



AMERICAN UNIVERSITY

W A S H I N G T O N , D C

DEPARTMENT OF CHEMISTRY

September 9, 2004

Enclosed please find a copy of the paper, "Platinum concentration in silicone breast implant material and capsular tissue by ICP-MS" by S. V. M. Maharaj.

Thank you very much for your interest in this study.

Yours sincerely,

A handwritten signature in black ink, appearing to read 'SME'.

Dr. Susan V. M. Maharaj
Assistant Professor of Chemistry

COLLEGE OF ARTS AND SCIENCES

4400 MASSACHUSETTS AVENUE, NW WASHINGTON, DC 20016-8014 202-885-1750 FAX: 202-885-1752

S. V. M. Maharaj

Platinum concentration in silicone breast implant material and capsular tissue by ICP-MS

Received: 5 January 2004 / Revised: 28 May 2004 / Accepted: 7 June 2004 / Published online: 8 July 2004
© Springer-Verlag 2004

Abstract Inductively coupled plasma-mass spectrometry (ICP-MS) was used to determine the concentration of platinum (Pt) in silicone breast implant gel (range, 0.26–48.90 $\mu\text{g g}^{-1}$ Pt; $n=15$), elastomer (range, 3.05–28.78 $\mu\text{g g}^{-1}$ Pt; $n=7$), double lumen (range, 5.79–125.27 $\mu\text{g g}^{-1}$ Pt; $n=7$), foam (range, 5.79–8.36 $\mu\text{g g}^{-1}$ Pt; $n=2$), and capsular tissue (range, 0.003–0.272 $\mu\text{g g}^{-1}$ Pt; $n=15$). The results show that very high levels of Pt are present in the encasing elastomer, double lumen, and foam envelope materials. Silicone breast implants can be a source of significant Pt exposure for individuals with these implants.

Keywords Platinum · Breast implants · Silicone · Polydimethylsiloxane · PDMS · ICP-MS

Introduction

Silicone breast implants have been used as prosthetic devices for aesthetic augmentation and reconstructive surgery since the early 1960s [1, 2]. In the US, it is estimated that as many as 2 million women have had silicone breast implants [3, 4, 5]. A possible relationship may exist between silicone breast implants and the risk of connective tissue disease, autoimmune disorders, and neurological problems.

The fluid component of the silicone gel, the encasing elastomer, and double lumen (the thicker outer layer) envelope of breast implants consist of polydimethylsiloxane (PDMS), the most common siloxane polymer used in medical products. Platinic chloride, a water-soluble form of platinum (Pt), is used as the catalyst for the cross-linking or “curing” of the PDMS chains in medical silicone gels and elastomers.

Exposure to complex Pt salts has been associated with allergic respiratory symptoms and a positive skin-patch test in Pt catalyst processing plant workers [6, 7], occupational asthma [8, 9], anaphylactic reactions [10], and contact dermatitis [11, 12]. Pt salt exposure has also been linked to immunogenicity in mice [13], and has produced inhibitory effects on brain enzymes in cats [14]. Moreover, some women with breast implants develop the signs, symptoms, and diseases consistent with toxicity from and allergy to Pt salts [15, 16].

Very few studies have addressed Pt in silicone breast implants or in the corresponding capsular tissue. Only two studies have addressed Pt in silicone breast implant gel, and one study has addressed Pt in tissue from women exposed to implants. El-Jammal and Templeton [17] and Lykissa et al [18], using conventional digestion methods, determined the Pt concentration from silicone breast implants by inductively coupled plasma-mass spectrometry (ICP-MS). El-Jammal and Templeton [17] used an acid digestion and extraction method that involved using beakers on a hot plate. They analyzed the gel from one implant and found a concentration of $\approx 4.5 \mu\text{g g}^{-1}$ Pt. Lykissa et al [18] dissolved gel from nine implants in an organic solvent, and reported a concentration of $\approx 700 \text{ ng g}^{-1}$ Pt. The difference in Pt concentration between the two studies may be due to the different digestion methods used and/or the variability of implants [19]. Recently, Flassbeck et al [20] determined the Pt concentration of fat, capsular, and/or muscle tissue in three women with silicone gel-filled implants using microwave digestion, ICP high-resolution isotope dilution mass spectrometry (ICP-HR-IDMS), and gas chromatography-mass spectrometry (GC-MS), and detected 2.1–90 ng g^{-1} Pt.

