The Role of Smoking Abeyance During Respiratory Virus Epidemics

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Introduction

Respiratory conditions impose an enormous burden on society. Oodles of people suffering and die because communicable and non-communicable respiratory diseases in every year. Fortunately, most of the respiratory diseases are avoidable by improving the quality of the air. Tobacco smoke, indoor and outdoor air pollution, air containing microbes, toxic particles, fumes and allergens can consider as common sources of unhealthy air. Latest findings show that air pollution exposure suppressed the immune systems regulatory T cells (T lymphocyte, is an essential part of the immune system). T cells are responsible for putting the bracs on the immune system and low function of T cell lead fail to block the inflammatory responses. Tobacco smoke contains more than 7,000 chemical compounds and many of them can harm the immune system and can make the body less successful at fighting against diseases.Tobacco smoking (TS) is associated with both release and inhibition of pro and anti-inflammatory mediators. Since the beginning of the 21st century, we are facing the convergence of several epidemics including tobacco smoking and influenza, SARS-CoV-2 like respiratory viral infections. Therefore, it is very important to understand the interrelationship between TS and respiratory viral infections.

A virus is always acommunicable agent with having both living and nonliving characteristics that is completely dependent on host cell for replication (intracellular parasite). Viruses are metabolically inert, force intracellular parasites, have only either DNA or RNA (but not both like living organisms), which use host living cell machinery to multiply.Moreover, they cannot make energy or proteins without support a host cell. In the case of respiratory viral infections (flu, SARS-CoV-2... etc.), viruses that can affect the breathing passages and cause respiratory illnesses and these viral infections commonly affect the upper or lower respiratory tract.

Viral pathogenesis can be defined as the process by which viruses produce disease in the host cell. There are several complex and dynamic interactions involve between the virus and the susceptible host as the factors that regulate viral transmission, multiplication, distribution and evolution. Considering the spread of a disease in society, it can be distinguished as **endemic** (disease limited to a certain group or region), **epidemic** (widespread in a society), or **pandemic** (spread worldwide).

Coronavirus disease 2019 is an infectious disease caused by severe acute respiratory syndrome coronavirus 2(SARS-CoV-2) which is a RNA virus. The outbreak was first identified in 2019 in Wuhan, the capital of Hubei, China, and has now spread more than 210 countries around the world. SARS-CoV-2 viral pathogens binds to the human angiotensin-converting enzyme-2 (ACE-2) receptor through densely glycosylated spike (S) protein, as the initiation step of the entrance mechanism to human cells.

In biology, **Immunity** is the balanced state of multicellular organisms with sufficient biological protection to fight off infections, diseases or other unwanted biological attacks. Nearly all the cells in the human body have mechanisms to detect viruses and other microbial agents. Pattern recognition receptors (PPRs) are associated with pathogen associated molecular patterns (PAMPs) or viruses, but are usually not found in host cells. Reactive oxygen species induced by TS are

Table 1: Respiratory viral infections

Respiratory virus	Type of virus	Time duration	Global mortality
Spanish flu	H1N1	1918-1919	50 million
Asian flu	H2N2	1957-1958	1-2 million
Hong Kong flu	H3N3	1968-1969	0.7 million
Swine flu	H1N1	2009-2010	0.28 million
SARS-CoV-2	Corona	08.12.2019 – 21.04.2020	>0.17 million

involved in interfering with PPR activity. PPRs important for virus detection include Toll-like receptors (TLRs), retinoic acid-inducible gene I (RIG-I), nucleotide-binding oligomerization domain-like receptors (NLRs) and other cytosolic virus sensors. Activity of the immune system is much critical in limiting virus spread and alerting the respond to the infection. Activation of PRRs in these cells by virus infection triggers production, release of type I, III interferon's(IFNs), and other pro-inflammatory mediators (e.g., cytokines, chemokine's , and antimicrobial peptides) which initiate the host innate and adaptive immune response. Thus, the level of PRR activation throughout the respiratory tract ultimately affects the level of immune cell recruitment and the release of the pro-inflammatory mediator, followed by any immunologic pathology.

Tobacco smoke (TS) isusually a health hazard. It generally has negative health effects, cause more than 7 million deaths per year worldwide (WHO Report on the Global Tobacco Epidemics, 2017).The chemicals that absorbed in to the blood stream by tobacco smoke directly linked to the biochemical changes of immune system.

