Diesel particle deposition in the airways and the induction of inflammation.

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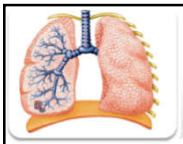
Centre for Research in
Occupational Safety & Health

October 6th, 2020

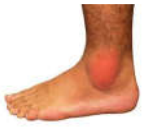
The Air We Breathe



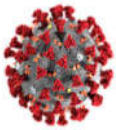
Airway Anatomy / Function

Particle Deposition

Particle Clearance



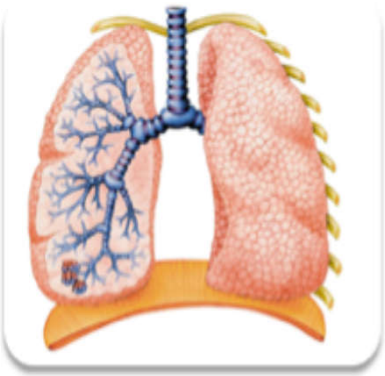
Inflammation, Chronic Inflammation, and disease



COVID 19

CROSH CRSST

Airway Anatomy

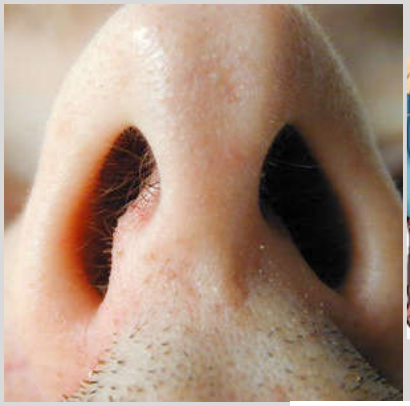


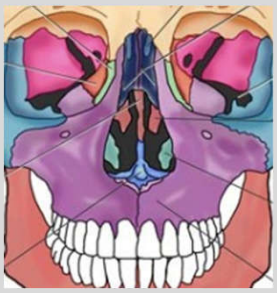
CROSH CRSST

The Nose

Filter

Exercise





The Lungs

23 branching generations

0-8 trachea and bronchi

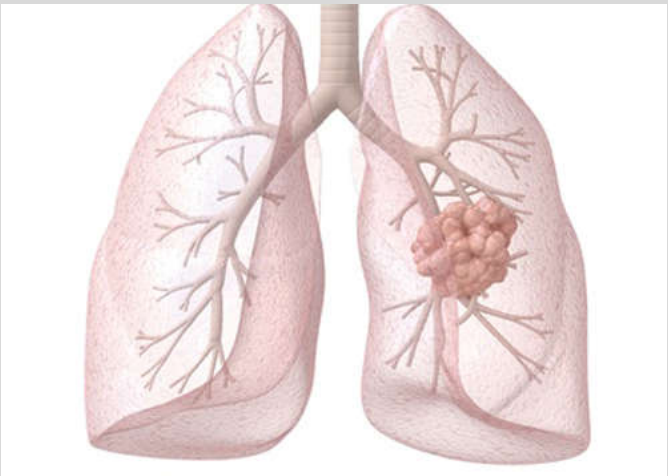
- Conduction

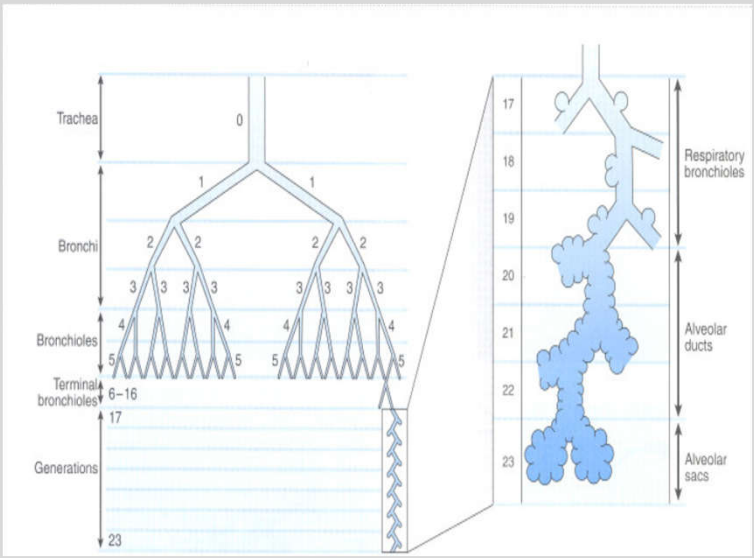
9-16 bronchioles

- Conduction & Diffusion

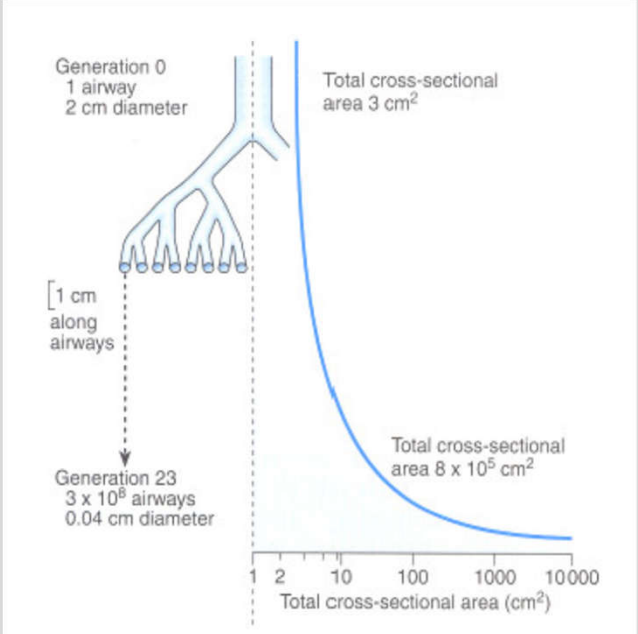
16-23

- Alveolar region diffusion



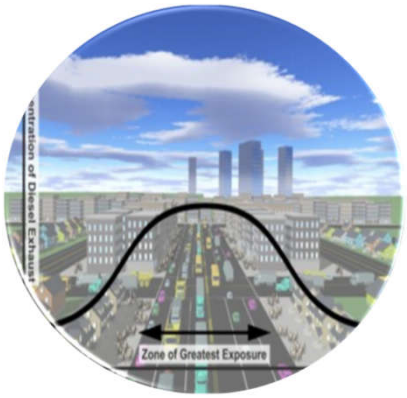


Weibel lung model 1963



The Respiratory System. Davies and Moore (2003) Elsevier press

Particle Deposition

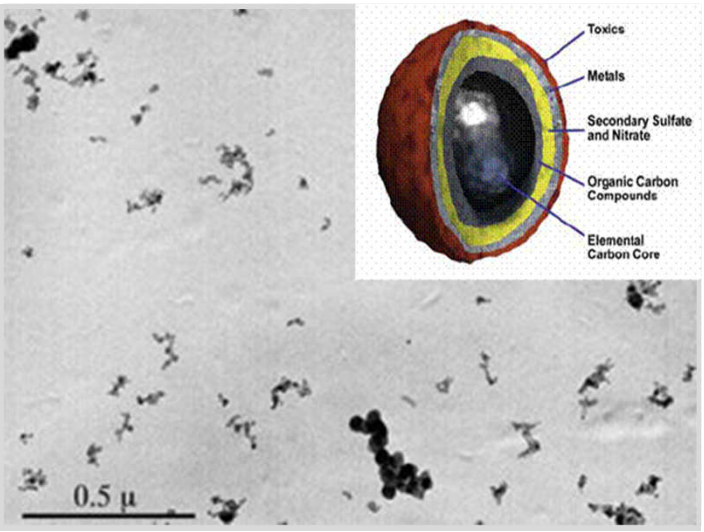


Mechanisms of Deposition

- Physical and chemical characteristics of the particle
- Properties of the particle kinetics in air
- Biological factors

