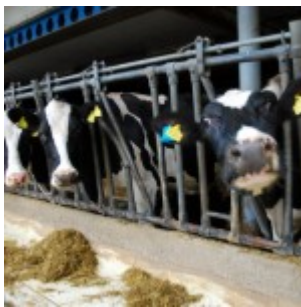


ALLERGY

# DUNG HILL COUNTING

9.08.2008

Wikipedia writes about [Imre Lakatos](#) the famous Hungarian mathematician and philosopher who [graduated 1961 in Cambridge](#) with “Essays in the Logic of Mathematical Discovery”



He showed that in some cases one research programme can be described as progressive while its rivals are degenerative. A progressive research programme is marked by its growth, along with the discovery of stunning novel facts, development of new experimental techniques, more precise predictions, etc. A

degenerative research program is marked by lack of growth, or growth of the protective belt that does not lead to novel facts.

One of these degenerate research program relates to the hypothesis that farming protects you from allergy

[E 2006:](#)

There is increasing evidence that environmental exposures determining childhood illnesses operate early in life. Prenatal exposure to a farming environment through the mother might also play an important role ... Both atopic sensitization ... and the gene expression of receptors of innate immunity were strongly determined by maternal exposure to stables during pregnancy, whereas current exposures had much weaker or no effects ... Each additional farm animal species increased the expression of TLR2, TLR4, and CD14 by a factor of 1.16

Keep in mind – it’s the farm animal.

#### K 2008:

Several epidemiological studies have shown that the farm environment impacts allergy protection mechanisms in children ... In investigating the link between farming lifestyle and prevention of childhood allergy, we examined the prevalence of *Listeria* spp. in dust specimens from the environment of rural children ... The dominant species found by culturing methods were *L. innocua* (n=12) and *L. monocytogenes* (n=8).

Sorry - it's *Listeria*.

#### K 2006:

There is increasing evidence that the farming environment has a protective effect as regards allergic diseases. Exposure to animal parasites, particularly helminth infections, is common in the farming environment. Exposure to nematodes, as determined by the levels of antibody to *A. lumbricoides*, was more frequent among farmers' children than non-farmers' children... This positive serology was found to be significantly associated with high total IgE levels ... and eosinophilia.

Sorry again - it's *ascaris*.

#### E 2007:

In recent years, studies have shown a protective effect of being raised in a farm environment on the development of hay fever and atopic sensitization...Inverse relations with a diagnosis of asthma were found for pig keeping ..., farm milk consumption ..., frequent stay in animal sheds ..., child's involvement in haying ..., and use of silage ... Protective factors were related with higher expression levels of genes of the innate immunity.

Sorry, it's everything: the pig, the milk, haying and silage.

#### W 2007:

Some studies in rural environments claimed an inverse association between consumption of farm-produced dairy products ... Farm milk consumption ever in life showed a statistically significant inverse association with asthma... rhinoconjunctivitis ... and sensitization to pollen and the food mix fx5 ..., and sensitization to horse dander.

Hey, milky ways ahead something new: the horse!

K 2007:

There is still uncertainty about the determinants of atopic eczema ... In multivariate analyses, helping with haying was the only variable related to a farming environment having a consistent inverse association with both current symptoms and a doctor's diagnosis of AE.

Yes, haying makes sense with hayfever.

W 2005:

An increasing number of studies report pet exposure to be associated with lower risk of asthma and allergies ... Current contact with dogs was inversely associated with diagnosed hay fever (OR 0.26, 95% CI 0.11-0.57), diagnosed asthma (OR 0.29, 95% CI 0.12-0.71), sensitization...

Oh no, the dog.

V 2008:

Numerous epidemiologic studies have demonstrated an allergy-protective effect of farm life early in childhood ...In vitro, B. licheniformis spores activated a T(H)1 cytokine expression profile. In vivo application of these spores resulted in less spore-specific but long-lasting immune activation preventing eosinophilia and goblet cell hyperplasia; however, they provoked an influx of neutrophils in lung tissue of asthmatic mice.

