Anaphylaxis Treatment with Steroids: Steroids should routinely be used for the treatment of anaphylaxis
Anaphylaxis Definition

- Classical definition of 2 or more of the below symptoms developing acutely following an exposure to an allergen\textsuperscript{1,2}

\begin{itemize}
  \item Sudden skin or mucosal symptoms and signs (e.g. generalized hives, itch-flush, swollen lips-tongue-uvula)
  \item Sudden respiratory symptoms and signs (e.g. shortness of breath, wheeze, cough, stridor, hypoxemia)
  \item Sudden reduced BP or symptoms of end-organ dysfunction (e.g. hypotonia [collapse], incontinence)
  \item Sudden gastrointestinal symptoms (e.g. crampy abdominal pain, vomiting)
\end{itemize}
Anaphylaxis Pathophysiology

- IgE binds to the high-affinity receptor FcεRI on the surfaces of blood basophils and tissue-resident mast cells\(^1\)

- Cross-linking of FcεRI-bound IgE leads to release of mediators

- Release of mediators leads to a variety of symptoms\(^1\)

Anaphylaxis Importance

- Life-time prevalence of anaphylaxis has been estimated at 0.05 to 2%\(^1\)
- Estimated to be fatal in 0.7 to 2% of cases
  - Case fatality rates in the US for patients treated for anaphylaxis either in the ED or hospital were estimated to be 63-99 deaths annually\(^2\)

\(^1\) Ann Allergy Asthma Immunol. 2006;97:596-602.
Anaphylaxis Treatment

- Epinephrine is first line in anaphylaxis\(^2\)

- Second line treatments include\(^1\)
  - Antihistamines
  - IV fluids
  - Oxygen
  - Bronchodilators
  - Steroids

---

Why Use Steroids?

1) All major guidelines continue to suggest the use of steroids as adjuvant treatment in anaphylaxis

2) The mechanism of action of steroids in anaphylaxis provides a rational basis for their continued use

3) There is no concrete evidence to oppose the use of steroids in anaphylaxis
Guidelines

- 6 major guidelines
  - ALL recommend considering use of glucocorticoids as adjunctive therapy
  - NONE of them state to NOT use steroids in the treatment of anaphylaxis!
AAAAI Practice Parameters

- “…consider [corticosteroids as] adjunctive therapy. [Strong Recommendation; B Evidence].”¹

What about Europe?

- UK – “Corticosteroids may help prevent or shorten protracted reactions … Consider oral steroid therapy for up to 3 days. This is helpful for treatment of urticaria and may decrease the chance of further reaction.”¹

- Europe – “Systemic glucocorticosteroids may be used [as third line treatment] as they may reduce the risk of late-phase respiratory symptoms.”²

²Anaphylaxis: guidelines from the European Academy of Allergy and Clinical Immunology. Allergy. 2014;69(8):1026-45.
What about Australia and Canada?

- Australia – “Steroids can be used for persistent wheeze.”¹

- Canada – “Other second-line therapies, such as … corticosteroids, may play a role in resolving respiratory and cutaneous signs and symptoms.”²


What about WAO?

- World Allergy Organization – “Glucocorticosteroids…could, theoretically, prevent protracted anaphylaxis.”

<table>
<thead>
<tr>
<th>Organization, country, year of publication, reference</th>
<th>First line of therapy, route</th>
<th>Glucocorticoids</th>
<th>Other therapies</th>
</tr>
</thead>
<tbody>
<tr>
<td>World Allergy Organization, 2015</td>
<td>Adrenaline, IM</td>
<td>To prevent biphasic reactions. No effect on initial symptoms</td>
<td>Not given</td>
</tr>
<tr>
<td>Australasian Society of Clinical Immunology and Allergy (ASCIA), Australia, 2019</td>
<td>Adrenaline, IM</td>
<td>Adjuvant</td>
<td>Prednisolone Oral</td>
</tr>
<tr>
<td>European Academy of Allergy and Clinical Immunology, 2014</td>
<td>Adrenaline, IM</td>
<td>Third-line</td>
<td>Nebulized</td>
</tr>
<tr>
<td>American Academy of Allergy, Asthma and Immunology (AAAAI) and the American College of Allergists, Asthma and Immunology (ACAAI), USA, 2014</td>
<td>Adrenaline, IM</td>
<td>Adjuvant or effective in the acute management of anaphylaxis</td>
<td>Methylprednisolone Intravenous</td>
</tr>
<tr>
<td>Canadian Pediatric Society, Canada, 2010</td>
<td>Adrenaline, IM</td>
<td>Second-line</td>
<td>Prednisone Oral</td>
</tr>
<tr>
<td>Working Group of the Resuscitation Council, UK, 2008</td>
<td>Adrenaline, IM</td>
<td>Second-line</td>
<td>Hydrocortisone Short intravenous or intramuscular</td>
</tr>
</tbody>
</table>
Why Use Steroids?

