

Inhalation exposure to transition metals can facilitate sensitization to an innocuous protein antigen

Fraleigh NL, S Lefebvre, S Khurana, B Ross and SA Ritz

# Inhalation Tolerance

- Respiratory tract is exposed to various antigens
- Inhalation tolerance results in the active suppression of responses towards harmless antigens
- ~15% of the industrialized world has an allergy

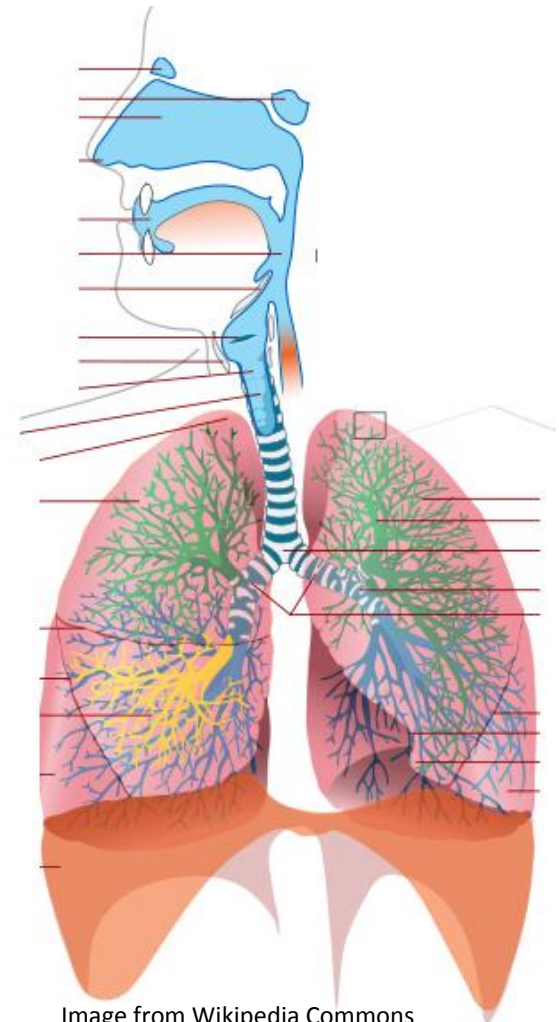
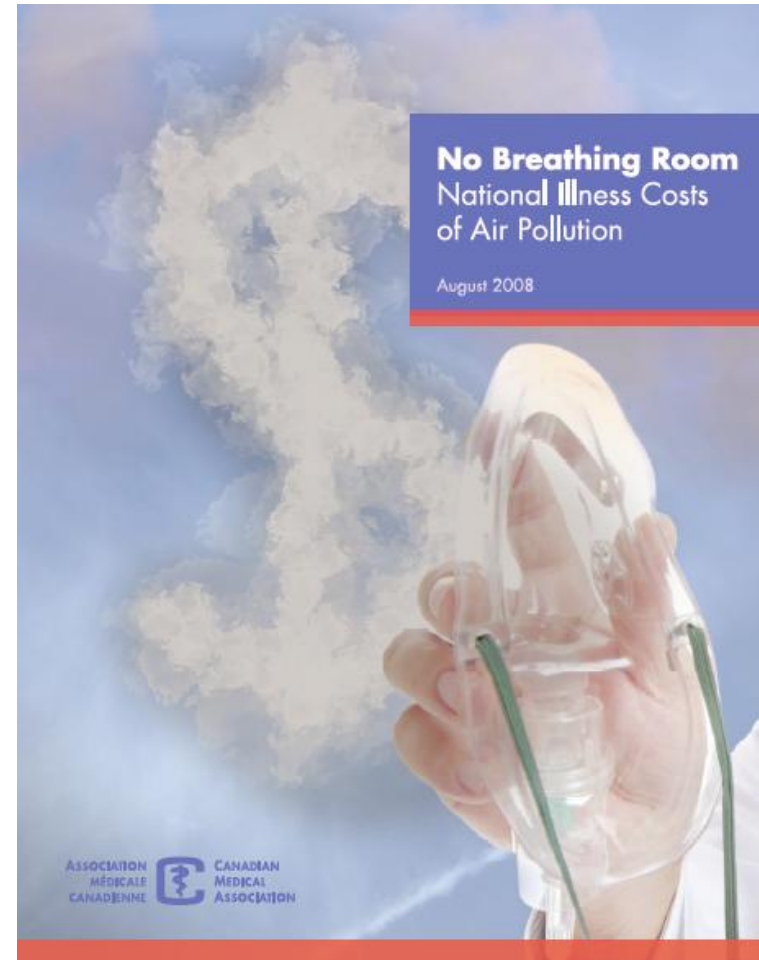


