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Research

Heavy Metals in Breast Implant Capsules and Breast Tissue: Findings from the Systemic Symptoms in Women–Biospecimen Analysis Study: Part 2

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Abstract

Background: Breast Implant Illness (BII), as described in recent medical literature and by social media, describes a range of symptoms in patients with breast implants for which there are no physical findings or laboratory results that explain their symptoms.

Objectives: Part 2 of this study aims to determine whether heavy metals are present in the capsules around saline and silicone implants and if there are statistical differences in the type or level of these metals between women with or without symptoms. Demographic data was collected to investigate potential alternate sources of metals: inhaled, absorbed, or ingested.

Methods: A prospective, blinded study enrolled 150 consecutive subjects divided equally into in three cohorts: (A) women with systemic symptoms they attribute to their implants who requested implant removal, (B) women with breast implants requesting removal or exchange who do not have symptoms they attribute to their implants, and (C) women undergoing cosmetic mastopexy who have never had any implanted medical device. Capsule tissue was removed from Cohort A and B for analysis of 22 heavy metals. Additionally, breast tissue was obtained from a control group with no previous exposure to any implanted medical device.

Results: The study was performed between 2019-2021. Heavy metal content was compared between the capsule tissue from Cohort A and B. The only statistically significant differences identified in Cohort A were higher levels of arsenic and zinc, and lower levels of cobalt, manganese, silver, and tin. There were no elevated levels or statistically significant differences in the other metals tested between Cohorts A and B.

Conclusions: This study analyzes the metal content in capsules surrounding both saline and silicone breast implants. Heavy metals were also detected in the non-implant control group breast tissue, with some metals at numerically higher levels than either breast implant cohort. Smoking, gluten free diets, dietary supplements, and the presence of tattoos were all identified as statistically significant sources of arsenic and zinc in Cohort A. The risk of heavy metal toxicity should not be used as an indication for total capsulectomy if patients elect to remove their breast implants.

Level of Evidence: 3

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Breast implants, it has been argued, are among the most studied medical devices to date. Nonetheless, since their introduction in the 1960s, concerns have been raised regarding various aspects of their safety.[1] Among those concerns has been whether breast implants may contain and release a significant number of heavy metals—either from catalysts in the curing reaction or as part of the raw shell material or possibly the gel—that might negatively impact patient health.[2,3]

Recently, social media has played a significant role in heightening the concerns of women about the safety of their breast implants.[4,5] Online groups focus on what is commonly termed breast implant illness (BII), providing specific treatment recommendations on their sites for women with systemic symptoms that they attribute to their implants. The most steadfast advice from these groups is the unconditional need for an "en bloc" capsulectomy (removal of the intact capsule with the implant inside) to remove the toxins that they believe leach from the implants into the body. The origin of this advice arises in part from a 2009 book entitled *The Naked Truth about Breast Implants* in which Dr Susan Kolb discusses the importance of the removing the implant and capsule together. The author described the need to remove the entire capsule intact to avoid the silicone "spillage" that she postulated would make the patient sick from "chemical toxicity."[6]

In recent years, these same BII websites have expressed growing concerns about heavy metals as a primary cause of a range of systemic symptoms and health problems. As a result, breast implant patients experiencing symptoms often seek out surgeons who guarantee an en bloc capsulectomy. Further, they are advised that if a surgeon does not guarantee this procedure, it is not because of concerns about surgical and aesthetic risks, but rather because the surgeon lacks the surgical skills required to perform the procedure. Scientific evidence to support an actual benefit of such en bloc removal of breast implants other than in the treatment of breast implant–associated anaplastic large cell lymphoma or other malignancies, however, has been absent. En bloc capsulectomy and similar procedures are associated with significantly increased risks to the patient, including hematoma and pneumothorax, as well as potential uncorrectable aesthetic deformities.[7-9] One of the specific aims of this biospecimen retrieval and analysis study was to evaluate the capsular tissue surrounding the breast implants in women with and without symptoms, as well as normal breast tissue in women never exposed to any implanted device, for the presence or absence of significant levels of heavy metals.

