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Exposure Dose and Significance of Platinum and Platinum Salts in Breast Implants

S. V. M. Maharaj, PhD

ABSTRACT. The objectives of this study were to illustrate and inform key scientific issues, as determined from the peer-reviewed literature, that are critical to developing an accurate understanding of the current state of knowledge regarding platinum (Pt) in medical devices (ie, breast implants). The author identified most studies for inclusion via a PubMed database search; she extracted descriptive statistics from the studies. The author calculated Pt and Pt salt exposure doses for environmental and occupationally related samples. She observed that a number of samples elicited biological effects over a wide range of concentrations. A single silicone breast implant may be expected to contain higher Pt and Pt salt doses than have produced adverse health effects in humans. The author posits a biologically plausible rationale for Pt salt-related health problems in women that have been exposed to silicone breast implants.

KEYWORDS: breast implants, environmental exposure, exposure assessment, medical devices, metal exposure, platinum, platinum salts, risk assessment

Environmental exposure may be defined as exposure originating from any source other than human biology. Exposure from air, water, food, and rocks are well-known examples. Lifestyle factors represent a subset of environmental exposure that have become increasingly important as determinants for illness and disease in humans.[1–5] One such lifestyle factor is whether individuals, including children,[6,7] have been exposed to medical devices.

Commonly implanted medical devices include breast, testicular, and chin implants. In the United States, 3–4 million women have elected to have breast implants placed[8–10] for augmentation purposes, following mastectomy due to breast cancer, or for other reasons (eg, to correct the appearance of chest wall deformities). Approximately 200,000 adverse events or reaction reports about breast implants have been submitted to the US Food and Drug Administration since 1985. However, there is no clear explanation for the symptoms reported by women who have had these medical devices placed or for the signs and diseases documented by their physicians. For example, a twofold-increased risk of lung cancer has been found in breast implant patients, even when smoking was controlled for.[11]

Medical-grade silicone or poly(dimethysiloxane) (PDMS) is the gel used in silicone breast implants and as the encasing envelope in both silicone and saline breast implants. The metal platinum (Pt) also is used in the manufacture of breast implants (ie, in the catalyst for the cross-linking of the PDMS chains in both gels and envelopes). Platinum may occur in the metal state as Pt (0), or it may occur in higher oxidation states (eg, Pt +2 or Pt +4). Platinum in the metal state or the (0) oxidation state is generally considered to be unreactive. Platinum in oxidation states Pt +1 through Pt +6 is considered reactive. In the compound hexachloroplatinate, which has been used in the manufacture of breast implants, the oxidation state of Pt is +4.

The majority of compounds that contain higher oxidation states of Pt are Pt salts. Pt salts can produce adverse health effects in humans.[12–18] Although Pt salts may act as cytotoxic agents, their importance to environmental and

S.V.M. Maharaj *is with the Center for Research on Environmental Medicine in New Market, MD.*

occupational medicine is based on their character as among the most potent sensitizers known.

To make an informed decision of whether to have breast implants placed, individuals need to weigh potential risks and benefits associated with the devices. True informed consent may only occur if individuals are aware of all potential health risks[19,20] from breast implants, including that from Pt. Therefore, in the interest of health education concerning the importance of possible environmental exposure from these medical devices, I reviewed the available scientific and medical literature to determine the amount and forms of Pt present in and from silicone and saline breast implants.

To my knowledge, this study represents the first systematic review of all experimental, clinical, and other evidence from the peer-reviewed literature on Pt in breast implants. The objectives of the study were to illustrate and inform key scientific issues that are critical to developing an accurate understanding of the current state of knowledge about the subject. This study provides important information on the amount and forms of Pt that individuals who have had breast implants—or those considering breast implants—may be exposed to, and the results may be useful for health risk assessment.

METHODS

Study Selection

I conducted a PubMed database[21] search for all articles published through January 2007 on the subject of Pt in breast implants. I used a combination of terms as keywords. The PubMed literature search was supplemented by searches of material identified in the references and in my library. Peer-reviewed original articles published in English were eligible for inclusion. I did not consider nonpeer-reviewed works (eg, letters to the editor).

