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Package 01	T-cell mediated immune response to silica in silicone breast implant patients

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Performing your original search, "**silica**" and "**breast implant**", in PubMed will retrieve [7 records](#).

Plast Reconstr Surg. 1999 Apr;103(4):1273-6.

Analysis of breast implant capsular tissue for crystalline silica and other refractile phases.

Pasteris JD, Wopenka B, Freeman JJ, Young VL, Brandon HJ.

Department of Earth and Planetary Sciences, Washington University, St. Louis, MO, USA.

Abstract

This study questions previous reports of the presence of micrometer-sized areas of crystalline silica in pathologic tissue sections that are based exclusively on polarized-light microscopy. By using optical principles, it can be argued that it is impossible to identify unambiguously or to detect the birefringence of crystalline silica in 5-microm-thin sections. To clarify whether silicone, amorphous silica, or crystalline silica occurs in micrometer-sized moieties in standard 5-microm-thick tissue sections, one needs to apply a structural means of analysis in addition to optical microscopy. This study recommends the use of the laser Raman spectroscopic technique, which is very well suited to clarify this highly controversial issue in future pathologic studies.

PMID: 10088520 [PubMed - indexed for MEDLINE]

Publication Types, MeSH Terms, Substances

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National Institutes of Health

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Curr Rheumatol Rep. 2002 Aug;4(4):293-8.

An association of silicone-gel breast implant rupture and fibromyalgia.

Brown SL, Duggirala HJ, Pennello G.

US Food and Drug Administration, Epidemiology Branch, Center for Devices and Radiological Health, HFZ-541, 1350 Piccard Drive, Rockville, MD 20850, USA. syb@cdrh.fda.gov

Abstract

Silicone-gel breast implant rupture is common. Silicone-gel from ruptured implants may escape the scar capsule that forms around breast implants and become "extracapsular silicone." Our previously published study found that women with extracapsular silicone gel were at higher risk of reporting that they were diagnosed with fibromyalgia. There has been a limited number of studies addressing this association in the literature. Some studies addressing the issue of silicone breast implants and connective tissue disease specifically exclude patients with fibromyalgia from the sample or do not include the syndrome in the analysis. Case series describing fibromyalgia in patients with implants have been published, but many of these papers lack information on extracapsular silicone and are not representative because the patients are typically from referral populations. In addition, most studies do not have control groups of women without implants for comparison or do not distinguish between saline and silicone implants. Additional observational studies of women from nonreferral populations are necessary to validate an association. These studies should provide information on how the rupture is diagnosed, state whether the rupture extended beyond the capsule, and provide an appropriate control group for comparison. The findings from such studies may be important to physicians as they describe potential risks associated with implants to their patients. These findings should also be important for regulatory decision making on silicone-gel breast implants.

PMID: 12126580 [PubMed - indexed for MEDLINE]

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Articles

Environmental Health Perspectives Volume 107, Number 2, February 1999

Cyclosiloxanes Produce Fatal Liver and Lung Damage in Mice

Michael W. Lieberman, Ernest D. Lykissa, Roberto Barrios, Ching Nan Ou, Geeta Kala, and Subbarao V. Kala

