Gillette Children's Specialty Healthcare

A PEDIATRIC Perspective

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Propranolol Is Treatment of Choice for Facial Hemangiomas or Those That Impair Function

by Robert Wood, M.D., and Cheryl Shell, R.N., C.N.P.

In 2008, propranolol emerged as a new therapy for treating infant hemangiomas, and in 2009, the craniofacial team at Gillette Children's Specialty Healthcare adopted it for facial hemangiomas and those that impair function.

Hemangioma Incidence and Risk Factors

By age 1, 10 to 12 percent of infants will have a hemangioma, a rapidly growing benign lesion that usually resolves and disappears by the time the child is 9. Hemangiomas occur primarily in white children, but a 1.4 percent incidence has been noted in black children. Pre-term infants, especially those born at less than 1000 grams, are at higher risk (up to 30 percent) of developing hemangiomas than full-term infants are. Girls with this disorder outnumber boys three to one. In addition to being disfiguring, hemangiomas can affect function. A hemangioma that develops near the eye can affect vision. One on the nose can obstruct breathing, and one on the lip can affect feeding.

Typical Pattern of Growth and Involution

Hemangiomas have a rapid growth phase that can begin at birth and plateau at 6 to 12 months of age. During this time, the growth of the hemangioma is faster than the overall growth of the child. The lesions can become raised and spongy, and there is no way to predict their eventual size at maturity. After this rapid period of growth, the mass begins to involute. It starts paling at the center of the lesion and then fades from bright crimson to a dull purple or gray.

Depending on the size and depth of the mature hemangioma, it can take several years to completely disappear. About 50 percent of hemangiomas completely regress by the time a child is 5. Approximately 90 percent of hemangiomas regress by the time a child is 9.

If the hemangioma exists primarily on the skin's surface, it might leave no evidence once it has totally regressed. Deeper or larger hemangiomas often leave a permanent change in the appearance of the skin, requiring intervention to achieve a more desirable appearance. After a hemangioma fades, the skin in the area might be pale, with a baggy or fatty appearance, or it might have clusters of tiny blood vessels. If there has been any associated ulceration, the skin might also show signs of residual scarring.

Course of Treatment Depends on Hemangioma's Size and Location

Historically, hemangiomas were treated as follows:

- **A hemangioma would be allowed to resolve on its own** if it did not impair function, was not in danger of ulcerating and was hidden by clothing.
- **Hemangiomas that posed any of the concerns above might be surgically reduced or removed**. Unfortunately, surgical excision often leaves a scar, which is a concern for facial hemangiomas.
- **Physicians might prescribe a six- to eight-week course of oral corticosteroids**. Steroids can have a number of side effects: temporary changes in behavior, such as irritability; an increase in appetite and corresponding weight changes; mild water retention; or facial flushing. Unless they are taken with food or milk, steroids may cause stomach aches. In addition, live virus vaccines, such as measles-mumps-rubella, must be delayed for three months after the patient completes oral steroid therapy.
- **Physicians might use injectable steroids** for facial hemangiomas or those that are at risk of ulcerating. Injectable steroids result in fewer side effects, and they can be used with laser therapy.
- **Laser therapy might be suitable for flat lesions** to minimize the appearance of the lesion or to prevent the "cobble-stoning" texture that can develop over time.

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- **Laser therapy might also be used to treat an ulcerated hemangioma**. Laser therapy is done on an outpatient basis using general anesthesia to reduce discomfort and allow the child's eyes to be securely protected. A single treatment typically leads to total healing within three weeks. The risks associated with laser treatment are scarring, incomplete resolution that requires additional treatments and hyperpigmentation.

Currently at Gillette, propranolol is the treatment of choice for facial hemangiomas or those that affect function. Injectable or oral steroids and laser therapy remain viable treatment options as well.

History of Propranolol Use for Infant Hemangiomas

Propranolol is a nonselective beta blocker mainly used in the treatment of hypertension. It also has been widely used in pediatric cardiology. In 2008, French physicians Christine Léauté-Labrèze, et al. reported their findings regarding the use of propranolol in the treatment of hemangiomas in the *New England Journal of Medicine*.[1] Their initial study consisted of 11 infants, and they, as well as other researchers, have conducted additional studies to ensure that propranolol is safe and efficacious for infants. See the selected bibliography on flap.

The French team saw impressive results with propranolol: within 24 hours of initiating treatment, the hemangiomas changed from intense red to purple and the lesions softened to the touch. After the initial changes, the lesions continued to improve until they were nearly flat.

Initially, some clinicians expressed concerns about the potential risks associated with using propranolol for infants: the possibility of bradycardia and hypotension. In addition, the drug may mask symptoms of hypoglycemia. Since 2008, additional studies have been published that address these concerns. See bibliography.

Gillette's Propranolol Guidelines

Although Gillette physicians are accustomed to managing patients who also have cardiac concerns, we consulted with Gillette pediatric cardiologist Rodrigo Rios, M.D., to establish a protocol for propranolol use. During a clinic visit, we note:

- Baseline blood pressure, temperature, pulse and respiratory rate
- Height and weight

The patient receives a prescription for oral propranolol based on these guidelines:

- Propanolol 0.67 mg/kg/dose (which equals 2 mg/kg/day) by mouth or per gastrostomy tube q 8 hours
- As patients gain weight, we adjust the dosage to keep it at 2-3 mg/kg/day (not to fall below 2 mg/kg/day)

We monitor patients regularly:

- In one week to re-evaluate the course of treatment and discuss any problems with administration or tolerance of the medication
- Periodically according to the aggressiveness of the lesion and/or the patient's response

Families receive a weight schedule so they know when to call for a dosage adjustment or new prescription. The course of treatment typically runs four to five months, followed by a weaning period.

