

# Everyday Exposure to Bacterial Endotoxins and Asthma in Children



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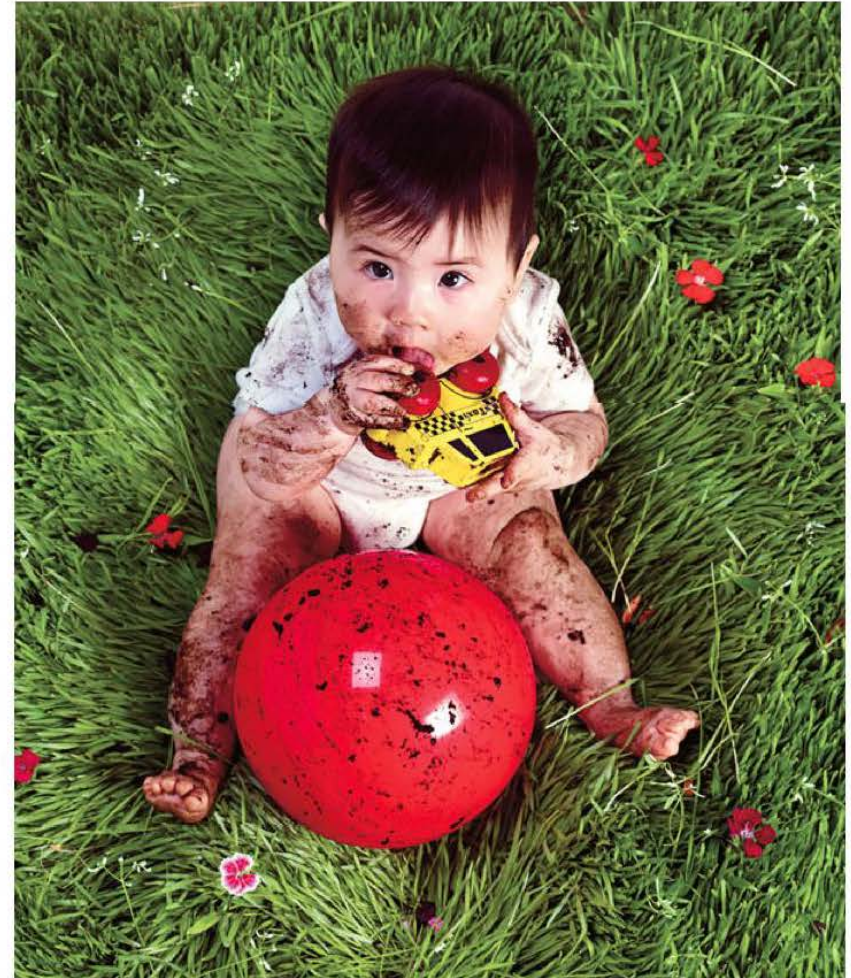
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BROUGHT



Some of My Best Friends Are Germs



Hannah Whitaker for The New York Times. Prop stylist: Emily Mullin.

# Overview

- Microbiomes in health and disease
- Everyday exposure to bacterial endotoxins in children with asthma
- Hygiene hypothesis update

# Microbiomes in Health & Disease

- Very dynamic in early life
- Early life matters
- Healthy microbiomes are diverse, rich & even
- Unhealthy microbiomes are punctuated by pathogens
- Keystone protectors and pathogens in asthma



# Asthma & allergies are less common in

*Rural areas*



- Africa
- Tokelau
- Venezuela
- China
- India

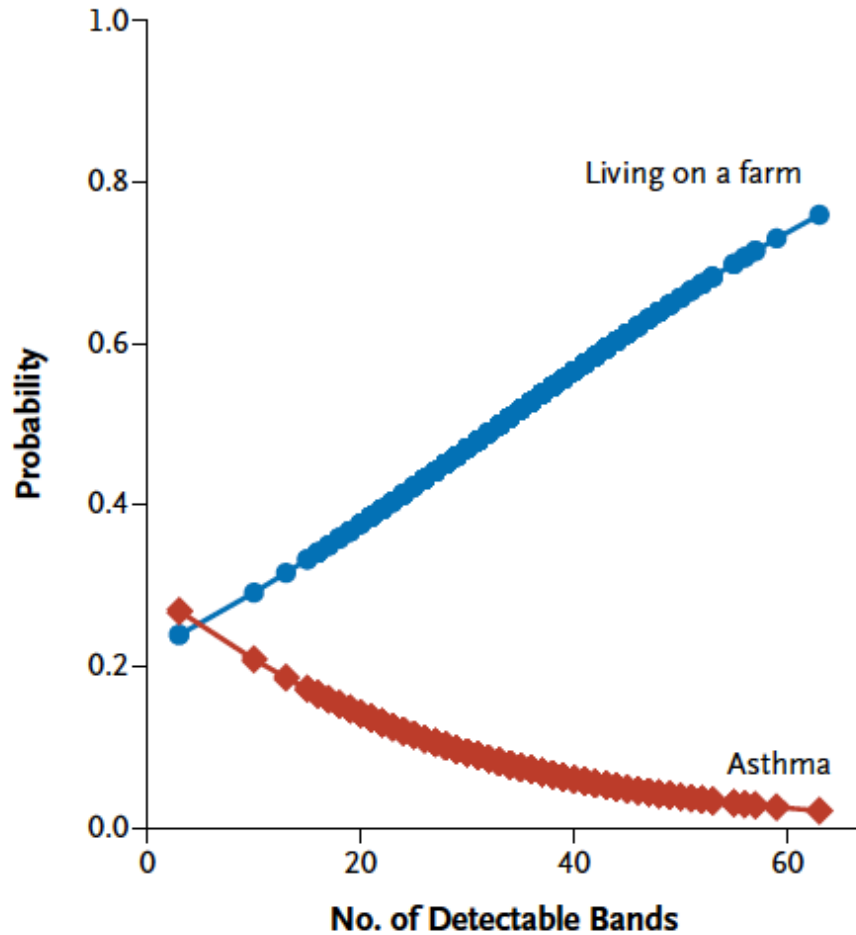
*Farms*



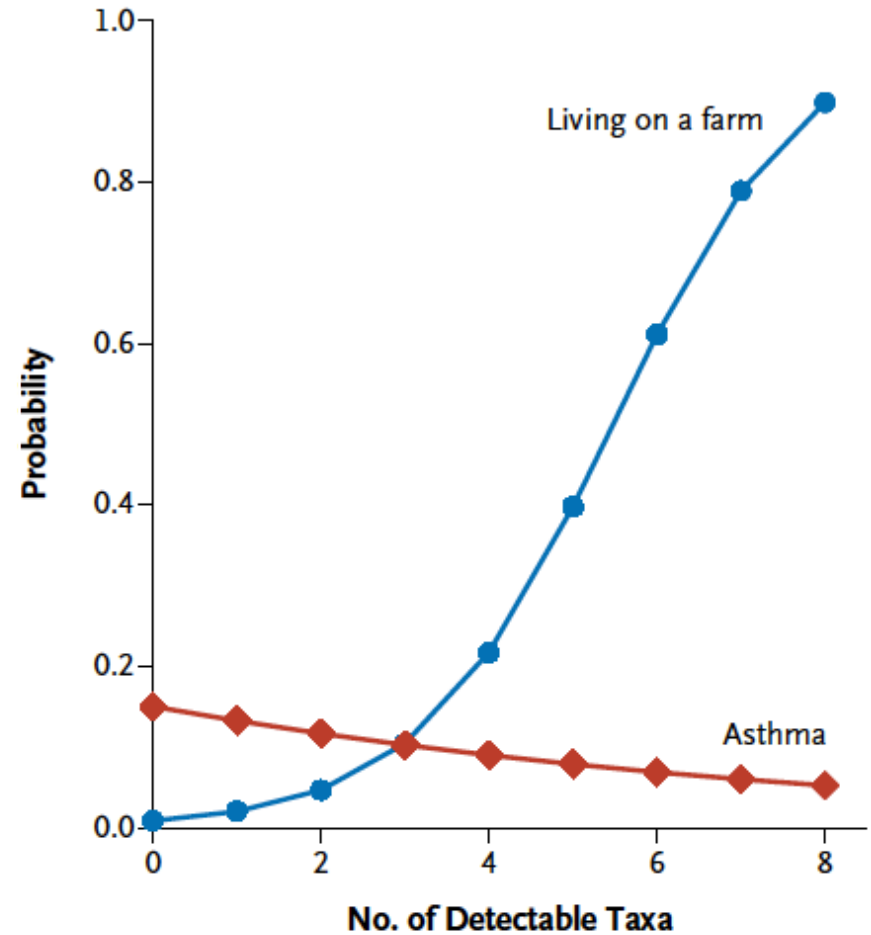
- Bavaria
- Switzerland
- Austria
- Finland
- Quebec
- U.S.
- Amish

