Information for Health Care Providers on Delayed Injection Site Reactions following administration of mRNA COVID-19 vaccines

Presenters: Elissa Abrams and Nooshin Ahmadipour
Q and A: Joseline Zafack, Gina Lacuesta
March 11, 2021
Conflicts of interest

• Elissa Abrams– no conflicts of interest to declare
• Nooshin Ahmadipour– no conflicts of interest to declare
• Joseline Zafack– no conflicts of interest to declare
• Gina Lacuesta– no conflicts of interest to declare
Objectives

• To provide an overview of delayed injection site reactions following administration of mRNA COVID-19 vaccines based on data from the Canadian Adverse Events Following Immunization Surveillance System (CAEFISS) and data from the Moderna clinical trial

• To describe the features and management of delayed injection site reactions following administration of mRNA COVID-19 vaccines

• To provide guidance on distinguishing these delayed injection reactions from other local reactions such as cellulitis
Outline

• Delayed injection site reactions
• Data from the Canadian adverse Event Following Immunization Surveillance System (CAEFISS)
• Data from the Moderna COVID-19 vaccine clinical trial
• Distinguish a delayed injection site reaction from a cellulitis
• Management of a delayed injection site reaction
Injection site reactions (local reactions)

- Injection site reactions or local reactions (swelling, redness, mild tenderness) after vaccination are common
  - Usually occur within a few hours; resolve quickly
  - Usually mild or moderate
  - Part of the normal immune response of the body

- Delayed local reactions have been described in the past
  - Occur within hours to days but can be delayed weeks
  - Can be immunologically or non-immunologically mediated (nonspecific inflammation, T cell mediated)
  - Self-limited, do not contraindicate administration of future vaccine doses

- Delayed local reactions following Moderna COVID-19 vaccination
  - Expected adverse event, usually mild or moderate and self-limited
  - T-cell mediated hypersensitivity
  - Does not contraindicate administration of future vaccine doses
  - Does not increase risk of anaphylaxis

Blumenthal KG, et al. Delayed large local reactions to mRNA-1273 vaccine against SARS-CoV-2. NEJM 2021
Data from the Canadian adverse Event Following Immunization Surveillance System (CAEFISS)

AEFI reports with at least one local reaction (CAEFISS, February 23)

V site reporting rate for Pfizer: 12/100,000 doses distributed
V site reporting rate for Moderna: 95/100,000 doses distributed
Data from the Canadian adverse Event Following Immunization Surveillance System (CAEFISS)

AEFI reports with at least one local reaction by delay of onset (CAEFISS, Feb 24, 2021)

<table>
<thead>
<tr>
<th>Time of onset after vaccination</th>
<th>Moderna</th>
<th>Pfizer-BioNtech</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-3 days</td>
<td>139 (25%)</td>
<td>127 (69%)</td>
</tr>
<tr>
<td>&gt;3 to &lt;8 days</td>
<td>150 (27%)</td>
<td>15 (8%)</td>
</tr>
<tr>
<td>8+ days</td>
<td>214 (38%)</td>
<td>17 (9%)</td>
</tr>
<tr>
<td>Missing</td>
<td>53 (10%)</td>
<td>26 (14%)</td>
</tr>
<tr>
<td>Total</td>
<td>556 (100%)</td>
<td>185 (100%)</td>
</tr>
</tbody>
</table>

At the time of report, outcome of Moderna injection site reactions was comparable between the various delays of onset.
Data from the Canadian adverse Event Following Immunization Surveillance System (CAEFISS)

Injection site reactions following Moderna COVID-19 vaccines (CAEFISS, February 23, 2021)

