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NEUROMUSCULAR DISORDERS

MOLECULAR DIAGNOSIS OF CHARCOT-MARIE TOOTH DISEASE

The frequency of mutations in certain genes in 153 unrelated patients with Charcot-Marie-Tooth disease (CMT) was determined by DNA sequencing before clinical testing at the Departments of Molecular and Human Genetics and Pediatrics, Baylor College of Medicine, Houston, TX, and other centers. Among this group not selected for a peripheral demyelinating neuropathy phenotype, 79/153 (52%) had a duplication of 17p12 (CMT1A duplication), 11 had a connexin 32 mutation (GJB1), 5 a myelin protein zero mutation (MPZ), 5 a peripheral myelin protein 22 mutation (PMP22), and 50 (33%) had no identifiable mutation. Several previously unreported mutant alleles were identified. Molecular diagnosis is considered a necessary adjunct for clinical diagnosis and management of inherited and sporadic neuropathy. (Boerkoel CF, Takashima H, Garcia CA et al. Charcot-Marie-Tooth disease and related neuropathies: mutation distribution and genotype-phenotype correlation. *Ann Neurol* February 2002;51:190-201). (Respond: Dr James R Lupski Department of Molecular and Human Genetics, One Baylor Plaza, Room 604B, Houston, TX 77030).

COMMENT. Primary peripheral demyelinating neuropathies include CMT type 1, Dejerine-Sottas syndrome, congenital hypomyelinating neuropathy, and hereditary neuropathy with pressure palsies (Lupski, Garcia, 2001). Fifteen genetic loci and 7 genes are associated with these disorders. Both dominant and recessive mutant alleles are described. Primary peripheral axonal neuropathies also present as a severe form in infancy and a mild adult-onset form, including CMT2 and giant axonal neuropathy. These disorders are associated with 11 genetic loci, 5 genes and mutations. CMT is genetically and clinically heterogeneous, with wide variability of phenotypic features and disease severity within and among families. Forty per cent of patients presenting with a chronic peripheral neuropathy have hereditary disease, and half of these patients (20%) will have CMT1A duplication of 17p12 as the cause. One third are sporadic and have unidentified mutations.

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