# Diverse Protective Farm Microbiomes

**A Bacteria (PARSIFAL)**

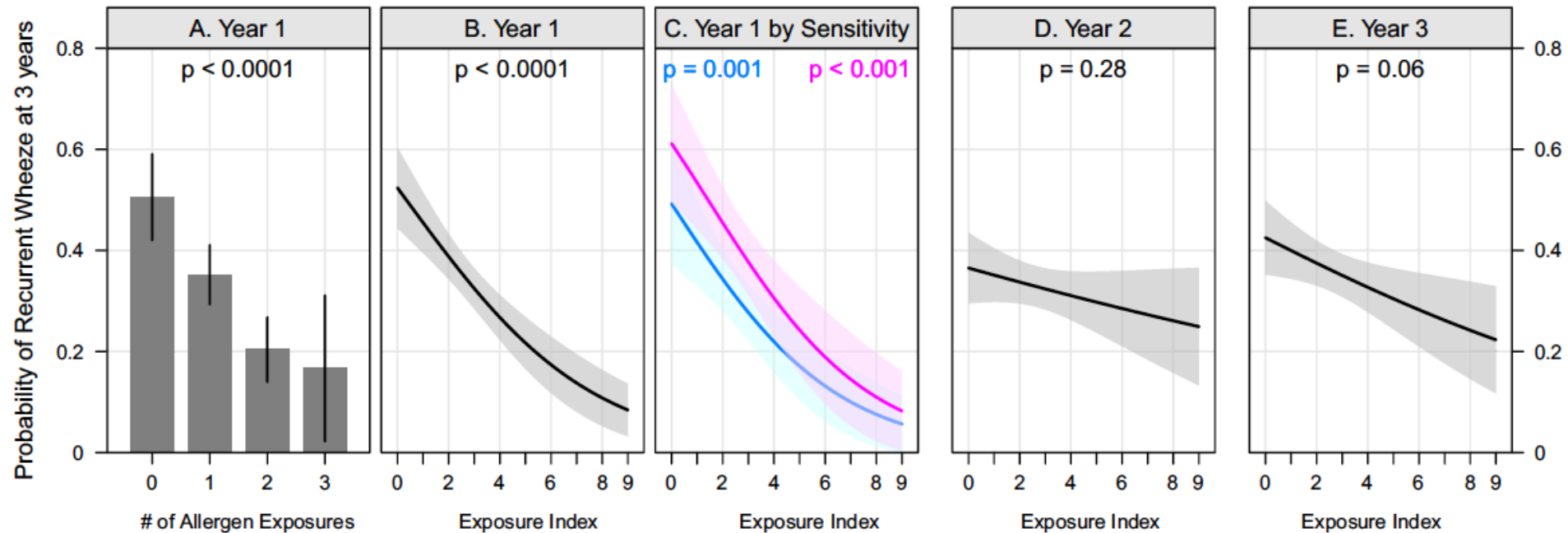


**B Fungi (GABRIELA)**



- Ege MJ et al. N Engl J Med 2011;364:701-9.

# In U.S. Inner-cities, greater cockroach, mouse &/or cat exposure and less wheeze



- Lynch SV et al. J Allergy Clin Immunol 2014;134:593-601.

# Mouse & cockroach allergen associated with more Bacteroidetes, Firmicutes, & Proteobacteria

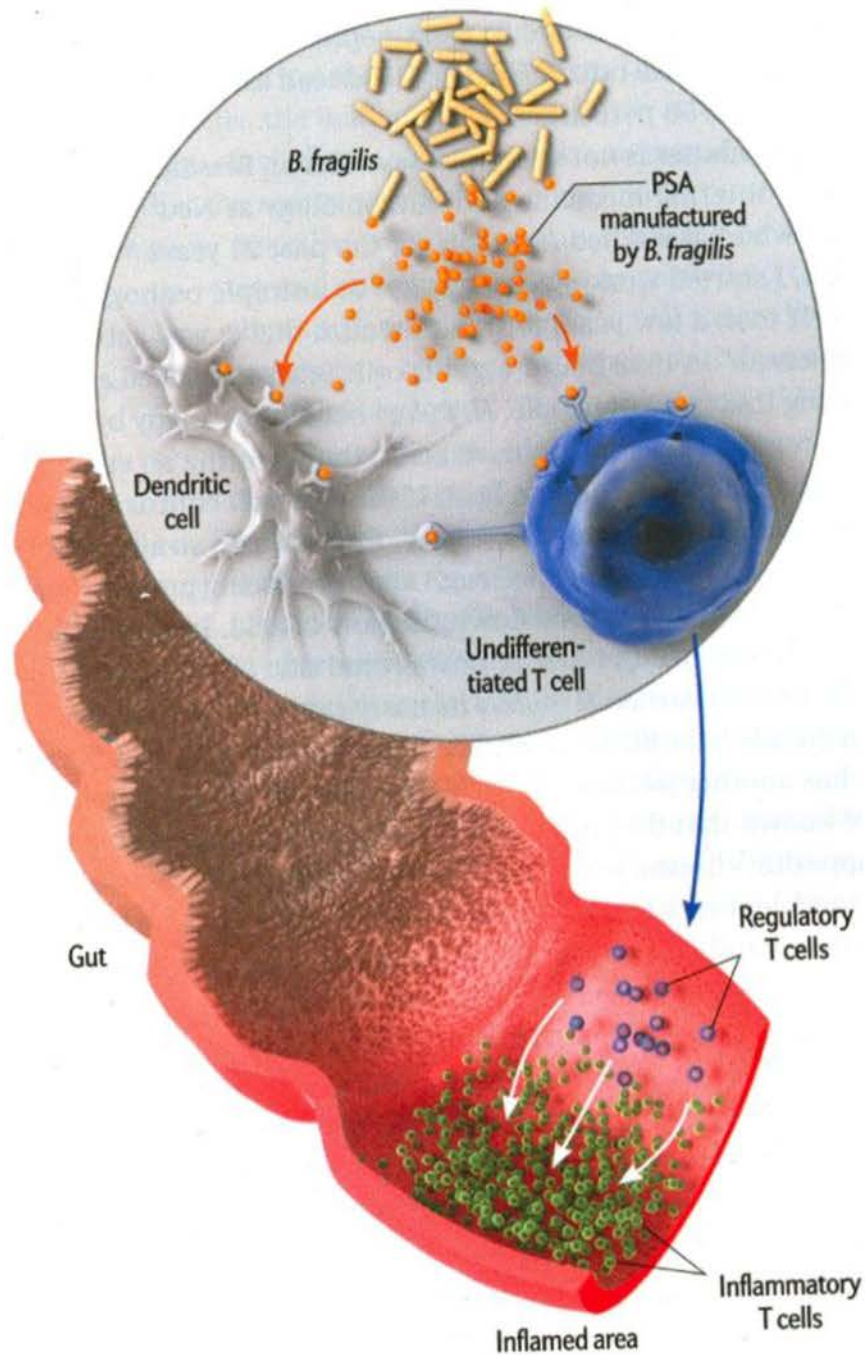
TABLE E7. Discriminatory taxa that exhibit a significant correlation with Mus m 1 or Bla g 1 allergen concentrations

