CHRONOLOGY OF SYSTEMIC DISEASE DEVELOPMENT IN 300 SYMPTOMATIC RECIPIENTS OF SILICONE GEL-FILLED BREAST IMPLANTS

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Aims: *To define the time sequence and incremental evolution of the systemic illness manifested by recipients of silicone gel-filled breast implants.* ***Methods:*** *Three hundred patients who became systemically ill following insertion of silicone gel-filled breast implants were examined. Mean age at the time of implantation was 33 years, and the average silicone gel device exposure spanned 12 3/4 years.* ***Results:*** *The onset of systemic disease began on average 2 1/2 years after implant insertion, occurring as early as two weeks after the implant or as late as 18 years afterwards, with 90% of the entire cohort symptomatic after six years. Implant rupture was not the stimulus for disease onset and preceded systemic illness in only nine patients (3%). Subsequent disease progression developed in an exponential manner, eventually encompassing an average of thirty symptoms and signs per patient. Disease acceleration occurred five to six years from the time of implantation, and coincided with failure of the fibrocollagenous capsule. Implant rupture (214 out of 300) served to exacerbate and aggravate any symptoms and signs that were already present but did not alter the rate of sequential disease progression compared to patients who never experienced rupture.* ***Conclusions:*** *In this cohort of symptomatic silicone gel breast implant recipients, the chronology of systemic disease development simulated a self-perpetuating runaway catalytic reaction and was uniquely different from the varied and established evolutions of spontaneous device-free classical connective tissue diseases. This time sequence of disease progression provides strong supportive evidence for the existence of a novel illness, and also offers rational advice for implant removal based primarily on the length of time of device insertion rather than whether or not implants have undergone rupture.*

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INTRODUCTION

Silicone gel-filled breast implants have been implicated by numerous investigators as the cause of a novel systemic illness (Lappe, 1993; Borenstein, 1994; Brawer, 1994; Bridges, 1994; Freundlich et al., 1994; Solomon, 1994a, 1994b; Shoaib et al., 1994; Brautbar et al., 1995; Davis et al., 1995; Lappe, 1995; Mease et al., 1995; Shoaib and Patten, 1995; Vasey, 1995). The foundation for this conclusion has predominantly relied upon (1) the repetitive observation of unique clinical features that cannot be attributed to other well-defined medical conditions, and (2) the amelioration of this illness in some patients following implant removal (Kaiser et al., 1990; Vasey et al., 1994; Brautbar et al., 1995; Cuellar et al., 1995; Vasey, 1995). Supportive laboratory findings in symptomatic implant recipients have been reported (Press et al., 1992; Vojdani et al., 1992; Kossovsky et al., 1993; Campbell et al., 1994; Cuellar et al., 1994; Kossovsky and Petrovich, 1994; Kossovsky and Stassi, 1994; Kossovsky et al., 1994; Ojo-Amaize et al., 1994; Bar-Meir et al., 1995; Brautbar et al., 1995; Cuellar et al., 1995; Smalley et al., 1995; Marcus, 1996), but some of these have recently been subjected to critical review.

Historically, a useful description of a new rheumatic disorder has incorporated the simultaneous observations of both the clinical manifestations and the disease chronology. A detailed time sequence of disease development and progression often strengthens the distinction of the new entity from other classical connective tissue diseases. A prime example of this is Lyme disease, where lab tests are not always definitive, and where overlapping clinical features not infrequently create confusion and controversy due to incomplete documentation of chronological data (Steere, 1989). The present study was designed to examine the time sequence and incremental evolution of the systemic illness manifested by recipients of silicone gel-filled breast implants. The reported findings attest to the existence and uniqueness of silicone-induced disease, contribute to its definition, provide guidance and advice for the timing of explantation, and offer insight into potential mechanisms of disease causation.

MATERIALS AND METHODS

Three hundred patients (299 women and one male) who became systemically ill following insertion of silicone gel-filled breast implants were examined. The patients were either self-referred, attorney-referred, or physician-referred. Table 1 lists the indications for surgery, with two-thirds of the women having undergone bilateral cosmetic breast enhancement. Multiple different manufacturing devices were represented in the cohort as a whole. The average silicone gel device exposure spanned 12 3/4 years with implantation time ranging from 11 months to 27 years. During this interval 164 patients had only one set or a single implant inserted, and 136 patients underwent multiple implant exchanges. A single rheumatologist interviewed and examined each patient directly, and prior medical records were reviewed whenever possible. Follow-up was arranged by either reexamination or telephone contact. In any patient with a final gel exchange for saline (44 out of 300), the additional saline device insertion time was not counted as part of the total implant exposure time.

