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## Propranolol Treatment of Infantile Hemangiomas: Anticipatory Guidance for Parents and Caretakers

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### Abstract

Infantile hemangiomas (IH) are benign tumors of endothelial-like cells. Occurring in 4.5% of children, they are the most common tumor of childhood. The great majority of patients with IH will not need treatment, but 10% require systemic treatment. Many treatments have been described for the treatment of IH, but the Food and Drug Administration has not approved any. Over the last decade, numerous reports of successful treatment of IH with propranolol have been published. Despite its widespread use, little is known regarding the proper dosing, safety monitoring, and during of treatment or long-term outcomes for propranolol treatment of IH. Given its potential side effects, detailed education regarding proper administration of the medication as well as warning signs to watch for is necessary for parents and caretakers. Herein, we provide a parental handout that practitioners can individually tailor for use in their clinics when educating parents and caretakers about the use of propranolol for IH. Updates will also need to be made as more is

learned regarding the optimal dosing and safety monitoring when using propranolol for this indication.

**Forward**—This article is a little different from the usual Techniques for Tots which have typically focused on examination or surgical techniques. We hope the readers will find it useful as an educational tool for families whose children are receiving propranolol for infantile hemangiomas.

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## Introduction

Infantile hemangiomas (IH) are benign tumors of endothelial-like cells. Occurring in approximately 4.5% of children, they are the most common tumor of childhood. The great majority of patients with IH will not need treatment, but a significant minority do require treatment, including systemic therapy (1). IH can lead to serious complications including permanent disfigurement, ulceration, airway obstruction and visual loss. Many treatments have been described for the treatment of IH, but to date, none have Food and Drug Administration approval. Over the last decade, numerous reports of successful treatment of IH with propranolol have been published (2–5). As more physicians have begun using propranolol for IH, reports of side effects have also increased (6–8). Despite its widespread use, little is known regarding the proper dosing, safety monitoring, duration of treatment or long-term outcomes for propranolol treatment of IH. As a first step toward answering each of these clinical questions, a consensus meeting was held in Chicago, Illinois on December 9, 2011. Twenty-eight members from 12 institutions, representing five specialties gathered to discuss their varying experiences regarding the use of propranolol for IH. These guidelines are currently in press and will be published soon (9). As a part of this meeting, all members noted the importance of parent education regarding the proper use of propranolol and potential side effects. A group of the participants felt that the development of a parental handout that practitioners could individually tailor and use in their clinics would be an important outcome of this meeting.

Herein, we provide a parental handout that can be used as a clinical tool for practitioners prescribing propranolol for IH. It is written at an eighth-grade reading level, which may need to be adjusted depending on the institution that uses it. Also, because safety monitoring currently varies greatly between providers, information regarding home heart rate monitoring, glucose checks, etc. may need to be modified. Practitioners should also note that changes may be needed based on new information on propranolol's use for IH.

## What is an Infantile Hemangioma?

An infantile hemangioma is a common type of birthmark. Hemangiomas are benign collections of extra blood vessels in the skin and are one of the most common skin problems of the first year of life. They appear most frequently during the first one to four weeks after

birth and occur in about 5% of all children. After appearing, hemangiomas grow fast for the first few weeks or months of life. A hemangioma is a tumor, but it is not cancer. It is benign. The cells of a hemangiomas multiply at a rate that is faster than normal. By around 8 months, these cells stop multiplying and most hemangiomas stop growing. They begin to shrink around 1 year and slowly improve over time on their own, and this often takes many years. Larger ones will take longer to go away and have a higher chance of scarring. Each hemangioma is unique. Even in the same baby, one hemangioma may not grow and another may become quite large. About one in four hemangiomas will need some form of treatment.

## **When is Propranolol Used to Treat a Hemangioma?**

A small number of hemangiomas require treatment for complications caused by the growth of the hemangioma. Sometimes treatment is needed if the hemangioma is growing too large on the eye, lip, and nose or in the airway. Treatment is also needed if there is a real risk of permanent scarring. Sometimes propranolol is used to help with healing when skin breakdown occurs on the hemangioma.

During the first couple of months of life when a hemangioma is growing rapidly, it can be difficult to determine how big it will become, so your child may need to be seen in the clinic often; as babies get older the office visits are usually less frequent.

## **What is Propranolol?**

Propranolol is a medicine that has been used for many years to treat high blood pressure and an irregular heart rate. Propranolol is also used to treat migraine headaches. Recently, propranolol has been shown to shrink hemangiomas in some infants. Propranolol is approved by the FDA, but not for treating hemangiomas in children. In fact, there is no medicine approved by the FDA for the treatment of infantile hemangiomas.

## **What are the Possible Risks or Side Effects of Propranolol?**

Your doctor will review potential risks and side effects of propranolol with you.

### **Allergic Reaction**

Your doctor will review potential risks and side effects of propranolol with you. As with any medicine, people can be allergic to propranolol, though this is very rare. Mild allergic reactions can include itching, hives or swelling of the face or hands. More severe allergic reactions include swelling or tingling of the mouth or throat, chest tightness or trouble breathing. You should stop your child's medicine and contact us if you suspect an allergic reaction.

