosacral Midline
- Tethered cord
- US/MRI

### Reticular
- Lower extremity
- Ulceration, anogenital/urinary anomalies

### PHACES Association
- V distribution + anomaly
- 2.3% IH, 20% V1,2,3, MRI 8% stroke
- P posterior fossa (cerebellum)
- H hemangioma
- A arterial (coarctation, carotid, vertebral)
- C cardiac (PDA, septal defects)
- E eye (microphthalmia)
- S sternum (nonunion, raphe)
Infantile Hemangioma

Complications

**Proliferating Phase (10%)**
- Ulceration
- Distortion

**Involuted Phase (50%)**
- Fibro-adipose
- Excess Skin
- Scar
- Alopecia
- Telangiectasias

**Obstruction**

**Destruction of Structures**
Infantile Hemangioma
Management Proliferating Phase

**Non-ProBLEMATIC (80%)**
- No Ulceration (80%)
  - Observation
- Ulceration (20%)
  - Barrier Dressing (heals ~2 weeks)

**Problematic (20%)**
- Topical Timolol (40%)
- Kenalog Injection (40%)
- Prednisone Propranolol (20%)
- Resection (<1%)
  - Superficial <8 weeks
  - Localized <3cm
  - Diffuse >3cm
  - Failed Other Tx

Infantile Hemangioma
Topical Timolol

- 0.5% gel-forming solution
- 1 drop BID
- Superficial lesions
- Early <8 weeks
- Discontinue 10 months
Infantile Hemangioma
Corticosteroid Injection

- 1st line small, well localized
- ≤ 3 cm diameter
- ≤ 3 mg/kg per injection
- N=100 triamcinolone
- 100% response
  - 1/3 stabilize
  - 2/3 regress
- No systemic side effects
- 2% fat atrophy
Infantile Hemangioma
Systemic Pharmacotherapy if Diffuse (>3cm)

- Propranolol (2008)
  - First-line
  - 15% non-response
  - Late rebound
  - Hypoglycemia, seizure
  - Monitoring
  - ? Neurocognitive effects

- Prednisone (1967)
  - Second-line
  - 90% smaller, 10% stabilize
  - 15% temporary growth, cushingoid
  - No long term side-effects
  - Simple

Greene et al. PRS 2011
Infantile Hemangioma

Resection

Ulceration

Ulceration

Distortion
Infantile Hemangioma
Involuted Phase (Age 3-4)
Congenital Hemangioma

- Fully-grown at birth - no growth
- Male = female, solitary, 5cm
- Pink-purple, telangiectasias, halo
- H/N(43%), limb(45%), trunk(13%)
- GLUT-1 negative
- Rapidly involuting (RICH)
  - Involved by 14 months
  - Fat atrophy
- Non-involuting (NICH)
  - Treatment is excision
Congenital Hemangioma

Treatment

RICH
- Birth
- Atrophy
- Fat Grafting

NICH
Kaposiform Hemangioendothelioma (KHE)

- 50% birth, male=female, >5cm
- Red-purple, trunk/extremities
- Incomplete regression (2 years)
- Kasabach Merritt phenomenon (50%)
  - PLT (<25k), petechiae, bleeding
- Treatment
  - Sirolimus (oral)
  - Vincristine (IV)
  - Operative (rare)
Kaposiform Hemangioendothelioma (KHE)
Operative Treatment
Pyogenic Granuloma

- Mean onset 6 yrs (rare < 6 mo)
- 2/3 head and neck (central face #1)
- Small, 6 mm
- Rapid growth, bleeding
- Reticular dermis
- Recurrence shave, superficial cautery (~50%)
- Recurrence after excision, deep cautery (0%)
Vascular Malformations

Capillary

Venous

Lymphatic

Arteriovenous
Capillary Malformation (CM)

- Dilated capillary-venules dermis
- Fading stain (50% Caucasians)
  - Forehead (“angel kiss”)
  - Nuchal area (“stork bite”)
- CM (0.3% population)
  - Darken, overgrowth
- CMTC
  - Violaceous, net-like pattern
  - Extremity, asymmetry, ulceration
- Syndromes (Sturge-Weber, CM-AVM)
- Treatment: (1) laser, (2) resection
Capillary Malformation (CM)
Pulse-Dye Laser

- Lightens lesion
- Multiple treatments
- Early = better result
- Can darken over time