Changes in the innate immune system along with direct and indirect tobacco smoke exposure lead to a pronounced and chronic inflammation in the respiratory system. This leads to other pathological changes, including re-modeling and destruction of lung tissue. Tobacco smoke exposure can also cause lung infections bacteria and viruses.In human lung, lower respiratory tract stay as sterile. Therefore, the processes of breathing and gas exchange can occur efficiently. When the respiratory system get expose to outside atmosphere, sophisticated system tend to changed, that protects and cleans the lung.

Chemicals in the tobacco smoke enter into the airway lumen by the direct or in direct exposure. Initial contact is with epithelial cells and there exist a numerous types of initial protective mechanisms. These include a mucociliary (self-clearing mechanism of the airways in the RS) transport system and innate defense mechanisms. Signaling from the epithelium triggersadditional innate

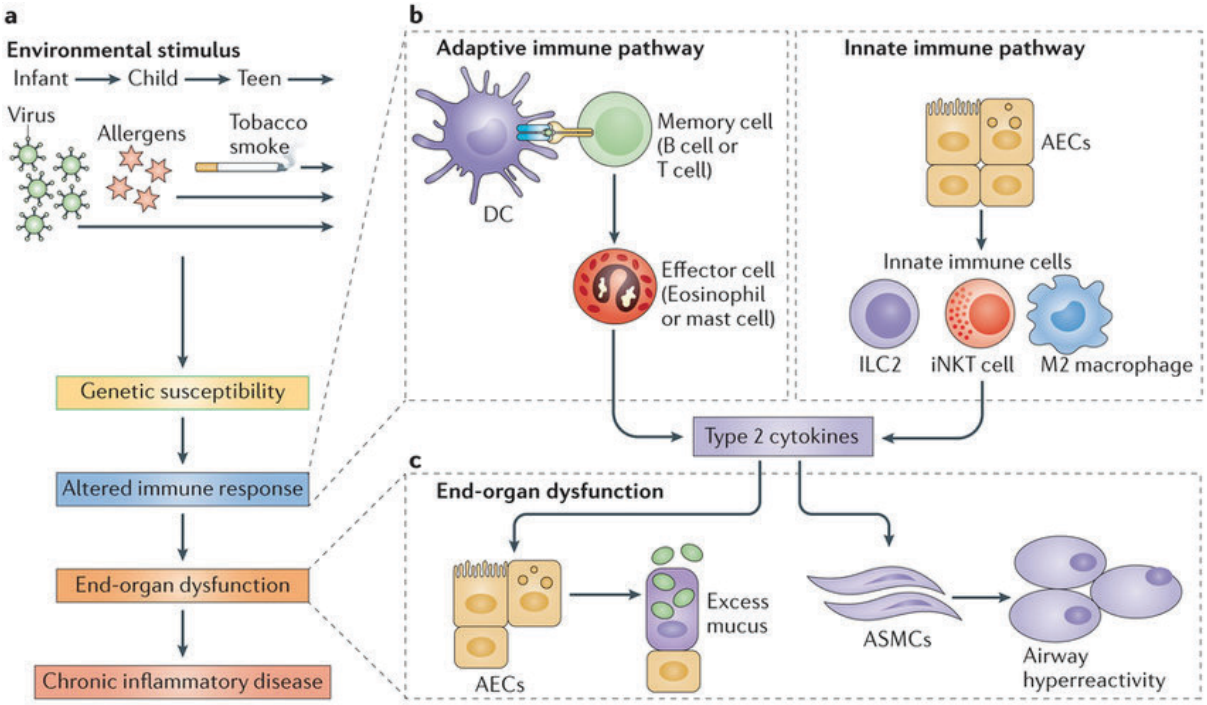

Figure 1: Adaptive and innate immune responses in chronic respiratory disease. a) Environmental stimuli — such as respiratory viruses, allergens and/or tobacco smoke — may act on genetically susceptible individuals to lead to an altered immune response. b) An altered adaptive immune response involves antigen-presenting cells, primarily dendritic cells (DCs), that process and present antigens to memory B cells and T cells that drive the activation of effector immune cells (such as eosinophil and mast cells). Additional T cell subsets that regulate the adaptive immune response include T helper 17 (TH17) cells, TH9 cells and regulatory T cells (not shown). Alternatively, altered innate immune responsesmay include airway epithelial cells (AECs) that activate innate immune cells, such as invariant natural killer T (iNKT) cells, M2 macrophages and innate lymphoid cells (ILCs). c) Effector cells or innate immune cells then produce type 2 cytokines — for example, interleukin 4 (IL 4) and IL 13 — that act on end-organ cells, especially AECs, to produce excess mucus, and on airway smooth muscle cells (ASMCs)

responses. First recruitment of neutrophils and then subsequently monocytes and macrophages. Later still adaptive immunity comes into play with T and B cells playing a role, which might also have an autoimmune component in more advanced and severe (Figure 1).By the down regulation of TRL3, TRL7, RIG-1 type receptors, TS interfere with the recognition of viruses.