Department of Pathology, Baylor College of Medicine, Houston, TX 77030 USA

Abstract

To examine the toxicity of cyclosiloxanes (CSs), the predominant low molecular weight cyclic silicones found in breast implants, we injected female CD-1 mice intraperitoneally with different doses of distillate (3.5-35 g/kg body weight) containing cyclosiloxane D3 (hexamethylcyclotrisiloxane; CS-D3), cyclosiloxane D4 (octamethylcyclotetrasiloxane; CS-D4), cyclosiloxane D5 (decamethylcyclopentasiloxane; CS-D5), and cyclosiloxane D6 (dodecamethylcyclohexasiloxane; CS-D6). The distillate was found to be lethal and all the mice injected with 35 g/kg died within 5-8 days. The median lethal dose (LD₅₀) for distillate was estimated to be approximately 28 g/kg. These mice developed inflammatory lesions of the lung and liver as well as liver cell necrosis with elevated serum levels of alanine aminotransferase, aspartate aminotransferase, and lactic acid dehydrogenase. Administration of CS-D4 alone also produced lethality in these mice with an LD₅₀ of 6-7 g/kg. CS-D4-treated mice also exhibited pulmonary and hepatic lesions and elevated serum enzymes. Analysis of LD₅₀ data indicates that CS-D4 is about as toxic as carbon tetrachloride or trichloroethylene. We measured hydroxyl radical formation in CS-D4-treated mice and found increases of approximately 20-fold in liver and approximately 7-fold in lung on day 4 following injection. Our findings are significant because in vitro experiments have demonstrated that CSs can migrate out of breast implants, and in mouse experiments CSs have been shown to be widely distributed in many organs after a single subcutaneous injection and to persist for at least a year. **Key words:** breast implants, cyclosiloxanes, silicone, toxicology. *Environ Health Perspect* 107:161-165 (1999). [Online 14 January 1999]

<http://ehpnet1.niehs.nih.gov/docs/1999/107p161-165lieberman/abstract.html>

Address correspondence to M.W. Lieberman, Department of Pathology, Baylor College of Medicine, Houston, TX 77030 USA.

We thank Donna Atwood, Susan Goodrum, and Estella Tam for their help with these experiments. This work was supported by a grant from the Consumer Advocates for Product Safety (CAPS) Foundation.

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Arch Dermatol. 1993 Jan;129(1):63-8.

Demonstration of silicon in sites of connective-tissue disease in patients with silicone-gel breast implants.

Silver RM, Sahn EE, Allen JA, Sahn S, Greene W, Maize JC, Garen PD.

Department of Medicine, Medical University of South Carolina, Charleston.

Comment in:

Arch Dermatol. 1993 Jan;129(1):97-8.

Abstract

BACKGROUND AND DESIGN: Silica, Silastic, and silicone (any organic compound in which silicon replaces carbon) have been associated with a number of connective-tissue diseases, most commonly systemic sclerosis (scleroderma). Silicone is known to leak from breast implants and spread to surrounding tissues, including lymph nodes, but silicone's role in the origin and pathogenesis of the inflammation and fibrosis related to such conditions remains controversial. Synovial tissue, alveolar macrophages, and skin, each from three different patients with silicone-gel implants, plus the breast implant capsules from each of the three patients, were examined by light microscopy, transmission electron microscopy, and electron probe microanalysis for the presence of silicon-containing material. **RESULTS:** Silicon was identified within the fibrous breast capsule of each case, associated with a chronic inflammatory cell infiltrate. Silicon was also identified within tissues involved by chronic inflammation and fibrosis, namely, synovium, skin, and alveolar macrophages, in association with clinical, serologic, and histologic evidence of connective tissue disease. All three patients improved after removal of the silicone-gel breast implants. **CONCLUSIONS:** The presence of silicon-containing material within sites of connective-tissue disease supports a role for silicon in the origin or pathogenesis of such conditions in patients with silicone-gel breast implants. All patients with connective-tissue disease should be questioned about exposure to various forms of silicon. In those patients with known exposure, tissue specimens should be examined carefully for silicon-containing material and, if found, the source should be removed.

PMID: 8420493 [PubMed - indexed for MEDLINE]

Publication Types, MeSH Terms, Substances

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U.S. National Library of Medicine
National Institutes of Health

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Toxicol Ind Health. 1994 Jan-Apr;10(1-2):25-42.

Immunologic and biologic markers for silicone.

Vojdani A, Brautbar N, Campbell A.

Drew University School of Medicine and Science, Beverly Hills, California 90211, USA.

PMID: 7570612 [PubMed - indexed for MEDLINE]

Publication Types, MeSH Terms, Substances

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U.S. National Library of Medicine
National Institutes of Health

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FASEB J. 1995 Mar;9(5):424-7.

Immunologic stimulation of T lymphocytes by silica after use of silicone mammary implants.

Smalley DL, Shanklin DR, Hall MF, Stevens MV, Hanissian A.

Baptist Memorial Health Care System, Memphis, Tennessee 38105.

