

A comprehensive model for the asthma paradox: Is asthma a protective or a risk factor for malignancy?



Dear editor

The asthma paradox refers to controversial reports of cancer risk in patients with asthma [1]. Long-term inflammation has been suggested as an underlying reason in malignancies development [2]. It has been hypothesized that long-term inflammation in the lungs due to asthma could increase likelihood of lung cancer in asthmatic patients [3]. Chronic inflammation in the asthmatic lungs has been suggested as a “cofactor” in causing lung cancer. On the other hand, it has been shown that asthma might be even protective for developing eight types of cancers [4]. It has been suggested that overactive immune system in asthmatic patients have enabled rapid identification and increased ability for immediate elimination of cancerous progenitor cells [5–7].

But what is the true answer for asthma paradox?

Traditionally disequilibrium in natural homeostasis is defined as disease. In traditional medicine, diagnosis and treatment of disorders was based on managing equilibrium [8]. Disequilibrium in these pathways could impair defense mechanism and increase likelihood of developing malignancies.

Actually, asthma refers to a wide spectrum of clinical manifestations from mild to severe forms. It can be assumed that the answer of the observed paradox in asthma and cancer is laid in equilibrium and complex systems biology; it could be hypothesized that mild inflammation might be protective while severe inflammation being carcinogen

Additionally there are differences in local and systemic effects which should be taken into consideration [1]. Although alert immune system in asthmatic patients could protect them from several cancers except lung cancer, it may increase risk of lung cancer by chronic damage to the pulmonary trunk and alveoli, especially in the case of severe inflammation. Thus, mild inflammation in contrast to severe inflammation might be protective rather than harmful even in lungs.

But where is the cutoff point for mild or severe inflammation?

The answer is laid in personalized medicine. Protective and harmful state of immune system activity should be defined for each person with respect to his/her life style and nature. There would be an optimum

point of protection and health; courtesy of evolution, in healthy normal human beings this point is set before; however, in new programmed person like asthmatic patients, or in smokers a new optimal point should be defined (Fig. 1).

For example, it has been shown that smokers who consume antioxidants such as vitamin E are at increased risk of developing cancer, compared to smokers who do not consume them; while it has been shown that moderate consumption of antioxidants decrease cancer development in healthy nonsmokers. Every day plenty of potentially cancerous cells are producing in our body, but our immune system eliminates them. It seems that our immune system utilizes oxidative stress as one of the mechanisms to kill cancerous cells which are developing in higher daily amounts in smokers. Hence, treatment with antioxidants might interfere with the increased protective oxidative stress in these patients and so increase likelihood of developing cancer [9]. This shows that a new level of oxidative stress is optimal for smokers compared to nonsmokers. Hence, increased oxidative stress and inflammation might be protective in selected patients. Every person with respect to its genetic and lifestyle would benefit from a different equilibrium set point between oxidative stress-anti oxidants and inflammation-anti inflammation. The more complex problem is that any organ might act different in a given person, and it is only evolution that can detect the optimal point by several trials. Although increased inflammation might protect some organs from developing cancer it might increase likelihood of developing cancer in some other ones, and also might increase likelihood of developing atherosclerosis in susceptible patients with risk factors for atherosclerosis.

In conclusion, asthma would be protective against cancers except for lungs as it is hypothesized in this paper. In lungs there would be a cutoff point wherein mild inflammation might be even protective rather than carcinogen and severe inflammation would be a risk factor. Further studies need to define and clarify this so called cutoff point based on clinical and para-clinical findings to establish new criteria for better diagnosis and specific treatment in each person.

This warrants a new area in personalized medicine, determining the optimal level of inflammation and oxidative stress for each person with respects to his/her genetic background, environmental factors, life style, and habits.

Defining a measurable factor or index for level of inflammation or oxidative stress to apply for this concept is warranted.

