



The Allergic Planet

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What is Allergy?

- The term “Allergy” was first coined on by Austrian physician von Pirquet who published an article entitled “Allergie” in July 24, 1906.
- He noticed that patients who had received injections of the smallpox vaccine had quicker, more severe reactions to second injections.
- He attributed this specific reaction to antibodies that and called it ‘allergy’
- Today, we define allergy as an immune-mediated and allergen-specific hypersensitivity



Clemens von Pirquet
(1874–1929)



Types of Allergens

- The cause of allergic disease is called an **allergen**, a normally harmless substance that causes an allergic reaction e.g. **Food**, dust, pollen, mould, insect stings, animal dander or drugs (penicillin, NSAIDs).
- Allergens have all properties of an antigen therefore elicits an immune response, either immediate or delayed.



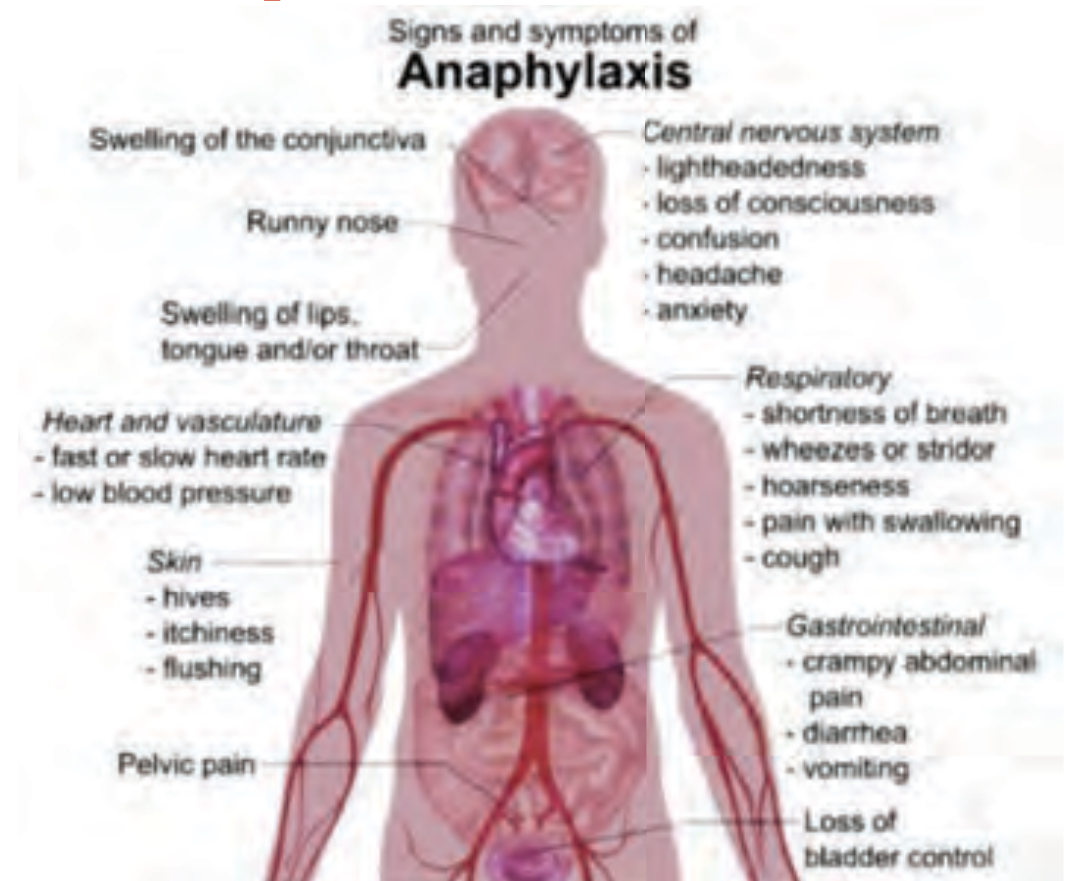
Why is this issue so important?

- Food allergies have **increased by 50%** in the past decade with hospitalisations due to anaphylaxis up 7 fold.
- **>250 million** people globally suffer from food allergies, 17 million in Europe alone.
- **339 million** people globally suffer from asthma
- **400 million** from allergic rhinitis
- Huge increase in skin allergic diseases e.g. eczema, atopic dermatitis
- Huge socio-economic impact, especially in 1st world countries.
- Allergies can develop at any stage in life!
- No current cure for food allergy.



Why is this issue so important?