TABLE 1. General Features and Indications for Surgery

No. of patients	261 out of 300 bilateral
199	Cosmetic augmentation
48	Cancer (32 unilateral)
24	Post partum breast atrophy
17	Congenital/acquired (6 unilateral)
11	Fibrocystic mastitis (1 unilateral)
1	Sex change

Note: Patient population 300 (299 women). Age 16–64 (mean 33). Initial insertion from 1967–1991.

For each systemic symptom and sign recorded, the precise time of onset of each item after implantation was determined. Any single clinical manifestation was included as part of the disease process only if it was (1) chronically unremitting and/or persistently repetitive, (2) was not present prior to device insertion, and (3) could not be attributed to any other well-defined medical condition. An average of thirty symptoms and signs developed in each patient. Individual patient elapsed time analysis was performed for each increment of six symptoms and signs, and the intervals were then averaged for the group as a whole. Thus, 20% of the total disease process represented (and coincided with) the average elapsed time interval until the sixth symptom or sign was recorded. Similarly, 40% of the total disease process represented (and coincided with) the average elapsed time interval until the twelfth symptom or sign was recorded. Analyses were also performed for the eighteenth and twenty-fourth phenomena, representing 60% and 80 % of the total disease process respectively. Data were also tabulated for presenting features, overall disease onset, and patterns of early, late, and random disease manifestations. Disease development data were not analyzed according to the type of implant inserted.

Implant rupture was determined by any of the following: obvious signs on physical examination, positive radiographic procedure, surgical findings, pathology findings, or classical history (such as sudden flattening). For patients with multiple sets of implants, rupture time was calculated only for the set that had failed, not from the total time interval since initial implantation. For example, if a patient underwent implant exchange two years from the time of initial implantation for painful capsular contracture without rupture, and the second set of implants subsequently ruptured six years later, the time to rupture was calculated at six years. If a patient experienced rupture in more than one set of implants, the incidence of rupture was counted only once, and the time to rupture was calculated for the first ruptured set only. The relationship of rupture and other local breast phenomena to the onset and progression of systemic disease was also analyzed.

RESULTS

The onset of systemic disease symptoms and signs occurred an average of 2 1/2 years after implant insertion, beginning as early as two weeks after implantation or as late as 18 years afterwards. Systemic disease development preceded implant rupture. Stated another way, implant rupture was not the stimulus for disease onset and preceded systemic illness in only nine patients (3 %). The average rate of rupture was noted to be 5% per year, and its relationship to disease onset is graphically illustrated in Figure 1.

