# Soft-tissue Hemangiomas in Infants and Children: Diagnosis Using Doppler Sonography

Josée Dubois[1]
Heidi B. Patriquin[1]
Laurent Garel[1]
Julie Powell[2]
Denis Filiatrault[1]
Michèle David[3]
Andrée Grignon[1]

**OBJECTIVE.** We describe the sonographic appearance and vascularization of hemangiomas and determine if vessel density and peak systolic Doppler shifts distinguish hemangiomas from other superficial soft-tissue masses.

**SUBJECTS AND METHODS.** Our pilot study included 20 infants and children with hemangiomas who were to undergo biopsy before treatment with interferon alpha-2b. We used Doppler sonography to determine the number of vessels per square centimeter, peak arterial Doppler shift, resistive index, and signs of arteriovenous shunting. All hemangiomas showed high vessel density (more than five per square centimeter) and high Doppler shifts (more than 2 kHz), and these two factors became our diagnostic criteria. A prospective study of 116 patients was then carried out. One hundred sixteen consecutive pediatric patients with superficial soft-tissue masses were examined using Doppler sonography; sonographic findings were compared with the final diagnoses that were established by biopsy, CT, or clinical follow-up.

**RESULTS.** The final diagnoses included 70 hemangiomas, 20 venous malformations, three arteriovenous malformations, three arteriolocapillary malformations, and 20 other masses. Fifty-nine lesions showing high vessel density (more than five per square centimeter) and a peak arterial Doppler shift exceeding 2 kHz were correctly diagnosed as hemangiomas (sensitivity, 84%; specificity, 98%). One arteriovenous malformation showed high vessel density and high Doppler shifts, but none of the other masses that were not hemangiomas did. Eleven patients with hemangiomas who were being treated with interferon at the time of the study fulfilled only one of the two diagnostic criteria.

**CONCLUSION.** High vessel density and high peak arterial Doppler shift can be used to distinguish hemangiomas from other soft-tissue masses.

Hemangiomas, which are among the most common soft-tissue tumors in infants [1–3], typically appear as slightly raised, bluish red subcutaneous masses that resemble the surface of a strawberry and regress as the child grows older. Some hemangiomas do not have this typical appearance because part or all of the lesion is deep in the soft tissue and the overlying skin appears normal. These lesions are difficult to distinguish clinically from more suspicious soft-tissue masses, such as vascular malformations, soft-tissue tumors (e.g., metastases from neuroblastoma or rhabdomyosarcoma), and infantile myofibromatosis. Children with such lesions are usually referred for imaging studies or biopsy.

Blood flow in superficial vessels is readily discernible using Doppler sonography. We sought to ascertain whether hemangiomas have characteristic features that can be seen using high-frequency gray-scale and Doppler sonography and whether they can be distinguished from other superficial soft-tissue masses in infants and children.

## Subjects and Methods

### *Pilot Study*

To determine the general appearance and vascularization characteristics of soft-tissue hemangiomas in infants, we performed high-resolution gray-scale and Doppler sonography and CT with IV contrast material on 20 infants and children with hemangiomas who were about to undergo biopsy before commencing therapy with interferon alpha-2b (Intron A, Schering, Canada). We used a Mark 9 HDI scanner (ATL, Seattle, WA) with a 10-MHz linear array transducer. Color Doppler sonograms were obtained with low-pulse repetition frequency and a wall filter. Pulse-repetition frequency was increased only if aliasing occurred. The area of greatest vasculariza-

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[1]Department of Medical Imaging, Hôpital Sainte-Justine, 3175 Côte-Sainte-Catherine, Montréal, Québec, Canada H3T 1C5. Address correspondence to J. Dubois.

[2]Department of Dermatology, Hôpital Sainte-Justine, Montréal, Québec, Canada H3T 1C5.

[3]Department of Hematology, Hôpital Sainte-Justine, Montréal, Québec, Canada H3T 1C5.

