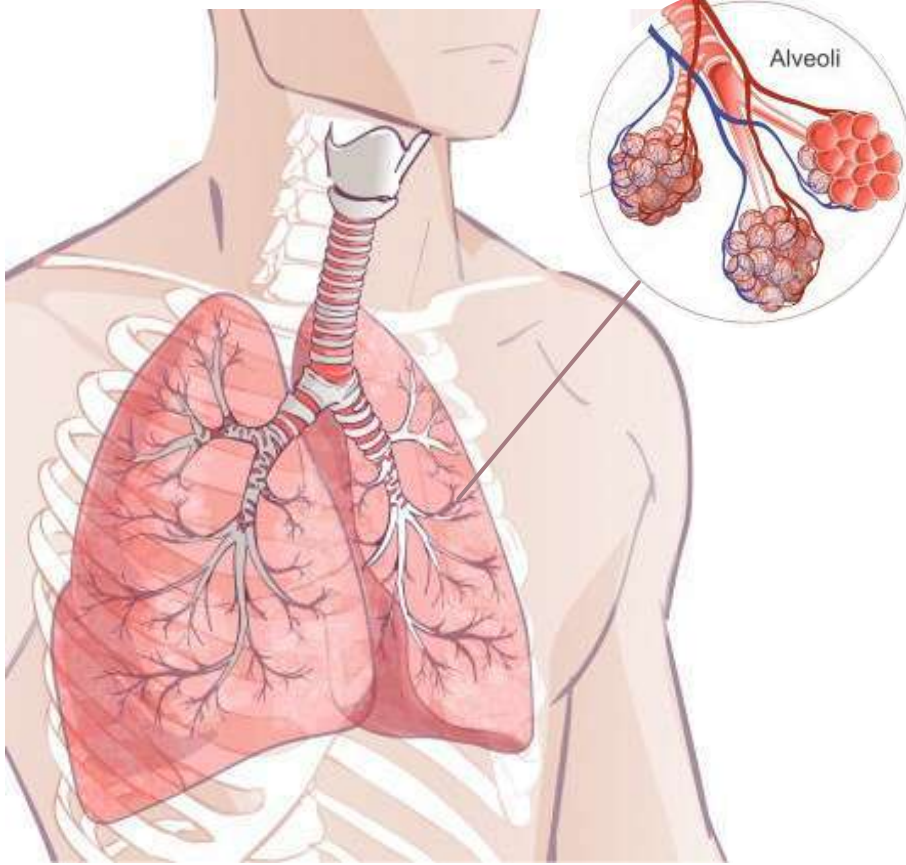


# Understanding Lung Inflammatory Diseases

The therapeutic potentials of mesenchymal stem cell (MSCs)-derived exosomes in lung inflammatory diseases



## Lung

The lungs are a pair of spongy, air-filled organs located on either side of the chest (thorax). Your lungs are part of the respiratory system, a group of organs and tissues that work together to help you breathe.

### Main job

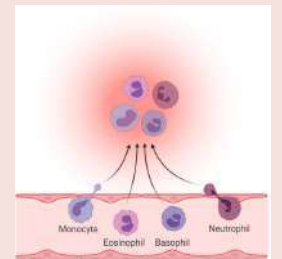
to move fresh air (O<sub>2</sub>) into your body while removing waste gases (CO<sub>2</sub>).

## Alveoli

Alveoli are the small air sacs surrounded by blood capillaries, where the exchange of oxygen and carbon dioxide takes place.

## What is Inflammation?

Inflammation is the body's immunity that are mounted in response to invading microbes, noxious stimuli, or tissue injury. During inflammation, numerous types of inflammatory cells are activated. Each releases cytokines and mediators to modify the activities of other inflammatory cells. Orchestration of these cells and molecules leads to the progression of inflammation. Because the lung is a vital organ for gas exchange, excessive inflammation can be life-threatening.



## Risk Factors that may cause Lung Inflammation



Microbe Infection



Air Pollution



Allergens



Toxins

## Acute Lung Inflammation

Acute inflammation is a rapidly induced inflammatory response in the lung when exposing to the triggering factors (e.g. virus).

