Infantile Hemangiomas and Vascular Malformations

Basic Dermatology Curriculum

Content for this module was developed by The Society for Pediatric Dermatology
The following module contains a number of blue, underlined terms which are hyperlinked to the dermatology glossary, an illustrated interactive guide to clinical dermatology and dermatopathology.

We encourage the learner to read all the hyperlinked information.
Goals and Objectives

- The purpose of this module is to help medical students and residents develop a clinical approach to the evaluation and initial management of hemangiomas and vascular anomalies.

- By completing this module, the learner will be able to:
  - Describe the growth characteristics, clinical features and possible complications of infantile hemangiomas
  - Understand the current treatments for infantile hemangiomas
  - Form a differential diagnosis for hemangiomas and other vascular tumors or malformations
  - Determine when to refer a pediatric patient with an infantile hemangioma or other vascular malformation to pediatric dermatology
Pediatric vascular anomalies are classified according to the underlying blood vessel abnormality as well as their growth patterns.

There are two major groups of vascular anomalies:

- **Vascular tumors** – neoplasms of a particular type of blood vessel or other vascular tissue
  - Tumors will proliferate and some never stop without therapy
- **Vascular malformations** – A lesion of abnormal blood vessels that does not have rapid proliferation
  - Malformations are static or very slow growing
Vascular Anomaly Classification

- **Vascular tumors**
  - Infantile hemangioma (IH)
  - Congenital hemangioma
    - NICH, RICH, PICH*
  - Tufted angioma
  - Pyogenic granuloma
  - Kaposiform hemangioendothelioma
  - Angiosarcoma

- **Vascular malformations**
  - Capillary malformations (CM)
    - Cutaneous or mucosal CM (“Port-wine” stain)
    - Nevus simplex (“salmon patch”)
  - Cutis marmorata telangiectatica congenita (CMTC)
  - Lymphatic malformations
  - Venous malformations
  - Arterial malformations
  - Arteriovenous malformations
  - Combined malformations

*RICH – rapidly involuting congenital hemangiomas, NICH - non-involuting congenital hemangiomas, PICH – partially involuting congenital hemangiomas*
Infantile Hemangiomas

- Infantile hemangiomas (IH) are common benign vascular tumors of infancy occurring in ~4% of infants.
- Low birth weight, female gender, twin gestation and fair skin are known risk factors for developing IH.
- At birth, a premonitory mark may be present such as a bruise-like patch, area of vasoconstriction/pallor or telangiectasias.
You see a 4 week old infant with this superficial hemangioma on the arm. It is growing. When should the parents expect the hemangioma to grow the most rapidly?
Case 1

You counsel the family that the period of most rapid growth for infantile hemangiomas is:

A. 4-6 months of age
B. 5-7 weeks of age
C. 0-3 weeks of age
D. 6-12 months of age
E. There is no period of accelerated growth, they enlarge slowly with time
Case 1

The period of most rapid growth for infantile hemangiomas is:
A. 4-6 months of age  
B. 5-7 weeks of age  
C. 0-3 weeks of age  
D. 6-12 months of age  
E. There is no period of accelerated growth, they enlarge slowly with time
Infantile Hemangiomas: Growth Characteristics

- Infantile hemangiomas proliferate during the first 2-3 months of life, with rapid growth of superficial IH observed between 5-7 weeks of age.
- Growth usually stabilizes around 4-6 months, followed by involution over years.
- Larger, deeper IH grow for longer and involute more slowly.
- Based on these growth characteristics, IH requiring intervention should be referred for treatment before 3 months of age.
Hemangiomas: clinical appearance

- Hemangiomas may have superficial, deep or mixed presentations
- Superficial hemangiomas are bright red and minimally elevated, deep hemangiomas are often larger with a bluish color. Mixed hemangiomas have both components.
Hemangiomas: clinical appearance

- Hemangiomas may occur anywhere on the body.
- They may be localized or segmental/regional in distribution.
- Regional/segmental IH of the head and neck or lumbosacral areas may have underlying structural anomalies (PHACE, LUMBAR/SACRAL associations).
Focal vs Segmental Distribution

- Hemangiomas are most commonly focal but when segmental/regional they are more likely to have or develop complications
Infantile Hemangiomas: Complications

Complications include:

• Ulceration
• Visual Impairment
• Airway involvement
• Multifocal presentation
• Aesthetic complications
• Complex Associations (PHACE, LUMBAR/SACRAL)
In this 4 week old infant with a large hemangioma on the arm what complication are you most concerned about?

