LEIDEN UNIVERSITY MEDICAL CENTER

Allergy in Developing Countries; *role of micro organisms and parasites in development of food allergy*

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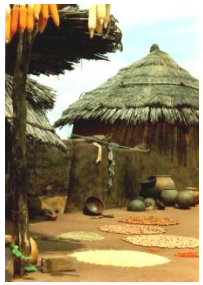
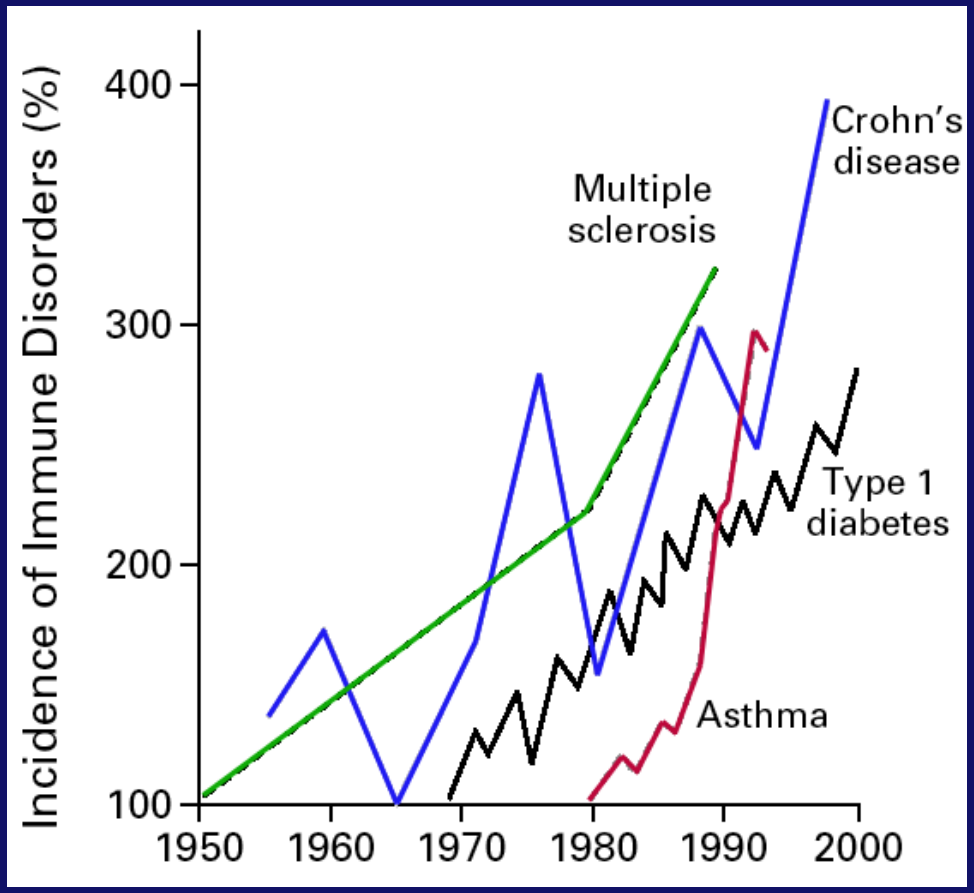




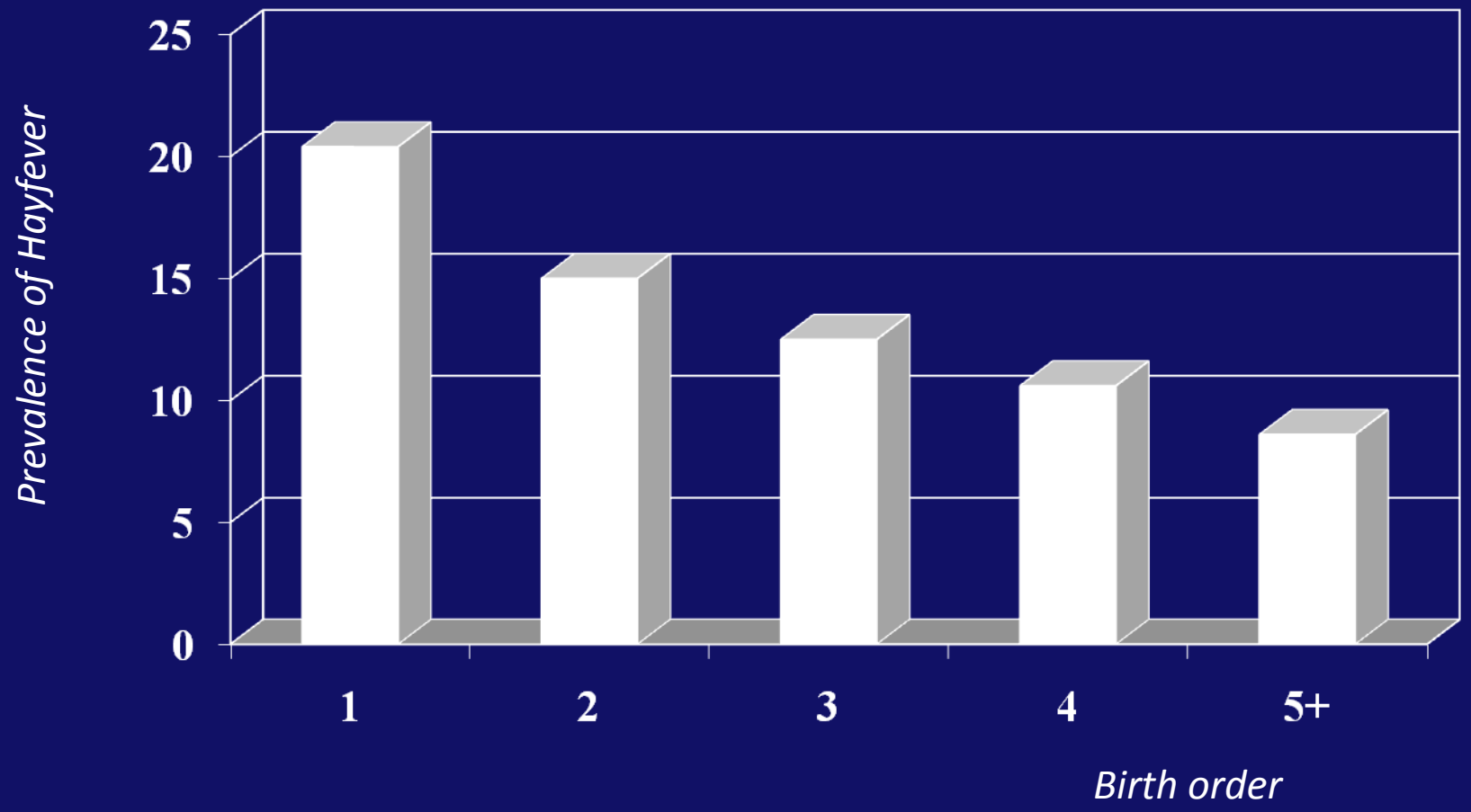
The increasing incidence of immunoregulatory disorders

From Bach J-F., (2002) 347:911-920



Hayfever and household size

Strachan 1989 "The Hygiene Hypothesis"

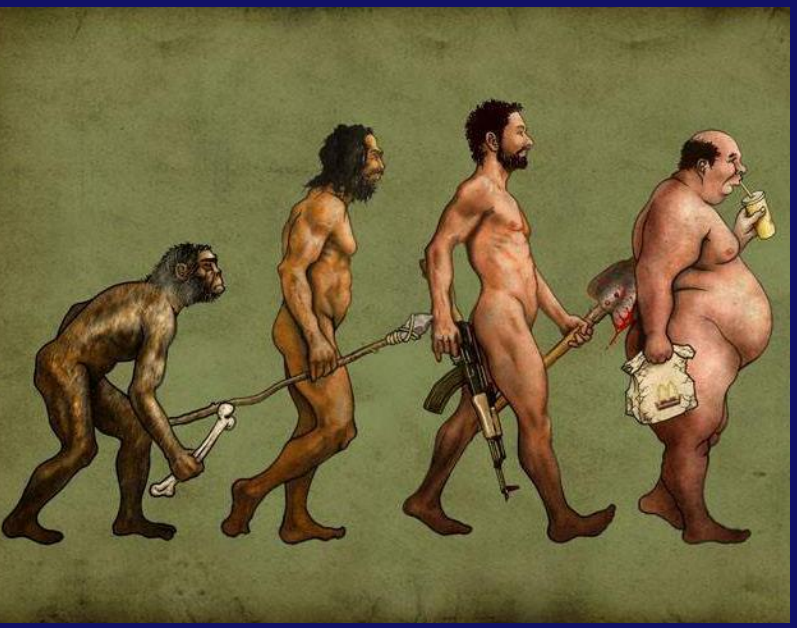


Why are inflammatory diseases increasing ?

