Effects of Rhinovirus on Bronchoalveolar Lavage Granulocyte and Cytokine Patterns in Children with Severe Wheeze

Kelly Boyd MD, Monica Lawrence MD, Larry Borish MD, Kristin Wavell BS, W. Gerald Teague MD

Background

- Recurrent episodes of cough and wheeze in preschool aged children are a major cause of morbidity
- The etiology of wheezing episodes in children is broad
  - Anatomic abnormalities
  - Host defense defects
  - Recurrent aspiration
  - Neonatal disorders
  - Infection

Background

- Lower respiratory pathogens, including rhinovirus, are common triggers for acute wheeze episodes in children[^3,^4]
- About ⅓ of preschool aged children with wheezing are later diagnosed with asthma in childhood[^5]

Hypothesis

- In preschool children with severe problematic wheeze, rhinovirus infection in the lower respiratory tract defines a clinical phenotype of those at risk for developing asthma

Purpose

- To examine the effect of respiratory pathogens on lower respiratory and systemic inflammatory patterns in preschool children with treatment-refractory cough and wheeze.

Methods

- Inclusion criteria
  - Children ages 1 to <6 years old with treatment refractory cough and wheeze
  - No current clinical symptoms of acute respiratory infection
- Exclusion criteria
  - Congenital heart disease
  - Cystic fibrosis
  - Congenital anomalies
  - Immunodeficiency
- 245 preschool aged children enrolled
Methods

- Patients underwent clinically-indicated diagnostic bronchoscopy with broncholavage (BAL) and bronchial brushing
  - BAL fluid for total cell counts with differential, bacterial and viral studies
  - Bronchial brushing for ciliary motion
  - Peripheral blood samples for eosinophil count, IgE, allergen-specific IgE, and CRP
- Subgroup (n=12) had BAL cytokines measured

245 children with treatment refractory cough/wheeze underwent bronchoscopy

- Bacteria
  - 68 (27.8%) positive for pathogenic bacteria
- Viruses
  - 98 (40%) positive for rhinovirus
  - 27 (11%) positive for non-enteroviral pathogen
## Baseline Characteristics

<table>
<thead>
<tr>
<th>Feature</th>
<th>Rhinovirus + (n=98)</th>
<th>Rhinovirus - (n=147)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average age</td>
<td>2.6 years</td>
<td>3.1 years</td>
<td>p&lt;0.05</td>
</tr>
<tr>
<td>Gender</td>
<td>72% male</td>
<td>64% male</td>
<td>NS</td>
</tr>
<tr>
<td>Ethnicity</td>
<td>24% non-white</td>
<td>20% non-white</td>
<td>NS</td>
</tr>
<tr>
<td>Daily use of high dose inhaled corticosteroids</td>
<td>64%</td>
<td>63%</td>
<td>NS</td>
</tr>
</tbody>
</table>

NS: Not Significant

## BAL Samples Granulocytic Patterns

<table>
<thead>
<tr>
<th>Feature</th>
<th>Definition</th>
<th>Rhinovirus +</th>
<th>Rhinovirus -</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pauci granulocytic</td>
<td>&lt;6% neutrophils 0% eosinophils</td>
<td>29%</td>
<td>45%</td>
<td></td>
</tr>
<tr>
<td>Isolated eosinophilia</td>
<td>&lt;6% neutrophils ≥1% eosinophils</td>
<td>2%</td>
<td>6%</td>
<td></td>
</tr>
<tr>
<td>Isolated neutrophilia</td>
<td>≥6% neutrophils 0% eosinophils</td>
<td>43%</td>
<td>33%</td>
<td></td>
</tr>
<tr>
<td>Mixed granulocytic</td>
<td>≥6% neutrophils ≥1% eosinophils</td>
<td>16%</td>
<td>7%</td>
<td>p&lt;0.05</td>
</tr>
</tbody>
</table>

*Cut-off points for BAL eosinophilia and neutrophilia derived from previously published ERS Task Force on BAL in children and studies done in healthy children*
## BAL Samples