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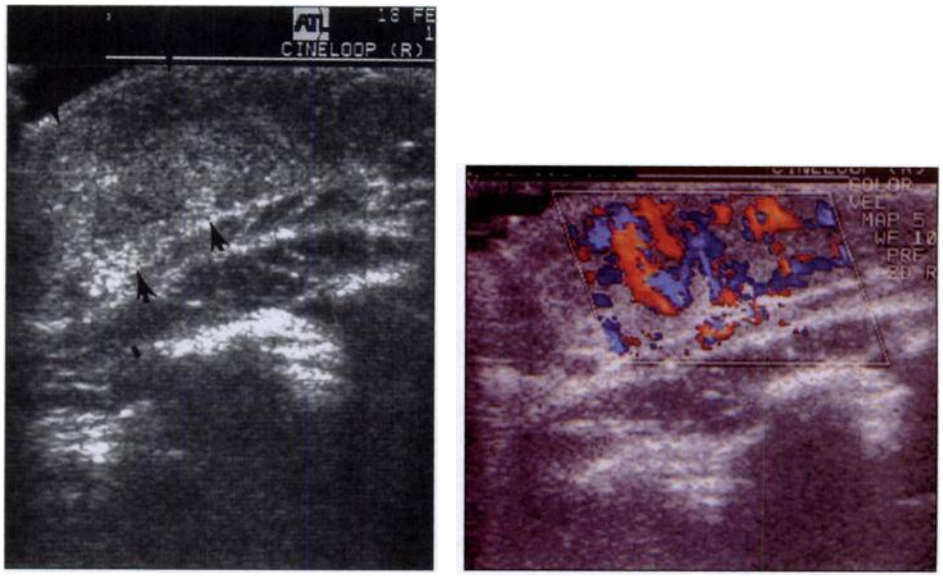
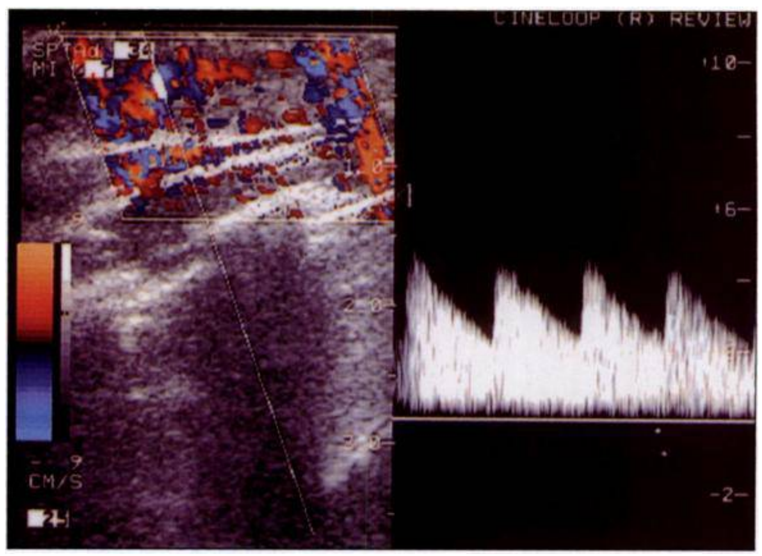



A B

Fig. 1.—Hemangioma of right cheek in 2-month-old girl (normal overlying skin).
A, Gray-scale sonogram reveals heterogeneous mass (*arrows*).
B, Color Doppler sonogram shows high vessel density (more than five visible vessels per square centimeter).
C, Spectroscopy shows peak arterial Doppler shift of 5 kHz.

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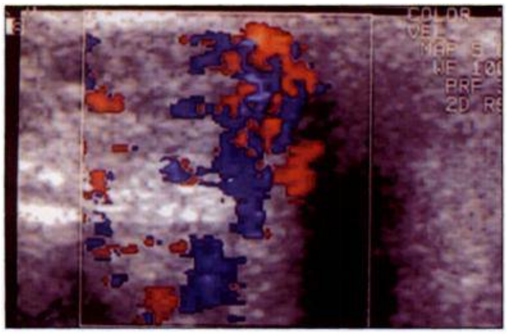
tion was selected, and the number of vessels per square centimeter outlined on color Doppler imaging was counted. Peak arterial Doppler shifts and the resistive index (RI) were ascertained with pulsed Doppler sonography. All of these lesions were verified as hemangiomas by biopsy. They had variable appearance on gray-scale sonography but were highly vascular, containing at least five vessels per square centimeter; the peak velocity was higher than 2 kHz. On CT, the hemangiomas showed rapid uptake and intense, persistent retention of contrast material. These findings were used as the criteria for the diagnoses of hemangiomas in the subsequent prospective study.