Systematic reviews and studies based on the literature typically exclude review articles,[22] articles that contain no original data,[23] and correspondence referring to previously published studies.[24] However, I included these types of articles in an effort to be as comprehensive and balanced as possible. For example, had I excluded articles that contained no original data, then I would have had to exclude all articles authored by individuals employed by or associated with the breast implant industry.

Data Analysis

I extracted descriptive statistics from the studies. Descriptive statistics were the most appropriate data analysis tool used in the studies examined because the number of observations (n) was small and were likewise the most appropriate data analysis tools for this study.

I mathematically combined the Pt concentration in silicone breast implants to extract the means for breast implant components, where applicable. I calculated the total Pt exposure dose (mean and ranges) that may be contained in 3 common implant sizes (200 g, 300 g, and 400 g) on the basis of the Pt concentration in breast implant components from the peer-reviewed literature. I considered 3 envelope types, which represent all types for which data exists. I used a 10% shell weight and 1.0 g/mL for density. A sample calculation follows: 270 g × 7.29 μg/g = 1,968.3 μg; 30 g × 11.49 μg/g = 344.7 μg; 1,968.3 + 344.7 μg = 2.313 mg Pt.

I also calculated Pt and Pt salt exposure doses for environmental and occupationally related samples. Because literature values were in a range of units, I converted all units to molarity (M) Pt or M Pt salts to compare dosimetries. For silicone breast implants, 1 g = 1 mL was assumed for conversion to M Pt (mean [M] and range) and M Pt salts. I calculated semiquantitative measures of Pt salts for silicone breast implants (n = 9, M) and whole blood (n = 7) from women exposed to silicone breast implants, using only percentages of higher oxidation states for which there was direct experimental evidence (ie, Pt +2 and +4) in the literature. I calculated Pt salts in silicone breast implants using the gel component only (eg, 270 g gel for a 300-g implant) because, to my knowledge, no researchers have analyzed implant envelopes for Pt oxidation states.

Where Pt salt compounds were unspecified (eg, National Institute for Occupational Safety and Health [NIOSH] limits), I assumed the molecular weight of hexachloroplatinate for conversion to M Pt salts. I calculated the NIOSH recommended exposure limit for the total weighted average (REL TWA) for Pt and Pt salts, and the immediately dangerous to life and health level (IDLH) for Pt salts to M Pt or M Pt salts assuming 1,000 cc = 1 L.

RESULTS

Sampling

The search procedures yielded 12 potentially relevant articles. Figure 1 characterizes the articles in the study selection process. Of the articles retrieved for evaluation, only 1 did not meet the inclusion criteria.[25] Five experimental studies,[26–30] 1 clinical study,[31] 3 reviews,[32–34] and 2 comments[35,36] met the inclusion criteria.

Six studies[26,27,29,32,33,35] addressed the Pt concentration present in silicone breast implant gels and/or envelopes. Five studies[27,32,33,35,36] discussed the total Pt exposure dose present in a single or a pair of silicone breast implants. Only 1 study reported the Pt concentrations of saline breast implant fluid.[30] The Pt concentration present in tissue and/or fluids from women exposed to silicone and/or saline breast implants was measured in 3 studies.[28–30] The forms of Pt, including the oxidation state of the Pt present in silicone and/or saline breast implants, tissue, or body fluids from exposed women, were evaluated in 10 studies.[27–36]

Pt in Silicone Implants

Of the studies that addressed the Pt concentration present in silicone breast implant gels and/or envelopes, 3 contained no original data,[32,33,35] and 3 presented experimental results.[26,27,29]

Two review articles[32,33] and 1 comment[35] gave values for the Pt concentration in gels and/or envelopes on the basis of previous work. One review[32] cited 2 of the previously mentioned 3 experimental studies,[26,27] and another review[33] and a comment[35] referenced the Institute of Medicine (IOM).[37]

In 1 experimental study,[26] researchers analyzed the gel from 1 implant and reported a concentration of ~4.5 μg/g Pt.