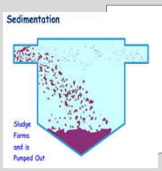
Physical/Chemical Properties

- Shape
- Size
- Contents

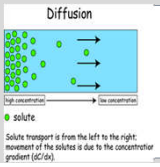


Particle Kinetics & Deposition

Impact



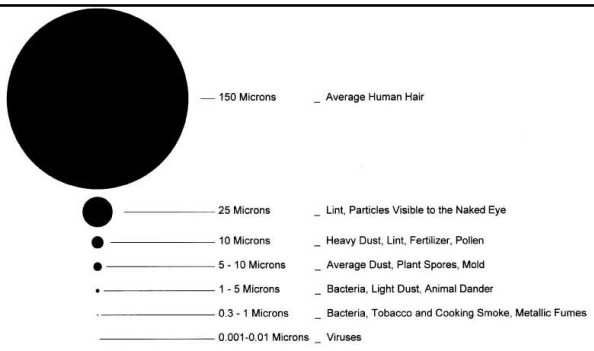
Sedimentation

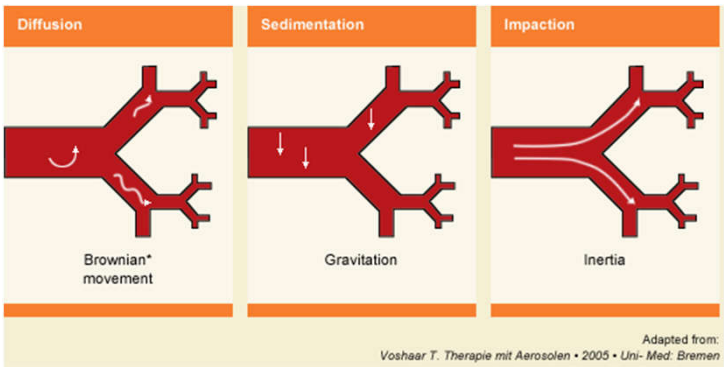


Diffusion

CROSH CRSST

Particle size





CROSH CRSST

Particle size

PM = Particulate Matter

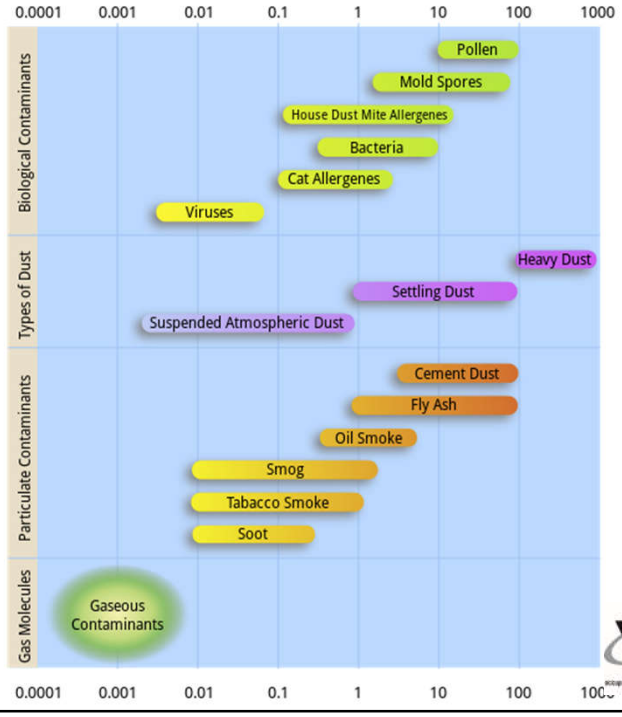
Inhalable particles are particles 10µm and smaller

PM_{10}: particles with a diameter between 2.5-10µm

$PM_{2.5}$: particles with a diameter between 0.1-2.5µm

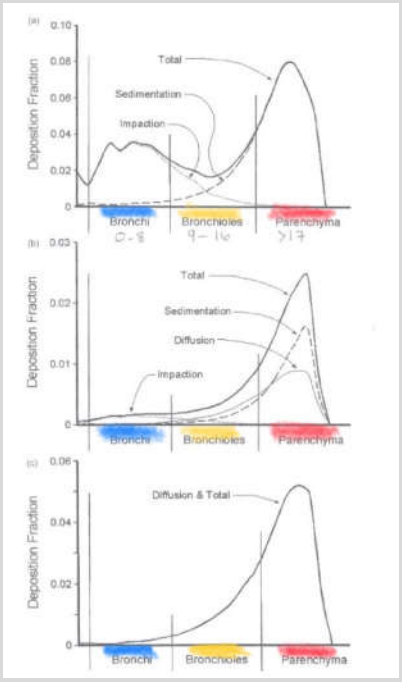
Ultrafine: less than 0.1µm

https://en.wikipedia.org/wiki/Particulates



Predicted lung Deposition by size

Smallest particles get into the deepest part of the airways

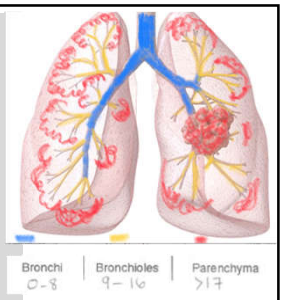


Foster & Costa. Lung Biology in Health and Disease. 2005

5µm

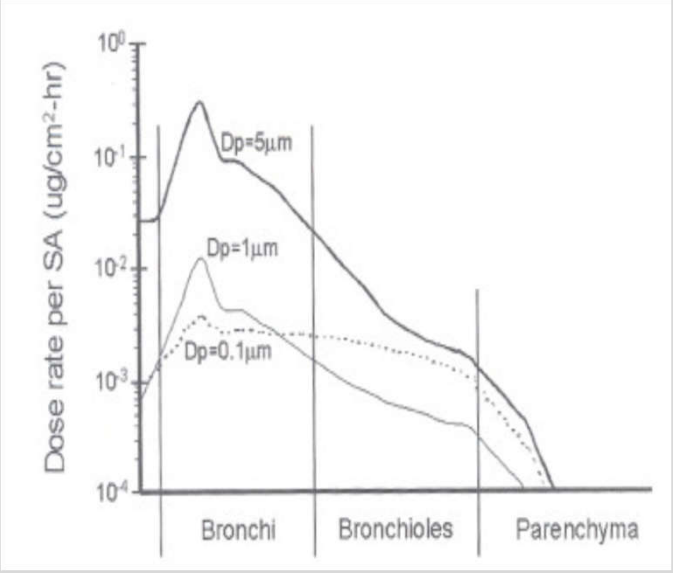
1µm

0.1µm



Deposition by size and surface area

Heavy deposition in the upper airways



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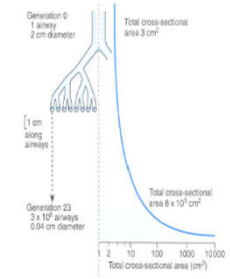