#### *Prospective Clinical Study*

All infants and children referred to our dermatology–vascular malformations clinic with clinically diagnosed hemangiomas or other superficial soft-tissue masses were screened by the attending dermatologist. Patients were referred for sonographic and CT examination if the lesion did not have the typical physical appearance of a hemangioma or appeared to have a subcutaneous extension that was difficult to assess clinically. Between June 1991 and January 1996, all such children were examined by sonography, and the sonographic diagnoses were compared with the final diagnoses.

Sonograms were obtained by one of four pediatric radiologists trained in Doppler sonography to whom the details of the sonographic technique for the study had been carefully explained. Either a Quantum II (Siemens, Issaquah, WA) with a 7.5-MHz linear gray-scale and Doppler transducer or a Mark 9 HDI (ATL) with a 10-MHz or 6-MHz transducer was used. A 1-cm-thick standoff pad was used when necessary. The length, width, and depth of the lesions were measured using electronic calipers. Echogenicity was assessed as hypoechoic or hyperechoic. Gray-scale sonography was used to look for visible vessels around or within the lesion. Internal architecture was classified as homogeneous or heterogeneous. Doppler sonography was performed using the lowest pulse-repetition frequency and Doppler gain settings that did not cause aliasing (pulse-repetition frequency, 2–16.6 kHz; wall filter, 50–100 kHz). Color Doppler sonography was used to scan the entire lesion with a restricted field of view. The area of greatest vascularity was retained for analysis. The field of interest was reduced to 1 $cm^2$. Vessels were identified by color-flow signals, and vessel density was defined semiquantitatively as sparse or low density (fewer than two vessels per square centimeter), moderate or medium (two to four vessels per square centimeter), and numerous or high (more than five vessels



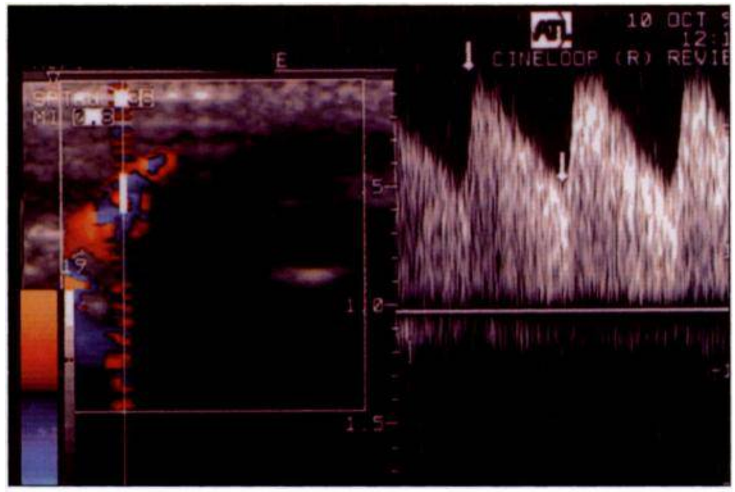


**Fig. 2.**—Hemangioma of orbital region in 2-month-old girl.
**A**, Color Doppler sonogram shows high vessel density.
**B**, Spectroscopy shows high systolic flow with peak of 4 kHz.

per square centimeter). A pulsed Doppler examination was then performed, placing the Doppler sample into arteries and veins. Peak arterial systolic Doppler shifts were noted and classified as low (<1 kHz), moderate (1–2 kHz), or high (>2 kHz). The RI was calculated (systolic − diastolic / systolic Doppler shifts). Evidence of arteriovenous shunting was sought, including high diastolic flow, RI less than 0.5, and pulsatile venous flow.