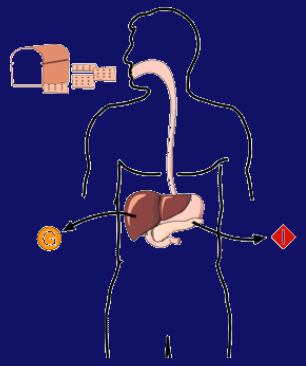
in the
West and Urban centres of developing countries
(between 1985 and 2000 nr of people with allergy doubled)

Exposure to infections
Physical exercise
Diet
Pollution

Remember !!The immune system has evolved in the presence of micro organisms and parasites

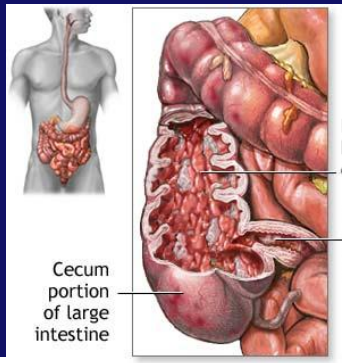


infections



diabetes

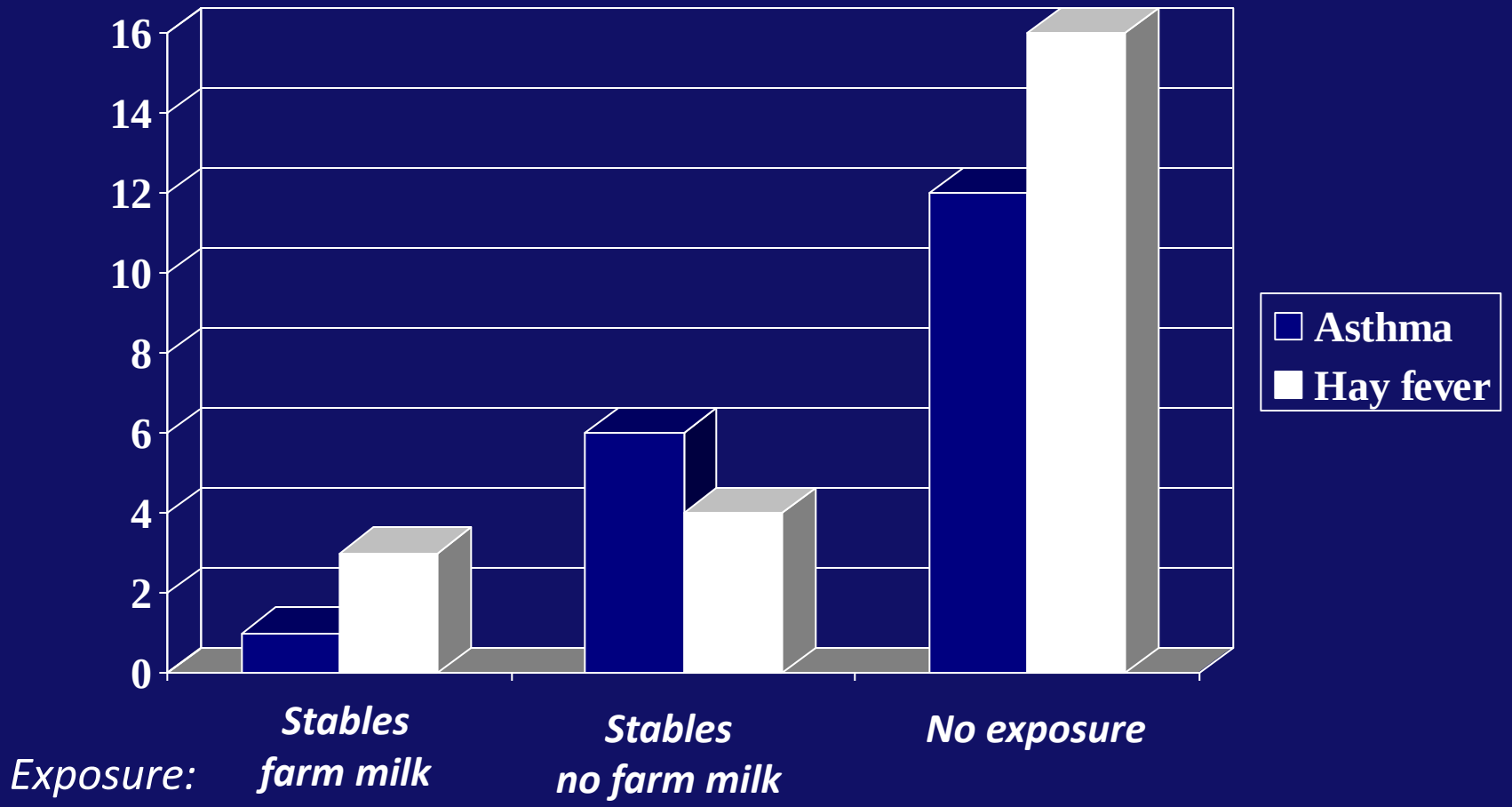
asthma



Inflammatory bowl disease

Exposure to traditional farming in Europe reduces the risk of allergies

(Riedler et al 2001)



Spot similarities !!