Abstract

Difficulties in showing the biologic activity of silicones in vitro have contributed to the controversy over effects of silicone mammary implants in vivo. We adapted a standard lymphocyte stimulation test to detect evidence of cellular immunity in patients with silicone gel implants. Initially, lymphocytes were harvested from 70 implant patients, 76 normal controls without implants or symptoms, and 18 patients with classic rheumatic disorders and without a history of silicone implants. The harvested lymphocytes were stimulated with PWM, PHA, Con A, and pharmaceutical grade colloidal silicon dioxide (silica). Implant patients showed increased SI compared to controls and those with rheumatic disorders. The mean SI of implant patients was 195.0 +/- 19.3, 18-fold that of normal controls (< 0.0001). Patients with rheumatic disease showed the same SI as controls (P = 0.3577). A follow-up study included 220 normal controls without implants, 942 silicone gel implant patients with demonstrable rheumatic symptoms, and 34 implant patients without symptoms at the time of the study. The average SI for the 220 normal controls was 10.0 +/- 0.41. Among the symptomatic implant women, 860 (91.3%) had SI significantly above those of the normal controls. Of these, 171 (18.2%) had SI between 25 and 50, 316 (33.5%) had SI between 50 and 100, and 373 (39.6%) had SI over 100. The data presented confirms that silicone implant patients respond immunologically to the silicon dioxide contained in mammary prostheses.

PMID: 7896014 [PubMed - indexed for MEDLINE] [Free Article](#)

MeSH Terms, Substances

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6/25/2019

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West J Med. 1995 May;162(5):418-25.

Immunopathologic effects of silicone breast implants.

Teuber SS, Yoshida SH, Gershwin ME.

Division of Rheumatology, Allergy, and Clinical Immunology, University of California, School of Medicine, Davis 95616, USA.

Comment in:

West J Med. 1995 Oct;163(4):395.

Abstract

Silicone-gel breast implants have been associated with a myriad of autoimmune and connective tissue disorders by anecdotal reports and small observational series. To date, no prospective epidemiologic studies have been done to substantiate these observations, but an increasing body of literature is being developed and older studies are being recognized that point to immunotoxic or inflammatory effects of these breast implant components. The development of disease due to implants would depend on the interaction of genetic host factors so that only a few patients would potentially be at risk. Based on the example of other chemically mediated disorders, such as scleroderma in association with silica exposure, latency periods of more than 30 years before disease develops may be possible. Herein we review studies on silicone and immunity.

PMID: 7785255 [PubMed - indexed for MEDLINE] PMCID: PMC1022791 [Free PMC Article](#)

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Performing your original search, "**silica**" and "**breast implant**", in PubMed will retrieve [7 records](#).

Immunobiology. 1996-1997;196(5):567-74.

Lymphocyte response to silica among offspring of silicone breast implant recipients.

Smalley DL, Levine JJ, Shanklin DR, Hall MF, Stevens MV.

Baptist Memorial Health Care System, University of Tennessee, Memphis, USA.

Abstract

The current study evaluated immune response to silicon dioxide in children born to women with silicone breast implants. In part one of the study, the T lymphocytes of 21 of 24 such children were significantly stimulated by silicon dioxide (silica). Part two consisted of eleven children, four born preimplantation and seven born postimplantation. None of the preimplant offspring showed T cell responses to silica; five of the seven postimplant children were positive for T cell memory for silica. Part three was a blinded study based on statistically significant differences in T cell stimulation with silicon dioxide between postimplant children and controls. These findings indicate a common immune reaction, that of T cell memory, occurs in mothers and their children born after exposure to silicone mammary implants placed prior to pregnancy. Since not all such children were breast fed the result favors transplacental passage of immunogens such as silicone oligomers or through maternofetal cellular traffic.

PMID: 9145333 [PubMed - indexed for MEDLINE]

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Do you realize
the significance of this
study?
1) Breast fed babies
had T-cell response
2) and babies not breast fed
got their dose in the womb.

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Top Magn Reson Imaging. 1998 Apr;9(2):92-137.

Magnetic resonance evaluation of breast implants and soft-tissue silicone.

Middleton MS.