A) Underlying structural anomaly
B) Aesthetic concern
C) Ulceration
D) Infection
E) Functional impairment of the elbow
Case 1 continued…

In this 4 week old infant with a large hemangioma on the arm what complication are you most concerned about?

A) **Underlying structural anomaly** (this hemangioma is localized and on the arm, an underlying structural anomaly is unlikely)

B) **Aesthetic concern** (this is not a particularly cosmetically sensitive location on the arm)

C) **Ulceration** (the white discoloration and location make ulceration very possible in this hemangioma)

D) **Infection** (hemangiomas very rarely become infected and are usually already ulcerated when/if infection occurs)

E) **Functional impairment of the elbow** (infantile hemangiomas are localized to the skin and soft tissue, functional impairment is uncommon)
Ulceration

- Ulceration is the most common complication occurring in ~10%
- Common on mucosal sites (40% on lip and anogenital) as well as sites prone to friction (upper back, arms)
- Early white discoloration may herald ulceration
- Large, segmental/regional hemangiomas are more likely to develop ulceration
Ulceration: Treatment

- Treatment of ulceration includes local wound care and pain control
  - Daily gentle cleansing/soaking, removal of crust
  - Liberal application of emollients/barriers (vaseline/aquaphor)
  - Pain control
  - Consider adjunctive measures in more extensive cases:
    - topical metronidazole cream, pulsed dye laser, oral propranolol
- In large, ulcerated IH, early referral to peds derm is recommended
- Ulceration can lead to significant pain and scarring
Visual Impairment

- Periorbital hemangiomas can lead to visual disturbances such as astigmatism due to pressure exerted on the globe.
- Proptosis, amblyopia or visual axis occlusion can also occur.
- Systemic therapy, referral to ophthalmology and pediatric dermatology may be warranted.
Airway Involvement

- Mandibular/beard distribution hemangiomas can be associated with airway involvement
- Laryngeal involvement can occlude airway and is a life threatening emergency
- Assess for stridor, hoarseness
- Systemic therapy is warranted: oral propranolol, oral corticosteroids or both
- Emergent referral to the emergency department if airway obstruction, urgent referral to pediatric dermatology, otolaryngology if stable
Multifocal Presentation

- Infantile hemangiomas may have a multifocal presentation
- > 5 cutaneous IH can be associated with hepatic involvement
- Hepatic hemangiomas are usually small and asymptomatic. Rarely, large IH in the liver may cause failure to thrive or high output cardiac failure
- Abdominal US recommended to screen for hepatic IH
Aesthetic complications:

- Large/exophytic hemangiomas may leave fibrofatty residuum post involution
- Scarring, anetoderma, hypopigmentation, telangiectasias are also seen in residual IH
- Treatment of residual IH with laser modalities or surgical excision can be considered prior to school age
- Early treatment with propranolol may reduce aesthetic impact and possibly prevent later need for surgery
This infant has a large, vascular plaque on the right face and scalp. You make a diagnosis of segmental infantile hemangioma. What association/syndrome should you consider in the setting of this type of birthmark?
Case 2

A. Sturge Weber syndrome
B. Goltz syndrome
C. LUMBAR/SACRAL association
D. PHACE association
E. Capillary Malformation-Arteriovenous malformation syndrome (CM-AVM)
Case 2

A. Sturge Weber syndrome
B. Goltz syndrome
C. LUMBAR/SACRAL association
D. PHACE association
E. Capillary Malformation-Arteriovenous malformation syndrome (CM-AVM)
Complex Associations: PHACE

- **Posterior fossae abnormalities (dandy walker malformation)**
- **Hemangioma (large facial IH >5cm)**
- **Arterial/Aortic anomalies**
- **Cardiac Anomalies**
- **Eye Abnormalities**
Case 2

What work up is recommended?
A. MRI of the head and neck
B. MRA of the head and neck
C. Ophthalmology evaluation
D. Echocardiogram
E. All of the above
Case 2