- Reactions can be mild moderate or severe i.e. anaphylaxis
- Anaphylaxis can be fatal within 20-30 mins without adrenaline ie.epipen.
- **But why is there such a surge in allergic and autoimmune diseases?**



Recent fatalities

ITV REPORT 7 November 2018 at 2:37pm

Takeaway bosses jailed for manslaughter after nut allergy death of 15-year-old Megan Lee

Parents of girl, 15, who died after allergic reaction to Pret sandwich say stricter food labels could be in place by next summer after meeting Michael Gove about 'Natasha's law'

- Natasha Ednan-Laperouse collapsed on flight from Heathrow to Nice in 2016
- 15-year-old ate sandwich containing sesame seeds, which she was allergic to
- The girl, from Fulham, West London, was later pronounced dead in hospital
- Packaging of baguette did not mention that the product contained the seeds

Nut allergy emergency: Woman recovers after Grafton St injection

Right to give life-saving shot as emergency first response only became legal last October

© Thu, Oct 4, 2018, 19:52 Updated: Thu, Oct 4, 2018, 20:01



Teenager, 14, who had allergic reaction to peanuts at Chinese buffet died in the street after chemist refused to give her a life-saving adrenaline injection

- Emma Sloan died in front of her mother and sisters in a Dublin street
- 14-year-old mistook Satay sauce for a curry missing the warning note

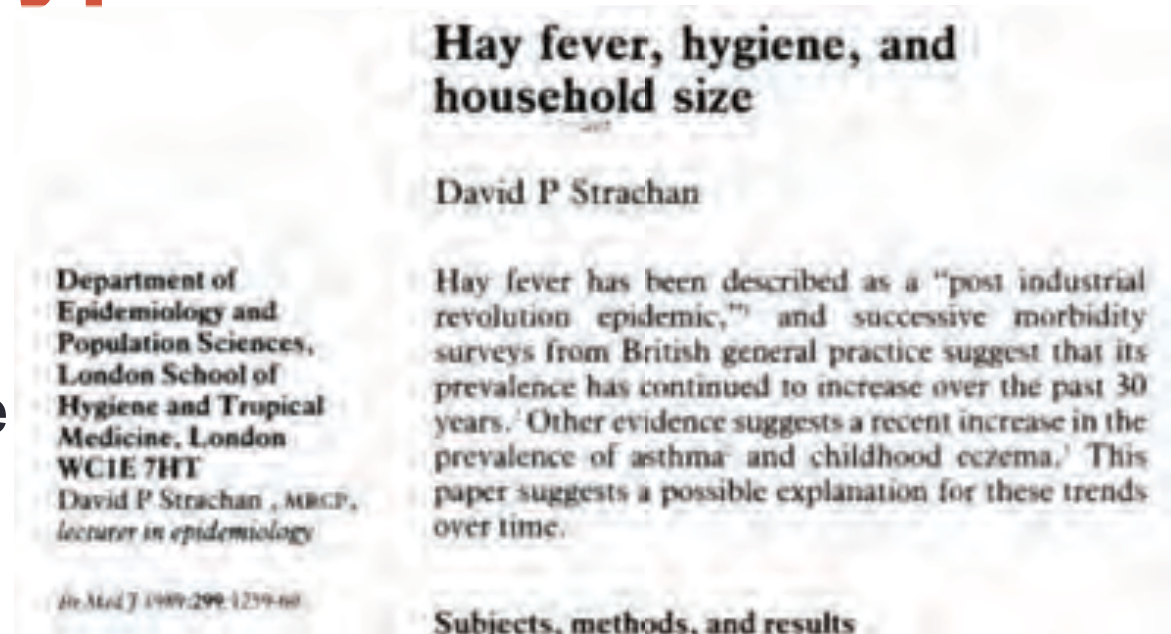
“The Hygiene Hypotheses”

- In 1976, Dr. John Gerrard a Canadian pediatrician studied allergies amongst white and metis communities in Saskatchewan.
- 1976 paper: *“were the price paid by some members of the white community for their relative freedom from diseases due to viruses, bacteria & parasitic worms”*



“The Hygiene Hypothesis”

- Further proposed by Professor David Strachan in 1989 who proposed the term “Hygiene Hypothesis”
- Found that children in large households had less cases of allergic rhinitis and eczema.
- Also known as the “old friends theory” or “depleted biome theory”.
- Also validates the theory of more allergies in “one child families”.



“Old friends theory”

- Proposed in 2003 By Graham Rook.
- Theory is that our gut microflora has changed from decades ago when we co-evolved with microbes from “hunter gatherer” times.
- The microbes that evolved alongside the mammalian immune system, known as “old friends,”
- These include; microbes that co-exist in the environment & parasitic worms called helminths

