

Infantile haemangiomas

Identifying high-risk lesions in primary care



CPD 

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Background

Infantile haemangiomas (IHs) are benign vascular tumours that affect up to 10% of infants and arise in the first few weeks-to-months of life. Some are associated with an increased risk of complications and poor cosmetic outcomes. General practitioners (GPs) are ideally placed to identify high-risk IHs and coordinate their management.

Objective

The aim of this article is to outline strategies to identify high-risk IHs and when to involve a multidisciplinary team.

Discussion

IHs that involve the lower face or neck can be associated with airway obstruction. Having five or more IHs is associated with hepatic haemangiomas, high-output cardiac failure and hypothyroidism. IHs that involve the eyes or mouth can cause functional impairments such as amblyopia and feeding difficulties, respectively. Large segmental IHs may be associated with syndromic presentations including PHACE syndrome when on the lower face, PELVIS syndrome when on the perineum and LUMBAR syndrome when on the lower back.

INFANTILE HAEMANGIOMAS (IHs) are the most common benign vascular tumour of childhood, and they affect up to 10% of infants.¹ They arise in the first few weeks-to-months of life² and are clinically diagnosed. Risk factors include female sex, breech delivery, amniocentesis, Caucasian ethnicity, premature birth, low birthweight and advanced maternal age. IHs can be classified according to their subtype: superficial IHs are bright red plaques or papules, deep IHs are raised nodular lesions and mixed IHs are a combination of the two. IHs can also be classified according to their clinical distribution. Localised IHs are well-defined focal lesions, segmental IHs occur on one side of the midline and are usually more than 5 cm in diameter, multifocal IHs are multiple focal lesions, and indeterminate IHs are neither segmental or focal. Differentials for IHs include congenital haemangiomas, which are present at birth; pyogenic granulomas; tufted angiomas; and vascular malformations that do not show any signs of regression and grow in proportion with the child.

Most IHs are usually small superficial lesions that spontaneously resolve and parents require only reassurance and education. Some of these lesions are high risk, and up to 10% can cause complications including ulceration, airway

obstruction, functional impairment or disfigurement.³ In this situation, treatment is initiated with oral or topical β -blockers, most commonly oral propranolol, and monitored closely. As a result of the various systems that high-risk IHs can affect, infants with high-risk IHs require multidisciplinary care. The general practitioner (GP) is in an ideal position to identify high-risk IHs during the six-week baby check, initiate investigations and be part of the multidisciplinary team to manage these lesions.

The aim of this article is to outline a strategy to identify high-risk IHs in the primary care setting, initial investigations to consider and when to refer using recently published guidelines from European,³ Australasian⁴ and American expert groups.⁵

IHs appear within the first few weeks of life and have three distinct phases. The proliferative phase involves rapid growth and occurs, on average, in the first nine months from onset.⁶ Superficial IHs reach their maximum growth within this time frame, but deep IHs can continue to grow for 18 months or more. The proliferative phase is followed by plateau, where the lesion is stable for months, and then the involution phase, where the lesion slowly decreases in size, leaving behind excess fibrofatty tissue. Traditional teaching

suggests that resolution increases by 10% every year after the age of five years (ie 50% chance of resolution at five years, 70% at seven years); however, recent evidence suggests IHs may not significantly improve after 3–4 years of age,⁶ and therefore waiting for resolution after this age is not recommended.

IHs are considered high risk if they can cause life-threatening complications or functional impairment, have a risk of ulceration/disfigurement or are associated with clinically significant structural anomalies (Figure 1). Patients with high-risk lesions should be referred to a specialist clinician with experience in treating IHs depending on the specific risk involved (Table 1). For example, a lesion with the potential for airway compromise

should be managed in a multidisciplinary setting with input from dermatologists; ear, nose and throat (ENT) surgeons; and paediatricians. According to guidelines, referral should occur as early as possible;⁶ an ideal time would be during the six-week baby check when this issue might be identified. The mean presentation to a dermatologist in one study was at five months of age, at which point the lesion may have significantly grown; earlier referral could prevent many of the aforementioned complications by allowing earlier treatment.² GPs are in an ideal position to communicate with the relevant specialist staff and ensure patients can be seen urgently to treat high-risk lesions before they reach their maximum growth potential.