eOTU	Phylum	Family	Genus	Mus m 1		Bla g 1	
				<i>r</i>	<i>FDR</i>	<i>r</i>	<i>FDR</i>
2279	Bacteroidetes	Bacteroidaceae	<i>Bacteroides</i>	0.3	0.0473	0.31	0.0589
1742	Bacteroidetes	Blattabacteriaceae	<i>Blattabacterium</i>	0.1	0.597	0.61	0.000
1223	Bacteroidetes	Blattabacteriaceae	<i>Blattabacterium</i>	0.11	0.5528	0.7	0.000
2282	Bacteroidetes	Porphyromonadaceae	<i>Dsygonomonas</i>	0.18	0.3334	0.57	0.000
1392	Bacteroidetes	Porphyromonadaceae	<i>Parabacteroides</i>	0.36	0.0077	0.67	0.000
455	Bacteroidetes	Prevotellaceae	<i>Prevotella</i>	0.37	0.0052	0.27	0.144
1710	Bacteroidetes	Prevotellaceae	<i>Prevotella</i>	0.31	0.0361	0.23	0.2376
2087	Bacteroidetes	Prevotellaceae	<i>Prevotella</i>	0.29	0.0598	0.33	0.0411
1708	Bacteroidetes	Prevotellaceae	<i>Prevotella</i>	0.32	0.026	0.24	0.2299
456	Bacteroidetes	Rikenellaceae	Unclassified	0.38	0.0029	0.32	0.0455
1071	Bacteroidetes	Rikenellaceae	Unclassified	0.38	0.0036	0.33	0.0369
2277	Bacteroidetes	Rikenellaceae	Unclassified	0.32	0.026	0.23	0.2521
1072	Bacteroidetes	Rikenellaceae	Unclassified	0.27	0.1059	0.34	0.0315
556	Bacteroidetes	Rikenellaceae	Unclassified	0.36	0.0077	0.24	0.2242
1340	Bacteroidetes	Rikenellaceae	Unclassified	0.35	0.0099	0.3	0.0743
903	Firmicutes	Enterococcaceae	<i>Melissococcus</i>	0.05	0.793	0.37	0.0085
1412	Firmicutes	Lachnospiraceae	Unclassified	0.3	0.0427	0.08	0.8021
1850	Firmicutes	Ruminococcaceae	<i>Oscillospira</i>	0.31	0.0389	0.16	0.5359
818	Firmicutes	Veillonellaceae	Unclassified	0.3	0.0466	0.2	0.3426
632	Firmicutes	Unclassified	Unclassified	0.3	0.0423	0.06	0.8598
524	Proteobacteria	Desulfovibrionaceae	Unclassified	0.14	0.44	0.69	0.000
Total no. of significant taxa					14		10

eOTU, Empiric Operational Taxonomic Unit; FDR, false discovery rate.

- Lynch SV et al. J Allergy Clin Immunol 2014;134:593-601.

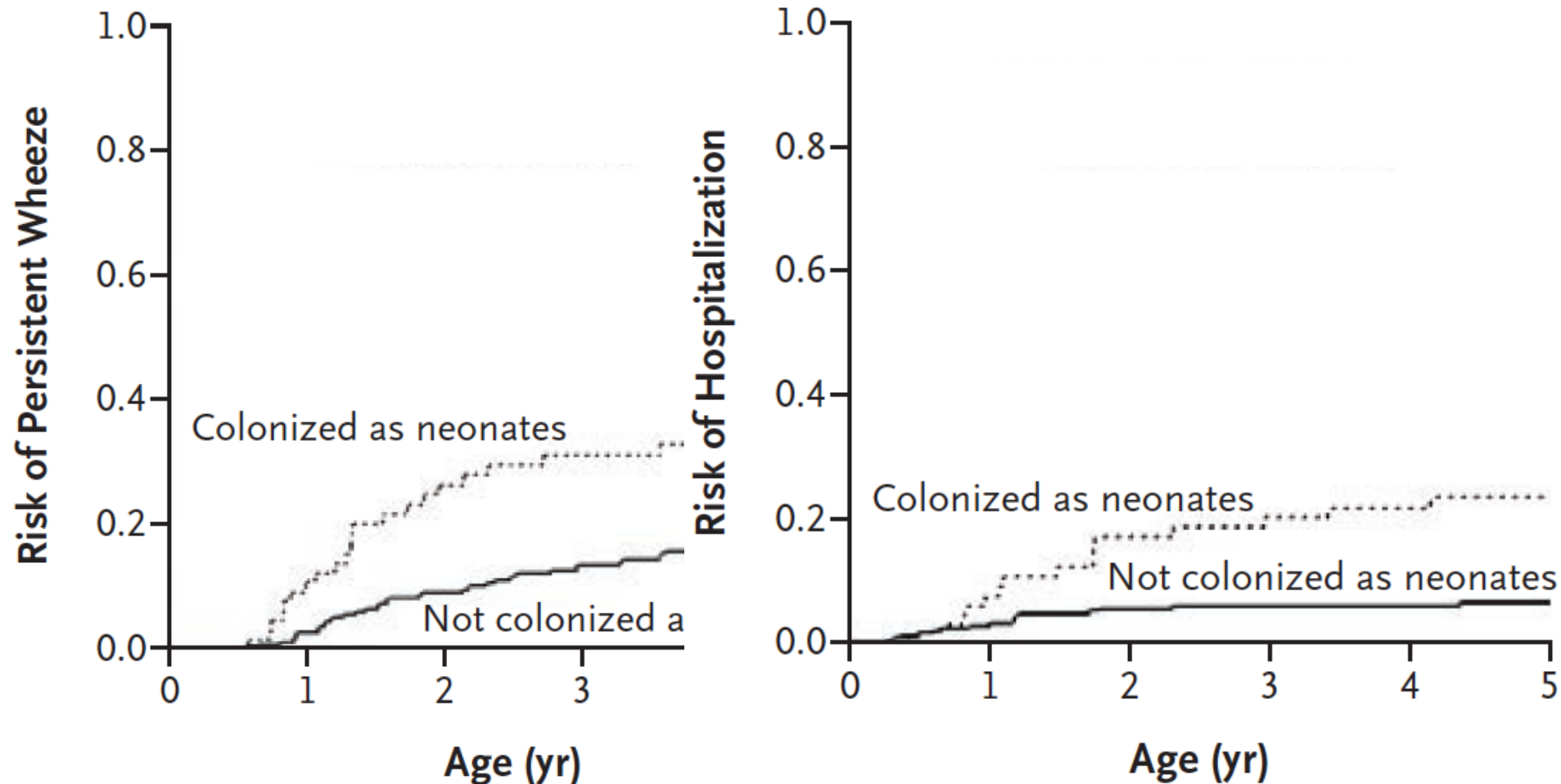




- Ackerman J. The Ultimate Social Network. Sci. Am. Page 25; June 12, 2012.

# Nasopharyngeal colonization with airway pathogens in infancy and asthma risk

(*Strep. Pneumoniae*, *Haemo. influenza*, *M. catarrhalis*)



# Denver Children's Environmental Health Center: Environmental Determinants of Airway Disease in Children

## ***Project 1: Endotoxin & Asthma in Children***

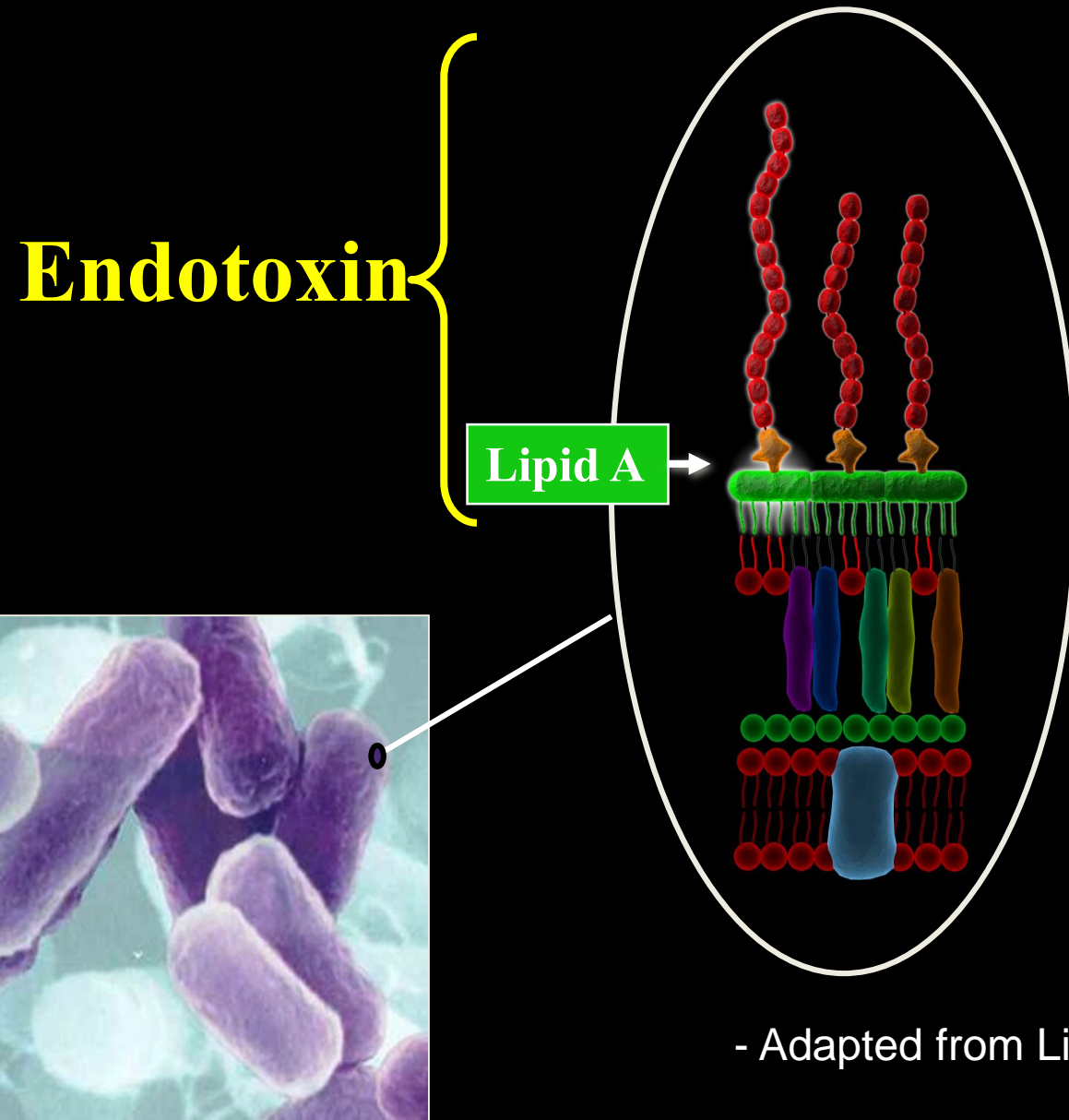
### Investigators & key personnel:

