Linkages between air pollution, COVID-19, and human health

Illustration courtesy CDC

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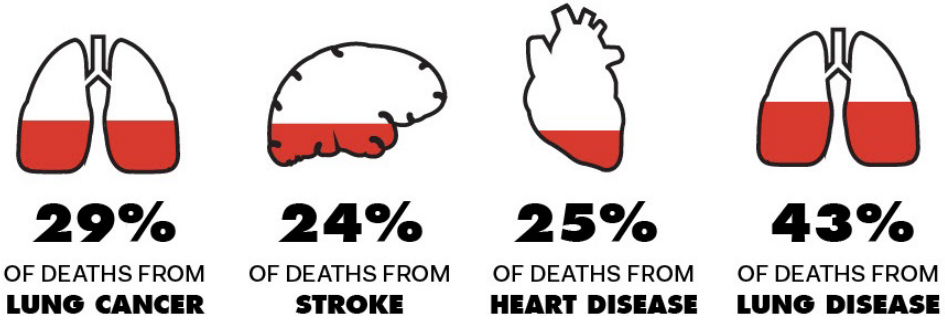
The What

Air Pollution vs COVID

Short-term and long-term exposure to air pollution (esp $PM_{2.5}$ and NO_2) may contribute to higher rates of COVID-19 infection and mortality.

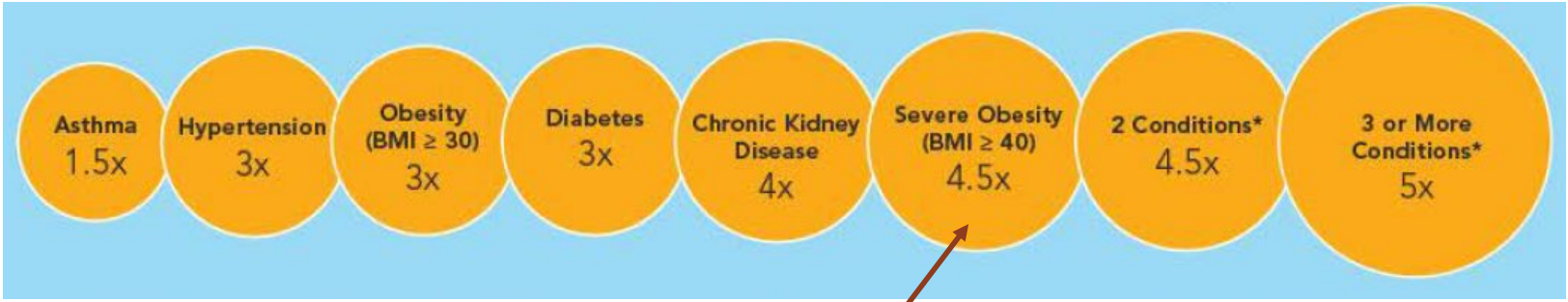
Disease Similarities

Air Pollution



- ✓ Asthma
- ✓ Hypertension
- ✓ Obesity
- ✓ Heart Attack
- ✓ Diabetes

COVID



Risk of COVID hospitalization

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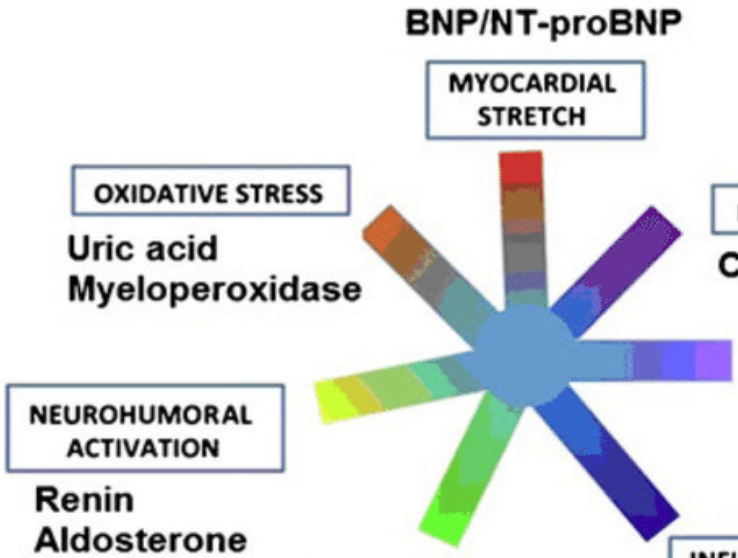
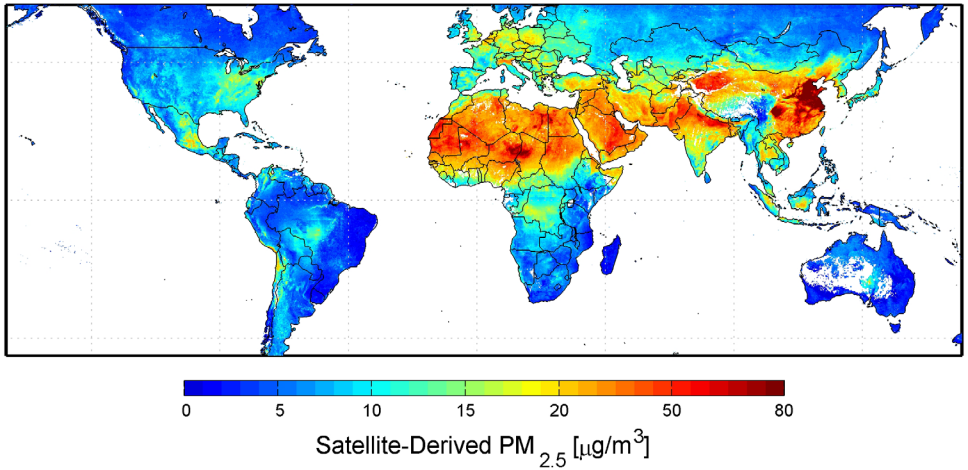
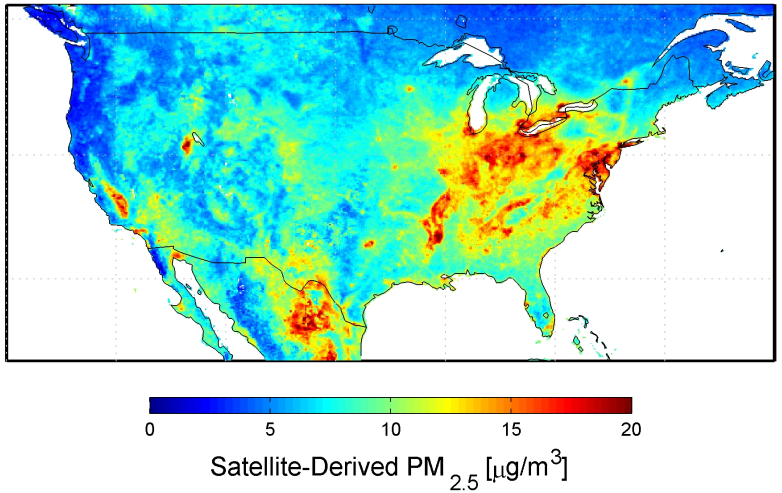
Air Pollution and COVID: Widespread Inflammatory Impacts



