Diagnosis, investigation and management of breast implant illness: a narrative review

Daniel WH Wong MD BDS,1 Tai K Lam MBBS MS FRACS2

1 Queen Elizabeth Hospital
Woodville South
South Australia
AUSTRALIA

2 Flinders Medical Centre
Adelaide
South Australia
AUSTRALIA

Abstract

Introduction: An increasing pool of literature proposes a link between silicone implants and autoimmune-related symptoms known colloquially as breast implant illness (BII). We describe the history of BII, the reported symptoms, risk factors and previously published diagnostic criteria with the aim to aid clinicians in the diagnosis, investigations and management of patients presenting with symptoms that they attribute to their silicone breast implants.

Methods: A literature search was performed using MEDLINE®, the Cochrane Database of Systematic Reviews, the Cochrane Central Register of Controlled Trials (CENTRAL), the Database of Abstracts of Reviews of Effect (DARE) and PubMed in September 2018. The search terms ‘autoimmune inflammatory syndrome induced by adjuvants’, ‘breast implants’ and ‘silicone’ were used alone and in combination.

Results: Thirty-four studies were reviewed, of which there were three case reports, 12 case series, 14 retrospective cohort studies, four case control studies and one prospective cohort study. Within this cohort, 18 studies were found regarding the explantation of implants relating to BII.

Conclusion: Studies have demonstrated no association between silicone breast implants and any known autoimmune diseases, but there exists a pool of literature suggestive of a relatively undefined condition colloquially known as BII. Serological testing and imaging play an important role in the assessment of patients to exclude other pathology, but these tests remain non-diagnostic for BII. Although medical treatment has shown promise, there is no established treatment for patients. The surgical explantation of implants appears to have positive outcomes for patients; however, the exact nature of the surgery required to achieve this remains unclear.

Keywords: plastic surgery, breast implantation, connective tissue, silicones, autoimmune diseases
Introduction

Silicone breast implants have been a powerful tool in both cosmetic and reconstructive surgery since the 1960s. Thus far, silicone implants have been considered safe, with accepted known risks.\(^1,2\) However, media and social awareness are now fuelling growing scepticism about the safety of silicone breast implants. Over the past 20 years, there has been an increasing pool of literature proposing a link between silicone implants and autoimmune-related symptoms\(^3\) known colloquially as breast implant illness (BII). This association was reported as early as 1964 by Miyoshi and colleagues\(^4\) and has various names including human adjuvant disease, silicone implant incompatibility syndrome and, more recently, autoimmune inflammatory syndrome induced by adjuvants (ASIA).\(^5\)

Currently, BII is not a defined disease and has no established diagnostic criteria or widely accepted treatment options. A recent article by Rohrich and colleagues\(^6\) reviewed the safety of silicone breast implants, while Magnusson and colleagues have analysed the scientific validity of BII.\(^7\) This supplementary review provides clinicians with