Children living on traditional farms in Germany, Austria and Switzerland

1900s

2006

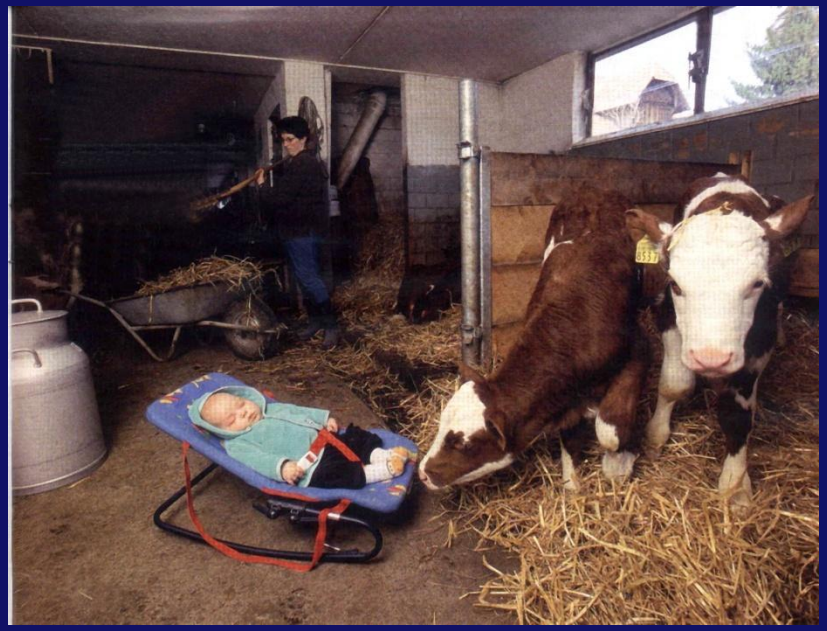
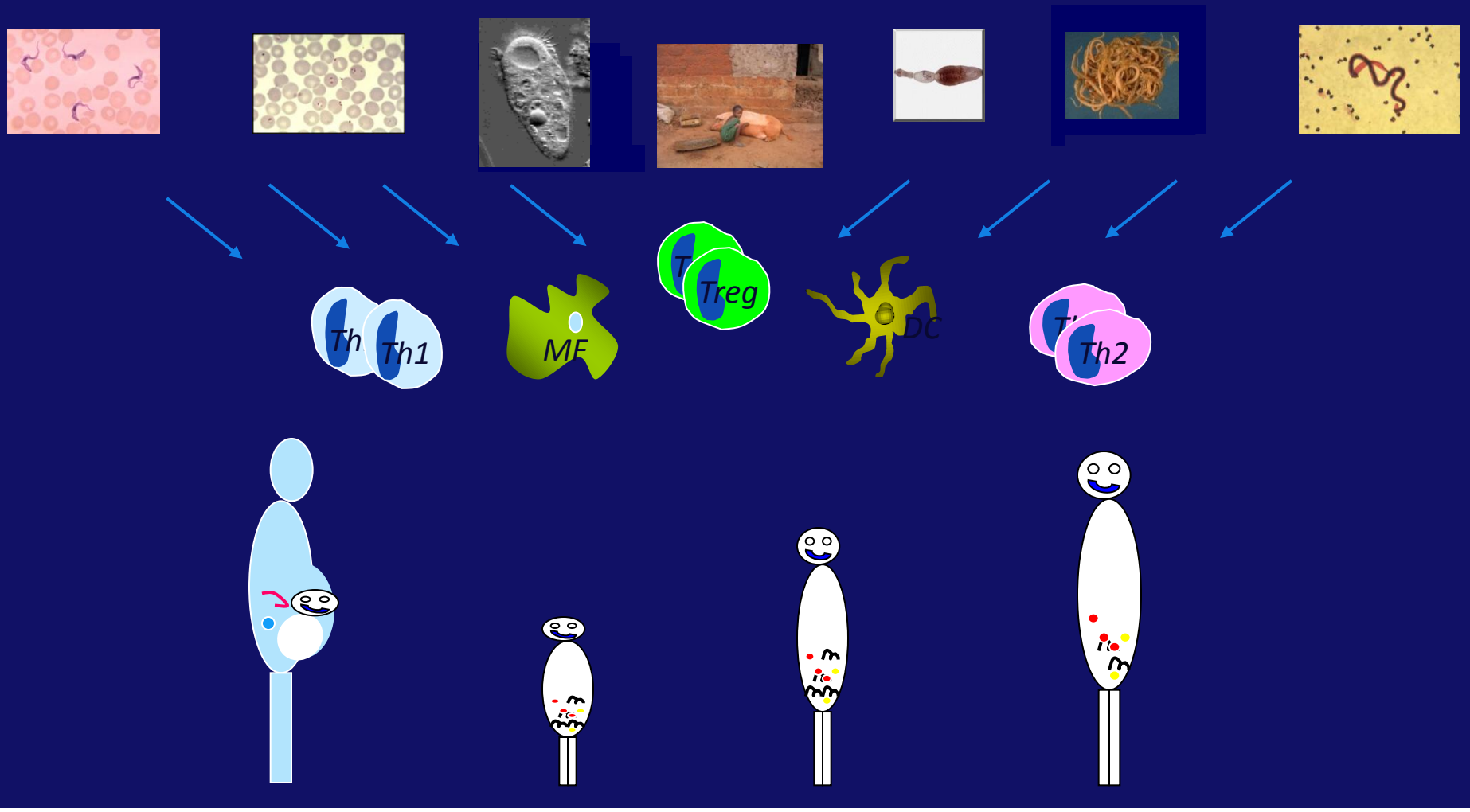


Photo from Erika von Mutius

Bacteria, *Moulds*, Farm milk, *Animal products*

In many parts of the world: infections

relentlessly challenge the immune system of a child for years



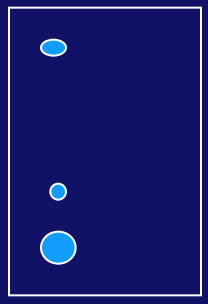
Skin prick test reactivity to allergens in epidemiological studies







