Silicone breast implants became available for use in the United States in 1962 [1], and it is estimated that approximately 1% of adult women aged 18 and above in the United States have undergone augmentation mammoplasty, most with implantation of silicone gel-filled prostheses [2, 3]. The vast majority of these procedures were performed for cosmetic augmentation, while only about 20% were performed for breast reconstruction after mastectomy. Because of concerns regarding both short- and long-term safety, including a possible increased risk for the development of ‘arthritis-like and other autoimmune diseases’, silicone gel-filled prostheses are no longer available for routine use in either the United States [4] or Canada [5]; they remain available, however, in the United Kingdom and almost all other countries within the European Community (Ludgate, personal communication).

Reports of connective tissue disease occurring in patients who had undergone augmentation mammoplasty with injections of silicone, paraffin and other materials began with that of Miyoshi et al. in 1964 who described the syndrome of human adjuvant disease [6]. The vast majority of cases with disease following injections of these materials have been reported in the Japanese literature [7]. A task force of the American Society of Plastic and Reconstructive Surgery concluded recently that this diagnostic category was imprecise and should not be used in future clinical reports [8].

The first report of patients developing well-defined connective tissue disease after augmentation mammoplasty with silicone gel-filled implants was by Van Nunen and colleagues in 1982 [9]. Recently, Sanchez-Guerrero and colleagues reviewed the English language literature from 1964 through June 1993 and identified reports of 293 patients with rheumatic symptoms following augmentation mammoplasty with silicone gel-filled breast implants [10]; these cases are summarized in Table I. The vast majority of these cases, including those reported by Bridges and colleagues [11], had rheumatic symptoms including arthralgias/itis, myalgias and fatigue, and did not fulfill diagnostic or classification criteria for any recognized connective tissue disease. Of those 72 patients who did fulfill such criteria, the majority had a diagnosis of systemic sclerosis or a scleroderma-spectrum disorder such as mixed connective tissue disease [10]; included herein are cases reported by Speira et al. [12, 13].

The above data are derived either from single case reports or case series, and do not provide an adequate basis to infer a causal association between the silicone gel-filled implants and the development of rheumatic symptoms and connective tissue diseases. In order to infer causality, we require knowledge of either the incidence of these rheumatic symptoms and connective tissue diseases in cohorts of women who have and have not undergone augmentation mammoplasty with silicone gel-filled prostheses, or the frequency of the surgical procedure in groups of women with and without rheumatic symptoms and connective tissue diseases. Thus, what is required are data from either cohort or case-control epidemiologic studies. Preliminary data from two studies were presented at the 1993 annual meeting of the ACR [14, 15] and will be briefly reviewed.

Gabriel and colleagues presented data from a retrospective cohort study which utilized the Rochester Epidemiology Project database and identified all women who had undergone augmentation mammoplasty with silicone gel-filled breast implants between January 1964 and December 1991 and were residents of Olmsted County, Minnesota [14]. A total of 824 women, aged 15 to 79 years, received silicone gel-filled prostheses during this interval; over 80% of procedures were for cosmetic breast augmentation. The medical records of each exposed women and two age-matched control women were reviewed for the occurrence of any connective tissue disease; all diagnoses were validated with ACR classification criteria. Over an average follow-up of 8 years in both groups, there were two cases of definite connective tissue disease among the exposed women (RA and Sjögren’s syndrome, 1 each) and five among the controls (all RA); no cases of systemic sclerosis were observed. The relative risk for development of connective tissue disease among the exposed women was 0.83 (95% CI: 0.14, 3.8) which was not statistically significantly different from unity.

Hochberg and colleagues presented preliminary results from a multi-centre case-control study of the association of augmentation mammoplasty with systemic sclerosis [15]. The study includes 840 women with systemic sclerosis and up to three age-, race- and sex-matched controls identified through the process of random digit dialing. Data on history of augmentation mammoplasty, including the type of prosthesis, occurr-

<table>
<thead>
<tr>
<th>TABLE I</th>
<th>Diagnoses in 293 patients with rheumatic symptoms following augmentation mammoplasty with silicone gel-filled breast implants*</th>
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</thead>
<tbody>
<tr>
<td>Definite connective tissue disease</td>
<td>57</td>
</tr>
<tr>
<td>(Systemic sclerosis, 38)</td>
<td></td>
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<tr>
<td>Possible connective tissue disease</td>
<td>15</td>
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<tr>
<td>Connective tissue disease-like</td>
<td>56</td>
</tr>
<tr>
<td>Human adjuvant disease</td>
<td>1</td>
</tr>
<tr>
<td>Rheumatic symptoms</td>
<td>164</td>
</tr>
</tbody>
</table>

*Modified from reference [10].
rence of complications and need for explantation were obtained through interview. Augmentation mammoplasty was reported by three (1.0%) of 290 cases residing in either Maryland, Virginia, District of Columbia, or California and five (1.3%) of 384 controls; the adjusted odds ratio for the association of augmentation mammoplasty with systemic sclerosis was 0.86 (95% CI: 0.20, 3.63).

Thus, neither these nor previous studies [16-18] demonstrate a statistical association between augmentation mammoplasty with silicone gel-filled prostheses and the development of connective tissue diseases, particularly systemic sclerosis. All studies, however, lack adequate statistical power to definitively exclude a small excess risk, and may not have adequate follow-up to account for a long latency period between implantation and development of disease. In addition, it is possible that only women with complications of these implants, including rupture with migration of silicone to regional lymph nodes, may be at increased risk of development of rheumatic symptoms and connective tissue diseases; these and similar studies would be unable to demonstrate such an association because of small sample size and low exposure frequency. Furthermore, it remains possible that women with silicone gel-filled breast implants are at increased risk of developing an atypical rheumatic disease which would not be recognized in studies wherein case status is based on medical record review. Thus, the issue of causation remains unresolved and, in addition, there are no uniform guidelines for the management of patients with rheumatic symptoms and/or connective tissue diseases with silicone gel-filled breast implants.

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REFERENCES