Image from Wikipedia Commons

# Health and Economic Effects

- In 2008, air pollution is estimated to be responsible for:
  - ~21 000 premature deaths
  - ~11 000 hospital admissions
  - ~92 000 ER visits
  - ~620 000 MD visits
  - ~\$8B in economic costs





# Particulate Matter

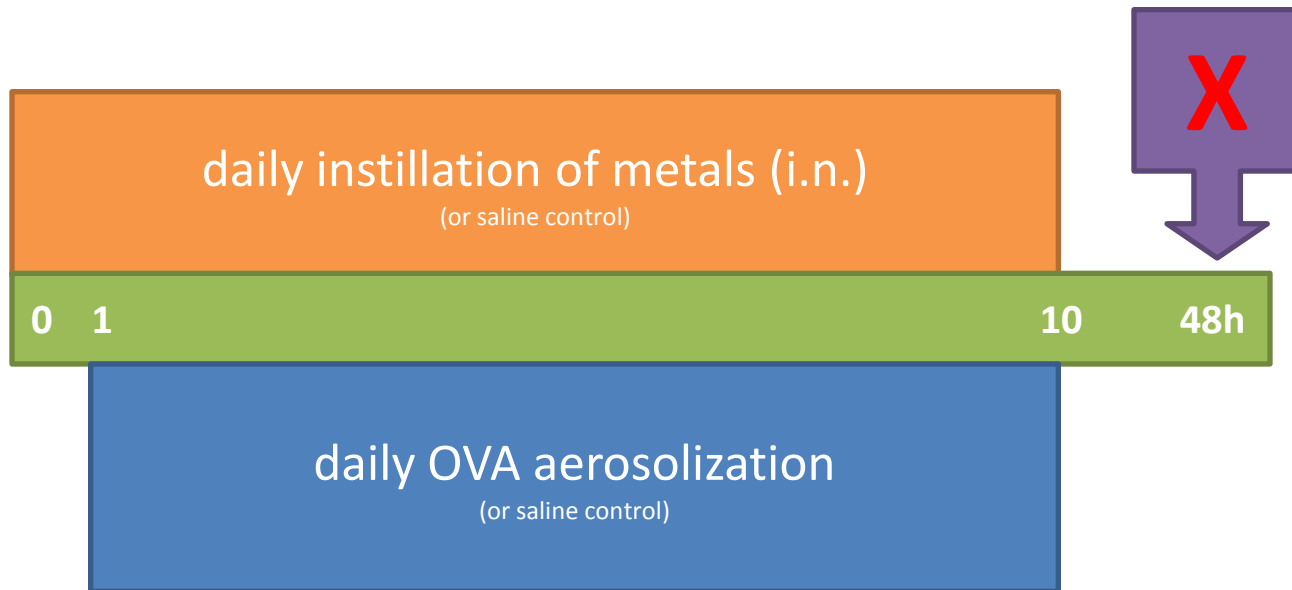
- Particulate matter is the solid portion of air pollution
- Exacerbates cardiovascular and respiratory disease in those at risk and causes inflammation
- Dependent upon local environment
- Sudbury Particulate Matter contains nickel
  - Nickel induces inflammation and the production of reactive oxygen species