Life-threatening complications

Segmental IHs of the lower face or anterior neck increase the risk of obstructive airway complications (Figure 2), especially when larger than 5 cm. Infants may present with early respiratory symptoms such as stridor and barking cough that could be easily mistaken for inflammatory croup. The mean time for diagnosis of obstructive complications is at four months of age.⁵ Infants with these IHs should be referred to a dermatologist and ENT surgeon as soon as possible. It is important to note that up to half of infants with airway compromise may not even have visible cutaneous IHs.⁷ Therefore, healthcare providers and parents must be vigilant and ensure immediate emergency medical attention is sought if an infant develops increasing signs of respiratory distress.

Having five or more cutaneous IHs increases the risk of having hepatic haemangiomas, high-output cardiac failure and hypothyroidism. Hepatic haemangiomas are usually focal, asymptomatic and require no treatment; however, some may cause high-output cardiac failure because of macrovascular shunting. Signs of cardiac failure include tachypnoea, increased work of breathing, difficulties feeding and failure to thrive. Higher-risk 'diffuse' hepatic haemangiomas can result in hepatomegaly severe enough to cause abdominal compartment syndrome and haemodynamic instability before the age of four months.⁸ Hypothyroidism can

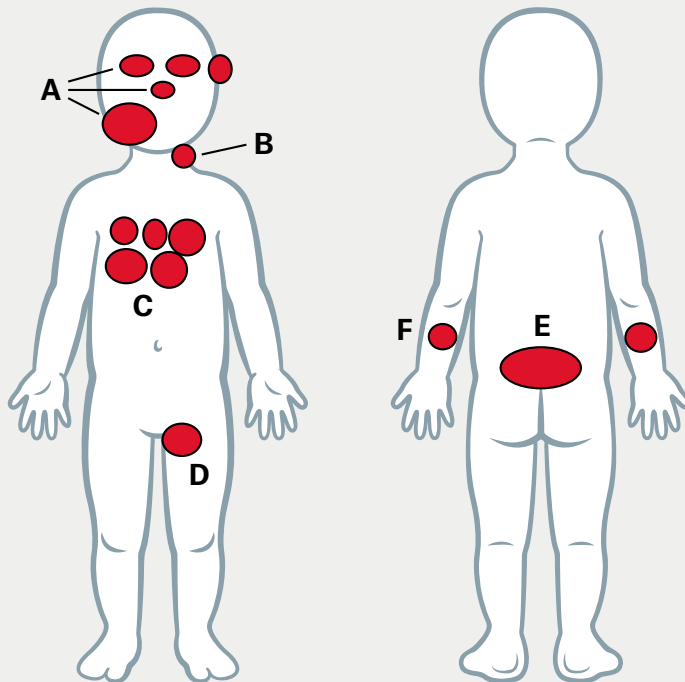


Figure 1. High-risk infantile haemangiomas (IHs)

A. IHs involving the lower face increase risk of airway obstruction and may indicate underlying PHACE syndrome; IHs involving the nose, lips and ears are at increased risk of ulceration and disfigurement; IHs involving the eyes increase risk of vision impairment and disfigurement; **B.** Neck haemangiomas have an increased risk of ulceration and may indicate underlying PHACE syndrome; **C.** Five or more haemangiomas indicate an increased risk of liver haemangiomas, cardiac failure and hypothyroidism; **D.** IHs involving intertriginous areas are at higher risk of ulceration; **E.** Lumbosacral IHs may indicate underlying spinal dysraphism; **F.** Segmental IHs on extremities are at high risk of ulceration.



Figure 2. Large segmental facial haemangioma in a patient with PHACE syndrome

Image courtesy of Dr Deshan Sebaratnam

occur as a result of inactivation of thyroid hormones by type-3-iodothyronine deiodinase in IH tissue.⁹ Affected infants may have intermittent bradycardia, hypothermia, reduced muscle tone, failure to thrive, jaundice and constipation. As a result of these risks, screening liver ultrasonography and thyroid hormone testing is recommended for infants

with five or more IHs.¹⁰ These infants should be referred to a dermatologist and paediatrician.