Eighty-five percent of these examinations were performed without sedation of the patient. The remainder were performed immediately after CT, taking advantage of the sedation necessary for that examination. Informed consent was obtained from patients' parents. The study was approved by the hospital committee on human experimentation. After Doppler sonograms were obtained, the examining radiologist reported the diagnostic impression to the clinician. At the end of the study period, all sonograms were reviewed by the principal investigator.

The diagnosis of hemangioma was made if the Doppler examination showed high vessel density (more than five vessels per centimeter) and a high Doppler shift (>2 kHz). All masses that did not fulfill these criteria were called "other masses–nonhemangioma." Lesions with several sites of arteriovenous shunting were called "nonhemangioma–likely arteriovenous malformation." Biopsy was performed if a lesion did not fulfill the criteria for hemangioma on clinical follow-up or on CT. The final diagnosis was established by clinical follow-up (regression or stability of the mass after age 2 years) in 49 patients; angiography or phlebography in 23 patients; and CT and biopsy in 44 patients. The sonographic findings were compared with the final diagnoses. Sensitivity, specificity, positive predictive value, negative predictive value, and diagnostic accuracy of the sonographic examinations were calculated.

## Results

One hundred sixteen infants and children who were 2 days to 7 years old (mean age, 18 months old) were examined. The final diagnoses included 70 hemangiomas, 20 venous malformations, three arteriovenous malformations, three arteriolocapillary malformations, and 20 other masses.

The size of the hemangiomas ranged from 2 to 640 $cm^3$. The gray-scale sonographic appearance was nonspecific. One lesion showed a small calcification. In four lesions, one or two vessels were visible on gray-scale sonography. In the remainder of patients, no vessels were seen on gray-scale sonography.

Doppler sonography revealed high vessel density (five vessels or more per square centimeter) in 65 (93%) of 70 hemangiomas and a maximum systolic Doppler shift greater than 2 kHz in 63 (90%) of 70 (Figs. 1–3). Using these two criteria established in the pilot study, we were able to make diagnoses of hemangioma in 59 (84%) of 70 hemangiomas. Maximum Doppler shifts ranged from 1.1 to 10 kHz with a mean ± SD of 3.8 ± 2.0 kHz. RI ranged from 0.25 to 0.89 with a mean of 0.59 ± 0.13 kHz). Eleven hemangiomas fulfilled only one of the two diagnostic criteria and were therefore diagnosed as "mass–nonhemangioma" on sonography. These 11 masses were clinically stable, and the children were receiving interferon treatment at the time.

Three hemangiomas with high vessel density and peak systolic shifts greater than 2 kHz had one or two sites of arteriovenous shunting. No feeding vessels were seen on gray-scale sonography. We correctly diagnosed these lesions as hemangiomas. Three other small lesions had many sites of arteriovenous shunting. Several dilated vessels were noted on gray-scale sonography and identified as feeding arteries and veins on Doppler sonography. One lesion had high vessel density and peak systolic shift greater than 2 kHz. The other two had moderate vessel density (three per square centimeter) with a high Doppler shift (2 kHz). We therefore made the diagnosis of "lesion–nonhemangioma, probably arteriovenous malformation" (Fig. 4) in these three patients. This diagnosis was confirmed by angiography.

The 49 nonhemangioma soft-tissue masses had zero to five vessels per square centimeter and a maximum systolic Doppler shift of 0.8 to 6.5 kHz, with a mean of 1.32 (SD = 1.4). The RI ranged from 0.2 to 1.00, with a mean of 0.45 (SD = 0.35) (Figs. 5 and 6). None fulfilled the two criteria for the diagnosis of hemangioma. Some lesions had only venous flow. Three atypical masses that were clearly not hemangiomas were difficult to diagnose on Doppler sonography. They did not fulfill the two sonographic criteria used for the diagnosis of hemangioma and were therefore labeled "other masses." In one mass, vessel density was moderate (three per square centimeter), with a high peak systolic Doppler shift (6.5 kHz). The diagnosis of "mass–nonhemangioma" was made. The mass was very hard on palpation. Biopsy showed a rhabdomyosarcoma. Another mass, which had appeared late in childhood, had high vessel density (more than five per square centimeter) and moderate Doppler shift (1.3 kHz). It

