

this would favor an elevated jugular venous pressure that perhaps was not recognized owing to improper positioning of the patient.

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**THE AUTHORS REPLY:** We agree with Drs. Daniels and Krummen that, barring a process such as hepatic-vein thrombosis with an incidental, hemodynamically insignificant pericardial effusion, elevation of jugular venous pressure should have been detected. Considerable variation exists in expertise in the measurement of jugular venous pressure, and studies indicate poor reliability of such assessments in critically ill patients.<sup>1</sup> This patient subsequently was found to have plethora of the inferior vena cava on echocardiography, reflecting elevated right atrial pressure<sup>2</sup> and signifying that the initial interpretation of the jugular venous pressure was probably incorrect.

Though one may be tempted to ensure complete agreement of all historical and physical findings with the patient's subsequent diagnosis, we chose to present details as they unfolded and as they were documented by the clinicians. We recognize that clinicians often consider broad differential diagnoses and commonly are faced with incongruent elements of a case. Consequently, one challenge is the integration of data and the determination of whether to discount or question inconsistencies. We hope that presenting the case in this manner accurately portrays the complex decision making that is necessary in routine practice, especially when conflicting or imprecise information exists.

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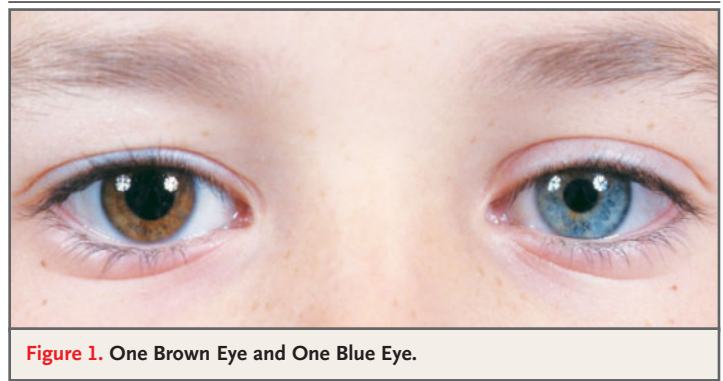
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## Medical Mystery: Brown Eye and Blue Eye — The Answer

**TO THE EDITOR:** The Medical Mystery in the October 6 issue<sup>1</sup> shows a 10-year-old boy with one brown and one blue eye, with mild ptosis and miosis of the lighter, left eye (Fig. 1). Both eyes respond equally to light and have normal vision; both are normal on funduscopic examination. The eyes of the boy's father are blue, and the mother's are gray. At 10 months of age, the boy was given a diagnosis of a left-sided paraspinal neuroblastoma (C7), extending to the upper thoracic vertebrae and entering the intraspinal canal, with bone marrow involvement (stage 4). After undergoing emergency decompression, chemotherapy, and surgery, the boy is in complete remission but has a loss of sweating (anhidrosis) on the left side of the face and torso. This finding is compatible with left Horner's syndrome, a regional disturbance of the sympathetic nervous system



**Figure 1.** One Brown Eye and One Blue Eye.

caused by the paravertebral tumor. A unilateral lack of sympathetic stimulation in childhood interferes with melanin pigmentation of the melanocytes in the superficial stroma of the iris, re-

sulting in heterochromia. This clinical finding might be useful in the early diagnosis of lesions affecting the sympathetic nerves.

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*Editor's note:* We received 1642 responses to this medical mystery, including 54 percent from physicians in practice, 19 percent from physicians in training, and 14 percent from medical students.

Responses were received from 77 countries. Of the respondents, 71 percent correctly identified Horner's syndrome (which is sometimes called the Horner–Bernard syndrome) with heterochromia; 21 percent correctly identified the lesion as a cervical neuroblastoma impinging on the sympathetic chain. Other respondents provided such answers as Waardenburg's syndrome, retinoblastoma, chimerism, Fuchs' syndrome, and varicella. In addition to the classic findings of Horner's syndrome and heterochromia, this case highlights the importance of sympathetic innervation for proper melanocyte activity in the iris. Pigmentation of the iris is usually complete by the age of two years.

## Domino Hepatic Transplantation in Maple Syrup Urine Disease

**TO THE EDITOR:** Orthotopic liver transplantation has been performed in at least 10 patients who have maple syrup urine disease (MSUD).<sup>1–4</sup> In the first patients, transplantation was for nonmetabolic reasons (hepatic failure with hepatitis A<sup>1</sup> and hypervitaminosis A<sup>2</sup>). In all patients, there was marked improvement in dietary protein tolerance and no

evidence of any decompensation episodes during follow-up extending 10 years.<sup>3</sup> Because the long-term outcome and effect on neurologic development remain to be identified, orthotopic liver transplantation remains a controversial therapy.<sup>1</sup> With recent reports of success, it has been established as an option for patients with MSUD whose condition fails to respond to medical management. Many patients with approved indications for orthotopic liver transplantation die before grafts become available (in 2004, approximately 18,000 patients were on the waiting list for transplants, 6168 of whom received them).

We performed an orthotopic liver transplantation in a 25-year-old man (Patient 1) with MSUD and frequent episodes of decompensation, including six hospitalizations over 18 months for ataxia and plasma levels of leucine higher than 1000  $\mu\text{mol}$  per liter (13 mg per deciliter). We used his liver as a domino graft (the use of an explanted liver from a patient with a metabolic disease as a graft in another patient in need of a transplant) in a 53-year-old man (Patient 2) with hepatitis C and hepatocellular carcinoma, who had low priority on the transplant waiting list and was unlikely to survive until routine procurement. Both transplantations were performed “piggyback,” with the domino graft reconstructed with caval segments from a cadaveric donor; accordingly, neither patient required venovenous bypass. Plasma levels of amino acids (Table 1) and apparent whole-body leucine oxidation levels<sup>5</sup> (low levels indicating MSUD) were measured before and after transplan-

**Table 1. Plasma Levels of Amino Acids before and after Liver Transplantation.\***

Patient	Leucine	Isoleucine	Valine	Alloisoleucine
	<i>micromoles per liter</i>			
Patient 1†				
Before transplantation	544±234	240±135	286±118	250±67
After transplantation	203±36	110±25	280±54	16±7
Patient 2‡				
Before transplantation	183±15	90±9	286±21	0
After transplantation	179±37	93±23	270±50	0
Patient 3§				
Before transplantation	092	38	141	0
After transplantation	112	34	146	0
Normal range	75–175	36–98	141–317	0

\* Patient 1 had maple syrup urine disease. Patient 2 had hepatitis C and hepatocellular carcinoma and received a liver graft from Patient 1. Patient 3 was a control who had hepatitis C and hepatocellular carcinoma and received a liver transplant from a cadaveric donor. Plus–minus values are means  $\pm$ SD.

† For Patient 1, amino acid levels were measured in 21 samples before transplantation and 28 samples after transplantation.

‡ For Patient 2, amino acid levels were measured in 2 samples before transplantation and 26 samples after transplantation.

§ For Patient 3, amino acid levels were measured in one sample before and after transplantation.