Mucosal administration of autoantigen (insulin) to animal models has been demonstrated to be effective in preventing autoimmune diabetes. Efficacy is dependent upon the dose and the age at which it is delivered. Because of its low toxicity, mucosal administration of insulin represents an attractive preventive therapy in human. Translation of what is efficacious in animal models is, however, challenging. We have proposed mucosal insulin vaccination as a primary prevention strategy in children on the basis that children with extreme type 1 diabetes risk (> 50%) can be identified and that insulin has been shown to be the first target of autoimmunity in children. Novel, and similar to what is efficacious in mice, is that insulin will be administered when the children are still autoantibody negative in order to induce protective immunity prior to initiation of autoimmunity. The efficacy of increasing doses of mucosal insulin to induce protective immunity will be assessed as the primary end point of the trial. The rationale for primary vaccination and the trial strategy are discussed.