Closed-vessel microwave digestion has several advantages over conventional digestion methods. In closed-vessel digestion, temperature and pressure are controlled; no sample material is lost, or contaminated; and samples are fully digested. Therefore, closed-vessel microwave digestion methods were developed for the

S. V. M. Maharaj
Department of Chemistry, American University,
Washington, DC 20016, USA
E-mail: Maharaj@american.edu

analysis of Pt from silicone breast implant material and capsular tissue samples.

This study represents: (1) the largest group of silicone breast implant gel and capsular tissue samples analyzed to date for Pt; (2) the first report of Pt levels in silicone breast implant gel using closed vessel microwave digestion, and; (3) the first report of Pt levels in silicone breast implant elastomer, double lumen, and foam (mainly polyurethane) encasing materials, the materials that are in direct contact with the chest wall of patients. Therefore, for the first time, analytical chemistry techniques are being applied to systematically include all intermediate breast implant components; elastomer, double lumen, and foam envelopes, leading from Pt in implant gel → Pt in implant envelopes → Pt in body tissue.

Materials and methods

Cases

Fifty available cases contained intact (unruptured) silicone implants, as determined from medical reports. Of the 50 cases 35 included the capsular tissue. From these 35 cases, 16 were selected for analysis, in order to have unruptured implants available for future work. The 16 cases represent implants containing elastomer ($n=7$), double lumen ($n=7$), and foam ($n=2$) encasing materials (Table 1), and the corresponding capsular tissue. Cases were chosen so that each type of encasing material would be represented, without knowledge of patient age, implant residence time, fixative used, or diagnosis. Of the 19 cases not selected, 16 contained elastomer shell envelopes.

Mean age of the women was 42.4 years (range, 25–69 years). Only one case (case no. 022) included infor-

Table 1 Cases, implants, and fixative

Case no.	Age ^a	Envelope ^b	Fixative ^c
001R	25	DL	Unfixed
005L	34	DL	Unfixed
005R	34	DL	Unfixed
012R	69	Elastomer	Saline
013L	35	Elastomer	Unfixed
022R	57	Elastomer	Formalin
024L	44	DL	Formalin
026L	35	Elastomer	Formalin
031L	56	Elastomer	Unfixed
031R	56	Elastomer	Unfixed
056L	27	Foam	Formalin
056R	27	Foam	Formalin
073L	35	DL	Formalin
112R	45	DL	Formalin
117R	47	DL	Formalin
128R	NA	Elastomer	Formalin

R right implant, L left implant, DL double lumen, NA not available

^aAge in years at time of explantation

^bOutermost encasing implant material

^cFixative is for implant only; all tissue was fixed in formaline

mation on the residence time of the implant before removal (20 years). No information was available on manufacturers or types of elastomers. Explanted implants were fixed in formalin or saline, or were unfixed (Table 1). All capsular tissue was fixed in formalin. Standard practice of not orientating capsular tissue specimens with respect to the inner or outer capsule layer was followed. All implants and tissue samples were stored in the dark. Medical reports of implant status (intact) for all implants in this study were verified by careful visual examination of each implant. Gel bleed on many shell surfaces was noted. Formalin tissue fixative solutions were also analyzed for background Pt levels. Implant fixatives were not analyzed. All studies were carried out after approval by the appropriate Institutional Review Board, Human Subjects and Research Committees.

Reagents

HF and HCl, Ultrex II Ultrapure Reagent grades, were purchased from J. T. Baker Inc. (Phillipsburg, N.J., USA). HNO₃, Optima grade, was purchased from Fisher Scientific (Pittsburg, PA, USA). HF and HNO₃ contained <1 pg ml⁻¹ Pt. HCl contained <5 pg ml⁻¹ Pt. The Pt standard (10,000 mg l⁻¹) was purchased from Spex CertiPrep (Metuchen, N.J., USA). Stock solutions were freshly prepared with distilled, deionized water from a MilliQ (Millipore, Bedford, MA, USA) filtering system.

