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Subclinical Infection of the Silicone Breast Implant Surface as a Possible Cause of Capsular Contracture

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Abstract. In order to reexamine the possible association between bacterial presence and capsular contracture, 55 silicone devices (mammary implants or tissue expanders) were cultured at the time of their removal from 40 patients. Special culture techniques were used in an attempt to recover bacteria adhering to the smooth-surfaced implant and encased in glycocalyx biofilm. Bacteria were detected on 56% (15 of 27) of implants surrounded by contracted capsules and on 18% (5 of 28) of those without capsular contracture ($p < 0.05$). Only three implants tested positive using routine plating techniques. The predominant isolate was *Staphylococcus epidermidis*. The concept that capsular contracture is associated with subclinical infection of silicone implants is supported by this study. With changes in the microbiological technique, bacterial recovery and growth occurs at a frequency greater than previously thought.

Key words: Breast—Implant—Capsule—Contracture—Infection

Formation of a fibrous capsule around implanted silicone devices is considered a part of the normal healing process. However, it remains unknown why some capsules contract and thicken leading to tissue contour distortion, induration, firmness, discomfort, or even pain. Many etiologies have been proposed to explain this perplexing phenomenon [1]. Infection as a factor has been investigated in the past and continues to be mentioned as a plausible, at least partial, explanation to formation of capsular contracture [7, 8, 11, 34].

Despite the fact that bacteria are frequently cultured from the breast glandular tissue and occasionally from the interior of contracted capsules, and despite the claimed decrease of capsular contracture incidence with the use of local antibiotics and antiseptics, no satisfying, objective evidence linking bacteria with contracture exists [3, 7, 8, 11, 24, 34, 38]. Skepticism was added by results of a morphological study showing no bacteria in capsules around silicone breast implants [31].

Clinically recognizable acute infection following breast implant placement appears to be rare (up to a few percent) [11, 14, 27]. However, there is accumulating evidence that subclinical infection of silicone devices may cause changes in their capsule biology without signs of full-blown infection [6, 9, 14]. Detection of this type of infection may be difficult: Microorganisms are "hidden." Bacteria adhere easily to silicone and produce extracellular polysaccharides and glycoprotein which form a slime layer. Encased in this biofilm they stay in a dormant, viable state but do not multiply (Fig. 1). They may not be readily accessible to nutrients from culture media or to treatment with antibiotics [10, 13, 20, 30]. The ability of bacteria to adhere to biomaterial surfaces and the development of biofilms have been implicated in the persistent nature of foreign body infections [4, 13, 20, 30, 32, 33, 38]. Infections of other implanted devices frequently originate from the patient's own endogenous flora and often involve or-

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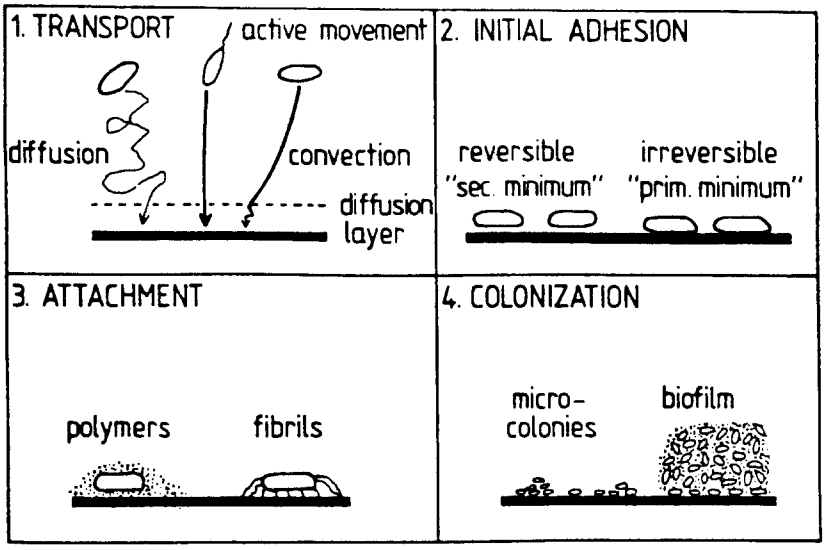

Fig. 1. Schematic representation of the sequence of steps in the surface colonization of slime-producing bacteria (from [20] with permission of the American Society for Microbiology)

ganisms of generally low virulence, such as coagulase-negative Straphylococci (e.g., *Straphylococcus epidermidis*) with clinical presentation similar to that of capsular contracture [26, 36, 38].

