COMMENTARY. The majority of infants exposed to the thiamine deficient formula in infancy were asymptomatic but a small minority developed encephalopathy and/or cardiomyopathy that were sometimes fatal. Infants who survive thiamine-deficient encephalopathy have a poor prognosis, with motor and cognitive impairment and epilepsy. Thiamine deficiency in a developed country is unusual, but as many as 12.5% of a population of critically ill Canadian children were found to have significant thiamine deficiency [1]. Wernicke encephalopathy and beriberi during total parenteral nutrition was attributed to multivitamin infusion shortage in a patient with Crohn's disease in California [2]. Almost immediately following intravenous thiamine, the hypotension resolved and the following day she no longer had diplopia, and the ophthalmoplegia had improved. Thiamine deficiency should be considered in patients with malabsorption, malnutrition, and malignancies.

References.
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NEUROMUSCULAR DISORDERS

CONGENITAL MYASTHENIC SYNDROME WITH AGRIN MUTATIONS

Investigators at Newcastle University, UK, and Hopitaux de Paris, France, report 5 patients from 3 unrelated families with a strikingly homogeneous clinical entity combining congenital myasthenia with distal muscle weakness and atrophy resembling a distal myopathy. MRI and neurophysiological studies were indicative of a mild distal myopathy, but decrement in response to 3 Hz repetitive nerve stimulation suggested a neuromuscular transmission defect. Post-exercise increment up to 285% in distal limb muscles was compatible with presynaptic congenital myasthenic syndrome. Immunofluorescence and ultrastructural analyses of muscle end-plate regions showed synaptic remodelling with denervation-reinnervation. Whole-exome sequencing identified five new recessive mutations in the gene encoding agrin. These findings expand the spectrum of congenital myasthenic syndromes due to agrin mutations. (Nicole S, Chaouch A, Torbergsen T, et al. Agrin mutations lead to a congenital myasthenic syndrome with distal muscle weakness and atrophy. **Brain** 2014 Sep;137(Pt 9):2429-43).

COMMENTARY. The authors recommend examination of patients with apparent distal myopathy for a neuromuscular transmission disorder and for agrin mutations.

Prevalence of congenital myasthenia. The UK prevalence of genetically confirmed congenital myasthenic syndrome (CMS) is 9.2 per million children under 18 years of age. CMS is equally prevalent in girls and boys. CHRNE, RAPSN and DOK7 are the most commonly identified mutations. Prevalence varies across geographical regions in England (2.8 to 14.8 per million). The mean incidence of antibody-positive autoimmune myasthenia was 1.5 per million children per year. Girls were affected more frequently than boys [1].

Investigators at the John Radcliffe Hospital, University of Oxford, UK, provide a review with updates of new mutations of known CMS causative genes and treatment strategies. The use of salbutamol and ephedrine alone or combined with physostigmine or 3,4-DAP is reported to benefit various CMS subtypes [2].

Of 51 patients attending the myasthenia clinic at the Massachusetts General Hospital, Boston, in 1958–1960, 35 were the juvenile type, 10 the transient neonatal type, and 6 a congenital myasthenia syndrome, under-recognized as a separate phenotype at that time [3].

References.
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SEIZURE DISORDERS

MOTOR CO-ACTIVATION OF JUVENILE MYOCLONIC EPILEPSY IN SIBLINGS

Investigators at UCL Institute of Neurology, Queen Square, London, UK, used functional magnetic resonance imaging to study the effect of cognitive effort during a working memory task as a trigger of myoclonic jerks in 15 unaffected siblings (10 female; age range 18-65 years, median 40 yrs) of 11 patients with juvenile myoclonic epilepsy (6 female; age range 22-54 yrs, median 35). fMRI activations were compared with 20 age- and gender-matched healthy control subjects.

Unaffected siblings showed abnormal primary motor cortex and supplementary motor area co-activation with increasing cognitive load, as well as increased task-related functional connectivity between motor and prefrontal cognitive networks, with a similar pattern to that in patients with JME ($P<0.001$). This finding in unaffected siblings suggests a mechanism for impairment of frontal lobe functions in both patients and siblings, independent of effects of medication or seizure, an endophenotype of JME. (Wandschneider B, Centeno M, Vollmar C, et al. Motor co-activation in siblings of patients with juvenile myoclonic epilepsy: an imaging endophenotype? **Brain** 2014 Sep;137(Pt 9):2469-79).

COMMENTARY. The abnormal frontal lobe function demonstrated by fMRI in adults with JME and their siblings is also demonstrated in children.

Neurodevelopment in new-onset juvenile myoclonic epilepsy. Investigators at Irvine University, CA, studied the maturation of cognitive and brain development in 19 children with new-onset JME in the first 2 years after diagnosis and 57 healthy controls. Abnormal patterns of brain development affecting frontoparietotemporal regions, as assessed by MRI, were evident in children with JME and included attenuation of age-related decline in cortical volume, thickness, and surface area. Children with JME have abnormal structural brain development and impaired cognitive development early in the course of the epilepsy [1].