Quality assurance

Digestion blanks, as well as internal and external standards, were used for quality assurance. Blanks and internal standards were subjected to the same digestion conditions as samples. Blanks contained either 5 ml HF and 1 ml aqua regia or 5 ml HNO₃ and 1 ml aqua regia, depending on the sample being analyzed (see below). An Aldrich (Milwaukee, WI, USA) PDMS gel, which was analyzed 18 times and contained a known amount of Pt, was used as an internal standard. Additional internal standards were made by adding 10, 100, and 1,000 pg ml⁻¹ Pt to blanks and the Aldrich PDMS gel before digestion. All internal standards were analyzed before and after each group of samples. External standards contained 5, 50, 250, 1,000, and 10,000 pg ml⁻¹ Pt in 1% HNO₃ and were interspersed between samples during analysis. Two samples from the same capsular tissue (case no. 128R) were analyzed.

Digestion method

Samples (0.5 g) were placed in numbered 500Plus vessels and digested in a MARS 5 microwave. Elastomer, double lumen, foam, and capsular tissue samples were

cut with an unused scalpel into $\approx 5 \text{ mm}^2$ sections to better ensure complete digestion. Two ramp-to-temperature microwave digestion methods were developed (Table 2). Samples containing PDMS gel, elastomer, double lumen, or foam were placed in the microwave with 5 ml HF; method Pt 1 was run, and vessels were allowed to cool to room temperature. One milliliter of aqua regia was added; samples were returned to the microwave; and method Pt 2 was run. Samples containing capsular tissue or formalin were also subjected to the above conditions, but were initially placed in the microwave with 5 ml HNO_3 (rather than HF). HF was used to dissolve the PDMS; HNO_3 was used to dissolve the tissue; and aqua regia was used to get the Pt into solution. All sample material was completely digested. Samples, blanks, and internal standards were diluted with 0.1% HNO_3 before analysis.

Instrumentation

All analyses were carried out with a Perkin Elmer (Shelton, CT, USA) SCIEX ICP-MS Elan 6100 DRC instrument equipped with a series 200 Autosampler. A radio frequency (RF) forward power of 1.3 kW was used. Argon flow rates for the plasma and auxiliary gas were 15 and 1.2 l min^{-1} , respectively, and were controlled with a MKS Type 146 mass flow controller. The sample was delivered at 0.9 ml min^{-1} by a peristaltic pump connected to a Meinhard quartz concentric neb-

ulizer and a cyclonic spray chamber (from Glass Expansion, Australia). Ion optics were optimized across the mass range 8.876–239 atomic mass units (amu), using a multi-element solution containing 56 elements at a concentration of 1 ng ml^{-1} each. Data were acquired at an amu of 195 with one mass unit resolution, 20 sweeps per reading, 4 s reading time, and three replicates per measurement. The detection limit was calculated at $1\text{--}2 \text{ pg g}^{-1}$ using three times the standard deviation of multiple blanks.

Results

The percentage relative standard deviation for all measured internal spiked standards was $\leq 10\%$ of known concentrations. A linear range ($r^2 \geq 0.999990$) was established between external standards, and extrapolated beyond them. Recovery of added Pt was complete (between 95 and 103%). Blank concentrations were calculated based on the final liquid weight and a 20-fold dilution factor and were $100\text{--}200 \text{ pg g}^{-1}$ Pt. Sample Pt concentrations (Table 3, Fig. 1) were calculated based on initial sample weight, final liquid weight, and mainly a 20- or 100-fold dilution factor.