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Allison Schiltz	Lisa Cicutto
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Kristy Freeman	<u>Channing Lab</u>
Julie Henley	Gus Litonjua
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Ronina Covar	
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Mike Van Dyke	Jonathan Thornburg
Matt Strand	Seung-Hyun Cho
Stan Szeffler	Ryan Chartier
David Schwartz	Charles Rodes

**Funded by EPA STAR  
(GAD# 834515010) and  
NIH NIEHS (P01 ES-018181)**

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# Endotoxin: *Prototypical PAMP*



- Adapted from Liu AH. JACI, 109:379-392, 2002.



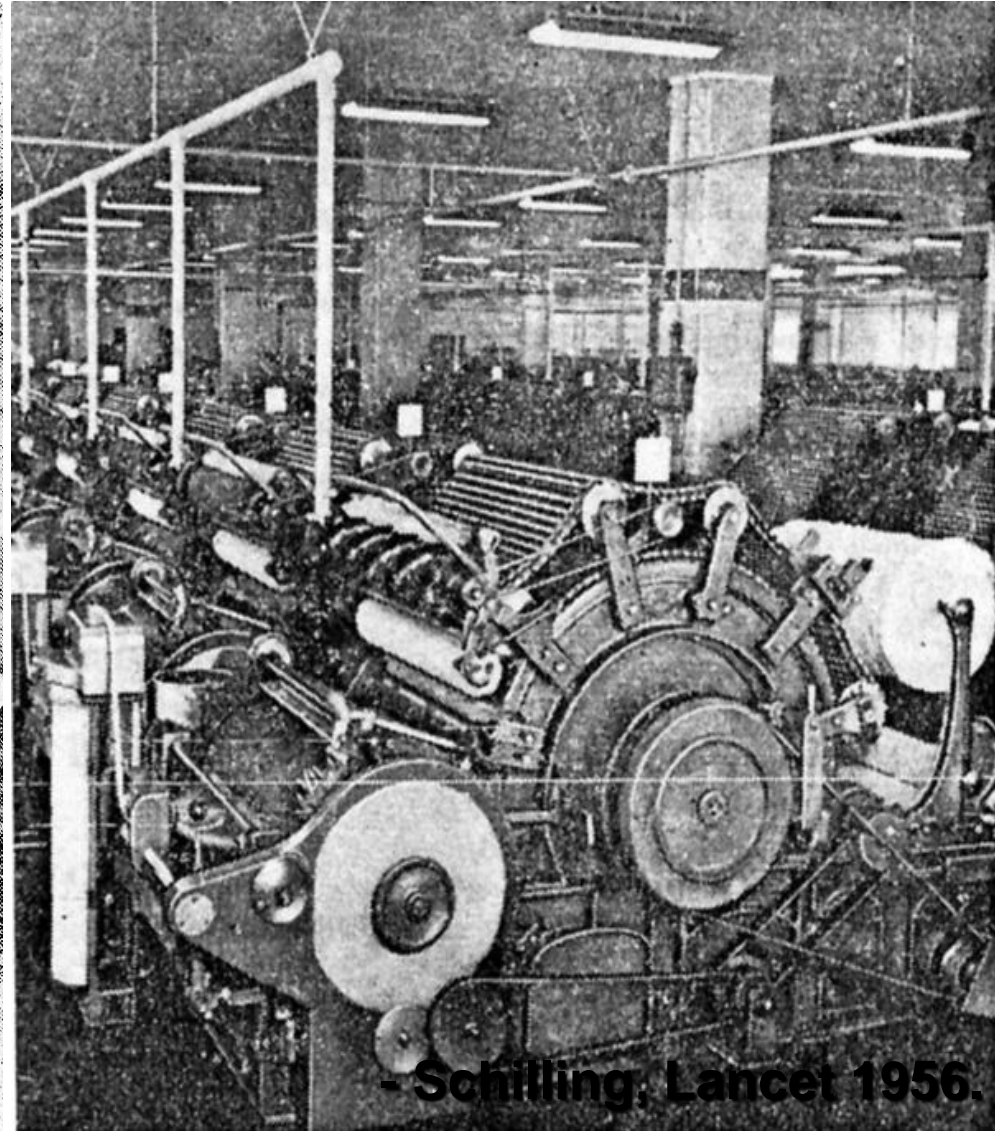
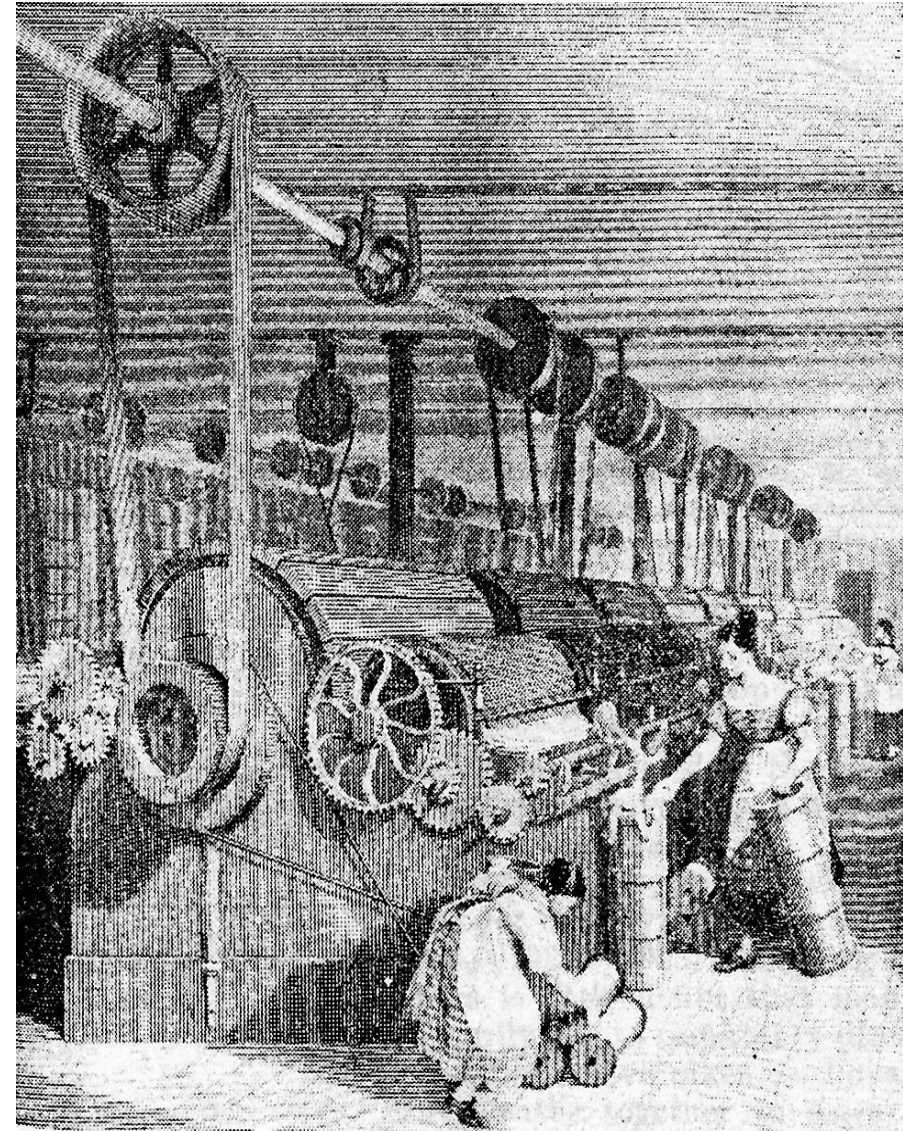
# Byssinosis: *Monday Asthma in Cotton Workers*