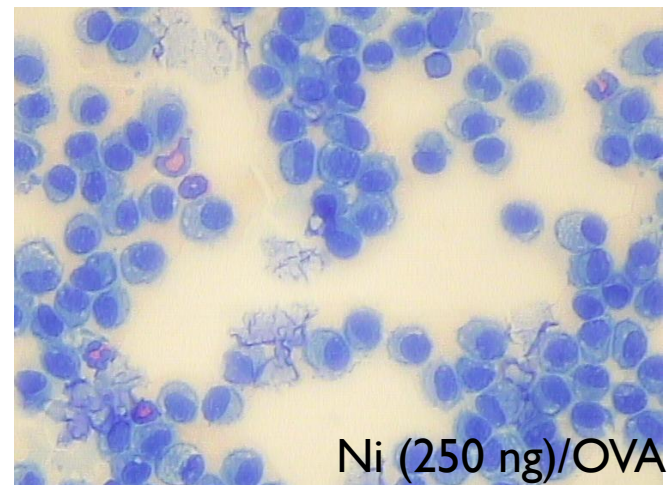
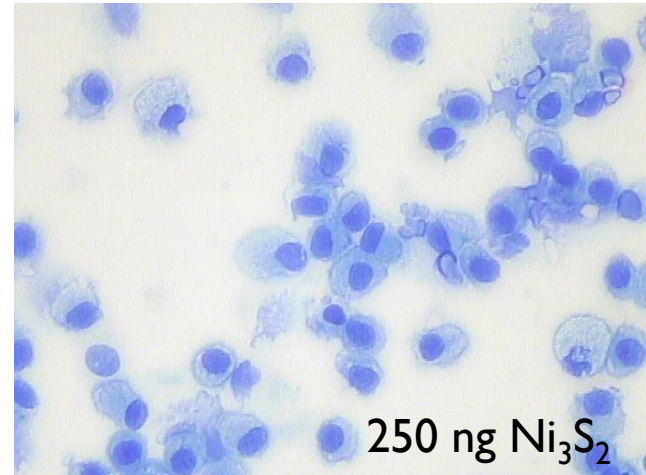
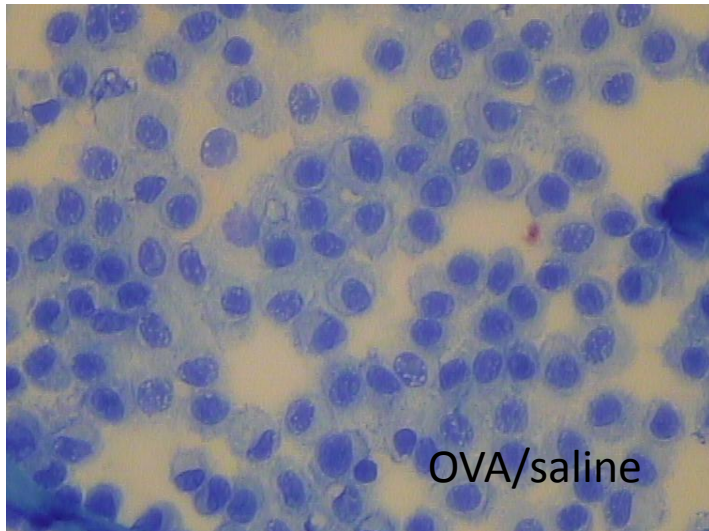
# Study Rationale

- Nickel may be able to act as an adjuvant and induce allergic sensitization
- Mice will be exposed to a harmless antigen (OVA) with or without  $\text{Ni}_3\text{S}_2$ , and inflammatory and immune responses assessed
  - Hallmarks of allergic responses: eosinophilia, IgE, Th2 cytokines