It is likely that true bacterial presence on implant surfaces may be underdetected by routine cultures [28, 29, 33]. To reexamine the possible association between bacterial presence and capsular contracture, segments of capsular tissue and implants were processed using culture techniques designed to recover adherent bacteria from smooth surfaces and exposed microorganisms trapped within the biofilm. Results were compared with those obtained by "routine" culture methods and verified morphologically by scanning electron microscopy.

Material and Methods

Patients

The study included 40 female patients (from 22 to 67 years, mean 39 years) with a total of 55 silicone devices (38 mammary implants and 17 tissue expanders). Twenty two patients were admitted for revision of augmentation mammaplasty and 18 for breast reconstruction procedures. Thirty four smooth-wall silicone mammary implants (gel or saline filled) were examined: 14 devices were exchanged for reasons other than signs of capsular contracture. Eighteen patients (17 had modified radical mastectomy and one had congenital breast aplasia) underwent a total of 20 reconstructive procedures. Four smooth-wall mammary implants and 17 tissue expanders obtained in this group were studied.

In 28 cases, segments of capsular tissue (total 40 capsules) were also harvested for microbiological testing.

Breasts that were firm with visible and obvious spherical distortion (Baker's classification grades III and IV) were categorized as having significant capsular contracture. Soft and natural-appearing breasts were categorized as without capsular contracture (grade I) [2].

Antibiotics

Patients were given semisynthetic cephalosporin antibiotic proplylaxis during their original implant procedures. Usually 1 g of cefazolin sodium diluted in normal saline was infused intravenously beginning 1 hour prior to the procedure or just prior to induction of anesthesia. No antibiotics were given until implants were removed and tissue samples obtained during revisional/secondary procedures which form the basis of this study.

Surgical Procedures

Procedures were performed following preparation of the operative field with povidone-iodine 7.5% "scrub" and 10% solutions. After skin incisions were made new instruments were used for further tissue dissection. Wound edges were retracted to expose the capsule surrounding the implant and to allow "no skin touch" technique. After the capsule lumen was entered, segments to implants as well as capsule tissue were obtained.

Specimens

Two 1.0-cm-diameter segments of silicone implant and adjacent capsular tissue wall were harvested from opposite sides of the capsule and implant. If the patient indicated localized pain preoperatively, a specimen was harvested from beneath the indicated area and from an opposite area, otherwise material was obtained from an area near the original incision and from the opposite side. Each specimen was divided and submitted for routine cultures to the UCSD Medical Center Microbiology Laboratory and for research processing in our laboratory.

"Routine" processing of samples by the microbiology laboratory included immediate transfer from the sterile specimen cup to a small, sterile, sealable bag containing normal saline. The sealed bag was subsequently placed for approximately 1 minute in the Colworth Stomacher Lab blender with a paddle speed set at 150–160 strokes per minute. The "supernatant" fluid was removed and 1.0 mL was added to 10–20 mL of a Brain Heart Infusate (BHI) and poured on plates containing Columbia nalidixic acid, eosin methylene blue, and rabbit blood with trypticase soy agar. Plates were incubated for 48 hours at 35 ± 0.3°C. If microorganism colonies grew they were subjected to identification procedures [35]. For anaerobic bacteria cultures Columbia agar was used, and for fungal cultures Sabauroud medium was used. The described technique represents standard processing of tissue and foreign body samples in a hospital microbiology laboratory [15, 28].

Samples for research laboratory processing were divided and 4–5-mm-diameter segments of the implant or capsule were placed in BHI or trypticase soy broth (TBS). During 72 hours of incubation at 37°C, specimens were continuously shaken by an Adams nutator. Any cultured specimen demonstrating increased turbidity, suggestive of bacterial growth, was submitted to the hospital microbiology lab for identification procedures.

Steps to prevent sample dessication, prolonged incubation with continuous agitation, and immediate sample placement in media favoring Staphylococcal growth were used to increase the detection of bacteria [12, 19, 20, 29, 30, 33].

Scanning Electron Microscopy (SEM)

Sections of implant walls were examined by SEM in the Electron Microscopy Laboratory, Scripps Clinic and Research Foundation, La Jolla, CA. Sample preparation included dehydration to cause "collapse" of hydrated exopolysaccharide matrix of the biofilm. Specimens were placed in a fixation solution consisting of 5% glutareldehyde in cacodyle buffer 0.1 M, pH 7.0, with 0.15% ruthenium red for 4 hours at 22°C, then washed in the buffer and metallized by using osmium tetroxide and thiocarbohydrazide. This was followed by dehydration in ethanol and freon 113 [21]. Microscopy was performed by means of a Hitachi S500 scanning electron microscope.

