Mechanisms of Particle Toxicity: Effects on the Respiratory System

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Airborne Particles in the California Central Valley: Friend or Foe?

PM Research at UC Davis

Why Study Particulate Matter Toxicity?

- Major Component of CA Air Pollution
- Complex Mixture
- Numerous Health Effects Seen
- Biologic Mechanisms are Unknown
- Different Mechanisms/Different PM
- Sensitive Populations
- Identify Which Portions are Most Harmful
- Minimize Public Health Threat

We Know PM Air Pollution Causes Health Effects

- Epidemiology Studies
- Statistical Tools Look at Human Populations

- Mortality and Illness Track PM Levels
- High Degree of Consistency and Coherence
  Among Studies

- Effects are seen Worldwide

We Don't Know How PM Air Pollution Causes Health Effects

- Which Characteristics Are Most Important?
  - Particle Size
  - Particle Composition
  - Particle Number

- What Cellular Mechanisms are involved?
  - Allergic response
  - Immune response
  - Inflammation
  - Injury and repair

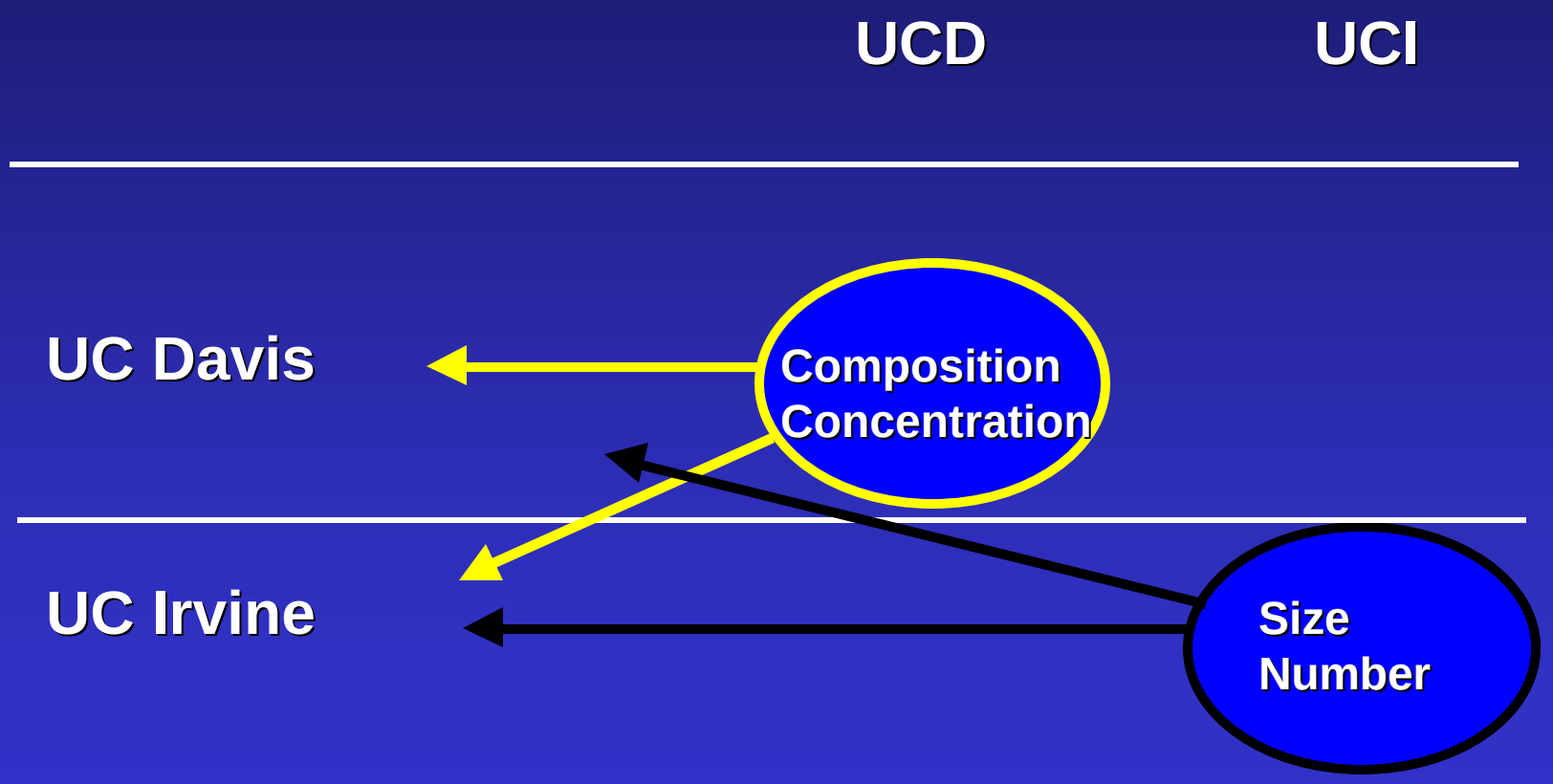
Related Human Health Effects

- **Asthma**
- **Chronic Pulmonary Disease (COPD)**
- **Allergic Challenge**
- **Airway Inflammation**
- **Cardio/Pulmonary Failure**
- **Age: Young, Adult, Senescent**
- **Developmental Concerns**

Biological Endpoints

- Cell Permeability (Injury)
- Cell Proliferation (Repair)
- Oxidative Stress
- Histopathology
- Injury Location
- Immunohistochemistry
- Immune Cell Responses
- Airway Inflammation
- Cellular Function
- Pulmonary Function
- Particle Clearance
- Asthmatic Symptoms
- Allergic Response (cellular)
- Cardiovascular Effects

PM Toxicology Research Design



Experimental Conditions

Ammonium Nitrate

(75, 150, 300 micrograms/cubic meter)

Carbon Black

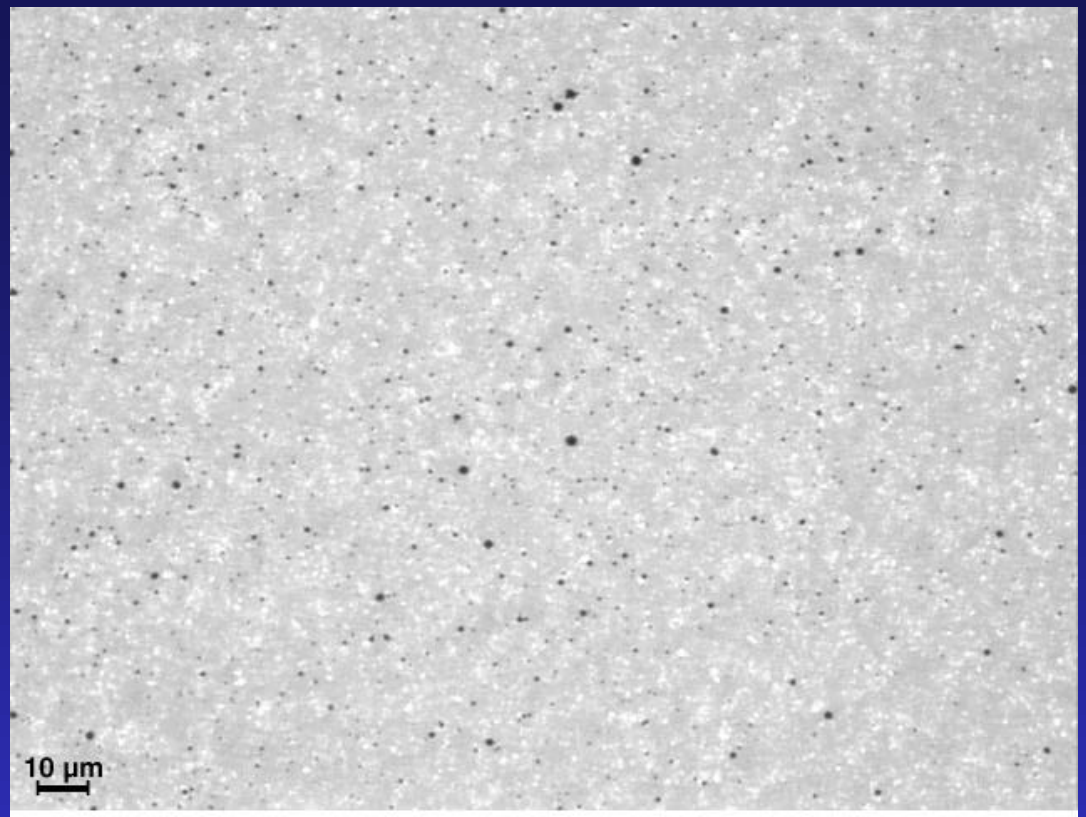
(50, 100, 200 micrograms/cubic meter)

Ozone

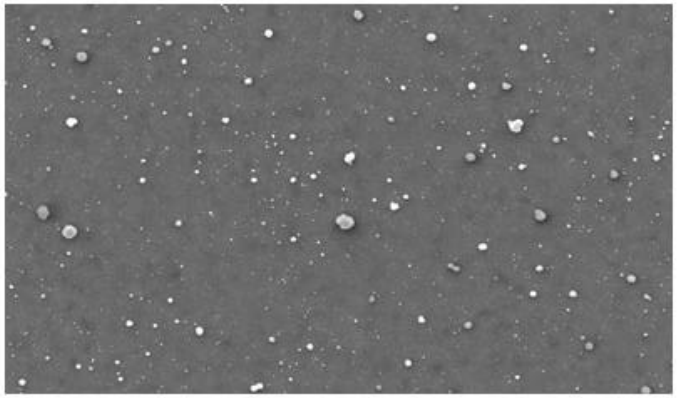
(0.20 ppm)