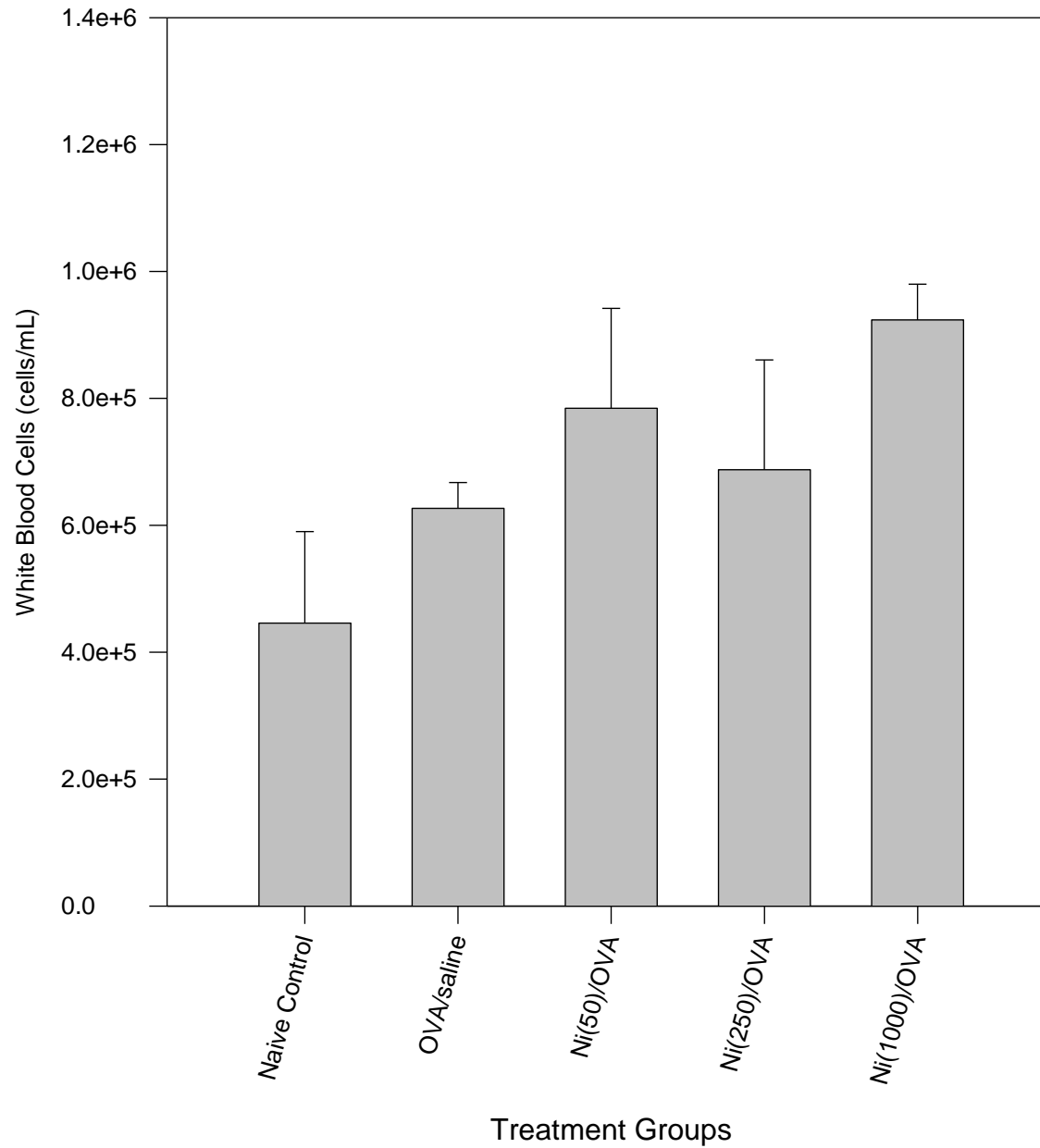
# Methodology



# Airway Inflammation

