

# Coal workers' serum immunoglobulins provide hints for pneumoconiosis

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## Commentary

Today, roughly 30% of the global energy needs are met by coal, according to the International Energy Agency [1]. Over the past few decades, although many measures have been taken to protect workers against dust inhalation, coal workers' pneumoconiosis (CWP) remains to be a significant threat to public health, especially in developing countries [2,3]. Data from the global burden of disease (GBD) study showed that the number of pneumoconiosis cases increased by 66.0% from 1990 to 2017, reaching 60,000 [4]. Evidence from the GBD Study 2019 showed that the incident cases, the age-standardized incidence rate and the age-standardized mortality rate of CWP were 7153 (95% uncertainty interval 5870, 8717), 0.09 (0.07, 0.11) per 105, and 0.04 (0.03, 0.05) per 105 globally [3].

Given the insidious symptoms of early stage CWP, early diagnosis and treatment are essential. Currently, the screening of pneumoconiosis primarily relies on observing a history of exposure to harmful dusts and chest radiography. The International Labour Organization (ILO) formulated the updated revision of the Classification of Radiograph of Pneumoconiosis in 2011. But chest X-rays cannot readily visualize early signs of the disease compared to high-resolution computed tomography (HRCT) [5]. A recent statement from radiologists disclosed that 43% of workers had chest X-rays classified as normal using the ILO Classification System, while the signs were visible on HRCT [6]. Although HRCT is more sensitive to the early signs of disease than chest x-rays, it does not evaluate pulmonary functions and global standards are lacking. The ILO did not support the introduction of HRCT for routine use in this setting. Spirometry tests contribute to the diagnosis and monitoring of pneumoconiosis [7], but have lower sensitivity in detecting abnormalities before extensive damages occur [8]. Potential new diagnostic methods for pneumoconiosis, such as electrical impedance tomography and microRNA, have been developed, but have not been applied widely to date [9].

Recently, a team led by Professor Jing Wang found that the ratio of between serum immunoglobulin G (IgG) proteins IgG2/IgG3 could be used as a tool for the diagnosis of CWP, with a sensitivity of 73.1% and a specificity of 73.4% [10]. While the current results cannot determine whether the changes in IgG2/IgG3 ratio is specific in CWP, the combination of this ratio with other methods, such as chest X-rays, may potentially improve CWP diagnosis. In another aspect, these findings highlight the important role of humoral immunity in CWP, illustrated by the subclass of IgG proteins. In another article from the same team, it was found that immunoglobulin E (IgE) and its receptor FcεRI play an important role in pulmonary inflammation and fibrosis in mice exposed to silica [11]. As for the role of IgG in pneumoconiosis, Koval et al. reported that IgG preferentially enhanced the internalization of large ( $\geq 1\mu\text{m}$ ) particles by macrophages [12], while Scherbart et al. found that the uptake of particles by macrophage was related to the IgG receptor FcγRII [13]. Phagocytosis of crystals in macrophages leads to lysosomal destabilization and NALP3 inflammasome activation [14], which is known to be involved in diseases caused by inhaled particles such as asbestos, crystalline silica, and airborne particulate matter [15]. More importantly, blocking FcγRII strongly inhibited quartz particle uptake in the rat alveolar macrophage cell line NR8383 [16]. Hence, anti-IgG or FcγR (Fc receptors for IgG)-targeted therapies may be effective in relieving or reversing pulmonary

fibrosis caused by inhaled particles, but a better understanding of these mechanisms is needed.

The study [10], however, has some limitations that remain to be addressed by future investigations. First, although this study provided a glimpse of IgG subtype changes and how this might facilitate the development of new diagnostic tools for CWP, a larger sample size and collaborative multi-center research are warranted in the future to validate the results. Considering the number of patients included, the study could not provide robust results regarding the different stages of pneumoconiosis. In addition, this study did not assess the relationship between IgG and pulmonary function. Further studies exploring the detailed mechanisms underlying these findings are warranted, in order to develop new strategies for the treatment of pneumoconiosis.

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