METHODS

A prospective, controlled study was designed to evaluate the demographics, breast implant capsules, peripheral blood, patient-reported systemic symptoms, and National Institutes of Health (Bethesda, MD)–validated PROMIS questionnaires (used to record patient levels of anxiety, depression, cognitive function, and sleep disorders) at baseline, 3 to 6 weeks, 6 months, and 1 year. The study was registered on ClinicalTrials.gov (NCT04255810) and was funded solely by the Aesthetic Surgery Research and Education Foundation (ASERF). An informed consent for the donation of biospecimens was obtained from all study subjects. The study protocol followed the guidelines of the Declaration of Helsinki and was approved by the Brown University IRB. Patients were consecutively enrolled between November 2019 and May 2022 into 1 of 3 cohorts: Cohort A comprised 50 women with breast implants and symptoms self-defined as BII; Cohort B comprised 50 women with implants undergoing either an implant replacement or explantation without symptoms they attributed to their implants; and Cohort C comprised 50 women undergoing an elective aesthetic mastopexy who had no previous exposure to any implanted device. The protocol followed strict inclusion and exclusion criteria previously described in the first study publication.[10] Patients were enrolled in 3 cohorts at 5 locations within the United States, and investigators agreed to closely follow the subjects for a period of 1 year. Follow up for all 3 cohorts was 98% to 100% at 3 to 6 weeks, 84% to 98% at 6 months, and at 1 year is currently 66% to 90%.

In addition to completing a detailed surgeon observation form on the day of surgery, biospecimens were collected, including capsular tissue in Cohorts A and B and systemic blood in all 3 cohorts. Specimens were deidentified, blinded with respect to cohort, and sent to a Brown University pathology laboratory within 24 hours of collection. Additionally, approximately 10 g of capsular tissue was removed from both the right and left capsules in patients who were enrolled in Cohorts A and B and breast tissue was collected from 8 Cohort C subjects and sent for heavy metal analysis (Figure 1). Capsule tissue was collected in special 50-mL metal-free containers with minimal handling and frozen at –80 °C and stored until the completion of sample collection. The specimens were then shipped, packed in dry ice, to Steris Applied Sterilization (Libertyville, IL) where they underwent sterilization by γ-irradiation prior to shipment to Eurofins Frontier Global Sciences, LLC (Tacoma, WA) for metal analysis. Eurofins prepared the samples using sealed Teflon (Chemours, Wilmington, DE) digestion vessels for full dissolution of the tissue followed by inductively coupled plasma triple quadrupole mass spectrometry. The homogenized samples were accurately weighed; approximately 0.500 g of sample placed into a tared Teflon bomb with 7.5 mL of concentrated nitric acid plus 15 to 20 mL reagent water. The Teflon digestion vessels were wrenched down and heated in an oven until the sample had fully gone into

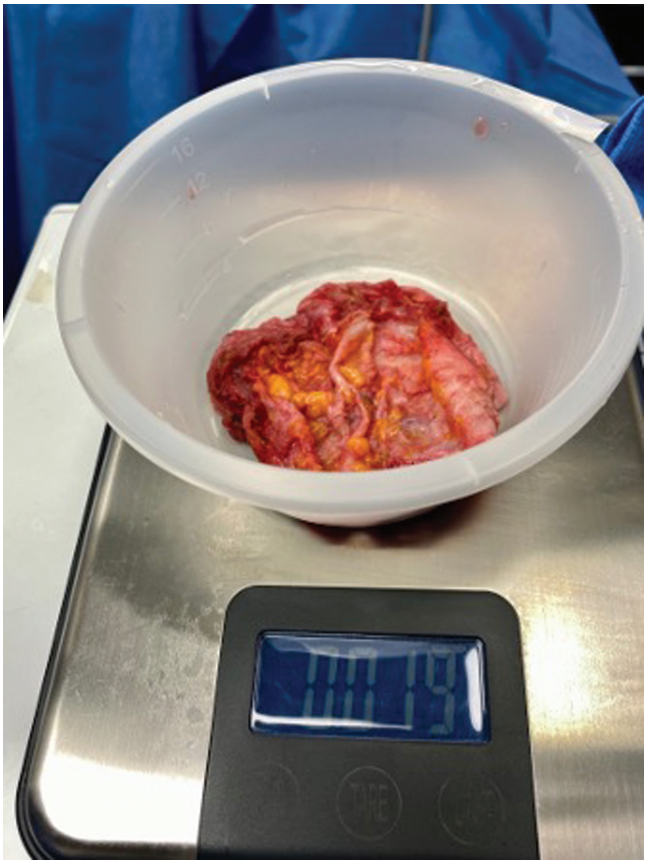

Figure 1. Capsule tissue being weighed.

solution. Digested solutions were then filtered and introduced into radiofrequency plasma where energy-transfer processes cause desolvation, atomization, and ionization. The ions were extracted from the plasma through a differentially pumped vacuum interface and separated based on their mass-to-charge ratio (*m*/*z*) by a mass spectrometer. The triple quadrupole system operates in multiple gas modes and rejects all unwanted masses and ions, reducing interference. A solid-state detector detected ions transmitted through the mass analyzer and the resulting current was processed by a data-handling system. Before analyzing the study specimens, an initial limited validation was performed by visual inspection of full dissolution of the capsules during the digestion process followed by experiments to fortify portions of the capsules with known reference materials for all elements under consideration.[11,12] Validation of the methodology was performed prior to cohort specimen analysis due to the variability in capsule thickness. Comparisons of the concentrations found in the fortified capsule samples to the known concentration added were then performed and found to be within expected ranges.