### **Slow Heart Rate**

Propranolol can make the heart rate slower, but most of the time the heart rate in infants taking propranolol for hemangiomas is still in a normal range. In some cases (if you agree) you may be taught how to take your child's heart rate and how many beats per minute is "normal" for your child's age group.

### **Low Blood Sugar**

Propranolol can lead to low blood sugar. Low blood sugar can cause drowsiness or rarely seizures. Early signs of low blood sugar may include coldness, shakiness, and sweating. Low blood sugar with propranolol is more likely to occur when your child is not eating normal amounts or has gone for several hours without eating. To help prevent this, always give propranolol during or right after your child has eaten. Other instructions to prevent low blood sugar are listed below under “Important information when giving your infant propranolol”.

### **Breathing Problems or Wheezing**

Propranolol can worsen asthma or wheezing. Wheezing is frequently associated with colds or flu-like illnesses. Sometimes your child will be treated for wheezing with an inhaled medicine (one that is breathed in). If your child is wheezing, immediately contact your doctor. Propranolol may be held during these types of illnesses.

### **Change in Sleep Pattern**

Propranolol can affect some children’s mood or sleep pattern. These effects are usually noticed when your child first begins taking propranolol, and may include difficulty getting to sleep or sleeping more than normal. Less often, night terrors (bad nightmares) have been reported. If you notice them and they are mild in your judgment, see if they decrease once your child has been taking propranolol for longer than a few weeks. Sometime the nightmares can be reduced by giving the last dose of propranolol before the evening feeding. If these side effects persist or are more than mild, report them to your doctor.

### **Other Possible Side Effects**

Propranolol can much more rarely cause other side effects. If your child is have a new problem or change in behavior, contact your pediatrician or the doctor prescribing the propranolol to see if it might be related.

### **What Can You Do to Reduce the Chances of a Side Effect During Treatment with Propranolol?**

If used properly, propranolol is a safe and effective medication for treatment of infantile hemangiomas. The following steps will help you use the drug safely.

- Propranolol’s side effects can increase as the dose is increased. Propranolol will be prescribed in a liquid form and should be measured very carefully. It is very important to give the correct amount at the correct time. Determine who/which caregiver will give the baby the medication and at what time of the day. Give every dose of propranolol with a feeding (breast milk, formula or solids), but do not mix in with food or milk.
- Always use a syringe to measure the medicine. Your doctor or pharmacist should provide you with the proper size syringe.
- Measure each dose of medicine carefully. It is best if the same person always gives the propranolol to avoid accidentally giving too much medicine. If this is not

possible, measure the amount of propranolol in the syringes you will need for the entire day and give a pre-filled syringe to the person that will be giving the dose.

- Doses should always be at least 6 hours apart.
- If you should miss a dose, never try to make up for missed doses by doubling the dose or giving more propranolol. Simply wait for the next time the dose is due and give it then.
- If your child spits up a dose or if you are uncertain whether they got it all of the medicine do not give another dose, just wait until the next scheduled dose.
- Feed your child frequently. Infants less than 6 months old should not go longer than 6 hours without feeding. Infants over 6 months old should not go longer than 8 hours without feeding. You may have to wake your baby during the night to feed them if they sleep longer than this.
- Have Pedialyte, or a similar drink, available at home. Give your child Pedialyte if they refuse to eat while on propranolol. This type of liquid is designed to promote quick fluid absorption while a child is sick and contains sugars and certain salts which are helpful during an illness.
- If your child is sick and will only drink small amounts, stop giving propranolol and contact your child's doctor. It is usually okay to stop the propranolol for a few days to give your child's body a chance to build up stores of sugar again after an illness.
- If your child needs to stop eating for a test or procedure (surgery, MRI scan or other procedure) be sure to let the doctors know that your child is on propranolol. It is possible that the propranolol will need to be stopped during procedure-related fasting (period of not eating).
- Check all drugs that your child is taking with your child's doctor or pharmacist. Propranolol may interact with some other drugs. This includes medicines that are over the counter, herbal and prescription.

### **What should you do if you notice any side effects that you think could be caused by propranolol?**

Call 911 if your child should develop trouble breathing, is unresponsive, or has a seizure. If you think your baby may have low blood sugar give him/her pedialyte or other source of sugar. However, do not give anything to your baby by mouth if he/she is unresponsive.

Contact/See your child's doctor right away if you notice any of these side effects:

- Allergic reaction: Itching or hives, swelling in the face or hands, swelling or tingling in the mouth or throat, chest tightness.
- Trouble awakening or losing consciousness.
- Cold sweats and/or bluish-colored skin.
- Slow, fast, or uneven heartbeat.

- Unusual tiredness or weakness.

If you notice these less serious side effects, contact your child's doctor to discuss:

- Constipation, diarrhea, nausea or vomiting, or upset stomach.
- Mood change.
- Skin rash.
- Trouble sleeping.

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