Others:
Electrolytes
Liver function tests
Thyroid function tests
Complete blood count
Iron studies

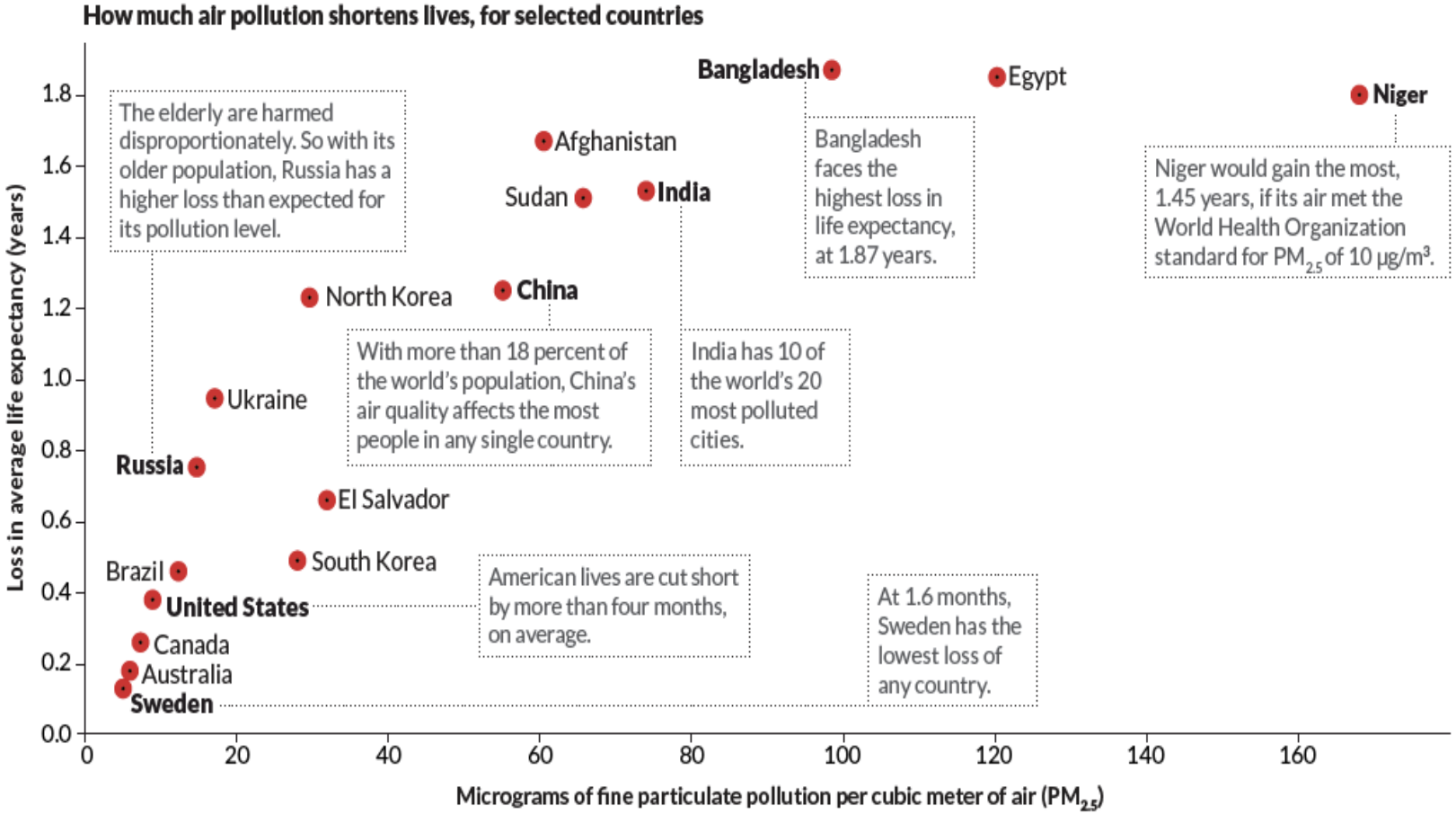
PM2.5 Levels Worldwide





Courtesy of nasa.gov

$PM_{2.5}$ is shortening lives around the world



Science News, 29 set. 2018. v. 194, n. 6, p. 32.