PM

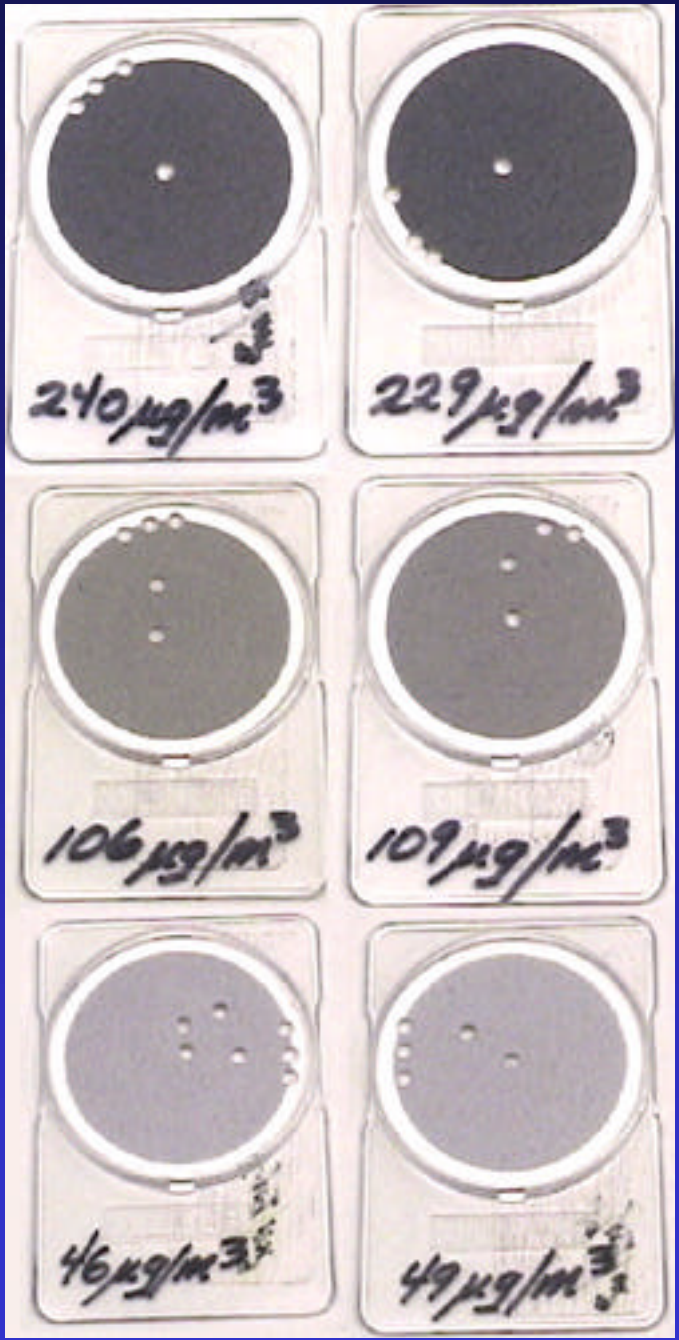
Aerosol

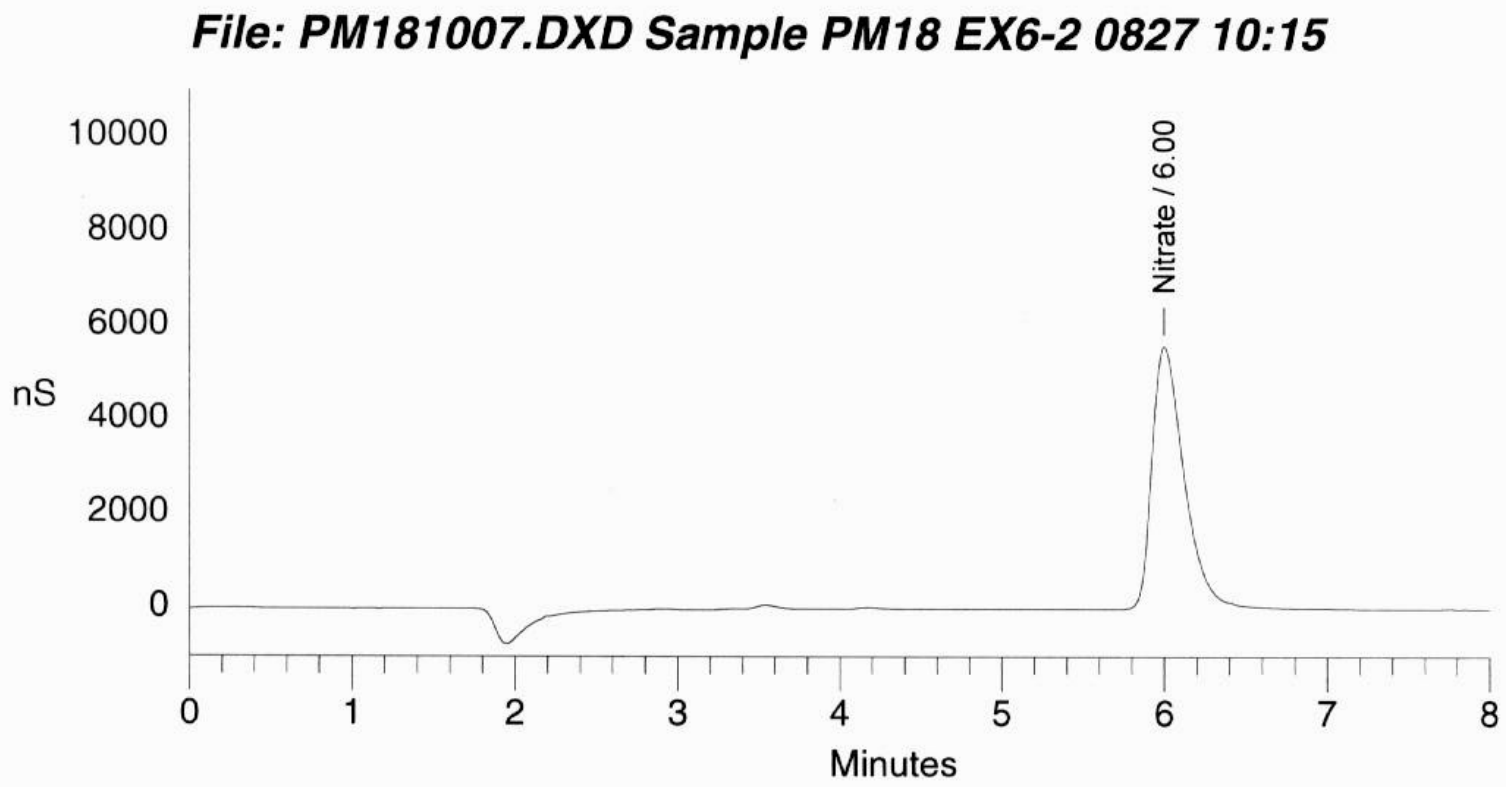


LM

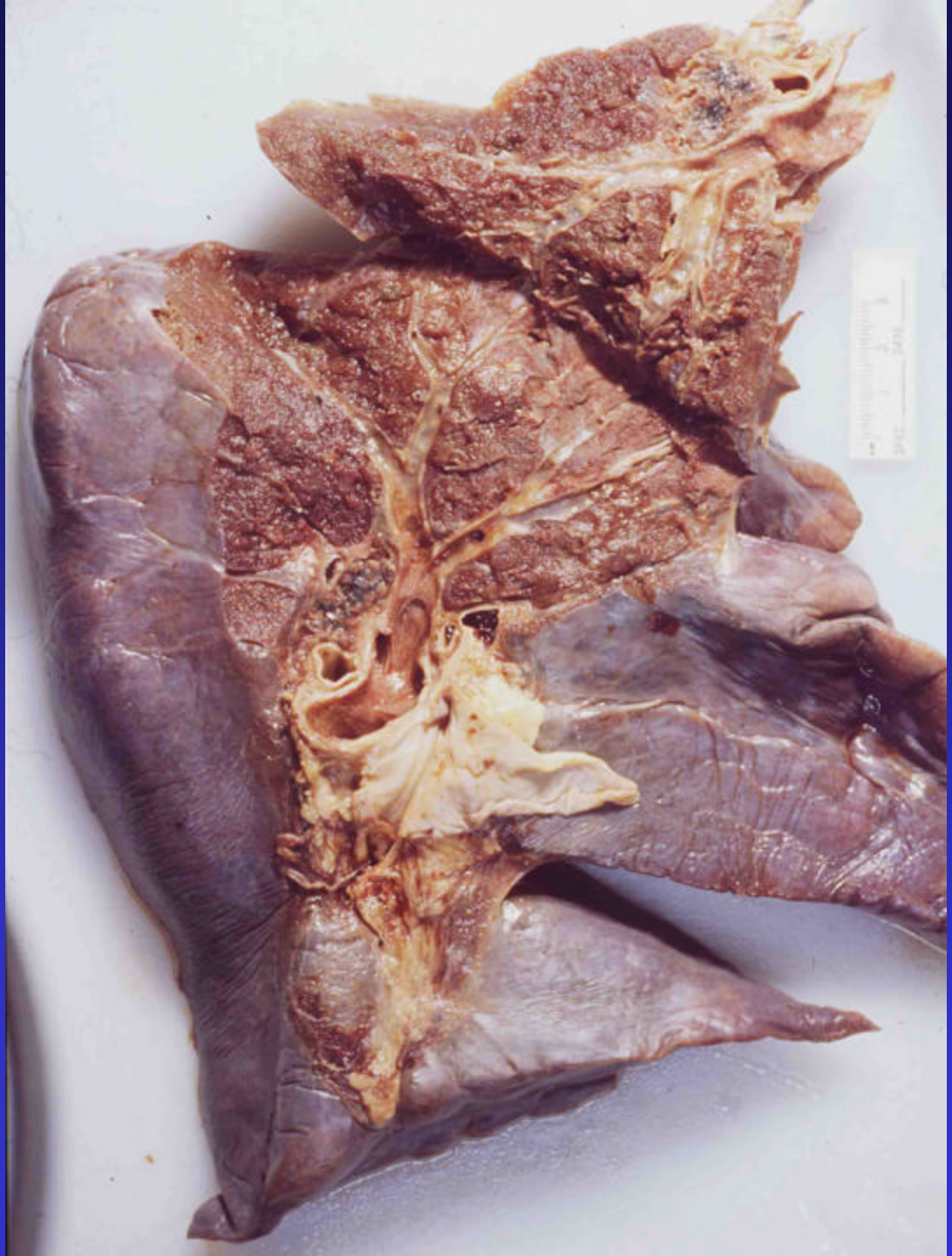


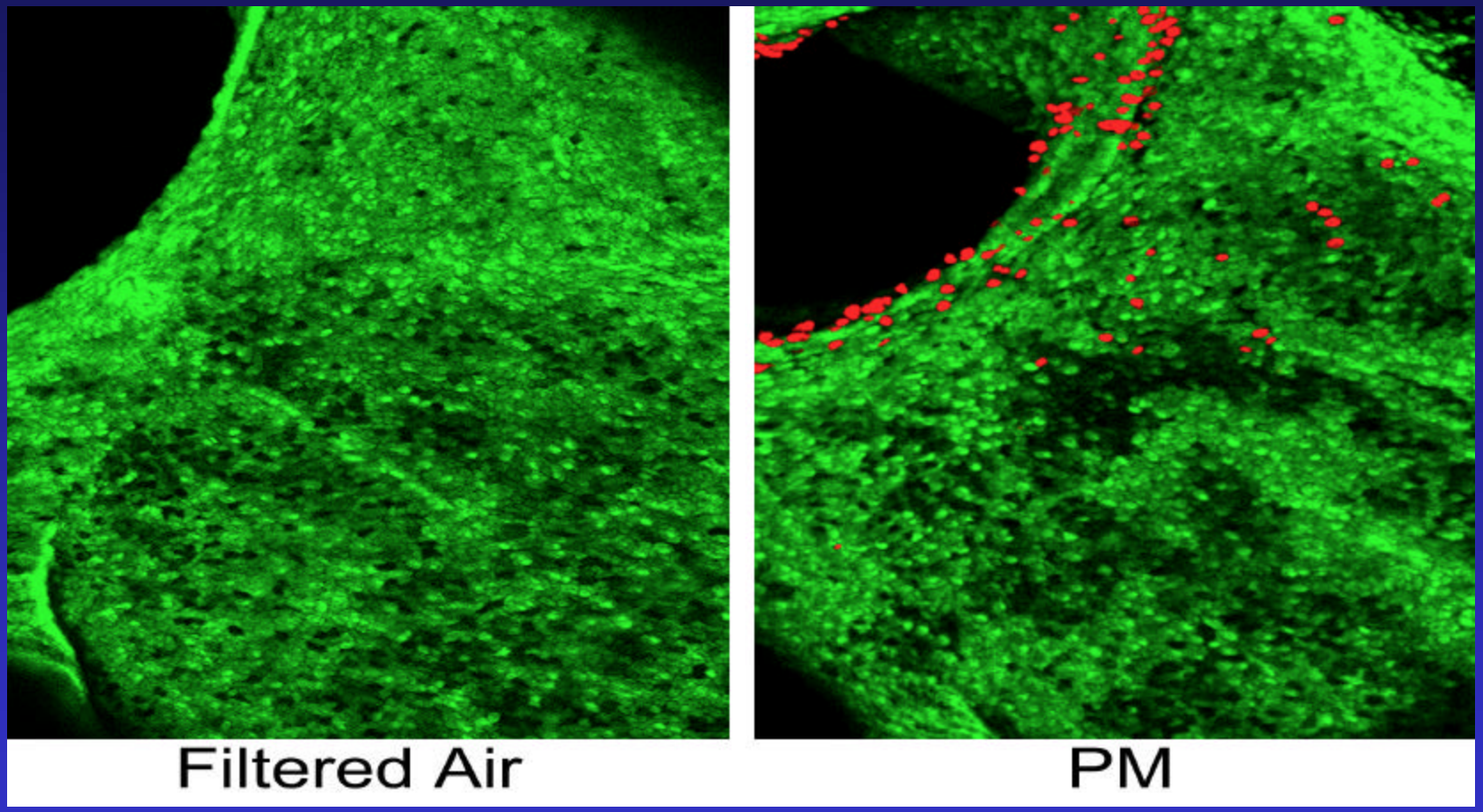
SEM

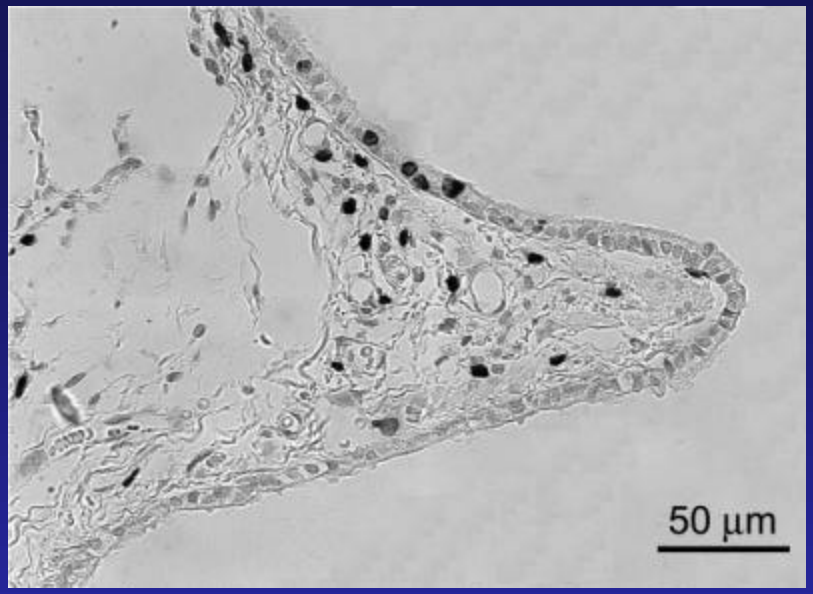

