dipstick in fresh urine, and elevated urine and plasma s-sulfocysteine. In infants with HIE these markers are absent and the plasma uric acid is elevated. On diffusion weighted imaging within 1 week after birth, patients with HIE show an increased signal in all cortical and subcortical areas, whereas in patients with MoCoD these findings are not uniform.

In addition to HIE, infants with MoCoD may present with neonatal hyperekplexia, unresponsive to clonazepam [1], and as pyridoxine-dependent epilepsy [2]. Two siblings with pyridoxine-responsive seizures and increased urinary excretion of a-AASA were diagnosed with MoCoD and a mutation in the MOCS2 gene. A trial of pyridoxine is recommended in patients with MoCo or sulfite oxidase deficiencies [2].

References.
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DEGENERATIVE DISEASES

ALZHEIMER GENE LINKED TO BRAIN DEVELOPMENT

Investigators at Brown University, Providence, RI, and other imaging genetic centers in the US, compare MRI measurements of white matter myelin water fraction (MWF) and gray matter volume (GMV) in healthy infant carriers and noncarriers of the apolipoprotein E (APOE) e4 allele, the major susceptibility gene for late-onset Alzheimer disease (AD). Infant e4 carriers, ages 2–25 months, had lower MWF and GMV measurements than noncarriers in precuneus, posterior/middle cingulate, lateral temporal, and medial occipitotemporal regions, areas affected by AD, whereas these measures were greater in frontal regions, and an attenuated relationship between MWF and age was evident in posterior white matter regions. The study demonstrates some of the earliest brain changes associated with a genetic predisposition to AD, and the role of APOE in normal human brain development and AD pathology. (Dean DC 3rd, Jerskey BA, Chen K, et al. Brain differences in infants at differential genetic risk for late-onset Alzheimer disease: a cross-sectional imaging study. **JAMA Neurol** 2014 Jan 1;71(1):11-22).

COMMENTARY. In a comment (Alzheimer gene APOE e4 linked to brain development in infants), Drs McDonald and Krainc of Northwestern University Feinberg School of Medicine find that this study highlights compelling evidence of the influence of the APOE e4 allele on brain structure in young infants. It remains to be determined whether these neurodevelopmental observations specifically influence AD pathogenesis in later life [1]. In an editorial, Growdon JH, and Hyman BT allude to data emphasizing effects of B-amyloid on neural plasticity during brain development, a peptide elevated in Down syndrome where trisomy 21 leads to an extra copy of the amyloid precursor protein and early onset AZ [2].

A study of effect of age and APOE genotype on neuropathological changes in Down syndrome hippocampal formation found that individuals who had inherited the APOE e4 genotype contained more than twice the amyloid burden of non-carriers. The level of amyloid deposition in Down syndrome patients is higher than in sporadic AZ

disease [3]. Inheritance of the APOE e4 genotype is an independent risk factor for developing higher levels of amyloid accumulation.

References.
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RIBOFLAVIN IN BROWN-VIALETTO-VAN LAERE SYNDROME

Investigators at Great Ormond Street Hospital, London, UK, and multiple centers internationally report the response to high-dose oral riboflavin therapy in 18 patients from 13 families with mutations in SLC5ZA2, encoding riboflavin transporter RTVT2, a new causative gene for Brown-Vialetto-Van Laere syndrome (BVVLS), a progressive neurodegenerative disorder leading to death in childhood. BVVLS is characterized by cranial neuropathies, pontobulbar palsy, sensorimotor neuropathy manifesting with sensory ataxia, weakness of upper limbs and axial muscles, with preserved strength of lower limbs, optic atrophy, sensorineural hearing loss, and respiratory insufficiency. Riboflavin therapy resulted in significant sustained clinical and biochemical improvement in 2 patients and preliminary response in 13 patients. (Foley AR, Menezes MP, Pandraud A, et al. Treatable childhood neuronopathy caused by mutations in riboflavin transporter RFVT2. **Brain** 2014 Jan;137(Pt 1):44-56).

COMMENTARY. BVVLS is a similar disorder to Fazio Londe syndrome caused by subtly different mutations of the same gene, and with the additional clinical feature of sensorineural deafness [1][2]. Diagnosis requires mutation analysis of transporter genes. The simple treatment with riboflavin supplementation may halt progression of both neurodegenerative disorders. An invited comment by Dr. John Wilson, Emeritus Chief of Neurology, Great Ormond Street Hospital, London, UK, and an authority on Fazio-Londe disease [2], is paraphrased as follows: “as our understanding of the basic concepts of disease become more complex, so we are lead to a beautiful simplicity (in the form of vitamin therapy) that brings light into dark places.” How many similar degenerative diseases may in the future be found responsive to a simple vitamin?

References.
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AUTISM SPECTRUM DISORDERS

ABNORMAL MOTOR FUNCTION AND AUTISM

Investigators from Albert Einstein College of Medicine, Bronx, NY, recorded the gait characteristics and prevalence of toe walking, the range of passive joint mobility, and age at walking in children with DSM IV autism spectrum disorders (ASDs) and in age- and gender-matched healthy peers (mean age 4 years 6 months, range 22 months – 10