Descriptive statistics are the most appropriate statistical tool for data analysis given the number of cases in this study. Standard deviations are small (Table 3). Mean gel and elastomer values were about the same, $11.42 \text{ } \mu\text{g g}^{-1}$ Pt (range, 0.26–48.90; $n=15$) and

Table 2 Microwave digestion methods

Method	Maximum power	Power (%)	Ramp (min)	Pressure (psi)	Temperature ($^{\circ}\text{C}$)	Hold (min)
Pt 1	1,200	100	15	350	170	15
Pt 2	1,200	100	15	350	130	5

Table 3 Pt concentration results ($\mu\text{g g}^{-1}$)

Case no.	Gel	Elastomer	Lumen	Foam	Tissue ^a	Formalin ^a
001R	48.903 ± 0.389	NA	72.878 ± 0.052	NA	0.014 ± 0.464	NA
005L	30.169 ± 0.159	NA	125.268 ± 0.764	NA	0.035 ± 0.465	NA
005R	34.713 ± 0.263	NA	79.138 ± 0.417	NA	0.018 ± 0.234	NA
012R	0.366 ± 0.004	5.566 ± 0.035	NA	NA	0.023 ± 0.934	NA
013L	0.260 ± 0.001	8.773 ± 0.076	NA	NA	0.023 ± 0.606	NA
022R	1.297 ± 0.009	28.776 ± 0.400	NA	NA	0.272 ± 0.354	NA
024L	40.071 ± 0.326	NA	40.650 ± 0.240	NA	0.023 ± 0.231	NA
026L	0.370 ± 0.002	13.518 ± 0.134	NA	NA	0.056 ± 1.101	NA
031L	0.390 ± 0.002	10.196 ± 0.132	NA	NA	0.010 ± 0.734	NA
031R	0.334 ± 0.002	NA	NA	NA	0.001 ± 0.217	0.004 ± 0.353
056L	4.113 ± 0.023	NA	NA	8.362 ± 0.038	0.022 ± 0.678	NA
056R	4.021 ± 0.021	NA	NA	5.792 ± 0.004	0.004 ± 0.233	NA
073L	5.291 ± 0.042	NA	15.069 ± 0.036	NA	0.010 ± 0.067	NA
112R	NA	NA	5.787 ± 0.042	NA	NA	NA
117R	0.542 ± 0.006	10.575 ± 0.110	7.241 ± 0.070	NA	0.005 ± 0.322	NA
128R	0.516 ± 0.002	3.045 ± 0.019	NA	NA	0.003 ± 0.092	0.001 ± 0.104

SD were calculated from three analyses per sample

NA not available

^aSD for tissue and formalin given in ng g^{-1} (in order to show values)

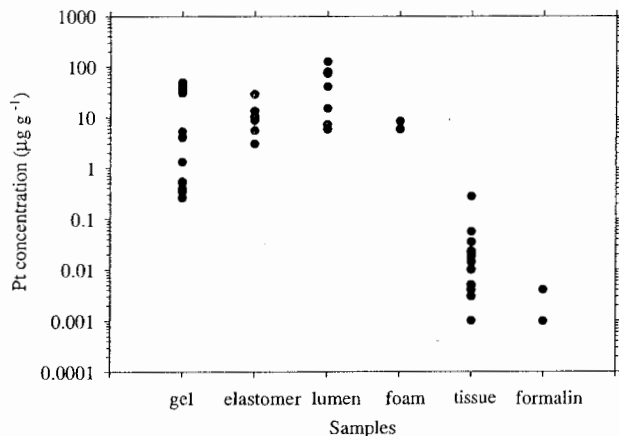


Fig. 1 Platinum concentration ($\mu\text{g g}^{-1}$) in silicone breast implant gel ($n=15$), elastomer ($n=7$), double lumen ($n=7$), foam ($n=2$), tissue ($n=15$), and formalin ($n=2$) samples; \bullet = this study