Since 2009, Gillette's craniofacial team has seen excellent outcomes in the seven infants with hemangiomas we have treated with propranolol therapy. See case studies on Page 3.

[1] Léauté-Labrèze, C. et al. Propranolol for severe hemangiomas of infancy. *N Engl J Med*, 2008; 358: 2649-2651, June 12, 2008.

Case Studies:

Boy With Hemangioma on Nose

This boy, one of twins, was born at just under 36 weeks of gestation. His parents noted a lesion a few weeks after he was born, and we first evaluated the patient when he was 7 weeks old. Because it was unclear whether the lesion was still growing, we opted to observe it before initiating treatment.

After three weeks, the lesion began enlarging aggressively (see photo), and we initiated propanolol therapy. The family did not notice any adverse side effects with the therapy, and the patient tolerated the medication throughout the treatment phase. After one week on propranolol, the lesion began to involute. The patient continued on propanolol therapy, and 5 ½ months after starting the medication, the hemangioma's mass had significantly decreased (see photo).

By the time the patient was 10 months old, the hemangioma had decreased even more in size and color. We discontinued propanolol, and at a follow-up check two months later, the hemangioma was essentially unchanged. No further treatment was needed, because the hemangioma's proliferative phase was finished. It will continue to fade over time.

When this little boy was 10 weeks old, the hemangioma lesion on his nose was clearly proliferating.

After 5 ½ months of propranolol treatment, the hemangioma had significantly decreased in size and color.

Girl With Hemangioma Over Eye

When this girl was 2 weeks old, her parents noticed a hemangioma over her left eye. The lesion continued to enlarge, and the patient was seen by a pediatric ophthalmologist, who prescribed topical timolol maleate twice daily. The family did not see any improvement, and we saw the girl when she was 5 months old (see photo). We initiated propanolol therapy, which the patient tolerated without any notable side effects.

She continued to do well throughout treatment. After one week, the lesion started to decrease in bulk and color. The lesion gradually began to flatten and fade, and the patient's ability to fully open her eye improved. After four months of propranolol therapy, the patient was dramatically improved (see photo). Because the lesion was at the end of its proliferative phase and will resolve on its own, we discontinued therapy.

When this little girl was 5 months old, the hemangioma was still proliferating, despite topical applications of timolol maleate prescribed by her ophthalmologist.

Four months after starting propranolol therapy, the hemangioma has begun to resolve, and the girl is able to open her eye fully.

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Author PROFILES

Robert Wood, M.D.

Robert Wood, M.D.
Craniofacial Surgeon
Robert Wood leads Gillette's Center for Craniofacial Services as program director. Before joining Gillette, he served as director of the Emory Egleston Center for Cleft and Craniofacial Anomalies in Atlanta.

Active in craniofacial research, Wood helped pioneer current techniques in endoscopic surgery to remove facial masses. He also developed an intra-oral bone expander and has an international reputation for his experience in resorbable fixation. In 2000, he worked closely with orthotists at Gillette to develop the Gillette CranioCap® orthosis to correct deformational plagiocephaly in infants.

Wood received his medical degree from the University of Minnesota Medical School and completed a general surgery residency at Hennepin County Medical Center in Minneapolis. He trained in plastic surgery at Emory University in Atlanta and completed a fellowship in craniofacial surgery at New York University Medical Center. He is a member of the American Cleft Palate and Craniofacial Association, American Society of Maxillofacial Surgeons and American Board of Plastic Surgery, among many other professional associations.

Cheryl Shell, R.N., C.N.P.

Cheryl Shell, R.N., C.N.P.
Cheryl Shell is a certified nurse practitioner and the coordinator of Gillette's cleft lip and palate team. In these roles, she provides outpatient assessments and postoperative care for patients who undergo craniofacial and plastic surgery. She serves as a feeding specialist and lactation consultant for infants with cleft lip and cleft palate. Shell offers community outreach services in the Twin Cities and outstate Minnesota, informing providers about Gillette's craniofacial programs. She also facilitates consultations and provides prenatal and preadoption counseling for families expecting children with craniofacial disorders.

Shell received a bachelor of science degree from Wichita State University and a master's degree in nursing from the University of Minnesota. She is certified by the Pediatric Nursing Certification Board and the International Board of Lactation Consultant Examiners.

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Gillette Craniofacial Services Welcomes Paul Lim, M.D.

Plastic surgeon Paul Lim, M.D., rejoined Gillette's Craniofacial Services team after serving as director of plastic surgery at CURE Ethiopia Children's Hospital in Addis Ababa, Ethiopia. There he gained extensive experience with cleft lip and palate reconstructions. He also specializes in treating children who have conditions such as craniosynostosis, congenital nevi, deformational plagiocephaly, torticollis, hemangiomas or congenital hand abnormalities.

Lim received his medical degree from Northwestern University Medical School in Chicago, Ill., where he completed a general surgery residency. He also finished a plastic surgery residency at the University of Minnesota in Minneapolis, Minn. He is certified by the American Board of Plastic Surgery and the American Board of Surgery. He is a fellow of the American College of Surgeons and the American Society of Plastic Surgeons, and he is a member of numerous other professional organizations.

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