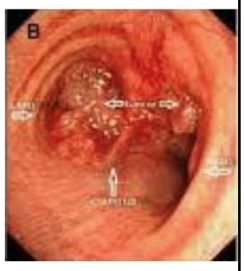

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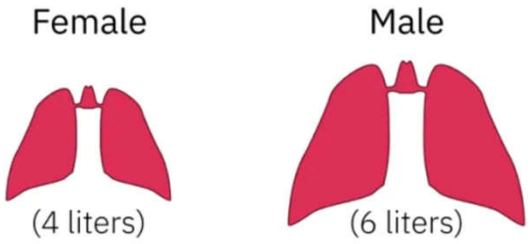
Biology of individual

Different people have different lung volumes & breathing rates

EXPOSURE ➔DOSE ➔RESPONSE



Deposition increases with:

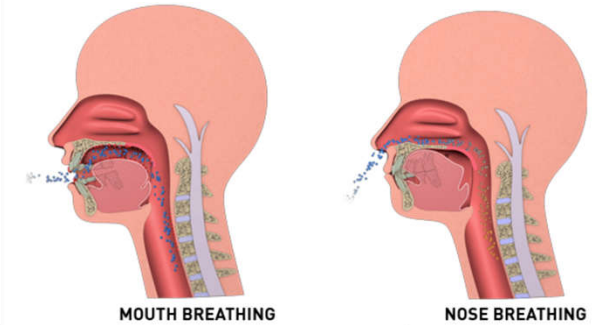
- increasing volume (larger person = larger volume);
- increased resistance;

Effect of Physical Activity

Deposition increases with increases in breathing rate (exercise).

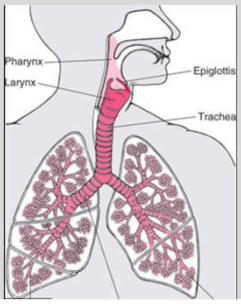
Upper airway deposition increases with increased airway velocity

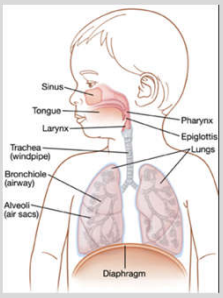
Nose to mouth breathing is an important aspect



Gender / Size

- Women have higher depositions per unit in the upper airways
- Men have higher deposition in their lower airways

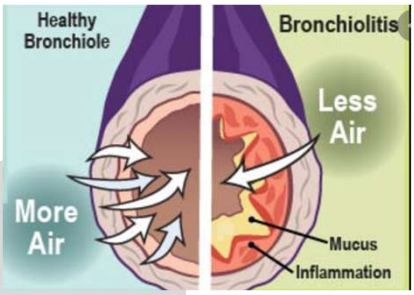




Age

- Children will have higher upper airway deposition due to anatomical size
- Older adults with normal lung function should have minimal changes in tidal volume and minute ventilation and so should not have altered deposition patterns

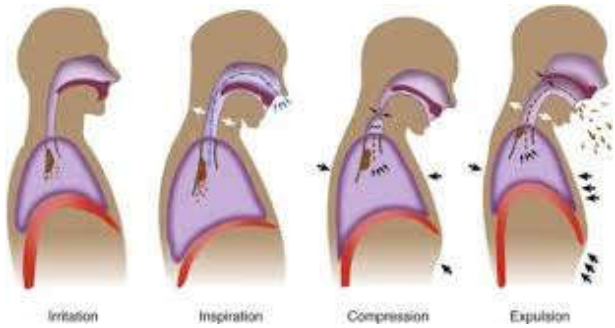
Lung Disease



- Breathing patterns change with lung disease
- These changes effect total deposition
  - COPD – higher minute ventilation
  - Bronchitis – increased deposition (narrowed airspaces)
  - Asthma – increased deposition
  - Smokers – increased deposition
  - Smokers - with small airways disease

Kin and Kang AJRCCM 1997

CROSH CRSST



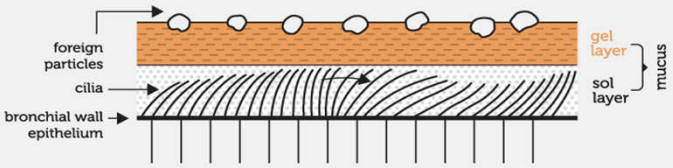
Particle Clearance

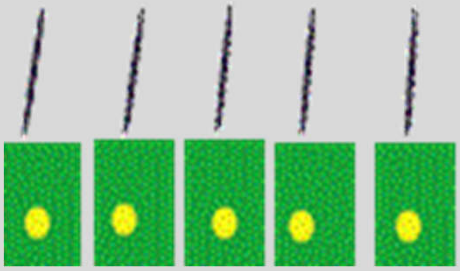
CROSH CRSST

Two main methods:

Upper Airways:
1.physical removal

clearance Time:
~ 2-24 hours

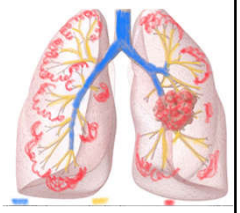




Lower Airways
2.Absorption

direct or via cell uptake

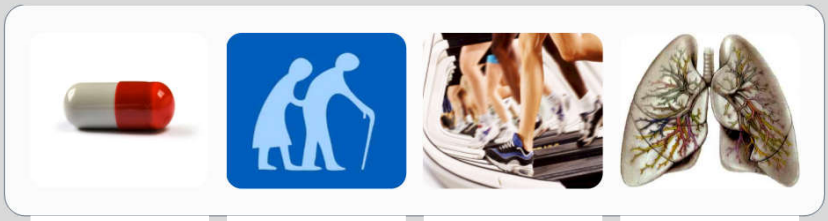
clearance Time:
>24 hours - Months



Clearance Rates

- Location matters
- Size matters
- Total number matters

Biologic alterations in clearance



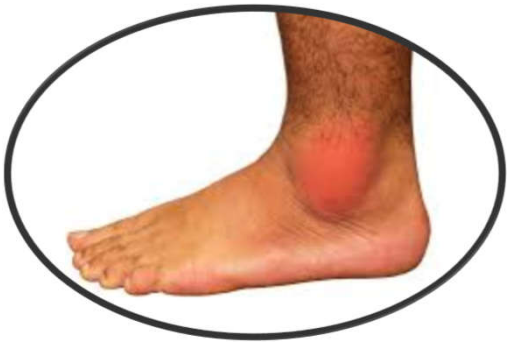
Drugs	Age Immune system	Physical activity	Lung disease

