

involved. Serum CPK was normal or slightly elevated and muscle biopsy changes were nonspecific. Subsequent reports included slightly variable manifestations, some children showing highly elevated CPK, up to 15 times normal, and muscle biopsies with dystrophic, necrotic and degenerating changes. Genetic tests find collagen type VI as the defective protein in Bethlem myopathy. The present study defines further variations in the clinical manifestations of the disease, with onset of symptoms at or even before birth, and a slowly progressive course in middle to late adulthood.

ATTENTION DEFICIT DISORDER

METHYLPHENIDATE AND CLONIDINE COMBINATION DEBATED

The Debate Forum of the J Am Acad Child Adolesc Psychiatry, in the May 1999 issue, addresses the concern regarding reported risk of fatalities in children receiving clonidine in combination with methylphenidate (MPH) for the treatment of ADHD with comorbid aggression, Tourette syndrome, or sleep disturbance.

Swanson JM, Connor DF, and Cantwell D consider the combination ill-advised, pending the results of controlled studies at the NIMH and the University of Massachusetts, and citing "the absence of clear demonstration of efficacy, and in the face of plausible but not-yet-validated serious side effects of the combination."

Wilens TE and Spencer TJ support the use of this combined therapy as a clinically sound medication option, citing promise in open trials and growing popularity with "widespread clinical use." These authors find the evidence for clonidine/MPH fatalities in 4 reported cases weakened by complicating factors, including congenital cardiac malformation. They do agree, however, on the need for further monitoring and study of the safety of the combination.

Swanson and associates, in a further negative rebuttal, respectfully disagree with the acceptance of uncontrolled trials as evidence for cited efficacy of the clonidine/MPH combination. They emphasize the relatively high (5%) drug-related electrocardiographic irregularities reported with clonidine, and the dangers of rising and falling levels of clonidine and MPH and their effects on cardiac function. (Debate Forum. Combining methylphenidate and clonidine. J Am Acad Child Adolesc Psychiatry May 1999;38:614-622).

COMMENT. This exchange of views regarding the use of combined methylphenidate and clonidine therapies for ADHD with comorbid aggression, Tourette syndrome, or sleep disturbance is very informative, but the opposing opinions of experts may leave the practicing neurologist or psychiatrist in a dilemma when faced with the decision to risk a possible fatality as a result of prescribed treatment. I tend to agree with the Swanson team that drug combinations with reported serious, and sometimes fatal, cardiac side effects should be withheld pending definitive controlled studies proving safety and efficacy. (see Millichap JG. Attention Deficit Hyperactivity and Learning Disorders. Chicago, PNB Publishers, 1998;p187-9).

Methylphenidate and behavior modification had beneficial effects on ADHD symptoms and comorbid ODD in a randomized, placebo-controlled study of 16 children studied at the Western Psychiatric Institute and Clinic, University of Pittsburgh Medical Center (Kolko DJ, Bukstein OG, Barron J. J Am Acad Child Adolesc Psychiatry May 1999;38:578-586).