Congressional Update on NIEHS Studies of Silicone Implants August, 2003

Immunology of Silicones

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Although a causal relationship between silicone implants and systemic rheumatic disease remains unproven, a variety of local and systemic adverse events have been reported following silicone implantation. Because risk factors and mechanisms for these adverse events remain undefined, we are utilizing multidisciplinary clinical, pathologic, immunologic and molecular approaches in an attempt to study these problems.

Medical implants containing silicones, especially breast implants, often induce the formation of a complex scar tissue around them called a capsule. These implants have been associated with local inflammation, scarring and painful capsular contraction, but the reasons for these reactions in some women but not others remain unclear.

In an attempt to understand the nature and implications of local and systemic immune responses to silicone implants, we have performed analyses of the inflammatory cells in capsules and at remote sites of disease activity. Microscopic examination of surgically explanted capsules showed much variation in the degree of inflammation. Inflammatory cells consisted of activated macrophages, multinucleated giant cells, T and B lymphocytes, which were often observed surrounding silicone in the capsules. Molecular analyses revealed shared patterns of T cell receptor expression in capsules and multiple tissues collected from silicone implant patients with connective tissue disease. DNA sequence analyses confirmed that identical T cells were present in both left and right silicone capsules and, in some cases, multiple, clinically affected tissues.

These data suggest that shared immune responses may contribute to chronic inflammation in silicone capsules as well as systemic sites of immune pathology. Further studies are needed to understand if silicone contributes directly or indirectly to these undesirable immune responses and how they can be better predicted and controlled.

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Myositis Following Silicone Implants

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The myositis syndromes, also known as the idiopathic inflammatory myopathies or IIM, are a group of autoimmune diseases defined by are chronic muscle weakness and muscle inflammation of unknown cause. Polymyositis and dermatomyositis (in which rashes are present) are the most common clinical forms of these diseases. Although the causes of these diseases remain unknown, evidence suggests that they may result after chronic immune activation in genetically susceptible individuals following exposure to specific environmental triggers. Their therapy consists of immunosuppressives to decrease tissue inflammation and rehabilitation to strengthen remaining muscles.

Evidence suggesting a role for genetics in these diseases includes: an increased prevalence in certain families; animal models in dogs and mice in which only certain strains are affected; associations with specific immune response genes including human leukocyte antigens (HLA), immunoglobulin and cytokine genes.

Evidence suggesting environmental influences in disease includes: strong temporal associations with some environmental exposures and disease onset; seasonal associations of myositis onset with some subgroups; strong evidence from animal models in which myositis can be induced by certain environmental exposures; epidemiologic associations between particular exposures and certain diseases; and possibly increasing incidence and prevalence of myositis.

Anecdotal cases have been reported of myositis developing after silicone implants.
A retrospective evaluation of 12 women who developed myositis after silicone implants suggested that these patients might have different HLA genes compared to race- and gender-matched women who develop myositis without implants. Most notably, patients who developed myositis after silicone implants lacked the strong genetic risk factors (called HLA DRB1*0301 and HLA DQA1*0501) associated with patients who developed myositis without silicone implants.

To evaluate this further, we are currently completing the collection and analysis of clinical, autoantibody and genetic data from a matched case-control study comparing 26 women who developed myositis following silicone implants with two control groups: (1) healthy women with silicone implants and (2) myositis patients without silicone implants.

In summary, gene-environment interactions appear to be important in the development of many autoimmune diseases and further studies in these areas may have important diagnostic, therapeutic and preventative implications.

Reference:

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