Statistical Analysis

Differences in the distribution between groups were tested with the chi-square test and considered as significant when $p < 0.05$ unless indicated otherwise.

Results

Signs of capsular contracture were observed in 23 patients (two with tissue expanders and 21 with mammary implants). This complication affected 27 silicone devices among them 24 mammary implants (63% of implants) and three tissue expanders (18% of expanders).

The time between the implantation of a device and the onset of capsular contracture symptoms and signs varied from two months to five years; 17 implants were affected by capsular contracture between two and 12 months after surgery. In a few cases, the time between the implantation and capsular contracture recognition was unknown; quite likely the breast remained firm after surgery.

Routine cultures of implants were positive in three cases all associated with capsular contracture. Research cultures were also positive in these cases. One patient (breast reconstruction with history of radiation) developed signs of capsular contracture followed by clinical infection (cellulitis) several months after subpectoral implant placement. Routine cultures of the implant and capsule revealed presence of *Straphylococcus epidermidis* (prior to implant removal the patient was receiving cefazolin intravenously). Two mammary implants, electively removed in the absence of clinical infection after subglandular breast augmentation, were positive by "routine culture": one for *Propionibacterium acne* and one for *Staphylococcus epidermidis*.

Results of this study demonstrate increased frequency of positive research cultures in cases with capsular contracture, although implants without signs of this complication also tested positive. In patients with capsular contracture, research cultures were positive in 15 cases: nine devices (implants) placed into subglandular augmentation and six subpectoral devices (one tissue expander and five mammary implants) (Table 1). Research cultures were significantly more frequently positive (56%) than routine cultures (three patients, 11%) ($p < 0.05$) of devices from patients with capsular contracture.

Overall the incidence of positive cultures of im-

Table 1. Incidence of positive "research" cultures

Type of surgery	Capsule		Significance
	Contracted	Non-contracted	
Submuscular	6/16	5/18	NS
Subglandular	9/11	0/10	$p < 0.05$
Total	15/27	5/28	$p < 0.05$

Table 2. Incidence of positive "research" cultures in submuscular breast augmentation versus breast reconstruction (4 implants, 17 tissue expanders)

Type of surgery	Capsule		Significance
	Contracted	Non-contracted	
Reconstruction	2/7	3/14	NS
Augmentation	4/9	2/4	NS

plants affected by capsular contracture (15 of 27 tested, 56%) was significantly higher than of those without capsular contracture (5 of 28 tested, 18%) ($p < 0.05$).

In patients without capsular contracture only five implants revealed the presence of bacteria (18%), while the majority of cultures (82%) were negative. Interestingly enough there were no positive cultures of implants removed from subglandular space in this group. There was no significant difference in the incidence of positive cultures of devices removed from the submuscular plane between those with and those without signs of capsular contracture (6 of 16, 38%, versus 5 of 18, 28%, $p > 0.05$) (Table 1).

The difference in the incidence of positive cultures between devices placed submuscularly and those placed into the subglandular plane was not significant (11 of 34, 32%, versus 9 of 21, 43%, $p > 0.05$). The incidence of positive cultures of implants from patients with breast reconstruction was not significantly higher in patients with capsular contracture (2 of 7, 29%) than of those without capsular contracture (3 of 14, 21%) ($p < 0.75$ for this relatively small population) (Table 2).

Correlation between the presence of pain and the culture results was striking: 91% of the cases with pain related to contracted capsules revealed positive cultures of implants while 25% of the implants that cultured positive in cases with capsular contracture did not have localized pain ($p < 0.1$) (Table 3).

The dominant species cultured was *Staphylococcus epidermidis*, which was identified in 17 of 22 positive cultures (Table 4).

Table 3. Incidence of positive implants cultures in relation to the presence/nonpresence of pain in patients with capsular contracture

Pain present	Negative culture	Positive culture[a]
Yes	1	10
No	12	4

[a] $p < 0.10$

Table 4. Bacteria cultured from silicone implant segments

Bacteria	Number of positive cultures[a]		Total
	Capsular contracture	No capsular contracture	
Staphylococcus epidermidis	13	4	17
Corynebacterium sp	1	—	1
Propionibacterium acnes	1	—	1
Bacillus sp	—	1	1
E. coli	—	1	1
Klebsiella pneumoniae	—	1	1
Total	15	7	22

[a] In two cases more than one isolate was cultured

Figure 2 shows the scanning electron micrograph of a silicone segment which is covered by amorphous material within which profiles suggestive of coccoid and bacilli bacteria are seen. The presence of bacteria-like bodies was only seen on SEM of implant surfaces which cultured positive and no bodies were found on those which cultured negative.