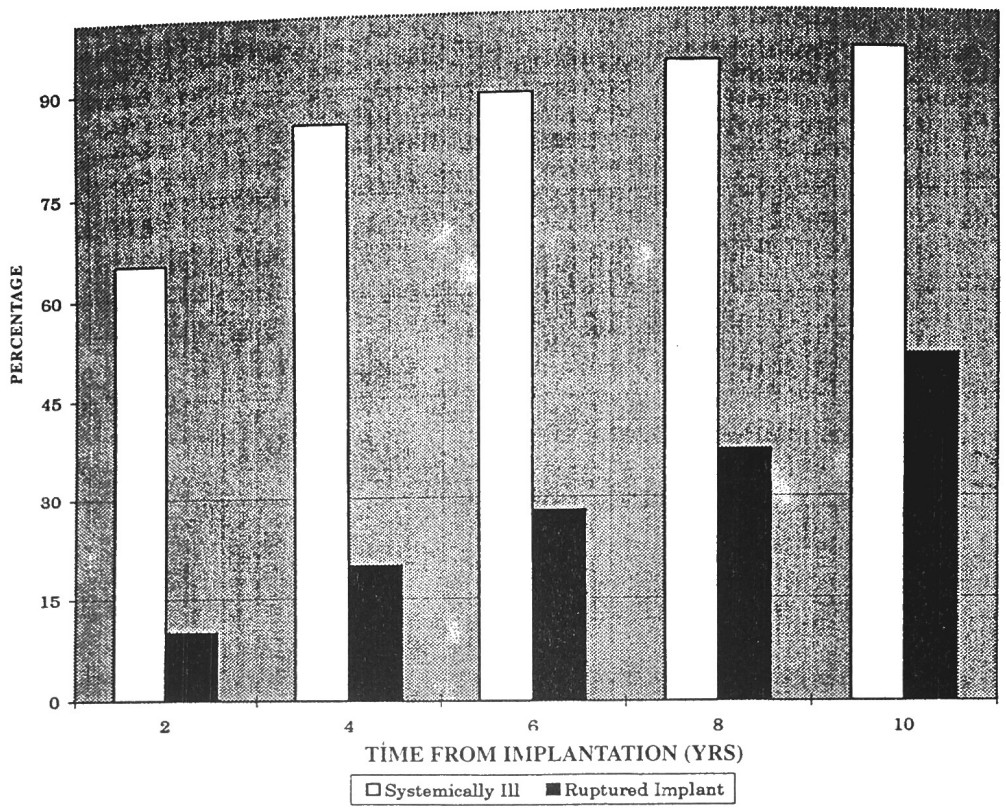

FIGURE 1. Bar graph comparing the percentage of patients who are systemically ill vs the percentage of patients who have a ruptured implant, at two-year intervals from the time of implantation.

An average of thirty symptoms and signs developed in each patient, with the predominant clinical features listed in Table 2. Table 3 provides the average calculation of the percentage of total systemic disease that had become established at varied points in time from implantation. These numbers are graphically illustrated in Figure 2, where the linear rate of rupture is superimposed. The disease development curve, noted in Figure 2, bears no resemblance to the usual clinical courses encountered in nonsilicone patients with classical connective tissue diseases, the latter of which is noted in Figure 3. The severity of the silicone gel related illness increased exponentially with increasing length of time of gel device insertion. Disease acceleration occurred five to six years from the time of implantation, and coincided with failure of the fibrocollagenous capsule (a local breast phenomenon clinically characterized by displacement and malposition) (Brawer, 1996). There was no difference in the rate of sequential disease development in the patients who never experienced a ruptured implant (86 out of 300) versus the patients who did experience one or more implant ruptures (214 out of 300). Rupture served to exacerbate and aggravate any systemic disease symptoms and signs that were already present, but did not change the disease development curve with regards to the production of additional new symptoms and signs. Findings also did not vary according to age at the time of implantation, the reasons for implantation, or the presence of a unilateral prosthesis. The following case history provides an example of disease evolution.

TABLE 2. Frequency of the Most Common Symptoms and Signs, Organized According to Pattern of Onset

Clinical Features					
Early	%	Random	%	Late	%
Fatigue	(88%)	Dry eyes/mouth	(76%)	Cognitive	(64%)
Arthritis	(86%)	Morning stiffness	(69%)	Telangiectasias	(59%)
Chest pain	(77%)	Myalgias	(60%)	Freckling	(51%)
Hair loss	(59%)	Skin rash	(58%)	Pigment changes	(50%)
Headaches	(46%)	Paresthesias	(56%)	Metallic taste	(40%)
Nails	(44%)	Itching	(46%)	Palmar erythema	(37%)
Chills	(39%)	Night sweats	(44%)	Loose stools	(32%)
Photosensitivity	(33%)	Dizziness	(43%)	Skin papules	(30%)
Spine pain	(33%)	Weight gain	(40%)	Muscle twitching	(28%)
Sinusitis	(32%)	Nausea/vomiting	(35%)	Palpitations	(25%)
Abdominal pain	(32%)	Bruising	(33%)	Lower respitory	
		Vaginitis	(32%)	infection	(24%)
		Periodontal	(31%)	Dysphagia	(23%)
		Sore throats	(31%)	Blurry vision	(22%)
		Lymphadenopathy	(27%)	Tinnitus	(20%)
		Urinary	(24%)	Periorbital edema	(20%)
		Menses	(23%)	Weakness	(20%)
		Hoarseness	(22%)		
		Dyspnea	(22%)		
		Fevers	(21%)		
		Constipation	(20%)		

TABLE 3. Elapsed Time Averaged 54 Months for the First Six Symptoms and Signs, 30 Months for the Next Disease Increment, and 16 Months for the Third Increment

	Sequential disease development				
	1 sx	6 sx	12 sx	18 sx	24 sx
Time (yrs) from implantation	2 1/2	4 1/2	7	8 1/3	9 1/2
percentage of total disease	3%	20%	40%	60%	80%

Note: Average illness = 30 symptoms and signs (sx).