<table>
<thead>
<tr>
<th>Feature</th>
<th>Rhinovirus +</th>
<th>Rhinovirus -</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total cell count</td>
<td>$2 \times 10^6$</td>
<td>$1.4 \times 10^6$</td>
<td></td>
</tr>
<tr>
<td>Total eosinophils</td>
<td>$13.8 \times 10^4$</td>
<td>$0.6 \times 10^4$</td>
<td></td>
</tr>
<tr>
<td>Total neutrophils</td>
<td>$424 \times 10^4$</td>
<td>$72 \times 10^4$</td>
<td></td>
</tr>
<tr>
<td>Absent ciliary motion on bronchial epithelial cells</td>
<td>21%</td>
<td>9%</td>
<td>p&lt;0.05</td>
</tr>
</tbody>
</table>

## Peripheral Blood Samples

<table>
<thead>
<tr>
<th>Feature</th>
<th>Rhinovirus +</th>
<th>Rhinovirus -</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>hs-CRP (mg/dL)</td>
<td>0.50</td>
<td>0.20</td>
<td>p&lt;0.05</td>
</tr>
<tr>
<td>Absolute neutrophil count (cells/ul)</td>
<td>2980</td>
<td>2470</td>
<td>NS</td>
</tr>
<tr>
<td>Absolute eosinophil count (cells/ul)</td>
<td>240</td>
<td>200</td>
<td>NS</td>
</tr>
<tr>
<td>IgE (IU/ml)</td>
<td>21</td>
<td>30</td>
<td>NS</td>
</tr>
</tbody>
</table>
**BAL Cytokines**

**Type 1 Inflammation**

- IFNγ
- CXCL-11
- TNFα
- LT

Uninfected vs HRV+ comparison for each cytokine with significance marked as *p<0.05*

**BAL Cytokines**

**Type 2 Inflammation**

- IL-4
- IL-5
- IL-13
- TSLP

Uninfected vs HRV+ comparison for each cytokine with significance marked as *p<0.05*
Thymic Stromal Lymphopoietin (TSLP)

- IL-7 like cytokine
- Promotes T2 inflammatory response
- Expressed by epithelial cells of skin, gut, and lungs
- Increased expression by keratinocytes in atopic dermatitis skin lesions and airway epithelial cells in asthma


BAL Cytokines

Type 3 Inflammation

![Graph showing IL-17a and IL-17c cytokine levels in infected and uninfected conditions.](image)
Summary

- In asymptomatic children with history of severe wheeze, rhinovirus transcript in the lung is highly prevalent (40% of cohort)

- Is rhinovirus an indolent infection or active infection?
  - Viruses vs bacteria
  - Inflammatory markers
  - Antiviral response

- In preschool children with severe wheeze/cough, the presence of rhinovirus transcripts in the lung fluid is associated with
  - mixed eosinophilic/neutrophilic bronchoalveolitis
  - Increased airway eosinophils
  - Ciliary dysfunction
  - Elevated blood hs-CRP
  - T1/T2/T3 cytokine response

- Rhinovirus transcripts in the lung fluid is NOT associated with
  - Increased IgE
  - Allergic sensitization
  - Serum eosinophilia
Future Studies

- One patient with +rhinovirus transcript and significantly higher Th2 cytokines (IL-4, IL-5, and IL-13)
  - Indicator for development of asthma?
  - Long-term follow-up
  - Increased study enrollment

Clinical Implications

- Increased BAL eosinophils and T2 cytokines, even in the absence of higher blood eosinophils or IgE, may identify those children at greater risk of persistent wheeze at school-age
OBESITY ALTERS PULMONARY MACROPHAGE LIPID METABOLISM AND FUNCTION DURING ASTHMA

ACAAI Annual Meeting
New Orleans, LA
November 7, 2021

Sam McCright
MD/PhD Candidate
Perelman School of Medicine at the University of Pennsylvania
Hill Lab - Supported by ACAAI Junior Faculty Grant
Division of Allergy and Immunology
Children’s Hospital of Philadelphia

OBESITY-ASSOCIATED ASTHMA (OAA) IS A DISTINCT ASTHMA ENDOTYPE THAT IS MORE SEVERE AND MORE DIFFICULT TO TREAT THAN ATOPIC ASTHMA