Other

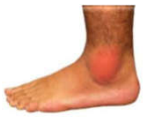
Smoking

Air pollution

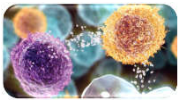
Inflammation



Acute Inflammation



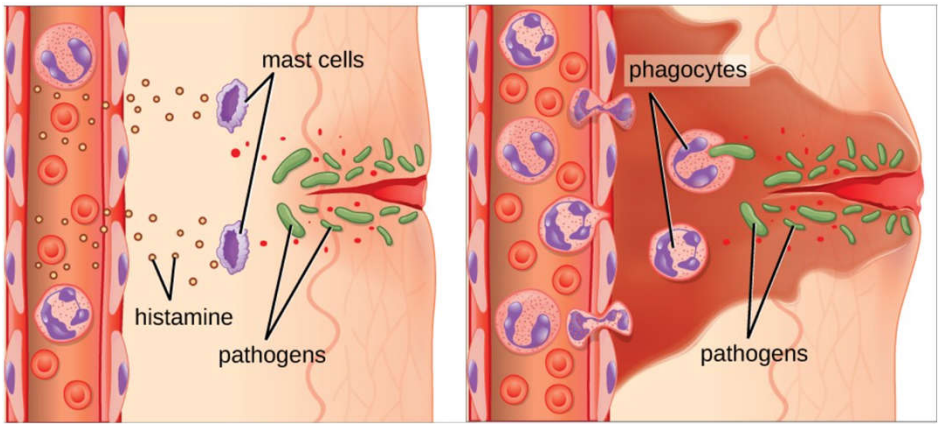
A serious threat triggers Inflammation (e.gs. cut, infection).



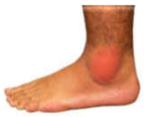
The body releases inflammatory compounds.

The job gets done and anti-inflammatory compounds are released and the body returns to normal.

Acute Inflammation



Acute Inflammation



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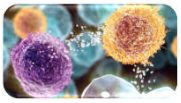
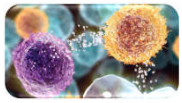


The body releases inflammatory compounds.

The job gets done and anti-inflammatory compounds are released and the body returns to normal.

Chronic Inflammation

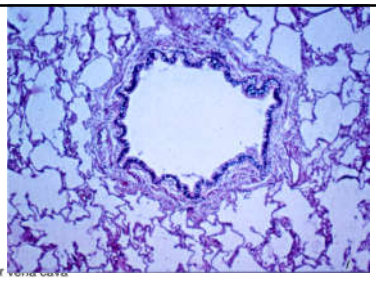
A repeated event that triggers inflammation (e.gs. Diesel particulate, air pollution, smoking, disease).

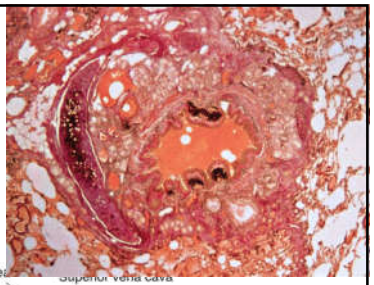


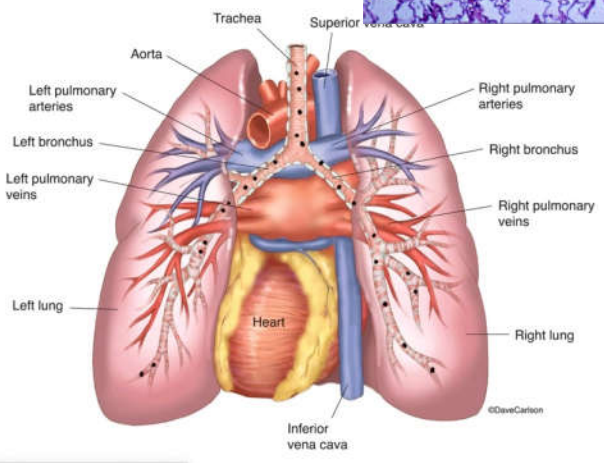
The body releases inflammatory compounds.

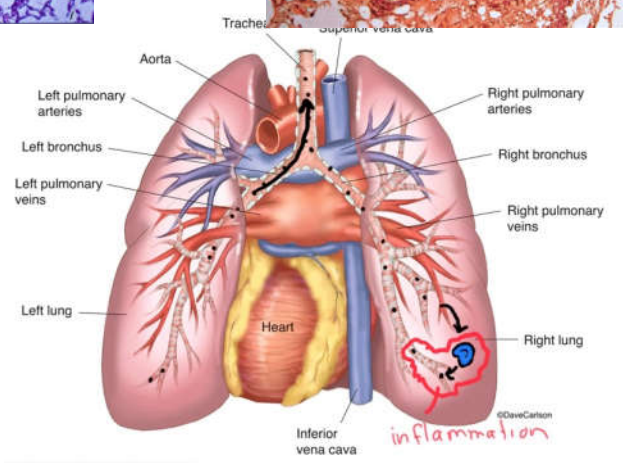
The body is overwhelmed and antioxidants are exhausted: inflammation continues causing progressive cell damage.

