Vaccine Reactions – why more antigen is not necessarily better

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What is a Vaccine Reaction?

• An adverse response to the vaccine
• Types can include:
  • Hypersensitivity
    – Type 1 – IgE mediated
    – Type 3 – immune complex mediated
  • Infection
    contamination
  • Local inflammation
    – Response to adjuvant
Type I Hypersensitivity

- IgE mediated responses
- Local
  - Hives, urticaria, localized edema
- Systemic
  - Systemic anaphylaxis
    - In horses, respiratory and GI systems can be affected
    - Shock with collapse and rapid death
    - Gastrointestinal smooth muscle/ colic
Increased capillary permeability
Smooth muscle contraction
Type 2 Hypersensitivity

- Local immune complex formation at injection site = Arthus Reaction
- Occurs when there are high titers of IgG to one or more components of vaccine
- Can be debilitating for several days and/or cause a significant lesion at the injection site
Vaccine Components

• Target antigen, e.g. virus
• Adjuvant, if inactivated
• + or - Stabilizers
• Non-target antigens
  – These are proteins that are carried along during processing of virus.
  – Growth of virus in tissue culture requires media that usually contains fetal bovine serum proteins
  – These are not removed from harvested virus
Hypothesis

• Repeated vaccination with viral vaccines containing fetal bovine serum proteins will, in some horses, stimulate the immune system to make bovine serum albumen (BSA) specific IgE, which could cause a type 1 hypersensitivity reaction upon subsequent administration of a vaccine containing BSA.
BSA Specific IgE in Horses Sampled before and after Vaccination

<table>
<thead>
<tr>
<th>Year</th>
<th># Horses Sampled</th>
<th>IgE Responder Level -1</th>
<th>IgE Responder Level-2</th>
<th>IgE Responder Level-3</th>
<th>Negative for BSA IgE</th>
</tr>
</thead>
<tbody>
<tr>
<td>2005</td>
<td>76</td>
<td>24 (32%)</td>
<td>3 (4%)</td>
<td>13 (17%)</td>
<td>36 (47%)</td>
</tr>
<tr>
<td>2005</td>
<td>64</td>
<td>10 (16%)</td>
<td>3 (5%)</td>
<td>11 (17%)</td>
<td>40 (62%)</td>
</tr>
<tr>
<td>2005</td>
<td>50</td>
<td>17 (34%)</td>
<td>0</td>
<td>11 (22%)</td>
<td>22 (44%)</td>
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<tr>
<td>2006</td>
<td>38</td>
<td>13 (34%)</td>
<td>2 (5%)</td>
<td>13 (34%)</td>
<td>10 (26%)</td>
</tr>
<tr>
<td>2008</td>
<td>50</td>
<td>15 (30%)</td>
<td>0</td>
<td>11 (22%)</td>
<td>24 (48%)</td>
</tr>
<tr>
<td>2009</td>
<td>49</td>
<td>12 (25%)</td>
<td>3 (6%)</td>
<td>7 (14%)</td>
<td>27 (55%)</td>
</tr>
</tbody>
</table>

Level1- O.D. values ≥60% positive control.
Level2- <60%, but post-vaccine O.D. at least twofold greater than pre-vaccine O.D.
Level 3- O.D. is >40% and <60% of positive control.
Negative - O.D. values ≤40% of the positive control.
IgE Responses to BSA in 6 Vaccinated Horses
Other Pertinent Results

• Approximately 50% of all horses tested also had IgG antibodies against bovine serum albumen.

• Intradermal skin testing with BSA was performed on a subset of horses with BSA specific IgE; results showed positive skin tests varying from 42 to 104% of the histamine control.
Implications

• Unless vaccine companies alter vaccine production to eliminate from vaccines all foreign non-target antigenic proteins, increasing the antigen load will increase the concentrations of these non-target proteins in each vaccine.

• Since horses receive multiple viral vaccines, many of which contain the same non-target proteins, the exposure to these antigens will be greatly increased.

• The result will be more horses making IgE and IgG antibodies to non-target proteins and more adverse vaccine reactions – many of which will be fatal.
Reference