240 µg/m3
229 µg/m3
106 µg/m3
109 µg/m3
46 µg/m3
49 µg/m3

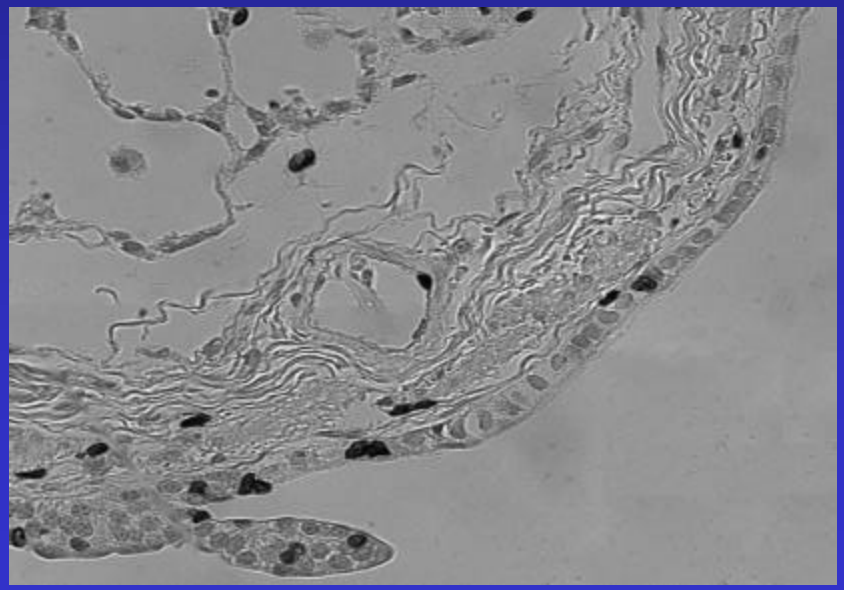

File: PM181007.DXD Sample PM18 EX6-2 0827 10:15
10000
8000
6000
4000
2000
0
nS
Nitrate / 6.00
0
1
2
3
4
5
6
7
8
Minutes