Breathing more polluted air worsen the effects of COVID-19

- ✓ China study of 120 cities and found a significant relationship between air pollution and COVID-19 infection. (Zhu, 2020)
- ✓ NO2 increased by 10 ug/m3 in the five years before the pandemic had 22% more Covid-19 cases vs PM had a 15% increase. (Tian, 2020; Wang, 2020)
- ✓ Yao et al found that air pollution was positively associated with increased COVID-19 mortality. (Yao, 2020)
- ✓ NO2 associated with the transmission ability of COVID-19. (Yao, 2021)
- ✓ The United Kingdom's Office for National Statistics found that without controlling for ethnicity, long-term exposure to fine particulate matter could increase the risk of contracting and dying from COVID-19 by up to 7%. (United Kingdom's Office for National Statistics, August 13, 2020)
- ✓ 1 µg/m3 PM2.5 x 9.4 more COVID-19 cases, 3 more hospital admissions, and 2.3 more deaths in Netherlands city (Cole, 2020)
- ✓ For deaths in 66 regions of Italy, Spain, France & Germany, 78% of them occurred in most polluted 5 regions (Ogen, 2020)
- ✓ Mortality in northern Italy assoc w/ with the highest levels of air pollution. (Conticini, 2020)
- ✓ Petroni et al found an increase in exposure to hazardous air pollutants (HAPs) is associated with a 9% increase in COVID-19 mortality. (Environmental Research Letters, September 11, 2020)
- ✓ US long-term elevated pollution assoc with 8% increase in mortality for every 1 ug/m3 increase in PM2.5 (Wu, 2020)
- ✓ 4.6 ppb increase NO2 from traffic assoc w/ 11% increase in mortality. (Liang, 2020)
- ✓ Increase in NO2 of 8.7 ppb assoc w/ 35–60% increase in incidence & mortality in LA County (Lipsitt, 2021).

Air Pollution associated with prior epidemics and influenza

SARS

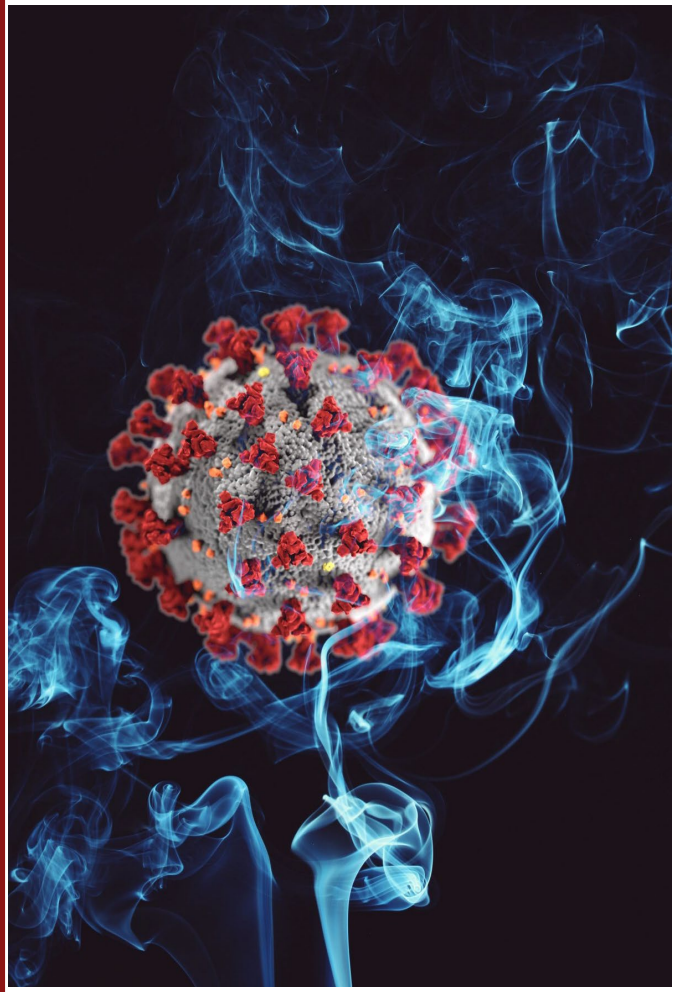
- ✓ **H**ighly polluted area of China twice as likely to die from SARS than someone in an area with cleaner air (Cui, 2003)
- ✓ SARS epidemic - increases in particulate matter air pollution increased risks of dying from the disease (Kan, 2019)

MERS

Influenza

- ✓ Researchers have found that several viruses, including adenovirus and influenza virus, can be carried on air particles. Zhao et al found that particulate matter likely contributed to the spread of the 2015 avian influenza. (Scientific Reports, August 13, 2019)

- ✓ Chen et al found that air pollution can accelerate the spread of respiratory infections. (Environment International, January 2017)



Smoking increases respiratory infections, including COVID

Smoking doubles your risk of developing respiratory infections.

- Healthy volunteers (n=391) had 1 of 5 respiratory viruses, including a coronavirus, dropped in a liquid into their noses. Smokers were twice as likely to develop an infection (Cohen, 1993)
- Exposures to SHS and air pollution are associated with significant hypermethylation and decreased expression of *IFN-γ* in Teffs and *Foxp3* in Tregs (Nadeau, 2012).