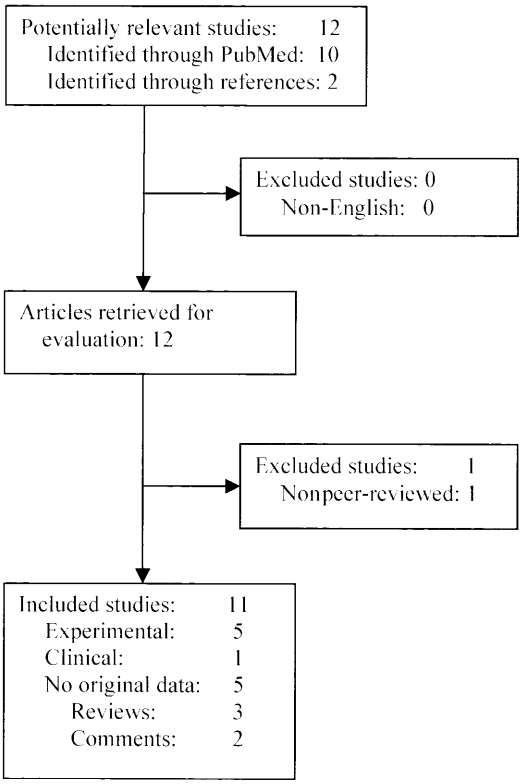

Fig. 1. Flow chart diagram of the study selection process.

In another experimental study,[27] researchers analyzed the gel from 9 explants and reported a concentration of ~0.7 μg/g Pt. In a third experimental study,[29] the researcher analyzed 15 gel and 16 envelope samples from explants. The envelopes were of 3 types: a single elastomer, a double lumen type where the thicker, outer envelope was sampled, and polyurethane foam. Table 1 lists mean Pt concentrations and ranges for silicone breast implant gel and envelopes on the basis of all available experimental studies.

Total Pt Exposure Dose in Silicone Implants

Of the studies that discussed the total Pt exposure dose present in a single or a pair of silicone breast implants, 3 cited amounts based on a single weight or volume of implant(s),[27,32,35] and 2 cited Pt ranges.[33,36]

Arepalli, Bezabeh, and Brown[32] cited the peer-reviewed literature and reported that 2 large implants weighing 500 g each would contain a total Pt exposure dose of 15 mg. Lane[35] cited the IOM[37] and reported that a 300-cm^3 implant might contain a total Pt exposure dose of ~300 μg. Lykissa et al[27] reported that a 250-g implant would contain a total Pt exposure dose of ~175 μg. Two additional reports[33,36] that also cited the IOM[37] stated that 2 implants would contain a total Pt exposure dose of approximately 0.1 to 10 mg.

However, the total Pt exposure dose of a silicone breast implant would be expected to vary by, for example, size, envelope type, generation of implant, and manufacturer. Consideration of the Pt concentration in silicone breast implant components available from all experimental studies (see Table 1) yields the total Pt exposure dose that may be expected from a single silicone breast implant for 3 common implant sizes and envelope types (see Table 2).

Pt in Saline Implants

To my knowledge, only Lykissa and Maharaj[30] have addressed the Pt concentration that may be present in saline

Table 1.—Summary of Platinum Concentration (μg/g) in Breast Implant Components

Type of breast implant	*M*	Range	*n*	Reference
Silicone				
Gel				
Implant gel	4.71	4.39–5.07	1	El-Jammal and Templeton[26]
Explant gel	0.70	NA	9	Lykissa et al[27]
Explant gel	11.42	0.26–48.90	15	Maharaj[29]
Total	7.29	0.26–48.90	25	El-Jammal and Templeton,[26] Lykissa et al,[27] Maharaj[29]
Envelope				
Elastomer	11.49	3.05–28.78	7	Maharaj[29]
Double lumen	49.43	5.79–125.27	7	Maharaj[29]
Polyurethane foam	7.08	5.79–8.36	2	Maharaj[29]
Total	27.54	3.05–125.27	16	Maharaj[29]
Saline				
Saline fluid	ND	ND	2	Lykissa and Maharaj[30]

Note. NA = not available; ND = not detectable (ie, below detection limit).