Autoimmune and allergic disorders incidence

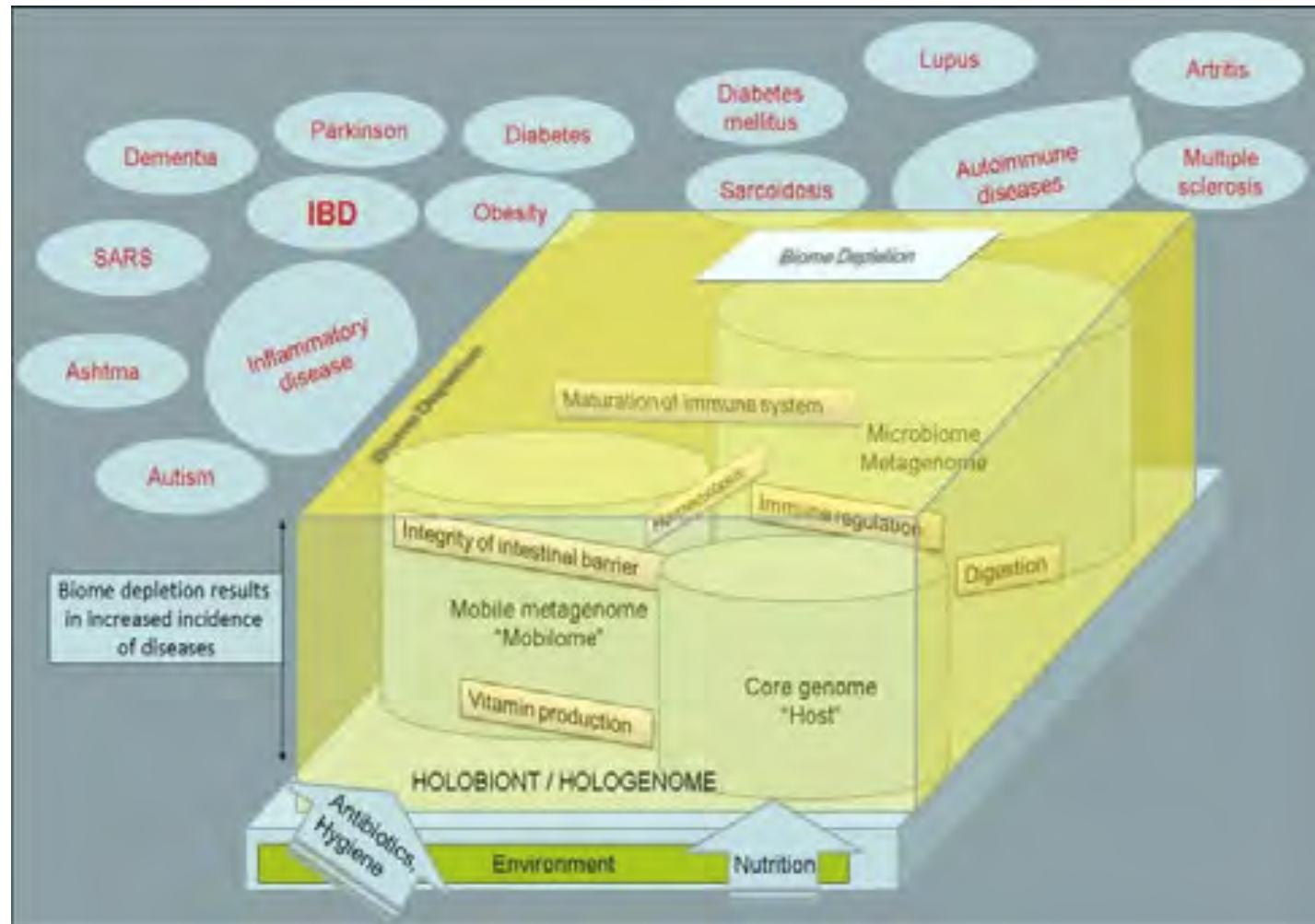


Helminths infestation incidence



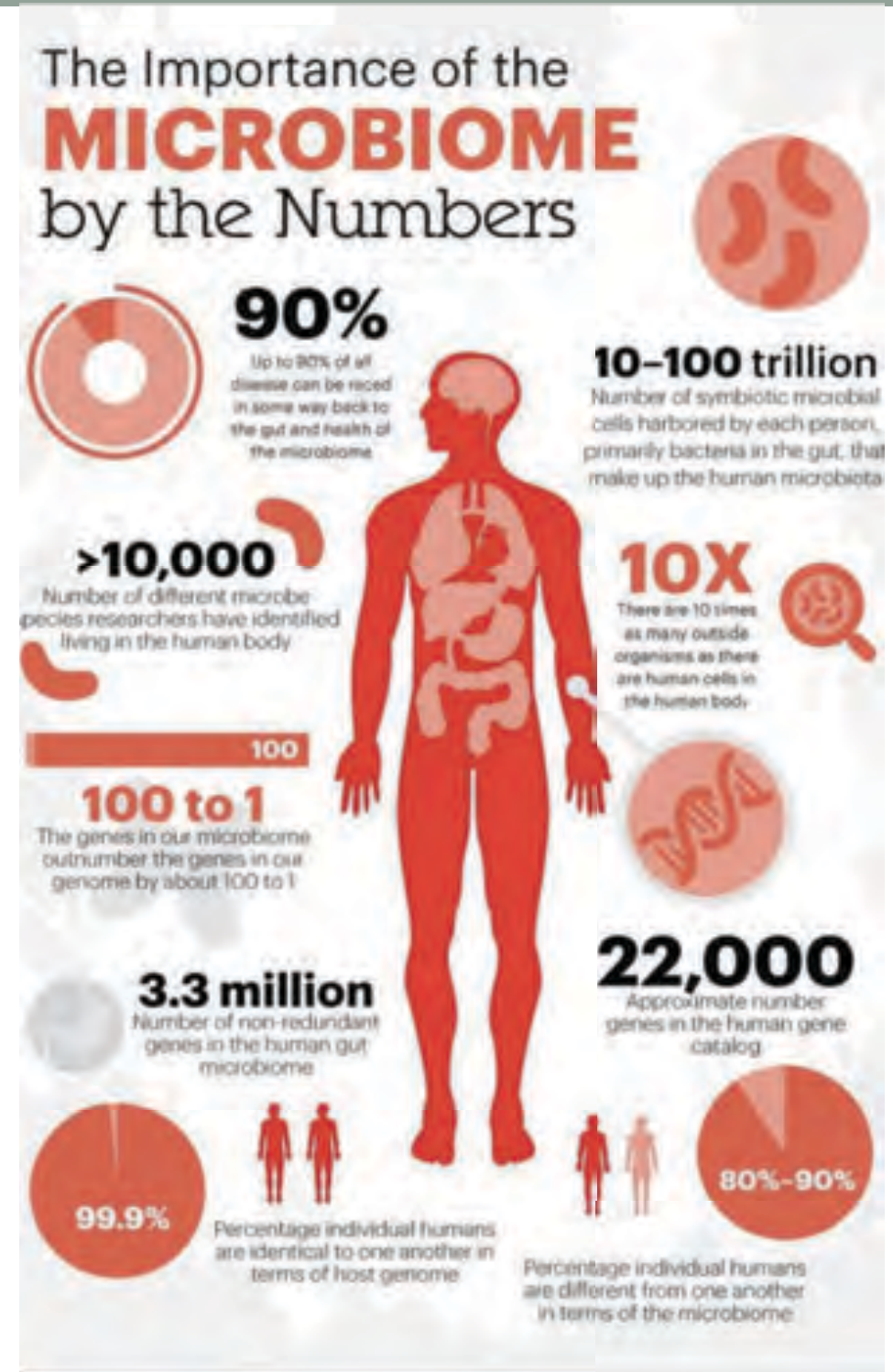
The “biome depletion” theory

- Due to a pathologically over-reactive immune response, which in turn is caused by a loss of components of our biome that normally interact with our immune systems.
- **Antibiotics?**