<table>
<thead>
<tr>
<th>Atopic asthma</th>
<th>OAA</th>
<th>Gap in knowledge</th>
</tr>
</thead>
<tbody>
<tr>
<td>T&lt;sub&gt;H&lt;/sub&gt;1 / 2 / 17?</td>
<td>T&lt;sub&gt;H&lt;/sub&gt;2 predominant</td>
<td>- T&lt;sub&gt;H&lt;/sub&gt;1 and T&lt;sub&gt;H&lt;/sub&gt;17 predominant</td>
</tr>
<tr>
<td>Cytokines?</td>
<td>Associated with allergy, IgE, IL-4, IL-5, IL-13</td>
<td>- Associated with increased CXCL1, CXCL2, TNFα, IL-1β,</td>
</tr>
<tr>
<td>Cell types?</td>
<td>Eosinophilic lung inflammation</td>
<td>- Neutrophilic lung inflammation</td>
</tr>
<tr>
<td>Treatment?</td>
<td>Responsive to corticosteroids and type 2-targeted biologic therapies</td>
<td>- Refractory to treatment with corticosteroids and type 2-targeted biologics</td>
</tr>
</tbody>
</table>

The immune mechanisms that cause OAA are not well understood.
LUNG MACROPHAGES AND OBESITY-ASSOCIATED MACROPHAGE ACTIVATION

- The innate immune response to allergic insults in the lung is shaped by lung macrophage abundance and activation state.

1. Monocyte-derived **interstitial macrophages** (IM) --> Promote type 1 inflammation
2. Self-renewing **alveolar macrophages** (AM) -------> Promote type 2 inflammation

- Metabolic stress leads to the development of pro-inflammatory tissue macrophages with unique functions involving lipid uptake and metabolism.

Lipid associated macrophages (LAMs)
- **Markers:** CD9+, intracellular lipid
- **Genes:** Trem2, Lpl, Lipa, Plin2
- **Cytokines:** CXCL1/2, TNFα, IL-1β

**Gap in knowledge**
**Effects of obesity on lung macrophage activation in the steady state, and their response to allergic stimuli, are unknown**

**HYPOTHESIS:**

Obesity alters lung macrophage cellular metabolism and inflammatory priming in the steady state, which results in a shift towards neutrophil-predominant response to an allergic stimulus.

**Questions:**

1) Do lung macrophages demonstrate features of obesity-associated macrophage activation?

2) What can we learn from model obesity-associated innate allergic lung inflammation in mice?
**IN OBESITY, CD9+ LUNG IM EXPAND AND ACCUMULATE INTRACELLULAR LIPID**

- **Cell counts**
  - CD9+ IM vs Total IM
  - n = 4 / group, data representative of 3+ independent experiments, presented as mean +/- SEM. Significance by unpaired t test, * = p < 0.05, ** = p < 0.01

- **Lipid quantification**
  - CD9+ IM vs Total IM
  - No differences seen in: neutrophils, eosinophils, alveolar mac, monocytes

Analysis of whole, perfused lung

**OBESITY INCREASES EXPRESSION OF GENES ASSOCIATED WITH LIPID METABOLISM IN LUNG MACROPHAGES**

- **Gene expression**
  - **Trem2**, **Lpl**, **Lipa**, **Plin2**

qPCR of CD64+ cells (IM, AM, monocytes) from lean and obese lung
n = 3 / group, data represent a single experiment, presented as mean +/- SEM. Significance by unpaired t test, * = p < 0.05, ** = p < 0.01
**HYPOTHESIS:**

Obesity alters lung macrophage cellular metabolism and inflammatory priming in the steady state, which results in a shift towards neutrophil-predominant response to an allergic stimulus.

Questions:

1) Do lung macrophages demonstrate features of obesity-associated macrophage activation? **Yes**

2) What can we learn from model obesity-associated innate allergic lung inflammation in mice?

**DEVELOPMENT OF A MURINE MODEL OF OBESITY-ASSOCIATED AIRWAY INFLAMMATION**

![Diagram of the Obesity-associated asthma model](chart)

- **CFD or HFD**
- **Weeks:** 6, 18, 21
- **D0, 1, 2:** sensitization
  - HDM + LPS intranasal
- **D14, 15, 18, 19:** challenge
  - HDM + LPS 25% dose
- **Analysis:** Flow cytometry
- **qPCR of tissue and immune cells**
TREATMENT WITH HDM + LPS INCREASES CD9+ LUNG IMMUNE CELL NUMBERS AND INTRACELLULAR LIPID CONTENT

HDM + LPS TREATMENT INCREASES EXPRESSION OF CYTOKINE GENES ASSOCIATED WITH OAA IN LUNG IMMUNE CELLS
OBESITY WORSENS LUNG NEUTROPHILIA AFTER TREATMENT WITH HDM + LPS