Functional impairment

IHs around the eyes can cause uniocular visual disturbance because of mechanical ptosis, strabismus, anisometropia and

astigmatism.¹¹ This can lead to amblyopia, and prompt referral of an infant with ocular involvement to a dermatologist and ophthalmologist can prevent these issues. IHs on the lips or around the mouth (Figure 3) can lead to feeding issues and failure to thrive and should be referred to a paediatrician and dermatologist for management.⁵

Table 1. Investigation and management of high-risk haemangiomas

High-risk categories (% prevalence where known)	Clinical findings	Investigations to consider initiating*	Disciplines involved	Management options†
Life-threatening complications	Lower face IHs (risk of airway obstruction)	Lateral neck X-ray	ENT surgeon Dermatologist	ENT examination Propranolol
	Five or more cutaneous IHs (risk of liver haemangioma, heart failure, hypothyroidism)	US liver Thyroid function tests	Dermatologist Paediatrician Cardiologist	Propranolol
Functional impairment	Eye involvement		Dermatologist Ophthalmologist Paediatrician	Propranolol
	Lip and mouth involvement		Dermatologist Paediatrician	Propranolol
Ulceration (16%)	High-risk areas – neck, intertriginous areas, lip, extremities High-risk types – segmental		Dermatologist Paediatrician	Propranolol Pain management and dressings Surgery Laser therapy
Disfigurement	High-risk areas – face, scalp, nasal tip, lip, ears, breast High-risk types – segmental		Dermatologist Paediatrician	Surgery Propranolol
PHACE syndrome	Large segmental facial IH	MRI Magnetic resonance angiography Electrocardiography Transthoracic echocardiography	Paediatrician Dermatologist Cardiologist Neurologist	
LUMBAR syndrome	Large segmental lumbosacral IH Sacral dimple, tuft of hair, skin tag	US spine US abdomen US pelvis and MRI spine	Paediatrician Dermatologist Neurologist	
PELVIS syndrome	Large segmental perineal IH with associated genetic deformation	US spine US abdomen US pelvis and MRI spine	Urologist Dermatologist Neurosurgeon Paediatric neurologist	

*Investigation for functional impairment, ulceration and disfigurement would be guided by the relevant specialties and is beyond the scope of this article.

†Management for PHACE, LUMBAR and PELVIS syndromes would be guided by the relevant specialties and is beyond the scope of this article.

ENT, ear, nose and throat; IH, infantile haemangioma; MRI, magnetic resonance imaging; US, ultrasonography

Ulceration, disfigurement and scarring

Ulceration can occur in up to 15.8% of infants,¹² and risk factors include the type of IH, its location and size. High-risk subtypes include segmental IHs, and high-risk locations include the neck, face, lips, extremities (Figure 4) and intertriginous areas (axillae, inguinal region, perineum, perianal) because of friction and maceration. Higher-risk sizes are those greater than 2 cm (in infants



Figure 3. Infantile haemangioma affecting the lower lip

Image courtesy of Professor Gayle Fischer



Figure 4. Large segmental haemangioma affecting the whole right extremity – high risk of ulceration

Image courtesy of Dr Deshan Sebaratnam

aged three months or older) or greater than 1 cm in size (in infants aged less than three months).⁶ Bleeding from ulceration is usually minor and manageable with pressure; however, there are rare cases of life-threatening blood loss reported.¹³ Disfigurement and scarring occur because of the potential size of the IHs, and high-risk areas include the nose, central face (if the IH is 2 cm or larger) and ears. Breast involvement in female infants can cause permanent changes in breast development. Although disfigurement and scarring may not be functionally impairing, they can cause significant psychological and social issues and should be managed appropriately.¹⁴

Structural syndromes

Patients with segmental IHs that involve the face, scalp or neck have an increased chance of having PHACE syndrome; one study has shown 30% of patients with segmental IHs involving the lower face have this syndrome.¹⁵ PHACE is an acronym for a syndrome that is characterised by **P**osterior fossa brain malformations, large segmental **H**aemangiomas affecting the face, **A**rterial anomalies including coarctation of the aorta, cardiac anomalies, **C**erebrovascular abnormalities and **E**ye abnormalities.¹⁶ Patients with segmental IHs that involve the face should be investigated with magnetic resonance imaging (MRI) or magnetic resonance angiography of the head and neck, electrocardiography and transthoracic echocardiography to assess cardiac involvement.⁵

