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Management of Infantile Hemangioma in the Community

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I practice as a general medical dermatologist in Northern British Columbia. During my first year of practice, I saw several infants requiring treatment for an infantile hemangioma, which required me to become familiar with topical and systemic therapies. The objective of this article is to provide an overview of the management of uncomplicated infantile hemangiomas in community settings, helping dermatologists become confident in prescribing first-line topical and systemic therapies.

Epidemiology, Clinical Presentation, and Natural History

Infantile Hemangiomas (IHs) are the most prevalent benign tumours in infancy, occurring in approximately 3% of infants.[1] Risk factors for IHs include female sex, multiple gestations, preterm birth, low birth weight, progesterone use in mothers, and a positive family history.[2]

IHs can be classified based on their depth (superficial, deep, and mixed) and their pattern of involvement (focal, multifocal, segmental, and indeterminate).[3] Superficial IHs typically present as red, lobulated papules or plaques, while deep IHs present as blue or skin-coloured subcutaneous lesions, often with overlying telangiectasia. Mixed IHs exhibit features of both superficial and deep types.

IHs appear within the first few weeks of life, and follow a characteristic growth pattern of proliferation then involution. Proliferation is most rapid within the first 3 to 5 months, during which the lesions reach approximately 80% of their final size, which is followed by slower growth up until 9 to 12 months of age, on average.[4] Involution typically begins at approximately 12 months of age, and continues for a period of 3 to 9 years.[4] It was previously thought that IHs regress by a rate of approximately 10% per year (i.e., 30% of IHs will involute by 3 years of age, 50% by 5 years, and 90% by 9 years).[5] However, more recent data shows that involution is complete by 4 years of age in 90% of patients.[6] Deep hemangiomas tend to present later and have a prolonged proliferative phase.[4] IHs with minimal or absent growth (IH-MAG), also known as Abortive Hemangiomas,

Morphologic or Anatomic feature(s)	Possible Associated Complication(s)
• Large or segmental infantile hemangiomas (IH) • Mixed IH • Lower lip, neck, anogenital area, 'biker glove' distribution	• Ulceration
• Segmental, especially face or scalp • Nasal tip, lip • Face ≥2 cm (>1 cm if ≤3 months of age) • Scalp, neck, trunk or extremity >2 cm • Breast (in females)	• Cosmetic deformity
• Periocular	• Astigmatism, visual axis obstruction, nasolacrimal duct obstruction, ptosis, amblyopia, strabismus
• 'Beard' distribution (preauricular, mandible, lower lip, chin, anterior neck)	• Airway hemangiomas, risk of airway obstruction
• Perioral	• Feeding difficulties
• ≥5 IHs	• Infantile hepatic hemangioma (may be associated with hypothyroidism)
• Large, segmental facial IH	• PHACES syndrome (Posterior fossa malformations, Hemangiomas, Arterial anomalies, Cardiac defects, Eye abnormalities, Sternal cleft)
• Segmental IH overlying lumbosacral spine or perineal	• LUMBAR syndrome (Lower body IH, Ulceration, Myelopathy, Bony deformities, Anorectal malformations, Renal anomalies, Arterial anomalies)

Table 1. Potential complications of infantile hemangiomas by morphologic and anatomic features[3,7]; *courtesy of Lisa Flegel, MD, FRCPC, DABD.*

represent a variant that has minimal to no proliferation but follows a similar involution pattern as other IHs.[5] After involution, patients may be left with telangiectasia, fibrofatty tissue, anetoderma, redundant skin, or scarring.[6]

Complications

Most IHs involute spontaneously and do not require intervention. Possible complications of IHs include cosmetic disfigurement, pain, ulceration, bleeding, infection, and functional impairment. IHs may also be associated with extracutaneous involvement, such as liver hemangiomas, and multi-system syndromes such as Posterior fossa malformations, Hemangiomas, Arterial anomalies, Cardiac defects, Eye abnormalities, Sternal cleft (PHACES) and Lower body IH, Ulceration, Myelopathy, Bony deformities, Anorectal malformations, Renal anomalies, Arterial anomalies (LUMBAR) (**Table 1**).

Management

The decision to treat and selecting a treatment for IH requires consideration of several factors, including size, location, risk of complications, as well as caregivers' preference. The American Academy of Pediatrics (AAP) has established a clinical practice guideline for managing IH, which outlines recommendations for topical, systemic, and physical therapy modalities.[7]

The majority of IHs do not need treatment given their tendency for spontaneous involution.

Considering this, and their common occurrence, most infants born with an IH will not be referred to Dermatology. However, for those with IHs requiring treatment, due to the rapid growth in the proliferative phase, early intervention is important to limit potential complications. In my practice I aim to see infants before they are 1 month old. For IHs with a low risk of complications, active non-intervention may be appropriate. If observation is chosen, lesions can be monitored through serial measurements and/or photographs.

Treatment is indicated for IHs located in cosmetically sensitive areas or for those at risk for functional impairment or ulceration. The presence of clinical features suggestive of PHACES or LUMBAR syndrome, or concern for extracutaneous IH involvement, should prompt a referral for further evaluation and management recommendations.

Topical Therapy

Topical beta blockers are the preferred treatment for thin, superficial IHs where treatment is not medically necessary but is desired. The most commonly used agent is timolol maleate 0.5% gel-forming drops, administered as one drop twice daily.[7] Topical timolol is well tolerated and is an effective treatment for select IHs. The best response is observed in thin (<1 mm) superficial IH.[8] Adverse events are mild and uncommon, occurring in <3% of patients, with the most common being mild irritation and xerosis.[8] Timolol has been documented to have systemic absorption, therefore, it is recommended to limit usage to a maximum of two drops per day.[8] Caution is advised when using topical timolol on large or ulcerated IHs, as well as on mucosal surfaces or occluded areas (e.g., the diaper region), due to the potential for increased systemic absorption.