Robert N. Berk Magnetic Resonance Institute, UCSD Department of Radiology, San Diego, California 92103-8749, USA.
msm@ucsd.edu

Abstract

After several years of research in many disciplines, concern for the safety of silicone gel-filled breast implants continues. Although systemic effects of silicone are debated, there is growing consensus that implant rupture and other local breast complications from implants are very real concerns. This paper reviews the history of breast augmentation with an emphasis on the great variety of implants manufactured during the last generation. A classification scheme consisting of 14 breast implant categories is described, and the MR appearance of many is illustrated. The MR signs of implant rupture and pitfalls associated with those signs are reviewed. Indications and contraindications for MR imaging of implants and soft tissue silicone are presented. The author's breast implant and soft-tissue silicone MR imaging experience with follow-up surgical experience over the last 6 years is summarized and discussed. For 1,626 single lumen silicone gel-filled implants imaged, the sensitivity for rupture was 74% and the specificity was 98%. For those implants, 64.9% showed no evidence rupture on MR, 7.9% were indeterminate, and 27.2% were definitely ruptured. Of those that were ruptured, 26.2% had silicone outside as well as within the fibrous capsule. Of the 442 implants that were shown to be ruptured, 54.8% were in a state of uncollapsed rupture, 12.9% minimally collapsed rupture, 4.1% partially collapsed rupture, and 28.3% fully collapsed rupture.

PMID: 9622095 [PubMed - indexed for MEDLINE]

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Plast Reconstr Surg. 1997 Nov;100(6):1558-65.

Pathological and biophysical findings associated with silicone breast implants: a study of capsular tissues from 86 cases.

Luke JL, Kalasinsky VF, Turnicky RP, Centeno JA, Johnson FB, Mullick FG.

Department of Environmental and Toxicologic Pathology, Armed Forces Institute of Pathology, Washington, D.C. 20306-6000, USA.

Abstract

Breast implant capsular tissues from 86 cases were studied to characterize the relationship between capsular findings and the type of implant used. Tissues were examined by light microscopy, immunohistochemistry, scanning electron microscopy/energy dispersive x-ray analysis and Fourier transform infrared, and Raman microspectroscopy. Capsular pathology was influenced by the structure and composition of the implant. A pseudoepithelium at the inner capsular surface (synovial metaplasia) was noted with silicone gel-filled, saline-filled, and polyurethane-coated implants, and disproportionately with textured surface implants. Immunohistochemical studies of pseudoepithelium supported a macrophage/histiocyte cellular origin. Talc was identified intracellularly within macrophages in 42 cases. Capsular calcification was strongly associated with the presence of implant stabilization patch material. Infrared spectra were used to identify silicone, talc, Dacron, and two different types of polyurethane in capsular tissues. Micropapillary structures identified at the pseudoepithelial surface have, to the authors' knowledge, not been previously described.

PMID: 9385972 [PubMed - indexed for MEDLINE]

MeSH Terms, Substances

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U.S. National Library of Medicine
National Institutes of Health

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Ultrastruct Pathol. 1997 May-Jun;21(3):263-71.

Silicone breast implants: pathology.

Raso DS, Greene WB.

Department of Pathology, Medical University of South Carolina, Charleston, USA.

Abstract

Questions as to the bioreactivity of silicone breast implants (SBIs) have recently been intensely scrutinized, most notably by the media and legal system. Pathologists must be aware of the controversy and treat each SBI and associated tissue as a potential lawsuit. Grossly, silicone is a clear, viscous substance that may be observed either within or extruding from a silastic bag. By light microscopy, silicone is a nonstainable, nonpolarizable, refractile substance. Thicker sections, especially when viewed by non-Köhler illumination, phase-contrast, and darkfield microscopy will enhance visualization. Ultrastructurally, silicone is an electron-dense, amorphous substance often located within phagocytic vacuoles or extracellularly within the stroma. Correlating electron probe microanalysis allows for reliable identification. In most cases, a fibrous capsule surrounds the SBI, with the interface lining varying from a virtually acellular to a synovial-like lining composed of phagocytic and secretory cells. Silicone can often be identified within the fibrous capsule and also in distant tissues biopsied for suspected autoimmune disorders, such as synovium, skin, and lymph nodes, often without ultrastructural evidence of cytologic effects. This study has demonstrated that silicone accumulates at distant tissue sites due to preexisting inflammation acting as a stimulus. Thus, silicone is not a primary inducer of inflammatory disease processes. These findings are supported by various large epidemiologic studies.