SPT results

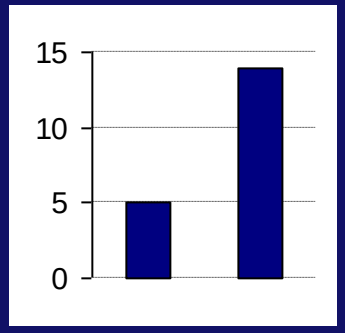


House dust mite
Cat
Dog
grass
Peanut
Histamine
-ve Control

Negative association between helminths and skin reactivity to allergens

% SPT positive

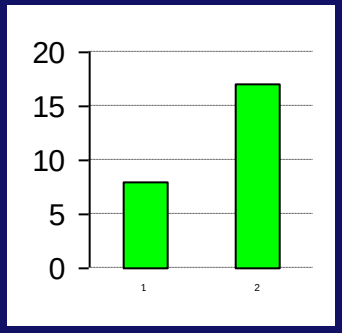
Cockroach SPT



Filariasis

Indonesia

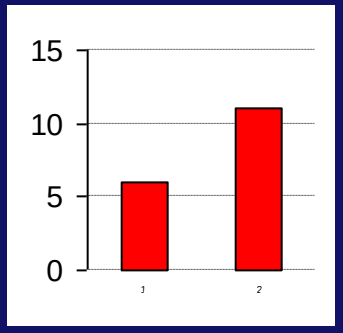
Mite SPT



Schistosomiasis

Gabon

Mite SPT



Hookworm & Trichiuris

Ghana

Experimental Schistosomiasis-Asthma model

OVA sensitisation

challenge

Infection
untill 16 weeks

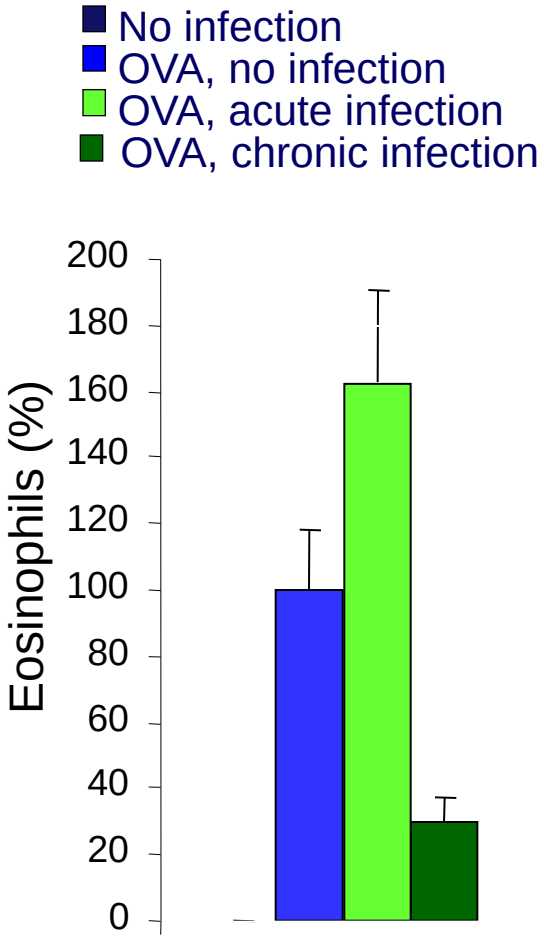
11 12 13 14

OVA aerosols

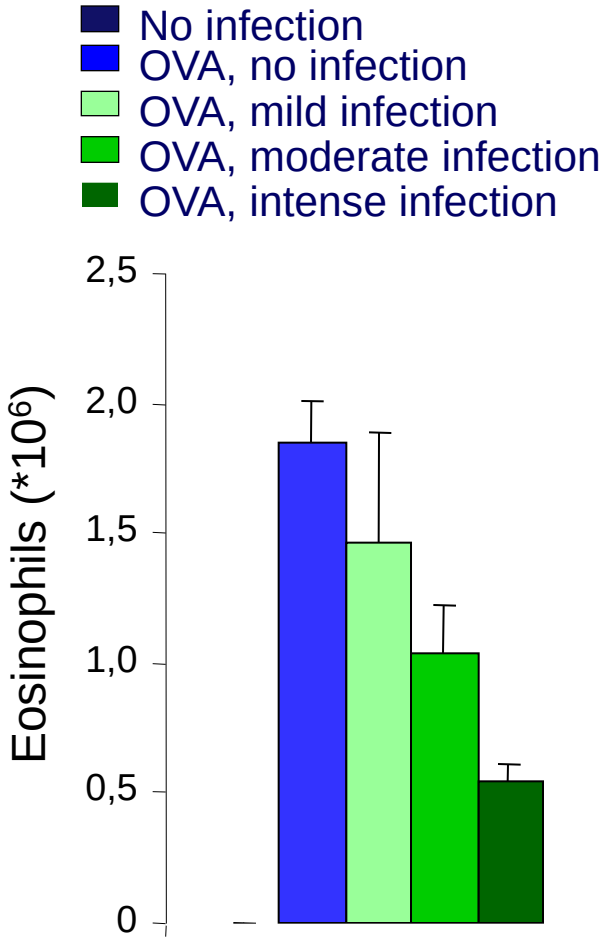
Eosinophilic airway inflammation??

OVA-induced airway inflammation is reduced during chronic schistosomiasis

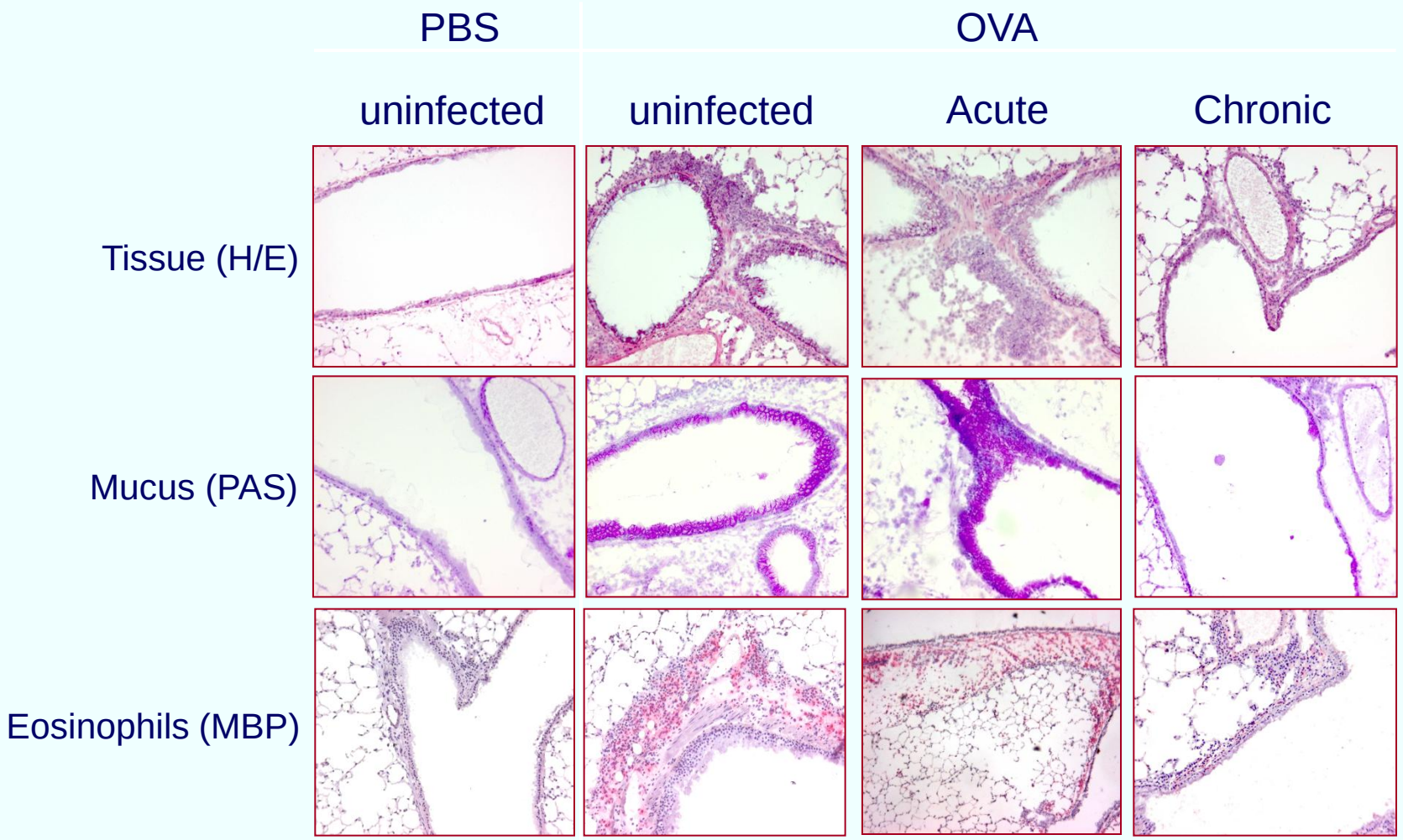
Acute vs chronic schistosome infection



Infection intensity



Reduction in OVA-induced eosinophilic airway inflammation in lung tissue



Helminths are among group of
micro organisms and parasites that can suppress
allergic inflammation

Joel Weinstock

Whipworm (*Trichuris app)*

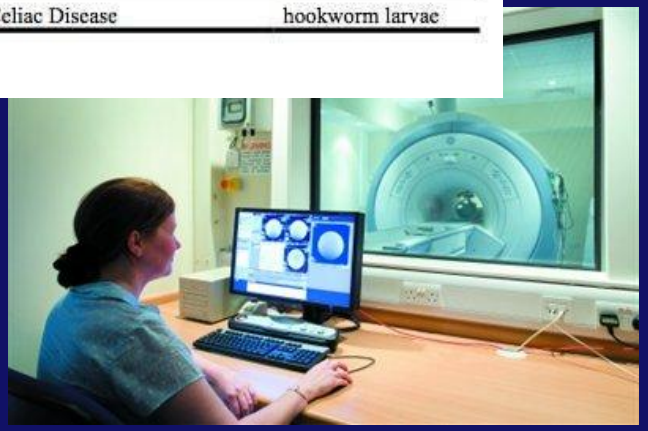
Clinical trials : infecting patients with helminths