### Table 1: Eligible studies published between 1987 and 2018

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>Type of study</th>
<th>No. of patients</th>
<th>Mean age (range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Endo et al(^8)</td>
<td>1987</td>
<td>Case series</td>
<td>8</td>
<td>45 (35–65)</td>
</tr>
<tr>
<td>Bridges et al(^9)</td>
<td>1993</td>
<td>Case control</td>
<td>156</td>
<td>44 (22–72)</td>
</tr>
<tr>
<td>Shoaib et al(^10)</td>
<td>1994</td>
<td>Retrospective cohort</td>
<td>100</td>
<td>32 (19–52)</td>
</tr>
<tr>
<td>Giltay et al(^11)</td>
<td>1994</td>
<td>Case control</td>
<td>235</td>
<td>43 (19–73)</td>
</tr>
<tr>
<td>Vasey et al(^12)</td>
<td>1994</td>
<td>Retrospective cohort</td>
<td>50</td>
<td>44 (30–66)</td>
</tr>
<tr>
<td>Freundlich et al(^13)</td>
<td>1994</td>
<td>Case series</td>
<td>50</td>
<td>43 (26–71)</td>
</tr>
<tr>
<td>Solomon et al(^14)</td>
<td>1994</td>
<td>Retrospective cohort</td>
<td>176</td>
<td>45 (24–72)</td>
</tr>
<tr>
<td>Cuellar et al(^15)</td>
<td>1995</td>
<td>Retrospective cohort</td>
<td>300</td>
<td>44 (25–69)</td>
</tr>
<tr>
<td>Wells et al(^16)</td>
<td>1995</td>
<td>Case series</td>
<td>52</td>
<td>45.6</td>
</tr>
<tr>
<td>Shoaib et al(^17)</td>
<td>1996</td>
<td>Case series</td>
<td>26</td>
<td>33.5 (21–50)</td>
</tr>
<tr>
<td>Kao et al(^18)</td>
<td>1997</td>
<td>Case report</td>
<td>1</td>
<td>56</td>
</tr>
<tr>
<td>Thomas et al(^19)</td>
<td>1997</td>
<td>Case series</td>
<td>25</td>
<td>Not specified</td>
</tr>
<tr>
<td>Meier et al(^20)</td>
<td>1997</td>
<td>Case report</td>
<td>2</td>
<td>Not specified</td>
</tr>
<tr>
<td>Peters et al(^21)</td>
<td>1997</td>
<td>Case series</td>
<td>100</td>
<td>28.9 (13–55)</td>
</tr>
<tr>
<td>Melmed et al(^22)</td>
<td>1998</td>
<td>Retrospective cohort</td>
<td>240</td>
<td>26–70</td>
</tr>
<tr>
<td>Contant et al(^23)</td>
<td>2000</td>
<td>Retrospective cohort</td>
<td>63</td>
<td>46 (25–71)</td>
</tr>
<tr>
<td>Contant et al(^24)</td>
<td>2002</td>
<td>Case series</td>
<td>57</td>
<td>43 (26–58)</td>
</tr>
<tr>
<td>Gaubitz et al(^25)</td>
<td>2002</td>
<td>Case series</td>
<td>90</td>
<td>50 (20–70)</td>
</tr>
<tr>
<td>De Jong et al(^26)</td>
<td>2002</td>
<td>Case series</td>
<td>42</td>
<td>31–73</td>
</tr>
<tr>
<td>Vermeulen et al(^27)</td>
<td>2003</td>
<td>Retrospective cohort</td>
<td>176</td>
<td>49</td>
</tr>
<tr>
<td>Englert et al(^28)</td>
<td>2004</td>
<td>Case control</td>
<td>458</td>
<td>Not specified</td>
</tr>
<tr>
<td>Kulmala et al(^29)</td>
<td>2004</td>
<td>Retrospective cohort</td>
<td>685</td>
<td>32 (16–65)</td>
</tr>
<tr>
<td>Siggelkow et al(^30)</td>
<td>2004</td>
<td>Retrospective cohort</td>
<td>53</td>
<td>51</td>
</tr>
<tr>
<td>Spear et al(^31)</td>
<td>2007</td>
<td>Retrospective cohort</td>
<td>940</td>
<td>34 (augmentation patients)</td>
</tr>
<tr>
<td>Wolfram et al(^32)</td>
<td>2008</td>
<td>Case control</td>
<td>143</td>
<td>44 (19–73)</td>
</tr>
<tr>
<td>Kappel et al(^33)</td>
<td>2012</td>
<td>Prospective cohort</td>
<td>111</td>
<td>49 (for replacement with monoblock hydrogel)</td>
</tr>
<tr>
<td>Zambacos et al(^34)</td>
<td>2013</td>
<td>Case series</td>
<td>14</td>
<td>N/A</td>
</tr>
<tr>
<td>Cohen Tervaert et al(^35)</td>
<td>2013</td>
<td>Retrospective cohort</td>
<td>32</td>
<td>49 (18–64)</td>
</tr>
<tr>
<td>Maijers et al(^36)</td>
<td>2013</td>
<td>Retrospective cohort</td>
<td>80</td>
<td>47 (22–78)</td>
</tr>
<tr>
<td>Kappel et al(^37)</td>
<td>2014</td>
<td>Case series</td>
<td>3</td>
<td>50</td>
</tr>
<tr>
<td>Colaris et al(^38)</td>
<td>2017</td>
<td>Retrospective cohort</td>
<td>100</td>
<td>33 (14–56)</td>
</tr>
<tr>
<td>Pavlov–Dolijanovic et al(^39)</td>
<td>2017</td>
<td>Case series</td>
<td>3</td>
<td>28–55</td>
</tr>
<tr>
<td>Nunes et al(^40)</td>
<td>2017</td>
<td>Case report</td>
<td>1</td>
<td>23</td>
</tr>
<tr>
<td>Alijotas-Reig et al(^41)</td>
<td>2018</td>
<td>Retrospective cohort</td>
<td>45</td>
<td>N/A</td>
</tr>
</tbody>
</table>
available and relevant information to form a framework for discussing the evidence behind the diagnosis, investigation, and management of patients who present with symptoms of BII.