- Pneumonia
- Acute Respiratory Distress Syndrome (ARDS)

## Chronic Lung Inflammation

Chronic inflammation initially follows the same pathway as an acute inflammatory response. Chronic inflammation occurs if the acute inflammatory response is inadequate to clear the tissue of invading microbes or substances.

- Asthma
- Chronic Obstructive Pulmonary Disease (COPD)

\*\*This poster is used for educational purpose only.

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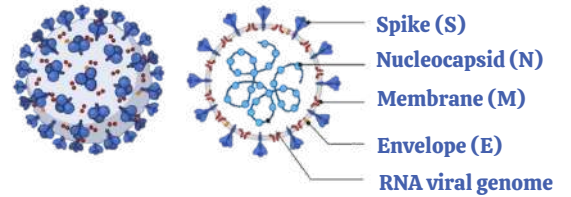
ROOTHEAL  
MEDICAL CLINIC

# An Acute Lung Inflammation Caused by COVID-19 Infection

COVID-19 infection may induce an aggressive inflammatory responses to the lungs that cause a severe lung damage.

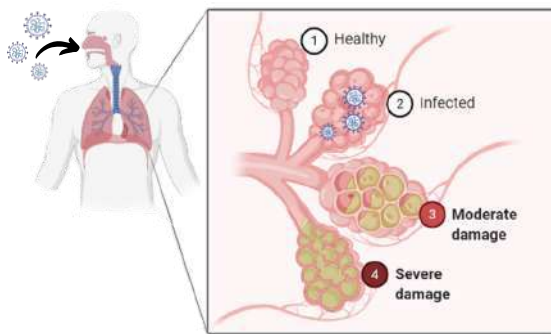
## WHAT IS COVID-19?

A disease caused by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2). SARS-CoV-2 infects people through air droplets. When virus-carrying droplets go into the human body via nose, eyes, or mouth, and travel down the bronchus into the alveoli in the lungs. The virus infects and destroys the cells in the lungs.



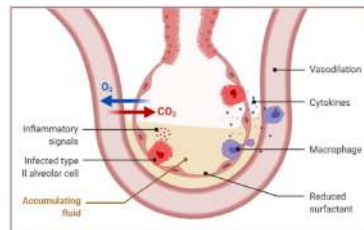
## What does COVID do to lungs

The body's immune system will recruit immune cells to attack the virus, causing acute inflammation happened in the lungs. COVID-19 infection can cause lung complications such as pneumonia and, in the most severe cases, acute respiratory distress syndrome, or ARDS.



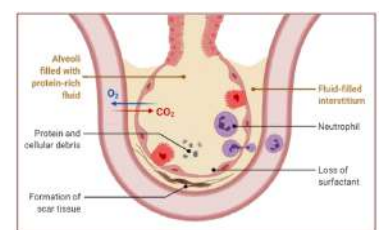
### 3 Moderate Damage

Accumulating fluid, reduced gas exchange



### 4 Severe Damage

Build up of protein-rich fluid, very limited gas exchange



During COVID-19 infection, the immune cells will secrete cytokines, the signaling molecules, to recruit more immune cells. This condition will cause an excessive inflammatory response, in which the release of large amount of pro-inflammatory cytokines by the immune cells can result in the damage of lung tissues. An accumulation of the protein-rich fluid containing dead cells and viruses fills up the space surrounding and inside the alveoli, causing a lessened uptake of oxygen. The infected patient will experience shortness of breathing. A severe infection leads to the formation of scar tissues and the fluid from alveoli can enter the bloodstream and flow through the whole body, causing a systemic inflammation.

## MULTI-ORGAN INFLAMMATION

When the protein-rich fluid enters the bloodstream and flow into elsewhere of the body, the systemic inflammation happens at the organs other than lungs.



Cardiovascular system



Liver



Lungs



Brain



Kidney



Reproductive system

## IS LUNG DAMAGE REVERSIBLE?



After a serious case of COVID-19, there are injuries to the lungs, followed by scarring. A patient's lungs can recover, but it takes time. Over time, the tissue heals, but it can take three months to a year or more for a person's lung function to return to pre-COVID-19 levels.