11.49 $\mu\text{g g}^{-1}$ Pt (range, 3.05–28.78; $n=7$), respectively. Mean Pt concentrations of the double lumen and foam encasing material were 49.43 $\mu\text{g g}^{-1}$ (range, 5.79–125.27; $n=7$) and 7.08 $\mu\text{g g}^{-1}$ (range, 5.79–8.36; $n=2$), respectively. Mean Pt concentration for all envelope shells was 27.54 $\mu\text{g g}^{-1}$ (range, 3.05–125.27; $n=16$). Mean Pt concentration for all capsular tissue samples was 0.035 $\mu\text{g g}^{-1}$ (range, 0.003–0.272; $n=15$). Mean formalin concentration was 0.003 $\mu\text{g g}^{-1}$ (range, 0.001–0.004; $n=2$) or $2,244 \pm 228$ pg g^{-1} Pt. The Pt concentration of freshly prepared formalin was 456 ± 162 pg g^{-1} . Mean concentration of the two samples from the same capsular tissue (case no. 128R) was $3,004 \pm 92$ pg g^{-1} Pt.

Cases (001R, 005L, 005R, 024L, and 073L) that contained the five highest values for the double lumen material (72.88, 125.27, 79.14, 40.65, and 15.07 $\mu\text{g g}^{-1}$ Pt, respectively) also contained the five highest gel values (48.90, 30.17, 34.71, 40.07, and 5.29 $\mu\text{g g}^{-1}$ Pt, respectively), (Table 3, Fig. 2). Cases 022R and 026L that contained the two highest values for the elastomer (28.78 and 13.52 $\mu\text{g g}^{-1}$ Pt, respectively) also contained the two highest tissue values (0.27 and 0.06 $\mu\text{g g}^{-1}$, respectively). Case 022R contained a much higher than average Pt tissue concentration.

Discussion

Internal and external calibration results show very good accuracy. Small standard deviations (Table 3) and a very low detection limit show the precision of the analytical methods used. Excellent reproducibility is demonstrated by a duplicate sample of capsular tissue from case no. 128R. Blanks contain very low Pt levels and show that contamination was minimal.

Platinum concentration in each group of breast implant material (gel, elastomer, double lumen, or foam) varied considerably (Fig. 1). All materials contained

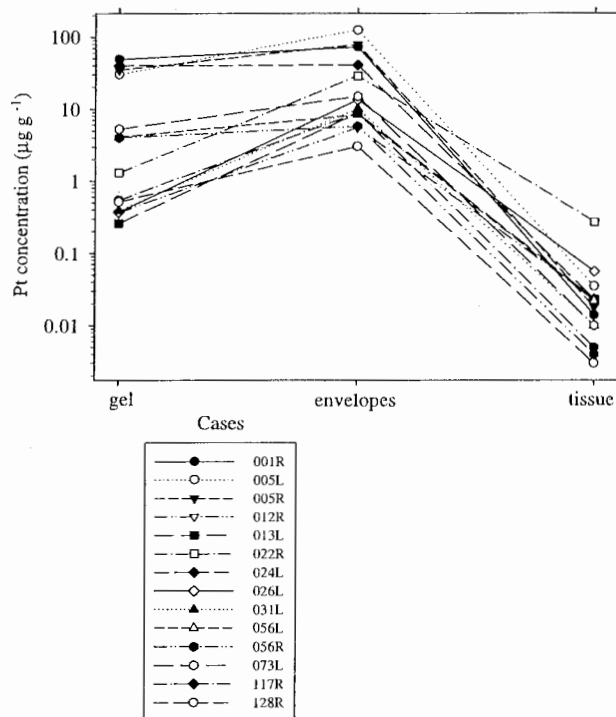


Fig. 2 Platinum concentration ($\mu\text{g g}^{-1}$) in gel, envelope, and tissue samples grouped by cases. The average envelope concentration was used for case no. 117R

much higher levels of Pt than has been reported by manufacturers, or in previous studies [17, 18]. This was most likely a result of the digestion methods, which yielded complete sample digestion and no sample loss. The slightly lower mean Pt concentration of the foam encasing material versus the other implant materials was probably due to the composition of the foam, which is mainly polyurethane and only partly PDMS. All encasing materials, and particularly the double lumen envelope, contained high levels of Pt. These are the materials in direct contact with the chest wall of patients with breast implants.