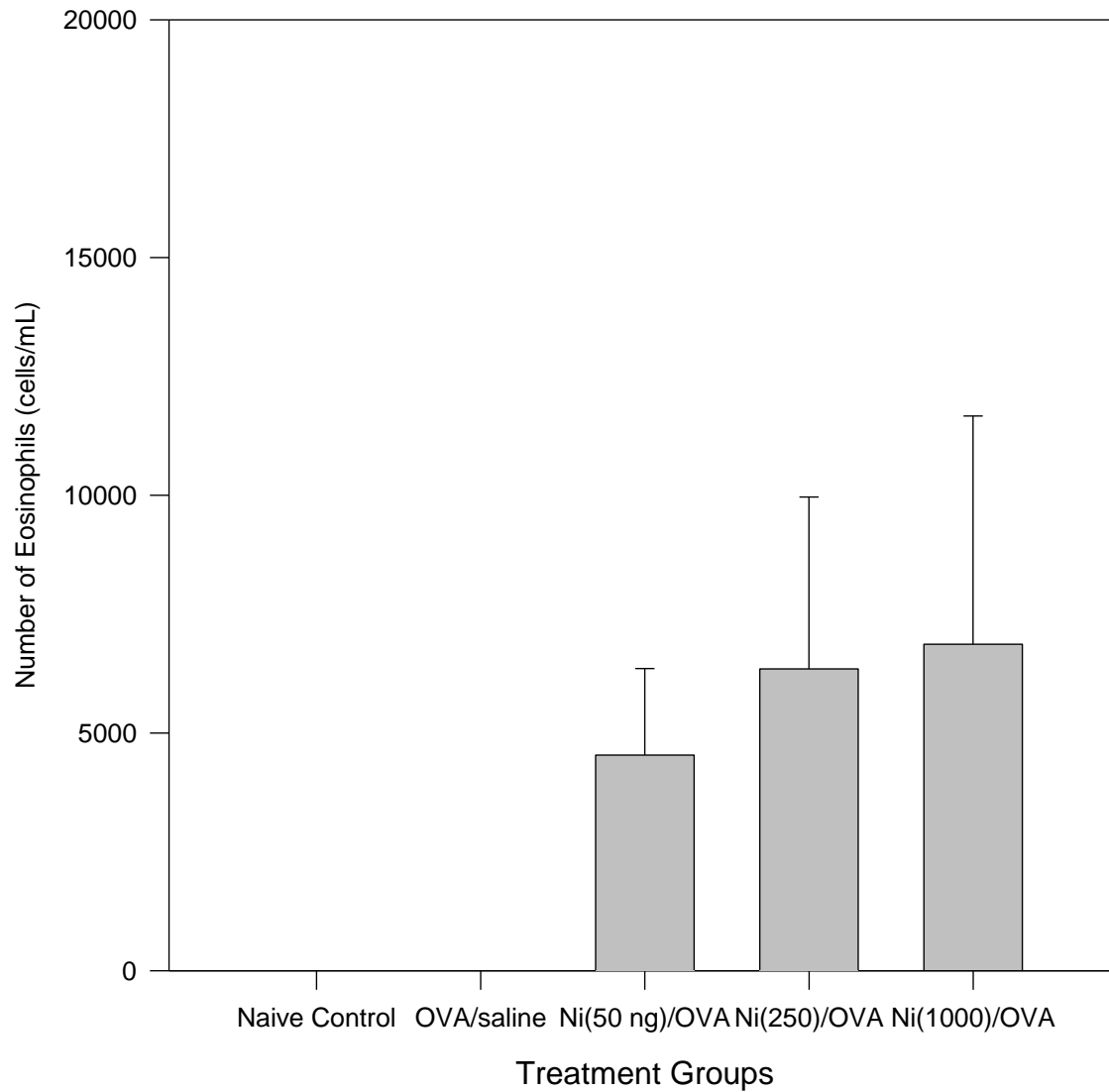


# Total Number of WBC in BAL of Acutely