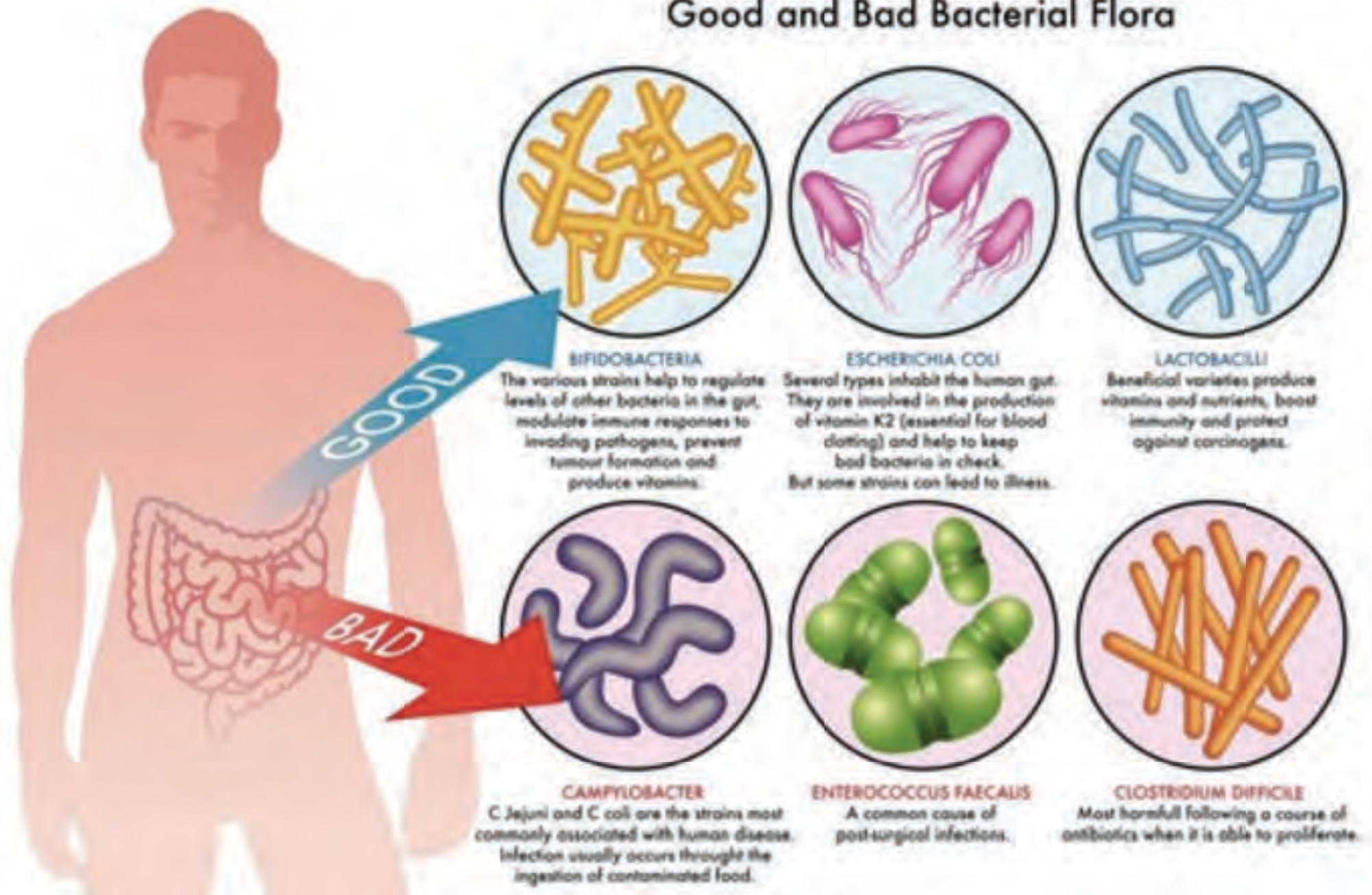


The Microbiome

- At the heart of all these hypotheses-suggests the composition of our microbiota affects the development of allergic diseases.
- **Dysbiosis**-microbial imbalance in the gut
- Has been associated with a plethora of allergic and autoimmune diseases.



Good and Bad Bacterial Flora



The studies of von Mutius

- In 1990, von Mutius (munich allergist) believed air pollution was responsible for asthma and allergic diseases
- She postulated that allergic diseases would be higher in the heavily polluted East Germany vs West Germany.
- When the Berlin wall came down she compared the incidences of allergic diseases and found it to be **LOWER** in the polluted east!



The studies of von Mutius

- von Mutius became intrigued by Gerrard's theory.
- **"The farm effect"** study compared the incidence of asthma and allergies in dairy farm children with city dwellers.
- Then with Holbreich (alberta allergist) compared allergy in the amish population vs rural dairy farmers vs city dwellers.
- ↑ City dwellers 50% less in farm children 50% less again in Amish
- **Why?** The composition of their microbiome



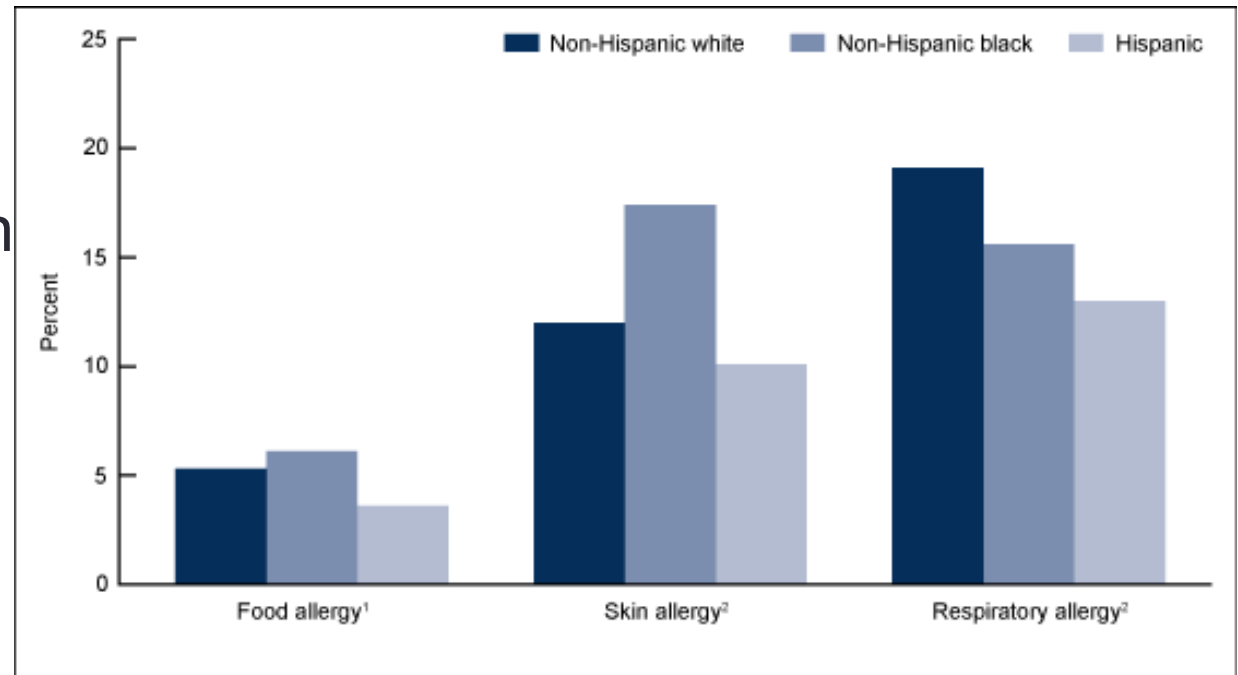
The studies of von Mutius

- **The Farm Effect** verifies the “Hygiene Hypothesis,” which states that a lack of early childhood exposure to infectious agents, microorganisms and parasites increases our susceptibility to allergic diseases by suppressing the natural development of our immune systems.