**Methods**

We performed a literature search using MEDLINE®, the Cochrane Database of Systematic Reviews, the Cochrane Central Register of Controlled Trials (CENTRAL), the Database of Abstracts of Reviews of Effect (DARE) and Pubmed in September 2018. The search terms ‘autoimmune inflammatory syndrome induced by adjuvants’, ‘breast implants’ and ‘silicone’ were used alone and in combination. Articles were excluded if they did not specifically focus on the potential relationship between silicone breast implants and symptoms of an undefined autoimmune disorder. Also excluded were articles that focused on well-defined autoimmune or connective tissue diseases, those that focused on silicone in medical devices other than breast implants, those pertaining to breast malignancies and non-English language papers. Further, additional citations were solicited from references in the selected articles.

**Results**

A total of 110 studies were screened and assessed for eligibility, of which 34 are included in this review. These studies were published between 1987 and 2017. They include three case reports, 12 case series, 14 retrospective cohort studies, four case control studies and one prospective cohort study (Table 1). Eighteen studies were found regarding the explantation of implants relating to ASIA or other defined autoimmune diseases. Of these, there were three case reports, five cases series, eight retrospective cohort studies and two prospective cohort studies (Table 2).

**Discussion**

Polydimethylsiloxane (PDMS) is the basic material of breast implants and is part of the family of polyorganosiloxanes (silicones). Although silicone is considered to be biologically inert, it undergoes oxidation to silica when exposed to reactive oxygen radicals released by activated local macrophages. Studies have demonstrated a link between silica and silicon exposure with the development of autoimmune conditions via the induction of a type two inflammatory response.
Silicone levels

Studies have shown that silicone levels are significantly higher in the peri-implant capsule in patients with saline-filled breast implants, while levels in adjacent breast tissue are the same compared with control breast tissue. Despite this, saline implants have not been linked with the development of BII.\textsuperscript{49–51} Comparatively, the levels of silicone in both the peri-implant capsule and adjacent breast tissue are significantly higher in patients with silicone-filled breast implants and have been associated with symptoms of BII.\textsuperscript{49,50} This observation speculates a possible dose-dependent pathogenesis for the symptoms of BII.

Silicone and autoimmune disease

The link between silicone breast implants and autoimmune disorders has historically been controversial. Following the moratorium on breast implants in 1992, the United States Institute of Medicine (IOM) released its report on the safety of silicone breast implants.\textsuperscript{52} This report noted that there was no evidence to implicate silicone breast implants with the development of autoimmune disease.\textsuperscript{52} When the US Food and Drug Administration (FDA) approved silicone-gel breast implants in 2006, it recognised that data on rare events and long-term outcomes were limited. To clarify this, each manufacturer of silicone-gel breast implants is required to conduct a number of post-approval studies to characterise the long-term safety profile of its devices.\textsuperscript{53} In response, MENTOR\textsuperscript{®} and Allergan produced core studies with a follow-up period of eight and 10 years, respectively.\textsuperscript{54,55} These studies did not demonstrate an association with autoimmune disease.\textsuperscript{53}

More recently, larger post-approval studies have been conducted to evaluate the incidence of rare adverse events. A study by Singh and colleagues assessed 55,279 patients with a minimum five-year follow-up who had Allergan implants, comparing the incidence of targeted adverse events to patients with saline implants and national norms. This study showed that Allergan Natrelle\textsuperscript{®} (Northshore Corporate Centre, 4/810 Pacific Hwy, Gordon NSW 2072) round silicone implants did not significantly increase the risk of any systemic disease compared with both national norms and saline implants.\textsuperscript{56} Another study by Coroneos and colleagues assessed both Allergan and MENTOR\textsuperscript{®} (a business of Johnson & Johnson Medical Pty Ltd 1–5 Khartoum Road, Macquarie Park NSW 2113) implants with a total of 99,993 patients, with a follow-up period of two years for Allergan and seven years for MENTOR\textsuperscript{®} implants. They found that women with silicone breast implants had rates of Sjögren’s syndrome, scleroderma and rheumatoid arthritis that were greater than double those in the general population. Furthermore, both the Allergan and MENTOR\textsuperscript{®} groups showed a higher incidence of patient-reported rheumatological symptoms in the revision-reconstruction cohort.\textsuperscript{57} These authors also countered the common criticism of patient-reported data. They suggested that although the accuracy of the findings might be difficult to interpret, the results represent a significant proportion of women who present with symptoms who nevertheless still require clinical evaluation and management.

