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Intrathecal Baclofen Therapy for Stiff man Syndrome and Progressive Encephalomyelopathy with Rigidity and Myoclonus

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Stiff-man syndrome (SMS) is a rare neurological disorder with progressive and fluctuating muscle rigidity combined with paroxysms of painful spasms that occur spontaneously or in response to unexpected stimuli. Some patients present with a more severe “plus” variant of SMS - termed progressive encephalomyelopathy with rigidity and myoclonus (PERM) - that includes additional neurological symptoms (e.g. ocular motor or sensory disturbances, vertigo or ataxia). Signs of autonomic dysregulation (tachycardia, tachypnea, hyperthermia, mydriasis and profuse sweating) are a potentially fatal danger of the disease. The pathogenesis remains unclear but the majority of SMS/PERM patients have auto-antibodies against the GABA-synthesizing enzyme, glutamic acid decarboxylase (GAD), suggesting an automimmune etiology. Oral GABA-mimetics such as diazepam and the GABA-B agonist, baclofen represent the standard therapy, but disease progression and/or drug tolerance often necessitate the administration of extremely high doses (up to 200 mg/day). Side effects (sedation, dysarthria, vertigo or ataxia) and drug dependence are common. Intrathecal administration of baclofen, a GABA-B agonist, is an effective form of therapy for spasticity patients refractory to oral medications but little is known

about the longterm effects of this form of therapy for SMS/PERM patients. We followed 8 out of 45 SMS/PERM patients (3 with SMS and 5 with PERM) receiving intrathecal baclofen therapy via subcutaneous pump for a period of up to 6 1/2 years. In all patients, intrathecal baclofen therapy resulted in long-lasting improvement of symptoms and increases in overall mobility. However, neither complete remission, nor cessation of disease progression was achieved in any of the patients. The side effects of intrathecal baclofen were milder than those of oral medications, but overdose was found to result in a transient coma-like state. Complications were not uncommon: both catheter dislocation - causing radicular symptoms - and pump malfunction - leading to inaccurate dosage administration and subsequent worsening of symptoms - were observed. More dangerous however, was sudden dosage reduction due to pump failure - a complication that can lead to fatal withdrawal symptoms. SMS/PERM patients receiving intrathecal baclofen therapy should be monitored closely to avoid errors in pump function and programming. In the event of sudden drug cessation, prompt readministration of intrathecal baclofen or intravenous diazepam can be lifesaving.