An 18-year old white female, previously in excellent health, underwent cosmetic breast augmentation with the insertion of bilateral silicone gel-filled breast implants. Within two weeks of the surgery both breasts became cold and numb, and in two months capsular contracture developed bilaterally. One year after the surgery, at the age of 19, sore throats developed, accompanied by fatigue, axillary lymphadenopathy, recurrent sinusitis, and hoarseness, none of which was significantly improved following a tonsillectomy. One year later recurrent vaginal yeast infections developed along with recurrent urinary infections, menometrorrhagia, brittleness of the nails, and freckling of the anterior chest wall. By the age of 21, or three years after implantation, the patient developed recurrent mouth sores and pains in her neck and shoulders. One year later lateral displacement and malposition occurred of the left breast, along with the appearance of small bilateral breast nodules and puckering and dimpling of the right breast. This was accompanied by the development of loose stools, abdominal cramps, and easy bruiseability.

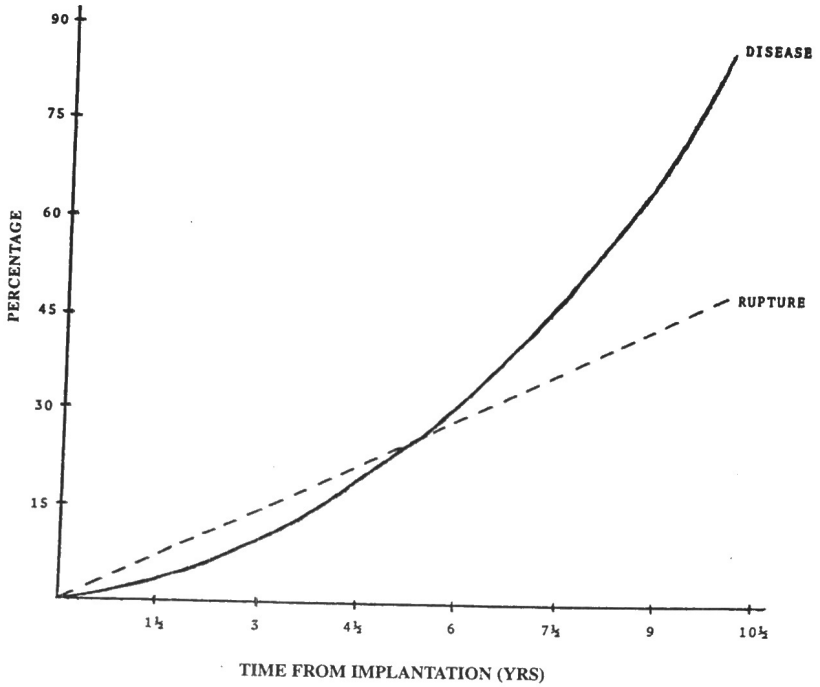

FIGURE 2. The disease development curve, averaged for the entire 300 patients, showing the percentage of systemic disease that has already become established at any point in time from initial implant insertion. For each successive increment of six symptoms and signs, the elapsed time interval becomes smaller and smaller. The linear rate of rupture is superimposed.

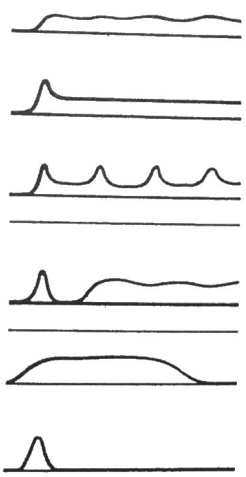

FIGURE 3. Common examples of the long-term clinical course manifested by patients with classical (nonsilicone) connective tissue diseases.