The much higher than average Pt concentration of the tissue sample for case 022R may be a result of the residence time in the patient – 20 years. This was the only case with available implant time data. As this individual was the second-oldest patient (Table 1), 20 years may very well be the longest implant residence time in this study, suggesting a possible relationship between Pt concentration in capsular tissue and implant residence time.

Platinum leaks through an intact 250 g implant into lipid-containing media at rates of approximately 20–25 $\mu\text{g day}^{-1}$ at 37°C [18]. The results of this study also indicate Pt migration from implant material, as the capsular tissue contains 35 ng g^{-1} Pt (mean). The formalin used for the tissue fixative contains about five times the amount of Pt (mean, 2,244 pg g^{-1} Pt), and also indicates possible Pt migration, perhaps via siloxane

bleeding. High Pt levels in tissue samples from a recent study also suggest a correlation between Pt and leaking of silicone gel breast implants [20]. The Pt levels in tissue detected by Flassbeck et al [20] are very similar to the Pt levels in tissue samples from this study, and demonstrate the robustness of these two independent investigations.

Platinum most likely occurs in implant material as hexavalent platinum (Pt⁺⁶) compounds, along with other ionized forms of Pt, and organoplatinum or silicon-Pt complexes [18]. Although the concentration of Pt⁺⁶ is unknown, given the high toxicity and biological reactivity of ionized forms of Pt, any amount may be too much [7, 21]. A major toxicologic issue is immunogenicity, where absolute amounts have little significance in the development of allergic and immune disorders [22, 23, 24]. As Pt in the form of soluble salts is a potent allergic sensitizer, a "safe" dose is unknown [25].

Alternative implants, such as those containing saline or soybean oil (Trilucent implants), have been proposed as a means to decrease exposure to silicone gel, and consequently to Pt. However, if silicone elastomer and double lumen encasing materials are used as part of these alternative implants, similar potential Pt toxicity risks may be expected.

Limitations of this study include the number of cases with different types of implant shells available for analyses, the limited information on manufacturer, type of elastomers, and the duration of implant exposure. The current dearth of studies in the peer-reviewed literature on the amount of residual Pt in implants and Pt levels in women with breast implants [26] needs to be corrected. Further research in this field needs to be performed on larger sample sizes, with complete information on manufacturer, type of elastomers, and exposure duration, and the chemical speciation should be addressed (including oxidation states of Pt in implants and capsular tissue).

Acknowledgements I thank Ms. Jessica Caplan and LT Dr. John W. Ejniak for assistance with the ICP-MS. COL Dr. Kip Hartman, Ms. Maggie A. Meitzler, Mr. Craig R. Morrissette, and several anonymous reviewers provided comments on an earlier version of this manuscript. I am grateful to Mr. Assen Assenov, Dr. Michael R. Harbut, and Ms. Marlene Keeling for discussions. Prof. Klaus Heumann and two anonymous referees provided constructive comments that greatly improved the manuscript, and are gratefully acknowledged. Partial support was provided by a grant from the American Registry of Pathology.