Large number of helminth therapy trials have been registered

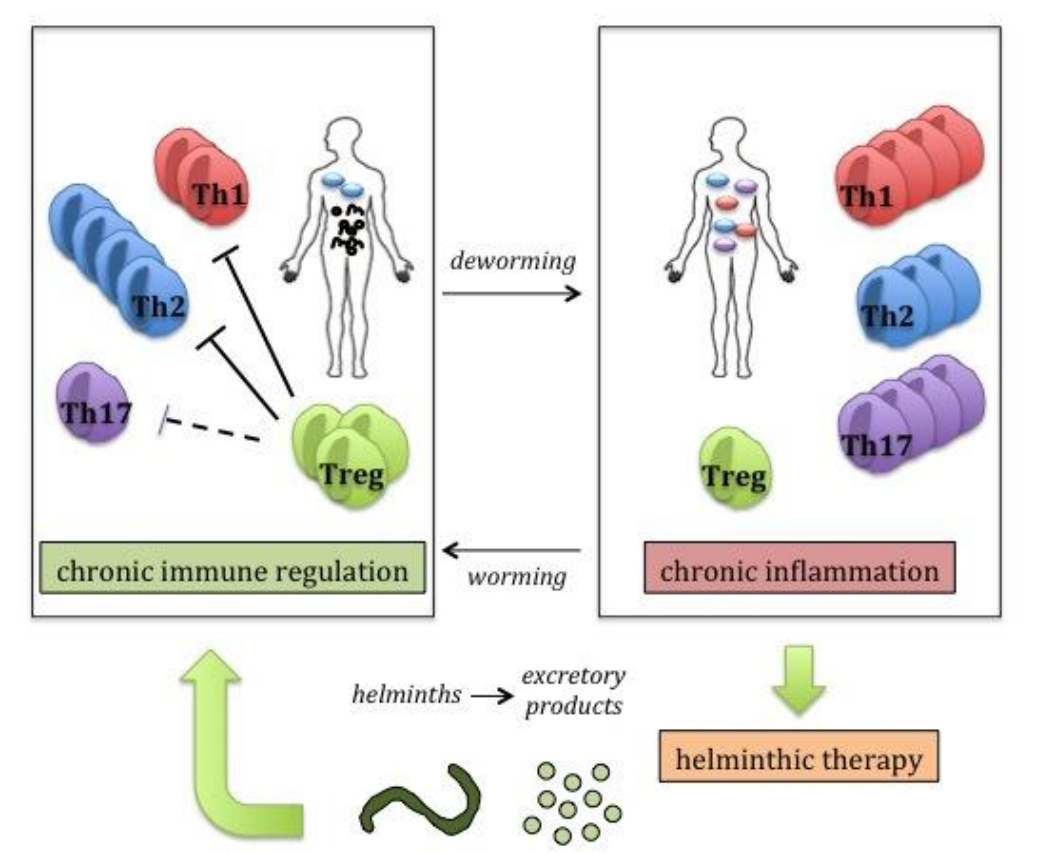
Trial identifier	Sponsor	Phase	Status	Condition	Intervention
ACTRN12608000241336	Asphelia Pharaceuticals	1	not yet recruiting	Crohn's disease	TSO
EUCTR2007-006099-12-DK	Statens Serum Institut, Denmark	2	completed	Allergic rhinitis	TSO
NCT00645749	University of Wisconsin, Madison, US	2	recruiting	MS	TSO
NCT01006941	Rigshospitalet, Copenhagen, Denmark	2	completed	MS	TSO
NCT01040221	Montefiore, New York, US	1	not yet recruiting	Autism	TSO
NCT01070498	Beth Israel,Boston, US	1	completed	Food allergy	TSO
NCT01279577 / EUCTR2006-000720-13-DE	Dr. Falk Pharma, Frankfurt, Germany	2	recruiting	Crohn's disease	TSO
NCT01413243 / EUCTR2009-015319-41-DE	Charite, Berlin, Germany	2	recruiting	MS	TSO
NCT01433471	NYU, New York, US	2	recruiting	Ulcerative colitis	TSO
NCT01434693	Coronado Biosciences, US	1	ongoing	Crohn's disease	TSO
NCT01576471	Coronado Biosciences, US	2	recruiting	Crohn's disease	TSO
NCT01734941	Hadassah Medical Organization, Jerusalem, Israel	2	not yet recruiting	Autism	TSO
NCT00232518	University of Nottingham, UK	1	completed	Allergic rhinoconjunctivitis	hookworm larvae
NCT00469989	University of Nottingham, UK	1	completed	Asthma	hookworm larvae
NCT00671138	Brisbane, Australia	2	unknown	Celiac Disease	hookworm larvae
NCT01470521 / EUCTR2008-005008-24-GB	University of Nottingham, UK	2	recruiting	MS	hookworm larvae
NCT01661933	Brisbane, Australia	1&2	recruiting*	Celiac Disease	hookworm larvae

*recruiting by invitation only

Hookworm trial of MS patients



Molecules derived from helminths to treat inflammatory diseases



Global burden of disease

Past

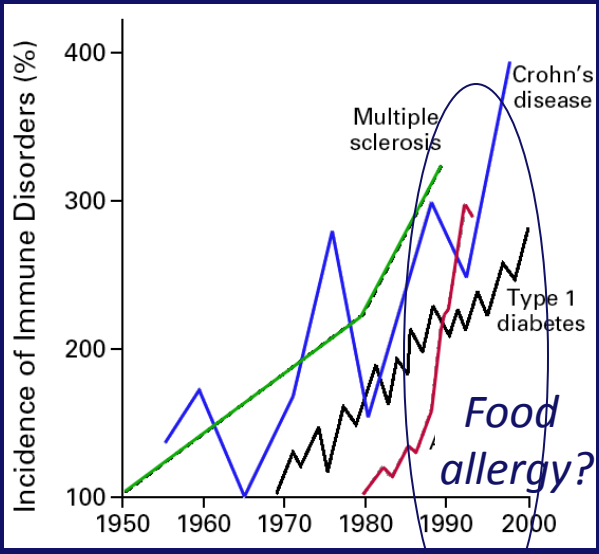
Present

Infectious Diseases

Autoimmune
Allergic
Inflammatory Bowel
Cardiovascular
Metabolic
Diseases

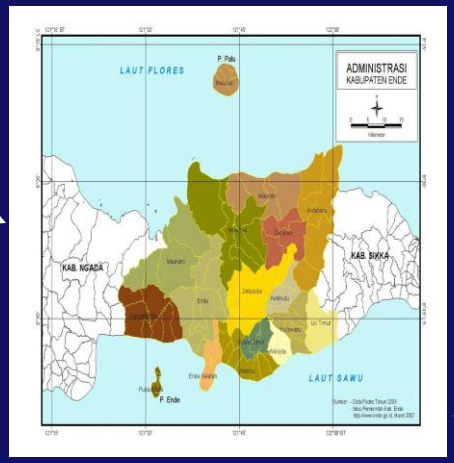
Conclusion on prevalence of food allergy

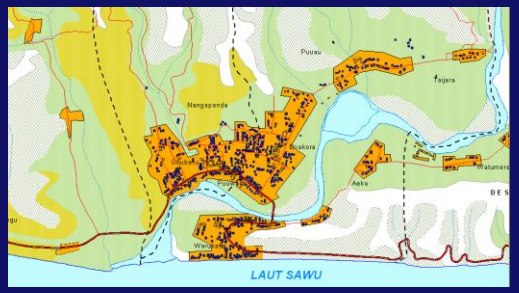
There is little information on food allergy
but
along with other allergies it is expected to increase
in rapidly urbanizing world



KNAW-funded project: web of immune regulation

To understand the relationship between parasitic infections, inflammation and immune responses







Indonesia : Flores Island

730 households, 3800 inhabitants

Population data:
Demographic data
GIS/GPS mapping
Malaria*: P. falciparum, P. vivax*
Intestinal helminths: Hookworm, Ascaris
BMI, waist/hip, skinfold
blood pressure
fasting blood glucose

ALLERGY

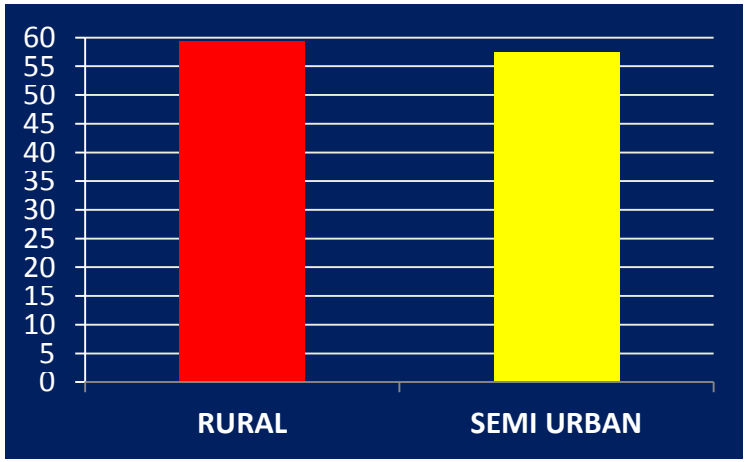
Immunology:
plasma, serum, EDTA blood
Whole blood culture with antigens, TLR ligands

