Oral Hemangiomas

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Background

Hemangiomas are tumors identified by rapid endothelial cell proliferation in early infancy, followed by involution over time; all other abnormalities are malformations resulting from anomalous development of vascular plexuses. The malformations have a normal endothelial cell growth cycle that affects the veins, the capillaries, or the lymphatics, and they do not involute.

Hemangiomas are lesions that are not present at birth. They manifest within the first month of life, exhibit a rapid proliferative phase, and slowly involute to near complete resolution. Hemangiomas exhibit both a proliferating phase and an involuting phase, whereas vascular malformations are more stable and fail to regress.[1]

Hemangiomas of the oral cavity are not common pathologic entities, but, among hemangiomas, the head and the neck are common sites. Most true hemangiomas involute with time, but a certain small percentage do not, which may present with complications that require treatment (see Complications). An estimated 10-20% of true hemangiomas incompletely involute and require postadolescent ablative treatment.[2]

Hemangiomas are associated with the following syndromes:

- Rendu-Osler-Weber syndrome (autosomal dominant inheritance, multiple telangiectasias, occasional GI tract involvement, occasional CNS involvement)
- Sturge-Weber-Dimitri syndrome (noninherited and nonfamilial, port-wine stain, leptomeningeal angiomas)
- Kasabach-Merritt syndrome (thrombocytopenic purpura associated with hemangioma, consumptive coagulopathy, microangiopathic hemolysis, intralesional fibrinolysis)
- Maffucci syndrome (hemangiomas of the mucous membranes, dyschondroplasia)
- von Hippel-Lindau syndrome (genetic transmission variable, hemangiomas of the cerebellum or the retina, cysts of the viscera)
- Klippel-Trenaunay-Weber syndrome (port-wine stain, angiomatosis of the extremities)
- PHACE(S) (posterior fossa brain malformations, hemangiomas of the face [large or complex], arterial anomalies, cardiac anomalies, and eye abnormalities): The association is referred to as PHACE(S) when ventral developmental defects, such as sternal clefting or supraumbilical raphe, are present.

The term hemangioma has been commonly used to describe a large number of vasoformative tumors. Unfortunately, the nomenclature and the classification of these entities have been complex and not entirely consistent over time. The complexity and the inconsistency have led to a large number of terms and classification schemes being used, resulting in confusion in understanding the pathophysiology of these lesions and in comparing data from different periods. The nomenclature lends little insight into the natural history and the management of these lesions.

What was referred to as a hemangioma 30 years ago is not necessarily what a hemangioma would be referred to as today. The term hemangioma described many lesions that bore little relationship to each other apart from their being involved with vessels. With this concept in mind, this article discusses oral vasoformative tumors under the broad and not entirely correct term oral hemangiomas.

In 1982, Mulliken and Glowacki[1] described the classification scheme that is most accepted today. This scheme is straightforward and essentially divides the vasoformative tumors into 2 broad groups: hemangiomas and vascular malformations (see Table 1 below). The vascular malformations can be further subdivided into arterial, venous, capillary, and lymphatic malformations.

Table 1. Classification of Vasoformative Tumors (Open Table in a new window)

Vasoformative Tumor	New Nomenclature	Old Nomenclature
Hemangiomas		
	Capillary hemangioma	Strawberry hemangioma
		Juvenile hemangioma

	Cavernous hemangioma	
	Mixed hemangioma	Parotid hemangioma
Vascular malformations		
	Venous malformation	Cavernous hemangioma
		Hemangiomatosis
	Intramuscular venous malformation	Intramuscular hemangioma
	Capillary malformation	Capillary hemangioma
		Port-wine stain
	Arteriovenous malformation	Arteriovenous hemangioma Arterial angioma Arteriovenous aneurysm Cirsoid angioma Red angioma Serpentine aneurysm
	Lymphatic malformation	Capillary lymphangioma Cavernous lymphangioma Lymphangioma Cystic hygroma

Pathophysiology

Vascular malformations need to be understood in terms of their embryology and development. The classic sequence of events usually falls into 3 stages: (1) the undifferentiated capillary network stage, (2) the retiform developmental stage, and (3) the final developmental stage. In the undifferentiated capillary network stage, the primitive mesenchyme is nourished by an interlacing system of blood spaces without distinguishable arterial and venous channels. Separate venous and arterial stems appear on either side of the capillary network in the retiform developmental stage. The retiform developmental stage begins at about 48 days of embryonic development. The final developmental stage begins at 2 months' development and involves the gradual replacement of the immature plexiform network by the mature vascular channels.