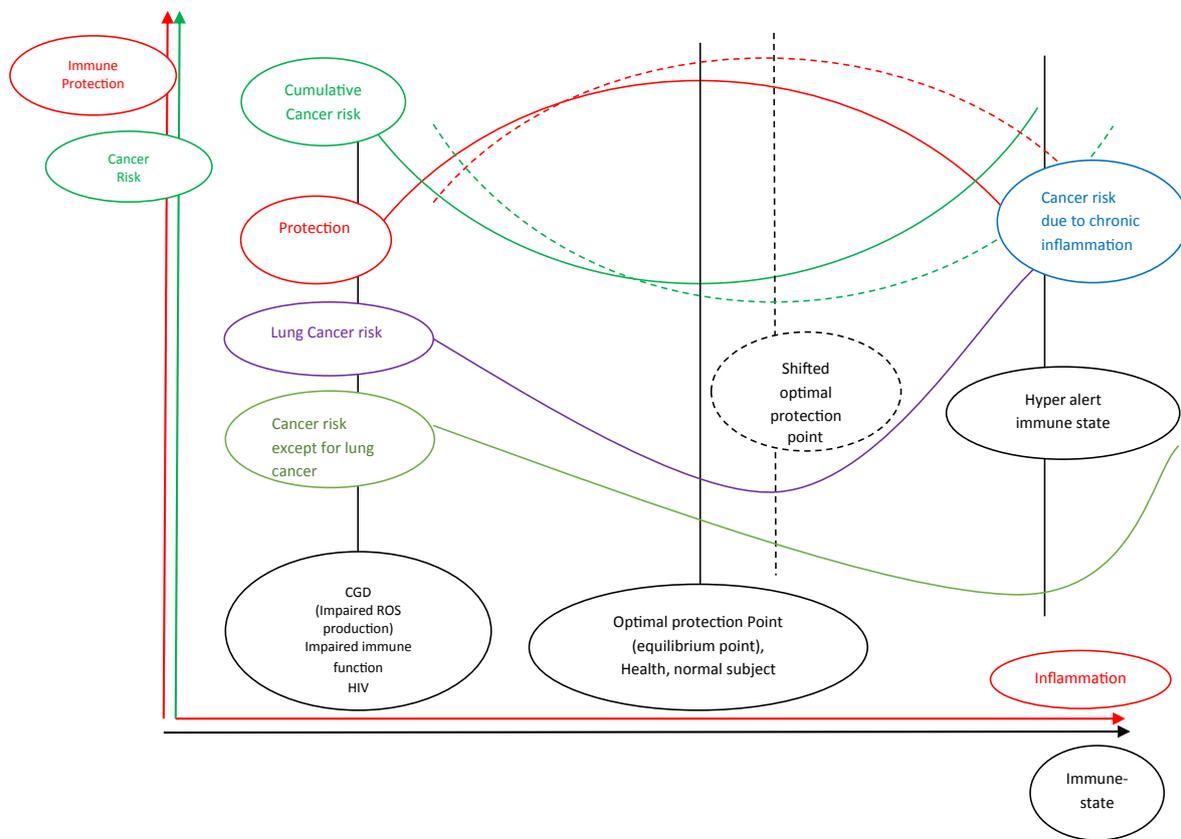


Fig. 1. A comprehensive model for asthma paradox. The following diagram depicts the relationship between inflammation, cancer protection, and carcinogenesis. This model shows how optimal immune system alertness could be shifted in a given person such as a smoker or a patient with severe or mild asthma. The optimal protective status is the result of a balance between inflammation and oxidative stress; Optimal protection point is where the highest protective effects of inflammation and oxidative stress match with the lowest risk of cancer due to inflammation and oxidative stress.

Declaration of Competing Interest

None declared

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Soroush Seifirad
 PERFUSE Study Group, Division of Cardiology, Department of Medicine,
 Beth Israel Deaconess Medical Center, Harvard Medical School, Boston,
 MA, USA
 E-mail address: sseifira@bidmc.harvard.edu.