series of cases, congenital myasthenic syndrome (CMS) was distinguished from the neonatal transient form by absence of MG in the mother, less severe generalized muscle weakness, and a poor response to anticholinesterase treatment. Ptosis, ophthalmoplegia and weakness of facial and masticatory muscles persist through childhood in to adult life. The family history may be positive for MG in siblings and cousins.

Since this clinical description of the congenital myasthenic syndrome in 1960, and the subsequent discovery of an autoimmune mechanism for MG, the absence of antibodies against the acetylcholine receptor further delineate the congenital syndrome. Engel and his colleagues have identified several CMS subtypes, including Lambert-Eaton CMS, end-plate AchE deficiency, slow and fast channel syndromes, and AchR deficiency. (Engel AG, Ohno K. **Adv Neurol** 2002;88:203-215; **Muscle & Nerve** 1993;16:1284-1292). See **Progress in Pediatric Neurology III**, PNB Publishers, 1997;346-349, for further case reports and commentaries on CMS. The identification of subtypes of the CMS is complex and requires studies of the kinetics of acetylcholine receptors (AchR), and ultrastructure of the endplate. Nevertheless, with an increased awareness of the syndrome, a diagnosis can be determined on clinical and neurophysiological grounds, leading to earlier treatment intervention and better genetic counseling.

TREATMENT OF AUTOIMMUNE MYASTHENIA GRAVIS

A treatment protocol for autoimmune myasthenia gravis (MG), patients sero-positive for AChR antibodies, is proposed from the University of California, Davis, CA. The greatest advances in outcome have resulted from therapies that reduce the autoimmune attack or modify its effect on the nicotinic acetylcholine receptor (AChR) and prevent damage to the structure of the endplate. More effective symptomatic treatment, including critical care and the use of cholinesterase inhibitors, has contributed to an improved prognosis. The initial therapy is determined on an individual cost/benefit ratio. Cholinesterase inhibitor drugs, first introduced in 1934 (Walker MB. **Lancet** 1934;1:1200-1201), and especially pyridostigmine, are usually effective early in the disease course or in mild cases. Tolerance develops and eventually the effect lessens even at maximal, frequently toxic, doses. The more effective treatments directly target the autoimmune response, reducing the likelihood of endplate damage. Immuno-directed treatment should begin when an early spontaneous remission is not obtained with pyridostigmine. High-dose daily prednisone is started, and short-term IV Ig or plasmapheresis is added if symptoms worsen in the first 2 weeks, or given concomitantly. Tapering of the prednisone is begun slowly when remission is established. Later, a steroid-sparing agent (eg azathioprine) and a bisphosphonate to prevent osteoporosis are added to the low-dose prednisone. The minimum amount of prednisone to maintain a remission is the goal in management. Thymectomy also acts as a steroid-sparing treatment and facilitates remission. Uncontrolled studies show that the earlier the operation, the better the result, and newer surgical techniques may carry less risk. The goal for optimal therapy is an increased specificity of immune-directed agents that reduce the antibodies or T-cell responses to the AChR, leaving other immune responses intact. (Rishman DP, Agius MA. Treatment of autoimmune myasthenia gravis. **Neurology** December (2 of 2) 2003;61:1652-1661). (Reprints: Dr David P Richman or Mark A Agius, University of California, One Shields Avenue, Davis, CA 95616).

COMMENT. The incidence of sero-positive acetylcholine receptor (AChR) binding antibodies is lower in juvenile-onset myasthenia gravis compared to adult-onset case-studies; 63% (Afifi and Bell 1993) v 85% (Richman and Agius 2003), respectively. In a series of 30 juvenile MG cases studied in Turkey (Anlar et al, 1996) AchR antibodies were positive in 34%, and response to treatment was not significantly different in seropositive cf seronegative cases. None of the antibody-positive cases was in remission. Myasthenic crises occurred in 33%. In a current report from Mexico (Guillermo GR et al. **Acta Neurologica Scandinavica** March 2004;109:217-221) the response to thymectomy was evaluated in 71 patients with MG of all ages (14 [20%] seronegative, and 57 [80%) seropositive). The response was similar in the two groups, with no differences in prognosis between the seronegative and seropositive patients.

In the Afifi and Bell, 1993 University of Iowa series of 27 juvenile MG cases, ocular myasthenics responded to pyridostigmine alone, while generalized myasthenics required corticosteroids and/or thymectomy. Those with normal thymus had a higher rate of remission than patients with thymic hyperplasia. Thymectomized patients had a 35% remission rate. In a series of 35 juvenile myasthenics (Millichap and Dodge 1960), 43% had respiratory difficulties, 40% of these requiring tracheostomy. Twenty-one underwent thymectomy and of these 18 (86%) showed complete or partial remission. Complete remission without the need for drug therapy was obtained in 29% of thymectomized compared to 14% of patients treated only with cholinergic drugs. Rodriquez et al, in 1983, found a cumulative 15-year remission rate of 55% following thymectomy, compared to a spontaneous remission rate of 30% in myasthenic children. The remission rate was higher following thymectomy performed within 12 months of the onset of symptoms. The reported high incidence of myasthenic crises and respiratory difficulties, and the satisfactory results of early thymectomy emphasize the importance of prompt introduction of immune-directed management when spontaneous remission is delayed.

MYOPATHY IN CRITICALLY ILL CHILDREN

The incidence of muscle weakness was determined in 830 children (3 months to 17 years of age) admitted for >24 hours to the intensive care unit over a 1-year period at the Hospital for Sick Children, Toronto, Canada. Generalized weakness developed in 14 (1.7%), and 4 failed repeated attempts to extubate. The age distribution was bimodal, with 3 under age 3 years and 11 age 10 or older. Eleven had multiple organ dysfunction and 9 had sepsis. Most received corticosteroids, neuromuscular blocking agents, or aminoglycoside antibiotics. Eight of the 14 were organ or bone marrow transplant recipients. EMG findings in 5 were abnormal and myopathic in 4, with short-duration, low-amplitude motor unit potentials and small polyphasic potentials. Nerve conduction studies done in 7 patients showed decreased compound muscle action potentials in 4, normal findings in 2, a compressive neuropathy in 1, and a demyelinating polyneuropathy in 1. Serum creatine kinase was elevated to 2 to 100 times the upper limit of normal in 3. A histological diagnosis of acute quadriplegic myopathy was made in all 3 patients with muscle biopsy. Three died; and in survivors, weakness persisted for 3 to 12 months after discharge. (Banwell BL, Mildner RJ, Hassall AC et al. Muscle weakness in critically ill children. **Neurology** December (2 of 2) 2003;61:1779-1782). (Respond: Dr BL Banwell, Department of Pediatrics (Neurology), Hospital for Sick Children, 555 University Ave, Toronto, Ontario, Canada M5G 1X8).