ENVIRONMENTAL EXPOSURE TO ENDOTOXIN AND ITS RELATION TO ASTHMA IN SCHOOL-AGE CHILDREN


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FROM ABSTRACT

In early life, the innate immune system can recognize both viable and nonviable parts of microorganisms.

Immune activation may direct the immune response, thus conferring tolerance to allergens such as animal dander or tree and grass pollen.

Methods
Parents of children who were 6 to 13 years of age and were living in rural areas of Germany, Austria, or Switzerland where there were both farming and nonfarming households completed a standardized questionnaire on asthma and hay fever. Blood samples were obtained from the children and tested for atopic sensitization; peripheral-blood leukocytes were also harvested from the samples for testing. The levels of endotoxin in the bedding used by these children were examined in relation to clinical findings and to the cytokine-production profiles of peripheral blood leukocytes that had been stimulated with lipopolysaccharide and staphylococcal enterotoxin B. Complete data were available for 812 children.

Results
Endotoxin levels in samples of dust from child ‘s mattress were inversely related to the occurrence of hay fever, atopic asthma, and atopic sensitization.

Cytokine production by leukocytes (production of tumor necrosis factor-alpha, interferon-gamma, interleukin-10, and interleukin-12) was inversely related to the endotoxin level in the bedding, indicating a marked down-regulation of immune responses in exposed children.

Conclusions
A subject ‘s environmental exposure to endotoxin may have a crucial role in the development of tolerance to ubiquitous allergens found in natural environments.

THESE AUTHORS ALSO NOTE:

“Asthma is the most common chronic disease in childhood and accounts for substantial morbidity and health care costs.”
An “intriguing hypothesis is that changes in the type and degree of stimulation from the microbial environment associated with improvements in public health and hygiene may increase the predisposition to chronic allergic conditions during childhood.”

One can have exposure to microbes or to nonviable parts of microbes and not become infected.

Exposure to these nonviable microbial substances are recognized by the innate immune system and they induce a potent inflammatory response. [As we have seen in other articles, the INNATE immune system.]

“Environmental exposure to microbial products may have a crucial role during the maturation of a child’s immune response, causing the development of tolerance to other components of his or her natural environment, such as pollen and animal dander.” [WOW, very important]

These authors measured endotoxin (a cell-wall component of gram-negative bacteria) in samples of dust from vacuumed mattresses of children.

The levels of endotoxin was then related to the prevalence of asthma and allergies and to serum levels of IgE.

812 children were assessed, 319 from farming and 493 from non-farming families.

“Endotoxin exposure showed a strong inverse association with hay-fever, hay-fever symptoms, and atopic sensitization.”

“Exposure to farming in the first year of life showed a strong inverse association with all health outcomes.”

DISCUSSION

“These findings suggest that environmental exposure to microbial products, as measured by the endotoxin levels in mattress dust, is associated with a significant decrease in the risk of hay-fever, atopic sensitization, atopic asthma, and atopic wheeze in childhood.”

“This protective effect was observed in children from farming and nonfarming households, indicating that even the lower levels of exposure that occur in nonfarming environments may favorably influence the risk of atopic diseases in childhood.”

High levels of environmental exposure to endotoxin in pre-school children results in a marked suppression of IgE following the activation of the innate immune system.

This causes “tolerance” or “down-regulation” to future exposure of antigens.
“Such a down-regulation occurs in vivo as a consequence of long-term exposure to environmental endotoxin.”

The innate immune response instructs the adaptive immune response [to produce IgG or IgE]. [IgG fights infection; IgE causes asthma, hay-fever, atopy]

“The innate immune system responds [favorably, for ones entire life] to the high microbial burden of the farming environment.”

Long-term, high-level environmental exposure of endotoxin may prevent the development of allergic immune responses.

Exposure to microbial products strongly affects the development of atopy and childhood asthma.

This study showed that both exposure to environmental endotoxins and also the timing of that exposure determines the beneficial or detrimental effects on immune system development.

The results of this study indicate that environmental exposure to microbial products is associated with the development of tolerance toward allergens found in nature.

These microbial compounds are recognized by the innate immune system and instruct the adaptive immune response how to deal with the resulting inflammatory responses.

This is of “key importance for the development of atopic illnesses such as hay fever and childhood asthma and wheeze.”

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**EAT DIRT — THE HYGIENE HYPOTHESIS AND ALLERGIC DISEASES**

Scott Weiss, MD

There is an epidemic of both autoimmune diseases and allergic diseases.

“The occurrence of these diseases is higher in more affluent, Western, industrialized countries.”

“One theory proposed to explain this increase in the prevalence of autoimmune and allergic diseases is that it results from a decrease in the prevalence of childhood infection.”

This is called the “hygiene hypothesis,” and is the result of indoor plumbing and antibiotics.

The decrease in antigenic stimulation related to the decrease in the frequency of
childhood infections.

“Stimulation of the innate immune system by endotoxin may be important in the ontogeny of the normal immune system.”

Endotoxin is a lipopolysaccharide that forms the outer layer of the cell membrane of all gram-negative bacteria.

Endotoxin levels tend to be highest in environments where there are farm animals.

Endotoxin is also found in the dust and can be inhaled or swallowed and “acts as a potent immunostimulatory molecule” through the innate immunity pathway.

Endotoxin exposure decrease Th2-mediated [IgE] diseases such as allergies and allergic asthma, and “enhance the developing immune response of a neonate.”

“Exposure to endotoxin early in life, during the development of the immune system, seems to be most important in providing protection against the development of allergic disease.”

KEY POINTS FROM DAN MURPHY

(1) [The innate immune response is encoded in our DNA, controlled by the nervous system, and develops in utero and early in life.]
(2) [The adaptive system is that which produces specific immunoglobulins, such as IgG and IgE].

(3) The innate immune system directs the adaptive immune response.

(4) Atopic disorders, such as hay-fever, allergies and asthma are associated with the overproduction of IgE by the adaptive immune system. (Th2 response).

(5) Asthma is the most common chronic disease in childhood and is an example of an atopic disorder.

(6) Atopic disorders are epidemic in Western industrialized nations.

(7) Early life (first few years) exposure to endotoxins from bacteria suppresses the Th2 IgE response, thereby reducing atopic disorders, forever, because it changes the way the immune system develops and responds.

(8) Another reason for increased Th2 IgE responses and atopic disorders is reduced infections from improved hygiene and the use of antibiotics.

This is yet another article that discusses the innate immune response, early life immune system maturation, the benefits of exposure to endotoxins and to having early life infections, and the adverseness of excessive cleanliness and antibiotics in non-life threatening infections.