In the studies we reviewed, there was a wide range in duration of latency periods between exposure and disease. In an analysis of 300 patients, Watad and colleagues\textsuperscript{58} showed a mean latency period of 31 months (range 1 week to 60 months). In their cohort of 200 patients, Colaris and colleagues\textsuperscript{38} showed a median latency period of four years (range 1–39 years) and several smaller studies had latency periods ranging from 5 to 15 years.\textsuperscript{4,55,35} The aforementioned post-approval studies by Allergan and MENTOR\textsuperscript{®} would therefore have captured data pertaining to ASIA; however, the FDA analysis was looking for an association with known autoimmune diseases and not a yet-to-be-defined syndrome such as BII.

The incidence of concomitant autoimmune conditions was assessed in several publications. A retrospective study of 300 patients with silicone breast implants referred to a rheumatology clinic for musculoskeletal complaints found similar incidences of human adjuvant disease and known connective tissue disease (10.6% and 11%, respectively).\textsuperscript{15} In other studies in which all
Table 3: Common symptom profile of ASIA

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Shoenfeld et al(^3)</th>
<th>Watad et al(^3)</th>
<th>Colaris et al(^3)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n=100</td>
<td>n=300</td>
<td>n=200</td>
</tr>
<tr>
<td>Myalgia</td>
<td>&gt;60%</td>
<td>49%</td>
<td>73%</td>
</tr>
<tr>
<td>Arthralgia</td>
<td>&gt;60%</td>
<td>61%</td>
<td>86%</td>
</tr>
<tr>
<td>Chronic fatigue/sleep disturbance</td>
<td>&gt;60%</td>
<td>59%</td>
<td>97%</td>
</tr>
<tr>
<td>Fever</td>
<td>Not reported</td>
<td>34%</td>
<td>58%</td>
</tr>
<tr>
<td>Neurological manifestations</td>
<td>30–60%</td>
<td>26%</td>
<td>26%</td>
</tr>
<tr>
<td>Cognitive impairment</td>
<td>30–60%</td>
<td>21%</td>
<td>80%</td>
</tr>
<tr>
<td>Generalised weakness</td>
<td>Not reported</td>
<td>33%</td>
<td>Not reported</td>
</tr>
<tr>
<td>Sicca symptoms (dry eyes, dry mouth)</td>
<td>Not reported</td>
<td>18%</td>
<td>73%</td>
</tr>
<tr>
<td>Skin (rash)</td>
<td>&lt;30%</td>
<td>16%</td>
<td>Not reported</td>
</tr>
</tbody>
</table>

patients met the criteria for ASIA, the incidence of concomitant autoimmune conditions ranged from 10 per cent to 53 per cent.\(^4,12,13,35,38\)

A meta-analysis by Janowski and colleagues\(^59\) showed no association between silicone breast implants and autoimmune or connective tissue disorders, supporting the safety of silicone breast implants. This is in keeping with three prior meta-analyses, which also found no increased risk of connective tissue diseases following silicone breast implantation.\(^60–62\)

However, in the meta-analysis by Janowsky and colleagues, several smaller studies\(^11,63,64\) and a significant study of 10,830 patients by Hennekens and colleagues\(^65\) were excluded as the patients’ symptoms were self-reported.\(^39\) In their analysis, Janowsky and colleagues found the relative risk of connective tissue, autoimmune or rheumatic disorders to be slightly elevated when the data from Hennekens and colleagues study were included, but when the data were excluded the results were equivocal.\(^39\) Janowsky and colleagues expounded on the shortcomings of self-reported data in light of the controversial nature of public awareness and concern over the potential health effects of breast implants, justifying the exclusion of this large study. In short, this meta-analysis failed to establish an association between silicone breast implants and autoimmune or connective tissue disorders.

Although the medical literature has failed to link silicone-gel breast implants with ‘known’ autoimmune or connective tissue disorders, there are numerous studies that examine the link between silicone breast implants and a collective group of symptoms that may be autoimmune in nature and are colloquially known as BII.