The more common capillary hemangioma represents an arrest in the development of the mesenchyme primordia in the undifferentiated capillary network stage. As differentiation progresses, primitive vessels penetrate deeper into the subcutaneous layer, the muscle, or the bone tissue and give rise to capillary hemangiomas. Termination of development in the retiform developmental stage may produce venous, arterial, or capillary malformations because this stage is characterized by an established venous, arterial, and capillary system. In the final developmental stage, the maturation of the venous and lymphatic systems predominates. Aberrations in this mature stage of development result in venous malformations and lymphangiomas.

Proliferating hemangiomas have been shown to have estradiol-17 beta-receptors

in the cytoplasm,[3] and corticosteroid treatment has been theorized to block these receptors. Lack of estradiol receptors in stable or involuting lesions has supported this theory, and steroid treatment has become a first line of treatment for proliferating lesions.

A number of growth factors, including vascular endothelial growth factor (VEGF), basic fibroblast growth factor (bFGF), transforming growth factor-beta (TGF-beta), and interleukin 6 (IL-6), have been demonstrated as regulators of angiogenesis.[4] Takahashi et al[5] outlined a number of cellular markers that distinguish the phases of hemangiomas; these markers include tissue metalloproteinase (TIMP-1), bFGF, proliferating cell nuclear antigen, type IV collagenase, VEGF, and urokinase.

Another theory suggests that the endothelial cells of hemangiomas are derived from a distant population of endothelial precursors carried by existing vascular pathways to a receptive environment. Potential sources include the bone marrow and the placenta. A small embolic nidus of placental endothelial cells could reach fetal tissues through the permissive right-to-left fetal shunt of fetal circulation.

This occurrence could, in part, explain the 3-fold increased risk of hemangiomas observed in infants subjected in utero to chorionic villus sampling, because local placental injury might predispose the shedding of cells into the fetal circulation. At least 5 markers of hemangiomas are uniquely co-expressed in the placenta: GLUT1, merosin, Lewis Y antigen, Fc-R11b, and type III iodothyronine deiodinase. Recently, a comparison of the transcriptomes of the human placenta and infantile hemangiomas supported a placental origin of the tumors.[6]

Epidemiology

US frequency

Hemangiomas are the most common tumors of infancy, occurring in as many as 2.6% of neonates and 12% of children aged 1 year.[7, 8] Up to 30% of preterm infants with low birth weight (1000 g) may have hemangiomas.[9] Fifty percent of venous malformations occur in the head and the neck.[10]

In the oral cavity, the bones and the muscles are affected as well as the mucosa and the skin. The incidence of intraosseous hemangiomas varies from 0.5-1.0% of all intraosseous neoplasms.[11] The bones most frequently affected are the vertebral column and the calvaria. The most commonly affected facial bones are the mandible, the maxilla, and the nasal bones. Intraosseous lesions affect the mandible more often than the maxilla, with a ratio of 2:1 reported in one study.[12] Involvement of the zygoma is rare.[13]

Intramuscular hemangiomas in the oral region are most commonly seen in the masseter, compromising 5% of all intramuscular hemangiomas.[14]

Race

Hemangioma, the most common tumor of infancy, affects as many as 12% of whites, but it rarely occurs in darker-skinned individuals. Vascular malformations also more commonly occur in whites.

Sex

Hemangiomas are approximately 3-5 times more common in females than in males.[15] The male-to-female ratio for venous malformations is reported in one study[10] to be 1:1. Arteriovenous hemangiomas of the oral cavity have a predilection for females.[16] Intraosseous hemangiomas are about 3 times more common in females than in males.[12, 17]

The patient's sex does not influence the speed or the completeness of involution of hemangiomas.[18]

Age

By their definition, hemangiomas occur in infants and children. The incidence of hemangiomas increases to 23% in premature infants with a birthweight of less than 1000 g.

Vascular malformations have a much broader range of incidence. Barrett and Speight[16] observed 35 oral vascular malformations over a 48-year period at their institution. The mean age was 52.6 years, with a range of 12-90 years.

Intraosseous vascular malformations most commonly occur in the fourth decade of life but range from infancy to the eighth decade of life.

