The Immunopathology of Siliconosis

History, Clinical Presentation, and Relation to Silicosis and the Chemistry of Silicon and Silicone

Abstract
Recent evidence confirms the fundamental involvement of the human immune system in the reaction to implantation of silicone-based medical devices. An as yet-to-be particularized epitope of many complex substances sharing siloxane structures is presented through the MHC-II apparatus with development and retention of T cell memory. This memory can be tested for in practical terms using one or more forms of silica, which links the immunohistopathology and autoimmune attributes of "silicosis" with those of "siliconosis." The lesions of siliconosis are typical of those for persistent antigens and delayed, cell mediated hypersensitivity. The basic descriptive pathology of the reaction to silicone has been known since soon after introduction of silicones in medical procedures, with the exception of some details related to the more recent discoveries on the role of cytokines in the immunopathic process. The clinical consequences of siliconosis are common and can be severe in some individuals implanted with silicone devices.

Key Words
Siliconosis
Silicosis
Silicone
Silica
Immune
Granulomas
Persistent antigen
Medical device failure
T cell-mediated process
Autoimmune
Conversion
Chemical toxicity

Introduction
Since the end of World War II, the increasing medical use of silicones has paralleled the development of modern knowledge in immunology and immunopathology (1-3). These vectors have met in a matrix of tissue injury, disease, and disability. The progressive application of the techniques of molecular immunology make for a compelling statement: "siliconosis" (4) is an immunopathic process with a potential to induce or stimulate autoimmune states over a long term, beyond its evident capacity to induce chronic inflammation, granulomas, and fibrosis (5). The autoimmune
states may be only epiphenomena. Silicone induction of cellular fibrous capsules or scar at sites of implantation has been established beyond doubt (6–11). The question is whether the tissue reaction to silicone is unusual or abnormal in any particular aspect compared to the reaction to other implanted, man-made materials, or the presence of persistent organisms. This is a matter of pathogenesis, prefatory to whether clinical distinctions exist or can be observed.

Parallels between silicone-lesion formation and other instances of delayed hypersensitivity, such as berylliosis (12–18) and tuberculosis (19–30), are apt, and they serve as models for the relative incapacity of the human immune system to destroy or fully isolate persistent alien irritants. Similar aspects have been shown to be operative in leprosy (31). Schistosomiasis has some similarities (32–35), but is a less appropriate comparative example of persistence owing to the special adaptive strategies available to Schistosoma during its active life cycle (36–41).

The following summary considers the history of clinical use of silicone devices, the chemistry and identification of silica and silicones, the histopathology and clinical presentation of siliconosis, and the rheumatological or autoimmune sequelae of this disease process. When viewed in the light of experienced awareness that inflammatory and immune cells do not travel or function as random acts, the pathogenesis becomes obvious in a global sense. There is, in fact, an abundance of detailed evidence for this statement; however, as with all evidence on complex matters, it must be examined carefully. There is an inconsistency of closely related matters referent to the effects of silicone. As techniques become more sensitive and more specific, these links in elucidation become clear, mutually reinforcing, and cross-validating. This is especially true in the interactions between macrophages, lymphocytes, and the chemical messengers that motivate and modulate their functions. When the source locations of cells and cytokines are considered, it becomes clear this process is systemic, regardless of where the dominant first or ultimate manifestation might be.

The most important clinical use of silicone medical devices over the past 40 yr has been through surgical insertion of mammary devices (1,3). In the case of mammary devices, the principal lesion formation, a fibrous peri-prosthetic capsulopathy, is around the device (42). Less well known, and used far less often, are devices to restore penile function and to replace absent testes, nasal septae, and parts of the skull after trauma or surgery, inter alia (43–46).

There have been attempts to enlarge women’s breasts since early in the 20th century. Initially, mixtures of paraffin, petroleum jelly, and olive oil were used. Later, silicone injections were used among Japanese women in the late 1940s during the American occupation and thence in the United States in the 1950s.

It was shown early on that injected silicone did not remain in bulk at the injection site (47). The ease with which lower molecular weight silicone moieties spread beyond injection sites was shown convincingly in the 1970s (48–57) and by the immunopathic consequences in children of women with implants (58–64). These indirect measures have been solidly reinforced by newer direct analyses for silicone in tissues throughout the body (65–67) and through $^{14}$C-labeled metabolic breakdown products in urine after subcutaneous injection of short chain silicones (68). Generally, reports regarding adverse effects of silicone products in clinical practice began almost immediately on their introduction into the medical realm, prior to 1969 (69–85).

To overcome the difficulty of spread from injection sites, a new formula, known as the