At the age of 23, or five years after implantation, an erythematous, nonraised confluent skin rash appeared on the neck and abdomen which was pruritic, accompanied by pinhead-sized erythematous papules on the anterior chest wall. This was followed by the development of photosensitivity, diffuse myalgias, three hours of morning stiffness, diffuse joint aches without swelling, chills, periodontal disease, metallic taste, and livedo reticularis on the legs. At the age of 24, telangiectasias developed on the upper anterior chest, accompanied by dysphagia, dry eyes and dry mouth, tinnitus, headaches, blurry vision, intermittent dizziness, nausea, and cognitive dysfunction. One year later the patient complained of recurrent eyelid twitching, contact allergies, paresthesias in the extremities, and skin hyperesthesia. At the age of 27, or nine years following implantation, she developed shortness of breath, weakness in the extremities, a 25-pound weight loss, insomnia, and anterior chest pain. Shortly thereafter intact silicone gel breast implants were removed without replacement. Figure 4 represents the patient's appearance one year after breast augmentation, and can be contrasted with Figure 5 which represents her appearance at age 27, shortly after explantation. Additional physical findings at that time revealed hemangiomas scattered on the arms, and anterior rib cage tenderness to palpation. Exhaustive laboratory tests, including muscle enzymes, were normal. Her condition remained unchanged until eighteen months after explantation, when she began to notice gradual improvement. Subsequently, over the next ten months, she noted resolution of her nausea, vaginal yeast infections, nail brittleness, chills, metallic taste, dysphagia, and weight loss. During this same 10-month interval she has noticed reduced frequency and/or severity (but by no means resolution) of her fatigue, skin rashes, arthralgias, morning stiffness, headaches, dizziness, paresthesias, dyspnea, urinary infections, axillary lymphadenopathy, periodontal disease, muscle twitching, insomnia, and skin hyperesthesia. The remainder of her symptoms and signs remain unchanged as yet.

FIGURE 4. Case history (see text), at age 19.

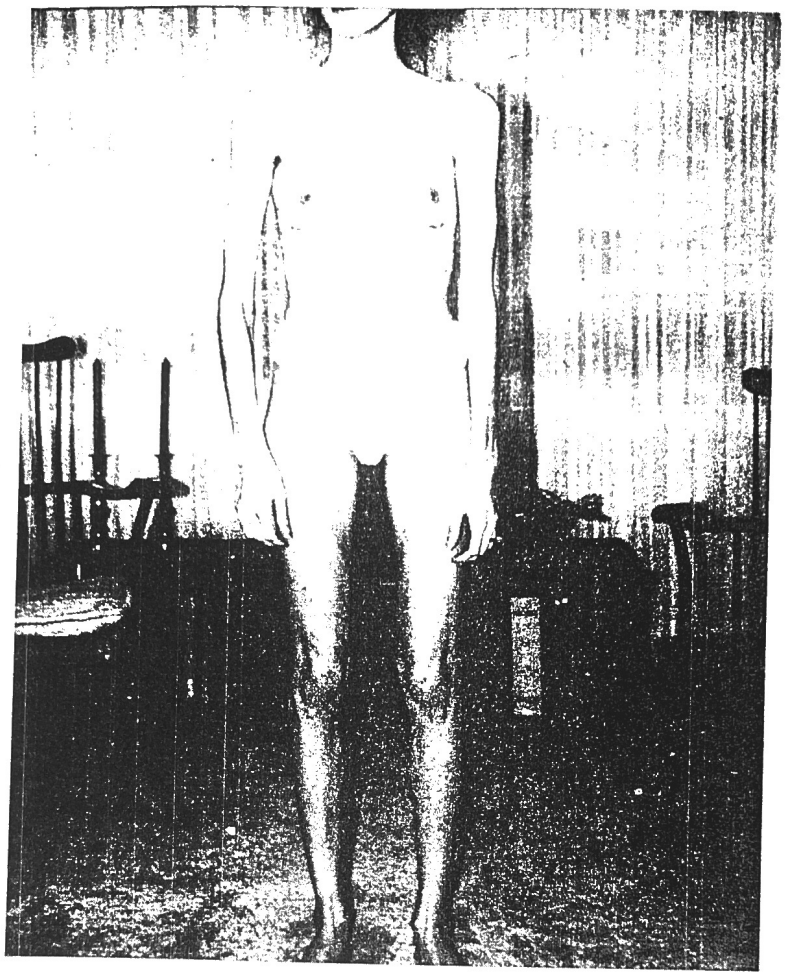

FIGURE 5. Case history (see text), at age 27.