Routine cultures of capsular tissue segments were negative. Research cultures of capsular tissue segments were positive in seven patients (eight devices, 20%); *Staphylococcus epidermidis* was the isolate. Seven samples (50%) of capsular tissue tested negative when an adjacent implant segment revealed the presence of bacteria. In only one case was the capsular culture positive while the adjacent implant segment culture did not reveal bacteria. Tissue from 21 noncontracted capsules tested negative 19 times (90%); two segments (10%) were positive. Among 19 contracted capsules, six segments tested positive (32%) versus 13 (68%) negative cultures. Contracted capsule tissue revealed the presence of bacteria more frequently than tissue segments from noncontracted capsules (6 of 19, 32%, versus 2 of 21, 10%, respectively) ($p < 0.1$).

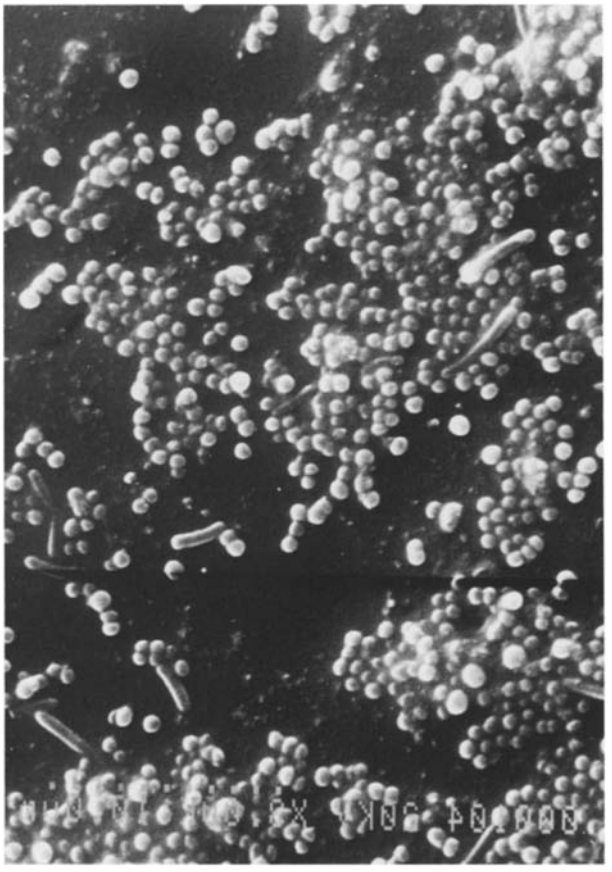

Fig. 2. Scanning electron microscopy of silicone mammary implant surface. Multiple coccoid and bacilli-like bacteria body shapes on the silicone surface. Original magnification 5000×

Discussion

Unilateral and bilateral contractures occur in ratios that are predictable based on the overall incidence of capsular contractures as independent events [5]. When one considers possible etiological causes of a unilateral contracture, causes other than those related to infection or hematoma lose credibility.

Overt infections following mammary implant placement seem to be rare nowadays [14, 27]. Nevertheless, when the implant is salvaged and retained by aggressive use of antibiotics, subsequent capsular contacture frequently occurs [11].

Accumulating clinical and experimental evidence lends support to the hypothesis that subclinical infection (bacterial presence without signs of infection) may be a cause of processes leading to capsular contracture [6–8, 34]. Even a study reporting the failure of a preoperative prophylaxis of antibiotics to decrease the incidence of capsular contracture, which at first glance may seem to disprove an "infectious theory," when analyzed may support it [17]. Diagnostic and therapeutic problems of subclinical infections are related to the fact that frequently slime-producing bacteria are involved. These bacteria may become very adherent to silicone surfaces and are difficult to recover by conventional microbiological assays and not accessible to antibiotics [13, 22, 26, 30, 32]. Bacteria encased in slime are equally hard to recover or to destroy. Therefore, the facts that systemic antibiotics have not been shown to reduce the rate of capsular contracture and that at the same time negative cultures of the breast tissue increased (perhaps due to easier penetration by antibiotics of breast tissue than of biofilm) should not be surprising.