Smoking doubles your risk of getting sicker from COVID-19

- Smoking is associated with getting sicker with COVID-19. In the largest study of 1099 people with COVID-19, people who smoke were 2.4 times more likely to be admitted to ICU, need mechanical ventilation or dying compared to those who did not smoke (Guan, 2020).

Smoking increases ACE2 receptors.

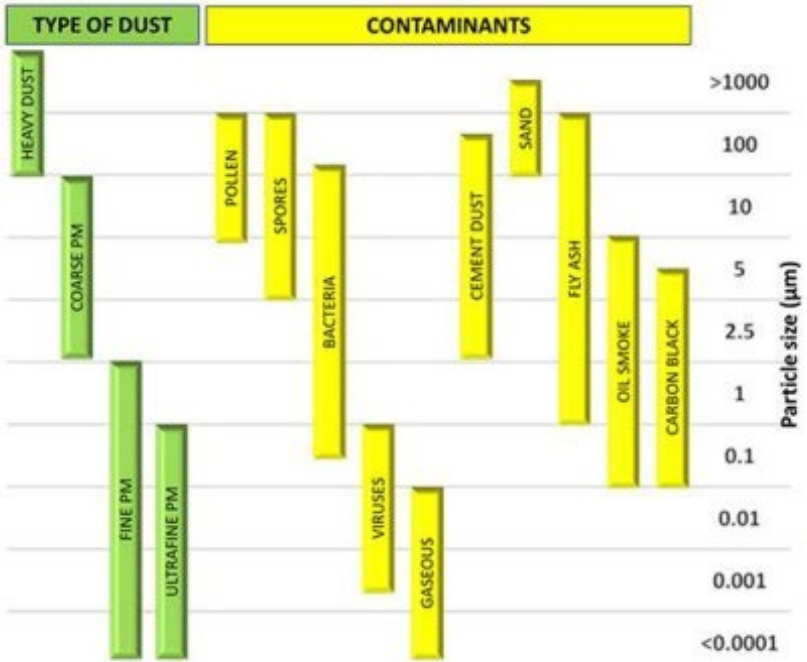
- Goblet cells (mucus-producing) make the most ACE2 receptors.
- Smoking increases goblet cells, increasing the amount of ACE2 in the lungs (Sheltzer, 2020)

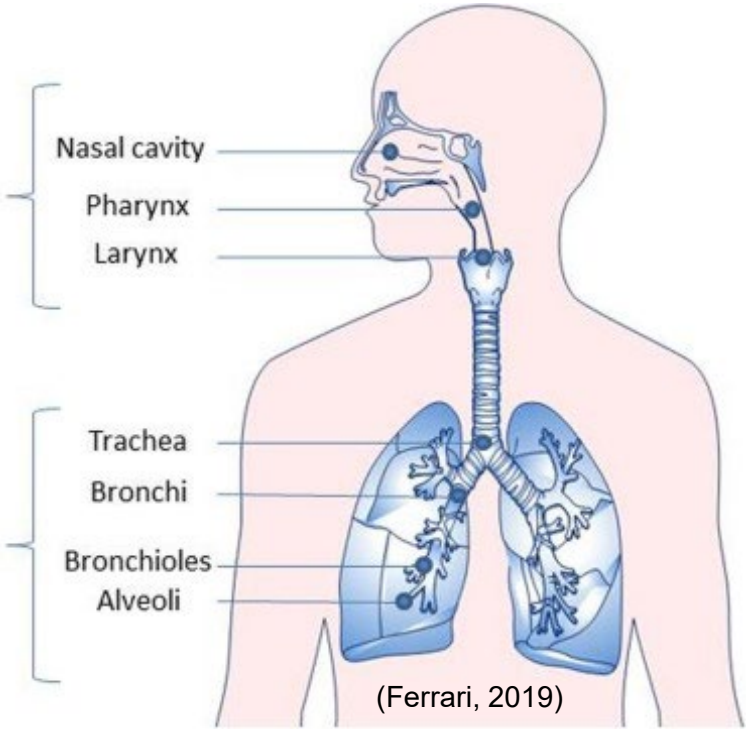
The Why

The Immune System

Air pollution exposure impairs the immune systems ability to defend against COVID