By recording the time of onset of each symptom and sign manifested in each of the 300 patients, it was also possible to determine the pattern of early and late disease features. Fatigue was an early symptom (as noted in Table 2), whereby when 20% of the systemic disease process was underway, 51% of the patients who were going to develop fatigue already were manifesting it. On the other hand, cognitive dysfunction was a late feature as nearly three-fourths of the patients with this feature developed it later than seven years from the time of implantation. As for the other symptoms and signs noted in Table 2, the diverse chronological scattering may eventually prove to be valuable clues in determining latent contributions of the multiple suspected mechanisms of disease causation.

DISCUSSION

The findings in this study strengthen the conclusions of other investigators stating that silicone gel-filled breast implants are the direct cause of a novel systemic illness. The disease development curve in this cohort of patients is uniquely different from the evolutionary patterns of classical connective tissue diseases. In addition, the sequential disease progression in the implant recipients bears remarkable similarity to exponential fluid bed reactor curves, the latter occurring whenever silica is used as a catalyst to produce chemicals such as amines, acrylics, carbonyls, acetates, and chromic acid. The envelope of breast implants contains varying concentrations of silica which was added to provide tensile strength and elasticity (Kossovsky and Stassi, 1994; Spiera et al., 1994; Smalley et al., 1995). Another source appears to come from macrophages that have ingested and subsequently hydrolyzed silicone gel molecules (Williams, 1978; Garrido et al., 1993). Although additional studies will be required to investigate the possibility that silica is released *in vivo* from the degradation of breast implant components, its presence could theoretically catalyze the production of various chemicals, as biological systems have the capacity for unanticipated molecular synthesis (Williams, 1978). These systems are far from homogeneous, and locally concentrated silicon can form polymerized species of unknown crystal forms (i.e., silicates) by interacting with calcium, magnesium, and phosphorus (Williams, 1978). Silicates bound to sugars can become catalytically active, taking on the properties of enzymes (Williams, 1978). The five chemicals listed above are known to produce toxic reactions such as skin rashes, dyspnea, nausea, short-term memory loss, headaches, dizziness, brittleness and cracking of nails, bone atrophy, teeth loss, and photosensitivity. Patients in this study who have had photosensitivity or other skin reactions describe the skin as if it is "on fire" or "burning like a cigarette is under the skin." At times this clinical observation had the tempo of a self-perpetuating runaway phenomenon. This is in keeping with the observation that the overall disease development in these patients simulates a reactor catalysis mechanism.

Although specific criteria for classification of silicone-induced disease have yet to be established, this study clearly indicates the need to incorporate the average time sequence of disease development and progression into such a classification. Chronological data need to be analyzed from larger populations of symptomatic silicone patients to determine whether or not the results in this report are representative. Knowledge of disease evolution also allows for a more focused perspective for any single patient exhibiting progressive symptoms and signs by creating a more logical rationale and more logical timing for explantation. For this cohort, interrupting the natural course of silicone disease before significant acceleration occurred essentially meant that the silicone gel-filled breast implants would (on average) have required removal around five to six years from the time of original implantation. This would have not only limited disease severity, but might also imply a better chance for improvement for whatever symptoms and signs had already appeared. Indeed, the disease development curve was found to have at least 90% predictability in patients at an early stage of implantation. Twenty-nine patients from this cohort had an average of 6 1/2 years implantation time when first evaluated by this author, with a familiar pattern of initial disease evolution. In those patients whose gel-filled implants remained inserted over a minimum follow-up period of at least two additional years, analysis of their subsequent clinical course revealed disease progression to new symptoms and signs at a rate comparable to the entire cohort.

Disease severity in this study was a reflection of the total number of symptoms and signs present at any point in time, and was not a measure of the magnitude of any single clinical feature. It was thus a function of the incremental development and appearance of new phenomena, which additively and progressively arose during increasing length of time of gel device insertion. Using this definition, patients who experienced implant rupture did not differ in disease severity compared to individuals without rupture because the rate of appearance of new symptoms and signs was identical in both groups. However, rupture did contribute to overall morbidity by exacerbating and aggravating whatever symptoms and signs were already present at the time the rupture occurred.