1) All major guidelines continue to suggest the use of steroids as adjuvant treatment in anaphylaxis

2) The mechanism of action of steroids in anaphylaxis provides a rational basis for their continued use

3) There is no concrete evidence to oppose the use of steroids in anaphylaxis
Steroid Mechanism

- Glucocorticoids are potent inhibitors of inflammatory processes and potent anti-allergic compounds
  - 1) Genomic effects\(^1\)
  AND
  - 2) Rapid non-genomic effects\(^1\)
Steroid Mechanism

- 1) Genomic effects\(^1\) – Take 4-6 hours for the effects to manifest

  - Direct binding of the glucocorticoid/glucocorticoid receptor complex to promoter region of genes and by interacting with other transcription factors

  - Think about allergic rhinitis and asthma!

Steroid Mechanism

- 2) Rapid non-genomic effects\(^1\) – Take 5-30 minutes for the effects to manifest

- Brought about by membrane interactions and mediated by interactions with intracellular receptors or membrane-bound receptors
Why Use Steroids?

1) All major guidelines continue to suggest the use of steroids as adjuvant treatment in anaphylaxis

2) The mechanism of action of steroids in anaphylaxis provides a rational basis for their continued use

3) There is no concrete evidence to oppose the use of steroids in anaphylaxis
What do we know about the benefits of steroids in anaphylaxis?

- Length of hospital stay tends to be shorter in those treated with corticosteroids for anaphylaxis\(^1\)

- A study that examined the association of corticosteroids with biphasic anaphylaxis supports the use of corticosteroids for this indication\(^2\)
Strength of Evidence

- There are **NO randomized controlled clinical trials** on steroid use in anaphylaxis\(^1\)
Evidence for Steroids in Anaphylaxis

- Currently estimated that 45-97% of patients receive glucocorticoids in the management of anaphylaxis\(^1\)

- The questions we need to ask are
  - Is there enough evidence to change current practice?
  - Or
  - Is it safe to stop?

Evidence for Steroids in Anaphylaxis

- Currently estimated that 45-97% of patients receive glucocorticoids in the management of anaphylaxis\(^1\)

- The questions we need to ask are
  - Is there enough evidence to change current practice?
  - Is it safe to stop?

To Review
Why Use Steroids?

1) **All major guidelines** continue to suggest the use of steroids as adjuvant treatment in anaphylaxis
   - Especially useful as adjuvant treatment for those with urticaria or respiratory symptoms

2) The *mechanism of action* of steroids in anaphylaxis provides a rational basis for their continued use

3) There is **no concrete evidence** to oppose the use of steroids in anaphylaxis
Why Use Steroids?

1) All major guidelines continue to suggest the use of steroids as adjuvant treatment in anaphylaxis

2) The mechanism of action of steroids in anaphylaxis provides a rational basis for their continued use
   - Glucocorticoids are potent inhibitors of inflammatory processes and potent anti-allergic compounds through both genomic and rapid non-genomic effects

3) There is no concrete evidence to oppose the use of steroids in anaphylaxis
Why Use Steroids?

- 1) **All major guidelines** continue to suggest the use of steroids as adjuvant treatment in anaphylaxis
- 2) The **mechanism of action** of steroids in anaphylaxis provides a rational basis for their continued use
- 3) There is **no concrete evidence** to oppose the use of steroids in anaphylaxis
  - No randomized control trials on steroid use in anaphylaxis
  - Therefore, it’s not safe to stop our current practice
Steroids should routinely be used for the treatment of anaphylaxis.