What work up is recommended?
A. MRI of the head and neck
B. MRA of the head and neck
C. Ophthalmology evaluation
D. Echocardiogram
E. All of the above
PHACE Association

• The risk of PHACE association depends on the location, size and distribution of the hemangioma.
• Large (>20cm$^2$), regional/segmental hemangiomas located on the face have a ~30% risk of underlying PHACE association.
• Having more than one region of the face involved (ie: forehead and mandibular region) is associated with an even higher risk for PHACE.
PHACE Association

- Recommended Work-Up
  -- echocardiography
  -- MRI/MRA of the head and neck
  -- ophthalmology evaluation

- Referral to pediatrics dermatology +/- interdisciplinary vascular anomalies team is helpful in these complex cases
Complex Associations: LUMBAR/SACRAL

- Regional/Segmental IH of lumbosacral and anogenital area can be associated with:
  - Anal anomalies
  - Abnormal genitalia
  - Imperforate anus
  - Lipomyelomeningocele
  - Tethered cord
  - Vesicorenal anomalies

WORK UP:
- Consider evaluation with US or MRI
- MRI is more specific in evaluating for spinal dysraphism
Infantile Hemangiomas: Management

- **Topical Therapies**
  - Topical beta blockers
  - Topical corticosteroids
  - Imiquimod

- **Local Therapies**
  - Intralesional corticosteroids
  - Pulsed dye laser for ulceration or residual lesions

- **Systemic Therapies**
  - Oral propranolol
  - Systemic corticosteroids
  - Immunosuppressive or anti-neoplastic* therapies (Interferon, Vincristine)

* rarely used since advent of propranolol
Topical Timolol

- Timolol maleate 0.05% gel has demonstrated efficacy as a local therapy
- Use in infantile hemangiomas is off-label
- Best used in small, superficial hemangiomas on head and neck
- Gel can lead to dryness, irritation
- Theoretic risk for systemic absorption in large or ulcerated hemangiomas, but generally regarded as safe
• Oral propranolol is FDA approved as a safe and effective therapy for infantile hemangiomas
• Acts to reduce size and halt growth, helpful in the setting of ulceration, mechanism of action unknown
• Propranolol is standard of care for hemangiomas requiring intervention and is well tolerated in most patients
• Side effects include:
  – hypoglycemia
  – hypotension
  – bradycardia
  – sleep disturbance/nightmares
Propranolol

- Propranolol can be initiated as inpatient or outpatient
- Guidelines suggest outpatient initiation in infants > 8 weeks corrected age, with pretreatment EKG and no comorbidities
- Dose is 1-3 mg/kg/d divided bid or tid with HR and BP check 1-2 hours post dose increases

- Contraindications
  - Premature infants with corrected age <5 weeks
  - Reactive airway disease
  - Infants <2kg
  - Bradycardia/heart block
  - Pheochromocytoma
  - Known hypersensitivity to the drug
Corticosteroids were the mainstay of treatment prior to 2008

- Dose of 1-3mg/kg day
- Use in setting of airway disease as adjunctive therapy or where propranolol is contraindicated
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<thead>
<tr>
<th>Infantile Hemangioma Location</th>
<th>Possible Complications</th>
<th>Suggested Workup</th>
</tr>
</thead>
<tbody>
<tr>
<td>Large Facial &gt; 5cm</td>
<td>PHACE Association, Ulceration, Aesthetic concern</td>
<td>MRI/MRA of head and neck, echocardiogram, ophthalmology exam, thyroid function tests</td>
</tr>
<tr>
<td>Central Facial</td>
<td>Aesthetic concern</td>
<td>Not usually required unless &gt; 5cm, see above</td>
</tr>
<tr>
<td>Periorbital</td>
<td>Visual compromise, astigmatism, amblyopia</td>
<td>Ophthalmology evaluation</td>
</tr>
<tr>
<td>Mandibular</td>
<td>Airway involvement</td>
<td>Physical exam to assess for stridor, hoarseness. Urgent referral (ED, ENT)</td>
</tr>
<tr>
<td>Mucosal (lip, anogenital)</td>
<td>Ulceration, pain</td>
<td>Not usually required unless segmental presentation</td>
</tr>
<tr>
<td>Lumbosacral</td>
<td>LUMBAR syndrome</td>
<td>MRI of the spine</td>
</tr>
<tr>
<td>Multiple</td>
<td>Hepatic Involvement</td>
<td>Abd US, Thyroid studies if numerous or large hepatic hemangiomas observed</td>
</tr>
</tbody>
</table>
Case Three
HPI: This is an 8 day old baby boy who presents for evaluation of a large, pink mark on his forehead present at birth. His parents are concerned by the size and location of the birthmark.