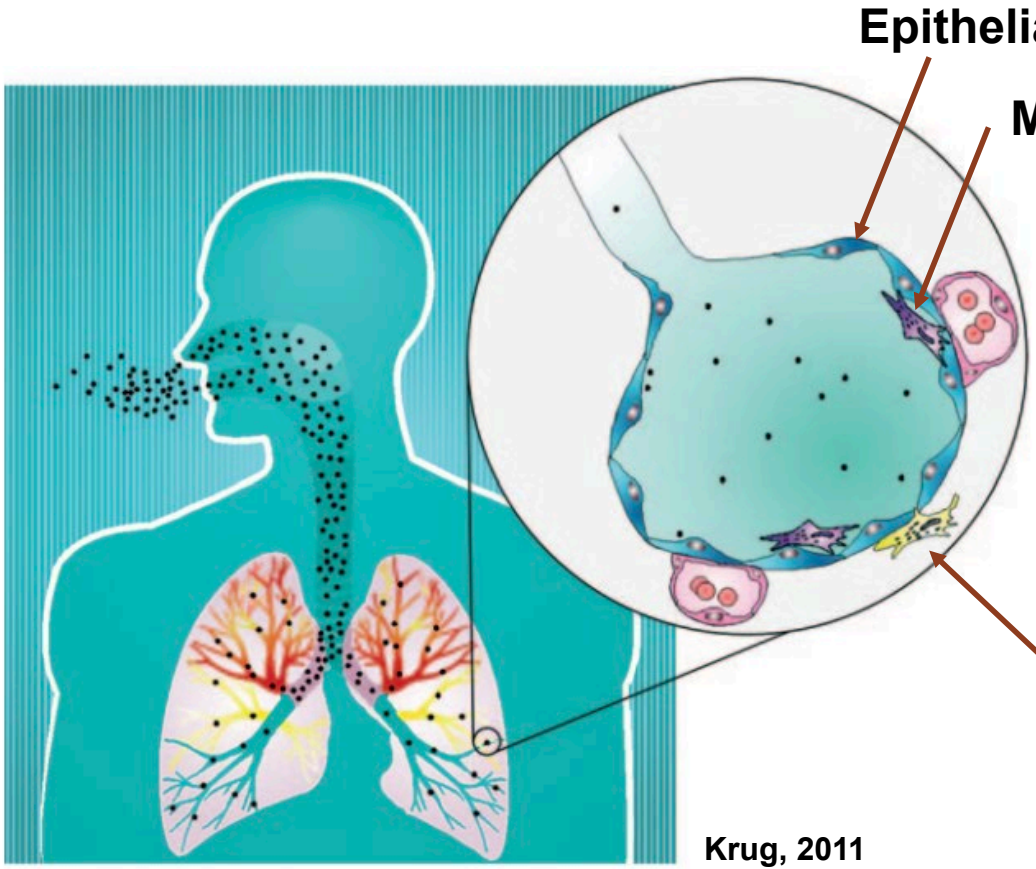
Depth of Inhalation Varies with Size





(Ferrari, 2019)

Wildfire Smoke Inhalation: Alveolar Barrier



Krug, 2011

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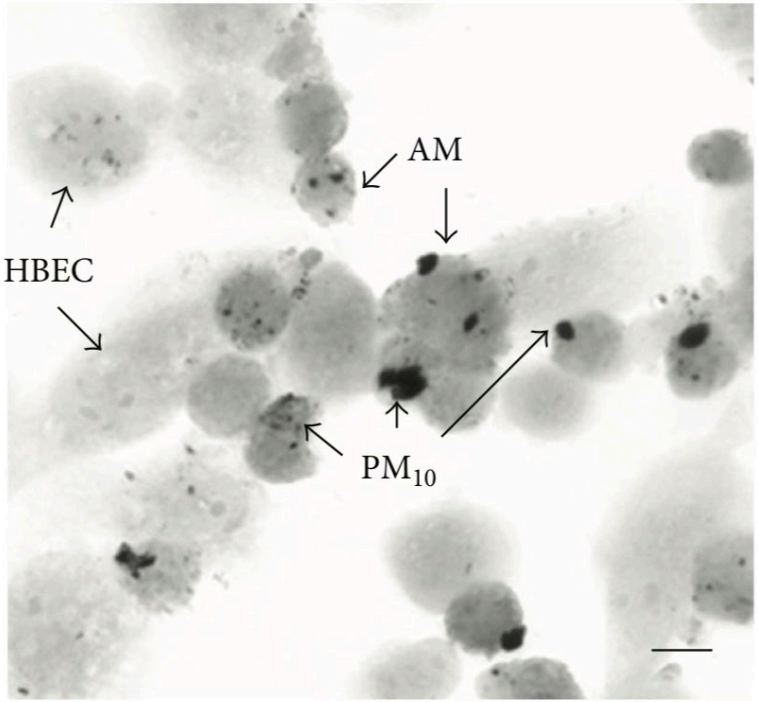
Alveolar Macrophages



Hiraiwa, 2013

- Interact with other lung cells (e.g. bronchial epithelial cells and dendritic cells) to try to clear the PM from the lung
- mobilization of inflammatory cells from the bone marrow into the circulatory system
- production of acute phase proteins by the liver
- increase in circulating inflammatory mediators

COVID-19

HOW DOES IT AFFECT YOU?

Designed by Avesta Rastan
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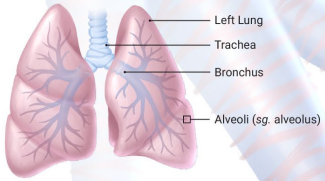
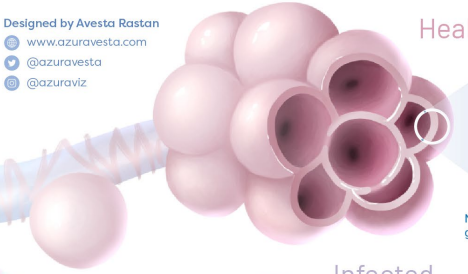
Coronavirus Disease 2019 (COVID-19) is a pandemic caused by Severe Acute Respiratory Syndrome Coronavirus 2, also called SARS-CoV-2. Despite the widespread awareness regarding COVID-19, many are still unaware about how it affects the human body.

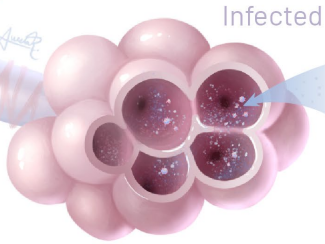


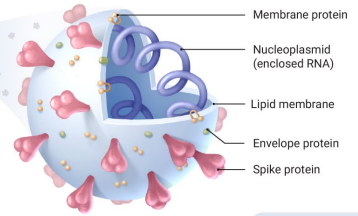
SARS-CoV-2 starts its journey in the nose, mouth, or eyes and travels down to the alveoli in the lungs. Alveoli are tiny sacs of air where gas exchange occurs.