Gene expression

PMN – CXCR2

PMN : Eos

Questions:

1) Do lung macrophages demonstrate features of obesity-associated macrophage activation?
   - In obesity, lung IM express CD9, accumulate intracellular lipid, and express gene programs observed in obesity-associated macrophage activation

2) What can we learn from model obesity-associated innate allergic lung inflammation in mice?
   - Combined HDM + LPS treatment induces neutrophil-predominant lung inflammation which is exacerbated in obese mice, which may occur via CXCR2 signaling
MODEL AND FUTURE DIRECTIONS

**Obesity**

- Obesity-associated macrophage activation

**Neutrophil-predominant lung inflammation**

1) **What signals?**
   - Metabolomics
   - Transcriptomics
   - Cytokine analysis

2) **What mechanisms?**
   - Genetic knockouts / pharmacologic inhibition of metabolic enzymes and immune mediators
   - Pulmonary function tests / histology

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- Thalia Mangan

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- Maggie Krall

**CHOP Division of Allergy and Immunology:**
- Kate Sullivan, MD, PhD

**Model figures: BioRender.com**
mRNA COVID-19 Vaccine Adverse Events Following Immunization: Should You Recommend the Second Dose?

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Jay R. Montgomery, MD²,

¹Department of Allergy, Asthma & Immunology, Walter Reed National Military Medical Center, Bethesda, MD
²Defense Health Agency Immunization Healthcare Division, Walter Reed National Military Medical Center Bethesda, MD

Disclaimer

The views expressed in this presentation are those of the authors and do not necessarily reflect the official policy of the Department of Defense or the U.S. Government.
Introduction

- Global COVID-19 pandemic was declared on March 11th, 2020
- In December 2020 two mRNA COVID-19 vaccines were granted emergency use authorization\(^1,2\)
- Adverse Events Following Immunization (AEFI) have occurred following receipt of both of these vaccines
- Anaphylaxis to mRNA COVID-19 vaccine is estimated to occur at a rate of 2.5 to 11 cases per 1 million doses\(^3\)
- AEFI can lead to vaccine hesitancy, decreased confidence in the vaccine, and resurgence of the disease\(^4\)

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Objective

Describe the evaluation and outcome of patients referred to an allergy/immunology clinic for adverse events following COVID-19 mRNA vaccine


Methods

• Retrospective observational study

• AEFI to either mRNA COVID-19 vaccine

• Patients referred to Walter Reed National Military Medical Center Allergy & Immunology clinic and the Defense Health Agency’s Immunization Healthcare Division

• Study period was from December 30th, 2020 to June 15th, 2021

• Cases were identified through a search of the medical record

• Data obtained for each patient included: age, sex, vaccine administered, first or second dose reaction, symptoms, skin testing, and vaccine challenge results

• Anaphylaxis criteria from the Adverse Reactions to Vaccines Practice Parameters 2012 update

• Patients AEFI were categorized into early vs late reactions (0-24 hours and >24 hours)

• Skin testing was performed in select patients

• Vaccine challenges were performed at full dose

• Location and observation period was dependent upon initial reaction severity

• Premedication was not used in all cases

• IRB protocol number: WRNMMC-EDO-2021-0677

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Methods

Probable anaphylaxis:5
- Reaction occurring within 4 hours of vaccine administration to include signs and/or symptoms from more than 1 of the following systems:
  - Dermatologic
  - Respiratory
  - Cardiovascular
  - Gastrointestinal

Possible anaphylaxis:
- Signs and/or symptoms from only 1 system (as above)
- Signs and/or symptoms from more than 1 system (as above) but occurring more than 4 hours after vaccination


Methods

- Skin testing was performed on selected patients using this protocol as a guide6
- Skin testing to the vaccine was also performed in select patients

### Results

**Characteristics**

<table>
<thead>
<tr>
<th>Description</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cases (total)</td>
<td>25</td>
</tr>
<tr>
<td>Female (%)</td>
<td>18 (75)</td>
</tr>
<tr>
<td>Average age (range)</td>
<td>46 (18-77)</td>
</tr>
<tr>
<td>mRNA - Moderna (%)</td>
<td>10 (40)</td>
</tr>
<tr>
<td>- Pfizer (%)</td>
<td>15 (60)</td>
</tr>
<tr>
<td>AEFI dose - First dose (%)</td>
<td>23 (92)</td>
</tr>
</tbody>
</table>