PMH: Born full term to healthy mother, no pregnancy or labor complications, received all vaccinations

Medications: None

Allergies: No known allergies

Family History: Non-contributory

Social History: Lives with mother, father, grandmother and 3-year-old brother

ROS: Negative
Case Three: Skin Exam

How would you describe this lesion?
Case Three: Skin Exam

Faint, dull, pink patches over the midline glabella, forehead and eyelids that are not confluent
Case Three, Question 1

What is the most appropriate next step in diagnosis and management of this skin lesion?

A. Skin biopsy
B. MRI of the head and neck
C. Ophthalmologic evaluation
D. Reassurance and education
Case Three, Question 1

What is the most appropriate next step in diagnosis and management of this skin lesion?

A. Biopsy (a biopsy is unnecessary as this is a clinical diagnosis)

B. MRI of the head (there are no associated abnormalities of the brain associated with this lesion)

C. Ophthalmologic evaluation (a nevus simplex does not confer any ophthalmologic risk)

D. Reassurance and education
Diagnosis: Nevus Simplex

- Nevus simplex (salmon patch) is a type of faint, transient capillary malformation
- Present in 30-40% of newborns, it is the most common pediatric vascular lesion
- Flat, pink to bright red patches typically on the midline forehead, scalp, upper eyelids, posterior neck and back.
- Children often have multiple
- Commonly referred to as a “stork bite” when on the nape of the neck or an “angel kiss” when on the eyelid or glabella
Nevus Simplex: Management

- In general, there are no findings associated with nevus simplex that require workup or evaluation
  - If there is a midline lumbosacral capillary malformation with other stigmata of spinal dysraphism (dimple, deviated, etc.), then evaluation for tethered spinal cord should be done
  - Can be seen in Beckwith-Wiedemann syndrome along with large protruding tongue, umbilical hernia and other findings
- The redness will become accentuated during episodes of increased internal pressure (crying, straining with defecation or physical exertion)
- 95% of facial lesions fade within 1-2 years making treatment unnecessary
Case Four
Case Four: History

HPI: This is a 6 month old baby who presents with a lesion on her face that has been present since birth and has been growing in size. The lesion is not itchy or painful.

PMH: Born at 38 weeks to healthy mother via C-section, no pregnancy or labor complications. No medical conditions.

Medications: None

Allergies: No known allergies

Family History: Non-contributory

Social History: Lives with mother and father

ROS: Negative
Case Four: Skin Exam

How would you describe this lesion?
Dull red patch on the face involving the upper eyelid, forehead, temple and scalp.
Case Four, Question 1

What is the most likely diagnosis?

A. Bruise
B. Nevus simplex (salmon patch)
C. Port-wine-stain (Cutaneous capillary malformation)
D. Superficial infantile hemangioma
Case Four, Question 1

What is the most likely diagnosis?

A. **Bruise** (this is too uniform and purple and has been present for too long to be a bruise of child abuse)

B. **Nevus simplex (salmon patch)** (dull pink patches)

C. **Port-wine-stain (Cutaneous capillary malformation)**

D. **Superficial infantile hemangioma** (a hemangioma should not be fully formed at birth, should be thickening and not as uniformly colored)
Diagnosis: Port-wine stain

- Natural course: Capillary malformation present at birth
- Present as pink to dark red patches that are often unilateral with midline cutoff
- Can be found on any part of the body
- Tend to darken and thicken slowly over years
- May develop vascular papules and significant skin hypertrophy over many years
- Other clinical findings: Can occur as isolated cutaneous findings or in association with specific syndromes
Case Four, Question 2

What is the most important next step in the evaluation in this patient given the location of her port-wine stain?