Airway Microdissection

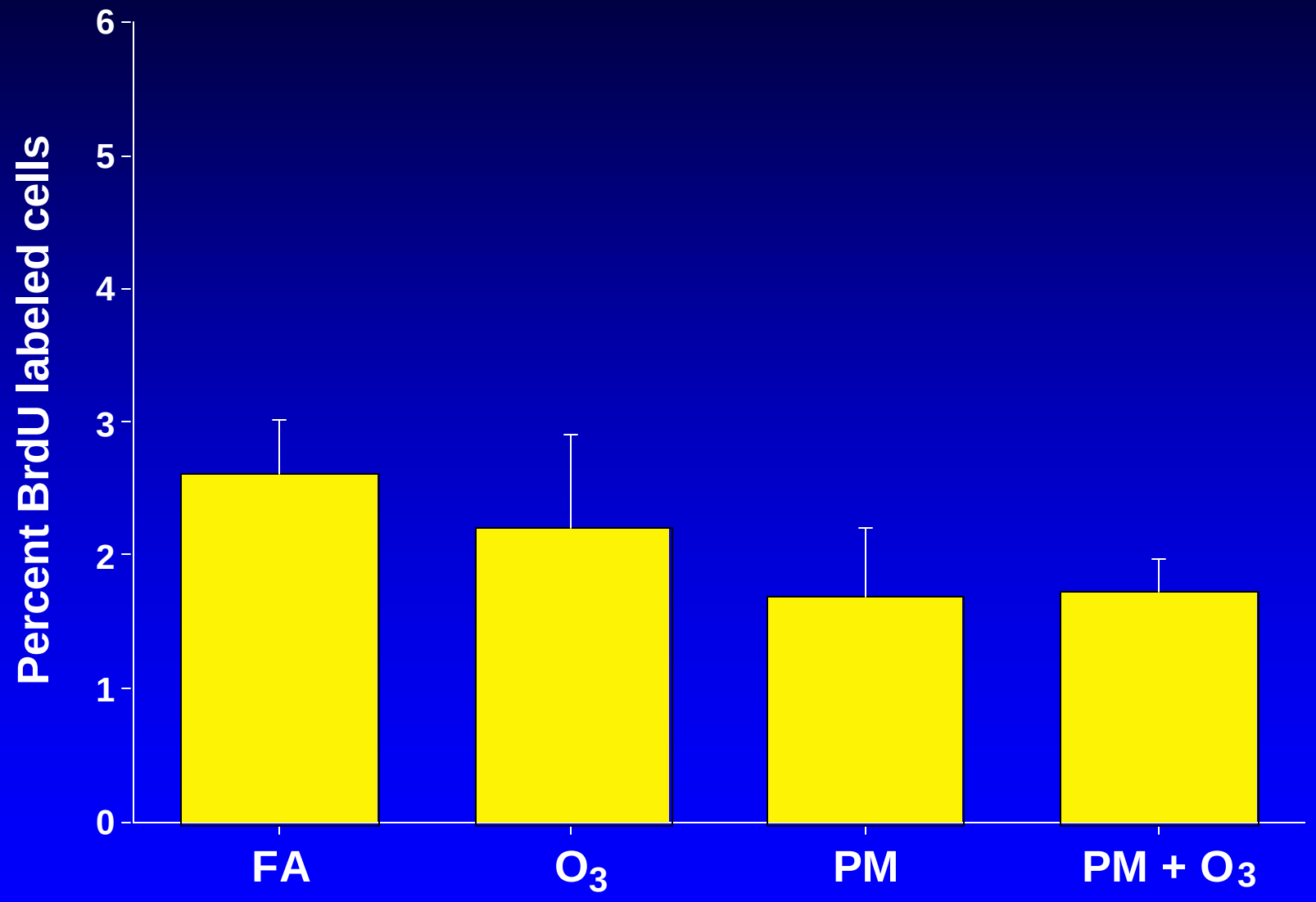



Filtered Air
PM

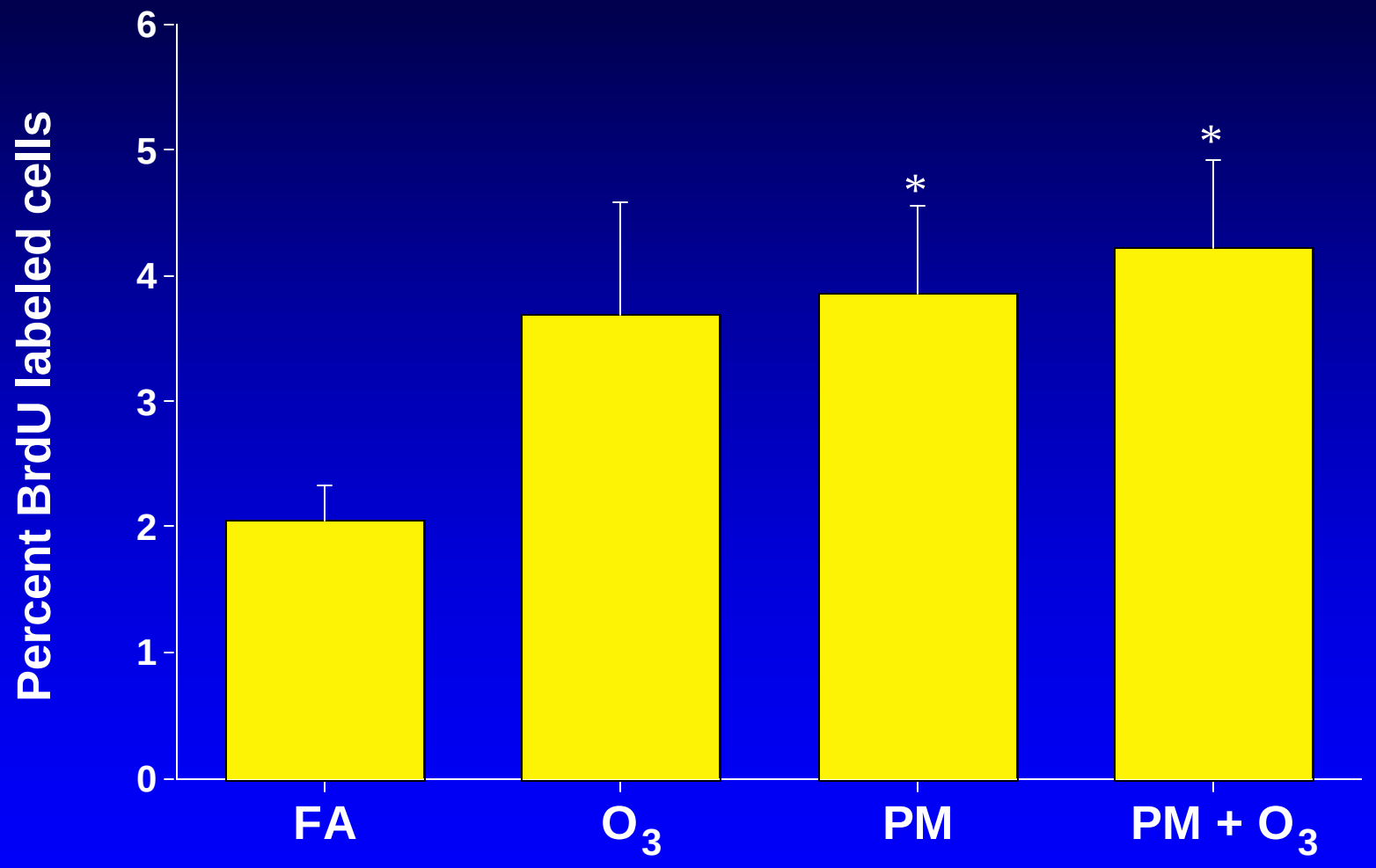

50 µm



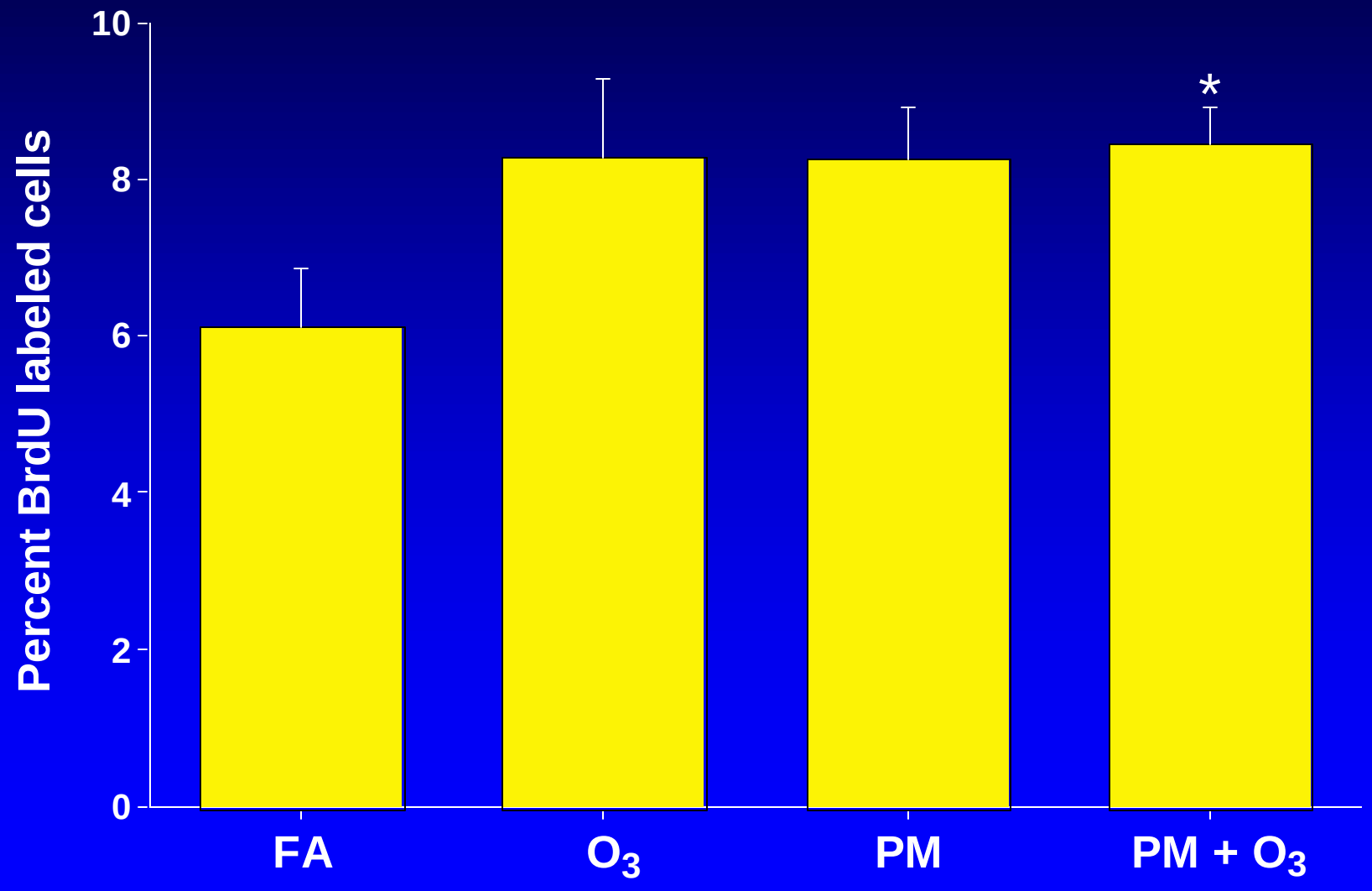
Epithelial cell labeling of airways



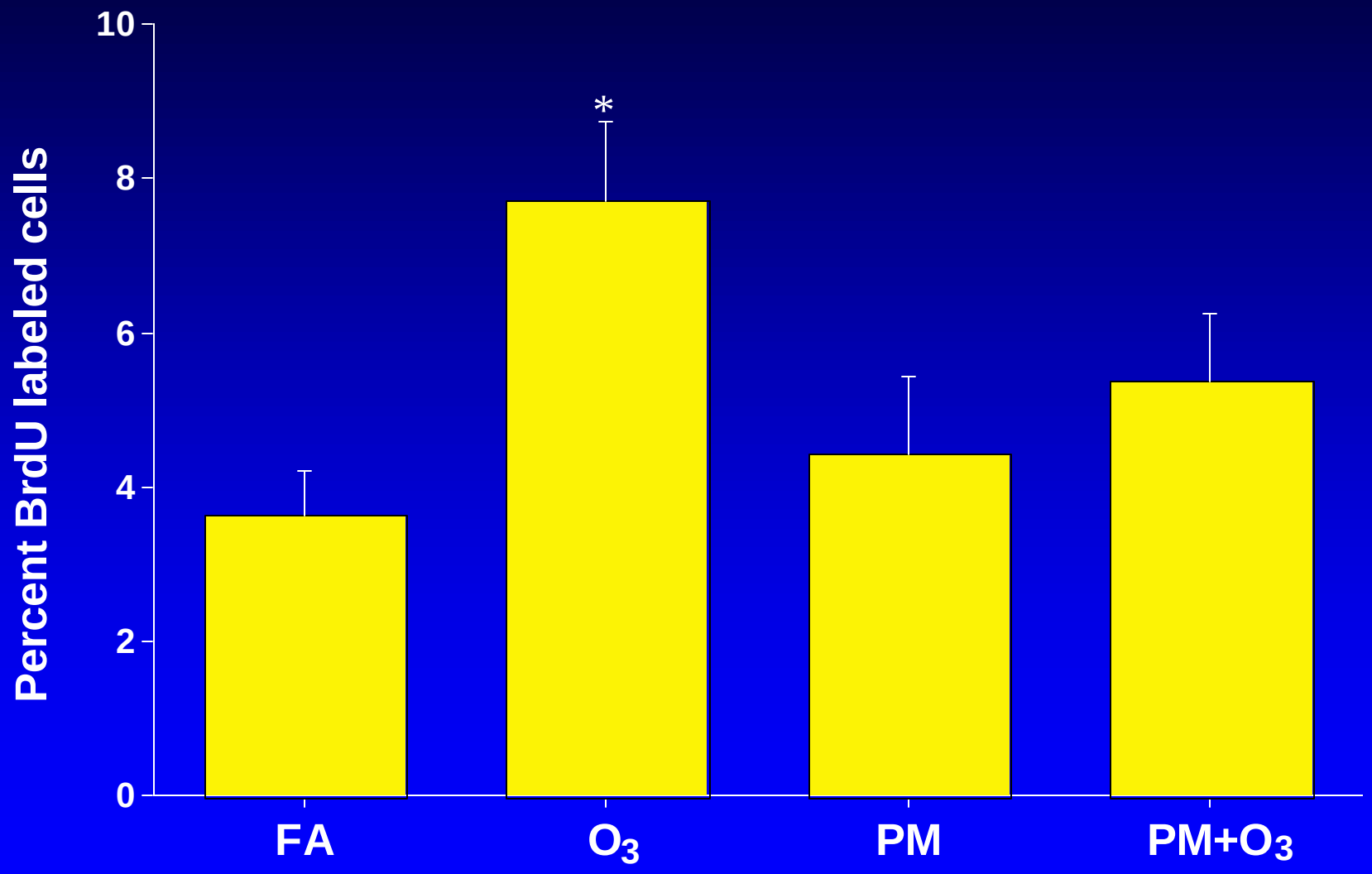
Epithelial cell labeling of airway bifurcations



