impairment or normal functional independence. (Debray F-G, Lambert M, Chevalier I et al. Long-term outcome and clinical spectrum of 73 pediatric patients with mitochondrial diseases. **Pediatrics** April 2007;119:722-733). (Respond: Grant A Mitchell MD, Medial Genetics Division, CHU Sainte-Justine, 3175 Cote Sainte-Catherine, Montreal, Quebec, Canada H3T 1C5).

COMMENT. A high level of suspicion for mitochondrial disease (MD) is recommended in the evaluation of patients with unexplained organ dysfunction. "Any age, any symptom, any organ" is an appropriate description of MD (Munnich A et al. 1996; cited by Debray et al). In diagnosis of MD, the above authors propose initial least-invasive techniques such as fibroblast culture, and blood DNA testing for specific etiologies. Muscle and/or liver biopsy should be deferred, pending the results of fibroblast culture and blood DNA. In a large series of MD patients published in 1995 (Jackson MJ et al. **Brain** 1995;118:339-357), the most useful confirmatory diagnostic test was histochemical analysis of muscle. Elevated plasma and CSF lactate are good indicators of MD (an especially high plasma lactate is a predictor of poor outcome), but specific etiologies require molecular diagnosis.

BRAIN TUMORS

OPTIC PATHWAY GLIOMAS IN NEUROFIBROMATOSIS 1 (NF-1)

Advances in the pathophysiology and clinical behavior of NF-1 associated optic pathway gliomas (OPG) made over the past 10 years are examined, and evidence-based recommendations for diagnosis and management are proposed by researchers from Children's Memorial Hospital, Chicago; St Thomas's Hospital, London; Children's Hospital of Philadelphia; University of Pennsylvania School of Medicine, Philadelphia; and Washington University School of Medicine, St Louis, MO, The initial diagnostic and management guidelines proposed by a task force in 1997 (Listernick R et al. **Ann Neurol** 1997;41:143-149) are extended, and unanswered questions are addressed. OPG may arise de novo or progress later in childhood or adulthood. The prevalence rate of OPG with NF-1 is estimated at 15% (between 5 and 25%). Children 6 years and younger are at greatest risk, but older children and adults with NF-1 are susceptible. Visual signs are present at the time of diagnosis in 59% of patients with OPG, including decreased visual acuity, proptosis, and nystagmus. Precocious puberty, manifested initially by accelerated growth, occurred in patients older than 6 years at diagnosis, and in 12-40% of those with chiasmal OPG. Progressive disease leading to treatment occurs in 35-52% cases, but risk factors for progression are not clearly defined. Late presentation at 10 years or older may correlate with progressive disease requiring treatment.

A synopsis of recommendations for diagnosis and management of NF-1 and OPG:

1. Annual complete eye exam for children with NF-1 younger than 8 years.
2. Eye exam every 2 years until 18 years of age, for children >8 years. No role for VEP.
3. Yearly height and weight in all NF-1 children, to detect sign of precocious puberty.
4. MRI of brain and orbits, and repeated eye exams, once abnormal eye exam recorded and OPG diagnosed, and at varying intervals (3 months or longer) thereafter.

5. Treatment should be deferred until clear evidence of progression. Chemotherapy is first-line therapy. Radiation is not recommended. Surgery is considered with excessive proptosis and blindness. (Listernick R, Ferrier RE, Liu GT, Gutmann DH. Optic pathway gliomas in neurofibromatosis-1: Controversies and recommendations. **Ann Neurol** March 2007;61:189-198). (Respond: David H Gutmann MD PhD, Department of Neurology, Washington University School of Medicine, 660 South Euclid Ave, Box 8111, St Louis, MO 63110).

C OMMENT. In a prospective, longitudinal study at Children's Memorial Hospital, Chicago, OPGs were found in 19% of 176 children with NF-1 who had CT or MRI at a median age of 4.1 years (Listernick R et al. **J Pediatr** 1994;125:63-66). OPG had not developed at follow-up in those not receiving an MRI. Eye lesions such as proptosis or glaucoma were most common in younger children (median age 1.9 years). OPG was asymptomatic at time of diagnosis in 76%, and eye findings were normal in 64%. At follow-up of 0.2-8 years, only 3 (9%) showed progressive tumor growth on MRI or deteriorating vision after diagnosis. Patients with symptomatic OPG were all diagnosed before age 6 years. Tumor growth after 6 years is unusual. Progressive abnormalities and precocious puberty occurred only with chiasmatic OPG. In accord with the present recommendations, serial eye exams in young children with NF-1 but not MRI were advocated in this earlier report.

BRAIN MALFORMATIONS

CHIARI TYPE I MALFORMATION AFTER RADIATION THERAPY

The development of a Chiari I malformation and cervical syringomyelia, 1.5 years after radiation for a malignant, rhabdoid tumor of the neck at 3 years of age, was diagnosed by MRI after the patient had 2 episodes of unresponsiveness. The radiation therapy followed chemotherapy and surgical exploration of the mass that involved the cranial base. The tumor could not be resected because it surrounded the internal carotid artery. The Chiari malformation was treated by suboccipital decompressive craniectomy and C1 laminectomy with duraplasty, and no further syncopal episodes occurred during a follow-up of 5.5 years. Postoperative MRIs indicated reconstitution of the CSF at the foramen magnum, ascent of the cerebellar tonsils, and resolution of the presyrinx state of the cervical cord. One previous case report in the literature describes a Chiari I malformation in a child after fractionated radiation therapy to the anterior cranial base. (Hoffman CE, Lis E, Wolden SL et al. Symptomatic Chiari I malfomation after radiation therapy in an infant: Case report. **Neurosurgery** April 2007;60:E782).

COMMENT. Known causes of acquired Chiari I malformation cited by the authors include lumboperitoneal shunts, craniosynostosis, rickets, supratentorial mass, spinal drainage, and acromegaly. A case of a 13-year-old girl whose Chiari I malformation presented after head trauma is also worthy of note (Mampalam TJ et al. **Neurosurgery** 1988;23:760-762). Radiation exposure is an additional acquired cause. Children who undergo radiation for medulloblastoma or brainstem tumor might also be observed for Chiari I malformation. Syncope described in the above patient is mentioned as cough syncope syndrome in a previous publication on Chiari malformations (Ireland PD et al. **Arch Neurol** 1996;53:526-531).