Genetics: DNA

Peanut allergy in Indonesia

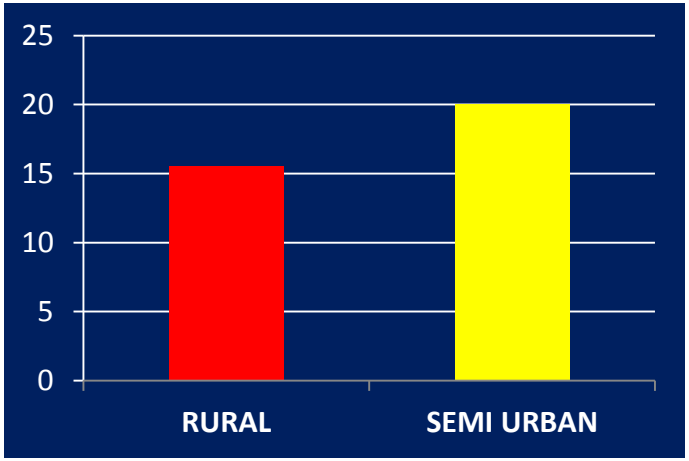
IgE: cut off 0.35

58.1%



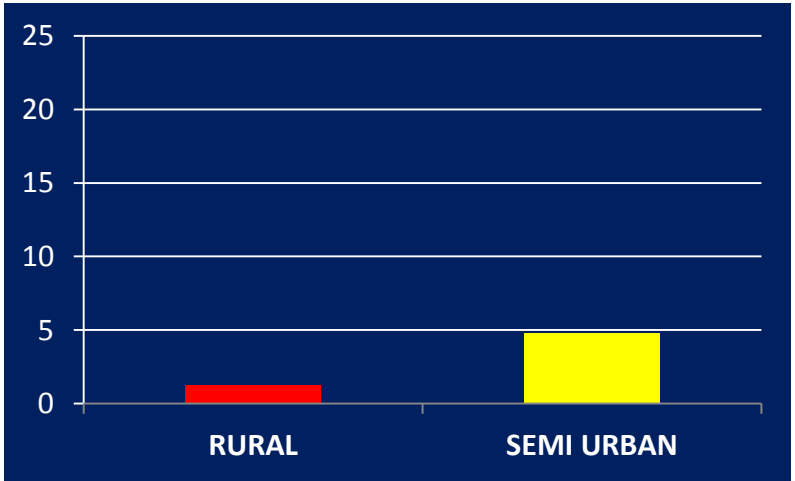
IgE: cut off 3.5

18.5%



SPT

3.7%

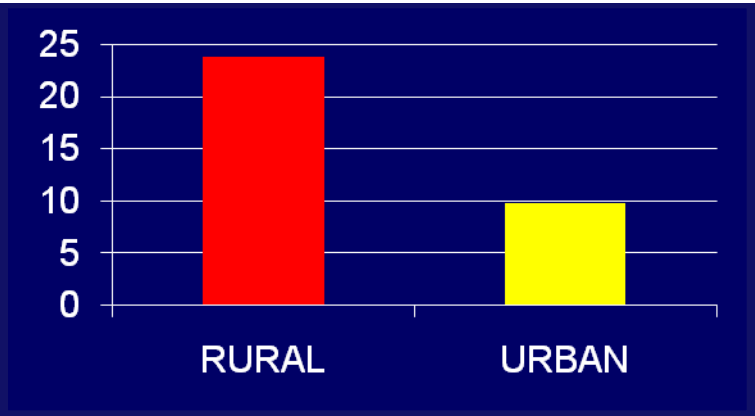


Peanut allergy in Ghana – large amounts of peanut specific IgE is seen but little SPT or symptoms