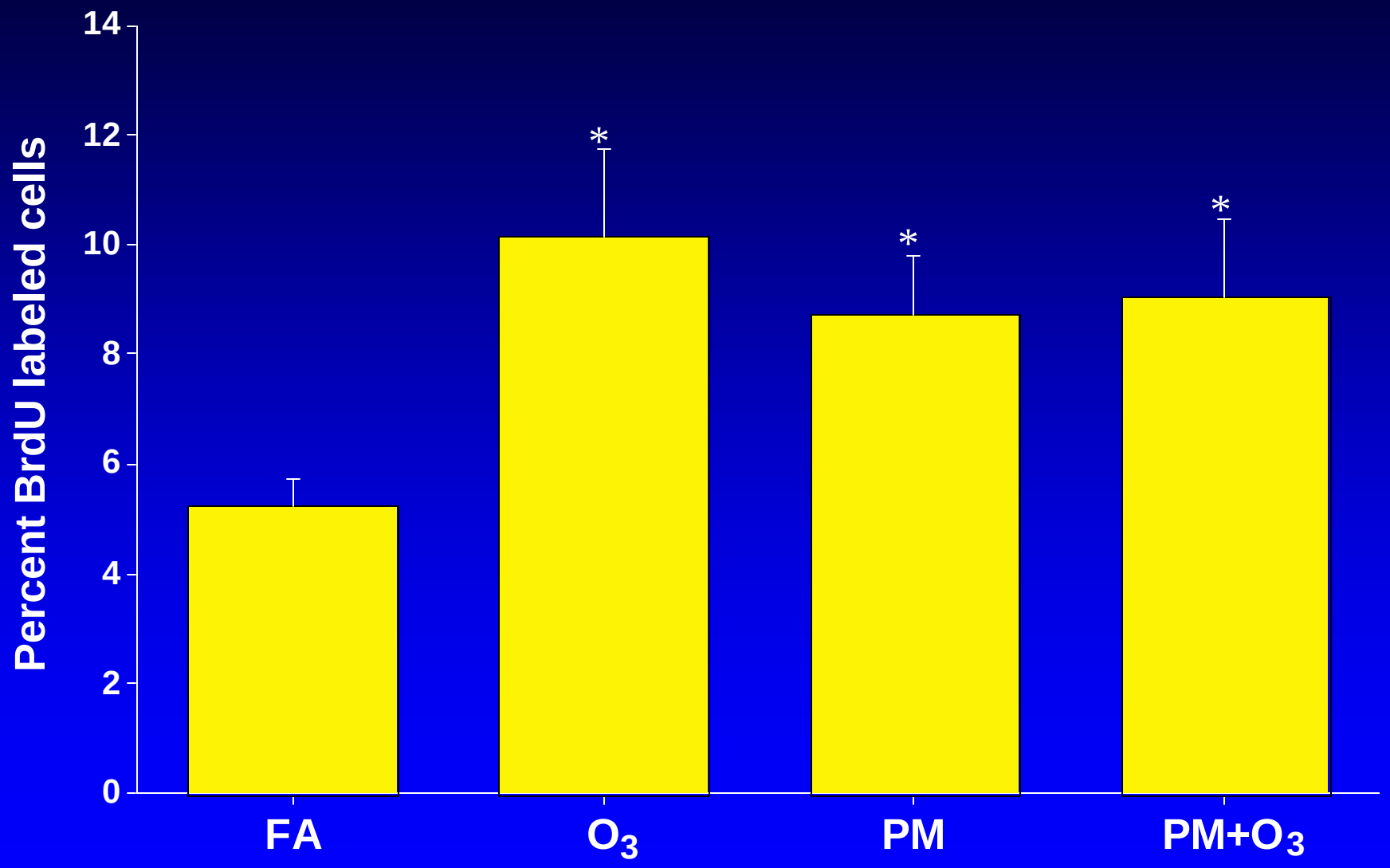
Interstitial cell labeling of airway bifurcations



Epithelial labeling of terminal bronchioles



Cell labeling of the proximal alveolar region



Epithelial cell labeling of respiratory bronchioles in Rhesus monkeys

(PM = 150 µg/m ^{3} + 100 µg/m ^{3} C)

Percent BrDU labeled cells

*

*$p < 0.05$

Conclusions

- Exposure to ammonium nitrate and carbon particles can cause injury to the lungs.
- Cellular injury can be seen even in healthy adults.
- Particle-induced lung injury is site-specific: airway bifurcations, centriacinar regions and respiratory bronchioles.
- Particle-induced lung injury is independent of ozone exposure.

Significance of Findings

- See PM effects even in healthy animals
- More sensitive effects seen here cannot be detected with epidemiological efforts
- Supports the need to continue toxicology studies to elucidate mechanisms
- Raises questions about the long-term implications of chronic PM exposure

Related Human Health Effects

- **Asthma**
- **Chronic Pulmonary Disease (COPD)**
- **Allergic Challenge**
- **Airway Inflammation**
- **Cardio/Pulmonary Failure**
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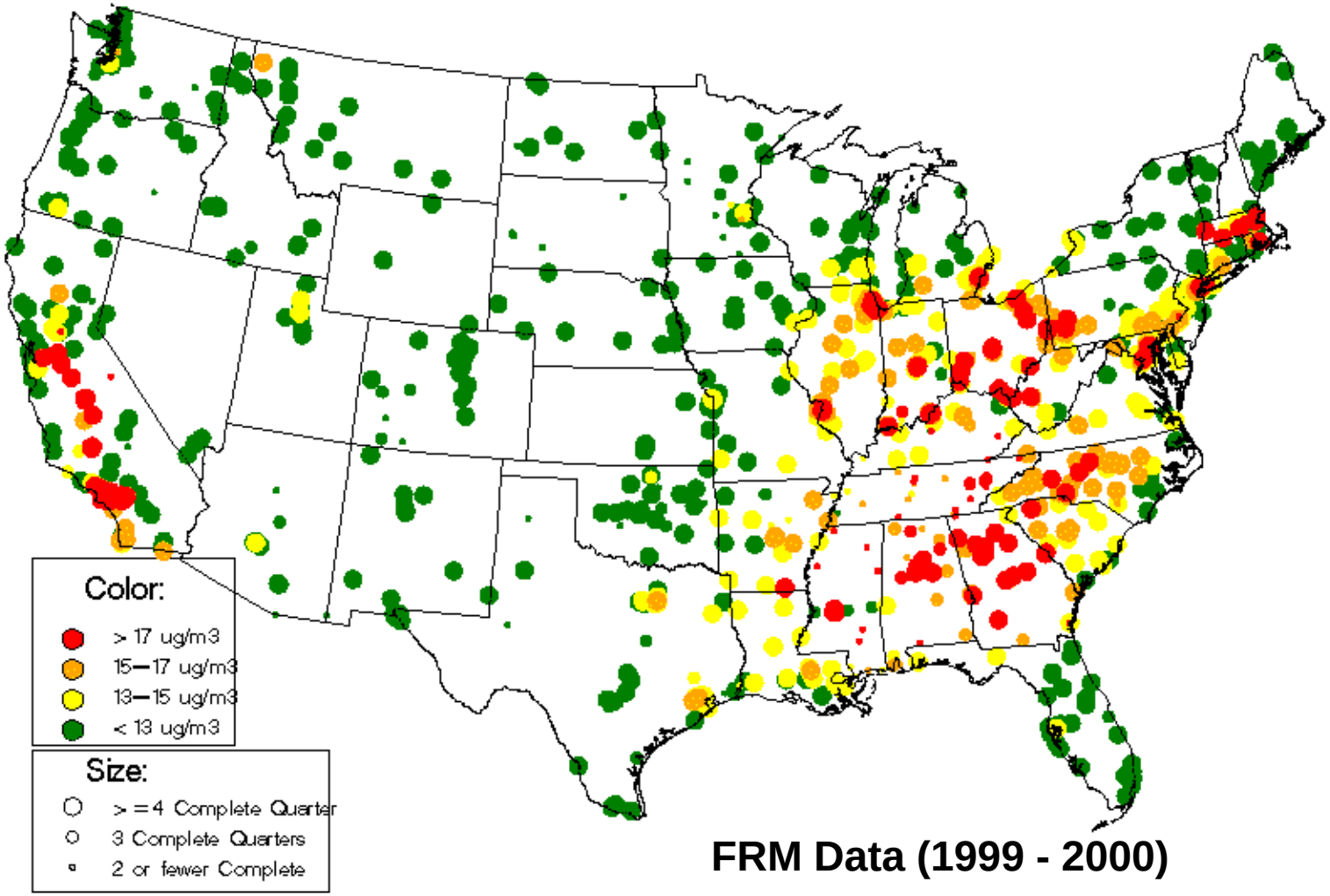
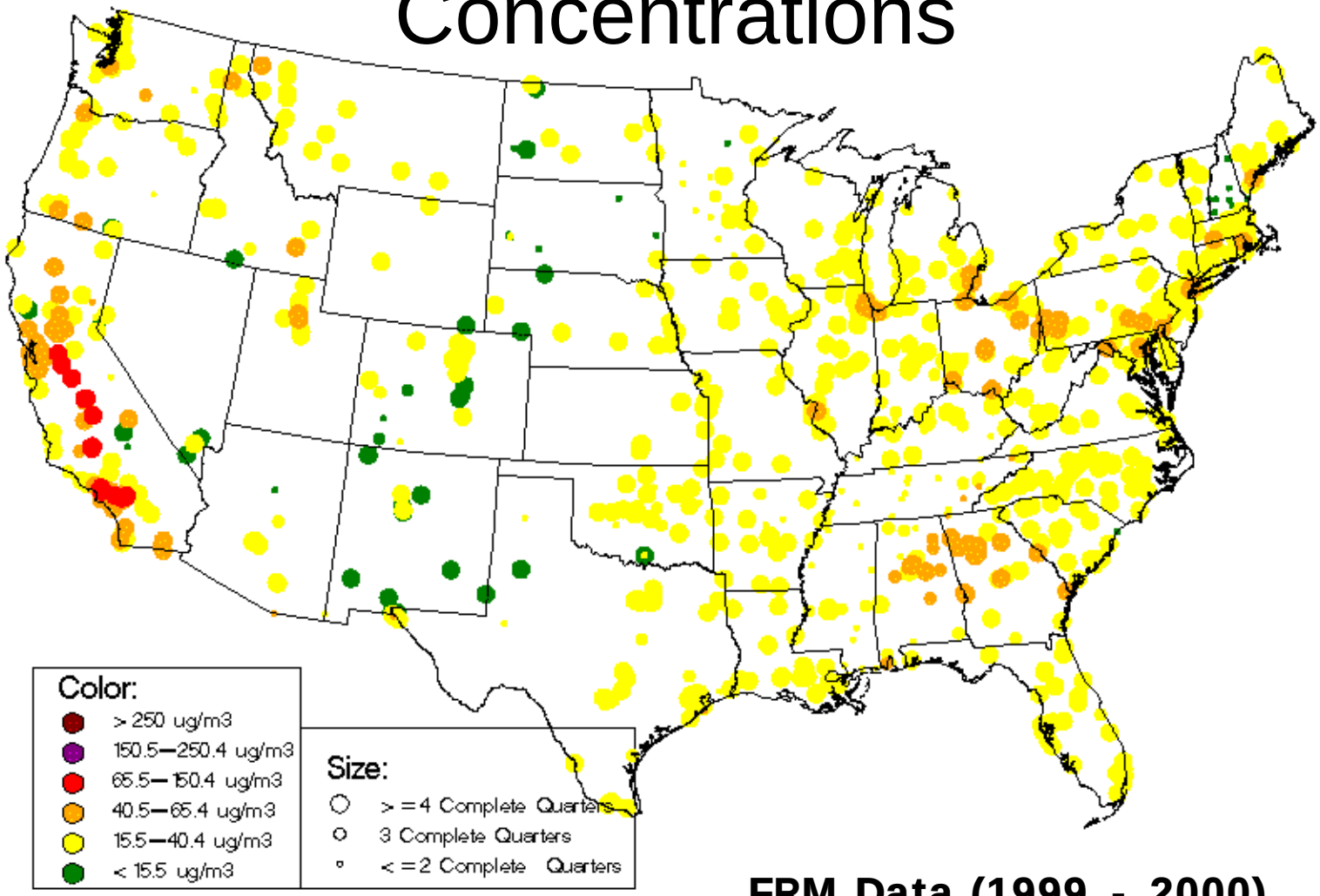
Annual Average PM2.5 Concentrations