A. Brain MRI
B. EEG
C. Complete blood count (CBC)
D. Ophthalmic examination
Case Four, Question 2

What is the most important next step in the evaluation in this patient given the location of her port-wine-stain?

A. Brain MRI (a brain MRI can help diagnose Sturge-Weber syndrome, however it is more important to rule out glaucoma first in a patient who is not seizing)

B. EEG (in a patient who has no seizures, this is not the most important first step)

C. Complete blood count (CBC) (Port wine stains don’t lead to associated CBC abnormality)

D. Ophthalmologic examination
Port-Wine Stain Distribution

- Port-wine stains in the distribution of the first branch of the trigeminal nerve or those stains that involve the upper (+/- lower) eyelid can be associated with Sturge-Weber syndrome (SWS).

- Patients with a port-wine stain involving the eyelid are at high risk for developing congenital glaucoma and should undergo initial ophthalmic evaluation emergently.

- Patients with widespread port wine stains may have associated overgrowth syndromes such as CLOVES, Macrocephaly- Capillary Malformation and others. These patients should be referred to a pediatric dermatologist or other vascular anomaly specialist for further evaluation.
Diagnosis: Port-wine stain

- Sturge Weber Syndrome (SWS)
  - Constellation of findings:
    - V1 Capillary malformation (if isolated, the risk is 10-20%)
    - SWS risk is higher with more extensive or bilateral capillary malformations
    - Glaucoma
    - Calcifications in the leptomeninges leading to risk of seizures, neurologic delay and hemiplegia
  - Workup:
    - Urgent evaluation by ophthalmology
    - Neurologic evaluation if seizures, developmental delay or parental concern
    - Referral to Pediatric dermatologist to discuss further workup and therapy
Management of Port-wine stains

- There are many factors to consider when deciding on management of PWS including size, location and cosmetic impact.
- If a patient has widespread PWS and overgrowth of the extremities, enlarged head or other underlying vascular malformations, they should be referred to a vascular anomaly specialist to rule out other associated syndromes.
- Management options include:
  - Conservative management – no treatment or use of cosmetics to conceal the lesions
  - Pulse dye laser (PDL) – causes intravascular coagulation in abnormal vasculature without damaging surrounding structures
Case Five
HPI: A 3 month old baby who presents for evaluation of skin discoloration. Her parents are concerned that her arm has a consistent mottled appearance that does not resolve with warming.

PMH: Born at 40 weeks to healthy mother via vaginal delivery. No known medical conditions.

Medications: None

Allergies: No known allergies

Family History: Non-contributory

Social History: Lives with mother, father and maternal grandmother

ROS: Negative
How would you describe this child’s skin?
Case Five: Skin Exam

Mottled skin in a reticulated pattern with white/faint blue vasoconstricted background and areas of ulceration
Case Five, Question 1

What is the most likely diagnosis?

A. Venous malformation
B. Cutis Marmorata
C. Cutis Marmorata Telangiectatica Congenita
D. Kaposiform Hemangioendothelioma (KHE)
Case Five, Question 1

What is the most likely diagnosis?

A. Venous malformation (a venous malformation typically looks blue or purple underneath the skin and feels soft when pressed)

B. Cutis Marmorata (Cutis Marmorata is a normal physiologic mottling that occurs in the cold but normalizes when the skin is warmed)

C. Cutis Marmorata Telangiectatica Congenita

D. Kaposiform Hemangioendothelioma (presents as a purple firm tumor and can lead to severe bleeding due to localized coagulopathy)
Diagnosis: Cutis marmorata telangiectatica congenita

- Purple mottling of unknown pathophysiology
- The color change does not reverse with re-warming
- The affected limb or body part can be smaller and have a smaller circumference
- There can be atrophy of the skin leading to ulceration and accentuation of the musculature underneath the lesion
Differential Diagnosis:  
Cutis Marmorata

- Normal temporary mottling of the skin often seen in infants, young children
- More persistent mottling is observed in patients with Trisomy 18, 21 and Cornelia de Lange syndrome
- Dilation of capillaries and small venules occurs in response to cold exposure
- Typically resolves with re-warming making treatment unnecessary
- If mottling is deep blue to purple in color and does not resolve with rewarming, may be more persistent form known as cutis marmorata telengiectatica congenita
Case Six: History

HPI: A 12 year old boy who presents with a “bleeding hemangioma” on his left thumb. His parents first noticed a red spot on his finger about a week ago. Since then, the spot has grown rapidly into a small bump. The bump bleeds easily and is extremely painful when manipulated.

