



A flashlight on Hygiene Hypothesis

(Review Article)

Ebtehal Edrees Ahmed Shubber

Ph.D. Microbiology. Science Faculty/ Kufa University

Introduction

Is it necessary to live in too clean environment ? using of various types of sensitizer, cleaning soaps? or just like that live naturally without any fear of that expectant opportunistic creatures that may invade our bodies with all their deleterious weapons! Over use of such means may be simply two edges sword. This is the premise of the puzzle (**hygiene hypothesis**), our environment is too clean and our immune systems are no longer as heavily taxed with fighting off germs and bacteria. Increased rates of allergies and other conditions like asthma partly attributed to deviation in immune response because of poor immune response towards the infectious agents might be caught by normal contact with them.

Living simply with natural micro living components of the environment leads to more activating of neutralizing potency immune system represented by all its types natural active and passive means.(Wander *et al.*,2012)

The decreased fighting ability of our immune system is also due to the emergence and overuse of antibiotics and vaccines. The immune system is no longer as challenged and becomes dependent on these products to assist in fighting off even the most common bacterial infections. Antibiotics , particularly those with broad spectrum do not target invading microorganism only but also have deleterious effect on microbial commensals which badly affect future response to later on infections.(Bloomfield *et al.*, 2006)

One of such immune overreactions is Eczema; a common skin disorder, Researchers recently reviewed 20 studies of first year of age and prenatals antibiotic use in connection with later skin problems. The results of these studies showed that risk for the disease was increased by up to 40% in children who had been exposed to antibiotics in their first year of life.

The Early Beginning :

This hypothesis was originally postulated by a lecturer in epidemiology. Where he used very big sample of population represented by British children born during the same week in 1958 and followed them up to age 23 years their number was 17414 , he came out with three results he further investigated first: self reported "hay fever d during the past 12 months" at age 23; second: parental report of "hay fever or allergic rhinitis in the past 12 months" at age 11; third: parental recall of "eczema in the first year of life" occurred when the child was at 7 years old(Strachan,1989) .

The conclusion of that study was that the children in larger families had more exposure to pathogens than smaller families this will make them less possibility to get hay fever , asthma or other atopic diseases(Umetu, 2012; Okada *et al.*, 2012; Benn *et al.*, 2004; Tulic *et al.*, 2004) the association between the decreased exposure to microbial agents during early infancy and increased allergic diseases later in life has been expanded to include also increased autoimmune diseases such as inflammatory diseases and type 1 diabetes mellitus.(Azad *et al.*,2013)



Examples of tangible clues supporting the hygiene hypothesis:

1-in Kilimanjaro increased delayed hypersensitivity to *Candida* is related with early life infection (Wander *et al.*, 2012)

2-Variation of microflora of gut support healthy immune system lowering predisposing to autoimmune diseases including T1D, the HEV infection could suppress the genetically driven autoimmune disease by activating immune system (Azad *et al.*, 2013)

3-Using *Escherichia coli* in infecting mice led to decrease of some parameters mediating the allergic response represented by allergic airway disease (AAD) (Pang *et al.*, 2013)

4- an inverse link between getting infected with *Helicobacter pylori* and allergic asthma (Matsushima and Nagai, 2012)

5-Hepatitis- A Virus was inversely linked with incidence of hay fever. (Umetsu, 2012)

6-Other relationship is based on the mild intracellular living pathogens like *Mycobacteria* mainly from soil and *Salmonella*, in other words those were ingested with food would protect from atopic diseases through the development of immune response further (Matricardi, 2010)

7-The hygiene hypothesis is thought to be a significant supporter to the growing incidence of inflammatory bowel disease (IBD) around the world (Koloski *et al.*, 2008)

Immunological Mechanisms underlying the hygiene hypothesis :

All immature T-cells contain CD3 designated as CD3⁺ and after differentiation are subdivided into two subsets, first effector T-cells which are characterized by the presence of CD8 having cytotoxic functions and so the name cytotoxic T-cells. These cells are capable of killing tumor cells, allografts, and viral infected cells. Second subset are the regulator T-cells also named helper T-cells characterized by their possession of CD4, which further subdivided into two types called the T helper-1 (Th-1), and T helper-2 (Th-2) cells. The first produce interleukin-2 (IL-2) which stimulate cytotoxic activity in the CD8⁺ cytotoxic T-cells, while production of IL-2 and interferon- γ (IFN- γ) will stimulate delayed type hypersensitivity response by macrophage. (Th-2) cells produce IL-4, IL-5 that stimulate B-cells to be plasma cells antibody producing cells

The atopic diseases that hypothesized to be correlated with lowered exposure to microbes in early immune system development is caused by antibody mediated immunity whereas the immune response against pathogens especially those in gastrointestinal tract is cellular mediated immunity. (Levinson, 2004)

The most famous elaboration was that the poor early exposure to infectious agents would lead to an immunological deviation towards Th-2 mediated immune response away from the Th-1-immune response. (Martinez and Holt, 1999)

Other explanations focusing on that the invariant natural killer T-cells can directly respond to some of bacterial glycolipids like that derived from *H. pylori* which leads to expand cell subset of suppressor iNKT-cells preventing the development of experimentally designed asthma in mice (Chang *et al.*, 2011)

other correlates the immune regulation by T-regulator cells by cytokines produced by other cells (Pang *et al.*, 2013)

in short the hypothesis needs for more researches that focusing on various aspects of the immunological disorders associated with the modern life style in order to modulate it in the way providing more protection against such disorders in the future.



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