craniocervical and systemic, should be considered in pediatric stroke when fibromuscular dysplasia is suspected. In a case-report of a 12-year-old boy with ischemic stroke caused by intracranial fibromuscular dysplasia, preliminary imaging investigations included CT and MR angiography, but a definitive diagnosis was reached following a conventional cerebral angiogram (Shea KJ, et al. **Pediatr Neurol** 2011 Mar;44(3):214-7).

MYOPATHIES

CONGENITAL RYR1-ASSOCIATED MYOPATHIES

Investigators from the Children's Hospital of Philadelphia, NINDS, and other centers in the US and France, report a series of 11 patients with severe neonatal RYR1-associated myopathy confirmed by genetic testing. Clinical features included decreased fetal movements, hypotonia, poor feeding, respiratory impairment, arthrogryposis, ophthalmoplegia, and femur fracture and hip dislocation at birth. RYR1 mutations were dominant in 4 patients and recessive in 7. Muscle ultrasound in 6 patients showed relative sparing of the rectus femoris muscle. All patients with dominant mutations had classic central cores on muscle biopsy; patients with recessive mutations showed histologic heterogeneity. (Bharucha-Goebel DX, Santi M, Medne L, et al. Severe congenital RYR1-associated myopathy. The expanding clinicopathologic and genetic spectrum. **Neurology** 2013 Apr 23;80(17):1584-9). (Resp.: Dr Bonnermann. Carsten.bonnermann@nih.gov).

COMMENT. Classic central core disease (CCD) due to mutations in the RYR1 gene typically presents with mild to moderate hypotonia, developmental delay, proximal muscle weakness, and occasional hip dislocation. The present series of patients has a more severe neonatal RYR1-associated myopathy caused by both dominant and recessive mutations of the gene and expands the clinical spectrum of central core disease. Sparing of the rectus femoris muscle on ultrasound should prompt evaluation for RYR1-associated myopathy.

Subtypes of congenital myopathies in UK. Of 54 patients with muscle biopsies available, diagnosed over a 5-year period at Great Ormond Street Hospital for Children, London, 29 (54%) had a core myopathy (central core disease, multi-minicore disease), 9 (17%) had nemaline myopathy, 7 (13%) had myotubular/centronuclear myopathy, 2 (4%) had congenital fibre type disproportion, 6 (11%) had isolated type 1 predominance and 1 (2%) a mixed core-rod myopathy. Of 44 with a genetic diagnosis, RYR1 was mutated in 26 (59%). The genetic defect was unidentified in 1/3 of congenital myopathies (Maggi L, Scoto M, Cirak S, et al. **Neuromuscul Disord** 2013 Mar;23(3):195-205).

RYR1 MUTATIONS, EXERTIONAL MYALGIA AND RHABDOMYOLYSIS

Investigators at Guy's & St Thomas' Hospital, London, UK, and other centers sequenced RYR1 in 39 unrelated families with rhabdomyolysis and/or exertional myalgia and identified 9 heterozygous RYR1 mutations in 14 families, 5 of them previously associated with malignant hyperthermia (MH). Index cases presented from 3 to 45 years

with rhabdomyolysis, with or without exertional myalgia (n=12), but no or little associated weakness; CK levels were markedly increased during episodes. Rhabdomyolysis was triggered by exercise and heat, viral infection and drugs. Familial RYR1 mutations were confirmed in relatives. (Dlamini N, Voermans NC, Lillis S, et al. Mutations in RYR1 are a common cause of exertional myalgia and rhabdomyolysis. **Neuromuscul Disord** 2013 Apr 28. pii: S0960-8966(13)00094-1 [Epub ahead of print]). (Response: Dr H Jungbluth, Children's Neurosciences Centre, St Thomas' Hospital, London SE1 7EH, UK. E-mail: Heinz.jungbluth@ghstt.nhs.uk).

COMMENT. Patients presenting with unexplained rhabdomyolysis and/or exertional myalgia and other family members should be tested for RYR1 mutations.

Malignant hyperthermia susceptibility of core myopathies. Due to their genetic linkage to mutations in the ryanodine receptor gene (RYR1), core myopathies (in particular, central core disease) carry a high risk of malignant hyperthermia susceptibility during anesthesia. (Brislin RP, Theroux MC. **Paediatr Anaesth** 2013 Apr 25 [Epub ahead of print]).

GLUCOCORTICOIDS FOR DUCHENNE MUSCULAR DYSTROPHY

Investigators at the Dubowitz Neuromuscular Centre, Great Ormond Street Hospital, and other centers in the UK, conducted a prospective longitudinal study across 17 neuromuscular centers in the UK of 360 boys aged 3-15 years with Duchenne muscular dystrophy who were treated with daily or intermittent (10 days on/10 days off) prednisolone for a mean duration of 4 years. The median loss of ambulation was 12 years in intermittent and 14.5 years in daily treatment; height restriction for intermittent versus daily regimen was 1.57 ($p=0.13$) and the median age for loss of ambulation did not differ. Boys on an intermittent regimen declined faster than those receiving daily treatment ($p<0.001$). Moderate to severe side effects were more common in the daily regimen, including Cushingoid features, hyperactive behavior and hypertension. Body mass index mean score was higher and height restriction was more severe in the daily regimen than in the intermittent regimen. (Ricotti V, Ridout DA, Scott E, et al. Long-term benefits and adverse effects of intermittent versus daily glucocorticoids in boys with Duchenne muscular dystrophy. **J Neurol Neurosurg Psychiatry** 2013 Jun;84(6):698-705). (Respond: Dr Francesco Muntoni, Dubowitz Neuromuscular Centre, UCL Institute of Child Health, 30 Guilford St., London WC1N 1EH, UK; E-Mail: f.muntoni@ucl.ac.uk).

COMMENT. Glucocorticoids are recommended in the international standards of care guideline for DMD and benefits are confirmed by Cochrane systematic reviews (Bushby K, et al. **Neuromuscul Disord** 2004 Sep;14(8-9):526-34). The most effective treatment postulated is prednisolone/prednisone or the equivalent deflazacort (Manzur AY, et al. **Cochrane Database Syst Rev** 2008 Jan 23;(1):CD003725). The intermittent and daily regimens are equally effective in gain of function until 6 years of age. After age 7 years, boys on an intermittent regimen decline more rapidly than those on daily therapy. Side effects are a greater problem with daily compared to intermittent therapy.