References

- Bridges AJ, Vasey FB (1993) Silicone breast implants: history, safety, and potential complications. *Arch Intern Med* 153:2638–2644
- Braley S (1963) Use of silicones in plastic surgery. *Archiv Otolaryngol* 78:669–675
- Deapen DM, Pike MC, Casagrande JT, Brody GS (1986) The relationship between breast cancer and augmentation mammoplasty: an epidemiologic study. *Plast Reconstr Surg* 77:361–368
- May DS, Stroup NE (1991) The incidence of sarcomas of the breast among women in the United States, 1973–1986. *Plast Reconstr Surg* 87:193–194
- Cook RR, Perkins LL (1996) The prevalence of breast implants among women in the United States. In: Potter M, Rose NR (eds) *Immunology of silicones*. Springer, Berlin Heidelberg New York, pp 419–425
- Bolm-Audorff U, Bienfait HG, Burkhard J, Bury AH, Merget R, Pressel G, Schultze-Werninghaus G (1992) Prevalence of respiratory allergy in a platinum refinery. *Int Arch Occ Env Hea* 64:257–260
- Niezborala M, Garnier R (1996) Allergy to complex platinum salts: a historical prospective cohort study. *Occup Environ Med* 53:252–257
- Merget R, Reineke M, Rueckmann A, Bergmann E, Schultze-Werninghaus G (1994) Nonspecific and specific bronchial responsiveness in occupational asthma caused by platinum salts after allergen avoidance. *Am J Resp Crit Care* 150:1146–1149
- Merget R, Caspari C, Kulzer R, Breitstadt R, Rueckmann A, Schultze-Werninghaus G (1995) The sequence of symptoms, sensitization and bronchial hyperresponsiveness in early occupational asthma due to platinum salts. *Int Arch Allergy Imm* 107:406–407
- von Hoff DD, Slavik M, Muggia FM (1976) Allergic reactions to *cis*-platinum. *Lancet* 1:90–95
- Sheard C (1955) Contact dermatitis from platinum and related metals: report of a case. *Arch Dermatol* 71:357–360
- Levene GM (1971) Platinum sensitivity. *Brit J Dermatol* 85:590–593
- Schuppe H, Haas-Raida D, Kulig J, Bomer U, Gleichmann E, Kind P (1992) T-cell-dependent popliteal lymph node reactions to platinum compounds in mice. *Int Arch Allergy Imm* 97:308–314
- Agnew WF, Yuen TGH, Pudenz RH, Bullara LA (1977) Neuropathological effects of intracerebral platinum salt injections. *J Neuropath Exp Neur* 36:533–546
- Bridges AJ, Conley C, Wang G, Burns DE, Vasey FB (1993) A clinical and immunologic evaluation of women with silicone breast implants and symptoms of rheumatic disease. *Ann Int Med* 118:929–936
- Harbut MR, Churchill BC (1999) Asthma in patients with silicone breast implants: Report of a case series and identification of hexachloroplatinate contaminant as a possible etiologic agent. *Israel J Occup Health* 3:73–82
- El-Jammal A, Templeton DM (1995) Measurement of platinum in biomedical silicones by ICP-MS. *Anal Proc Incl Anal Commun* 32:293–295
- Lykissa ED, Kala SV, Hurley JB, Lebovitz RM (1977) Release of low molecular weight silicones and platinum from silicone breast implants. *Anal Chem* 69:4912–4916
- Brandon HJ, Young VL, Jerina KL, Wolf CJ (2001) Variability in the properties of silicone gel breast implants. *Plast Reconstr Surg* 108:647–655
- Flassbeck D, Pfeleiderer B, Klemens P, Heumann KG, Eltze E, Hirner AV (2003) Determination of siloxanes, silicon, and platinum in tissues of women with silicone gel-filled implants. *Anal Bioanal Chem* 375:356–362
- Kazantzis G (1978) The role of hypersensitivity and the immune response in influencing susceptibility to metal toxicity. *Environ Health Persp* 25:111–118
- Biagini RE, Bernstein IL, Gallagher JS, Moorman WJ, Brooks S, Gann PH (1985) The diversity of reaginic immune responses to platinum and palladium metallic salts. *J Allergy Clin Immun* 76:794–802
- Merget R, Schultze-Werninghaus G, Muthorst T, Friedrich W, Mefer-Sydow J (1988) Asthma due to complex salts of platinum: a cross-sectional survey of workers in a platinum refinery. *Clin Allergy* 18:569–580
- Pepys J, Pickering CAC, Hughes EG (1972) Asthma due to inhaled chemical agents: complex salts of platinum. *Clin Allergy* 2:391–396

25. Goering PL (1992) Platinum and related metals: palladium, iridium, osmium, rhodium, and ruthenium. In: Sullivan JB, Krieger GR (eds) Hazardous materials toxicology, clinical principles of environmental health. Williams and Wilkins, Baltimore, MD, pp 874-881
26. Arepalli SR, Bezabeh S, Brown SL (2002) Allergic reaction to platinum in silicone breast implants. *J Long Term Eff Med* 12:299-306