Gas Exchange

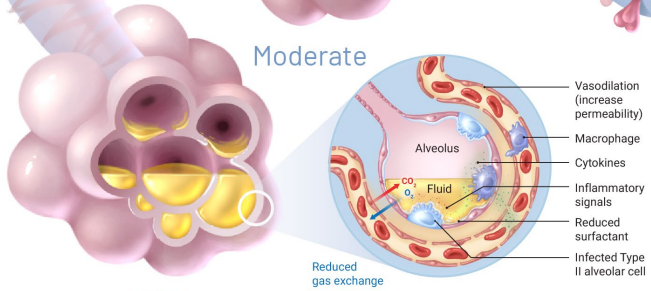
Each sac of air, or alveolus, is wrapped with capillaries where red blood cells release **carbon dioxide** (CO_2) and pick up **oxygen** (O_2). Two alveolar cells facilitate gas exchange; **Type I** cells are thin enough that the oxygen passes right through, and **Type II** cells secrete **surfactant** – a substsance that lines the alveolus and prevents it from collapsing.

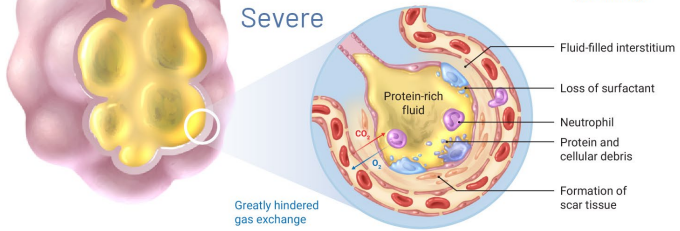




Viral Infection

The spike proteins covering the coronavirus bind ACE2 receptors primarily on type II alveolar cells, allowing the virus to inject its RNA. The RNA "hijacks" the cell, telling it to assemble many more copies of the virus and release them into the alveolus. The host cell is destroyed in this process and the new coronaviruses infect neighbouring cells.





Impaired Gas Exchange

When the immune system attacks the area of infection it also kills healthy alveolar cells. This results in three things that hinder gas exchange:

1) Alveolar collapse due to loss of surfactant from Type II cells
2) Less oxygen enters the blood-stream due to lack of Type I cells
3) More fluid enters the alveolus

Stay Home

Symptoms may start to show (e.g. dry cough, fever, etc.)

Pneumonia develops

Shortness of breath

Hospitalization

Dangerous for high-risk individuals; secondary infections may occur

Intensive Care (ICU)

Patients may require ventilators and life-support

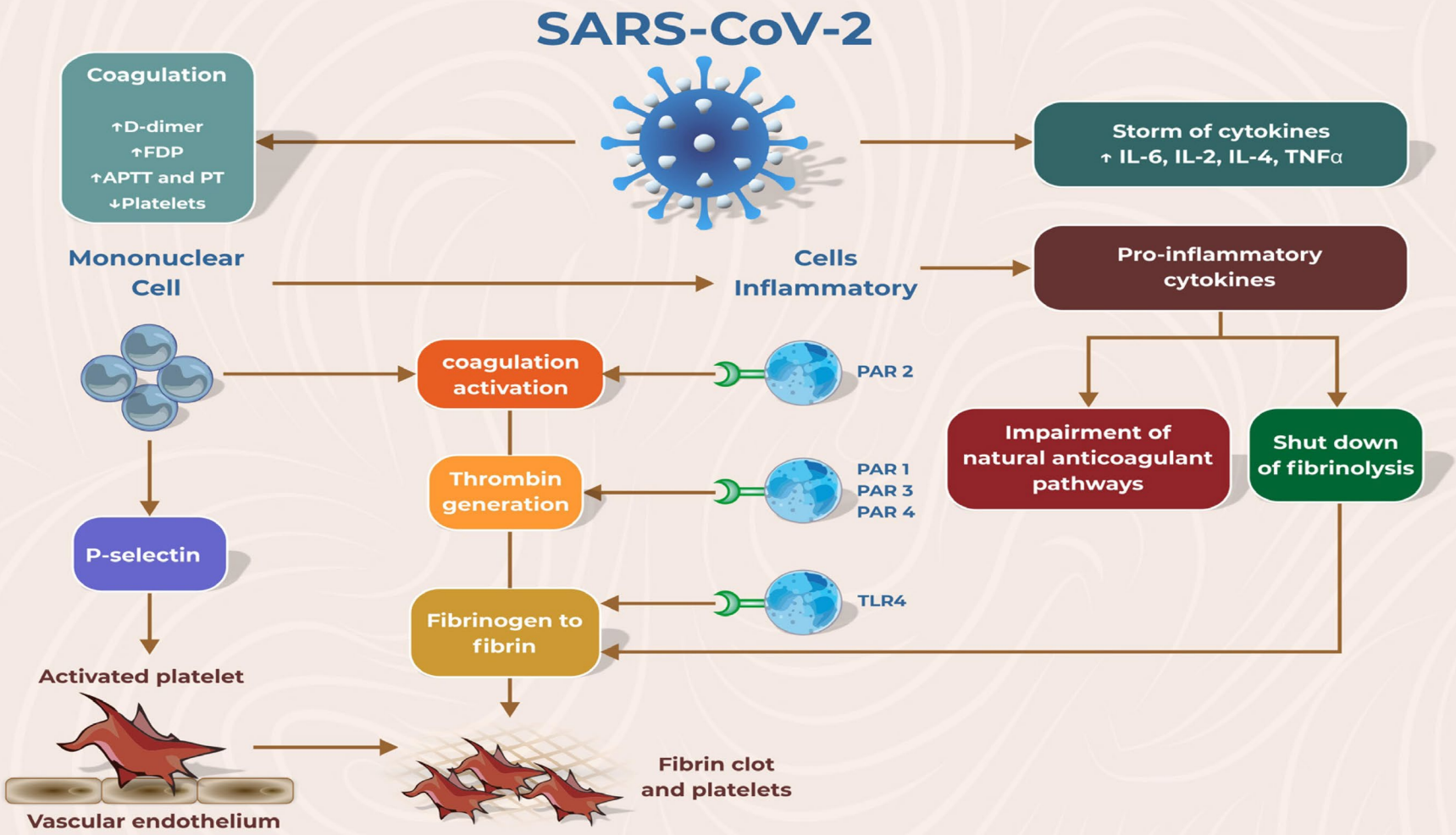
Complications unrelated to COVID-19 may occur