### Clinical findings

The symptom profile of ASIA has been reported by numerous studies. The most common symptoms experienced include chronic fatigue, myalgia, arthralgia, fever and generalised weakness (Table 3).

A common belief is that the symptomatology of ASIA is non-specific and therefore possibly related to any number of conditions or circumstances in the normal population. This generalisation has been difficult to dispel, as only a limited number of controlled studies have assessed the incidence of symptoms in patients with silicone breast implants compared with those without. Giltay and colleagues\(^11\) presented an age-matched study of 235 patients with silicone breast implants and 210 patients who had undergone an aesthetic operation without the use of silicone. They found that patients with silicone breast implants had a significantly higher rate of symptoms, especially arthralgia, dry eyes and skin abnormalities. Of note, this study was excluded from the meta-analysis by Janowsky and colleagues due to the use of self-reported outcomes. Englert and colleagues\(^28\) presented a study of 458 patients with silicone breast implants and a control group of 687 patients who had undergone plastic surgery without the use of silicone. Although they found a higher rate of a ‘cluster’ of symptoms including night sweats,
Diagnostic criteria

Despite having a varied presentation and symptomatology, several authors have described diagnostic criteria for ASIA. Miyoshi and colleagues were the first to do so for a condition they called human adjuvant disease. In 2011, Shoenfeld and colleagues refined this by introducing major and minor criteria. In 2015, Alijotas-Reig further modified this by replacing subjective terms from Shoenfeld’s criteria with objective terms to minimise false-positive diagnoses (Table 4). These diagnostic criteria should guide clinical recognition of common symptom groupings that patients may present with. Rather than a tool to exclude or confirm a diagnosis of ASIA, these criteria should direct counselling and appropriate

<table>
<thead>
<tr>
<th>Table 4: Published diagnostic criteria for ASIA</th>
</tr>
</thead>
</table>
| **Miyoshi et al** <sup>66</sup> | - Variable latency time ranging from months to years  
- Foreign body-type granuloma present in injected or implanted area ± drainage lymph nodes  
- Presence of any auto-antibody  
- Symptoms may resolve after implanted material is removed  
- Infection of neoplastic causes are excluded |
| Schoenfeld et al <sup>56</sup> | **Major criteria** | 1. External stimulus exposure (infection, vaccine, silicone) before clinical signs  
2. Appearance of typical clinical manifestations  
   - Myalgia, myositis or muscle weakness  
   - Arthralgia and/or arthritis  
   - Chronic fatigue, sleep disturbance  
   - Neurological manifestations  
3. Cognitive impairment or memory loss  
4. Pyrexia or dry mouth  
5. Removal of agent induces improvement of symptoms  
6. Typical biopsy of involved organs |
| | **Minor criteria** | 1. Auto-antibodies or antibodies directed at the adjuvant  
2. Other clinical symptoms (for example, irritable bowel syndrome)  
3. Specific HLA (that is, HLA-DRB1, HLA-DQB1)  
4. Evolvement into a defined autoimmune disease |
| Alijotas-Reig <sup>66</sup> | **Major criteria** | 1. Exposure to external stimuli (biomaterials, vaccines, anilines or other organic/inorganic materials) prior to clinical manifestations  
2. Minimum latency time of days when referring to vaccines and one month for other suspected adjuvants  
3. Clinical involvement  
   - Local/regional (inflammatory nodules, skin oedema, skin indurations, pseudo-abscesses, lymphadenopathy, panniculitis, morphea, sarcoid-like lesions)  
   - Systemic (distant inflammatory nodules, arthritis, Sicca or Sjögren’s syndrome, myositis, extended panniculitis, demyelinating neurological involvement)  
   - Evolvement into autoimmune disease  
4. Foreign body-type biopsy of involved area or lymph nodes or histological findings consistent with autoimmune/ granulomatous disorders  
5. Removal of inciting materials induces improvement  
6. Compatible HLA (HLA-B8, HLA-DRB1, HLA-DR3, HLA-DQB1 or haplotype combination) |
| | **Minor criteria** | 1. Recent history of triggering factors preceding the onset of clinical manifestations  
2. Large, de non livedo reticularis and/or hand erythema appearing at the onset of clinical manifestations  
3. Presence of any auto-antibody and/or hypergammaglobulinaemia and/or increased angiotensin-converting enzyme or increased LDH and/or low complement levels |