The remainder of the capsule tissue was sent off for analysis of microbes and routine histology. Blood collected on the day of surgery in all 3 cohorts was sent for complete blood count, thyroid level, Vitamin D, C-reactive protein, cytokines, and antibodies to bacterial enterotoxin superantigens. The findings of these analyses will be detailed in Part 3 of the ASERF biospecimen study.

Statistical analysis

The detailed metals analysis report was generated by Eurofins and sent for statistical analysis along with demographic data obtained at baseline. The odds ratios and *P* values are from a logistic regression analysis with group as the dependent variable and the baseline characteristic as the explanatory variable. The *P* value is for a 2-sided test of the null hypothesis that the true odds ratio equals 1.

RESULTS

Heavy metal analysis revealed statistically significant higher levels of 2 metals in Cohort A (BII) vs Cohort B (non-BII): arsenic and zinc (Table 1). The detected arsenic levels in the capsules of Cohort B ranged from 0.01 to 0.33 mg/kg with a mean of 0.12 mg/kg; for Cohort A the levels ranged from 0.04 to 0.36 mg/kg with a mean of 0.20 mg/kg, which was statistically significantly higher. Cohort C included normal breast tissue from patients with no implanted medical device. Arsenic levels detected in the control breast tissue ranged from 0.11 to 0.51 mg/kg with a mean of 0.36 mg/kg, numerically higher than either implant cohort. For zinc, Cohort B ranged from 2.7 to 33.4 mg/kg with a mean of 11 mg/kg, Cohort A ranged from 2.9 to 117 mg/kg with a mean of 21 mg/kg, which was statistically significantly higher than Cohort B. Cohort C ranged from 1.45 to 2.94 mg/kg in the breast tissue with a mean of 2.3 mg/kg. Platinum was detected in only 1 of 50 patients in Cohort A and 1 of 50 patients in Cohort B.

Multiple confounding variables were identified as sources of possible heavy metal ingestion, inhalation, and absorption with statistical significance between the cohorts (Table 2).

The incidence of current or former smokers using tobacco and marijuana was 56% of patients in Cohort A, 41% of patients in Cohort B, and 14% of patients in Cohort C. There was a statistically significant difference between the number of smokers in Cohort A compared with Cohort C. The incidence of tattoos was 63% of patients in Cohort A, 8% of patients in Cohort B, and 42% of patients in Cohort C. The patients enrolled in all 3 cohorts ranged in age from 30 to 65 years. The average for each cohort was similar: Cohort A, 44.5 years; Cohort B, 46.9 years; and Cohort C, 46.5 years. There was a statistically significant number of patients in Cohort A who reported gluten and wheat allergies vs Cohorts B and C (Table 2).