With proper care, patients may recover at any point during this process

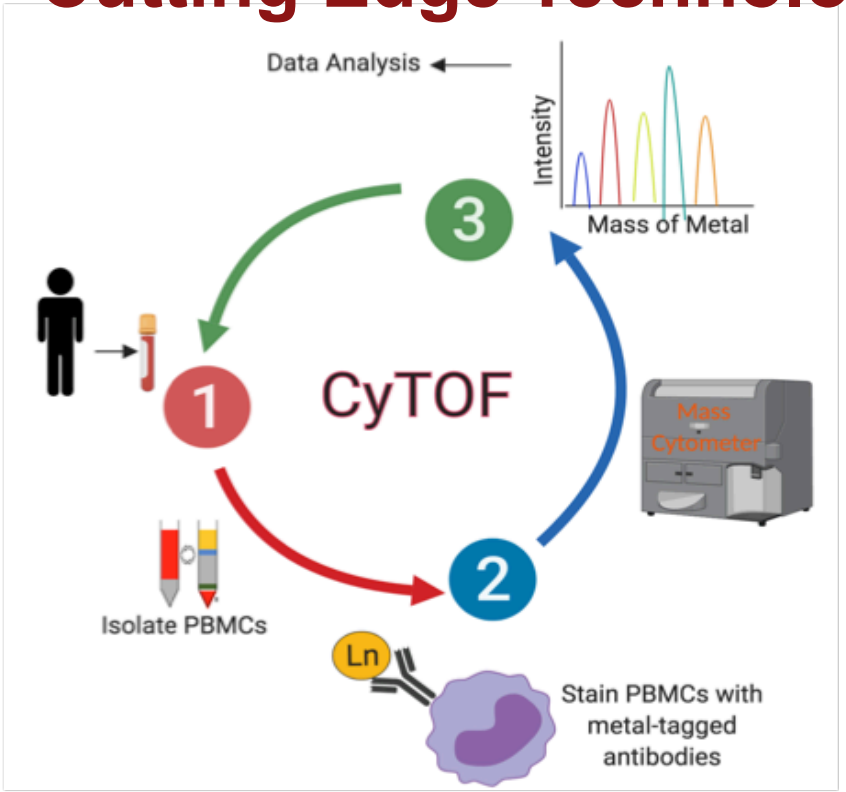
Immune Response

1. After infection, Type II cells release **inflammatory signals** that recruit **macrophages** (immune cells).
2. Macrophages release **cytokines** that cause vasodilation, which allows more immune cells to come to the site of injury and exit the capillary.
3. Fluid accumulates inside the alveolus.
4. The fluid dilutes the surfactant which triggers the onset of alveolar collapse, decreasing gas exchange and increasing the work of breathing.
5. **Neutrophils** are recruited to the site of infection and release Reactive Oxygen Species (ROS) to destroy infected cells.
6. Type I and II cells are destroyed, leading to the collapse of the alveolus and causing **Acute Respiratory Distress Syndrome** (ARDS).
7. If inflammation becomes severe, the protein-rich fluid can enter the bloodstream and travel elsewhere in the body, causing **Systemic Inflammatory Response Syndrome** (SIRS).
8. SIRS may lead to **septic shock** and **multi-organ failure**, which can have fatal consequences.