1830' s

*Carding Machines: covered*

1890' s

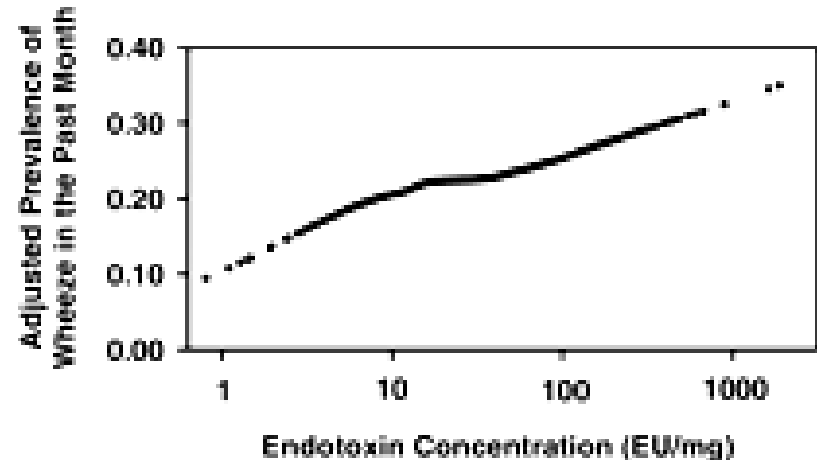
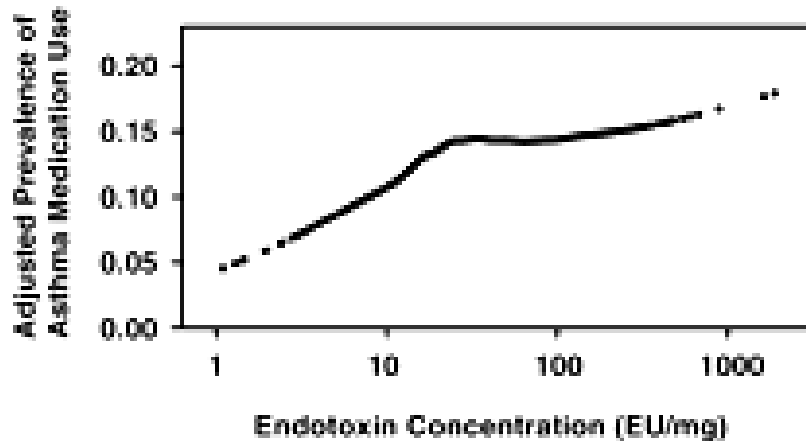
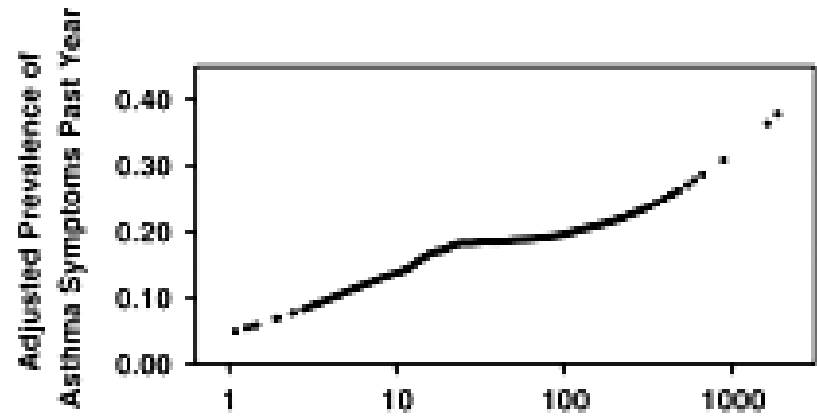
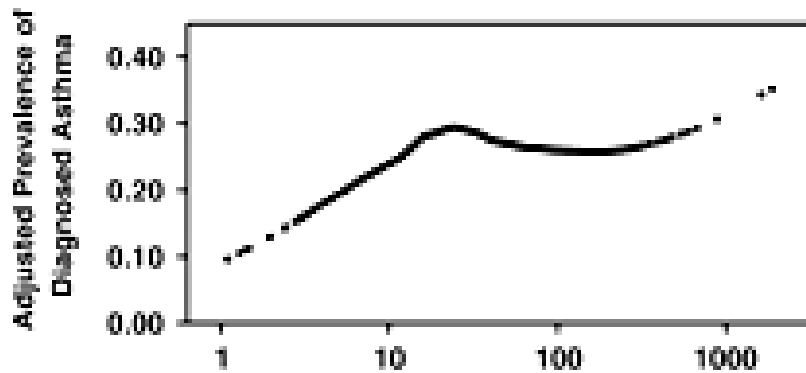
*Carding Machines: open*



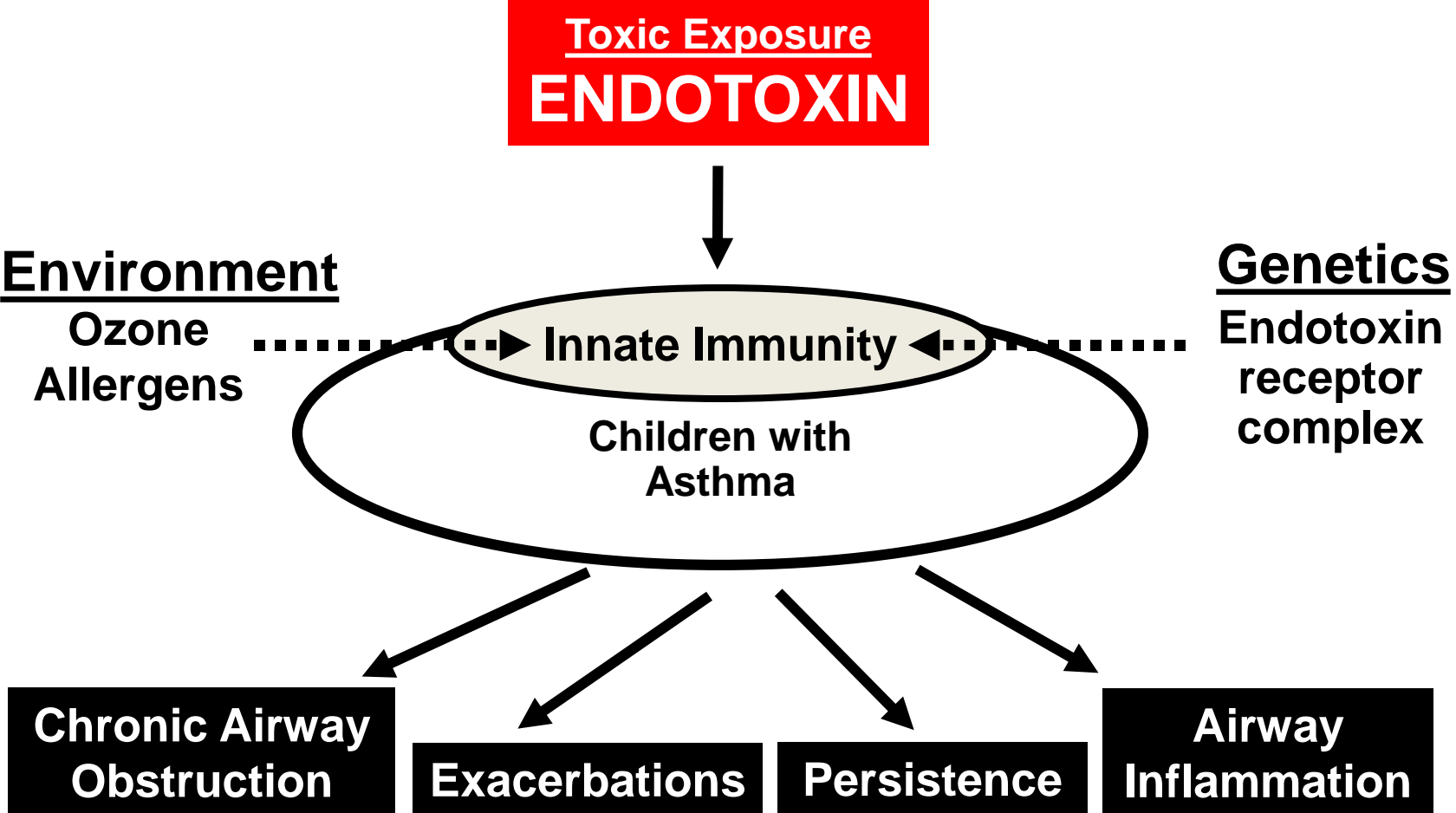
- Schilling, Lancet 1956.