Overall prevalences

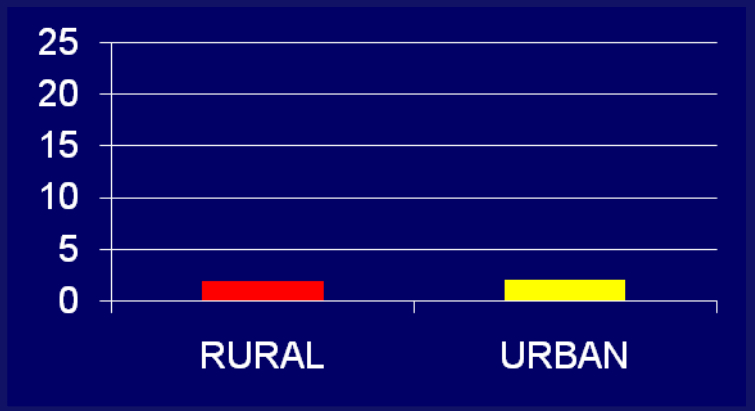
IgE

17.7%



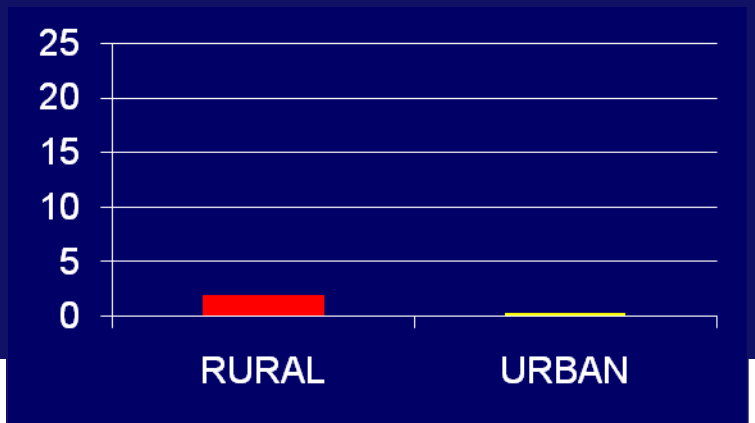
SPT

1.9%

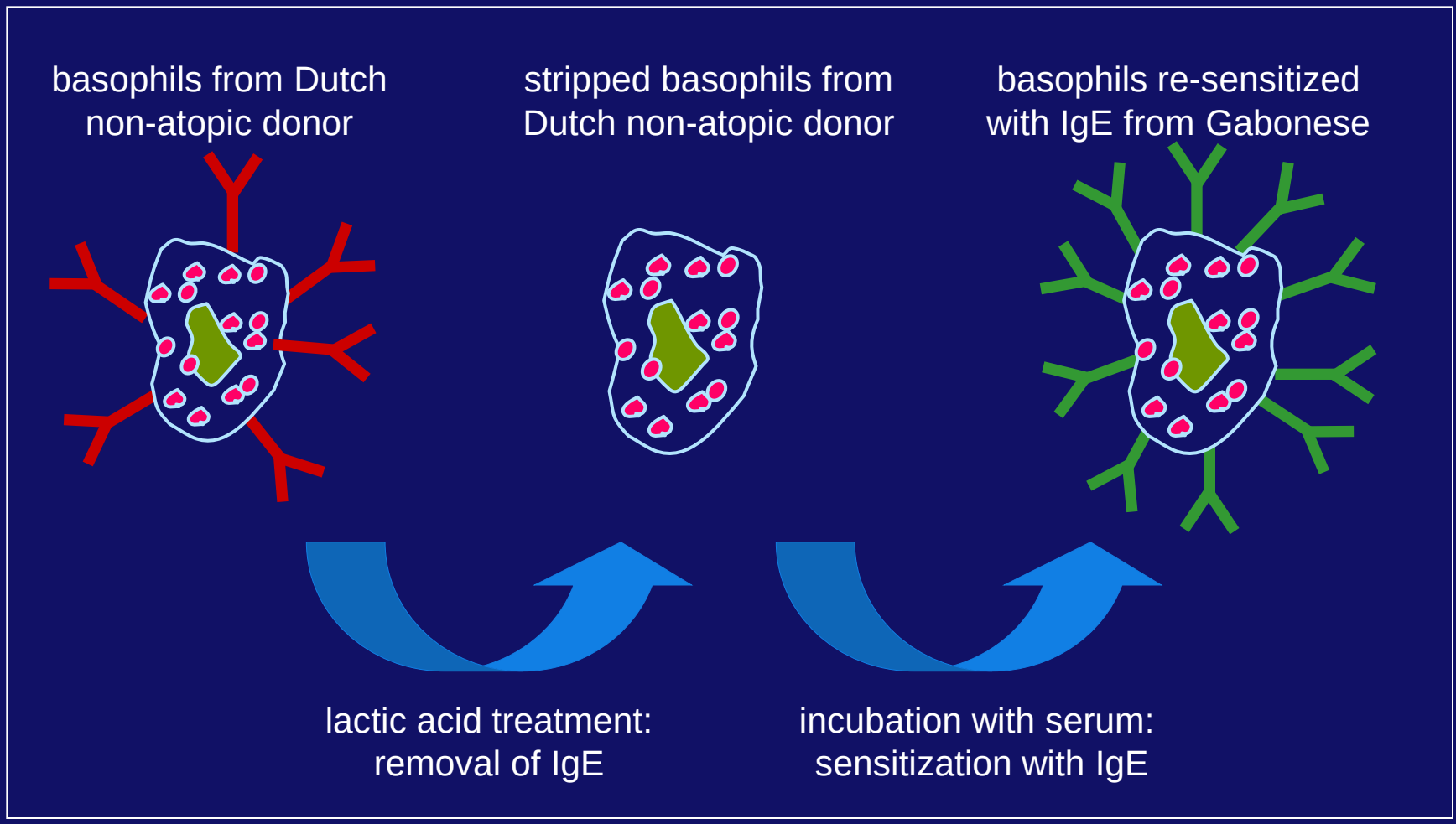


Symptoms

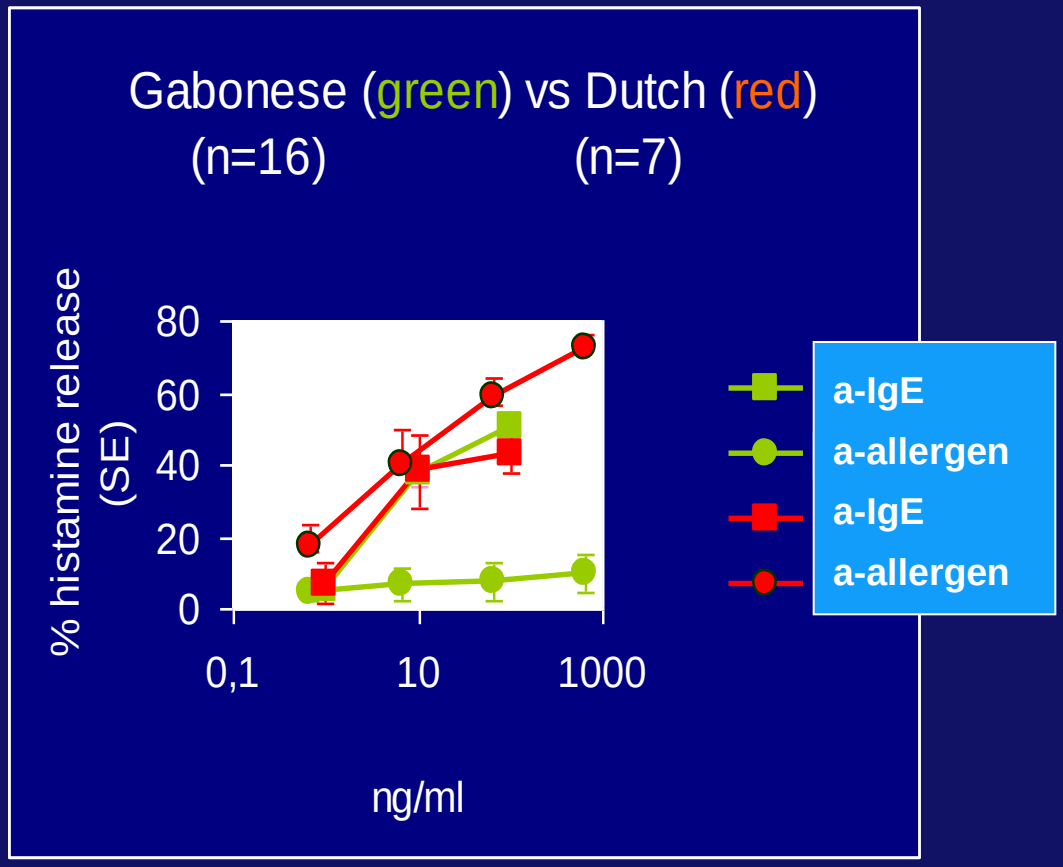
1.5%



Stripped basophil protocol



Despite higher IgE titers, there is little biological activity of IgE

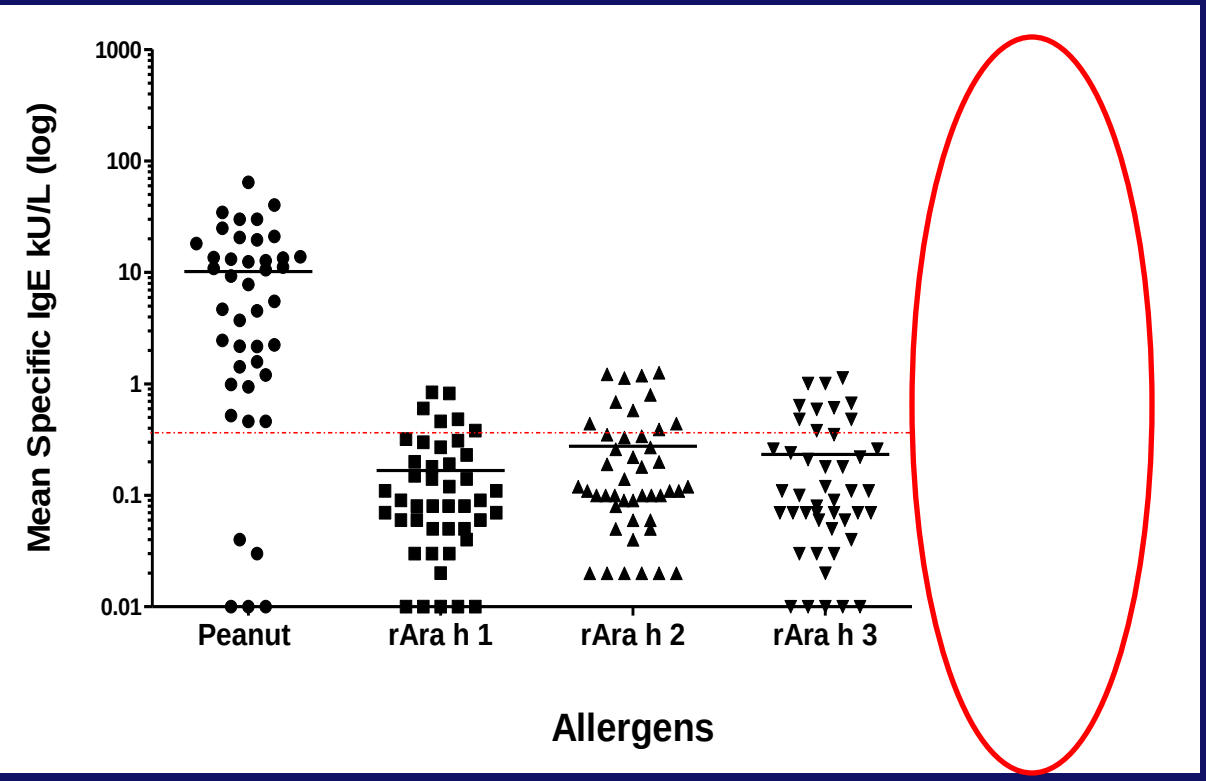


Abena Amoah, van den Biggelaar, van Ree et al unpublished data

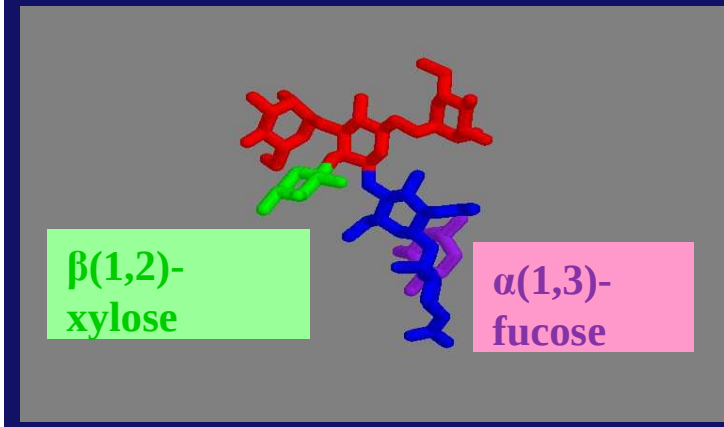
What is the Peanut Specific IgE against?