FRM Data (1999 - 2000)

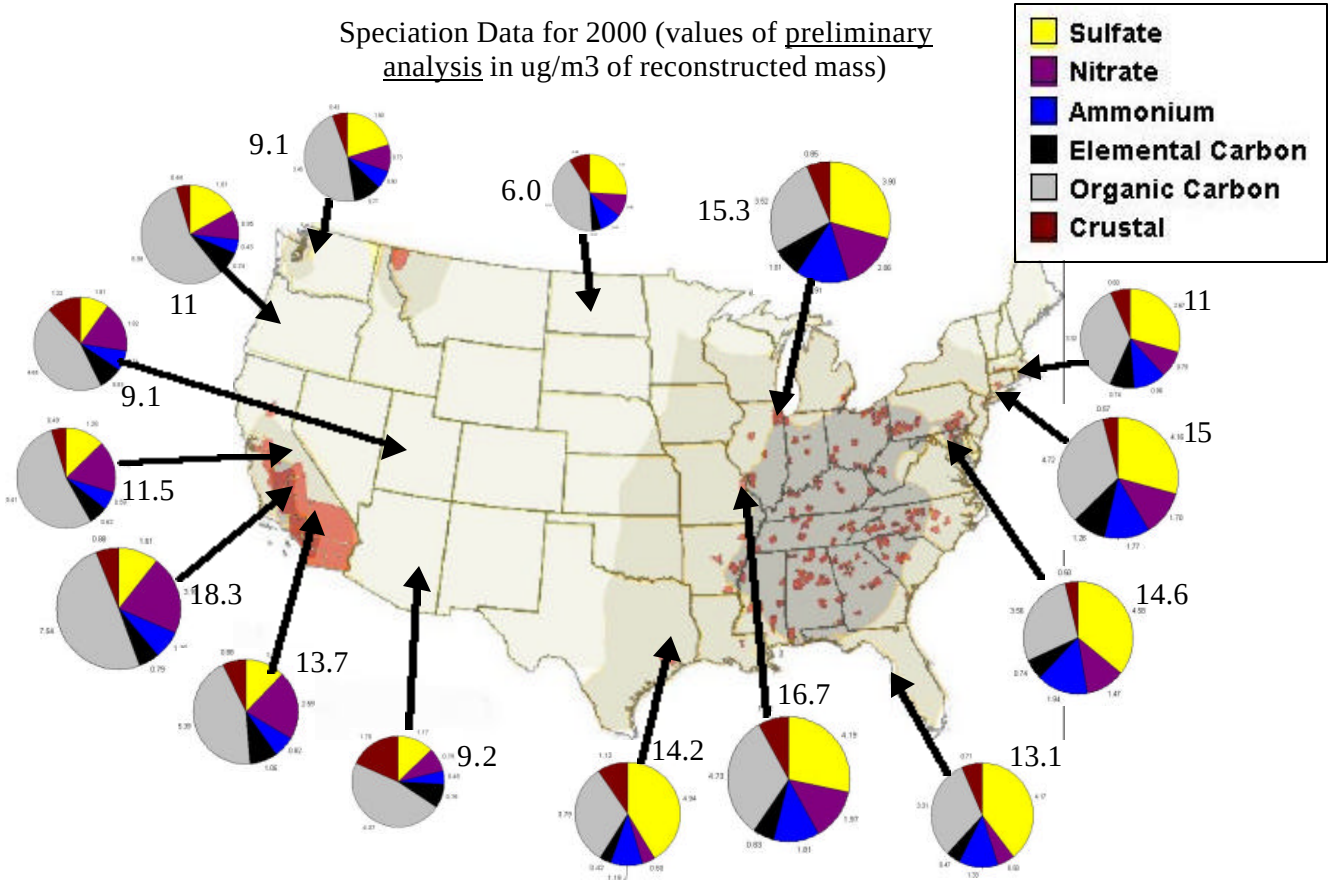
24-Hour Average PM2.5 Concentrations



FRM Data (1999 - 2000)

PM2.5 Chemical Speciation Networks: Results

PM2.5 Composition Varies by Region



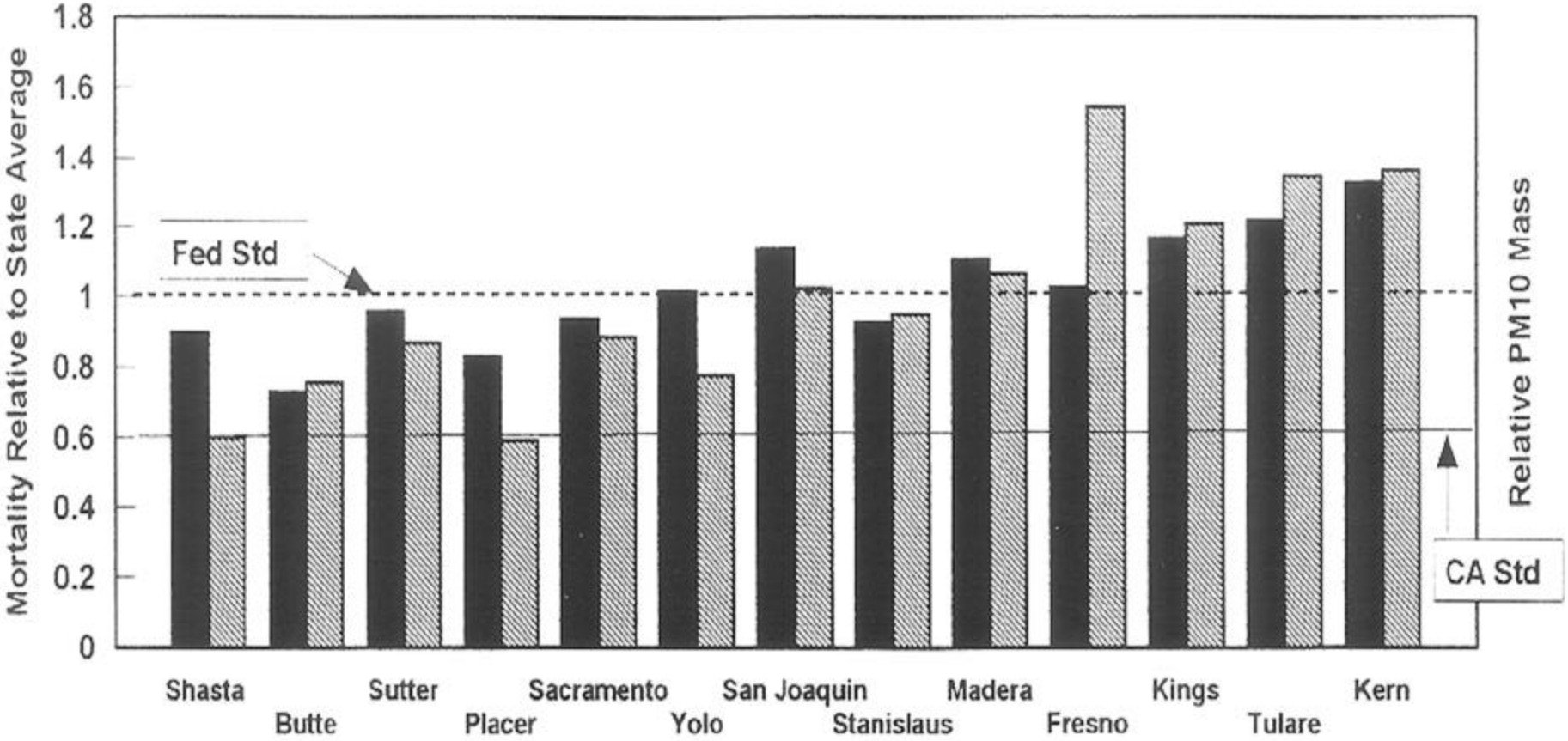
Red Implies Counties With 1999/2000 FRM PM2.5 Levels Exceeding Standard; Note Need 3 Yrs of Data;

