The recommendations in this publication do not indicate an exclusive course of treatment or serve as a standard of care. Variations, taking into account individual circumstances, may be appropriate.

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Infantile hemangiomas (IHs) are the most common tumors of childhood. Unlike other tumors, they have the unique ability to involute after proliferation, often leading primary care providers to assume they will resolve without intervention or consequence. Unfortunately, a subset of IHs rapidly develops complications, resulting in pain, functional impairment, or permanent disfigurement. As a result, the primary clinician has the task of determining which lesions require early consultation with a specialist.

Although several recent reviews have been published, this clinical report is the first based on input from individuals representing the many specialties involved in the treatment of IH. Its purpose is to update the pediatric community regarding recent discoveries in IH pathogenesis, treatment, and clinical associations and to provide a basis for clinical decision making in the management of IH.

This Quick Reference Guide refers to the AAP Clinical Report on the Diagnosis and Management of Hemangiomas of Infancy.
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INFANTILE HEMANGIOMA (IH) IS THE CURRENTLY ACCEPTED TERMINOLOGY FOR THE LESIONS THAT ARE THE FOCUS OF THIS CLINICAL REPORT.

**NOMENCLATURE**

**Congenital Hemangiomas**
are biologically and behaviorally distinct from IH.

**Pyogenic Granuloma**
may be misdiagnosed as IH and is more accurately categorized as a hyperplasia rather than a true neoplasm.

**Cavernous Hemangiomas**
are usually, in fact, deep IHs or venous malformations.

**Kasabach-Merritt phenomenon or KMP**
(a consumptive coagulopathy) is not associated with IH but rather 2 other vascular neoplasms, kaposiform hemangioendothelioma (KHE) and tufted angioma (TA).
02.

**TYPES**

- Epidemiology
- Pathogenesis
- Histopathology
Epidemiology

THE INCIDENCE OF IH IN THE GENERAL POPULATION IS APPROXIMATELY 5%.

- Risk factors for IH include being white, being female, and having low birth weight.
- Associations are also reported with older maternal age, multiple gestation births, placenta previa, pre-eclampsia, use of fertility drugs or erythropoietin, breech presentation, and being the first born.

Pathogenesis

IHS MAY DEVELOP EITHER FROM INTRINSIC ENDOTHELIAL PROGENITOR CELLS (EPCS) OR FROM ANGIOBLASTS OF PLACENTAL ORIGIN.

- IH growth is affected by intrinsic influences, such as angiogenic and vasculogenic factors within the IH, and by external factors such as tissue hypoxia and developmental field disturbances.
- A unifying theory proposes that circulating EPCs migrate to locations in which conditions are favorable for growth into placenta-like tissues.

Histopathology

PROLIFERATING IH ARE WELL CIRCUMSCRIBED AND LACK A CAPSULE.

- Involuting IH are fibrofatty and less defined.
- Glucose transporter protein isoform 1 (GLUT1) is a commonly used immunochemical marker for IH.
Phases of Growth

**CLINICAL APPEARANCE**

- IHs are characterized as superficial, deep, or mixed, and as focal, multifocal, or segmental.
- Superficial IHs appear earlier and begin involution sooner than their deeper counterparts.
- Segmental IHs are more commonly involved in PHACE and other IH syndromes and associations.
- The presence of more than 5 focal IHs suggests a higher risk of hepatic involvement.

**DETECTION**

- IHs usually make their initial appearance prior to 4 weeks of age.
- IHs complete most of their growth by 5 months of age.
- Involution of IHs begins as the child approaches 12 months of age.
- In most cases, the majority of involution is completed by age 4.
Complications

**SEGMENTAL IHS** are far more likely than focal IHs to result in a complication, usually ulceration.

**FOCAL IHS** cause complications primarily by virtue of their location on or near vital structures.

**FACIAL IHS** cause complications more frequently than nonfacial IHs and are several times more likely to receive some form of therapy.