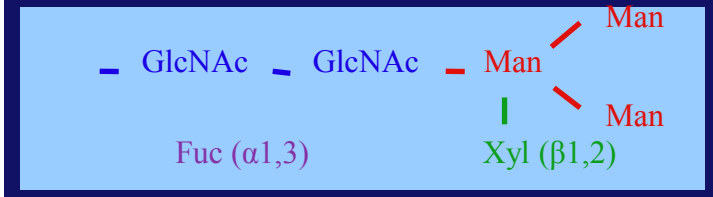
In a subset :

- Specific IgE responses to recombinant peanut allergens Ara h 1 – 3 (most European peanut allergic patients react strongly to these allergens)
- Cross reactive carbohydrate determinants (CCD), measured with Bromelain



N-glycan found in plants/invertebrates





Peanut Specific IgE in Ghana is :

primarily to cross reactive carbohydrate epitopes present in parasites

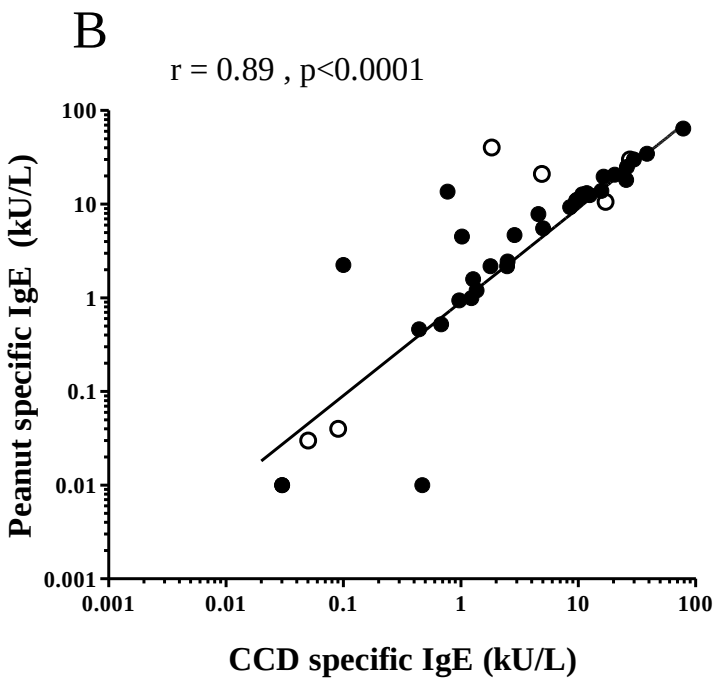
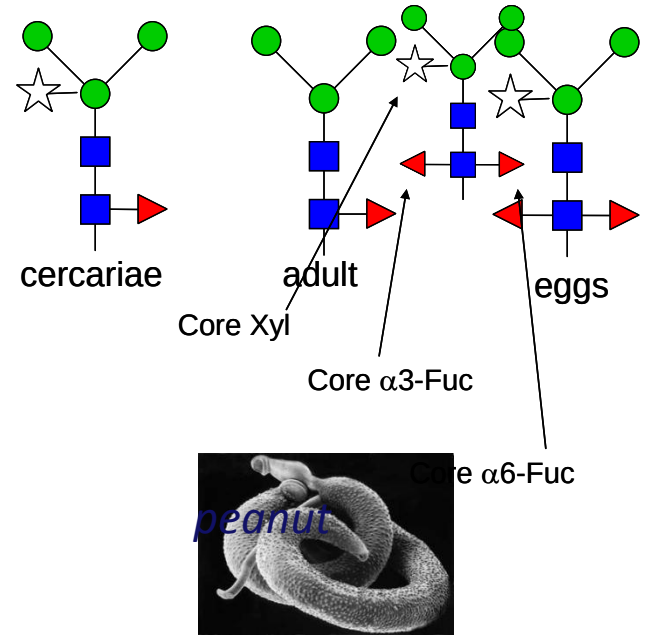
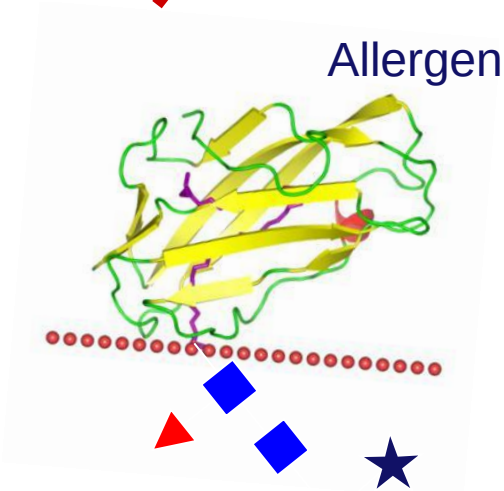


Fig. 2B



IgE

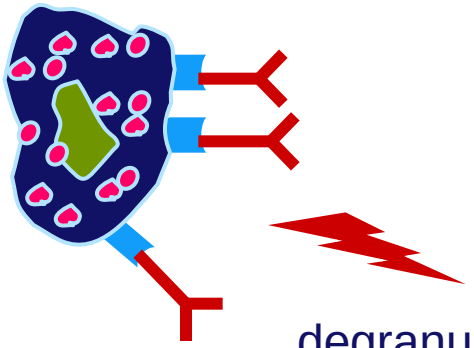
IgE



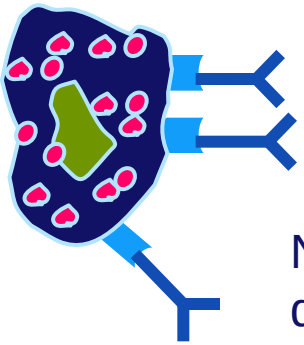
Allergen protein

cercariae

Allergen carbohydrate



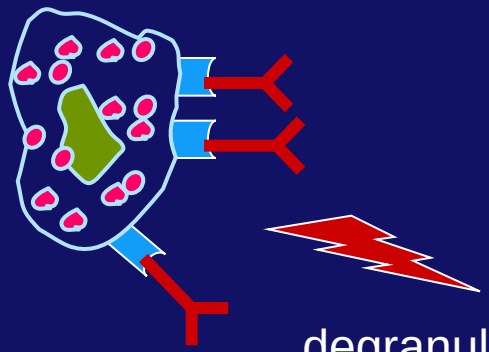
degranulation



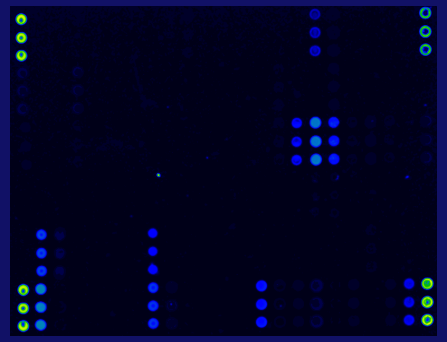
No degranulation

Conclusion on detection of allergies- caution !

In urbanizing areas,
detection of food allergy as well as other allergies
needs new tools



degranulation



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