Segmental IHs involving the lumbosacral region are associated with LUMBAR syndrome, which includes **L**ower body haemangioma, **U**rogenital anomalies, **M**yelopathy, **B**ony deformities, **A**norectal malformations and **R**enal anomalies.¹⁷ Segmental IHs involving the perineum are associated with PELVIS syndrome, which includes **P**erineal haemangioma, **E**xternal genital malformations, **L**ipomyelomeningocele, **V**esicorectal abnormalities, **I**mpervious anus and **S**kin tags.¹⁸ These syndromes should be investigated with ultrasonography of the abdomen, pelvis and spine, and MRI.¹⁹

Management

Most simple IHs require only education, support and ongoing monitoring. Worried parents should be encouraged to schedule frequent visits with the GP, take photographs and contact the GP if concerned regarding a lesion's appearance, unexpected rapid growth, ulceration, bleeding or pain. The role of dermatologists and paediatricians is to assess referred high-risk IHs (Figure 5), commence appropriate treatment, follow up progress and correspond with the GP who will be caring for the infant in the community.

Oral propranolol is considered a first-line agent when IHs are high risk or develop complications.²⁰ Its precise mechanism of action is unknown, and adverse effects include hypoglycaemia, sleep disturbances, bronchial irritation, bradycardia and hypotension.⁵ Oral propranolol requires vigilant monitoring to ensure significant adverse effects are not missed; a potential alternative is atenolol, which might be as effective and better tolerated but has less evidence for its application.^{21,22} A meta-analysis has shown that propranolol has a clearance rate of 95% (complete or nearly complete resolution).²³ Where β -blockers are poorly tolerated, contraindicated or not effective, oral corticosteroids can be used and have a clearance rate of 43%.²³ Adverse effects of oral steroids include cushingoid appearance, infections, growth retardation and hypertension.⁵ Topical timolol is a treatment option for superficial IHs and has a clearance rate of 64%.²³ There is less evidence for this treatment option, and its adverse effect profile is promising but has not yet been clearly established. Wound care should also be used in ulcerated haemangiomas with wound cleaning, dressings and adequate analgesia.²⁴ Surgical intervention can be considered for solitary IHs when they are refractory to pharmacotherapy and develop complications including ulceration or obstruction or have the potential for disfigurement. Pulsed dye lasers have been shown to be superior to other lasers and are used to treat some IHs.²⁵ They have been advocated for treatment of ulcerated lesions and early proliferative lesions; however, the evidence comes