Table 1. Assessment and Comparisons of Heavy Metal Levels for Each Cohort

Metal	Detection limit (µg/g)[a]	Odds ratio BII vs non-BII (Cohort A vs Cohort B)	*P* value BII vs non-BII (Cohort A vs Cohort B)	Acceptable internal exposure[b] (µg/day)	Mean (median) BII (Cohort A) (µg/g)	Mean amount in a 40-g capsule[c] BII (Cohort A) (µg)	Mean (median) non-BII (Cohort B) (µg/g)	Mean amount in a 40-g capsule non-BII (Cohort B) (µg)	Mean (median) mastopexy (Cohort C) (µg/g)	Mean amount in a 40-g breast tissue mastopexy (Cohort C) (µg)
Aluminum	0.05	0.892	0.308	50	0.33 (<0.05)	13	0.83 (<0.05)	33.2	<0.05 (<0.05)	<2
Antimony	0.001	0.067	0.177	94	0.11 (0.089)	4.3	0.14 (0.087)	5.6	0.094 (0.091)	3.8
Arsenic[d]	0.01	>999	0.0001	15	0.20 (0.20)	7.8	0.12 (0.090)	4.8	0.36 (0.39)	14.0
Barium	0.002	2.751	0.419	730	0.15 (0.085)	5.9	0.12 (0.073)	4.7	0.042 (0.050)	1.7
Beryllium	0.003	NA	NA	0.14	<0.003 (<0.003)	<0.12	<0.003 (<0.003)	<0.12	<0.003 (<0.003)	<0.12
Cadmium	0.0003	0.600	0.978	1.7	0.016 (0.014)	0.65	0.016 (0.013)	0.7	0.011 (0.01)	0.4
Chromium	0.03	0.913	0.621	1070	1.08 (0.97)	43	1.19 (0.90)	48	0.11 (<0.03)	4.4
Cobalt[e]	0.0006	<0.001	0.0011	5	0.0020 (<0.0006)	0.08	0.024 (<0.0006)	0.9	<0.0006 (<0.0006)	<0.024
Copper	0.002	1.364	0.462	340	0.79 (0.70)	32	0.72 (0.64)	29	0.17 (<0.002)	6.7
Iron	0.3	0.999	0.893	6300	49 (47)	1977	50 (45)	2015	13 (<0.3)	525.0
Lead	0.0008	16.915	0.625	5	0.016 (<0.0008)	0.63	0.013 (<0.0008)	0.5	0.0024 (<0.0008)	0.1
Lithium	0.01	3.913	0.287	280	0.077 (<0.01)	3.1	0.040 (<0.01)	1.6	0.20 (<0.01)	7.8
Manganese[e]	0.0008	0.011	0.0009	18	0.13 (0.14)	5.2	0.32 (0.21)	13.0	0.092 (<0.0008)	3.7
Mercury	0.0005	1.029	0.669	3	0.0015 (<0.005)	0.062	0.0013 (<0.005)	0.1	<0.005 (<0.005)	<0.02
Molybdenum	0.001	1.195	0.947	1700	0.01 (<0.001)	0.58	0.013 (<0.001)	0.5	0.36 (<0.001)	14
Nickel	0.0009	1.604	0.439	22	0.41 (0.33)	17	0.36 (0.29)	14.5	<0.0009 (<0.0009)	<0.036
Platinum	0.25	0.289	0.502	10	0.0069 (<0.25)	0.28	0.031 (<0.25)	1.2	<0.25 (<0.25)	<10
Selenium	0.01	5.629	0.264	85	0.64 (0.62)	25	0.60 (0.59)	24	0.71 (0.69)	28
Silver[e]	0.0004	<0.001	<0.0001	14	0.0024 (<0.0004)	0.095	0.030 (<0.0004)	1.2	0.001 (<0.0004)	0.04
Thallium	0.0001	NA	NA	8	<0.0001 (<0.0001)	<0.004	<0.0001 (<0.0001)	<0.004	0.003 (<0.0001)	0.1
Tin[e]	0.005	0.006	0.0105	640	0.026 (<0.005)	1.05	0.096 (<0.005)	3.8	<0.005 (<0.005)	<0.2
Titanium	0.02	21.706	0.574	1200	0.016 (<0.02)	0.64	0.012 (<0.02)	0.5	<0.02 (<0.02)	<0.8
Uranium	0.001	NA	NA	0.6	<0.001 (<0.001)	<0.04	<0.001 (<0.001)	<0.04	<0.001 (<0.001)	<0.04
Vanadium	0.004	<0.001	0.212	12	0.0006 (<0.004)	0.022	0.0022 (<0.004)	0.1	0.031 (<0.004)	1.2
Zinc[d]	0.01	1.118	0.0007	6400	21 (16)	826	11 (8.4)	424	2.3 (2.3)	93

BII indicates those patients seeking explantation because they believe their implants are responsible for their symptoms. Cohort A: patients with self-reported BII requesting explantation; Cohort B: patients requesting implant exchange or explantation without self-reported BII; Cohort C: patients with mastopexy (without soft-tissue support or implants). BII, breast implant illness; NA, not available. [a]µg/g = micrograms per gram, equivalent to milligrams per kilogram, equivalent to parts per million (ppm). [b]Acceptable internal exposure (µg/g) sourced or derived primarily from International Conference on Harmonization Q3C guidance and National Institutes of Health Office of Dietary Supplements Fact Sheets for Health Professionals (Bethesda, MD). [c]Mean amount in a 40-g capsule = mean concentration × 40 g capsular tissue (approximate average weight of 2 capsules). [d]Significantly ($P < 0.05$) elevated level in Cohort A relative to Cohort B. [e]Significantly ($P < 0.05$) decreased level in Cohort A relative to Cohort B.