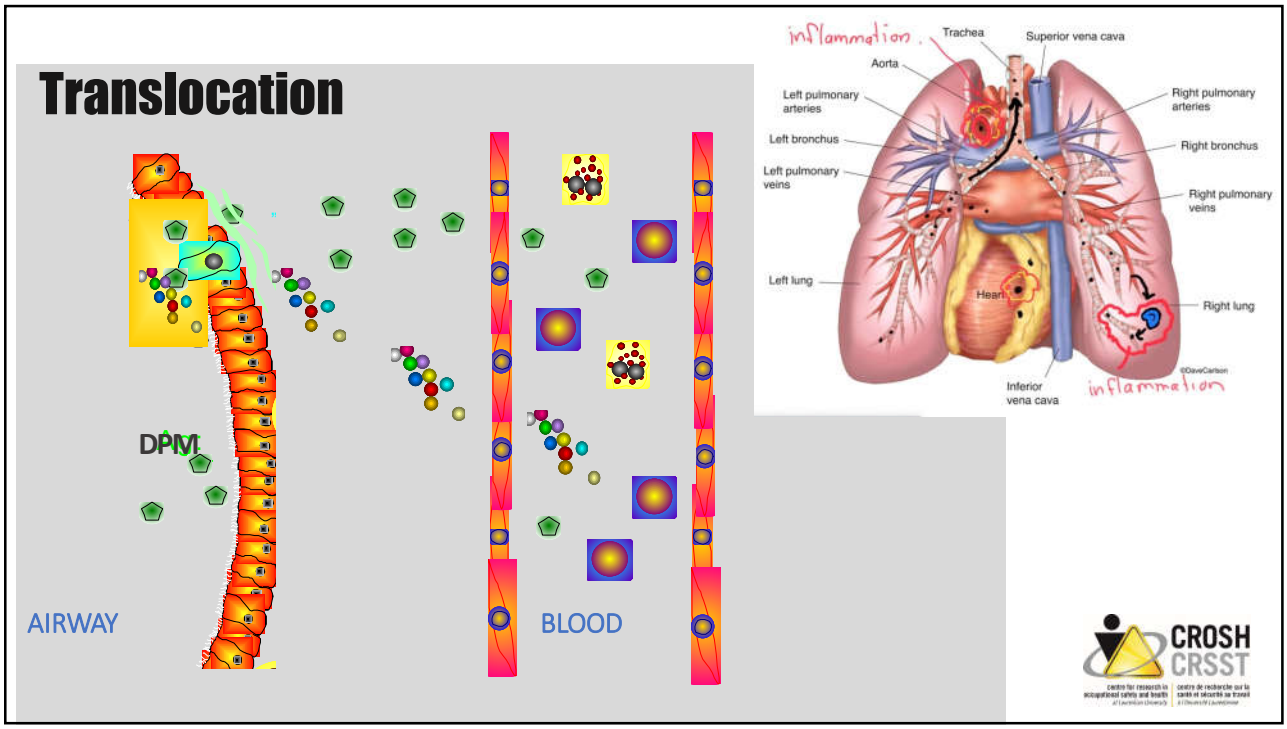
Lung Injury

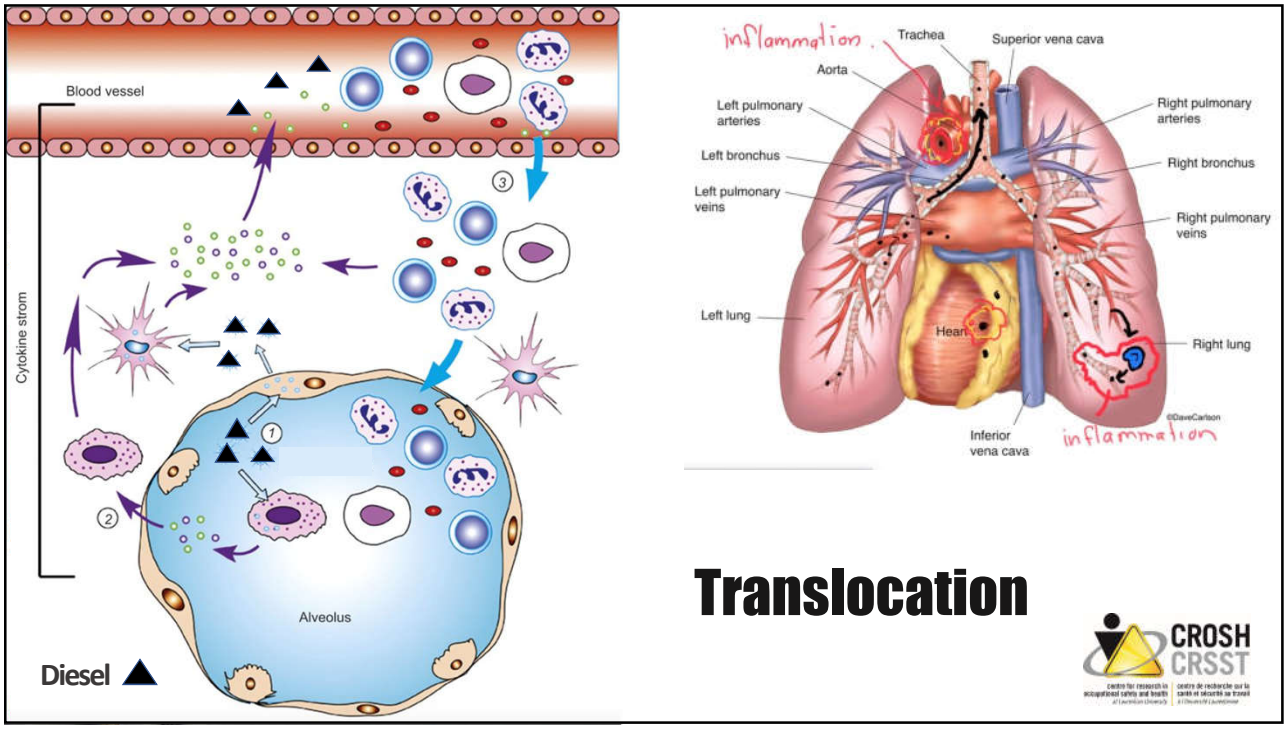








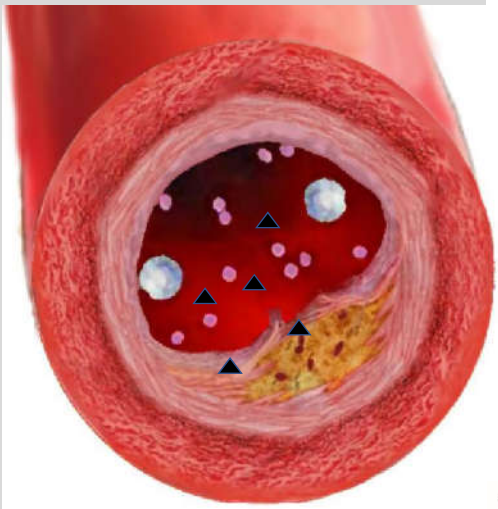

Translocation
DPM
AIRWAY
BLOOD
inflammation
Trachea
Superior vena cava
Aorta
Left pulmonary arteries
Right pulmonary arteries
Left bronchus
Right bronchus
Left pulmonary veins
Right pulmonary veins
Left lung
Heart
Right lung
Inferior vena cava
inflammation
CROSH
CRSST


Blood vessel
Cytokine strom
Alveolus
Diesel
inflammation
Trachea
Superior vena cava
Aorta
Left pulmonary arteries
Right pulmonary arteries
Left bronchus
Right bronchus
Left pulmonary veins
Right pulmonary veins
Left lung
Heart
Right lung
Inferior vena cava
inflammation
Translocation
CROSH
CRSST

Diesel Particles

Effects:

- directly damage vessel wall
- **Induces chronic inflammation**
- increases stickiness of the vessel wall