Treated Balb/c Mice

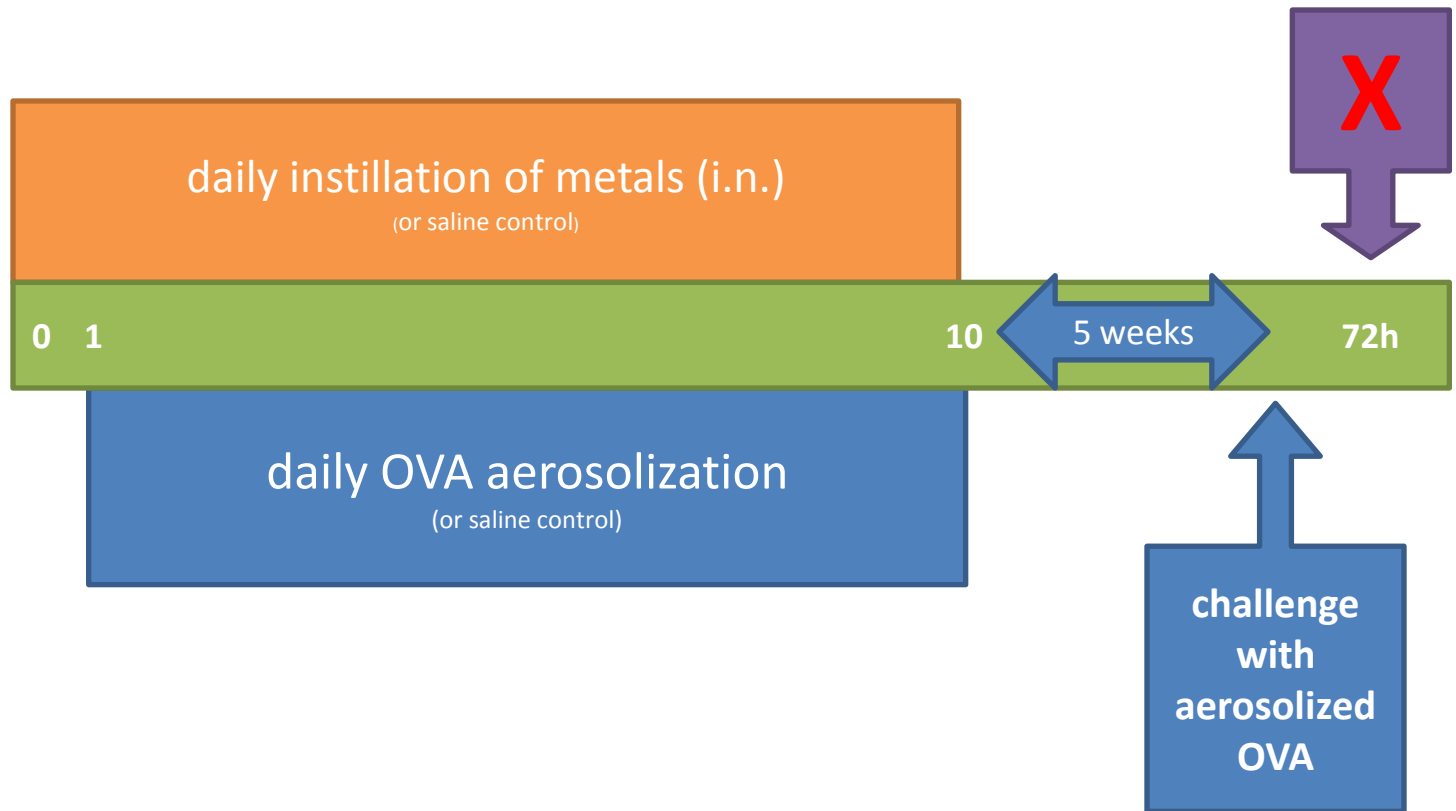




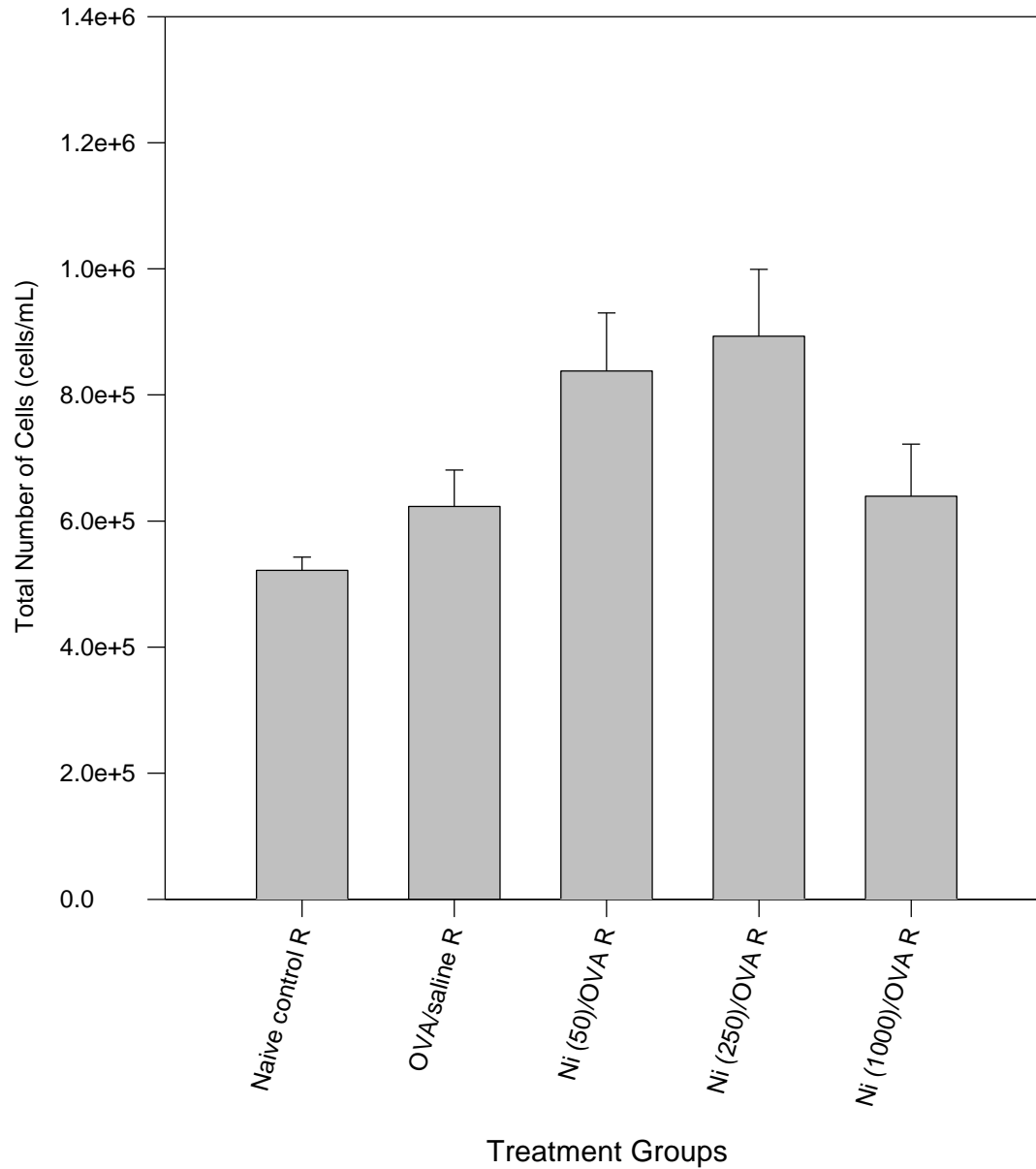
# Total Number of Eosinophils in Acutely Treated Balb/c Mice