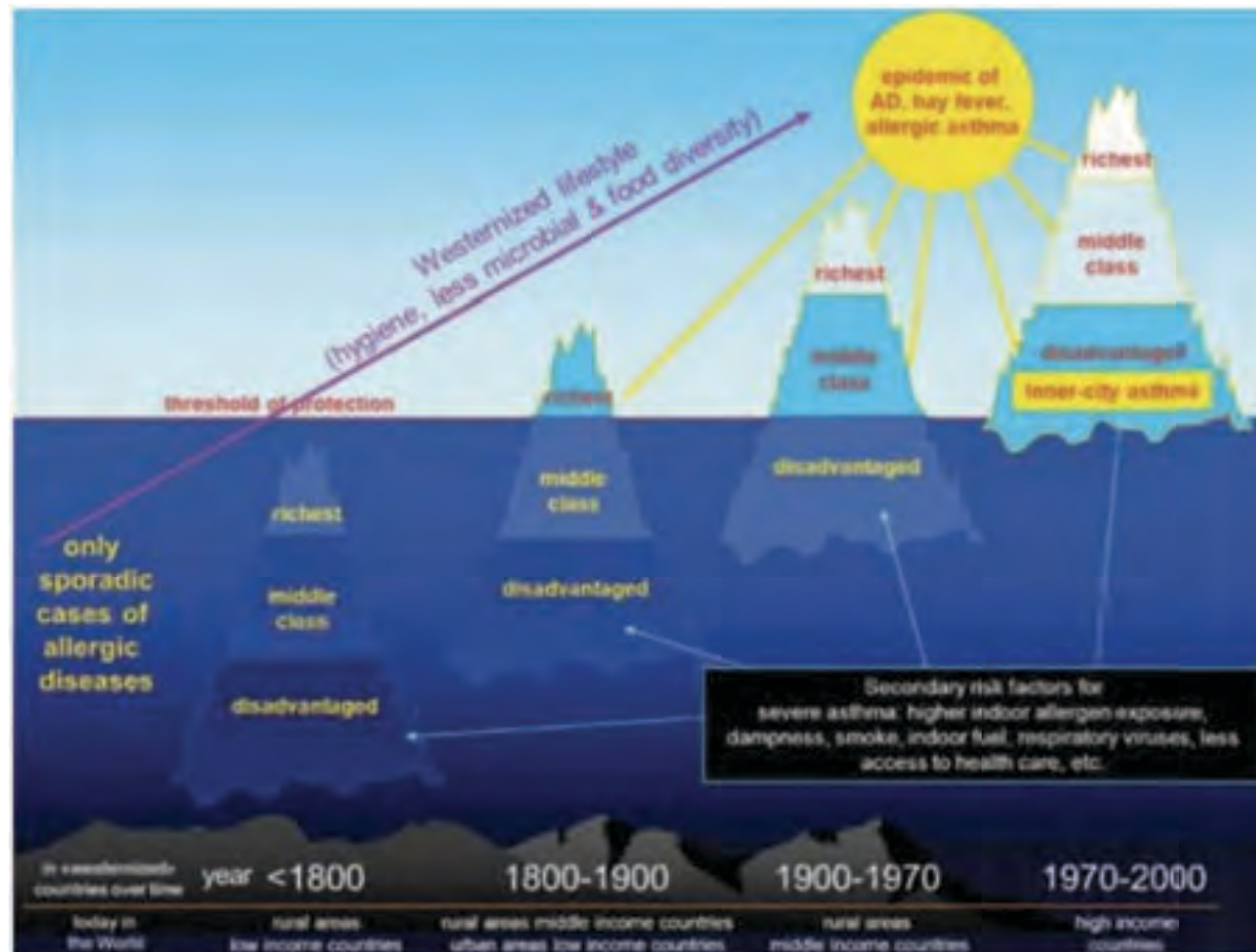
Ethnicity

- 2013 report by the CDC suggested that “Hispanic children had lower rates of all of allergies compared with children of other race or ethnicities.
- Non-Hispanic black children were more likely to have skin allergies and less likely to have respiratory allergies compared with non-Hispanic white children



Socio-economic Status

- Matricardi, 2014 stated that “allergies affect the rich strata of the population first, spreading to the middle class and ultimately to the poorest in countries undergoing epidemiological transition” Rich face low antigenic burden-dysregulation of the immune system!