Table 2.—Total Platinum Exposure Dose (mg) in a Single Silicone Breast Implant by Size and Envelope Type

Implant with envelope	200 g	300 g	400 g
Elastomer			
M	1.542	2.313	3.084
Range	0.108–9.378	0.162–14.066	0.216–18.755
Double lumen			
M	2.301	3.451	4.602
Range	0.163–11.307	0.244–16.961	0.325–22.615
Polyurethane foam			
M	1.454	2.181	2.908
Range	0.163–8.969	0.244–13.454	0.325–17.938

breast implants. In that study, the saline fluid component from 2 saline breast explants were analyzed and no detectable levels of Pt were found (see Table 1). To my knowledge, no researchers have analyzed any other components of saline breast implants for Pt, (eg, saline breast implant envelopes).

Pt From Silicone Implants

The Pt concentration present in tissue and/or fluids from women exposed to silicone breast implants was analyzed in 3 experimental studies.[28–30] Flassbeck et al[28] measured the Pt concentration in fat, capsular, and/or muscle tissue of 3 women exposed to silicone breast implants as 0.02 μg/g (range = nd−0.09). Control tissue samples of 3 women not exposed to silicone breast implants were 0.0004 μg/g (range = nd−0.001). In 2004, I measured the Pt concentration in capsular tissue in 12 women exposed to silicone breast implants as 0.035 μg/g (range = 0.003−0.272).[29] I did not analyze control tissue samples in that study; however, a cross-study comparison, a standard method for exposure analysis and interpretation, with the Flassbeck et al[28] study shows higher mean Pt tissue values from exposed women than from controls. In addition, a comparison of the mean Pt values in samples from exposed women in the 2 studies[28,29] shows similar amounts.

In another study, Lykissa and Maharaj[30] analyzed the Pt concentration in whole blood, urine, hair, nails, sweat, and/or breast milk samples from women exposed to silicone breast implants; control samples from women not exposed to breast implants were available for only whole blood and urine samples. Mean Pt values in whole blood and urine samples from women exposed to silicone breast implants were higher (568 pmol/L, $n = 9$; 1.77 μg/g, $n = 10$, respectively) than the mean in samples from the control groups (506 pmol/L, $n = 5$; 0.37 μg/g, $n = 2$, respectively). Mean Pt values for hair, nails, and breast milk samples from women exposed to silicone breast implants, when compared with the peer-reviewed literature, were also higher (2.1 ng/g, $n = 9$; 0.88 ng/g, $n = 9$; 1.09 μg/L, $n = 6$, respectively) than in individuals from the general population with no known Pt exposure (0.15 ng/g, $n = 114$; 0.31 ng/g, $n = 96$; < 0.01 μg/L, $n = 27$, respectively).[30]

Pt From Saline Implants

To my knowledge, only Lykissa and Maharaj[30] have addressed the Pt concentration present in tissue or fluids from women exposed to saline breast implants. In that study, we analyzed a whole blood sample from a woman exposed to saline breast implants and found a lower Pt concentration (412 pmol/L) than the mean for women exposed to silicone breast implants and for control subjects from the study.

Pt Oxidation States

All but one study[26] that met the inclusion criteria addressed the forms of Pt that may be present in breast implants. Experimental results have indicated that at least some Pt may occur in silicone breast implants as organoplatinum or silicone Pt complexes.[27,28] Other studies have hypothesized that Pt may occur in silicone breast implants as Pt +4,[31] Pt +6,[29] and other ionized forms of Pt.[29]

Five reports[32–36] stated that Pt occurs in silicone breast implants in the (0) oxidation state. However, none of these reports contained any original data in which to substantiate their claims, and instead cited previous studies as providing evidence that Pt occurs in silicone breast implants in the (0) oxidation state. For example, one report[35] asserted that "implants do contain catalytic amounts of platinum in the zero oxidation state" and cites a reference.[38(p5607)] However, the reference cited[38] contains no data regarding Pt oxidation states and was not peer reviewed.