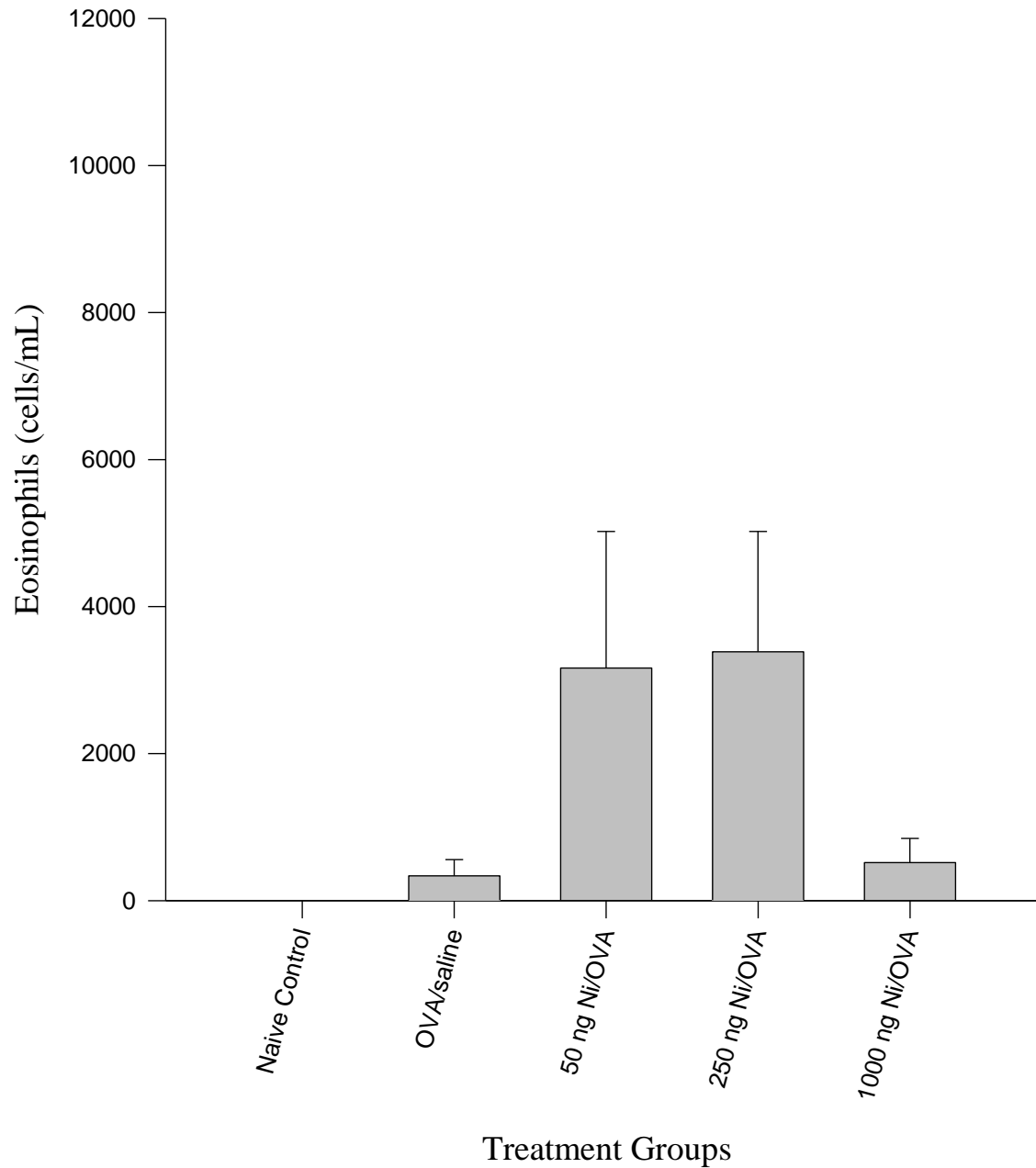
# Methodology



# Total Number of Cells in BAL of Rechallenged Balb/c Mice



# Number of Eosinophils in BAL of Rechallenged Balb/c Mice





- Histological processing of lungs
- OVA-specific Immunoglobulin ELISA
- Repeat the experiment with a dose reflecting the results obtained from the pilot study



# Take Home Message

- Nickel is able to induce an inflammatory response leading to increased levels of inflammation
- Groups that were treated with low doses of Ni and rechallenged with OVA had increased levels of eosinophilia
- Low doses of Ni may act as an adjuvant and elicit allergic sensitization to another antigen

# Acknowledgements

- I would like to thank the members of Team Ritz for all of their help and support
  - Dr. Stacey Ritz
  - Sandhya Khurana
  - Sebastien Lefebvre
  - Sarah White
- Manel Jordana Lab at McMaster University
- Joe Eibl and NOSM lab
- CIHR Team in Gender Environment and Health
- NOSM/NOSM FA Research