**Early Reaction (0-24 hours)**

- Probable anaphylaxis (4)
- Possible anaphylaxis (12)

**Late reaction (>24 hours)**

- Non-urticarial rash (4)
- Acute transverse myelitis (1)

**Referred for AEFI evaluation (25)**

- Mild or known side effects (4)
- Unexpected adverse side effects (21)
Results

Referred for AEFI evaluation (25) → Mild or known side effects (4) → Negative challenge (4)

Results

Early Reaction (0-24 hours)

Probable anaphylaxis (4)

Skin testing (2) → Negative skin test (2) → Not challenged (2)

Possible anaphylaxis (12)

No skin testing (2) → Negative challenge (1) → Not challenged (1)
Results

Early Reaction (0-24 hours)

Probable anaphylaxis (4)

Possible anaphylaxis (12)

Skin testing (4)

No skin testing (8)

Negative skin test (4)

Negative challenge (4)

Not challenged (4)

Negative challenge (4)

Late reaction (>24 hours)

Non-urticarial rash (4)

Acute transverse myelitis (1)

Negative challenge (3)

Not challenged (1)

Not challenged (1)
Results

- 2 patients were advised against receiving the 2nd dose
  - Probable anaphylaxis during the early stages
  - Possible anaphylaxis complicated by history of seizures
- 6 patients declined 2nd dose or were advised to wait until resolution of symptoms
- 2 patient had an adverse reaction following the 2nd dose

Discussion

- Allergy to one of the vaccine components or an allergic reaction to the first dose are the only contraindications to receiving the second dose
- Several retrospective studies have demonstrated 2nd dose tolerance after anaphylaxis to the first dose[^8][^9][^10]
- This highlights that first dose anaphylaxis does not always mean they are allergic, or will have anaphylaxis to second dose
- Perhaps anaphylaxis to the first dose should no longer be a contraindication to the second dose

Discussion

• Risk stratification algorithms have been proposed to help guide providers\(^6\)

• The mechanism of these reactions remains unclear and in most cases is not likely IgE-mediated

• The NIH is conducting a randomized, placebo-controlled crossover study to assess safety of second dose administration of the mRNA COVID-19 vaccines

• Consider administering a different COVID-19 vaccine in patients with allergy to vaccine component or severe anaphylactic reaction to the mRNA vaccine

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Discussion

• Various cutaneous reactions have been reported to include local injection site reactions as well as distant cutaneous eruptions

• The majority of patients with first dose cutaneous reactions did not experience recurrence after the second dose

• These cutaneous reactions are generally minor and self-limited\(^1\)

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Conclusions

• All of the patients with first dose reaction, who agreed to second dose, tolerated vaccine challenge with either no or minimal side effects

• Skin testing may be of limited utility in mRNA vaccine allergy evaluation

• The majority of patients who did not receive the second dose were offered, but declined

• Allergists play a crucial role in the evaluation and management of these patients

• This type of research may help guide patients and doctors to offer second dose

• Further research is needed to better understand AEFI to ensure safe and effective vaccination programs, as well as improve public trust in vaccines

References


Patch Testing Results in Adult Patients with Dermatitis during the COVID-19 Pandemic

Stephanie Kong, DO, Shahidul Islam, DrPH, MPH, Stephanie L. Mawhirt, DO
NYU Langone Hospital—Long Island
ACAAI Oral Concurrent Sessions: November 7, 2021

Disclosure

• None
Introduction

• Allergic contact dermatitis (ACD) occurs in the general population at a prevalence of approximately 17-24%. [1]

• Prevalence of ACD due to common allergens [1-7]:
  – nickel (11.4%)
  – formaldehyde (7%)
  – para-phenylenediamine (PPD) (6.2%)
  – textile dye mix (TDM) (3.6%)
  – glutaraldehyde (3.6%)
  – fragrance mix (FM) (3.5%)
  – propylene glycol (0.8-3.5%)
  – disperse blue (0.7-16.7%)

Allergic contact dermatitis among health care workers

• Prevalence of ACD among healthcare workers (HCWs) is up to 63%. [8]

• Facial ACD incidence [8]:
  – female HCW (17%)
  – male HCW (21%)