Brook stated that "the papers that have examined the species of platinum in silicone breast implants have found no evidence of any species not at the zero oxidation state."[33(p3283)] However, an examination of the papers cited as evidence[39–46] in the above reports[32–34,36] reveals that no researcher actually analyzed a silicone breast implant (or explant) for various Pt oxidation states but instead analyzed silicone precursor materials. In addition, instrument sensitivities are critical to understanding the context of the reported results in these studies. It is debatable whether the detection limits of the instruments used (eg, cyclic voltammetry, extended x-ray absorption fine structure, nuclear magnetic resonance, small-angle x-ray scattering, ultraviolet-visible spectroscopy) in these previous studies[39–46] would be sensitive enough today to analyze for Pt in breast implants, even more so when these studies were conducted. Moreover, none of the instruments used in the previous studies would have been sensitive enough to detect Pt present in higher oxidation states in breast implants.

To my knowledge, only Lykissa and Maharaj[30] have analyzed silicone and saline breast implants, as well as tissue and body fluids from exposed women for ionic forms of Pt, and found direct experimental evidence for Pt (0), Pt +2, and Pt +4. Higher oxidation states of Pt were detected in all silicone explants ($n = 9$), whole blood

(n = 7), breast milk (n = 6), urine (n = 1), and brain tissue (n = 1) samples analyzed from women exposed to silicone breast implants. The fluid component from 2 (n = 2) saline breast explants showed no detectable levels of higher oxidation states of Pt.

Dosimetry Comparisons

Table 3 compares the concentration of Pt and Pt salts for a range of samples and the biological effects produced, where applicable. Tolerance limits for tissue concentrations of Pt or Pt salts for implantable biomedical devices are not available. The NIOSH REL TWA for Pt of 1 mg/m^3 calculates to 5×10^{-9} M Pt. The NIOSH REL and OSHA permissible exposure limit (PEL) TWA for Pt salts of 0.002 mg/m^3 calculates to 4.9×10^{-12} M Pt salts. The NIOSH IDLH for Pt salts of 4 mg/m^3 calculates to 10^{-8} M Pt salts.

COMMENT

Pt in and From Breast Implants

Table 1 presents the most comprehensive report to date of the Pt concentration present in breast implant components. Considerable variability may exist in the Pt concentration of silicone breast implant gels[26,27,29] and envelopes.[29] Although the amount of Pt may vary with other factors (eg, generation of implant and manufacturer), little information about these additional implant characteristics is available, and n values are too small at present to justify further subcategorizing of implants. Table 2, therefore, provides the best measure to date of the total Pt exposure dose that may be expected in a single silicone breast implant, by implant size and envelope type.

Mean Pt concentrations in breast fat and muscle tissue[28] and in whole blood and urine[30] from women exposed to

Table 3.—Comparison of Platinum and Platinum Salt Exposure Doses and the Effects Produced

