Mitochondrial calcium overload has been suggested as the general mechanism for cell necrosis in muscle disease.² There is excess calcium entry into the cell as well as a failure of calcium removal. Prostaglandin E1 is well known for its bell-shaped dose response curve with very low and very high levels having the same effect.³ Very high levels of Prostaglandin E1 can inhibit Thromboxane A2 (TXA2) activity which is involved in both calcium release and calcium removal. A substantial overproduction of Prostaglandin E1 has been proposed to exist in myotonic dystrophy as it explains the presence in myotonia of weakness, reproductive abnormalities, reduced glucose tolerance, increased metabolic effect of growth hormone, and anatomical motor end plate abnormalities.⁴ Finally, lithium inhibits the production of Prostaglandin E1 by an opiate-like effect and has, in fact, been suggested by Horrobin⁴ to improve the clinical state in myotonic dystrophy.

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Brumback and Gerst reply

We appreciate the comments by Dr Backon. Although it is attractive to hypothesise that lithium-mediated changes in prostaglandins modified the myotonia, we suggest that a lithium effect on other "second messengers" such as adenine and guanine nucleotides^{1,2} might also alter myotonic phenomena. Prostaglandins apparently do have a role in calcium regulation, and calcium overload has been proposed as a mechanism of muscle fiber destruction in certain neuromuscular diseases;¹ however, necrosis is not a feature of myotonia congenita (the disease in our

reported case), and atrophy and myofibrillar network disturbances are the major histologic changes in myotonic dystrophy.^{4,5} Also, in myotonia congenita the disturbance is confined to muscle, while myotonic dystrophy is a multisystem disorder. The 20,25-diazacholesterol model of myotonia appears to be more analogous to myotonia congenita than to myotonic dystrophy.⁶

We have previously postulated that the disturbance underlying myotonic dystrophy is abnormal function of cellular aminergic and peptidergic receptors.⁷ We originally proposed an intrinsic defect in the receptor mechanism itself, but it is equally possible that abnormality in a second messenger system could explain the symptomatology of myotonic dystrophy. Additionally, we have found that patients with myotonic dystrophy manifest significant neuropsychiatric impairment due to chronic depression (affective disorder) that is responsive to tricyclic antidepressant pharmacotherapy.⁸⁻¹⁰ Lithium pharmacotherapy has been shown to be beneficial in many patients with primary unipolar depressive illness,¹¹ and it is possible that the depression associated with myotonic dystrophy might also respond to lithium administration.

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