- Minor bleeding from an ulcerated IH is common, but rarely of clinical significance; bleeding from a nonulcerated IH is rare.
- Patients with extensive IH in the “beard” distribution are more likely to have involvement of the airway.
- High risk periocular IHs are those that are larger than 1 cm in diameter, located near the nose, associated with ptosis or eyelid margin change, or displacing the globe.
- Diffuse IH of the liver may be associated with severe consumptive hypothyroidism.
The hallmark of PHACE syndrome is a large, segmental IH, characteristically located on the face, scalp, and/or neck.

The most common extracutaneous features of PHACE syndrome are cerebrovascular anomalies, followed by cardiac anomalies and structural brain anomalies.

LUMBAR syndrome may be best considered the “lower half of the body” variant of PHACE syndrome and may be associated with urogenital, anal, skeletal, and spinal cord anomalies.
04.

DIAGNOSIS

13  Imaging
14  Clinical
Imaging

IMAGING OF IH IS NOT USUALLY NECESSARY.

When imaging of IH is performed, ultrasound is the preferred modality for diagnosis, while MRI is better to assess extent of the lesion.

Imaging may be required when the diagnosis is uncertain, when evaluation of extent is necessary, when the IH is a possible marker of PHACE or LUMBAR syndrome, or when response to therapy needs to be monitored.
THE INDICATIONS FOR INTERVENTION FOR IH INCLUDE:

Emergency treatment of potentially life-threatening complications.

Urgent treatment of existing or imminent functional impairment, pain, or bleeding.

Evaluation to identify structural anomalies potentially associated with IH.

Elective treatment to reduce the likelihood of long-term or permanent disfigurement.

THERE IS NO ALGORITHM TO DETERMINE THE MOST APPROPRIATE INTERVENTION FOR IH. FACTORS AFFECTING THIS CHOICE INCLUDE:

1) age of the patient
2) growth phase of the lesion
3) location and size of the lesion
4) degree of skin involvement
5) severity of complication and urgency of intervention
6) potential for adverse psychosocial consequences
7) parental preference
8) physician experience
TREATMENT

16 Management
17 Medical Therapy
18 Corticosteroid
19 Other Medical Therapies
20 Laser Therapy
20 Surgical Therapy
Management of ulcerated IH consists primarily of:

- **BARRIER DRESSINGS**
- **PAIN CONTROL**
- **CONTROL OF IH GROWTH**

Adjuvant therapies may include:

1) **TOPICAL AGENTS INCLUDING ANTIBIOTICS, ANESTHETICS, OR WOUND DRESSINGS**

2) **PULSED DYE LASER**
Medical Therapy

Propranolol, administered orally at a dose of 1 to 3 mg/kg/day, is efficacious in reducing size and discoloration of IH. The mechanism of propranolol’s effect on IH likely involves several processes including vasoconstriction, inhibition of angiogenesis, and stimulation of apoptosis.

A consensus report suggests heart rate and blood pressure be determined at baseline, 1 and 2 hours after the first dose of propranolol, and 1 and 2 hours after each dosage increase of ≥0.5 mg/kg/day.

Administration of propranolol with feedings, and holding doses if oral intake is compromised, reduces the likelihood of hypoglycemia.

Topical application of timolol has demonstrated efficacy in the management of superficial IHs.

Sidebar
COMMON SIDE EFFECTS

Common side effects of propranolol include sleep disturbance and discoloration with cooling of the hands and feet.

Contraindications to the use of propranolol for IH include cardiogenic shock, sinus bradycardia, hypotension, heart block greater than first-degree, heart failure, bronchial asthma, and known hypersensitivity to the drug.
Corticosteroids, administered orally at a dose of 2 to 3 mg/kg/day, are efficacious in reducing size and discoloration of IH. The mechanism of IH growth inhibition by corticosteroids likely involves reduced vasculogenesis and enhanced adipogenesis. Corticosteroids administered intralesionally and topically also appear effective in certain subsets of patients with more localized IH, but their dosing and safety profile are not well studied. Periodic reexamination of children on corticosteroid therapy for IH has been suggested for monitoring of growth and blood pressure as well as changes in the lesion(s) being treated.
Other Medical Therapies

Medications other than beta blockers and corticosteroids may have efficacy in treating IH, but their utility is limited by their safety profile.