Biomaterials included paraffin, silicone, silicone medical grade, methacrylate, poly-L-lactic acid, polyacrylamide, poly-alkyl-imide, collagen, hydroxyl-apatite, hyaluronic acid, non-animal stabilised hyaluronic acid, and alginate

lethargy, impaired cognition, myalgia, breast pain, reflux and paraesthesia in the ‘exposed’ group, these symptoms were also found in the ‘non-exposed’ group, albeit at a lower frequency.
investigation. In their discussion, Shoenfeld and colleagues aptly described the clinical signs and symptoms as ‘enigmatic’, but ‘nevertheless prominent’.5

**Risk factors**

The development of autoimmunity is believed to result from complex multifactorial interactions involving both a genetic predisposition and external triggers. To better characterise ASIA and rationalise why some individuals exposed to silicone develop post-exposure autoimmune symptoms, Soriano and colleagues described four groups of patients deemed to be at risk of developing ASIA after vaccination based on their review of the literature.67 These groups were identified. They were patients with:

1. a prior documented autoimmune reaction to an adjuvant
2. an established autoimmune condition
3. a history of allergic conditions/atopic disorders
4. a genetic predisposition to autoimmune disorders.

From their own review of the literature, Goren and colleagues suggested that these same groups would be at risk of developing ASIA following exposure to silicone.3 The commentary provided by these two papers reflects the current literature surrounding risk factors for post-exposure autoimmune syndromes, but both papers acknowledge the need for larger epidemiological studies to validate these concepts.

In addition to a genetic predisposition, external factors such as smoking and obesity have been linked to the development of autoimmune syndromes.68-70 Having an appreciation of these potential risk factors adds to our understanding and gives depth to our discussion with patients presenting with symptoms of BII (Table 5).

**Serological markers**

The role of serological markers in the diagnosis and management of connective tissue and autoimmune diseases is well established. Many investigators have hoped to discover unique patterns of markers to diagnose and characterise ASIA. To date, no specific pattern of serological markers has been identified. In their case series of 156 patients with breast implants and rheumatic disease complaints, Bridges and colleagues found that most women had normal results from serological tests. These tests included immunoglobulins, complement, C-reactive protein, rheumatoid factor and autoantibodies.9 The Dutch Working Party on Silicone Breast Implants reported a cohort study of 63 women who underwent mastectomy followed by immediate reconstruction with silicone breast implants. They found no difference in symptoms between antinuclear antibody-positive or -negative patients.23 Despite this, serological investigation is vital in the workup of a patient presenting with symptoms of an autoimmune condition and future research endeavours may yet discover a significant serological marker for BII.

**Imaging**

Although BII has been commonly reported in the presence of an intact and uncomplicated implant,25 thorough imaging will define the integrity of the implant, delineate the containment of a silicone rupture within a fibrous capsule, highlight silicone lymphadenopathy and identify a mass or peri-prosthetic fluid. If on imaging an implant appears intact and uncomplicated, patients presenting with BII often still request explantation. However, if imaging identifies an abnormality, this will direct further investigation to exclude traumatic, inflammatory or malignant conditions. Ultrasound and CT scanning have a role, but MRI is the

<table>
<thead>
<tr>
<th>Risk group</th>
<th>Example</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prior documented autoimmune reaction to an adjuvant</td>
<td>Vaccines, silicone breast implants, cosmetic fillers</td>
</tr>
<tr>
<td>Established autoimmune condition</td>
<td>Systemic lupus erythematosus, Hashimoto’s or Grave’s disease, type 1 diabetes, rheumatoid arthritis</td>
</tr>
<tr>
<td>History of allergic or atopic disorders</td>
<td>Eczema, hay fever, pollen and dust mite allergy, drug allergy, rubber or latex allergy</td>
</tr>
<tr>
<td>Prone to develop autoimmunity</td>
<td>HLA-DR4, HLA-DRB1, HLA-DR53, HLA-DQA1*0102, HLA-C7</td>
</tr>
<tr>
<td>Active smoking</td>
<td>Obesity</td>
</tr>
</tbody>
</table>