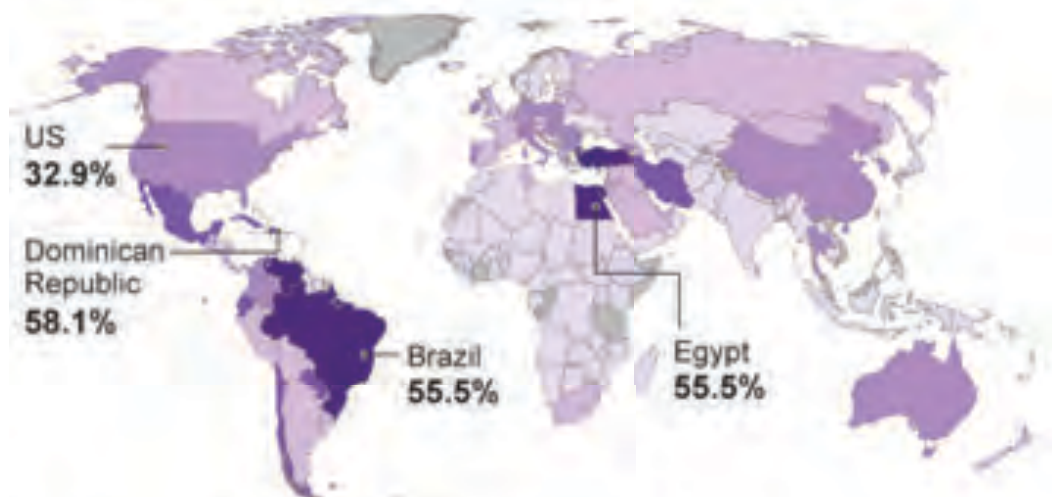
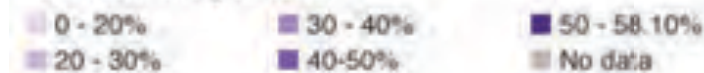
Increase in C-sections

- 4 fold increase in caesarean section in the past 30 years!
- 30-40% of all births in Ireland are by c-section.
- Theory is that the babies microbiome composition is different to naturally born babies who are exposed to the flora in the birth canal.
- Babies born by c-section are exposed to primarily skin and air borne bacteria first.



