

The Cancer Hygiene Hypothesis: From Theory to Therapeutic Helminths

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Abstract: Background: The “Hygiene Hypothesis” was postulated by David Strachan in 1989 to explain for the rapid 20th century increase in allergic diseases such as asthma. In this hypothesis, children from developed countries living in ultra-hygienic environments and avoiding exposure to viruses, bacteria, and parasites, especially helminthes, have an increased risk of atopic disorders.

Materials & Methods: Research and online content related to cancer hygiene hypothesis is highlighted and to illustrate key themes. Guidelines for meaningful participation in DOC activities for people with diabetes, families, health care providers, and industry are provided.

Results: The lack of worms leads to failure of stimulation of mucosal Th2 responses. These infections exert their effect through critically altering T-helper (Th)1/Th2 regulation, and it is postulated that, thus, they protect against atopy and asthma, through the induction of Th1 regulatory response. It is now also recognized that this “hygiene hypothesis” concept applies to a wider range of chronic inflammatory diseases than atopy and asthma, such as diabetes, multiple sclerosis and cancer.

Conclusion: Here we discuss the major implications of these findings for the association between microorganisms and cancer, and also between some immune pathologies, like autoimmune diseases, and cancer.

Keywords: Hygiene hypothesis, cancer, parasites, helminths, anticarcinogenic effects, infection.

1. INTRODUCTION

1.1. The “Hygiene Hypothesis”

In 1989, David Strachan observed that hay fever was inversely correlated to the number of children in the family circle. These observations could be anticipated, if allergic maladies were barred by infection in the beginning of upbringing, transmitted by germ-infested contact with elder children, or obtained before birth from a mother infected by contact with her elder siblings. Afterwards, infection or reinfection by younger children might allow further defense against hay fever. These observations formed the basis for the “Hygiene Hypothesis” to explain the rife clinical appearance of atopic disease for the last century where the diminishing family number, enhancements in domestic facilities, and privileged typical individual hygiene have decreased the chance of cross infection in juvenile household relatives [1].

1.2. Helminths as the Basis for the “Hygiene Hypothesis”

The “Hygiene hypothesis” was extended to the fact that individuals exposed to helminth parasite infection decreased their propensity to be infected by allergy/asthma and autoimmune diseases [2].

Helminths are multicellular parasites and have successfully adapted to a parasitic lifestyle. They are classified into three taxonomic groups: cestodes, such as the pork tapeworms that cause cysticercosis (e.g., *Taenia solium*), nematodes that include the major intestinal worms (e.g., *Ascaris lumbricoides*) and trematodes that include the flukes, such as the schistosomes (e.g., *Schistosoma mansoni*) [3].

Since the beginning of human history, helminths have been infecting humans. As described by Hippocrates and in Egyptian medical papyri, we can identify numerous clinical attributes of helminth infections [3]. These clinical sets of infection by helminth parasites represent one of the utmost tests to our immunologic system, together in the context of the body dimension of the organisms and their ability to generate immunomodulatory molecules that are basically immunosuppressive or present innate and adaptive immune cells reaction with the regulatory role [2].

These clinical observations are explained by the fact that helminths have typically been regarded to T-helper 2 (Th2)-inducing pathogens. Th2 innate cells comprise eosinophils, basophils, mast cells, otherwise activated or type 2 (M2) macrophages, and type 2 ILC2. M1 and ILC1 in concert with Th1 cells act as protective immunity to viruses, bacteria, and tumors, while ILC2 and M2 macrophages in concert with Th2 cells take part in the removal of helminth parasites [2].

1.3. The Link Between Infection and Cancer

The mammalian immunologic system has been developed to manage infection and avert the growth of cancer. It accomplishes this by an arrangement of innate and adaptive effector cells and molecules which have to be firmly synchronized to avoid ineffective infection and cancer-associated immunopathology [2]. Still, despite the fact that the path of carcinogenesis is indisputably multifactorial, foremost awareness is concerned on the onus of infectious diseases and the immunologic system in cancer enlargement. Numerous categories of cancers are associated with infections, while inflammation is renowned as a definite property of cancer, and insertion of immunologic evaluations in cancer diagnosis and prognosis has been recommended [2].

Several infectious agents can directly control carcinogenesis. Human papillomavirus protein E7 is able to combine with the retinoblastoma tumor suppressor and the cyclin-dependent kinase inhibitor p21 in infected cells, stimulating DNA replication and cell proliferation [4], while Hepatitis B virus is capable of activating hypoxia-inducible factor-1 α , stimulating angiogenesis [5]. The helminth *Schistosoma haematobium* is able to cause urothelial dysplasia and inflammation following intravesical instillation in mice [6] and is linked to bladder cancer [7].

Quite the opposite, immunologic reactions, encompassing those generated by microorganisms, are acknowledged to reduce cancer risk or give rise to tumor regression. The link associating infection and tumorigenesis are not soundly explicit, and both positive and adverse immunologic-mediated or direct anticarcinogenic outcomes from pathogens have been recognized [8].

1.4. The “Cancer Hygiene Hypothesis” Explained

In recent times, the hygiene hypothesis has been revisited to accommodate the connection between microorganisms and cancer. Subsequent to the identical model observed with some immune pathologies, there are emergent data of a rising cancer incidence in “Westernized” economically urbanized countries. The similitude of the “Hygiene Hypothesis” to the one revealed by hygiene and cancer is not unexpected, because groundwork observations have linked tumorigenesis with chronic immune-mediated disorders like, an augmented risk of cancer within patients affected by autoimmune disorders [8].

In a further pathogen-based observation, parasites and their extracts have been studied as antitumor inducers to substantiate the cancer hygiene hypothesis. Indeed, *Fasciola hepatica* extracts induced death of Chinese Hamster Ovary (CHO) cells suggesting that some molecules present in *F.*

hepatica extracts could have a potential as a preventive or even curative anti-cancer substance [9, 10].

Other researchers observed the direct effect of molecules released by *Echinococcus granulosus* whose activity directly inhibits cancer cell migration and growth. These authors concluded that *E. granulosus* probably secretes molecules that can develop as anti-cancer therapeutics in the future [11].

CONCLUSION AND FUTURE PERSPECTIVES

These annotations sustain the defensive shield of infections, as anticipated by the cancer hygiene hypothesis. Incidentally, cancer might be linked with the improved aseptis/reduced contact to particular pathogens, akin to which is recognized in the case of autoimmune diseases and allergies [8].

These findings have major implications for the association between microorganisms and cancer. The rationale to back up this viewpoint is to exploit the parasites or their singled out constituents to be used as a tool to cure/hinder cancer.

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