The relatively low consistency between results of implant cultures and adjacent tissue segment cultures in this study and the absence of bacteria and histological signs of inflammation in capsular tissue described by others is probably another illustration of the same problem: Slime-producing bacteria have a better chance of survival on a foreign body surface and they are generally difficult to recover [20, 29–32]. Some investigators even raise the possibility that changes of bacteria resistance to antibiotics may occur in the presence of biomaterials *per se*, for example, by induction of ultrastructural changes [10]. Alternative ways of preventing bacterial colonization of implants, other than traditionally administered antibiotics, may have to be sought, such as implant coating with a substance preventing bacterial adherence (Fig. 3) [7, 8, 10, 13, 17, 18].

There was no difference in the incidence of positive cultures between devices placed into subglandular and submuscular planes. It should also be noted, however, that the difference in the incidence of positive cultures of devices removed from the submuscular plane between cases with and without capsular contracture was not significant. This "inconsistency" reminds us that there may be more factors than silicone and bacteria determining the biological outcome of silicone implantation. There may be different interactions between silicone, bacteria, and fibroblasts depending on silicone surface or wound location. Immune system cells and inflammation mediators may have different access to the wound, depending, for example, on its vascularity [4, 16, 23].

SEM is the technique of choice to study microbes immobilized in polymeric matrices, however, it does have some technical problems [21, 25]. SEM screening essentially yielded similar sensitivity as did our research culture technique. Both culture techniques and SEM may give false negative results [9, 12, 20, 21, 30, 33]. Use of more complicated forms of testing might increase bacteria detection yield [10, 19, 22, 29].

Results of this study, generally supporting the concept that subclinical infection is involved in the development of capsular contracture, demonstrate

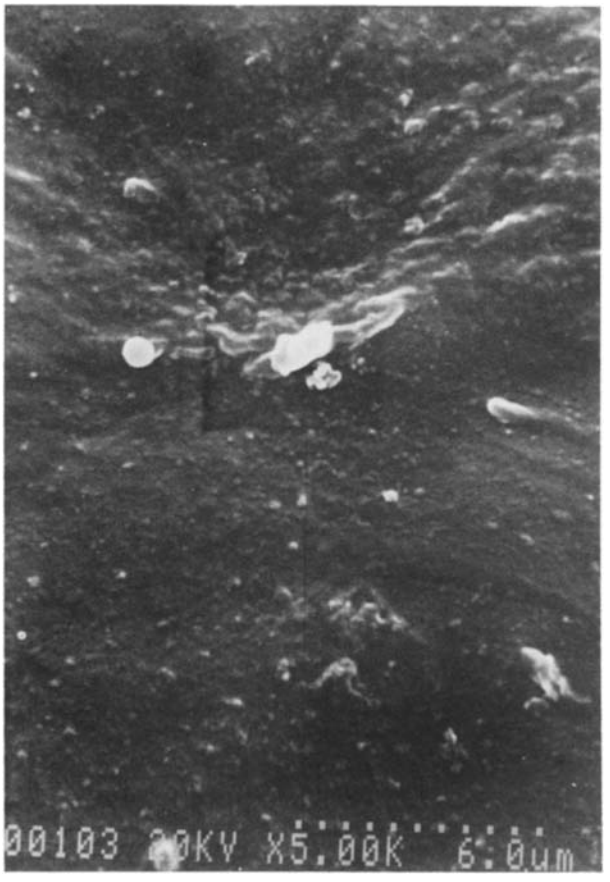

Fig. 3. Scanning electron microscopy of surface of silicone mammary implant immersed in a heparin solution (100 Units/1 mL of normal saline) prior to immersion in cultured *Staphylococcus epidermidis* suspension. Minimal colonization of the silicone surface. Original magnification 5000×

the importance of technical and microbiological aspects of silicone device investigation. There is a striking difference between the bacteria recovery rate from the routine, short incubation/plating technique and that from the prolonged incubation/continuous flow of substrates around the silicone culture technique [19, 20]. Use of sonication to disintegrate biofilm prior to culturing would perhaps further increase the bacteria recovery rate [10]. Perhaps it is unrealistic to think that there might be an absolutely sterile silicone mammary implant, considering the proximity of skin and its appendages (breast gland), the relative richness of endogenous bacterial flora in the operative area, and the affinity to silicone of slime-forming bacteria [6, 9, 29, 32, 37].

Several questions remain unanswered: What is the clinical significance of the presence of bacteria? Could silicone-adherent, biofilm-encased, metabolically dormant bacteria—or just the slime alone—affect the process of capsule healing? Is there a critical amount of bacterial products needed to trigger an unfavorable course of healing? Which products are important? Is there any local, cellular, genotypic or phenotypic predisposition necessary to "allow" the contracture to occur? Those issues will have to be addressed by those who try to establish "the bacteria connection."

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