Courtesy of Marilyn Liang, MD
Capillary Malformation (CM) Operative Treatment

Overgrown Lip
Pyogenic Granuloma
Liposuction
Lymphatic Malformation (LM)

- Types
  - Macrocytic
  - Microcytic
  - Lymphedema
  - Generalized, Gorham

- Infection, bleeding, drainage, overgrowth

- Macrocytic
  - Sclerotherapy
  - +/- Resection

- Microcytic
  - Resection
  - Laser, RFA
  - Bleomycin
  - Sirolimus
Lymphatic Malformation
Macrocystic - Sclerotherapy
Lymphatic Malformation
Microcystic - Resection
Lymphatic Malformation
Microcystic - Other Treatments

Carbon Dioxide Laser

Radiofrequency Ablation

Bleomycin Injection

Oral Sirolimus

Courtesy Reza Rahbar, MD

Courtesy Cameron Trenor, MD
Lymphatic Malformation
Primary Lymphedema - Liposuction
**Venous Malformation (VM)**

- Thin-wall, abnormal smooth muscle
- 90% sporadic/solitary (50% TIE2)
  - Glomuvenous (glomulin)
  - Cutaneomucosal (TIE2)
  - Cerebral cavernous (CCM/KRIT1)
  - VVM (MAP3K3)
- Stagnation
  - Intravascular coagulopathy
  - Phlebothrombosis, pain
- Treatment
  - Compression, aspirin
  - Sclerotherapy
  - Resection

 Typical

 Local | Diffuse | Subcutis

 Typical

 Bockenheimer | Verrucous | GVM

 Subtypes

 BRBNS
Venous Malformation
Sclerotherapy
Venous Malformation
Sclerotherapy + Resection

Pre-Treatment  Post-Sclerotherapy  Post-Resection

[Images of pre-treatment, post-sclerotherapy, and post-resection stages of venous malformation treatment]
Venous Malformation
Resection Only
Arteriovenous Malformation (AVM)

- Artery abnormally connected to a vein
- No capillary bed (nidus, fistula)
- Treatment: embolization, resection

### Schobinger Stage

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage I</td>
<td>Warm, shunt on Doppler</td>
</tr>
<tr>
<td>Stage II</td>
<td>Enlargement, pulsation/thrill/bruit, tortuous veins</td>
</tr>
<tr>
<td>Stage III</td>
<td>Ulceration, bleeding, pain</td>
</tr>
<tr>
<td>Stage IV</td>
<td>Cardiac failure</td>
</tr>
</tbody>
</table>

CM-AVM

PTEN-AVA
Arteriovenous Malformation
Diffuse - Embolization Only
Arteriovenous Malformation (AVM) Embolization + Resection

Local

Regional

Diffuse
Vascular Malformation Overgrowth Syndromes

< 1% of Vascular Anomalies
CLOVES Syndrome

- Congenital lipomatosis, overgrowth, vascular malformations, epidermal nevi, and scoliosis/skeletal/spinal anomalies

- Common features: truncal lipomatous mass, slow-flow vascular malformation (capillary), hand/foot anomalies

- Less common features: paraspinal AVMs, epidermal nevus, Wilms, phlebectasia

- Management
  - MRI spine (lipoma, AVM)
  - Wilms tumor screening
  - Treat symptoms
Klippel-Trenaunay Syndrome

- Capillary-lymphatic-venous malformation + extremity + overgrowth

- Lateral embryonic vein (Servelle)

- Affects tissues below muscle fascia

- Management
  - MRI
  - Leg-length discrepancy
  - Remove lateral vein (DVT/PE)
  - Sclero, resection
Maffucci Syndrome

- Multiple enchondromas + soft tissue vascular malformations
- Sporadic: IDH1 (98%), IDH2 (2%)
- Spindle cell hemangioma (reactive in VM)
- Risk for chondrosarcoma and other tumors
- Management
  - Screening plain radiographs
  - Curettage/resection bone lesions
  - Sclero/resection VMs
Parkes Weber Syndrome

- Diffuse AVM + CM + overgrowth extremity
- RASA1
- MRI
- CHF-embolization
- Leg-length monitoring
Proteus Syndrome

- Rare (~100 cases)
- Sporadic: \textit{AKT1}
- Features
  - Progressive, asymmetric bone overgrowth
  - Cerebriform nevus (palms, soles)
  - Epidermal nevi
  - Vascular malformations
  - Cerebral anomalies
  - 20% mortality (PE, cystic lung, cancer)
- Management based on symptoms
Sturge-Weber Syndrome