Table 2. Analysis to Find Baseline Characteristics That Are Predictive of a Patient Self-Reporting BII—Metals

Baseline characteristic		BII vs non-BII (Cohort A vs Cohort B)		BII vs mastopexy (Cohort A vs Cohort C)	
	Reference category	Odds ratio	*P* value	Odds ratio	*P* value
Tobacco history	Never				
Former		1.304	0.5634	2.529	0.0725
Current		>999	0.0864	>999	0.0734
Marijuana use	Never				
Former		1.277	0.6479	3.486	0.0758
Current		>999	0.0156	1.163	0.8390
Medications					
Antibiotics (yes/no)	No	2.538	0.1096	13.820	0.0138
Aspirin/NSAID (yes/no)	No	14.461	<0.0001	10.615	<0.0001
Prescription pain medications (yes/no)	No	>999	0.0032	1.568	0.5076
Other herbal/nonprescription medicines (yes/no)	No	4.636	0.0060	1.325	0.5171
Any allergy (yes/no)	No	1.405	0.4769	4.909	0.0005
Allergy: gluten (yes/no)	No	7.977	0.0566	>999	0.0015
Allergy: wheat (yes/no)	No	4.261	0.2023	>999	0.0177
Tattoos (yes/no)	No	2.681	0.0172	1.043	0.2309

BII indicates those patients seeking explantation because they believe their implants are responsible for their symptoms. Cohort A: patients with self-reported BII requesting explantation; Cohort B: patients requesting implant exchange or explantation without self-reported BII; Cohort C: patients with mastopexy (without soft-tissue support or implants). The odds ratios and *P* values are from a logistic regression analysis with group as the dependent variable and the baseline characteristic as the explanatory variable. The *P* value is for a 2-sided test of the null hypothesis that the true odds ratio equals 1. BII, breast implant illness; NSAID, nonsteroidal anti-inflammatory drug.

DISCUSSION

Heavy metals have been postulated as a potential cause of systemic symptoms in women with breast implants. This study measured the levels of 22 heavy metals in the capsules surrounding breast implants to determine if there were differences in levels between women with systemic symptoms they attribute to their implants and women with implants who do not have systemic symptoms attributed to their implants, as well as in relation to breast tissue from a control group of women who never had any implanted medical device. There was very careful discussion and deliberation before we settled on the study design and tissue to be sampled for this study. Capsule tissue only, and not breast tissue, was collected from Cohorts A and B. The reasons for the selection of the tissue to be sampled are: (1) the capsule tissue in direct contact with the implant would be expected to show the highest concentration of heavy metals (vs surrounding tissue) were the breast implants to be the source of such metals; (2) we received an expedited IRB review and exemption based on the fact that the patient's deidentified biospecimens being collected and analyzed were those removed as part of the normal surgical procedure (which was true for Cohorts A, B, and C under the protocol implemented), but would not have been true if extra breast tissue were collected from Cohorts A and B, many of whom had very limited tissue coverage anyway from which to obtain such a specimen. The measured levels were all below what are considered acceptable exposure levels by regulatory agencies; however, higher measured levels of arsenic and zinc were observed in Cohort A compared with cohort B.

Environmental exposure to heavy metals by ingestion, inhalation, and absorption through the skin is ubiquitous and has been well documented (Appendix). Arsenic is a naturally occurring element in the environment and it is estimated that the average daily exposure of adults in the United States is 11 to 14 µg/day. By comparison, the total amount measured in the capsular tissue (based upon an approximate average total capsule weight of 40 g) was 7.8 µg. Soluble forms of arsenic are well absorbed (60%-90% absorption) from the gastrointestinal

tract and the lungs.[13] Significant arsenic exposure occurs in certain populations where there are higher levels present in the ground water and drinking water, and both the World Health Organization (Geneva, Switzerland) and the Environmental Protection Agency (Washington, DC) have established limits to control exposure.[14] Arsenic exposure from drinking water containing 1 to 2 mg/L (approximately 0.1-0.2 mg/kg/day) has been shown to induce oxidative DNA damage in the brain.[15] Although drinking water safety standards have been determined, arsenic levels in foods are variable and regulatory limits have not been established. Interestingly, it is estimated that fewer than 1% of Americans have been diagnosed with celiac disease, yet up to 13% of US consumers report consuming gluten-free foods.[16,17] Certain crops such as rice absorb arsenic more readily and rice-based products can make up a large part of the modern-day diet. Additionally, many of the gluten-free foods contain rice-based formulas and rice flour is the primary substitute for grains such as wheat and rye ingested by consumers who avoid gluten. Rice often contains elevated levels of arsenic and methylmercury as well as additional heavy metals including chromium, cadmium, and lead. Other sources of inorganic arsenic in the diet include fruits, fruit juices, and vegetables due to residual arsenic in the soil from older fertilizers and insecticides.[18,19]