The peak incidence of central vascular malformations of the jaws is in the second decade of life.[17]

Intramuscular vascular malformation of the head and the neck most commonly present in the third decade of life.[14]

Clinical Presentation

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References

1. Mulliken JB, Glowacki J. Hemangiomas and vascular malformations in infants and children: a classification based on endothelial characteristics. *Plast Reconstr Surg*. 1982 Mar. 69(3):412-22. [Medline].
2. Waner M, Suen JY, Dinehart S. Treatment of hemangiomas of the head and neck. *Laryngoscope*. 1992 Oct. 102(10):1123-32. [Medline].
3. Sasaki GH, Pang CY, Wittliff JL. Pathogenesis and treatment of infant skin strawberry hemangiomas: clinical and in vitro studies of hormonal effects. *Plast Reconstr Surg*. 1984 Mar. 73(3):359-70. [Medline].
4. Folkman J, Klagsbrun M. Angiogenic factors. *Science*. 1987 Jan 23. 235(4787):442-7. [Medline].
5. Takahashi K, Mulliken JB, Kozakewich HP, Rogers RA, Folkman J, Ezekowitz RA. Cellular markers that distinguish the phases of hemangioma during infancy and childhood. *J Clin Invest*. 1994 Jun. 93(6):2357-64. [Medline]. [Full Text].
6. Christison-Lagay ER, Fishman SJ. Vascular anomalies. *Surg Clin North Am*. 2006 Apr. 86(2):393-425, x. [Medline].
7. Stal S, Hamilton S, Spira M. Hemangiomas, lymphangiomas, and vascular malformations of the head and neck. *Otolaryngol Clin North Am*. 1986 Nov. 19(4):769-96. [Medline].

8. Jacobs AH, Walton RG. The incidence of birthmarks in the neonate. *Pediatrics*. 1976 Aug. 58(2):218-22. [Medline].
9. Amir J, Metzker A, Krikler R, Reisner SH. Strawberry hemangioma in preterm infants. *Pediatr Dermatol*. 1986 Sep. 3(4):331-2. [Medline].
10. de Lorimier AA. Sclerotherapy for venous malformations. *J Pediatr Surg*. 1995 Feb. 30(2):188-93; discussion 194. [Medline].
11. Dahlin DC, Unni KK. Bone Tumors: General Aspects and Data on 8,542 Cases. Springfield, Ill: Thomas. 1986.
12. Hayward JR. Central cavernous hemangioma of the mandible: report of four cases. *J Oral Surg*. 1981 Jul. 39(7):526-32. [Medline].
13. Cuesta Gil M, Navarro-Vila C. Intraosseous hemangioma of the zygomatic bone. A case report. *Int J Oral Maxillofac Surg*. 1992 Oct. 21(5):287-91. [Medline].
14. Wolf GT, Daniel F, Krause CJ, Kaufman RS. Intramuscular hemangioma of the head and neck. *Laryngoscope*. 1985 Feb. 95(2):210-3. [Medline].
15. Marchuk DA. Pathogenesis of hemangioma. *J Clin Invest*. 2001 Mar. 107(6):665-6. [Medline].
16. Barrett AW, Speight PM. Superficial arteriovenous hemangioma of the oral cavity. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*. 2000 Dec. 90(6):731-8. [Medline].
17. Yih WY, Ma GS, Merrill RG, Sperry DW. Central hemangioma of the jaws. *J Oral Maxillofac Surg*. 1989 Nov. 47(11):1154-60. [Medline].
18. Bowers RE, Graham EA, Tomlinson KM. The natural history of the strawberry nevus. *Arch Dermatol*. 1960. 82:667-680.
19. Lister WA. The natural history of strawberry nevi. *Lancet*. 1938. 1:1429-1434.
20. Bivings L. Spontaneous regression of angiomas in children; twenty-two years' observation covering 236 cases. *J Pediatr*. 1954 Dec. 45(6):643-7. [Medline].
21. Blackfield HM, Morris WJ, Torrey FA. Visible hemangiomas: a preliminary statistical report of a 10-year study. *Plast Reconstr Surg*. 1960. 26:326-329.
22. Grabb WC, Dingman RO, Oneal RM, Dempsey PD. Facial hamartomas in children: neurofibroma, lymphangioma, and hemangioma. *Plast Reconstr Surg*. 1980 Oct. 66(4):509-27. [Medline].
23. Yonetsu K, Nakayama E, Kawazu T, Kanda S, Ozeki S, Shinohara M. Value of contrast-enhanced magnetic resonance imaging in differentiation of hemangiomas from lymphangiomas in the oral and maxillofacial region. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*. 1999 Oct. 88(4):496-500. [Medline].
24. Johann AC, Salla JT, Gomez RS, de Aguiar MC, Gontijo B, Mesquita RA. GLUT-1 in oral benign vascular lesions. *Oral Dis*. 2007 Jan. 13(1):51-5. [Medline].
25. Kane WJ, Morris S, Jackson IT, et al. Significant hemangiomas and vascular malformations of the head and neck: clinical management and treatment outcomes. *Ann Plast Surg*. 1995 Aug. 35(2):133-43. [Medline].
26. Mulliken JB, Boon LM, Takahashi K, et al. Pharmacologic therapy for endangering hemangiomas. *Curr Opin Dermatol*. 1995. 109-113.
27. Leaute-Labreze C, Dumas de la Roque E, Hubiche T, Boralevi F, Thambo JB, Taieb A. Propranolol for severe hemangiomas of infancy. *N Engl J Med*. 06/08. 358(24):2649-51.
28. Siegfried EC, Keenan WJ, Al-Jureidini S. More on propranolol for hemangiomas of infancy. *N Engl J Med*. 12/08. 359(26):2846-7.
29. Antaya RJ. Infantile Hemangioma. *Medscape Reference*. June 2010. [Full Text].
30. Herrero Hernández A, Escobosa Sánchez O, Acha García T. Successful treatment with vincristine in PHACES syndrome. *Clin Transl Oncol*. April 2007. 9(4):262-3. [Medline].
31. Fost NC, Esterly NB. Successful treatment of juvenile hemangiomas with prednisone. *J Pediatr*. 1968 Mar. 72(3):351-7. [Medline].
32. Edgerton MT. The treatment of hemangiomas: with special reference to the role of steroid therapy. *Ann Surg*. 1976 May. 183(5):517-32. [Medline].
33. Pope E, Krafchik BR, Macarthur C, Stempak D, Stephens D, Weinstein M, et al. Oral versus high-dose pulse corticosteroids for problematic infantile hemangiomas: a randomized, controlled trial. *Pediatrics (Epub)*. May 2007. 119(6):e1239-47. [Medline].
34. Bartoshesky LE, Bull M, Feingold M. Corticosteroid treatment of cutaneous hemangiomas: how effective? A report on 24 children. *Clin Pediatr (Phila)*. 1978 Aug. 17(8):625, 629-38. [Medline].
35. Hawkins DB, Crockett DM, Kahlstrom EJ, MacLaughlin EF. Corticosteroid management of airway hemangiomas: long-term follow-up. *Laryngoscope*. 1984 May. 94(5 Pt 1):633-7. [Medline].
36. Hasan Q, Tan ST, Gush J, Peters SG, Davis PF. Steroid therapy of a proliferating hemangioma: histochemical and molecular changes. *Pediatrics*. 2000 Jan. 105(1 Pt 1):117-20. [Medline].
37. Blei F, Isakoff M, Deb G. The response of parotid hemangiomas to the use of systemic interferon alfa-2a or corticosteroids. *Arch Otolaryngol Head Neck Surg*. 1997 Aug. 123(8):841-4. [Medline].