- CM in V₁ distribution + ocular anomalies (glaucoma, choroidal anomalies) + leptomeningeal vascular malformations
- Soft tissue/skeletal overgrowth
- Seizures
- Management
  - Brain MRI
  - Ophthalmology consultation
  - Pulse-dye laser
  - Resection overgrown tissues
Emerging Genetic Framework
Causative Mutations for Most Vascular Anomalies Recently Discovered

**FAMILIAL (<1%)**
- 1994 HHT
- 1996 CMVM
- 1996 PTEN-AVA
- 1999 CCM
- 2000 Lymphedema
- 2003 CM-AVM

**SPORADIC (>99%)**
- 2009 VM
- 2011 *Proteus*
- 2012 CLOVES
- 2013 CM
- 2014 FIL
- 2015 LM/KTS/FAVA
- 2015 VVM
- 2016 PG
- 2016 CH
- 2016 KHE
- 2017 AVM
- 2017 BRBNS
# Genetic Classification of Vascular Anomalies

**PROS (PIK3CA Related Overgrowth Spectrum)**

<table>
<thead>
<tr>
<th>PIK3CA</th>
<th>GNAQ</th>
<th>GNA11</th>
<th>GNA14</th>
<th>TIE2</th>
<th>MEK1</th>
<th>MEK3</th>
<th>Glomulin</th>
<th>AKT</th>
<th>PTEN</th>
<th>RASA</th>
<th>KRT</th>
<th>ENG</th>
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<tbody>
<tr>
<td>CLOVES</td>
<td>CM</td>
<td>CM-VM</td>
<td>AVM</td>
<td>VVM</td>
<td>GVM</td>
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<td>AVEA</td>
<td>CM-AVM</td>
<td>CCM</td>
<td>HHT</td>
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</tbody>
</table>
Case Examples
Diagnostic Algorithm By History

Present At Birth?

Yes

Tumor
- Congenital Hemangioma
- Kaposiform Hemangioendothelioma

Malformation
- Capillary Lymphatic
  - Venous
  - Arteriovenous

No

Infantile Hemangioma
Pyogenic Granuloma
Diagnosis Algorithm by Physical Exam

Hand-Held Doppler

Blood Flow?

Fast-Flow

Tumor
- Infantile Hemangioma
- Congenital Hemangioma
- Kaposiform Hemangioendothelioma

Malformation
- Arteriovenous

Slow-Flow

Capillary Malformation
- Lymphatic Malformation
- Venous Malformation
14 y/o with a 3 month history of a trunk lesion
14 y/o with a lesion of the lip since birth
3 m/o with a forehead lesion since age 2 weeks
15 y/o with an anterior trunk lesion since birth
## Summary

<table>
<thead>
<tr>
<th>Biological Name</th>
<th>Incorrect Term</th>
<th>Treatment</th>
<th>Biological Name</th>
<th>Incorrect Term</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infantile Hemangioma</td>
<td>“Strawberry hemangioma” “Capillary hemangioma” “Cavernous hemangioma”</td>
<td>Observe Injection Propranolol Prednisone Timolol Resect</td>
<td>Capillary Malformation</td>
<td>“Port-wine stain” “Capillary hemangioma”</td>
<td>Observe Laser Resect</td>
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<tr>
<td>Congenital Hemangioma</td>
<td>“Infantile hemangioma”</td>
<td>Observe Resect</td>
<td>Lymphatic Malformation</td>
<td>“Cystic hyroma” “Lymphangioma”</td>
<td>Observe Sclero CO₂ Laser RFA Resect Sirolimus</td>
</tr>
<tr>
<td>Kaposiform Hemangioendothelioma</td>
<td>“Capillary hemangioma”</td>
<td>Sirolimus Vincristine</td>
<td>Venous Malformation</td>
<td>“Cavernous hemangioma”</td>
<td>Observe Sclero Resect</td>
</tr>
<tr>
<td>Pyogenic Granuloma</td>
<td>“Hemangioma”</td>
<td>Cauterize Resect</td>
<td>Arteriovenous Malformation</td>
<td>“Arteriovenous hemangioma”</td>
<td>Observe Embolize Resect</td>
</tr>
</tbody>
</table>
Conclusions-Learning Objectives

- Comprehend biological classification and terminology
- Accurately diagnose major types of vascular anomalies
- Understand basic management