Action for Pulmonary Fibrosis

Introduction

This paper by Steve Jones, Chair at APF summarises recent research published by Prof. Gisli Jenkins which looks at potential links between Covid-19 and pulmonary fibrosis.

The full research paper can be found here: https://www.medrxiv.org/content/10.1101/2020.07.15.20152967v1

Research Summary

Covid-19 and pulmonary fibrosis are both severe diseases involving malfunctioning in the processes by which the body repairs injuries to the lung.

In the case of Covid-19 the injury can be rapid and lead to Acute Respiratory Distress Syndrome (ARDS)[1], a type of respiratory failure involving rapid onset of widespread inflammation of the lungs.

In pulmonary fibrosis, the injury is often slow and involves prolonged exposure to inhaled matter, including chemicals, dust and viruses. The original cause of the injury is often not known (this refers to idiopathic pulmonary fibrosis, IPF) until it is too late, if at all.

Both Covid-19 and IPF disproportionately affect older people, especially men, and people with a cluster of conditions, including obesity, high blood pressure and type 2 diabetes.

Although doctors expect Covid-19 to result in persistent respiratory complications, including progressive forms of pulmonary fibrosis, we do not yet know how many Covid-19 patients will develop progressive pulmonary fibrosis. But, given the large number of people hospitalised with Covid-19, there is likely to be a significant expansion in the number of people living with pulmonary fibrosis in the UK.

Acute lung injury by itself is not sufficient to cause progressive lung fibrosis (we know some severe cases of ARDS and ALI resolve without causing significant loss of lung function). The body' repair systems must also fail in

[1] ARDS is the severe form of Acute Lung Injury (ALI).

ways that promote tissue fibrosis rather than repair, including breakdown in the mechanism by which the process of fibrosis is switched off once lung injury has been resolved.

Scientists think that these malfunctions are linked to genetic variations. We are beginning to understand how this works in pulmonary fibrosis and can be reasonably confident in the case of Covid-19, but research is needed.

The malfunctioning of the body's repair processes may cause:

- a stronger than usual response by the body's immune system, which makes the viral injury worse in Covid-19 (the so-called cytokine storm);
- over-production of fibroblasts – the cells that make the collagen and other materials surrounding the air sacs (alveoli) in the lung, leading to progressive lung scaring, as in IPF.

It is possible the mechanisms driving these two pathways are linked and molecular level research may provide evidence leading to repurposing or development of drugs to improve outcomes in each condition. Such drugs might include: new antifibrotics (there is a healthy pipeline of new drugs undergoing clinical trials); senolytics, which selectively kill senescent (rapidly aging) cells; and other drugs (e.g., metformin, a diabetes drug).

The impact of genetics on lung damage and repair is not yet fully understood. We know that a large number of genes are known to promote pulmonary fibrosis. But, the proportion of genetic risk explained by known genes is low and further research is needed to identify other genes and the way they influence pulmonary fibrosis development. APF-funded research by Dr Richard Allen at the University of Leicester is addressing this issue in IPF. We can be reasonably confident that genetics plays a key role in Covid-19 but continued research is needed.

It is important that we understand the shared mechanisms that exist between the two conditions in respect of cell injury and failures in lung repair. If we are to deal with the emerging epidemic of fibrotic lung disease and the very immediate Covid-19 pandemic.

Steve Jones, Chair or APF – 19/08/20