<table>
<thead>
<tr>
<th>Reaction at the vacc. site</th>
<th>N total</th>
<th>0-3 d Row %</th>
<th>&gt;3 to &lt;8 d Row %</th>
<th>8+ d Row %</th>
<th>Missing onset Row %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Erythema</td>
<td>262</td>
<td>20.23</td>
<td>30.92</td>
<td>41.22</td>
<td>7.63</td>
</tr>
<tr>
<td>Pain</td>
<td>258</td>
<td>43.02</td>
<td>28.29</td>
<td>20.93</td>
<td>7.75</td>
</tr>
<tr>
<td>Swelling</td>
<td>204</td>
<td>21.57</td>
<td>34.31</td>
<td>38.73</td>
<td>5.39</td>
</tr>
<tr>
<td>Warmth</td>
<td>165</td>
<td>22.42</td>
<td>35.15</td>
<td>36.97</td>
<td>5.45</td>
</tr>
<tr>
<td>Pruritus</td>
<td>111</td>
<td>11.71</td>
<td>45.05</td>
<td>34.23</td>
<td>9.01</td>
</tr>
<tr>
<td>Cellulitis</td>
<td>104</td>
<td>24.04</td>
<td>31.73</td>
<td>40.38</td>
<td>3.85</td>
</tr>
<tr>
<td>Inflammation</td>
<td>83</td>
<td>18.07</td>
<td>21.69</td>
<td>53.01</td>
<td>7.23</td>
</tr>
<tr>
<td>Induration</td>
<td>68</td>
<td>22.06</td>
<td>33.82</td>
<td>32.35</td>
<td>11.76</td>
</tr>
<tr>
<td>Rash</td>
<td>53</td>
<td>9.43</td>
<td>47.17</td>
<td>37.74</td>
<td>5.66</td>
</tr>
<tr>
<td>Extensive swelling</td>
<td>14</td>
<td>78.57</td>
<td>14.29</td>
<td>0</td>
<td>7.14</td>
</tr>
<tr>
<td>Oedema</td>
<td>12</td>
<td>16.67</td>
<td>33.33</td>
<td>33.33</td>
<td>16.67</td>
</tr>
<tr>
<td>Urticaria</td>
<td>12</td>
<td>50</td>
<td>41.67</td>
<td>8.33</td>
<td>0</td>
</tr>
<tr>
<td>Total (all)*</td>
<td>1,534</td>
<td>24.32</td>
<td>31.36</td>
<td>37.16</td>
<td>7.17</td>
</tr>
</tbody>
</table>

*Includes frequencies 1-2 that were removed from the two tables
Data from the Canadian adverse Event Following Immunization Surveillance System (CAEFISS)

Injection site reactions following Pfizer-BioNTech COVID-19 vaccines (CAEFISS, February 23, 2021)

<table>
<thead>
<tr>
<th>Reaction at the vacc. site</th>
<th>Total</th>
<th>0-3 d Row %</th>
<th>&gt;3 to &lt;8 d Row %</th>
<th>8+ d Row %</th>
<th>Missing onset %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain</td>
<td>140</td>
<td>76.43</td>
<td>4.29</td>
<td>6.43</td>
<td>12.86</td>
</tr>
<tr>
<td>Erythema</td>
<td>53</td>
<td>64.15</td>
<td>9.43</td>
<td>18.87</td>
<td>7.55</td>
</tr>
<tr>
<td>Swelling</td>
<td>49</td>
<td>67.35</td>
<td>10.2</td>
<td>12.24</td>
<td>10.2</td>
</tr>
<tr>
<td>Warmth</td>
<td>32</td>
<td>81.25</td>
<td>6.25</td>
<td>9.38</td>
<td>3.13</td>
</tr>
<tr>
<td>Pruritus</td>
<td>22</td>
<td>54.55</td>
<td>18.18</td>
<td>22.73</td>
<td>4.55</td>
</tr>
<tr>
<td>Induration</td>
<td>14</td>
<td>71.43</td>
<td>21.43</td>
<td>0</td>
<td>7.14</td>
</tr>
<tr>
<td>Extensive swelling</td>
<td>12</td>
<td>91.67</td>
<td>0</td>
<td>8.33</td>
<td>0</td>
</tr>
<tr>
<td>Cellulitis</td>
<td>12</td>
<td>75</td>
<td>8.33</td>
<td>8.33</td>
<td>8.33</td>
</tr>
<tr>
<td>Paraesthesia</td>
<td>9</td>
<td>66.67</td>
<td>11.11</td>
<td>11.11</td>
<td>11.11</td>
</tr>
<tr>
<td>Rash</td>
<td>9</td>
<td>66.67</td>
<td>0</td>
<td>33.33</td>
<td>0</td>
</tr>
<tr>
<td>Inflammation</td>
<td>6</td>
<td>83.33</td>
<td>0</td>
<td>0</td>
<td>16.67</td>
</tr>
<tr>
<td>Nodule</td>
<td>3</td>
<td>100</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Total (all)*</td>
<td>407</td>
<td>71.25</td>
<td>8.6</td>
<td>10.57</td>
<td>9.58</td>
</tr>
</tbody>
</table>

*Includes frequencies 1-2 that were removed from the two tables
Data from the Moderna COVID-19 vaccine trial

- Local reactions occurred in up to 80% of trial participants overall
  - Majority of mild to moderate local reactions
  - Pain mainly, erythema, swelling, lymphadenopathy at the site of injection
  - Not harmful, not a contraindication for future vaccination