Caesarean section rates

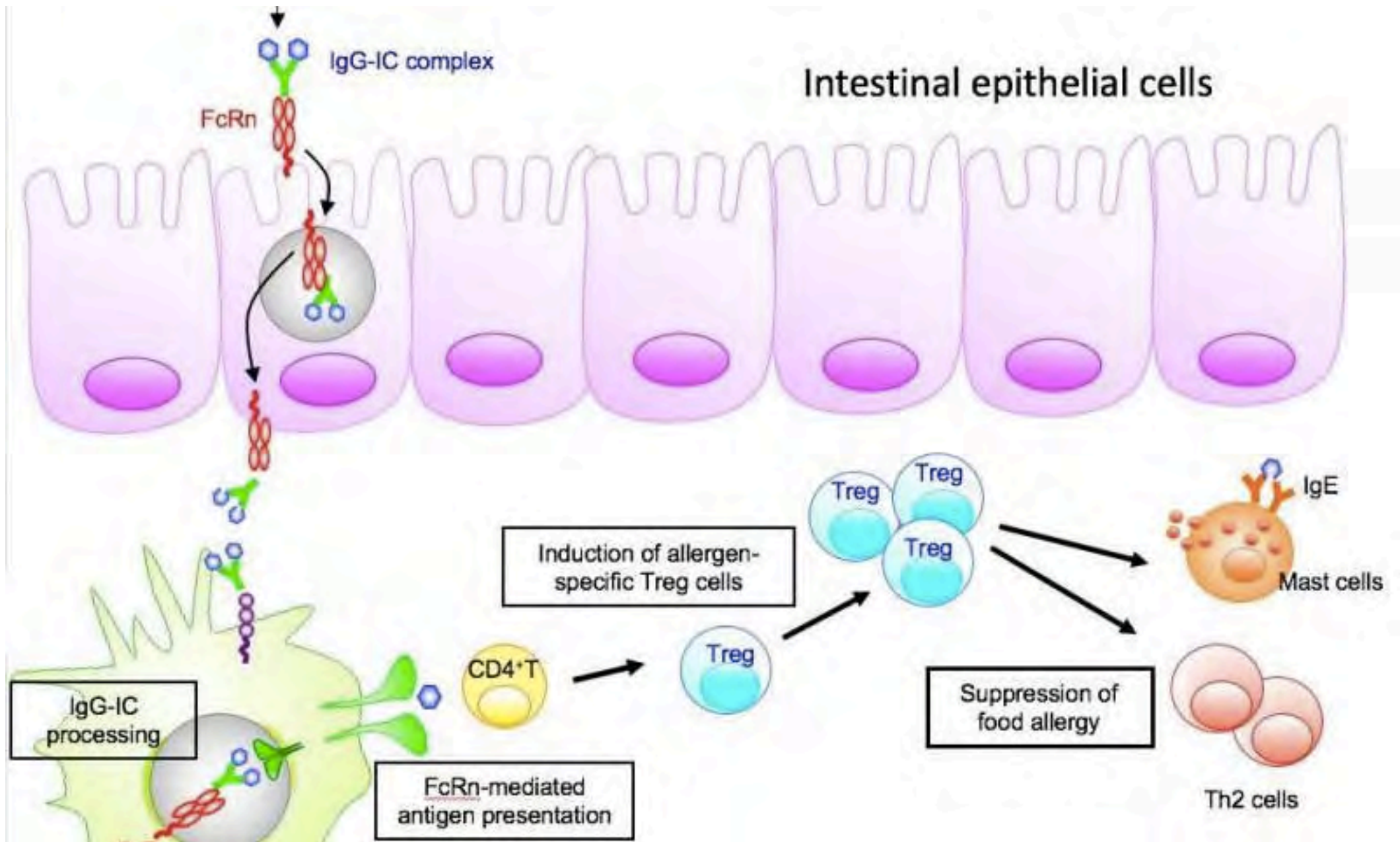
% of births using c-section



Breastfeeding

- 2017 study from Boston childrens' hospital showed that eating allergenic foods during pregnancy and breastfeeding can prevent the development of allergies.
- In the study, pregnant mice were fed allergenic foods including eggs and peanuts. Antibodies were subsequently transferred to their offspring through breast milk.
- The antibodies caused the baby mice to produce allergen-specific regulatory T immune cells, which made them tolerate the allergenic foods.





Breastfeeding Vs Bottle feeding

- Breastfeeding vs bottle feeding also promotes the growth of good bacteria in the gut.
- Breast milk is a source of vitamins, minerals, probiotics, antibodies, growth factors, and prebiotics that selectively feed *Bifidobacterium infantis* and also helps digest food during early weaning.
- *Bifidobacterium infantis* also produces short-chain fatty acids like butyrate that helps modulates the immune system.



Weaning

- Not weaning babies early enough & exposing them to allergic foods.
- The EAT (enquiring about tolerance) study showed that exposing babies to six allergenic foods (cooked eggs, milk, wheat, peanuts, fish and sesame) from the age of three months reduced the risk of developing an allergy by 67% vs breastfeeding alone.