• ACD related to facial masks is a COVID-19 pandemic emerging issue. [9-10,18-20]
  – Formaldehyde, elastic/rubber accelerators (thiuram), polyurethane (diisocyanates), textile dye

• Glutaraldehyde and formaldehyde detected in N95, surgical masks, other PPE. [11-12, 20]

• Increased exposure to contact allergens may lead to new sensitization.
Methods

• IRB-approved, retrospective review

• Patients with suspected ACD evaluated with NACD panel patch testing (PT) before and during the COVID-19 pandemic.
  – Pre-COVID-19: January 2018 – February 2020
  – COVID-19 pandemic: March 2020 – March 2021

• Inclusion criteria: Adult patients (age >18 years) who underwent PT for the evaluation of suspected ACD during the time period of January 2018 through March 2021.

• Exclusion criteria: children/vulnerable populations, metal PT

Methods

• Data gathered included:
  – Demographics (age, sex, occupation (HCW))
  – Atopic dermatitis history
  – Dermatitis characteristics (location, duration, features)
  – PT results (any positive allergens)

• At least 2 separate PT readings were performed (48 hours and 72 or 96 hours)

• PT reading was graded using the International Contact Dermatitis Research Group’s system. [13,14]
Methods

- Statistical analyses were performed using the Chi-Square or Fisher's exact tests.
- Results with $p<0.05$ were considered statistically significant.

### Results: patient demographics

- **Total 99 patients who underwent PT for suspected ACD identified:**
  - **Pre-COVID: n=65**
  - **COVID-pandemic: n=34**
  - **Median age: 49 years (IQR: 37—59 years)**
  - **91% women**
  - **21% HCW**
  - **14% atopic dermatitis**

<table>
<thead>
<tr>
<th></th>
<th>Pre-COVID (n=65)</th>
<th>COVID-pandemic (n=34)</th>
<th>All patients (n=99)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years; median/IQR)</td>
<td>50 (35—60)</td>
<td>47 (41—59)</td>
<td>49 (37—59)</td>
<td>NS</td>
</tr>
<tr>
<td>Sex: female</td>
<td>58 (89%)</td>
<td>32 (94%)</td>
<td>90 (91%)</td>
<td>0.72</td>
</tr>
<tr>
<td>Occupation: HCW</td>
<td>14 (22%)</td>
<td>7 (21%)</td>
<td>21 (21%)</td>
<td>0.91</td>
</tr>
<tr>
<td>Atopic dermatitis</td>
<td>7 (11%)</td>
<td>7 (20%)</td>
<td>14 (14%)</td>
<td>0.228</td>
</tr>
</tbody>
</table>
# Results: dermatitis clinical characteristics

<table>
<thead>
<tr>
<th>Location of dermatitis</th>
<th>Pre-COVID (n=65)</th>
<th>COVID-pandemic (n=34)</th>
<th>All patients (n=99)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Facial</td>
<td>35 (54%)</td>
<td>23 (68%)</td>
<td>58 (59%)</td>
<td>0.186</td>
</tr>
<tr>
<td>Extremities</td>
<td>20 (31%)</td>
<td>8 (24%)</td>
<td>28 (28%)</td>
<td>0.448</td>
</tr>
<tr>
<td>Trunk</td>
<td>10 (15%)</td>
<td>9 (27%)</td>
<td>19 (19%)</td>
<td>0.184</td>
</tr>
<tr>
<td>Generalized</td>
<td>12 (19%)</td>
<td>5 (15%)</td>
<td>17 (17%)</td>
<td>0.638</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Duration of dermatitis</th>
<th>Pre-COVID (n=65)</th>
<th>COVID-pandemic (n=34)</th>
<th>All patients (n=99)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;3 months</td>
<td>11 (17%)</td>
<td>5 (15%)</td>
<td>16 (16%)</td>
<td>0.776</td>
</tr>
<tr>
<td>3-6 months</td>
<td>7 (11%)</td>
<td>4 (12%)</td>
<td>11 (11%)</td>
<td>1.00</td>
</tr>
<tr>
<td>&gt;6 months</td>
<td>23 (35%)</td>
<td>8 (24%)</td>
<td>31 (31%)</td>
<td>0.227</td>
</tr>
<tr>
<td>Unknown</td>
<td>24 (37%)</td>
<td>17 (50%)</td>
<td>41 (41%)</td>
<td>NS</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Features</th>
<th>Pre-COVID (n=65)</th>
<th>COVID-pandemic (n=34)</th>
<th>All patients (n=99)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pruritus</td>
<td>38 (59%)</td>
<td>25 (74%)</td>
<td>63 (64%)</td>
<td>0.139</td>
</tr>
<tr>
<td>Erythema</td>
<td>19 (29%)</td>
<td>14 (41%)</td>
<td>33 (33%)</td>
<td>0.231</td>
</tr>
<tr>
<td>Vesicular</td>
<td>0 (0%)</td>
<td>3 (9%)</td>
<td>3 (3%)</td>
<td>0.038</td>
</tr>
</tbody>
</table>