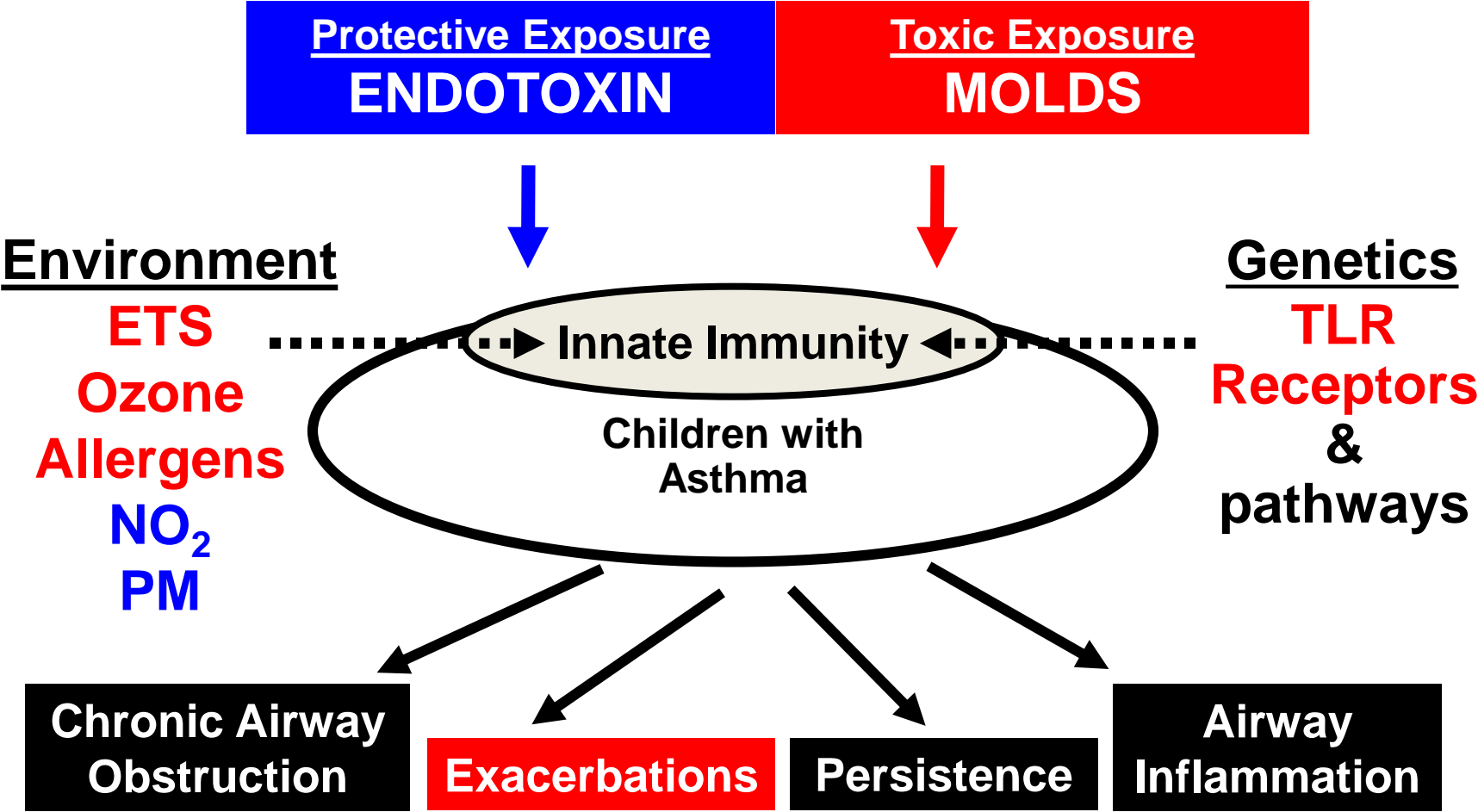
# Bedroom-dust endotoxin & asthma prevalence, symptoms & med use (NSLAH)