In summary, the chronological findings in this cohort of symptomatic silicone gel breast implant recipients attest to the existence and uniqueness of silicone-induced disease, and offer rational advice for the timing of explantation based primarily on the length of time of gel device insertion.

REFERENCES

BAR-MEIR, E., TEUBER, S.S., LIN, H.G., ALOSACIE, I., GODDARD, G., TERYBERY, J., BARKA, N., SHEN, B., PETER, J.B., and BLANK, M. (1995). "Multiple autoantibodies in patients with silicone breast implants." J. Autoimmunity 8(2):267–277.

BORENSTEIN, D. (1994). "Siliconosis: a spectrum of illness." Seminars on Arthritis & Rheumatism (suppl.1) 24:1-7.

BRAUTBAR, N., CAMPBELL, A., and VOJDANI, A. (1995). "Silicone breast implants and autoimmunity: causation, association, or myth?" J. Biomaterials Sci. Polymer Edn. 7:133–145.

BRAWER, A.E. (1994). "Bones, groans, and silicone: beauty and the beast (abstract)." Arthritis & Rheumatism (suppl.) 37:R38.

BRAWER, A.E. (1996). "Clinical features of local breast phenomena in 300 symptyomatic recipients of silicone gel-filled breast implants." J. Clean Technol. Environ. Toxicol. Occup. Med. 5(3):236–250.

BRIDGES, A.J. (1994). "Autoantibodies in patients with silicone implants." Seminars on Arthritis & Rheumatism (suppl.1) 24:54–60.

CAMPBELL, A., BRAUTBAR, N., and VOJDANI, A. (1994). " Suppressed natural killer cell activity in patients with silicone breast implants: reversal upon explantation." Toxicol. Ind. Health 10:149–154.

CUELLAR, M.L., STEIN, T.W., ESPINOZA, L.R., TAN, E.M., and OCHS, R.L. (1994). " Immunoblot analysis of sera from women with silicone breast implants (abstract)." Arthritis & Rheumatism (suppl.) 37:5422.

CUELLAR, M.L, ESPINOZA, L.R., OCHS, R., and TAN, E.M. (1995). "Clinical outcome of silicone breast implant women following implant removal. (abstract)." Arthritis & Rheumatism (suppl.) 38:S264.

CUELLAR, M.L., SCOPELITIS, E., TENNENBAUM, S.A., GARRY, R.F., SILVEIRA, L.H., CABRERA, G., and ESPINOZA, L.R. (1995). "Serum antinuclear antibodies in women with silicone breast implants." J. Rheumatology 22:236–240.

DAVIS, J., CAMPAGNA, J., PERRILLO, R., and CRISWELL, L. (1995). "Clinical characteristics of 343 patients with breast implants (abstract)." Arthritis & Rheumatism (suppl.) 38:5263.

FREUNDLICH, B., ALTMAN, C., SANDORFI, N., GREENGERG, N., and TOMASZEWSKI, J. (1994). " A profile of symptomatic patients with silicone breast implants: a Sjogren's-like syndrome." Seminars on Arthritis & Rheumatism (suppl.1) 24:44–53.

GARRIDO, L., PFLEIDERER, B., PAPISOV, M., ACKERMAN, J.L.(1995). " *In vivo* degradation of silicones." Magn. Reson. Med. 29:839–843.

KAISER, W., BIESENBACH, G., STUBY, U., GRAFINGER, P., and ZAZGORNIK, J. (1990). " Human adjuvant disease: remission of silicone-induced autoimmune disease after explantation of breast augmentation." Ann. Rheumatic Diseases 49(11):937–938.

KOSSOVSKY, N. and STASSI, J. (1994). "A pathophysiological examination of the biophysics and bioreactivity of silicone breast implants." Seminars on Arthritis & Rheumatism (suppl.l) 24:18–21.

KOSSOVSKY, N., ZEIDLER, M., CHUN, G., PAPASIAN, N., and NGUYEN, A. (1993). "Surface dependent antigens identified by high binding avidity of serum antibodies in a subpopulation of patients with breast prostheses." J. Appl. Biomaterials 4:1-8.