Table 5: Potential risk factors for patients presenting with symptoms of BII

---

_Australasian Journal of Plastic Surgery_ 2021 Volume 4 Number 1
In line with a multifactorial model of pathogenesis for a post-exposure autoimmune syndrome, Colaris and colleagues explored the role of vitamin D as an immune regulator in patients with ASIA.\textsuperscript{79} Based on their literature review and measurement of vitamin D levels in 135 patients with ASIA, they found that vitamin D deficiency was related to the presence of auto-antibodies in patients with ASIA, as well as those with other autoimmune diseases such as autoimmune thyroid disease, connective tissue disorders, inflammatory arthritides and multiple sclerosis. Although speculative in nature, the authors acknowledge the limitations of the study and suggest that more robust trials are required to assess the role of vitamin D supplementation.\textsuperscript{79}

**Implant integrity**

Although it has been proposed that the risk of ASIA is greater and symptoms are more severe in patients with ruptured implants,\textsuperscript{75} ASIA has been described in patients with intact implants.\textsuperscript{25} Gaubitz and colleagues explored this further in their MRI study of 90 patients with silicone breast implants. They found that symptoms and signs of an autoimmune response did not differ between those with or without ruptured implants.\textsuperscript{25}

Considering that a patient with silicone implants is exposed to silicone from the shell and silicone bleeding,\textsuperscript{76–78} the integrity of an implant should not determine the presence and course of an autoimmune response.

**Medical therapy**

Medical therapy with prednisolone alone and in combination with agents such as hydroxychloroquine, allopurinol, cetirizine and tacrolimus has been used for patients presenting with symptoms of ASIA.\textsuperscript{4} Alijotas-Reig and colleagues presented a case series of 45 patients with ASIA from biomaterials. Of these patients 42 per cent had silicone breast implants. Medium-high doses of prednisolone (0.5–1mg/kg/day) were typically used, with some patients requiring long-term corticosteroid therapy to manage their symptoms. They found that almost 100 per cent of patients were symptom free within a few months and 70 per cent remained symptom free at two years when treatment was withdrawn. Although promising, within this small sample, 22 per cent (10/45) of patients also had complete surgical removal of the offending biomaterial, with 60 per cent of this group demonstrating an improvement in symptoms.\textsuperscript{4}

In its recent draft, the FDA has recommended an ultrasound or MRI at five to six years postoperatively, then every two years thereafter.\textsuperscript{53} The current recommendations from the FDA are for MRI screening of asymptomatic patients with breast implants at three years post-implantation and every two years thereafter.\textsuperscript{53}
Maijers and colleagues recruited their patients through a national media campaign, while Cuellar and colleagues recruited patients referred to a rheumatology clinic. A study by Peters and colleagues was based on consecutive cases of patients requesting explantation. The data are therefore difficult to interpret, despite appearing to strongly support the role of capsulectomy and explantation.

The way in which the explantation and capsulectomy are performed has not been consistently reported and there is no evidence to support an en-bloc capsulectomy over a total capsulectomy that removes the capsule in components or even explantation without a capsulectomy. However, in line with the theory of an adjuvant inciting an autoimmune response, understanding the permeating nature of silicone within a fibrous capsule and acknowledging silicone bleed as a real phenomenon, an en-bloc style capsulectomy and explantation theoretically would provide the most thorough technique to remove any potential local source of silicone while minimising silicone contamination to the surgical field. De Boer and colleagues even suggested that the persistence of symptoms following capsulectomy may reflect the presence of residual silicone perpetuating the production of autoantibodies.

Most patients presenting to a surgeon seeking explantation surgery would usually have contemplated the potential aesthetic impact. A thorough exploration of a patient’s sense of body image and emotional readiness for surgery should be completed. If a patient expresses deep regret or fear of losing their breast implants, these concerns should be explored until it is clear that the patient understands and accepts the aesthetic ramifications of explantation surgery. A discussion of the merits and limitations of immediate or delayed options in restoring form and/or volume to the breasts should also be conducted.

Conclusion

Breast implant illness remains a condition of marked debate. This review serves to outline the literature surrounding BII so that clinicians have the relevant information at hand to discuss with their patients. Patients with possible BII can present in a number of ways with mild to severe and even debilitating symptoms. The uncertain nature of a BII diagnosis has repercussions in establishing satisfactory management pathways for these patients. Regardless of the true nature of BII, clinicians have a responsibility to assess these patients to exclude other pathology and also offer counselling and appropriate management guided by the available literature to date. A multidisciplinary approach is recommended to assess and support these patients and surgery is a key component to be considered in their overall management.

Disclosures

The authors have no financial interest to declare in relation to the content of this article. The article is not based on a previous communication. The authors are not recipients of a research scholarship.

References