CROSH CRSST

Blood Vessels

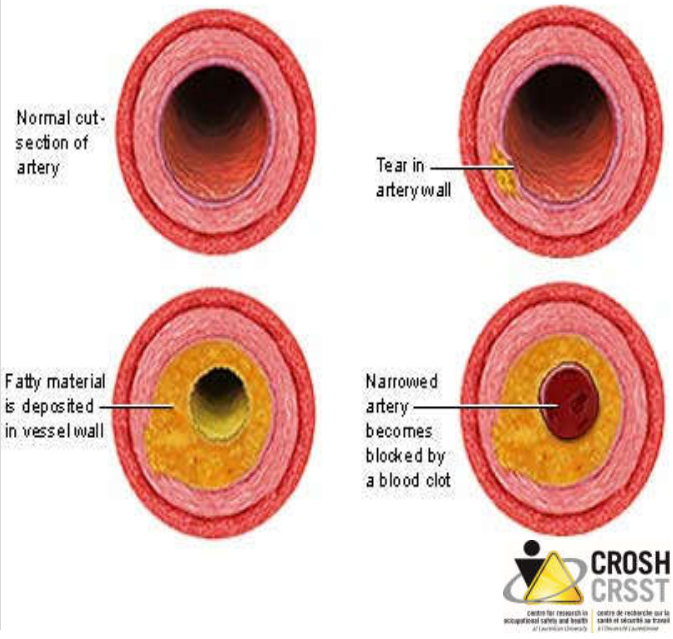
- **Atherosclerosis**

Heart

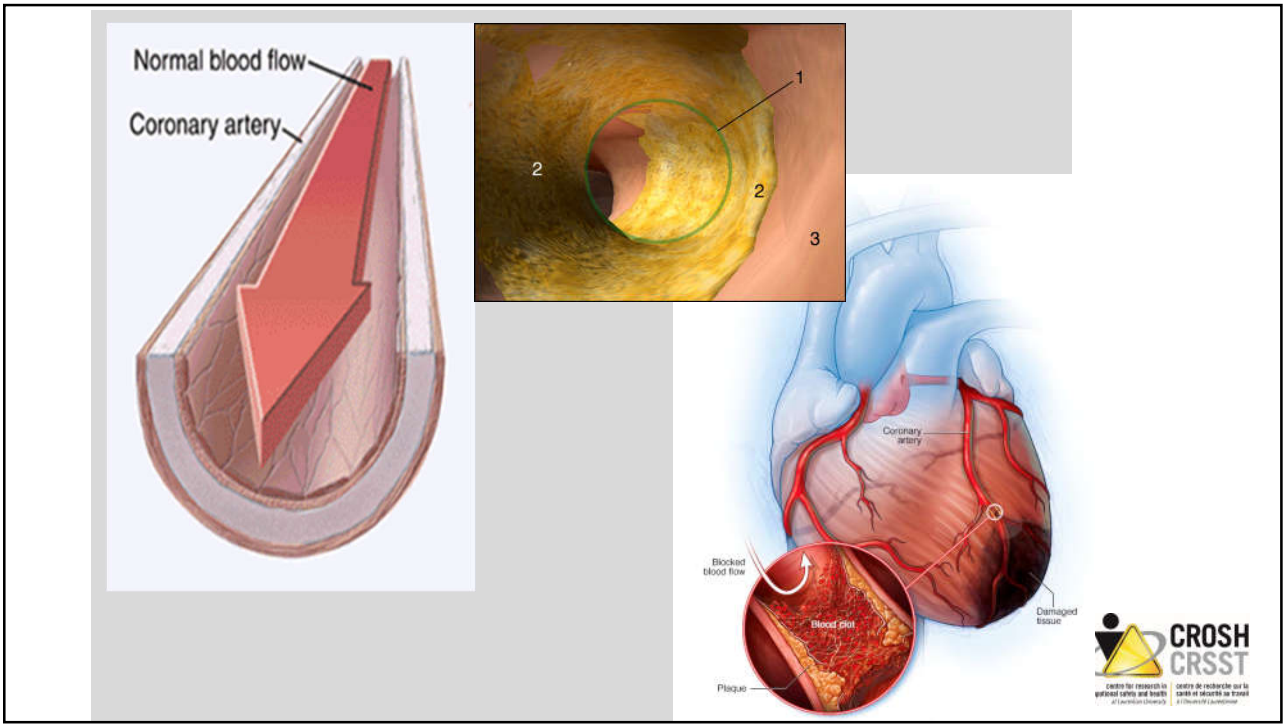
- **Angina**
- **Heart Attack**

Brain

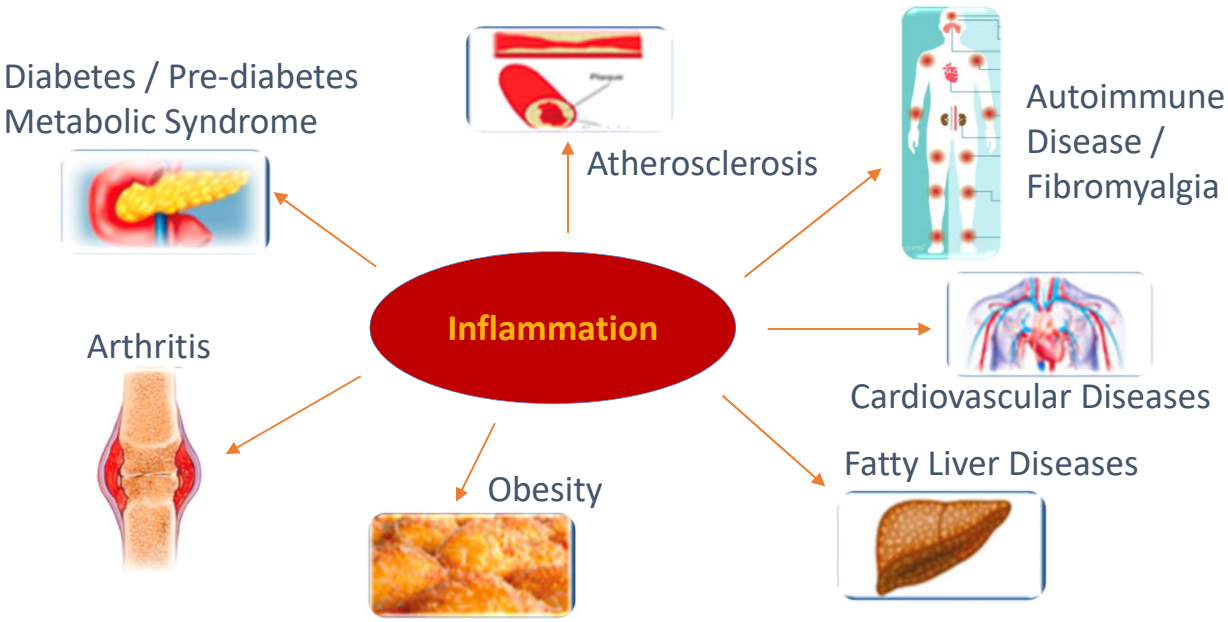
- **Stroke**



CROSH CRSST



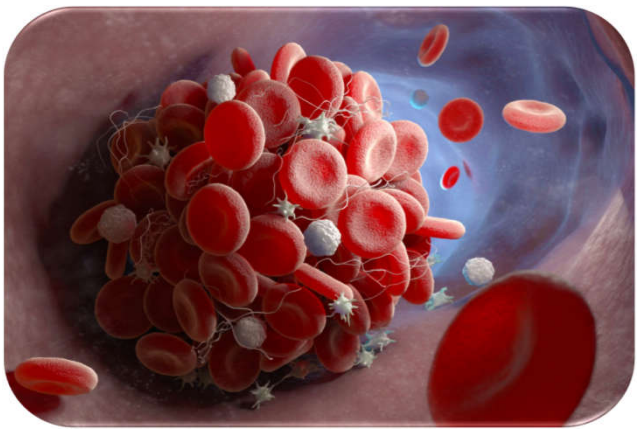
Chronic Inflammation Can Cause or Worsen Chronic Disease