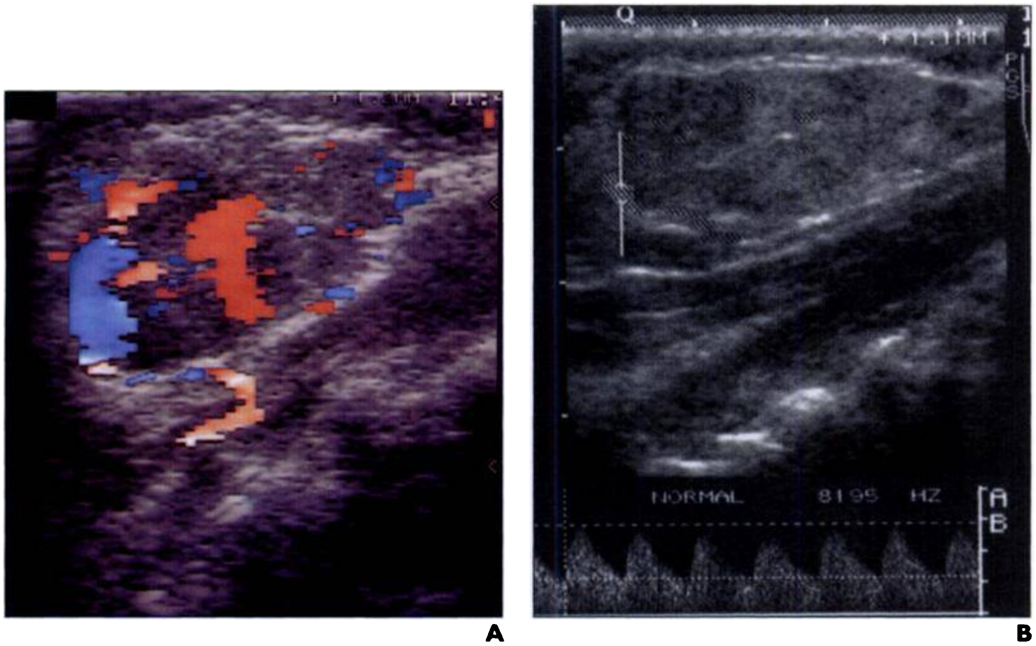



**Fig. 3.**—Hemangioma with normal overlying skin on back of 6-month-old boy.
**A**, Color Doppler sonogram shows high vessel density (more than five per square centimeter).
**B**, Spectroscopy shows peak systolic Doppler shift of 5.7 kHz.

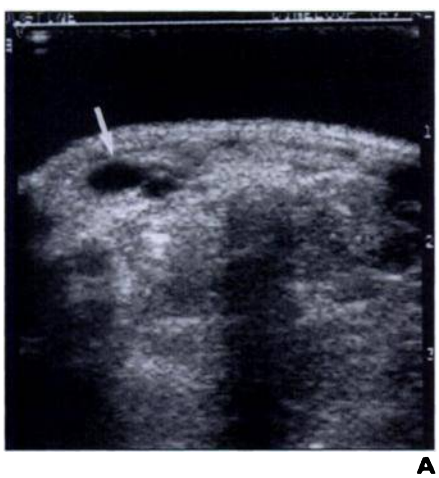
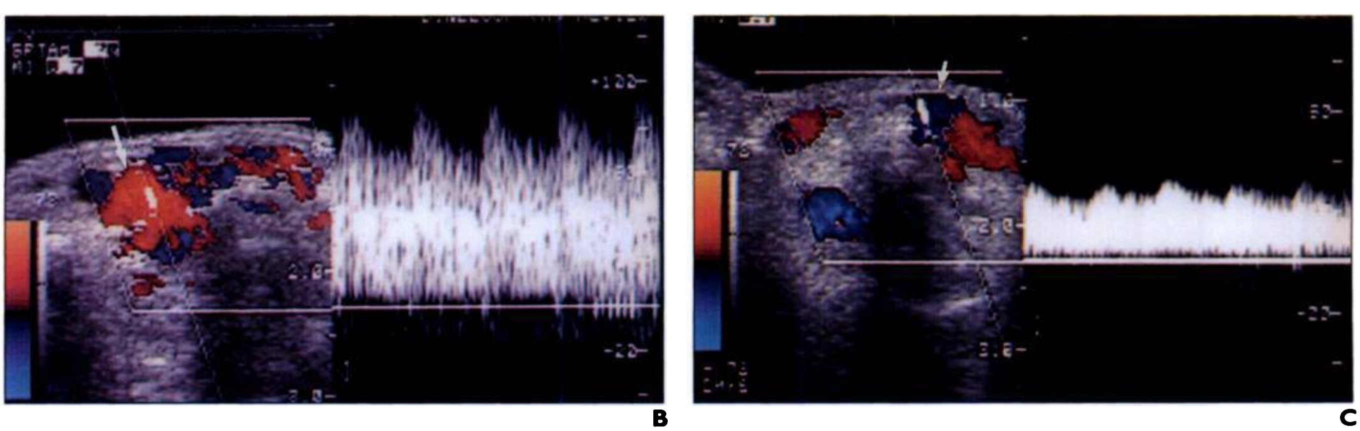