Sample	Molarity	Range	Reference	Effects produced
Platinum				
SGFBI[a]				
With double lumen shell	5.9×10^{-5}	2.9×10^{-4}–4.2×10^{-6}	This study	Not studied
With elastomer shell	4×10^{-5}	2.4×10^{-4}–2.8×10^{-6}	This study	Not studied
With polyurethane shell	3.7×10^{-5}	2.3×10^{-4}–4.2×10^{-6}	This study	Not studied
Platinum	5×10^{-9}		NIOSH REL[47]	Toxicity
Platinum salts				
Sodium hexachloroplatinate (IV)	10^{-3}		Eberl et al[48]	Sperm reaction effects
$(NH_4)_2PtCl_4$, $(NH_4)_2PtCl_6$	10^{-4}		Di Gioacchino et al[49]	In vitro immune effects
Cis-diaminedichloroplatinate, Na_2PtI_6, $PtCl_4$	10^{-4}		Di Gioacchino et al[49]	In vitro immune effects
Tetra- and hexachloroplatinate	10^{-4}		Di Gioacchino et al[49]	In vitro immune effects
3:1 K_2PtCl_4:H_2PtCl_6	5.1×10^{-5}		Agnew et al[50]	Inhibitory effect on brain enzymes
Ammonium hexachloroplatinate	4.5×10^{-5}–2.3×10^{-6}		Rosenberg et al[51]	Inhibit cell division
Platinum chloride	10^{-5}–10^{-6}		Nordlind[52]	Influence DNA synthesis
Platinum salts in an SGFBI[a]	9.1×10^{-6}		Lykissa and Maharaj[30]	Not studied
Ammonium hexachloroplatinate	2.3×10^{-6}		Levene and Calnan[53]	Positive skin prick tests
Potassium hexachloroplatinate	2.1×10^{-6}		Freedman and Krupey[12]	Anaphylactic reaction
Hexachloroplatinate	10^{-2}–2×10^{-7}		Merget et al[16]	Skin reactivity
Sodium hexachloroplatinate (IV)	5×10^{-7}		Eberl et al[48]	Sperm reaction effects
Tetra- and hexachloroplatinate, $PtCl_4$	10^{-7}		Di Gioacchino et al[49]	In vitro immune effects
Hexachloroplatinate	10^{-2}–10^{-8}		Santucci et al[54]	Positive skin prick tests
Cisplatin, carboplatin, oxaliplatin	10^{-5}–5×10^{-8}		Mandal et al[55]	Hemoglobin-Pt complex formation
Hydrogen hexachloroplatinate (IV)	2.5×10^{-5}–2.5×10^{-8}		Theron et al[56]	Reactive oxygen species produced
Platinum salts	10^{-8}		NIOSH IDLH[47]	Immediate danger to life or health
Ammonium hexachloroplatinate	2.3×10^{-3}–2×10^{-9}		Biagini et al[14]	Positive skin prick tests
Ammonium hexachloroplatinate	2.3×10^{-4}–2×10^{-9}		Cleare et al[13]	Positive skin prick tests
Potassium tetrachloroplatinate	10^{-7}–10^{-9}		Freedman and Krupey[12]	Respiratory allergy
Potassium hexachloroplatinate	10^{-7}–10^{-10}		Freedman and Krupey[12]	Respiratory allergy
Platinum salts in whole blood (exposed to SGFBI)	10^{-9}–10^{-10}		Lykissa and Maharaj[30]	Not studied
Platinum salts	4.9×10^{-12}		NIOSH REL, OSHA PEL[47]	Allergic responses

Note. SGFBI = silicone gel-filled breast implant; NIOSH REL = National Institute for Occupational Safety and Health's recommended exposure limit; IDLH = immediately dangerous to life or health; OSHA PEL = Occupational Safety and Health Administration's permissible exposure limit.
[a]200, 300, or 400 g.

silicone breast implants have been shown to be higher than in the respective control groups. Mean Pt concentration in capsular tissue[29] and in hair, nails, and breast milk samples[30] from women exposed to silicone breast implants have been shown to be higher than in individuals from the general population with no known Pt exposure.

Pt has also been shown to migrate from intact implants[27] to capsular tissue[28,29] and breast fat and muscle tissue.[28] Experimental results have indicated that Pt migrates from silicone implants via the lymphatic and blood systems into urine, sebaceous secretions, and breast milk, and subsequently is deposited and accumulates in hair and nails.[30] It also has been hypothesized that Pt may persist after explantation as Pt-protein complexes and in bone.[30]

As saline breast implant fluid contained no detectable amounts of Pt, and a whole blood sample from a woman exposed to saline breast implants was lower than that of the mean of control subjects from the study, the devices analyzed most likely did not expose the individuals to Pt. However, Pt catalysts have been used in saline breast implant envelopes.[37] Therefore, individuals with older saline breast implants (in particular) may be exposed, but, to my knowledge, no researchers to date have analyzed saline breast implant envelopes for Pt.

The Catalyst

Four generations of silicone breast implants are commonly recognized.[37] First- and second- generation implants are no longer available. Third- and fourth-generation implants are currently on the market. There are no reports showing the type of catalyst used for a given generation of implant by manufacturer, construction type, and product characteristics.

In older implants, higher oxidation states of Pt may result directly from the hexachloroplatinate that was used as a catalyst and/or Pt-implant degradation products. In newer implants, higher oxidation states of Pt may result from the hexachloroplatinate that was used as starting material for the catalyst and/or from the incomplete conversion of the Pt catalyst to Pt (0). In addition, higher oxidation states of Pt in newer implants may result from Pt-implant degradation products.