Arsenic was detected in some of the capsule tissue in both Cohorts A and B as well as in the control group breast tissue. The mean arsenic levels were 0.20 µg/g (range, 0.05-0.36 µg/g) in Cohort A, 0.12 µg/g (range, 0.0-0.33 µg/g) in Cohort B, and 0.36 µg/g (range, 0.11-0.0.52 µg/g) in Cohort C. Based on these measurements, the average estimated total amount of arsenic in an average total of 40 g of capsule (around 2 implants) was 7.8 µg for Cohort A and 4.8 µg for cohort B (Table 1). By way of perspective, the acceptable daily internal exposure (ie, via the parenteral route) for arsenic is 15 µg/day (Table 1). Based on data published in the FDA Summary of Safety and Effectiveness documents (see below), arsenic was below detection limits in an analysis of saline-filled implants and the estimated total amount of arsenic in a 350-cc gel implant containing trace levels of arsenic at 0.123 µg/g would equate to only approximately 1.4 µg/day if it was all released from the implant over a 30-day period. Any release would actually be expected over a much longer time span that would reduce this number further.[25,26]

The metals analysis also demonstrated a statistically significant difference between Cohort A and Cohort B with respect to levels of zinc. The mean zinc levels from Cohorts A, B, and C were 21, 11, and 2.3 µg/g, respectively. Based on these measurements, the average estimated total amount of zinc in an average total 40 g of capsule (around 2 implants) was 826 µg for Cohort A and 424 µg for cohort B (Table 1). By way of perspective, the acceptable daily internal exposure (ie, absorbed from an oral dose) for zinc is 6400 µg/day (Table 1). Based on data published in the FDA Summary of Safety and Effectiveness documents (see below), the estimated total amount of zinc in a 350-cc saline-filled implant containing trace levels of zinc at 0.26 µg/g would equate to <0.2 µg/day if it was all released from the implant over a 30-day period.[25] Similarly, the estimated total amount of zinc in a 350-cc gel implant containing trace levels of zinc at 0.034 µg/g would equate to <0.4 µg/day if it was all released from the implant within 30 days. Any release would be expected over a much longer time span, which would reduce this number further.[26]

The recommended daily dietary allowance for zinc is 8 mg/day for women with a tolerable upper intake level of 40 mg/day.[27] Zinc is present in food sources and dietary supplements as well as homeopathic medications. Excessive dietary zinc may lead to copper deficiency and neurologic disease; however, zinc has also been reported to reduce the severity and duration of viral illnesses and cold symptoms.[28]

In Cohort A, 18% of patients self-reported gluten allergies and 12% self-reported an allergy to wheat. In Cohort B, only 2% of patients reported either a wheat or gluten allergy, and in Cohort C there were no gluten or wheat allergies reported (Table 2).

Patients in all cohorts were asked to report their current and past smoking history including both tobacco and cannabis products. Tobacco smoke is a complex mixture of thousands of components and over 30 metal ions depending on where the tobacco is grown. Present in the highest concentration are a variety of trace substances including formaldehyde, copper, mercury, antimony, nickel, zinc, cadmium, lead, arsenic, ammonia, benzene, carbon monoxide, and polycyclic aromatic hydrocarbons.[20] Cannabis, whether smoked or ingested, contains contaminants including microbes, aflatoxins, ash, pesticides, and heavy metals (arsenic, cadmium, lead, and mercury), and the threshold for clean medicine standards for cannabis has not yet been established.[21] Regular exposure to low doses of inorganic arsenic can lead to a variety of systemic symptoms ranging from skin disease, neurologic effects, diabetes, cardiovascular disease, and cancers of the lung, liver, kidneys, and bladder. Studies have also found an association between arsenic and reproductive issues and possible compromise to the immune system.[22]

This study also documented the presence of tattoos in all three cohorts. Data included the total body surface area of the tattoos and whether the tattoos contained green pigment. The FDA (Silver Spring, MD) classifies the inks that are most frequently used in tattoos as cosmetics, and the specific pigments used in the inks as color additives which are subject to premarket approval under the Federal Food, Drug, and Cosmetic Act.[23] The FDA has investigated microbial contamination and risks associated with specific

tattoo inks, and although the color additives are approved for cosmetics, none are approved for injection into the skin. Some modern tattoo pigments have removed heavy metals from their formulas but most still contain a variety of heavy metals. These include chromium (green), cobalt (blue) cadmium (red, orange, yellow), and nickel (black). Colorants may be added that contain arsenic, sulfur, beryllium, antimony, calcium, titanium, and occasionally lead. Black ink may also be manufactured from soot, known to contain hydrocarbons. There are also numerous potential impurities in organic tattoo pigments including polycyclic aromatic hydrocarbons and primary aromatic amines, both of which are known carcinogens. Further, statistics show that 12% of Europeans and up to 24% of US citizens are estimated to be tattooed, and females are almost twice as likely to have tattoos as males.[24]