Vincristine is used for lesions associated with KMP; however, such lesions are kaposiform hemangioendotheliomas and TAs rather than IHs and are associated with potential risks of irritation and neurotoxicity.

Interferon-alpha and imiquimod, although effective in IH treatment, are associated with an undesirable rate of complications.
Laser Therapy

Laser treatment of IH may be useful in early nonproliferating superficial lesions, management of critical skin, treatment of ulcerating lesions, “multimodal” therapy, and management of persisting postinvolution telangiectasia.

**PULSED DYE LASER (PDL) IS USED MOST COMMONLY, BECAUSE ITS LIGHT IS PREFERENTIALLY ABSORBED BY HEMOGLOBIN.**

Use of laser on proliferating and superficial IHs may lead to ulceration. Atrophic scarring and hypopigmentation are also potential complications of laser use in IH.

Surgical Therapy

Indications for surgery for IH during infancy are limited to:

01. **FAILURE OF, OR CONTRAINDICATION TO, PHARMACOTHERAPY**
02. **FOCAL INVOLVEMENT IN AN AREA ANATOMICALLY FAVORABLE FOR RESECTION**
03. **A HIGH LIKELIHOOD THAT RESECTION WILL ULTIMATELY BE NECESSARY AND THE SCAR WILL BE THE SAME REGARDLESS OF TIMING**

During involution, surgery may be indicated for excision of residual fibrofatty tissue, resection of scarred/excess skin, and/or reconstruction of damaged structures.

Timing of surgery is based on the age of the patient, the location and degree of deformity, and whether the tumor is still regressing. Elective surgical intervention for IH is reasonable after age 4 years because, by this age, self-esteem and long-term memory begin to form and the tumor has completed most of its involution.
IHs of the periocular area have the potential to cause compression of the globe, obstruction of the visual axis, and extension into the retrobulbar space, resulting in refractive errors, strabismus, and amblyopia, leading to vision loss. The permanence of ophthalmic complications due to IH is often related to their severity and duration, underscoring the need for early ophthalmologic evaluation.
Common Locations of IH

AIRWAY
Most patients with IHs of the airway have subglottic involvement causing biphasic stridor and barking cough, often mistaken as croup. Voice and swallowing are generally normal. Diagnosis of airway IHs is usually made by endoscopy in the operating room. In most cases, IHs of the airway may be managed medically; in cases of severe obstruction, surgical reduction or excision may be entertained.

NOSE
Early management of nasal tip IH reduces the likelihood of poor cosmesis resulting from skin excision and/or replacement and effects on the underlying cartilage. Goals of surgery for nasal tip IHs include complete IH excision, reconstruction of the cartilaginous framework, and judicious skin excision and redraping.

LIP
IHs involving the lips and perineum have a tendency to ulcerate, and these regions are difficult to reconstruct. Such lesions are appropriately managed aggressively with medical therapy.

Although these are common locations for IH, they are not the only locations. Be aware that IH can occur anywhere.
HEPATIC IHS HAVE BEEN CHARACTERIZED AS OCCURRING IN 3 PATTERNS:

**focal**

Focal hepatic IHS are the hepatic manifestation of rapidly involuting congenital hemangioma (RICH); they are fully grown at birth, and involution is almost complete by 1 year of age.

**multifocal**

Multifocal hepatic IHS have normal hepatic parenchyma between them. Many patients are asymptomatic; however, those with high-flow and/or high-output cardiac failure require pharmacologic therapy with propranolol or corticosteroid. Patients with diffuse hepatic IHS present with hepatomegaly that can lead to compromised ventilation, renal failure attributable to renal vein compression, poor inferior vena caval blood return to the heart, and death.

**diffuse**

Diffuse hepatic IHS may cause acquired hypothyroidism. Most hepatic IHS are managed medically; rarely embolization, surgical resection, and transplantation have been necessary.

Although these are common locations for IH, they are not the only locations. Be aware that IH can occur anywhere.