The Environment, Genetics and Age – The Ménage à Trios of Autoimmunity

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Autoimmune diseases, which comprise over 80 clinically distinct conditions, are characterized by autoimmunity, which is the presence of autoantibodies or autoreactive T cells directed against self-structures (autoantigens). These generally incurable disorders are rapidly increasing in recognition throughout the world, yet their heterogeneity and complex etiologies have limited our understanding of their pathogeneses. The mechanisms for the development of autoimmune diseases are not known, however, evidence from many complementary lines of investigation suggests that autoimmune diseases result from the interactions of specific environmental exposures, selected polymorphisms of immune response genes, and aging. While considerable progress has been made in understanding the genetic risk factors for many autoimmune diseases, relatively little information is now available regarding the role of the environment and aging in the development of these illnesses. Nonetheless, the growing evidence for the role of the environment in the development and progression of autoimmune diseases has focused attention on the particular exposures that are likely involved, and the possible mechanisms by which these agents may induce and sustain autoimmune processes. Coordinated multidisciplinary studies of critical developmental windows in the timing of exposures, understanding dose-response relationships, and elucidating mechanisms for disease development in specific phenotypes, genotypes, and after combinations of different exposures, are all needed to elucidate pathogenic processes. Identifying the necessary and sufficient genetic and environmental risk factors for autoimmune diseases holds the promise of preventing illness by minimizing exposure to environmental risk factors in genetically susceptible individuals.