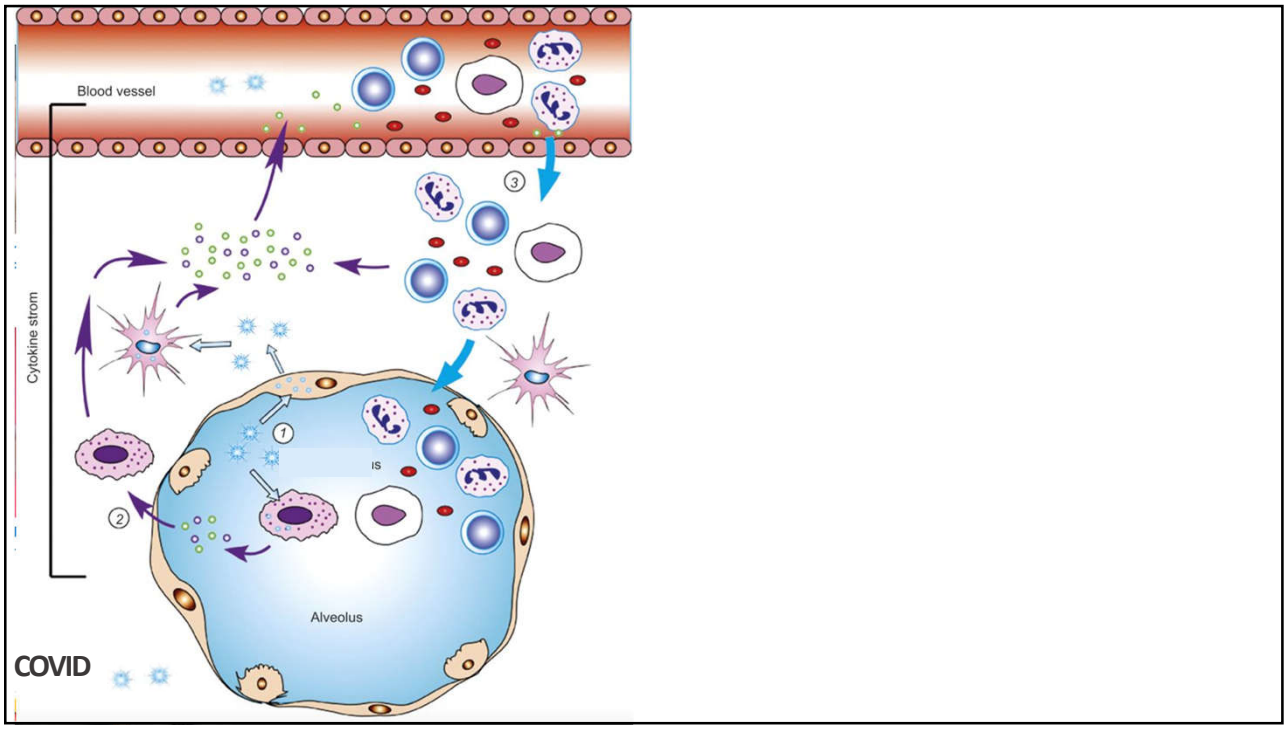


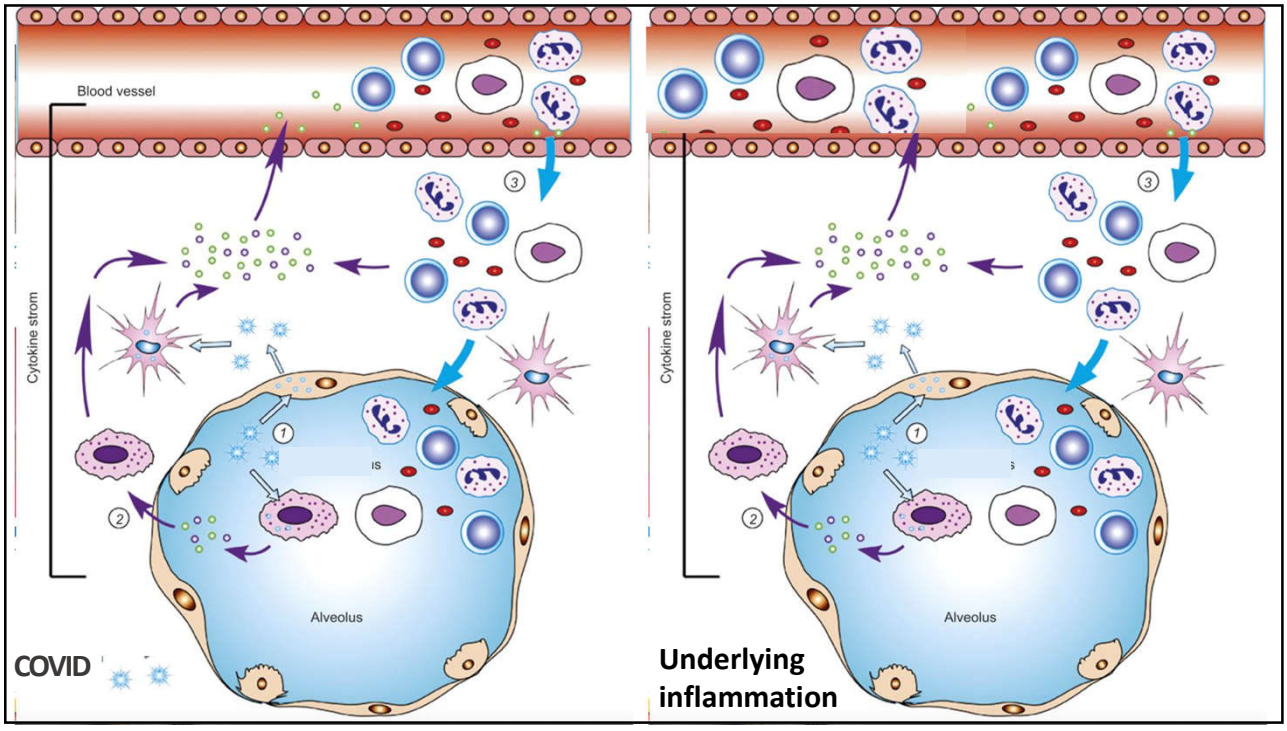
COVID 19

SARS COVID-19

- An Acute Inflammation – that is wide-spread.
- The virus starts in the lungs; but can travel into the rest of the body, via the blood.
- Inflammatory response can also start in the lungs but become wide spread.

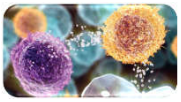



Blood vessel
Cytokine strom
1
2
3
IS
Alveolus
COVID


Blood vessel
Cytokine strom
1
2
3
IS
Alveolus
COVID
Cytokine strom
1
2
3
Alveolus
Underlying
inflammation

Covid-19 No Baseline inflammation

Covid-19 enters the body; stimulates an immune response.