Grey Zone Denotes Areas of Concern

Dusty environments In California agriculture

Cardiac (IHD) Mortality vs PM10 Particle Concentrations

Central Valley, California (1989-1991)



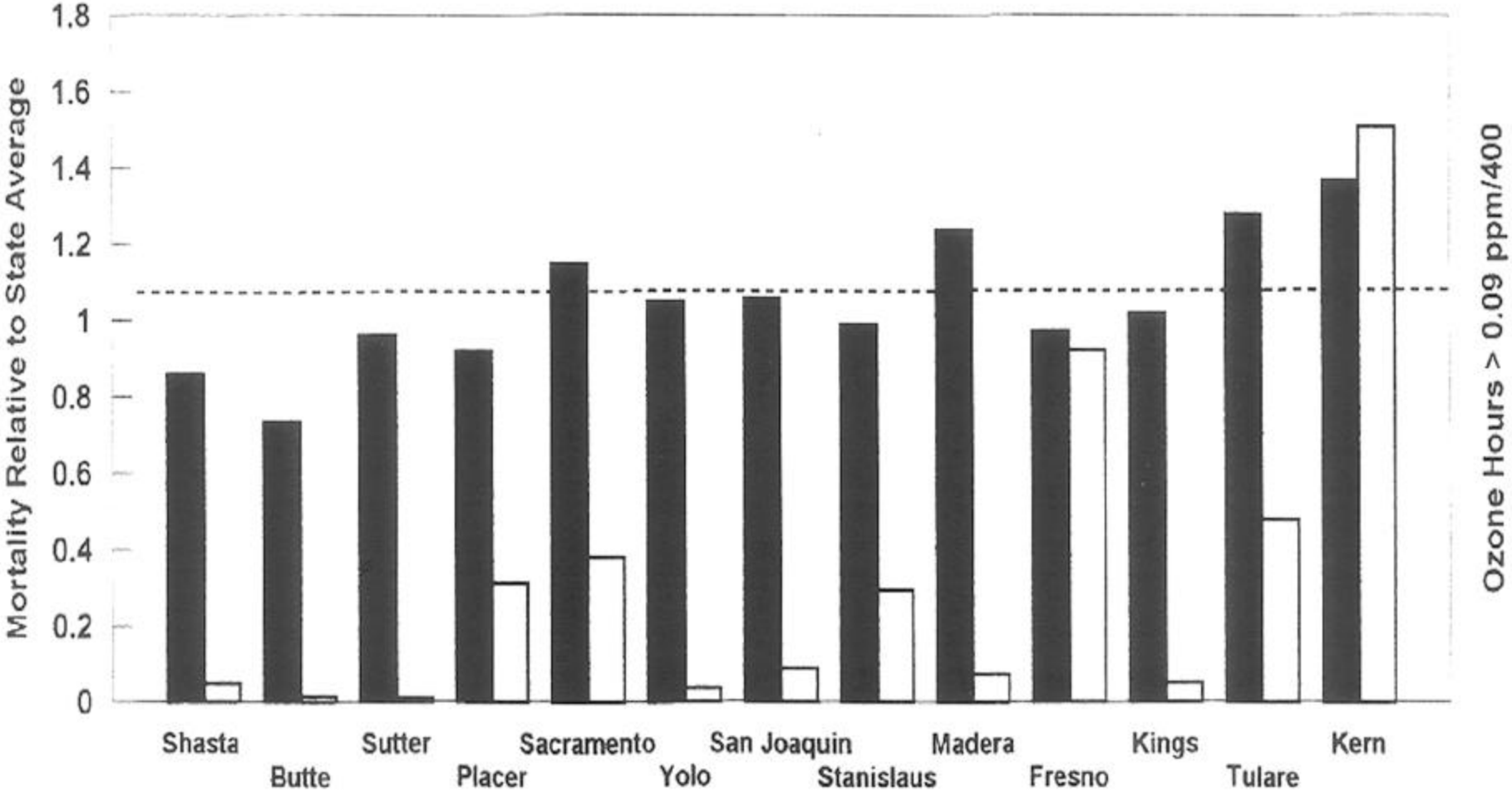
■ Cardiac (IHD) Mortality Relative to CA Average

▨ Annual PM10 Concentration Divided by 50 micrograms/m3

IHD - Ischemic Heart Disease

Cardiac (IHD) Mortality versus Ozone Hours > 0.09 ppm

Central Valley, California, (1989-1991)



■ Cardiac (IHD) Mortality Relative to CA Average □ Ozone Hours > 0.09 ppm (CA Std) Divided by 400

Studies of Concentrated Ambient Particles of Fresno, California

Concentrated Ambient Particles
Fall 2000, Fresno, CA

Date	Number/cc	Mass/m^3
Oct 17 - Oct 19	120,000	847
Oct 24 - Oct 26	120,000	260
Oct 31 - Nov 2	110,000	369

Chemical Composition of Fine Aerosol in Fresno

Oct 17-19, 2000

(Total Mass = 847 μg/m^3)

141
Organic Carbon

61
Elemental Carbon

60
Metals

49
Sulfate

8
Non-metals

527
Nitrate

Chemical Composition of Fine Aerosol in Fresno

Oct 24-26, 2000

(Total Mass = 260 μg/m^3)

95
Organic Carbon

9
Elemental Carbon

70
Metals

19
Sulfate

5
Non-metals

63
Nitrate

Chemical Composition of Fine Aerosol in Fresno

Oct 31- Nov 2, 2000

(Total Mass = 369 µg/m^3)

80
Organic Carbon

8
Elemental Carbon

25
Metals

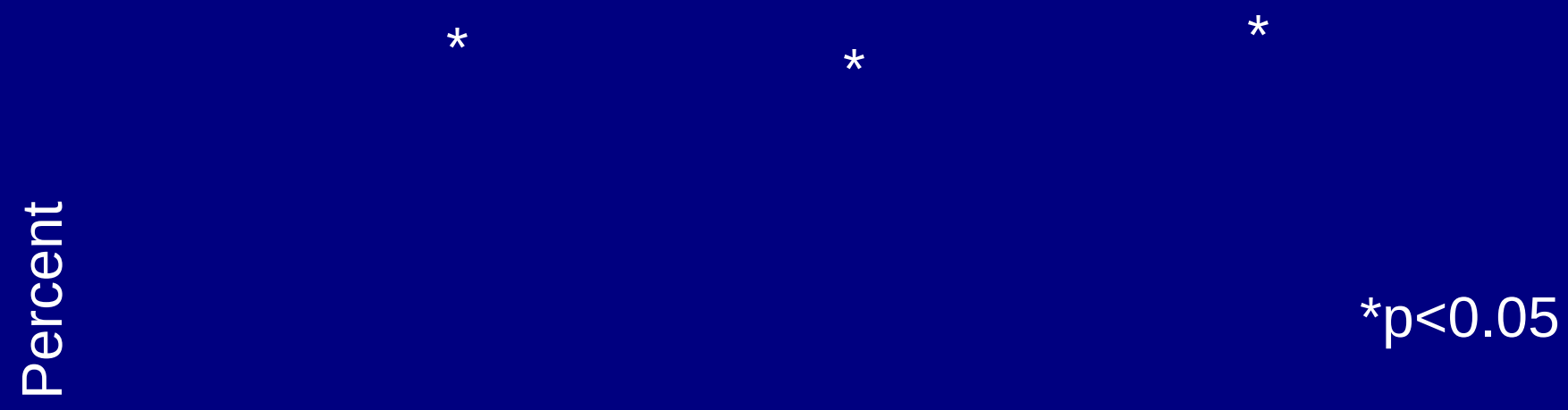
26
Sulfate

20
Non-metals

211
Nitrate

Fresno PM Study: Cell Permeability for Bronchoalveolar Lavage

Fall, 2000



Concentrated Ambient Particles
Winter 2001, Fresno, CA

Date	Number/cc	Mass/m^3
Jan 30 - Feb 1	84,000	815
Feb 6 - Feb 8	100,000	190
Feb 13 - Feb 15	120,000	371

Chemical Composition of Fine Aerosol in Fresno

Jan 30 - Feb 1, 2001

(Total Mass = 815 $\mu g/m^3$)

Chemical Composition of Fine Aerosol in Fresno

Feb 6 - 8, 2001

(Total Mass = 190 $\mu g/m^3$)

Chemical Composition of Fine Aerosol in Fresno

Feb 13 - 15, 2001

(Total Mass = 371µg/m^3)