In today's global emergency, such as the SARS-CoV-2 outbreak, identification of vulnerable groups is essential. Recent scientific studies show that the SARS-CoV and SARS-CoV-2 share the same receptor, ACE2(angiotensin-converting enzyme 2), and that this receptor is common in the respiratory system of tobacco smokers(Figure 2). According to the latest findings by the research done by University of South Carolina, scientists observed significantly higher ACE2 gene expression in former smoker's lung compared to non-smoker'slung.

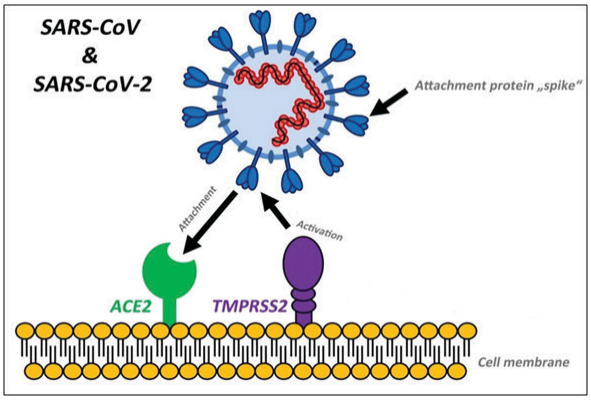

Figure 2: ACE2 receptor, expressed on the cell membrane of lungs, as a binding site of spike protein of SARS-CoV-2 virus.

In addition, they found that the ACE2 gene expressed in specific cell types related to the history of tobacco smoking. Findings of the research explainACE2 actively expressedin current smokers goblet cells and in non-smokers club cells in the bronchial epithelium. Other than that, ACE2 actively expressed in reconstituted type II alveloar cells (in which genes regulating viral reproduction and transmission are highly expressed) of former smokers in alveoli.

Discussion

Tobacco smoke adversely affects the immune system, resulting in immune deficiency, high infection rates (bacterial, viral…etc.) and in many cases of different autoimmune diseases. Surprisingly, immunological pathogenesis of respiratory virus infection reflects a complex interaction that directly influenced by virus and other viral factors, including the response of resident respiratory cells and the recruitment of innate and adaptive immune cells to the lungs. By quitting bad habits like tobacco smoke, people can enhance their immune related defense mechanismsagainst respiratory virus(like SARS-CoV-2 pandemic) and other related infections. In addition, it will help to reduce abnormal expression of ACE-2 receptor(one of the major binding site of SARS-CoV-2 virus to human body) in the respiratory system to reduce riskof the infection of SARS-CoV-2 virus.

References

1. Tobacco-use disparity in gene expression of ACE2, the receptor of 2019-nCov, GuoshuaiCai, Department of Environmental Health Sciences, Arnold School of Public Health, University ofSouth Carolina, Columbia,SC29208.
2. COPD and the response of the lung to tobacco smoke exposure, John D. Taylor, Integrative Pharmacology, Biosciences R&D Lung, Respiratory & Inflammation Research Area, AstraZeneca. Lund, SE-22187, Sweden
3. Virtual screening of inhibitors against spike glycoprotein of SARS-CoV-2: a drugrepurposing approach, Kanishka S Senathilake, Sameera R Samarakoon and Kamani H Tennekoon, Institute of Biochemistry, Molecular Biology and Biotechnology, University of Colombo, Colombo 03. Sri Lanka.
4. Alteration of the nasal responses to influenzavirus by tobacco smoke, Terry L. Noah, Haibo Zhou, and Ilona Jaspers,Department of Pediatrics, University of North Carolina at Chapel Hill, Chapel Hill, NC, USA
5. The role of airway epithelial cells and innate immune cells in chronic respiratory disease, Michael J. Holtzman, Derek E. Byers, Jennifer Alexander-Brett and Xinyu Wang, Pulmonary and Critical Care Medicine, Department of Medicine, Washington University School of Medicine, Saint Louis, Missouri 63110, USA.