**Fig. 4.**—Arteriovenous malformation of face in 2-year-old girl.
**A**, Gray-scale sonogram shows several vessels (*arrow*).
**B**, Spectroscopy shows large feeding artery (*arrow*). Blood flow has low resistance and high diastolic flow, suggesting arteriovenous shunting.
**C**, Spectroscopy shows large draining vein (*arrow*). Blood flow is pulsatile, compatible with venous flow distal to arteriovenous malformation.



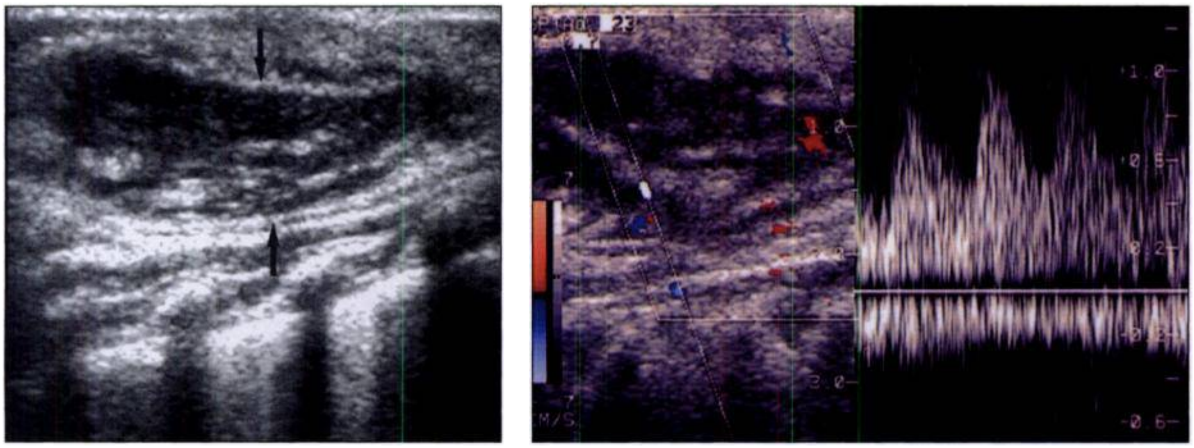


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**Fig. 5.**—Infantile myofibromatosis on back of 1-month-old girl.
**A**, Gray-scale sonogram reveals nonspecific mass (*arrows*).
**B**, Color Doppler spectroscopy shows low vessel density with systolic peak of 1 kHz.

was identified as an angiofollicular hamartoma on biopsy. A lesion in a neonate had low vessel density (fewer than two per square centimeter) with very high Doppler shifts (6.5 kHz). No specific sonographic diagnosis was made. Biopsy showed a sarcoma.

Using the two criteria of high vessel density (more than five per square centimeter) and peak arterial Doppler shift greater than 2 kHz for the diagnosis of hemangioma, we found the sensitivity of the Doppler sonography to be 84% (59/70); specificity, 98% (45/46); positive predictive value, 97% (59/61); and negative predictive value, 82% (45/55).