# Results: patch testing

<table>
<thead>
<tr>
<th>Positive Patch Test (to any allergen)</th>
<th>Pre-COVID (n=65)</th>
<th>COVID-pandemic (n=34)</th>
<th>Overall (n=99)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>35 (54%)</td>
<td>30 (88%)</td>
<td>65 (66%)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Specific allergens</th>
<th>Pre-COVID (n=65)</th>
<th>COVID-pandemic (n=34)</th>
<th>Overall (n=99)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fragrance mix (FM)</td>
<td>6 (9%)</td>
<td>11 (32%)</td>
<td>17 (17%)</td>
<td>0.004</td>
</tr>
<tr>
<td>Disperse blue</td>
<td>5 (8%)</td>
<td>5 (15%)</td>
<td>10 (10%)</td>
<td>0.305</td>
</tr>
<tr>
<td>Textile dye mix (TDM)</td>
<td>3 (5%)</td>
<td>6 (18%)</td>
<td>9 (9%)</td>
<td>0.06</td>
</tr>
<tr>
<td>Formaldehyde</td>
<td>3 (5%)</td>
<td>6 (18%)</td>
<td>9 (9%)</td>
<td>0.06</td>
</tr>
<tr>
<td>Glutaraldehyde</td>
<td>2 (3%)</td>
<td>6 (18%)</td>
<td>8 (8%)</td>
<td>0.019</td>
</tr>
<tr>
<td>p-Phenylenediamine (PPD)</td>
<td>4 (6%)</td>
<td>0 (0%)</td>
<td>4 (4%)</td>
<td>0.296</td>
</tr>
<tr>
<td>Propylene glycol</td>
<td>2 (3%)</td>
<td>1 (3%)</td>
<td>3 (3%)</td>
<td>1.00</td>
</tr>
</tbody>
</table>
# Results: sub-analysis of facial ACD