38. Greinwald JH, Burke DK, Bonthius DJ, Bauman NM, Smith RJ. An update on the treatment of hemangiomas in children with interferon alfa-2a. *Arch Otolaryngol Head Neck Surg*. 1999 Jan. 125(1):21-7. [Medline].

39. Barlow CF, Priebe CJ, Mulliken JB, Barnes PD, Mac Donald D, Folkman J. Spastic diplegia as a complication of interferon Alfa-2a treatment of hemangiomas of infancy. *J Pediatr*. 1998 Mar. 132(3 Pt 1):527-30. [Medline].

40. Bigorre M, Van Kien AK, Valette H. Beta-blocking agent for treatment of infantile hemangioma. *Plast Reconstr Surg*. 2009 Jun. 123(6):195e-6e. [Medline].

41. Léauté-Labrèze C, Hoeger P, Mazereeuw-Hautier J, et al. A randomized, controlled trial of oral propranolol in infantile hemangioma. *N Engl J Med*. 2015 Feb 19. 372 (8):735-46. [Medline].

42. Sommers Smith SK, Smith DM. Beta blockade induces apoptosis in cultured capillary endothelial cells. *In Vitro Cell Dev Biol Anim*. 2002 May. 38(5):298-304. [Medline].

43. Ran Y, Chen S, Dai Y, Kang D, Lama J, Ran X, et al. Successful treatment of oral itraconazole for infantile hemangiomas: a case series. *J Dermatol*. 2015 Feb. 42 (2):202-6. [Medline].