PMID: 9183827 [PubMed - indexed for MEDLINE]

Publication Types, MeSH Terms, Substances

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U.S. National Library of Medicine
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Life Sci. 1995 Mar 10;56(16):1299-310.

Yoshida SH, Swan S, Teuber SS, Gershwin ME.

Division of Rheumatology, Allergy and Clinical Immunology, School of Medicine, University of California, Davis 95616, USA.

Comment in:

Life Sci. 1995;57(19):1737-40.

Abstract

Silicone gel implants for breast augmentation and reconstruction have been in use since 1962. Significant local complications include capsular contracture, rupture, gel "bleed", and spread of the implant material to regional lymph nodes (1-7) as well as histologic findings of foreign body granulomas in the capsular tissue and in lymph nodes (7-9). Through magnetic resonance spectroscopy and atomic emission spectroscopy, silicon compounds were found in the blood of some women with silicone breast implants; silicone and silica have also been found in liver (10). Well-publicized case reports have raised significant concerns regarding an association between implants and systemic disease. However, despite the availability of silicone implants for over 30 years, controlled epidemiological studies were not carried out until 1992. Currently available epidemiologic data are extremely limited. In part, because the majority of implants were used after 1981, the incidence of long-term problems is not yet known. In 1992, due to the unavailability of studies demonstrating the safety of implants, the U.S. Food and Drug Administration advised that silicone breast implants should be used only in reconstructive surgery and as part of clinical trials (11). This decision spurred a wave of research on the bioreactivity of silicone and clinical observations of patients with implants. Herein, we review the adverse immune effects following contact with silicone as well as the epidemiologic data available.

PMID: 8614251 [PubMed - indexed for MEDLINE]

Publication Types, MeSH Terms, Substances

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U.S. National Library of Medicine
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Minerva Med. 1998 Apr;89(4):117-30.

[Silicone breast prosthesis and rheumatoid arthritis: a new systemic disease: siliconosis. A case report and a critical review of the literature]

[Article in Italian]

Iannello S, Belfiore F.

Istituto di Medicina Interna e Specialità Internistiche, Università degli Studi, Catania.

Abstract

Today the number of women receiving breast implants of silicone gel, for augmentation or reconstruction of the breast, is increasing. Silicon implants may cause local complications (such as capsular contracture, rupture, closed capsulotomy, gel "bleed", nodular foreign body granulomas in the capsular tissue and lymph nodes) or general symptoms. An adverse immune reaction with signs and symptoms of rheumatoid disorders is also possible, although an increased frequency of true autoimmune systemic connective tissue diseases is controversial. The US Food and Drug Administration advised that these silicone implants should be used only in reconstructive surgery and as part of clinical trials. Silicone is not an inert substance and silicone compounds were found in the blood and liver of women with silicone breast implants. The development of disease related to silicone implants would depend on genetic factors, so that only a very few women are potentially at risk. HLA-DR53 may be a marker of predisposed subjects. Breast-feeding by women with silicone implants should not be recommended for possible autoimmune disorders in the children. We report the case of an adult female patient with silicone breast implantation for bilateral mastectomy (performed 12 months before) and a unique syndrome characterized by low-grade fever, chronic fatigue, arthralgias of the hands, dysphagia, dry eye, increased level of rheumatoid factor and decreased value of complement C3 and C4. No increased erythrocyte sedimentation rate occurred, and no ANA, nDNA, ENA and AAT autoantibodies were evidence. A critical review of literature (source: MEDLINE 1980-1997) was performed and our case seems to be the first one reported in Italy. The internist should become familiar with the immunological disorders related to silicone breast implants, often so marked to require the explantation of the prostheses to improve symptomatology. However, perhaps due to the leak and spreading of silicone, the progression to a severe systemic involvement may remain despite the implant removal.