## Discussion

Infantile hemangiomas are benign vascular lesions characterized by a phase of initial growth and angiogenesis, a plateau phase of inactivity, slow resolution of angiogenesis, and regression of both the size and vascularity of the tumors [4–6]. Their severity varies; hemangiomas range from an asymptomatic, discolored spot on the skin to large, highly disfiguring masses that can be life-threatening when they occur near vital structures such as the airway. Their high vascularity can cause high output heart failure. Sequestration of platelets in the lesion may lead to thrombocytopenia (Kasabach-Merritt syndrome). Microscopically, the hallmark of a growing hemangioma is a proliferation of endothelial cells, forming syncytial masses composed of numerous vessels or cords of endothelial cells. The vessel lumens are often compressed. Occasional mitotic figures are seen. However, the nuclei have a benign appearance and are not pleomorphic. As the proliferative phase progresses, vascular channels are less compressed and capillary lumens lined by plump endothelial cells may be seen [7]. Mast cells are also abundant in proliferating hemangioma tissue [8]. Most hemangiomas have a typical "strawberry" appearance with well-

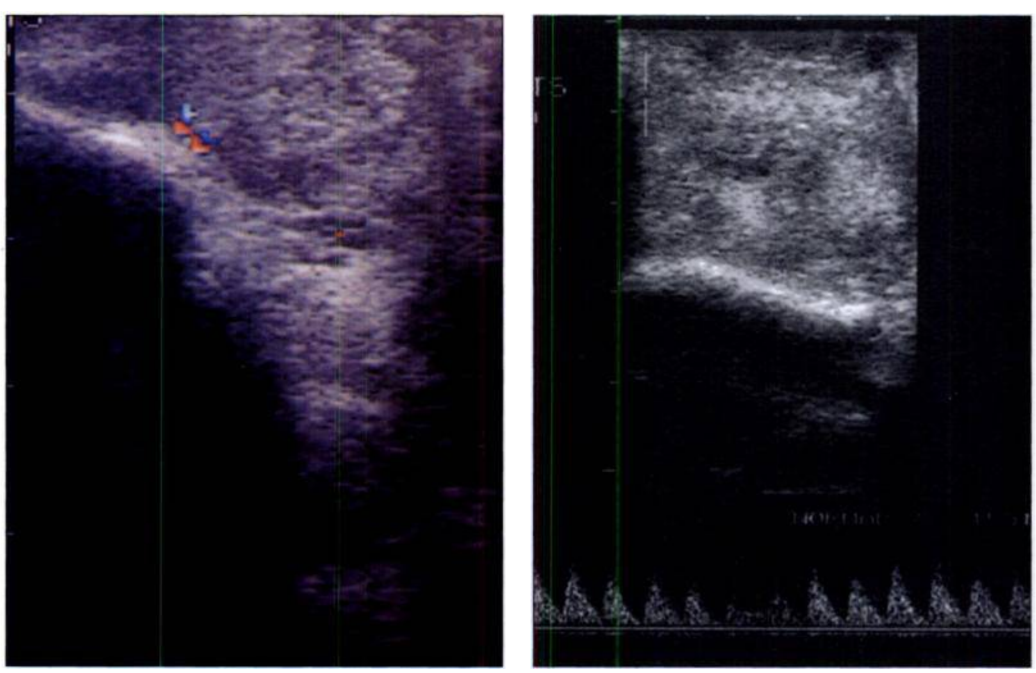

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**Fig. 6.**—Atypical mass on forehead of 1-week-old boy.
**A**, Color Doppler sonogram shows low vessel density.
**B**, Spectroscopy shows peak Doppler shift of 1.5 kHz. Rhabdomyosarcoma was diagnosed by biopsy.

defined borders. This type presents little diagnostic difficulty on clinical examination. Diagnostic problems arise when lesions are atypical and when all or part of a lesion lies deep in the subcutaneous tissues and therefore cannot be clearly defined on physical examination. This type of lesion is difficult to distinguish from vascular malformations and tumors such as infantile myofibromatosis, neuroblastomas, metastases, and sarcomas. Children with such lesions are usually referred for imaging studies.