Additional confounding factors, including the consumption of nonprescription medications and dietary supplements, were reported: Cohort A, 74%; Cohort B 58%; and Cohort C 62%, and may account for these differences.

Limitations of this study include several factors that were related to the research protocol. Capsule tissue was sampled for heavy metals and, unlike urine testing, it provided a measure of integrated exposure. The evaluation of arsenic exposure included exposure to both organic and inorganic species.[29] Another limitation of this study is the relatively small number of control specimens (breast tissue) obtained from patients with no previous exposure to any implanted device. The documentation of similar heavy metals detected in healthy normal breast tissue was sufficient to corroborate the hypothesis that age-matched control subjects have similar environmental exposure through the air, water, tobacco, cannabis, tattoos, and their diet. Interestingly, the level of arsenic detected in normal breast tissue was higher than in the capsules of the implant cohorts. The strengths of this study are that it is the first prospective, blinded, study with a control group and robust follow up. The laboratory used for heavy metals analysis is a well-recognized laboratory with focused expertise in analytical chemistry and in compliance with the strict requirements of regulatory agencies. The protocol required consistent handling of tissue samples and the collection of extensive medical history and symptom data, including validated diagnostic instruments for the same patients undergoing metals analysis.

Other potential etiologies for signs and symptoms experienced by women with breast implants aside from heavy metals have been proposed, including the presence of gel bleed and/or silicone in tissues. However, these entities, which were explicitly not included in the analysis of capsular tissue in this study, can be excluded as causative factors with a high level of confidence based on existing observations. The most significant underlying observation is that BII is reported similarly in patients with both saline-filled and with silicone gel-filled breast implants.[30] Indeed, in this present study, there were actually a greater number of BII patients with saline-filled vs silicone gel-filled breast implants.[10]

The diffusion of minute amounts of low-molecular-weight silicone molecules (siloxanes), including D4, D5, D6, etc, from silicone gel-filled breast implants is commonly referred to as gel bleed. The very small amount of gel bleed that occurs has been characterized for silicone gel–filled breast implants manufactured in the United States, and the results have been presented on the FDA website for several years located in the Summary of Safety and Effectiveness documents for each manufacturer. Saline-filled breast implants, however, do not contain silicone gel (the principal source of such low-molecular-weight siloxanes in gel bleed) and the shells of saline-filled breast implants contain less than 1/100th the amount in silicone gel-filled breast implants.[25,26] Therefore, gel bleed can be excluded with a high level of confidence as a causative factor for BII.

The same is true for the silicone shell of both saline-filled and gel-filled breast implants. In 1997, Peters et al studied 100 women with silicone gel–filled breast implants (mean implantation time, 12.0 years) who were experiencing symptoms they attributed to their breast implants and had their devices explanted.[31] At an average of 2.7 years postexplantation, 75 patients completed a questionnaire capturing information including symptom resolution and psychological well-being. Among 6 patients with diagnosed autoimmune disease, no improvement was observed. Among 12 patients with rheumatic disease, ie, fibromyalgia and inflammatory arthritis, only short-term improvement was observed. In the remaining patients reporting symptoms but without diagnosed autoimmune or rheumatic disease, more than 80% reported “major improvement” in their symptoms and more than 93% reported significantly improved psychological well-being. An often-missed observation from this study is that of the 100 patients whose silicone gel–filled breast implants were explanted, 43 were immediately reimplanted with saline-filled breast implants, yet those patients also were among those experiencing the extremely high levels of symptom resolution. If a reaction to silicone were responsible for BII, replacing a silicone gel–filled breast implant (which has a silicone elastomer shell) with a saline-filled implant (which also has a silicone elastomer shell) would not be expected to lead to symptom resolution. This is especially significant as even more patients in the BII group in this current study had saline-filled vs silicone gel–filled implants.