Oral Beta Blockers

Oral propranolol is the first-line therapy for IHs requiring systemic therapy and has been established as a safe and effective treatment. Its use is reviewed in two consensus guidelines: one by the British Association of Dermatologists (2018) and another by the Australasian College of Dermatologists (2017).[9,10] **Table 2** summarizes the treatment parameters for oral propranolol. If contraindications are present, referral to a pediatrician and/or pediatric dermatologist should be considered.

Systemic therapy is indicated for IHs that pose risks such as visual impairment, airway compromise, nasal obstruction, auditory canal involvement, ulceration, or those with a potential for permanent disfigurement.[9] In Canada, propranolol oral solution (3.75 mg/mL) is commercially available as *Pr* Hemangiol (Pierre Fabre Dermo-Cosmétique Canada Inc.) and has Health Canada approval for treating life- or function-threatening hemangiomas, ulcerated hemangiomas with pain and/or lack of response to simple wound care measures, and hemangiomas with a risk of permanent scarring or disfigurement.[11]

Prior to starting propranolol, a thorough history and physical exam, including infant heart rate, should be performed to assess for potential contraindications.[9,10] Outpatient initiation of propranolol is considered appropriate for term infants with a normal birth weight who are older than 4 weeks and have no significant comorbidities.[9,10] For younger or low weight (<2.5 kg) patients or those with comorbidities, consider a referral to Pediatrics or Pediatric Dermatology for treatment initiation. In such cases, a lower initial dose, three times daily dosing, and slower dose escalation may be warranted.[12]

During the COVID-19 pandemic, in-person evaluations were not always feasible, prompting the Hemangioma Investigator Group to develop consensus guidelines for managing IHs by telemedicine.[13] Propranolol initiation via telemedicine can be considered for infants older than 5 weeks with a normal birthweight, without ulceration or features concerning for PHACES or LUMBAR syndrome. Patients should have a recently documented weight (within 2 weeks) and a normal cardiovascular and respiratory exam within the previous 4 weeks.[13]

Propranolol therapy is typically initiated at 1 mg/kg/day, with an increase to 2 mg/kg/day

Indications	• Life or function-threatening • Ulcerated or high risk of ulceration • High risk of deformity or psychosocial impact
Contraindications	Consider specialist consultation for patients with contraindications **Relative** • Infants prone to hypoglycemia • Infants with cardiovascular disease (persistent bradycardia, aorta coarctation) • Bronchospasm • Intracranial arterial anomalies • Other systemic disease **Absolute** • Second or third degree heart block • Hypersensitivity to propranolol
Side effects	**More common** • Sleep disturbance • Cold extremities • Diarrhea **Less common** • Hypoglycemia • Bradycardia • Hypotension • Bronchospasm
Dose	Start at 1 mg/kg/day, given as twice daily dosing; increase the dose after 1 to 2 weeks to 2 mg/kg/day (unless the lower dose is clinically effective)
Monitoring	Clinical monitoring monthly until signs of involution, then every 3 months until discontinuation of therapy
Duration of therapy	At least 12 months of age for most patients
Instructions for parents	• Give propranolol twice a day, at least 8 hours apart • Give propranolol with feeds • Temporarily hold the dose if the child is feeling unwell (e.g., vomiting, decreased feeds, wheezing) until feeding normally • If a dose is missed do not give an extra dose, simply resume at the next scheduled time • Routine immunizations can be given during therapy

Table 2. Summary of oral propranolol for the treatment of infantile hemangiomas[9-11]; *courtesy of Lisa Flegel, MD, FRCPC, DABD.*

after 1 to 2 weeks.[9,10] The lowest clinically effective dose should be used. If there is no response, the dose may be increased up to 3 mg/kg/day if needed.[7,11] Clinical signs of response include softening, lightening in colour, a reduction or cessation in growth rate, and over time, a decrease in size.

Caregivers should be counselled on potential adverse effects and advised on when the medication should be held or medical consultation sought. Common side effects include sleep disturbances, peripheral vasoconstriction (manifesting as cold hands and feet), and diarrhea. More serious adverse events, though less frequent, include hypoglycemia, bradycardia, hypotension, and bronchospasm. If an infant is feeling unwell, has reduced oral intake or is wheezing, propranolol should be temporarily withheld until they are feeding normally.

Patients can be monitored monthly until clinical signs of involution are observed, with dose adjustments made based on weight, and then less frequently until treatment cessation. The duration of therapy varies among individuals and rebound growth may occur following discontinuation. A large multicentre retrospective cohort study found the lowest risk of rebound when treatment was discontinued between 12 to 15 months of age.[14] Consequently, many experts recommend continuing therapy until at least 12 months of age.[7,9] Propranolol can be discontinued at the end of treatment without any weaning.

Nadolol is an oral beta blocker that has also been used to treat IHs. While a full review of nadalol is beyond the scope of this article, a Canadian prospective study demonstrated that oral nadolol is non-inferior to propranolol and has a comparable safety profile.[15]

Other Therapies

With the use of oral and topical beta blockers for IHs, the need for alternative treatments has decreased.

Systemic corticosteroids were the standard treatment for IHs prior to the introduction of propranolol and remain an option in select cases, such as when beta blockers are contraindicated or ineffective.[7] Intralesional corticosteroids have been used to treat small, bulky IHs.[7]

Surgical intervention is generally reserved for older children requiring reconstruction for functional or cosmetic purposes, but it may be considered in select infant cases.[7] Laser therapy, including pulsed dye laser and long-pulse Nd:YAG laser, can be used for small, superficial IHs, although access to these treatments is limited in some communities.[12]

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