Baden LR et al. Efficacy and safety of the MRNA-1273 SARS-CoV-2 Vaccine. NEJM 2021;384: 403-16
Delayed local reactions following COVID-19 vaccines

- Reaction seen to COVID-19 mRNA vaccines around the injection site
  - Induration
  - Swelling
  - Erythema
  - Pain/tenderness
  - Median onset on day 8 (range 4 to 11)
  - Resolve within 6 days (range 2 to 11)
  - Systemic AE in some patients

- Thus far appear to be more common with Moderna COVID-19 vaccine

- Observed in the Moderna clinical trial
  - Dose 1: 0.8% of vaccine recipients
  - Dose 2: 0.2% of vaccine recipients

- 50% recurrence after dose 2 (similarly or less severe than the 1st reaction)

Blumenthal KG, et al. Delayed large local reactions to mRNA-1273 vaccine against SARS-CoV-2. NEJM 2021
Delayed Cutaneous Reactions to Moderna COVID-19 Vaccine (1)

Blumenthal KG, Freeman EE, Saff RR et al. Delayed large local reactions to mRNA-1273 vaccine against SARS-CoV-2. NEJM 2021 [epub ahead of print]
Delayed Cutaneous Reactions to Moderna COVID-19 Vaccine (2)

Blumenthal KG, et al. Delayed large local reactions to mRNA-1273 vaccine against SARS-CoV-2. NEJM 2021
Distinguish a delayed injection site reaction from cellulitis

• On clinical presentation delayed local reaction may resemble cellulitis
  – Risk of unnecessary antibiotic treatment

• The main difference between the two is presence or absence of systemic symptoms
  – Cellulitis: fevers, chills, malaise
  – Local reaction: in general no systemic symptoms
  – Cellulitis: Faster onset, day 3-5
  – Cellulitis: Less demarcation or clear edges

• If no systemic symptoms monitor for progression of fever, systemic symptoms, or worsening local discomfort over time

Photo c/o Dermnetz.org

Lapphira K, Scheiffele D. Vaccination site reaction or bacterial cellulitis? Paediatr Child Health 2009;14:245
Management of delayed injection site reactions

- Reassurance
- Ice packs or cold compresses
- Analgesics
- Antihistamines (for the pruritus and burning)
- Avoid systemic steroids (as it may blunt response to vaccine)
  Topical steroids if symptomatic relief needed.
- Monitor the evolution of signs and symptoms
Key messages

• Delayed local reactions are an injection site reaction occurring days after vaccination
  – Inform vaccinated patients that these reactions can occur
  – Reassure all patients (especially those who have experienced it) that the reaction is benign

• Delayed local reactions may look similar to cellulitis but resolve without the use of antibiotics and in general have no systemic symptoms

• Delayed local reactions are usually not serious and will self-resolve

• Delayed local reactions do not preclude future vaccination and do not increase the risk for anaphylaxis with future vaccination

• There is a decreased frequency of these delayed local reactions following the 2nd dose of vaccine.
• Refer to Part 2 - Vaccine Safety in the Canadian Immunization Guide (CIG) for definitions of AEFIs and additional general information.
Subscribe for NACI publications and updates to the CIG

Canadian Immunization Guide updates and National Advisory Committee on Immunization - publications mailing list

On this page
- Subscribe
- Cancelling your subscription

Subscribe
To receive information regarding updates to the Canadian Immunization Guide and new National Advisory Committee on Immunization (NACI) recommendations, statements and literature reviews, please enter your e-mail address below and click on the "Subscribe" button.

* Your E-mail address (required)

* Preferred update(s) (required)
- Canadian Immunization Guide
- NACI Recommendations, Statements and Updates
Resources for healthcare providers

COVID-19 Vaccination Information Resources
Ressources documentaires sur la vaccination contre la COVID-19

Tool Kit for Health Care Providers
Trousse à outils pour les fournisseurs de soins de santé

- COVID-19 vaccination tool kit for health care providers can be found at Canada.ca/coronavirus
Additional resources

• How to report an AEFI: https://www.canada.ca/en/public-health/services/immunization/reporting-adverse-events-following-immunization.html

• AEFI report form: Reporting Adverse Events Following Immunization (AEFI) in Canada

• Submission of AEFI reports: User guide to completion and submission of the AEFI reports
Acknowledgements

• PHAC Vaccine Safety Section
• NACI Vaccine Safety Working Group
• National Collaborating Centre for Infectious Diseases (NCCID)
THANK YOU

QUESTIONS?