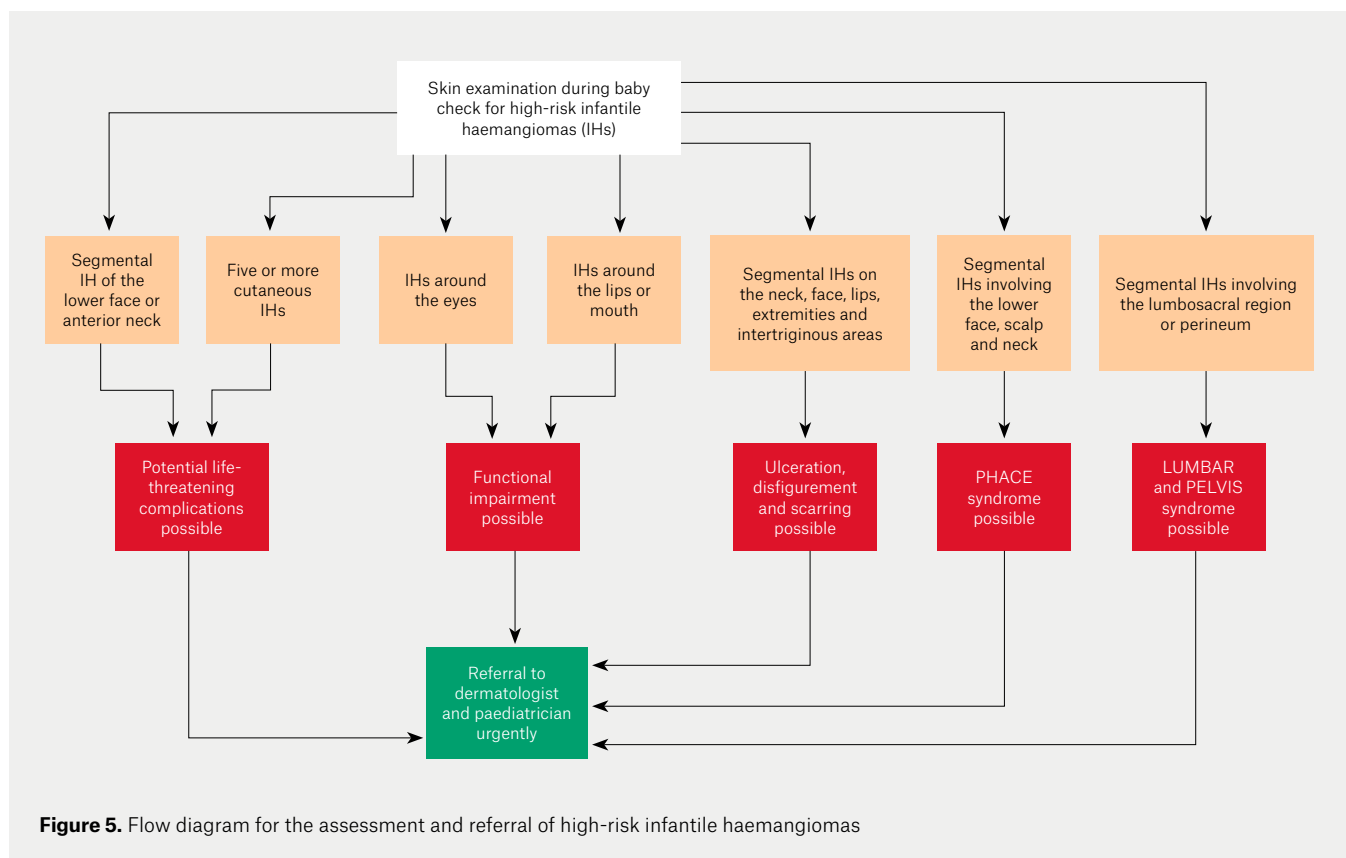


Figure 5. Flow diagram for the assessment and referral of high-risk infantile haemangiomas

mainly from case reports, and some controversy exists regarding increased risk of scarring and hypopigmentation.⁶

Conclusion

Although most IHs seen in clinical practice will be benign and self-limiting, it is important that clinicians are vigilant in identifying high-risk IHs and potential complications. IHs have significant interpatient variability; even within the same patient, multiple IHs may have significantly different characteristics and growth patterns. GPs are ideally placed to identify high-risk IHs, monitor therapy and monitor low-risk IHs. A skin check for IHs can be easily incorporated into the six-week baby check while assessing all the other facets of this examination such as the abdominal, genital and neurological examinations. Worried parents should be encouraged to actively monitor lesions, take photographs and liaise with their GPs with concerns regarding lesion growth,

ulceration, bleeding or pain. Patients with high-risk IHs should be referred to dermatologists as early as possible, as this will ensure management can be commenced prior to the maximum growth of the lesion and prevent potential complications. Where this is not possible, such as in geographically isolated regions, telemedicine could be used to ensure appropriate guidance is sought.

Key points

- IHs are usually small, superficial, self-limiting lesions that may require no further investigation or intervention.
- High-risk IHs are those that have possible life-threatening complications; risk of ulceration, disfigurement or functional issues; and may be associated with underlying structural syndromes.
- GPs are ideally placed to identify high-risk IHs during routine baby checks.
- Early referral is key to optimising management of high-risk lesions.

- Infants with respiratory symptoms and IHs on the lower face should be immediately referred to the emergency department for acute airway management.
- High-risk types of haemangiomas are segmental, and high-risk locations include the face (nose, lips, ears, lower face), scalp, neck, intertriginous areas, extremities and lumbosacral area.

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