The updated September 2022 FDA guidance documents for saline and silicone gel breast implants describes the agency’s recommendations for new labeling of breast implants. Included in the recommendations is guidance that requires manufacturers to provide qualitative and

quantitative analysis for heavy metals on the final finished shell, gel, and patch. This includes the names of each chemical, material, additive, plasticizer, and antioxidant as well as the function and location of each chemical and material. The recommendations include testing for antimony, arsenic, barium, beryllium, cadmium, chromium, cobalt, copper, lead, magnesium, mercury, molybdenum, nickel, platinum, selenium, silver, tin, titanium, vanadium, and zinc.[32] These levels are obtained from extractable analysis after the shells are subject to dissolution in acids and analyzed by inductively coupled plasma mass spectrometry. All manufacturers are required to report these data to the FDA and the data are published in the Summary of Safety and Effectiveness. Unlike the heavy metals data provided by the FDA, the BII websites and social media groups portray the heavy metals tables as a list of "ingredients" rather than trace residuals, and they do not put the levels reported in any perspective, such as providing the acceptable levels of exposure as determined by regulatory agencies. This ignores the most basic, fundamental of toxicology, the concept of dose-response, first stated by Paracelsus (1493-1541), a physician who noted that: "All substances are poisons; there is none which is not a poison. The right dose differentiates a poison and a remedy." Stated differently, any substance at sufficiently low dose will be safe, and any substance at sufficiently high dose will exhibit toxicity. For patients doing research for potential sources of their systemic symptoms, seeing arsenic and 21 other heavy metals listed as an "ingredient" of their breast implants without context is an understandable cause for concern. The site, healingbreastimplantillness.com, has a section entitled "Silicone breast implants are made with heavy metals." The site makes the claim that heavy metals in implants lead to fatigue, damage the brain, lungs, kidney, liver, blood composition, and most organs. They further state that long-term exposure can cause progression to multiple sclerosis, Parkinson's, Alzheimer's, and muscular dystrophy.[33] Another site, breastimplantillness.com, states that heavy metals are the cause of symptoms because "They compete for the same receptors as our vital minerals, therefore they displace and hinder their physiologic roles. They accumulate and disrupt functions in vital organs such as the brain, bone, liver, kidney, heart, etc." This site also states that these metals are neurotoxic, and the brain and central nervous system are particularly vulnerable.[34] In addition to making claims about heavy metal toxicity, social media platforms and some surgeons suggest that a total intact or en bloc capsulectomy is required to remove the heavy metals which they suggest have leached from the implant into the capsule tissue. It is therefore important that the trace heavy metal analysis data be put into proper context. Heavy metals tables should always be presented accurately in context with levels of potential toxicologic concern and reflect those metals that are present at nondetectable levels or levels well below what is known to cause toxicity. It is also important to note that there are environmental sources of heavy metals that are ingested, inhaled, and often intentionally placed into the skin, and each contribute to the patient's total heavy metal exposure.

CONCLUSIONS

Analysis of capsule tissue from Cohorts A and B and breast tissue from Cohort C was analyzed to answer the question of whether heavy metals were present in capsule tissue in high enough levels to warrant the need for total capsulectomy. This paper reports the results of the analysis of 200 capsules for 22 heavy metals from the 2 implant cohorts, and 8 specimens of breast tissue from patients without implants or any other implanted medical device. The findings of the ASERF biospecimen study conclude that there is not a significant risk of heavy metal exposure from breast implants, either saline or silicone. Patients in the BII cohort demonstrated a minor elevation in arsenic and zinc. Environmental exposure and personal choices related to cigarette smoking, marijuana use, tattoo pigments, and dietary sources of arsenic and zinc have been confirmed to be significant confounding variables in a patient's total heavy metal exposure. This study confirmed that there may be fewer heavy metals in breast implant capsules than detected in normal breast tissue never exposed to any implanted device, and therefore the risk of heavy metal toxicity should not be used as an indication for total capsulectomy if patients elect to remove their breast implants.

Supplemental Material

This article contains supplemental material located online at www.aestheticsurgeryjournal.com.

Disclosures

Dr Glicksman is the medical director for the US Motiva Breast Implant Clinical Trial (Establishment Labs, Alejuela, Costa Rica). Dr McGuire is a consultant and clinical investigator for Establishment Labs. Dr Wixtrom is a toxicologist with LSCI (Springfield, VA), and is a consultant for Mentor Worldwide LLC (Irvine, CA) and PhaseOne Health (Nashville, TN). Dr Haws is on the business advisory board for RealSelf (Seattle, WA), is on the Sientra (Santa Barbara, CA) Education Advisory Board, and is an investor in Strathspey Crown (Newport Beach, CA). The other authors declared no potential conflicts of interest with respect to the research, authorship, and publication of this article.

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