# Endotoxin Exposure & Asthma in Children: *paradigm*

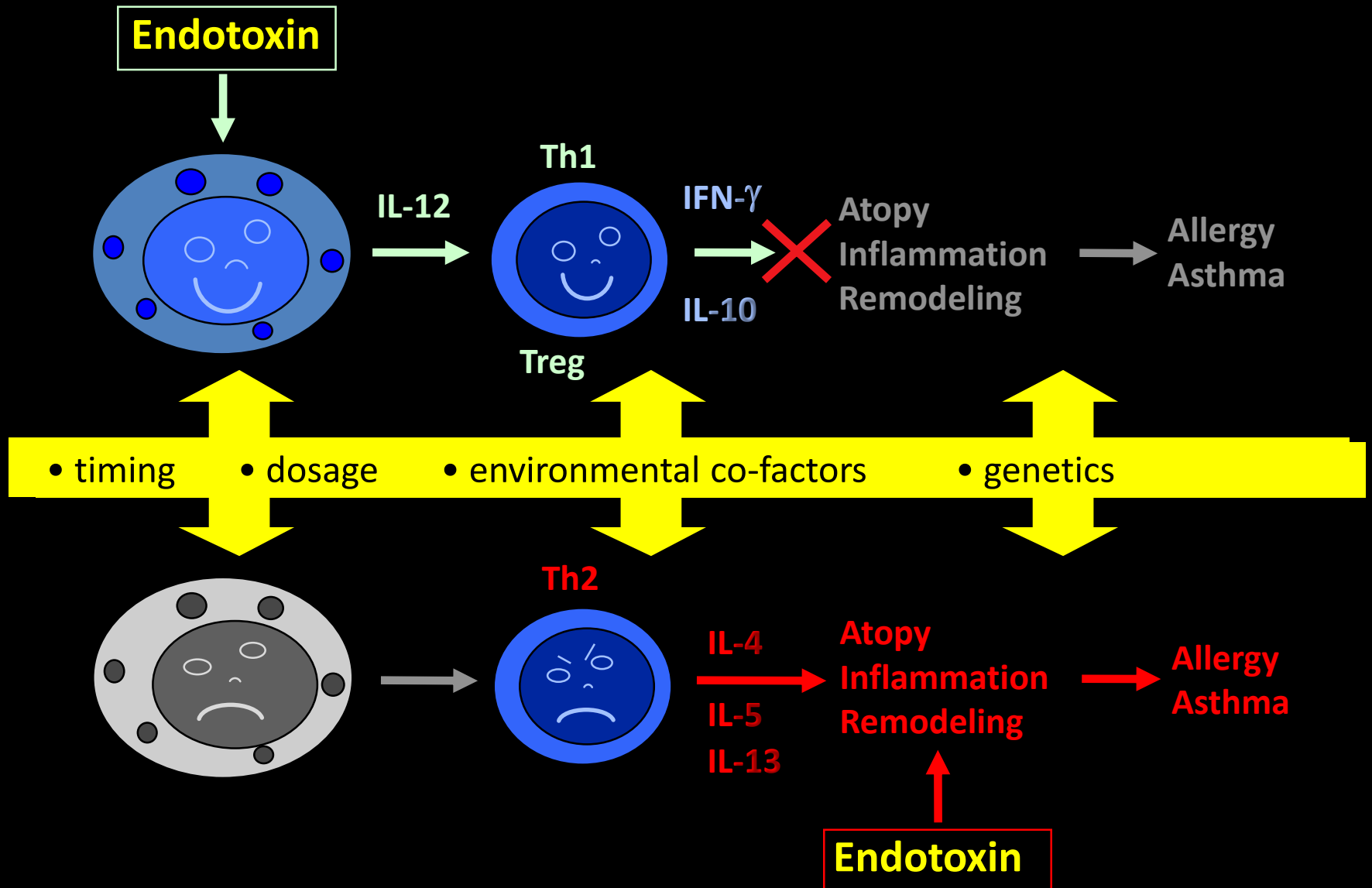


# Endotoxin Exposure & Asthma in Children: *Paradigm revised*

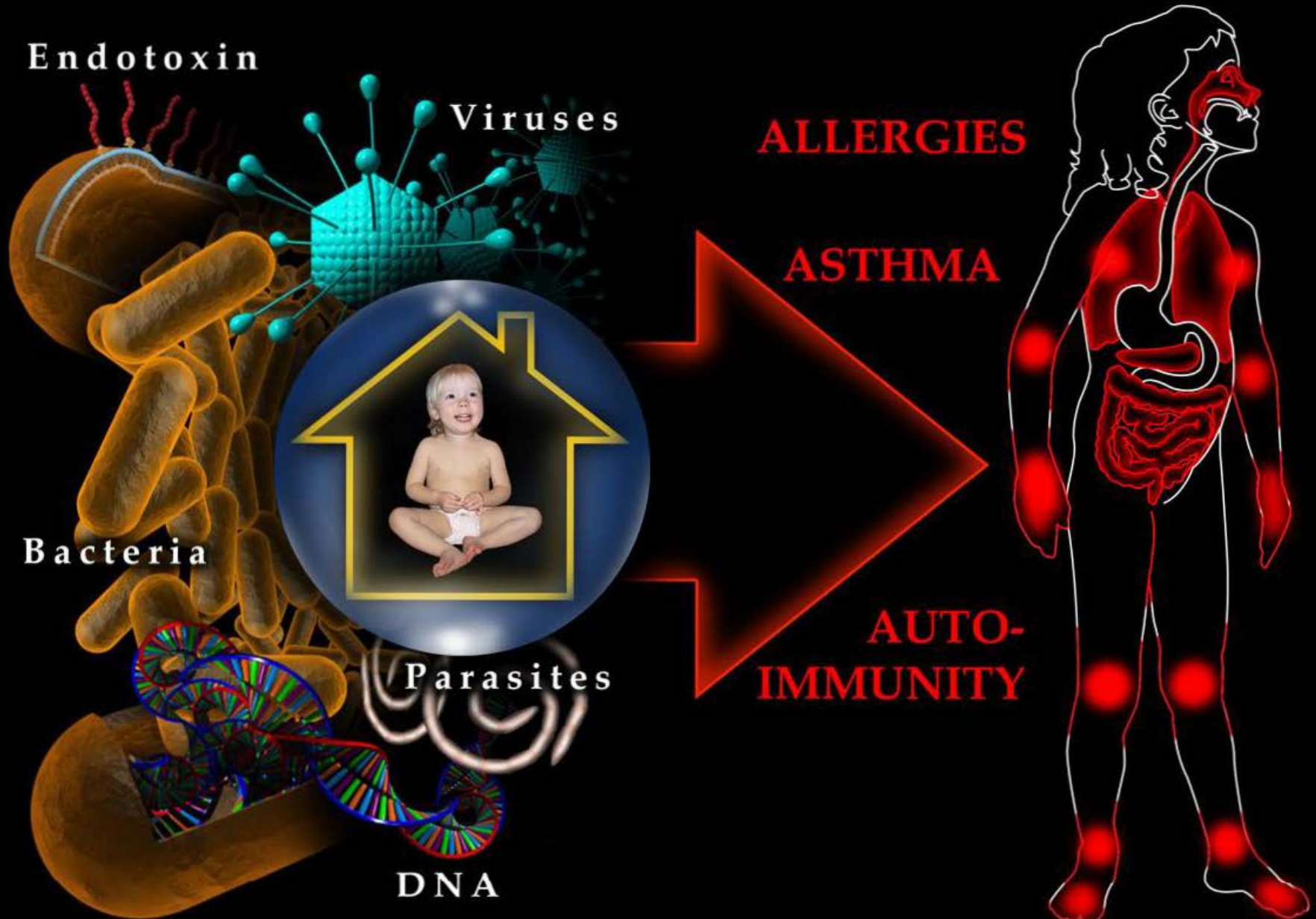




# Endotoxin: *Friend & Foe?*

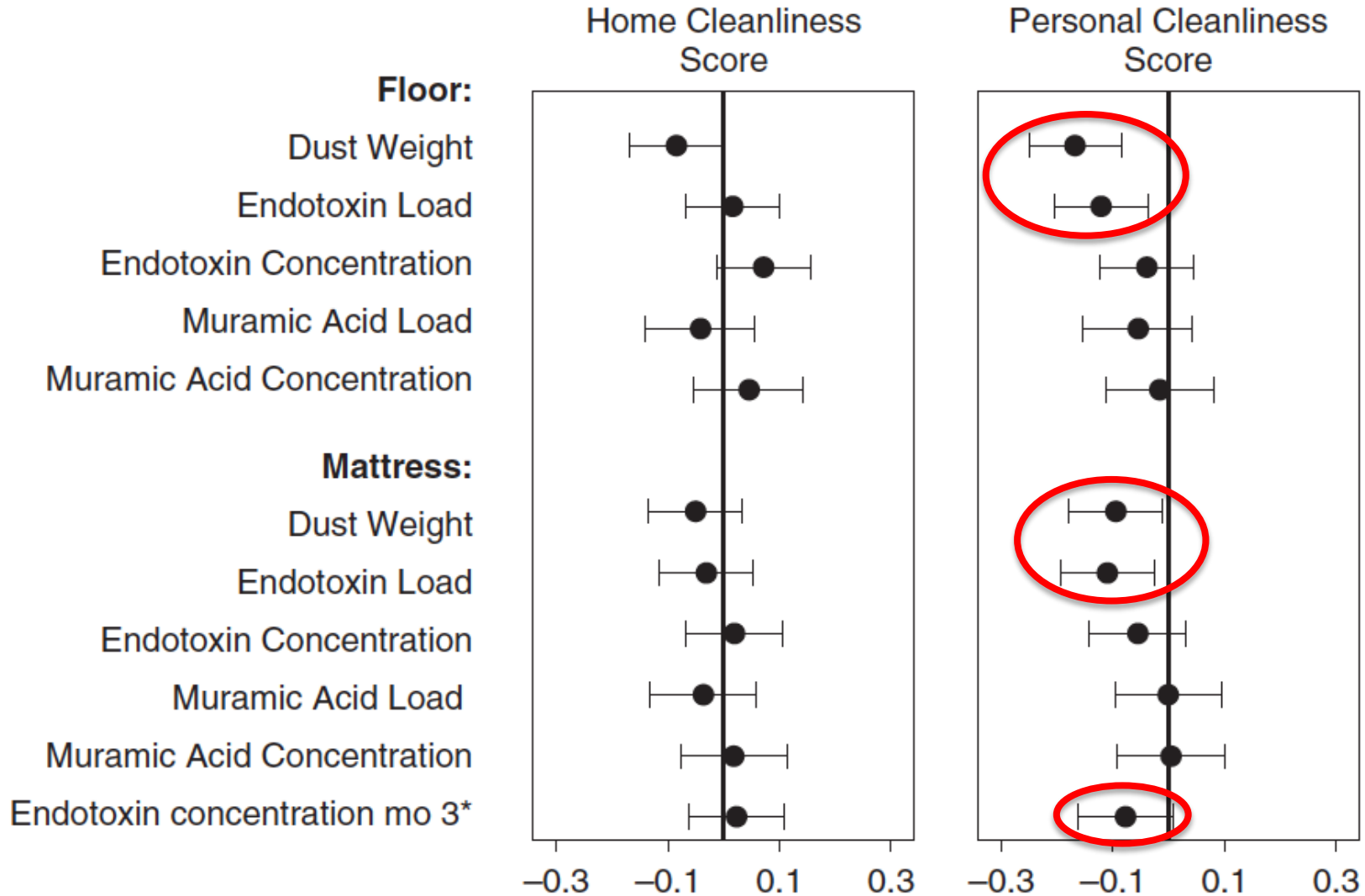


# Hygiene Hypothesis: *Fact or Fiction?*



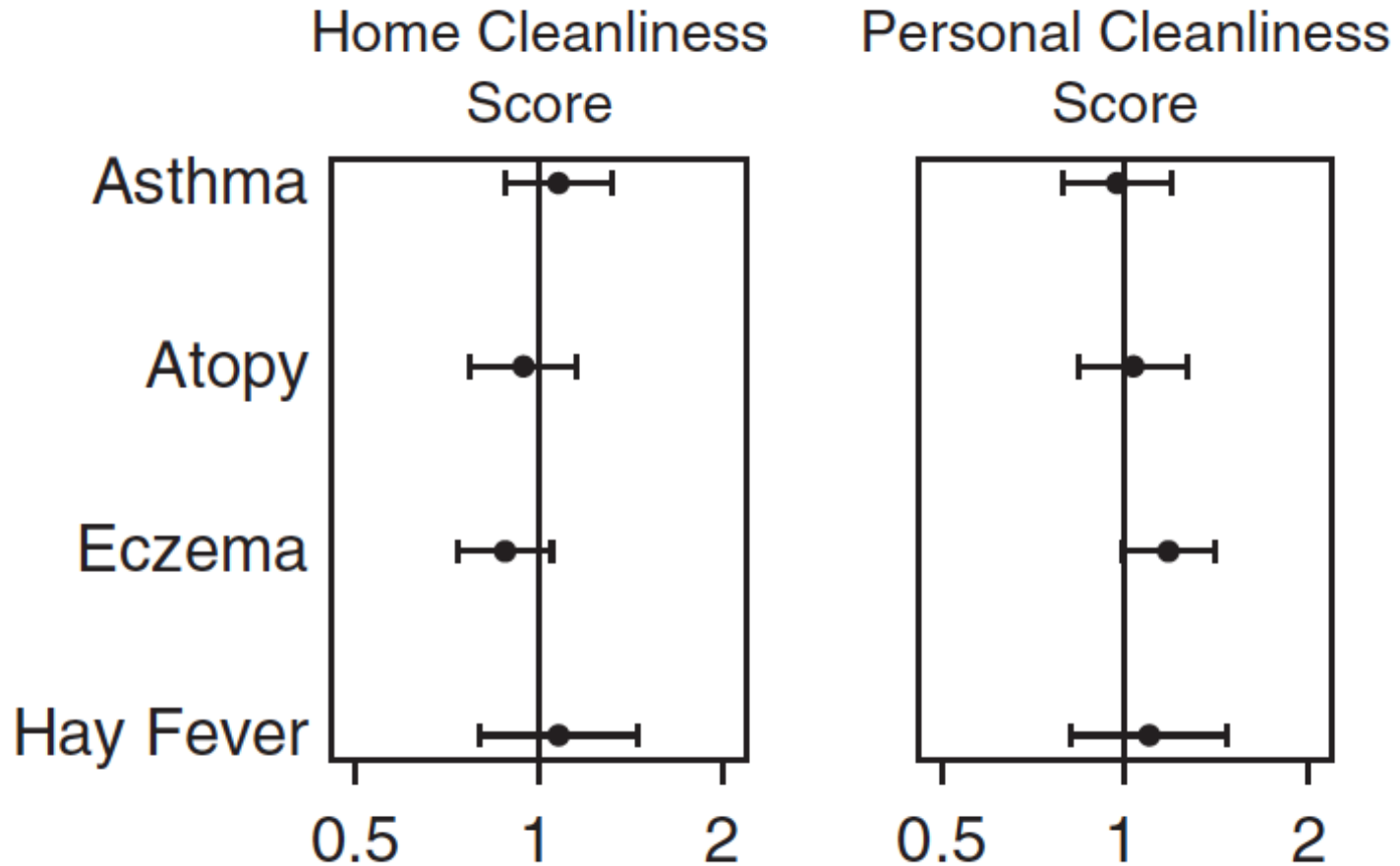