Because modern sonographic equipment is ideally suited to examining superficial lesions, this noninvasive method is useful in examining children with such lesions. Feeding arteries and veins are more easily identified by Doppler sonography than by CT because the lesions can be examined in many planes.

In our pilot study of biopsy proven hemangiomas, we found that all hemangiomas had blood flow through many vessels too small to be seen on gray-scale sonography. We devised a method of estimating vessel density by counting the number of vessels per square centimeter shown on color Doppler sonography in the area of greatest vascularization in each lesion. Technical factors were kept constant. The vessel count is semiquantitative at best, considering that one tortuous vessel may yield more than one color Doppler signal. We classified vessel density as low, medium, or high. Maximum systolic Doppler shift rather than velocity was measured because the vessel beam angle was rarely known. The 20 patients with hemangiomas in the pilot study had a maximum Doppler shift exceeding 2 kHz. During the prospective study of 116 children with various subcutaneous masses, we found that the two criteria of high vessel density and Doppler shift greater than 2 kHz allowed us to distinguish hemangiomas from other lesions, which had fewer vessels or lower Doppler shifts.

A number of pitfalls were encountered. Arteriovenous malformations also showed more than five vessels per square centimeter and Doppler shift exceeding 2 kHz. However, feeding vessels large enough to be seen on gray-scale sonography were found to be feeding arteries and draining veins on spectroscopy. Multiple sites of arteriovenous shunting were identified by very high diastolic Doppler shifts (RI < 0.5) and abnormally pulsatile draining veins. Each arteriovenous malformation was associated with a small soft-tissue mass. We were unable to confirm the work of Meyer et al. [9], who found that arteriovenous malformations can be differentiated from hemangiomas by the absence of a soft-tissue mass. Only one of 70 hemangiomas showed one vessel large enough to be identified on gray-scale sonography, and no pulsatile draining veins were identified. Some hemangiomas had one or two sites of arteriovenous shunting that were not of the same density as arteriovenous malformations. Two sarcomas and one angiofollicular hamartoma had the high Doppler shifts characteristic of hemangiomas, but their vessels were sparse in number and at the periphery of the lesions [10, 11].

Why do hemangiomas (benign lesions) and sarcomas sometimes share similar blood flow characteristics as seen on Doppler sonography? The answer probably lies in the concept of angiogenesis [12, 13]. Some lesions are capable of stimulating the host to create new vessels, usually from existing endothelial cells, by secreting angiogenesis factors. The molecular structure of several angiogenesis factors has been defined [14, 15]. Angiogenesis factors have been isolated from many tissues including fibroblasts, wound fluids, placentas, numerous malignant tumors, hemangioendotheliomas, and infantile hemangiomas. The new vessels produced through angiogenic stimulation do not have a muscularis layer, and therefore blood flow through the network of vessels feeding them has high velocity and low resistance. Flow within the individual microscopic vessels is slow. Thus it is likely that the blood flow in hemangiomas that is detected by Doppler sonography occurs in the vessels feeding the neovasculature stimulated by angiogenesis factors. During their phase of proliferation, hemangiomas receive maximal angiogenic stimulation, as evidenced by the large number of vessels and cords of endothelial cells seen by microscopy. Other benign superficial tumors of childhood do not appear to manifest the intense degree of angiogenesis noted in hemangiomas. This may explain the difference in vessel density and peak systolic Doppler shift between hemangiomas and other benign masses.

Although malignant tumors may show intense angiogenesis, the network of new vessels is usually found at the periphery of the mass. Very high Doppler shifts have been detected at the periphery of numerous malignant tumors, especially in the abdomen [10, 11]. It is not likely that a malignant tumor would mimic the high density of vessels throughout its mass that is seen in hemangiomas. The 11 hemangiomas in our series that had fewer than five vessels per square centimeter or less than 2 kHz Doppler shift were clinically stable lesions in children undergoing interferon alpha-2b treatment. It remains to be seen whether the diminishing angiogenic stimulation in treated or spontaneously involuting hemangiomas is reflected in changing Doppler patterns.

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