44. Berenstein A, Lasjaunias P, Kricheff II. Functional anatomy of the facial vasculature in pathologic conditions and its therapeutic application. *AJNR Am J Neuroradiol*. 1983 Mar-Apr. 4(2):149-53. [Medline].

45. Muto T, Kinehara M, Takahara M, Sato K. Therapeutic embolization of oral hemangiomas with absolute ethanol. *J Oral Maxillofac Surg*. 1990 Jan. 48(1):85-8. [Medline].

46. Gilbert LD, Bakos LH, Graves RW. Sodium morrhuate--an alternative in the treatment of soft tissue hemangiomas. Review of the literature and case reports. *W V Dent J*. 1981 Apr. 55(2):11-5. [Medline].

47. Chin DC. Treatment of maxillary hemangioma with a sclerosing agent. *Oral Surg Oral Med Oral Pathol*. 1983 Mar. 55(3):247-9. [Medline].

48. O'Donovan JC, Donaldson JS, Morello FP, Pensler JM, Vogelzang RL, Bauer B. Symptomatic hemangiomas and venous malformations in infants, children, and young adults: treatment with percutaneous injection of sodium tetradecyl sulfate. *AJR Am J Roentgenol*. 1997 Sep. 169(3):723-9. [Medline].

49. Baurmash H, Mandel L. The nonsurgical treatment of hemangioma with Sotradecol. *Oral Surg Oral Med Oral Pathol*. 1963 Jul. 16:777-82. [Medline].

50. Minkow B, Laufer D, Gutman D. Treatment of oral hemangiomas with local sclerosing agents. *Int J Oral Surg*. 1979 Feb. 8(1):18-21. [Medline].

51. Govrin-Yehudain J, Moscona AR, Calderon N, Hirshowitz B. Treatment of hemangiomas by sclerosing agents: an experimental and clinical study. *Ann Plast Surg*. 1987 Jun. 18(6):465-9. [Medline].

52. Baurmash H, DeChiara S. A conservative approach to the management of orofacial vascular lesions in infants and children: report of cases. *J Oral Maxillofac Surg*. 1991 Nov. 49(11):1222-5. [Medline].

53. Seccia A, Salgarello M. Treatment of angiomas with sclerosing injection of hydroxypolyethoxydodecan. *Angiology*. 1991 Jan. 42(1):23-9. [Medline].

54. Glassberg E, Lask G, Rabinowitz LG, Tunnessen WW Jr. Capillary hemangiomas: case study of a novel laser treatment and a review of therapeutic options. *J Dermatol Surg Oncol*. 1989 Nov. 15(11):1214-23. [Medline].

55. Apfelberg DB. Intralesional laser photocoagulation-steroids as an adjunct to surgery for massive hemangiomas and vascular malformations. *Ann Plast Surg*. 1995 Aug. 35(2):144-8; discussion 149. [Medline].

56. Suen JY, Waner M. Treatment of oral cavity vascular malformations using the neodymium:YAG laser. *Arch Otolaryngol Head Neck Surg*. 1989 Nov. 115(11):1329-33. [Medline].

57. Dixon JA, Davis RK, Gilbertson JJ. Laser photocoagulation of vascular malformations of the tongue. *Laryngoscope*. 1986 May. 96(5):537-41. [Medline].

58. Goldwyn RM, Rosoff CB. Cryosurgery for large hemangiomas in adults. *Plast Reconstr Surg*. 1969 Jun. 43(6):605-11. [Medline].

59. Murphy JB. The management of a large hemangioma of the oral cavity with cryotherapy. *J Oral Med*. 1978 Jul-Sep. 33(3):104-6. [Medline].

60. Gongloff RK. Treatment of intraoral hemangiomas with nitrous oxide cryosurgery. *Oral Surg Oral Med Oral Pathol*. 1983 Jul. 56(1):20-4. [Medline].

61. Hartmann PK, Verne D, Davis RG. Cryosurgical removal of a large oral hemangioma. *Oral Surg Oral Med Oral Pathol*. 1984 Sep. 58(3):280-2. [Medline].

62. Greene LA, Freedman PD, Friedman JM, Wolf M. Capillary hemangioma of the maxilla. A report of two cases in which angiography and embolization were used. *Oral Surg Oral Med Oral Pathol*. 1990 Sep. 70(3):268-73. [Medline].

63. Strand M, Smidt AC. Pain management for ulcerated infantile hemangiomas. *Pediatr Dermatol*. 2012 Jan-Feb. 29(1):124-6. [Medline].