# An Acute Lung Inflammation Caused by COVID-19 Infection

## Post-COVID syndrome (Long COVID)

Severe lung damage caused by COVID-19 infection leads to the development of the post-COVID syndrome. Signs and symptoms that develop during or after COVID-19 infection, up to 12 weeks or more. The reported symptoms are up to hundreds, while 3 common symptoms are:



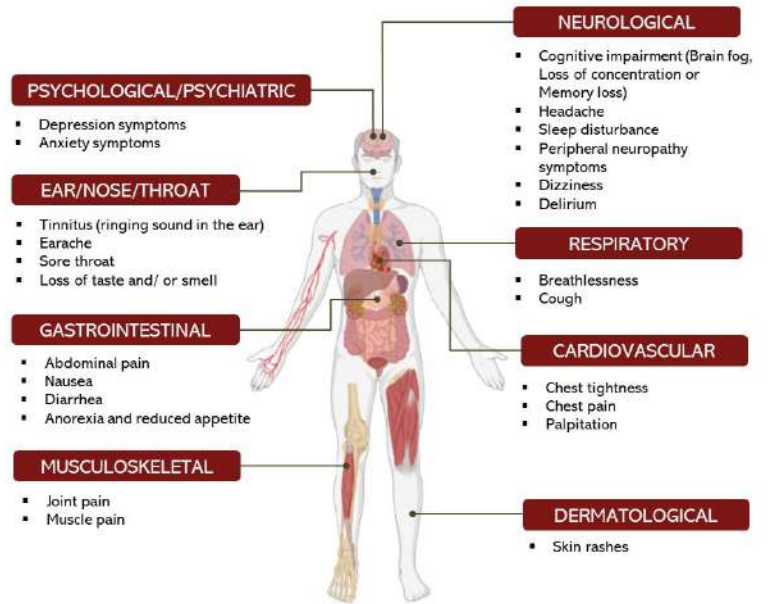
**Shortness of breathing**



**Fatigue**



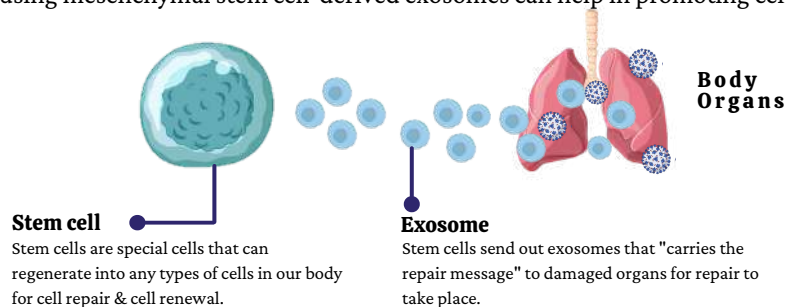
**Cognitive dysfunction**  
(e.g. memory loss)



The lung injury caused by COVID-19 infection may take a longer time to recover. People with long COVID can experience a decrease in lung capacity, worsened lung functions and complications in several organ systems. They may require a long-term rehabilitation in order to get back the quality of life at pre-COVID stage.

## Exosome therapy and Post COVID-19

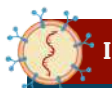
In regenerative medicine, therapy using mesenchymal stem cell-derived exosomes can help in promoting cell regeneration.