- Liu AH, Murphy JR. JACI (2003) 111:471-8.

# Asthma & the Hygiene Hypothesis: Does Cleanliness Matter?



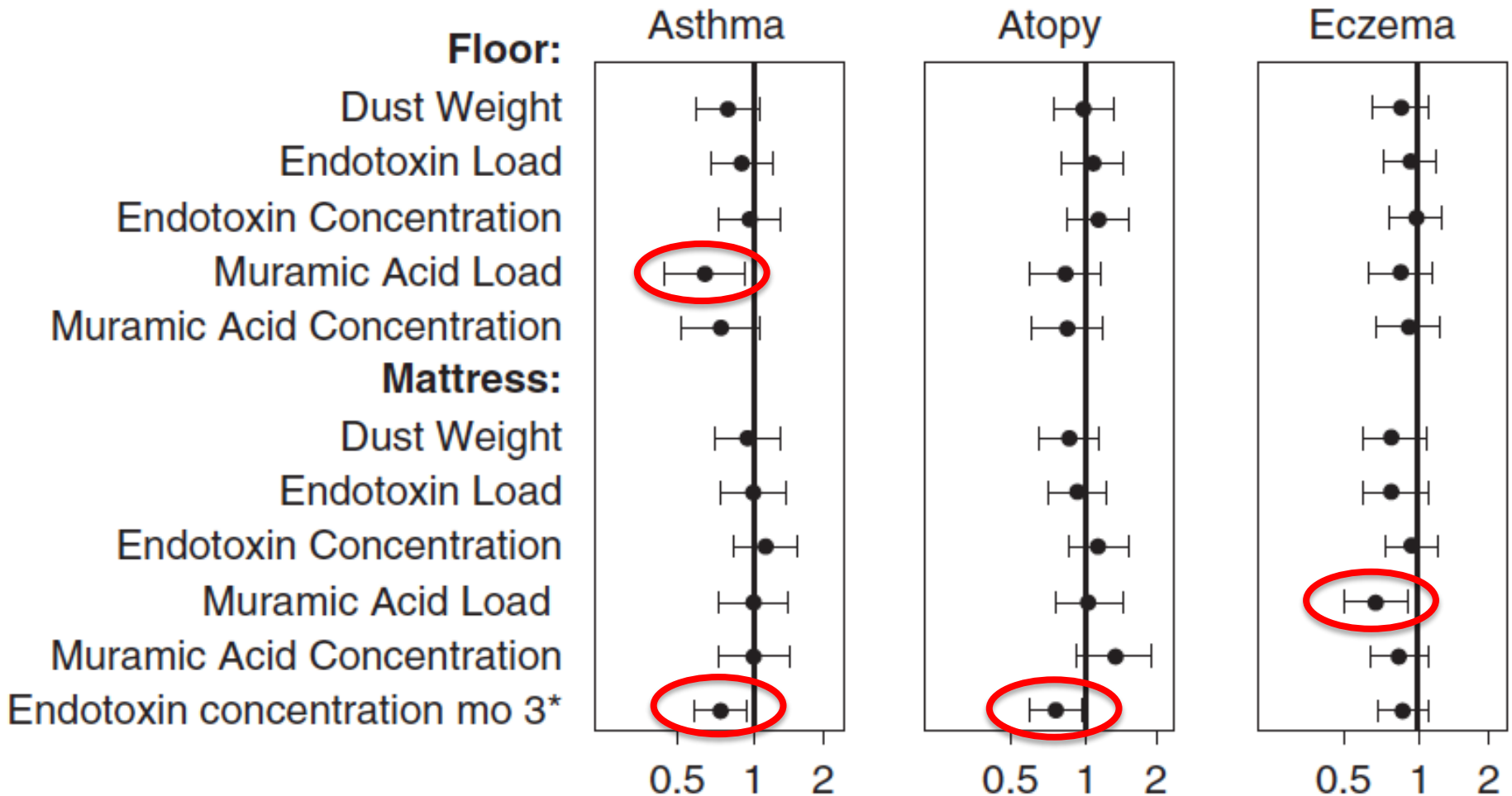
- Weber J, et al. AJRCCM 191:522-9 (2015).

# Asthma & the Hygiene Hypothesis: Does Cleanliness Matter?





# Endotoxin & Muramic Acid Effects on Asthma & Allergy







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