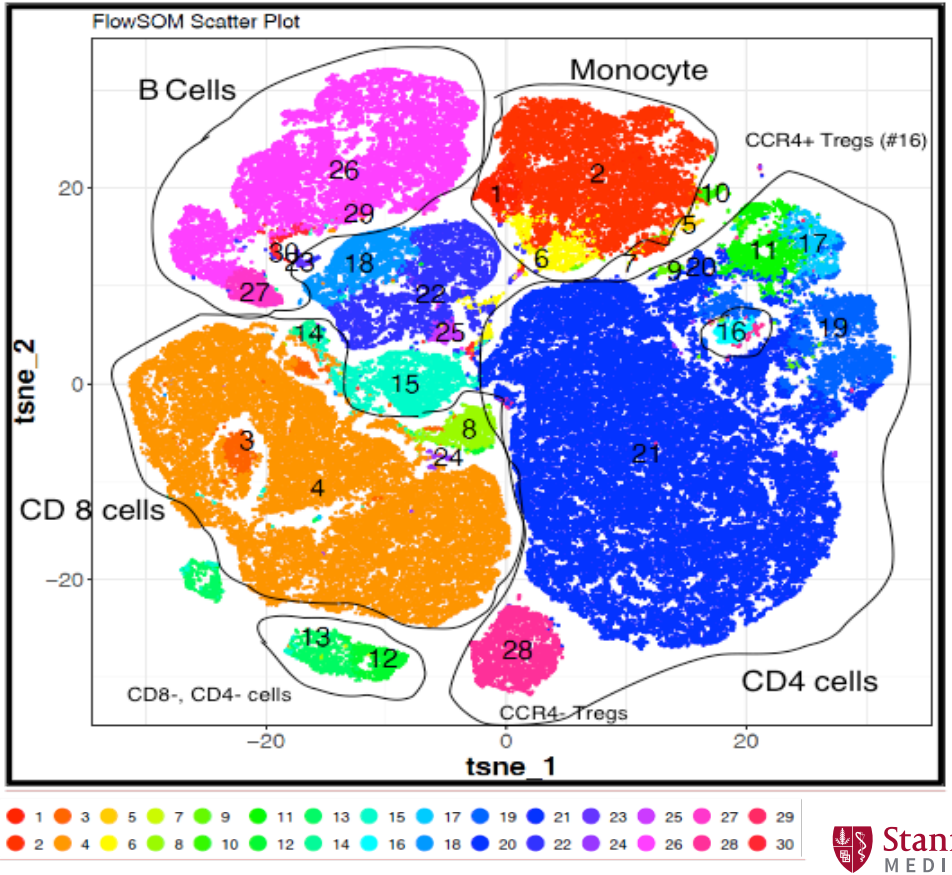
Courtesy of visualcapitalist.com


SARS-CoV-2
Coagulation
↑D-dimer
↑FDP
↑APTT and PT
↓Platelets
Storm of cytokines
↑ IL-6, IL-2, IL-4, TNFα
Mononuclear Cell
Cells Inflammatory
Pro-inflammatory cytokines
coagulation activation
PAR 2
Impairment of natural anticoagulant pathways
Shut down of fibrinolysis
Thrombin generation
PAR 1
PAR 3
PAR 4
P-selectin
Fibrinogen to fibrin
TLR4
Activated platelet
Vascular endothelium
Fibrin clot and platelets

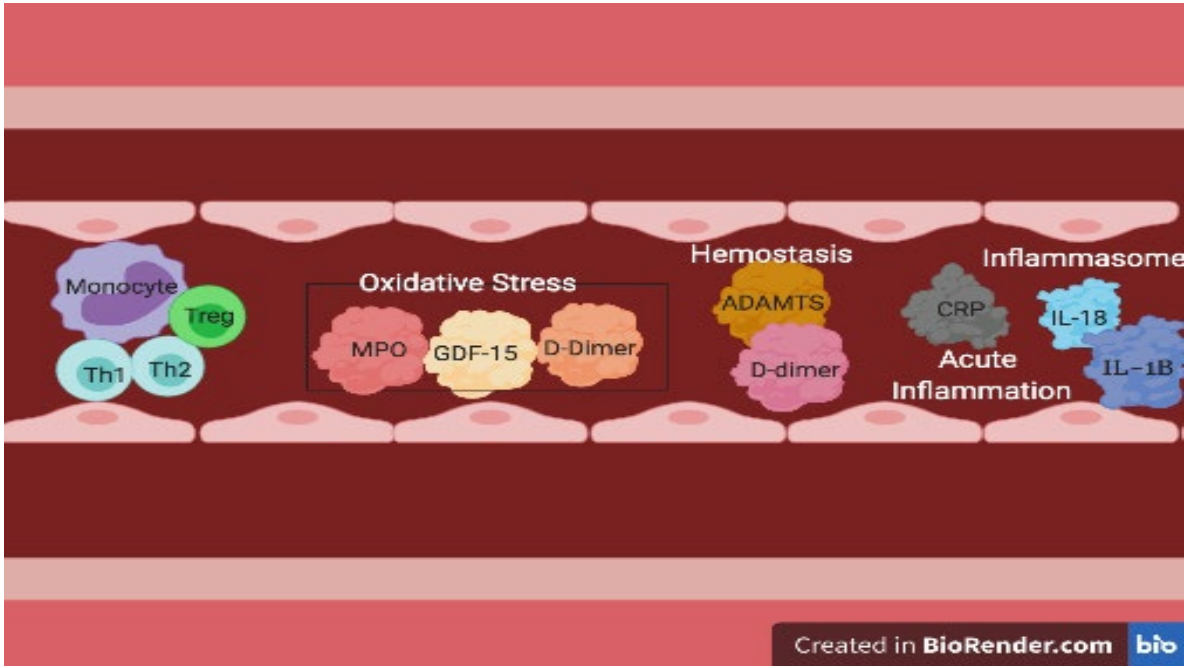
Cutting Edge Technology



Immune Cell Plot



Inflammatory Biomarkers are Assoc with Air Pollution and COVID



Air pollution exposure is linked with methylation of immunoregulatory genes, altered immune cell profiles, and increased blood pressure in children. (Prunicki, 2021).

With Appreciation, Patients and Families, Clinical and Laboratory Team, Collaborators and funding

NIH National Institute of Environmental Health Sciences

NIH National Institute of Allergy and Infectious Diseases

NIH National Heart, Lung, and Blood Institute

EPA United States Environmental Protection Agency

MATERNAL & CHILD HEALTH RESEARCH INSTITUTE

AMERICAN ACADEMY OF ALLERGY ASTHMA & IMMUNOLOGY

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CHAPS Children's Health & Air Pollution Study