Immune system reacts; including inflammatory response.

COVID is eradicated; immune system retreats.

Covid-19 + Low-Level Inflammation

Covid-19 enters the body and stimulates an immune response.

The inflammatory response **builds on top of the current inflammation – inflammatory storm.**

The body is overwhelmed and inflammation continues causing progressive cell damage.

Pre-existing conditions

People who smoke / have lung disease

People with diabetes / pre-diabetes/ obese

People with high blood pressure/atherosclerosis/heart disease

Older individuals (inflam-aging)

? people regularly exposed to air pollution, like DPM

CROSH CRSST

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Conference Reference

To reference:

S.C. Dorman. The Air We Breathe: particle deposition in the airways.

Center for Research in Occupational Safety and Health (CROSH)

Goodman School of Mines Webinar, September 16th, 2020.

Centre for Research in Occupational Safety and Health
CROSH

CROSH brings together industry, labour groups, safe workplace associations, government organizations and researchers to solve important occupational health and safety issues with the goal of achieving

PREVENTION THROUGH RESEARCH

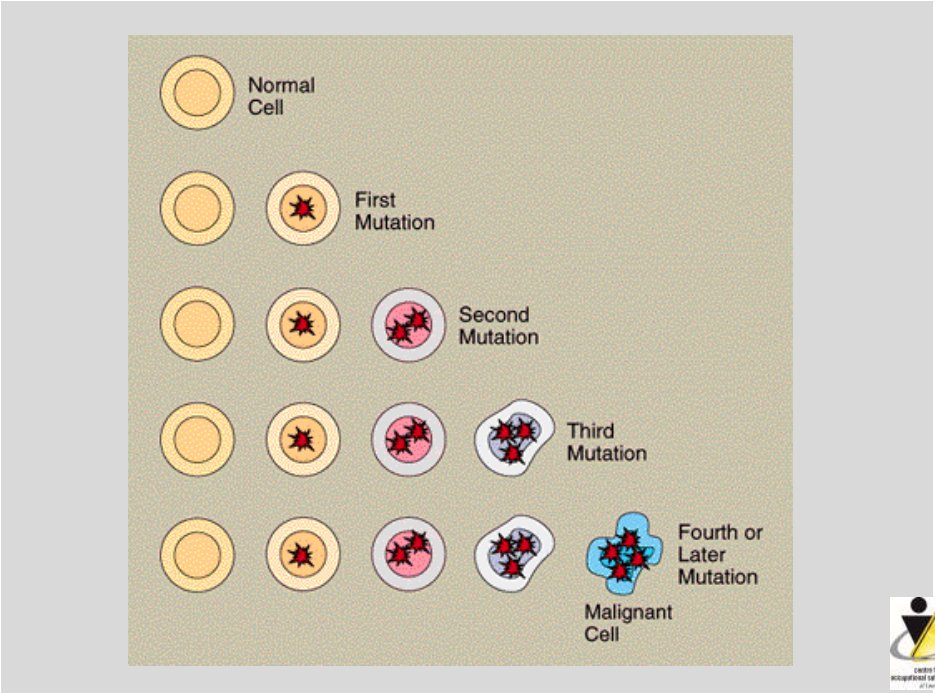
Cancer risk

Organization & year	Animal Data	Human Data	Overall evaluation
NIOSH ‘88	Confirmatory	Limited	Potential Occupational carcinogen
IARC ‘89	Sufficient	Limited	Probably carcinogenic to Humans
IPCD ’96	Not evaluated	Not evaluated	Probably carcinogenic to humans
EPA ‘98	Demonstrated carcinogenicity	Consistent evidence for a causal association	DPM classified as a toxic air contaminant
NTP ‘00	Supporting animal & mechanistic data	Elevated lung cancer in occupationally exposed groups	DPM-reasonable anticipated to be a carcinogen
EPA ‘02	Adequate evidence for carcinogenicity	Probable human carcinogen	Probably human carcinogen (Group B1) “Likely to be carcinogenic to humans by inhalation” and this evaluation applies to environmental exposures.”
IARC ’12	Adequate evidence for carcinogenicity	Human Carcinogen	Designated human carcinogen (Group 1)

Adapted from: Foster & Costa: Lung Biology in Health and Disease; Vol 204

Cancer: Properties of Cells

- Starts from a single cell that has had multiple attacks causing changes to the cell’s genome.
- Causes abnormal replication.
  - Cancer cells do not respond to normal growth regulatory signals, from other cells
- As the cells multiply they continue to mutate allowing them to flourish at the expense of surrounding cells



Diesel Particulate

- Diesel particulate matter has within it many different chemicals
- Some of which are known carcinogens (NO2-PAHS)
- Many of which are capable of producing oxygen radicals & oxidative stress (which can also cause genetic mutations)

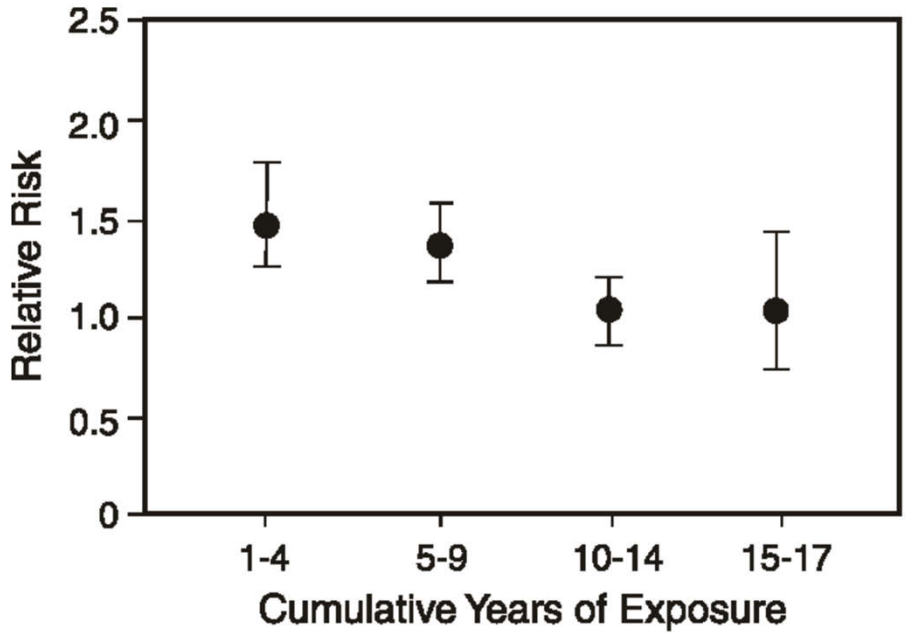


Figure 4. Relative risk of lung cancer by years of exposure to diesel

Published in Diesel Emissions and Lung Cancer : Epidemiology and Quantitative Risk AssessmentArchibald Cox, Douglas M. Costle