What about bacillus spores?

vM 2008

Contact with farm animals, at least in childhood, likely confers protection; other factors have not been completely identified. Also, the consumption of milk directly from the farm during childhood has been shown to be beneficial with respect to childhood asthma and allergies.

Ok, it is milk. Are you still readings here?

This week I am back with the most exciting research

Previous cross-sectional surveys have suggested that maternal exposure to animal sheds during pregnancy exerted a protective effect on atopic sensitization in children lasting until school age ... Different sensitization patterns in cord blood of farm and nonfarm children were observed. In multivariable analysis consumption of boiled, but not unboiled, farm milk during pregnancy was positively associated with specific IgE to cow's milk independently from maternal IgE.

[This paper counts dung hills](#) The authors even invent a new classification (sorry, not dung hill height but "50 m distance between dung hill and house").

**TABLE I. Multivariable models for the outcome: Cord blood IgE to seasonal allergens**

Exposures and covariables	Full model* (n = 831)
Farm child	1.18 (0.45-3.06), $P = .738$
Exposure to animal sheds during pregnancy	0.38 (0.18-0.81), $P = .013$
Open dung hill in surrounding area	0.49 (0.25-0.96), $P = .039$
Maternal IgE to seasonal allergens	1.49 (0.82-2.70), $P = .189$
Paternal history of atopic diseases	1.04 (0.54-2.01), $P = .903$
Maternal history of atopic diseases	1.28 (0.67-2.43), $P = .460$
No. of previous pregnancies	0.84 (0.65-1.07), $P = .159$

And did you also wonder why paternal history is no more a risk in these studies? There are only a few allergic parent due to healthy worker effect...

No adjustment for multiple testing "because it will lead to fewer errors of interpretation when the data under evaluation are not random numbers but actual observations on nature" That is one of the most stupid sentences I have ever read.

The overall response rate in this study is 32% and the strongest risk for cord blood IgE is

maternal IgE. Is there any statistical model that [can account for poor data by contamination of newborn cord blood with maternal IgE](#)? And uhh, 32% response is that really a representative sample?

Did you notice that being a farm child now suddenly becomes a risk for seasonal sensitization (OR=1.18, NS) and food allergy as well (OR=1.25, NS)? And that farm milk consumption is suddenly a risk! for IgE to cow's milk (OR=3.64, p=0.01)?

The mantra at the beginning at each of the abstract above is certainly necessary to let us believe in the rest of these papers.

Addendum 8/8/2008

Poster E3269: Prenatal exposure to a farm environment affects atopic sensitization at birth at ERS Berlin Tuesday, October 7, 2008.

Furthermore, inverse associations of CB IgE to seasonal allergens with positive maternal records for *Toxoplasma (T.) gondii* (adjusted odds ratio = 0.37 [0.17-0.81]) and rubella virus (adjusted odds ratio = 0.35 [0.13-0.96]) were found.

gotcha - *Toxoplasma* + Rubella.

Addendum 11/12/2009

a [new paper](#) & a new cowshed derived bacterium: *Acinetobacter*

Using the cowshed-derived bacterium *Acinetobacter lwoffii* F78 together with a mouse model of experimental allergic airway inflammation, this study investigated the hygiene hypothesis.

Addendum 28/2/2011

a new press release [Eurotium](#)

Mikrobielle Vielfalt allein reicht vermutlich allerdings nicht aus, um Asthma zu verhindern. Wahrscheinlich ist es eine Kombination spezifischer Arten, die eine Schutzwirkung entfalten kann. „Im gesamten untersuchten Spektrum fanden sich einige Keime, die besonders interessant sein könnten“, berichtet Ege, „dazugehören außer bestimmten Bazillen und Staphylokokken – etwa die Art *Staphylococcus sciuri* – auch Schimmelpilze der Gattung *Eurotium*.“

## Addendum 1/1/2018

The research above has now lead to the highest German Science Prize, an honorary doctorate, an ERC advanced grant, a Leopoldina and Bavarian Academy membership.

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