Sensitization

The importance of Pt and Pt salts is illustrated, in part, by the number of samples that have elicited adverse health effects over a wide range of concentrations (see Table 3). A single silicone breast implant may be expected to contain a higher dose of Pt than has produced toxicity in humans. A single silicone breast implant also may be expected to contain a higher dose of Pt salts than has produced, for example, anaphylactic reactions, respiratory allergy, and other allergic responses in humans (see Table 3). Whole blood samples from women exposed to silicone breast implants contained a Pt salt concentration above the NIOSH and OSHA air concentration limits for Pt salts, which have elicited allergic responses in sensitized workers. Pt salts are well-known for their ability to act as potent sensitizers. For example, after Pt salt workers who were asthmatic and had positive skin prick tests were removed from exposure, and even after their skin prick tests had returned to negative, their asthma persisted.[57]

IOM Report and Health Problems

A number of reports that contained no original data referenced the IOM[37] to support arguments regarding Pt concentrations in silicone implant gels and envelopes,[33,35,36] the total Pt dose in an implant,[33,35,36] and the biologic plausibility of Pt-related health problems.[33–35] However, the IOM[37] reviewed reports published only through part of 1999, and as I have demonstrated, there have been several articles in the field published since then. Thus, the IOM[37] report is an outdated reference for the Pt concentration in breast implant components and for the total Pt exposure dose from an implant.

In addition, the IOM[37] states that there are no data in its report consistent with the disease process caused by Pt salts. However, Table B-1 of the report lists prominent problems in breast implant patients and reveals many symptoms and diseases (eg, allergic reactions, asthma, breathing difficulties, chemical and environmental sensitivities) known to be caused by Pt salts.

The IOM[37] report is also an outdated reference with respect to the plausibility of Pt-related health problems. It states that "then a biologically plausible rationale for platinum related health problems in women with silicone breast implants does not presently exist."[37(p110)] However, the first half of the sentence is prefaced by the qualifications, "If the platinum in breast implants is in zero valence form" and "if it is in microgram quantities." Direct experimental evidence shows that Pt in silicone breast implants may be present as Pt +2 and Pt +4,[30] and that Pt is present in much higher amounts than microgram quantities (as shown in this study and in others[26,27,29]). Therefore, using the same logic as the IOM,[37] a biologically plausible rationale for Pt-related health problems in women with silicone breast implants presently exists.

Limitations

This study is limited by the number of peer-reviewed articles that have been published on the subject of Pt in breast implants and by the information that was available in these studies. The strength of this review is based in part on the aggregation of the published literature (eg, in the PubMed database).

Future Work

Much more research in this field is warranted. Saline breast implant envelopes have not been analyzed for Pt concentration, nor have silicone and saline breast implant envelopes been for ionic forms of Pt. More studies on baseline levels from the general population are needed for a number of biological matrixes (eg, hair, nails, breast milk). Development of additional Pt standards and certified reference

materials that contain Pt concentrations in human biologic matrixes certified near current human exposure values is needed to support method validation. Development of methods to further characterize Pt oxidation states at the levels present in breast implants is also needed. Physiologically based pharmacokinetic modeling would be valuable to relate Pt and Pt salt exposure dose via implantation to bioavailability. Finally, future research should examine the ramifications of Pt and Pt salt exposure on the health outcomes of women with implants to provide a more complete understanding of this issue.

Conclusions

This comprehensive review of the existing peer-reviewed literature regarding Pt in breast implants supports the conclusions that (1) Pt is present in silicone breast implants in milligram quantities, (2) Pt migrates out of intact silicone implants and accumulates in the tissue and body fluids of exposed women, and (3) higher oxidation states of Pt (ie, Pt +2 and Pt +4) have been documented in silicone explants, tissue, and body fluids from exposed women. In addition, saline breast implants have not been associated with the release of Pt or Pt salts to other compartments. A single silicone breast implant may be expected to contain higher Pt and Pt salt doses than have produced symptoms and disease in humans. At present, a biologically plausible rationale exists for Pt salt-related health problems in women who have been exposed to silicone breast implants.

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For comments and further information, address correspondence to Dr S.V.M. Maharaj, Center for Research on Environmental Medicine, P.O. Box 224, New Market, MD 21774 USA.

Email: svmm@environmed.org

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