PMH: Seasonal allergies.

Medications: Cetirizine as needed

Allergies: Strawberries.

Family History: Non-contributory

Social History: Lives with mother and younger sister

ROS: Pain with manipulation of left thumb
How would you describe this lesion?
Red, friable nodule on the finger that looks like it is growing out of a cup of normal skin
Case Six, Question 1

What is the most likely diagnosis?

A. Compound nevus
B. Epidermal inclusion cyst
C. Pyogenic granuloma
D. Wart
Case Six, Question 1

What is the most likely diagnosis?

A. Compound nevus (darkly pigmented papules, bleeding and rapid development are uncommon)

B. Epidermal inclusion cyst (typically flesh colored, often with central punctum)

C. Pyogenic granuloma

D. Wart (painless, verrucous growth that does not typically bleed with trauma)
Pyogenic Granuloma

• Common acquired vascular tumor
• Occurs on skin particularly prone to trauma (hands, fingers, face) and mucous membranes
• Develop rapidly (days to weeks)
• Extremely friable, bleed with little manipulation
• Can recur despite treatment
Treatment of Pyogenic Granulomas

- Pyogenic granulomas can be treated with:
  - Currettage or shave removal with electrodessication of base (to prevent recurrence)
  - Surgical removal with primary closure
  - Pulsed-dye laser

- The lesions should ALWAYS be sent for pathologic confirmation as the clinical appearance can mimic a melanoma

- Patients should be counseled that the risk of recurrence is high since Pyogenic granuloma is a response to trauma and the therapy is traumatic
Take Home Points

- While many vascular lesions represent isolated findings, some lesions are associated with syndromes that require special management and referral to other specialists. Referral to a pediatric dermatologist can be helpful to guide any potential workup.
- Infantile hemangiomas grow most rapidly between the ages of 5 and 7 weeks so lesions in locations requiring intervention should be referred early.
- Mandibular hemangiomas with stridor or hoarseness need emergent ENT referral to evaluate for airway compromise.
- Port-wine stains in a V1 distribution require urgent ophthalmologic evaluation.
- The decision to treat a vascular lesion is one that is made after many discussions between the patient, family and provider.
- Many vascular lesions evolve over time. Parents should be counseled on what skin changes should be expected and how treatment may impact such changes.
# Common Vascular Lesions

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<tr>
<th>Lesion</th>
<th>Pathophysiology</th>
<th>Onset</th>
<th>Further evaluation</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Infantile Hemangioma</strong></td>
<td>Tumor of blood vessels</td>
<td>Within first few weeks</td>
<td>If on face consider PHACE If in perineum consider LUMBAR If greater than 5 evaluate for liver involvement</td>
<td>Propranolol, topical timolol, PDL, excision, active nonintervention</td>
</tr>
<tr>
<td><strong>Nevus simplex (salmon patch)</strong></td>
<td>Capillary malformation</td>
<td>Birth</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td><strong>Port-wine stain (Cutaneous capillary malformation)</strong></td>
<td>Capillary malformation</td>
<td>Birth</td>
<td>Depends on distribution (V1; SWS ophthalmologic +/- neurologic exam) Widespread referral to pediatric derm</td>
<td>Pulsed dye laser (PDL)</td>
</tr>
<tr>
<td><strong>Cutis Marmorata Telangiectatica Congenita</strong></td>
<td>Unclear</td>
<td>Birth</td>
<td>None</td>
<td>Possible referral to Orthopedics if leg length discrepancy</td>
</tr>
<tr>
<td><strong>Pyogenic granuloma</strong></td>
<td>Vascular tumor</td>
<td>Any age</td>
<td>None</td>
<td>Excision, PDL</td>
</tr>
<tr>
<td><strong>Venous Malformation</strong></td>
<td>Malformation of veins</td>
<td>Birth</td>
<td>Referral to vascular anomalies expert</td>
<td>Sclerotherapy, surgery</td>
</tr>
</tbody>
</table>
Acknowledgements

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References