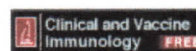
PMID: 9676177 [PubMed - indexed for MEDLINE]

Publication Types, MeSH Terms, Substances

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Clin Diagn Lab Immunol. 1994 Nov;1(6):689-95.

Silicone-specific blood lymphocyte response in women with silicone breast implants.

Ojo-Amaize EA, Conte V, Lin HC, Brucker RF, Agopian MS, Peter JB.
Specialty Laboratories, Inc., Santa Monica, California 90404-3900, USA.

Abstract

A blinded cross-sectional study was carried out with 99 women, 44 of whom had silicone breast implants. Group I consisted of 55 healthy volunteer women without breast implants; group II comprised 13 volunteer women with breast implants or explants who felt healthy; group III comprised 21 volunteer women with breast implants who had chronic fatigue, musculoskeletal symptoms, and skin disorders; and group IV comprised 10 women who had their prostheses explanted but still presented with clinical symptoms similar to those of the women in group III. Proliferative responses of peripheral blood mononuclear cells from all 99 women were measured by [³H]thymidine uptake after exposure to SiO₂ silicon, or silicone gel. The levels of proliferative responses were expressed as stimulation indices, which were obtained by dividing the counts per minute of stimulated cells by the counts per minute of unstimulated cells. Abnormal responses to SiO₂, silicon, or silicone gel were defined as a stimulation index of > 2.8, > 2.1, or > 2.4, respectively. Abnormal responses were observed in 0% of group I, 15% of group II, 29% of group III, and 30% of group IV (P < 0.0005 for group I versus groups II and IV). Thirty-one percent of symptomatic women with silicone gel breast implants had elevated serum silicon levels (> 0.18 mg/liter); however, there was no significant correlation between abnormal cellular responses and silicon levels in blood serum, type of implant, time since first implantation, prosthesis explantation, number of implants, or report of implant leakage or rupture. (ABSTRACT TRUNCATED AT 250 WORDS)

PMID: 8556522 [PubMed - indexed for MEDLINE] PMCID: PMC368392 [Free PMC Article](#)

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Summary

Pathology

1996, Vol. 28, No. 3, Pages 232-235

Spectrum of histological changes reactive to prosthetic breast implants: A clinopathological study of 84 patients

Gary Yeoh, Peter Russell and Elaine Jenkins

¹Hampson Pathology, Westmead, NSW

Summary

A wide range of host reactions can be produced in response to prosthetic breast implants. Although the spectrum of histological changes is well described in the literature, the chronology and relative occurrence of these changes are not well documented. Examination of 161 capsulectomy specimens from 84 women suggested the following chronological sequence of tissue response: fibrous scar tissue; histiocyte response; foreign body giant cell reaction to extruded or exposed material including polyurethane and Dacron patch; synovial-like metaplasia; and calcification. Fibrous scar tissue was seen in all implants. Histiocytic response was noted in 107/161 of the specimens and a foreign body giant cell reaction to polyurethane was seen only in the two Meme implants. Synovial-like metaplasia was less common than previously reported, occurring in 45/161 of specimens after a mean *in situ* duration of 11.7 years. This peculiar process was seen only in association with a prominent histiocytic response and was not associated with calcification. Dystrophic calcification, which has been reported as occurring rarely in implant capsules, was seen in 15/161 of our specimens after a mean *in situ* duration of 17.7 years.

[References](#) | [PDF \(2417 KB\)](#) | [PDF Plus \(1044 KB\)](#)

Forward Links to Citing Articles

Patrick P. L. Lau, Alexander C. L. Chan, M. H. Tsui. (2009) Diagnostic cytological features of polyacrylamide gel injection augmentation mammoplasty. *Pathology* 41:5, 443-447

Online publication date: 1-Jan-2009.

[Summary](#) | [Full Text](#) | [PDF \(552 KB\)](#) | [PDF Plus \(553 KB\)](#)

Aleš Ryška, Josef Špaček. (1998) Letters to the editor. *Pathology* 30:1, 82-83

Online publication date: 1-Jan-1998.

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