<table>
<thead>
<tr>
<th></th>
<th>Pre-COVID (n=35)</th>
<th>COVID-pandemic (n=23)</th>
<th>Overall (n=58)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age (median; years)</strong></td>
<td>47</td>
<td>49</td>
<td>48</td>
<td>NS</td>
</tr>
<tr>
<td><strong>Sex (female)</strong></td>
<td>33 (94%)</td>
<td>23 (100%)</td>
<td>56 (97%)</td>
<td>NS</td>
</tr>
<tr>
<td><strong>HCW</strong></td>
<td>8 (23%)</td>
<td>6 (26%)</td>
<td>14 (24%)</td>
<td>NS</td>
</tr>
<tr>
<td><strong>Atopic dermatitis</strong></td>
<td>1 (3%)</td>
<td>5 (22%)</td>
<td>6 (10%)</td>
<td>0.032</td>
</tr>
<tr>
<td><strong>Duration of dermatitis</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;3 months</td>
<td>8 (23%)</td>
<td>4 (17%)</td>
<td>12 (21%)</td>
<td>NS</td>
</tr>
<tr>
<td>3-6 months</td>
<td>5 (14%)</td>
<td>3 (13%)</td>
<td>8 (14%)</td>
<td>NS</td>
</tr>
<tr>
<td>&gt;6 months</td>
<td>10 (29%)</td>
<td>6 (26%)</td>
<td>16 (28%)</td>
<td>NS</td>
</tr>
<tr>
<td>Unknown</td>
<td>12 (34%)</td>
<td>10 (43%)</td>
<td>22 (38%)</td>
<td>NS</td>
</tr>
<tr>
<td><strong>Features</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pruritus</td>
<td>17 (49%)</td>
<td>15 (65%)</td>
<td>32 (55%)</td>
<td>NS</td>
</tr>
<tr>
<td>Erythema</td>
<td>12 (34%)</td>
<td>10 (44%)</td>
<td>22 (38%)</td>
<td>NS</td>
</tr>
<tr>
<td>Vesicular</td>
<td>0 (0%)</td>
<td>2 (9%)</td>
<td>2 (3%)</td>
<td>NS</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>Pre-COVID (n=35)</th>
<th>COVID-pandemic (n=23)</th>
<th>Overall (n=58)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Positive Patch Test (to any allergen)</strong></td>
<td>19 (54%)</td>
<td>21 (91%)</td>
<td>40 (69%)</td>
<td>0.004</td>
</tr>
<tr>
<td><strong>Specific allergens</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fragrance mix (FM)</td>
<td>4 (11%)</td>
<td>9 (39%)</td>
<td>13 (22%)</td>
<td>0.023</td>
</tr>
<tr>
<td>Formaldehyde</td>
<td>2 (6%)</td>
<td>5 (22%)</td>
<td>7 (12%)</td>
<td>0.102</td>
</tr>
<tr>
<td>Glutaraldehyde</td>
<td>2 (6%)</td>
<td>4 (17%)</td>
<td>6 (10%)</td>
<td>0.202</td>
</tr>
<tr>
<td>Textile dye mix (TDM)</td>
<td>0 (0%)</td>
<td>3 (13%)</td>
<td>3 (5%)</td>
<td>0.057</td>
</tr>
<tr>
<td>Disperse blue</td>
<td>2 (6%)</td>
<td>1 (4%)</td>
<td>3 (5%)</td>
<td>1.00</td>
</tr>
<tr>
<td>p-Phenylenediamine (PPD)</td>
<td>2 (6%)</td>
<td>0 (0%)</td>
<td>2 (3%)</td>
<td>0.513</td>
</tr>
<tr>
<td>Propylene glycol</td>
<td>1 (3%)</td>
<td>1 (4%)</td>
<td>2 (3%)</td>
<td>1.00</td>
</tr>
</tbody>
</table>
Results: sub-analysis of HCW

- No differences detected in positive PT allergens in HCW (n=21) in the pre-COVID and COVID-pandemic groups.

Discussion

- Positive PT to glutaraldehyde and FM were detected at significantly higher rates among any dermatitis in the COVID-pandemic compared to the pre-COVID group.
  - Fragrance mix: 32% v. 9%, p=0.004
  - Glutaraldehyde: 18% v. 3%, p=0.019

- Positive PT to FM was detected at a significantly higher rate in the COVID-pandemic group for those with facial dermatitis.
  - Fragrance mix: 39% v. 11%, p=0.023
  - Individuals in the COVID-19 pandemic group more commonly had atopic dermatitis.

- Other allergens detected at comparatively high rates in the COVID-pandemic group:
  - Any dermatitis: TDM (18%), Formaldehyde (18%), Disperse blue (15%)
  - Facial dermatitis: Formaldehyde (22%), Glutaraldehyde (17%), TDM (13%)
Study limitations

• Small sample size
  – Unable to perform sub-analysis on other dermatitis locations (i.e. extremities, trunk)
• Retrospective nature
• Documentation of PPE exposure not sufficient in most cases

Conclusions

• Glutaraldehyde and fragrance mix represent potentially relevant contact allergens in patients with ACD during the COVID-19 pandemic.
  – Glutaraldehyde is present in disinfectants. [15]
    • Used in sterilization of some facial PPE. [11]
  – Fragrance is present in personal products, cleaning products. [16]

• Other allergens of interest include textile dye mix and formaldehyde. [20]
  – Textile dyes are used in surgical masks. [17]
  – Formaldehyde is released from textile processing in PPE. [12]

• Providers should consider these contact allergens in the evaluation of new onset dermatitis during the COVID-19 pandemic.
References


14. International Contact Dermatitis Research Group

15. Occupational Safety and Health Administration, Best Practices for the Safe Use of Glutaraldehyde in Health Care


17. flavorful Ink, Inc., FLTR76 FaceMask with Crossflow Non-Return Valve Cleaning, Sterilization/Distribution & Maintenance


Acknowledgement

- American College of Asthma, Allergy and Immunology
- ACAAI Meeting Abstract Committee
Thank You

Stephanie.Kong@nyulangone.org