Fresno PM Study: Cell Permeability for Bronchoalveolar Lavage

Winter, 2001

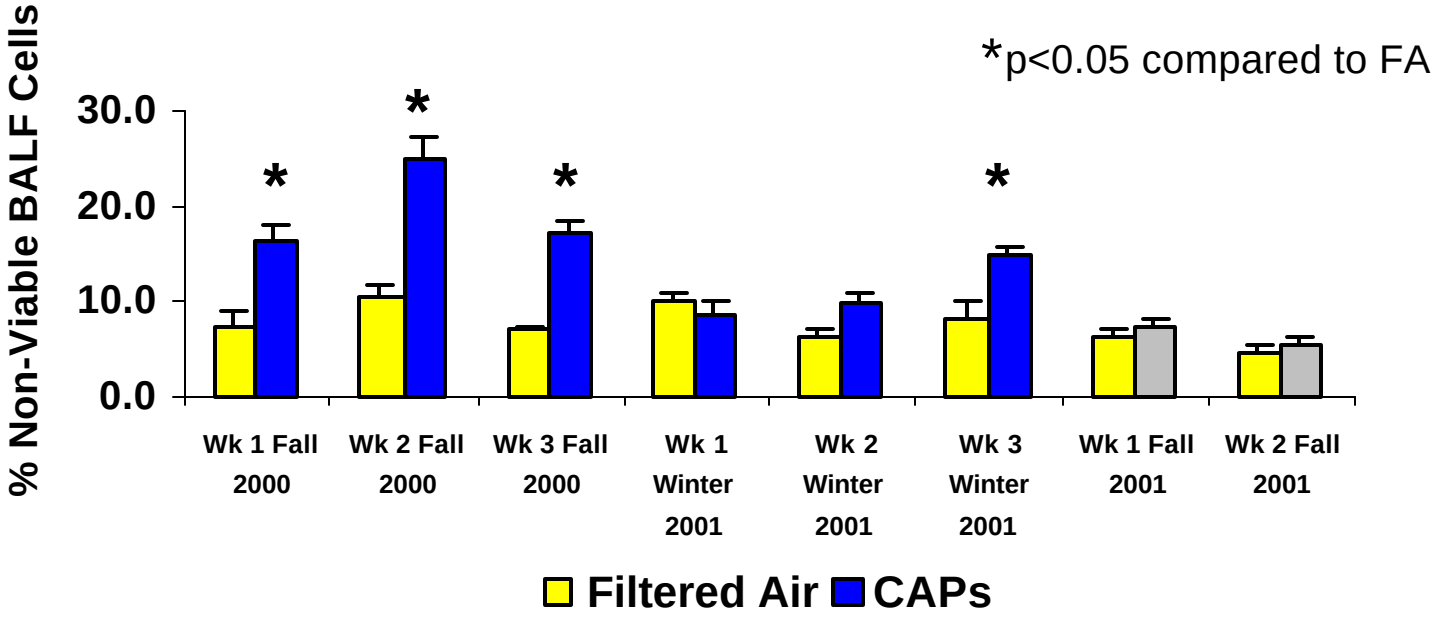
*

Percent

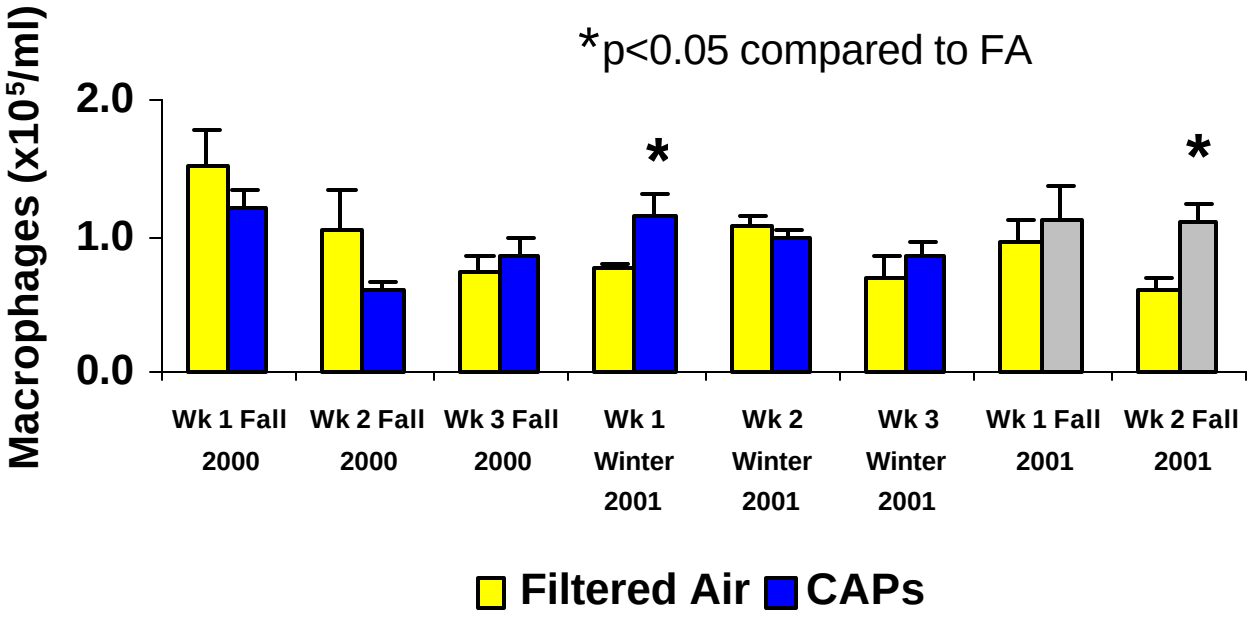
*p<0.05

Fine Versus Coarse Particle Effects on the Lungs in Fresno, California

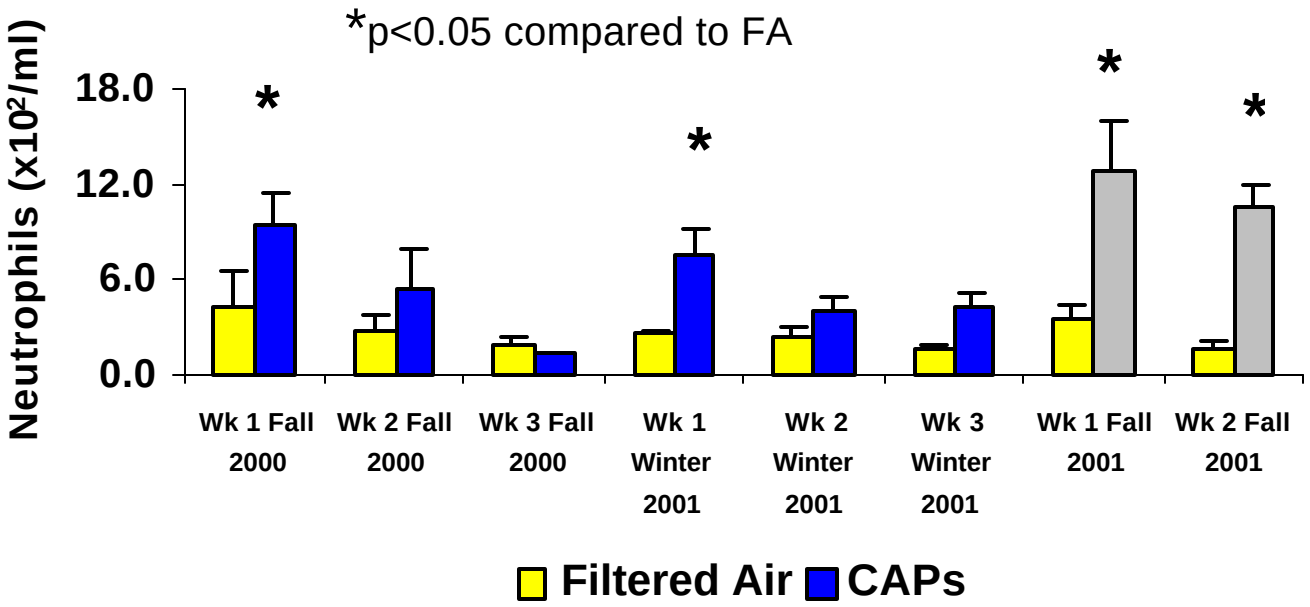
Non-Viable Cells in BAL from SD Rats Exposed to Fine or Coarse Aerosol in Fresno



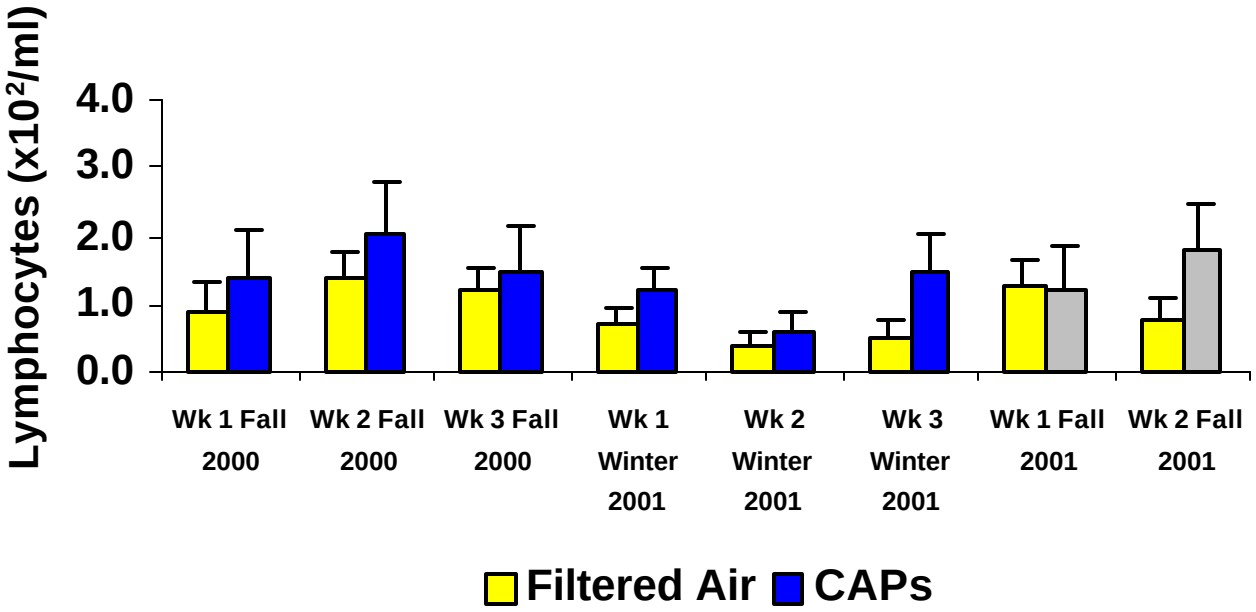
Macrophages in BAL from SD Rats Exposed to Fine or Coarse Aerosol in Fresno



Neutrophils in BAL from SD Rats Exposed to Fine or Coarse Aerosol in Fresno



Lymphocytes in BAL from SD Rats Exposed to Fine or Coarse Aerosol in Fresno



Conclusions

- Fine and coarse particles can be concentrated to study health effects.
- Respiratory changes have been observed during both the fall and winter seasons in Fresno, California.
- Concentrated ambient fine or coarse particles in Fresno, California, produce respiratory change in healthy adult rats.

Acknowledgements

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