### Anti-inflammation & Tissue repair

Exosomes possess distinctive and intrinsic homing property, to move it toward inflammation site in the body, in order to promote healing process. For prolonged inflammation after COVID-19 infection, exosomes help to

- reduce inflammatory reactions & promotes edema clearance
- protect lung tissues from further damage by aggressive inflammation
- promote tissue regeneration by miRNA, growth factors and other bioactive molecules



### Immunomodulation

Exosomes that carry essential growth factors and biological signals can help to 'reprogram' the immune response

- decrease the destructive inflammatory components
- maintain the host response to infections
- enhance the repair and resolution of lung injury



### Anti-fibrotic effect

Lung injury caused by severe inflammation, will develop into scars and thicken over time, which make people hard to breath. Exosomes secrete specific cytokines with anti-fibrotic properties to

- suppress fibroblast proliferation (which is a key to fibrosis)
- have a protective effect to slow down the rate of scarring in the lungs

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# Chronic Lung Inflammation: COPD & Asthma

MSCs and their secreted exosomes are also a potential therapeutic agent in treating chronic inflammation

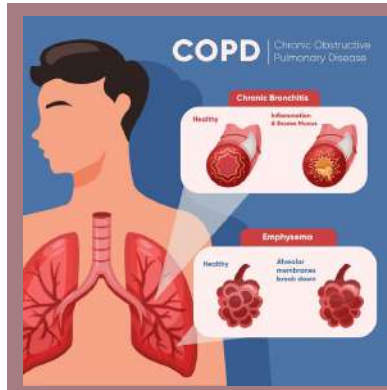
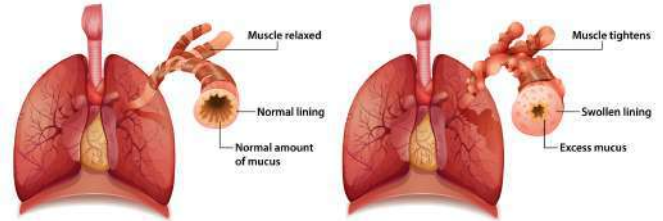
## CIGARETTE SMOKING: A RISK FACTOR FOR VARIOUS LUNG DISEASE



Cigarette smoking is one of the main causes of preventable death, it can cause chronic lung inflammation. It is the leading cause of COPD while one of the main risk factors in developing asthma. A long-term exposure to the cigarette smoking and other lung irritants, such as secondhand smoke, can increase the chance of causing chronic lung inflammation and diseases.

### Understanding Asthma

Asthma is a long-term condition affecting children and adults. Inflammation and narrowing of the small airways in the lungs cause asthma symptoms, such as cough, wheeze, shortness of breath, and chest tightness. High levels of eosinophils (immune cells) cause the inflammation in asthma patients.



### Understanding COPD

Chronic obstructive pulmonary disease (COPD) is the fourth leading cause of death worldwide and a major cause of chronic morbidity and mortality. It is a chronic inflammatory lung disease that causes obstructed airflow from the lungs. **Airway inflammation and alveolar membrane break down** are occurred. Symptoms include breathing difficulty, cough, mucus (sputum) production and wheezing.

## Exosome therapy and Chronic lung inflammatory diseases

During chronic lung injury, inappropriate immune response and/or abnormal repair process causes irreversible damage in lung tissue and most usually results in the development of fibrosis followed by decline in lung function. MSC-derived exosomes have showed several therapeutic potentials on chronic lung inflammation.



### Asthma

High levels of eosinophils causes an inflamed airways blocked with the mucus in asthma patients, resulting in a severe asthma condition. MSC-derived exosomes decrease the levels of pro-inflammatory cytokines (IL-4, IL-5, and IL-13) and the serum levels of immunoglobulin to

- Reduce the mucus production
- Decrease the level of eosinophils that cause the inflammation
- Modulate the immune system and suppress the inflammatory responses



### COPD

MSC-derived exosomes were shown to mediate the up-regulation of the growth factors, VEGF and TGF $\beta$ -1, and the down-regulation of pro-inflammatory mediators (TNF- $\alpha$ , IL-1 $\beta$ , MCP-1, and IL-6) and proteases (MMP9 and MMP12) in lung to:

- Reduce the cell damage caused by inflammation
- Suppress the prolonged inflammation by regulating the immune system
- Improve the lung capacity which determined by the expiration rate

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- [1] Moldoveanu, B., Otmishi, P., Jani, P., Walker, J., Sarmiento, X., Guardiola, J., ... & Yu, J. (2009). Inflammatory mechanisms in the lung. *Journal of inflammation research*, 2, 1.
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