KOSSOVSKY, N., GELMAN, A., and HNATYSZYN, H.J. (1994). "Adjuvant effect of silicone on the formation of anti-insulin and anti-fibronectin antibodies (abstract)." Arthritis & Rheumatism (suppl.) 37:S271.

KOSSOWSKY, R. and PETROVICH, D. (1994). "Novel antibodies to native macromolecules (anti-SSAA) in patients with silicone breast implants (abstract)." Arthritis & Rheumatism (suppl.) 37:5422.

LAPPE, M.A. (1993). "Silicone-reactive disorder: a new autoimmune disease caused by immunostimulation and superantigens." Medical Hypotheses 41:348–352.

LAPPE, M. (1995). "Causal inference in syndromes associated with silicone breast implants: psychogenic and environmental factors." Intl. J. Occup. Med. Toxicol. 4:165–175.

MARCUS, D.M. (1996). "An analytical review of silicone immunology." Arthritis & Rheumatism 39:1619–1626.

MEASE, P.J., OVERMAN, S.S., and GREEN, D.J. (1995). "Clinical symptoms/signs and laboratory features in symptomatic patients with silicone breast implants (abstract)." Arthritis & Rheumatism (suppl.)38:S324.

OJO-AMAIZE, E.A., CONTE, V., LIN, H.C., BRUCKER, R.F., AGOPIAN, M.S., and PETER, J.B. (1994). "Silicone specific blood lymphozyte response in women with silicone breast implants." Clinical Diagnosis Lab. Immunol. 1(6):689–695.

PRESS, R.I., PEEBLES, C.L., KUMAGAI, Y., OCHS, R.L., and TAN, E.M. (1992). "Antinuclear autoantibodies in women with silicone breast implants." Lancet 340(8831):1304–1307.

SHOAIB, B.O. and PATTON, B.M. (1995). "Multiple sclerosis-like syndrome in women with silcone breast implants: a novel neurological disease with rheumatological symptoms (abstract)." Arthritis & Rheumatism (suppl.) 38:52–64.

SHOAIB, BO, PATTEN, B.M., CALKINS, D.S. (1994). "Adjuvant breast disease: an evaluation of 100 symptomatic women with breast implants or silicone fluid injections." Keio J. Med. 43:79–87.

SMALLEY, D.L., SHANKLIN, D.R., HALL, M.F., STEVENS, M.V,.and HANISSIAN, A. (1995). "Immunologic stimulation of T-Lymphocytes by silica after use of silicone mammary implants." The FASEB J. 9:424–427.

SOLOMON, G. (1994). "A clinical and laboratory profile of symptomatic women with silicone breast implants." Seminars on Arthritis & Rheumatism (suppl.1) 24:29–37.

SOLOMON, G.(1994). "Clinical and serologic features of 639 symptomatic women with silicone gel implants: evidence for a novel disease Siliconosis (abstract)." Arthritis & Rheumatism (suppl.) 37:S423.

SPIERA, R.F., GIBOFSKY, A., and SPIERA, H..(1994). "Silicone gel-filled breast implants and connective tissue disease: an overview." J. Rheumatology 21:239–245.

STEERE, A.C. (1989). "Lyme disease." New Engl. J. Med. 321:586–596.

VASEY, F.B. (1995). "A rheumatologist's view of silicone." Intl. J. Occup. Med. Toxicol. 4:203–209.

VASEY, F.B., HAVICE, D.L., BORANEGRA, T.S., SELEZNICK, M.J., BRIDGEFORD, P.H., MARTINEZ-OSUNA, P., and ESPINOZA, L.R. (1994). "Clinical findings in symptomatic women with silicone breast implants." Seminars on Arthritis & Rheumatism (suppl.1) 24:22–28.

VOJDANI, A., CAMPBELL, A., and BRAUTBAR, N. (1992). "Immune functional impairment in patients with clinical abnormalities and silicone breast implants." Toxicol. Ind. Health 8:415–429.

WILLIAMS, R.J.P. (1978). "Silicone in biological systems." In: Biochemistry of Silicone and Related Problems (G. Bendz and I. Lindqvist, eds.) Plenum Press, New York, NY pp. 561–576.