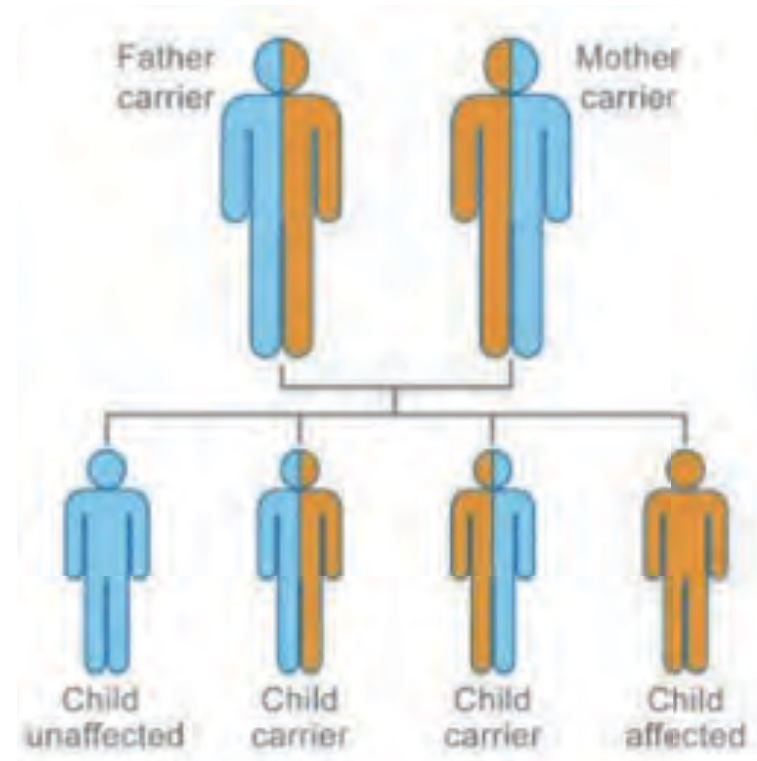


Genetic predisposition

75% risk of the child developing an allergy if both parents suffer. Reduces to 50% if only one parent.

Recent 2018 Canadian study has identified a gene called c11orf30/EMSY (EMSY) already associated with atopic diseases. This study is the first to link EMSY with peanut & food allergy!

Could hold potential for gene therapy not only for food allergies but other diseases e.g. asthma



J Allergy Clin Immunol. 2018 Mar;141(3):991-1001. doi: 10.1016/j.jaci.2017.09.015. Epub 2017 Oct 10.

Genome-wide association study and meta-analysis in multiple populations identifies new loci for peanut allergy and establishes C11orf30/EMSY as a genetic risk factor for food allergy.

Asai Y¹, Eslami A², van Ginkel CD³, Akhabir L², Wan M², Ellis G², Ben-Shoshan M⁴, Martino D⁵, Ferreira MA⁶, Allen K⁵, Mazer B⁴, de Groot H⁷, de Jong NW⁸, Gerth van Wijk RN⁶, Dubois AEJ³, Chin R⁹, Cheuk S¹⁰, Hoffman J¹¹, Jorgensen E¹², Witte JS¹¹, Melles RB¹³, Hong X¹⁴, Wang X¹⁴, Hui J¹⁵, Musk AWB¹⁶, Hunter M¹⁷, James AL¹⁸, Koppelman GH³, Sandford AJ², Clarke AE¹², Daley D¹⁹.

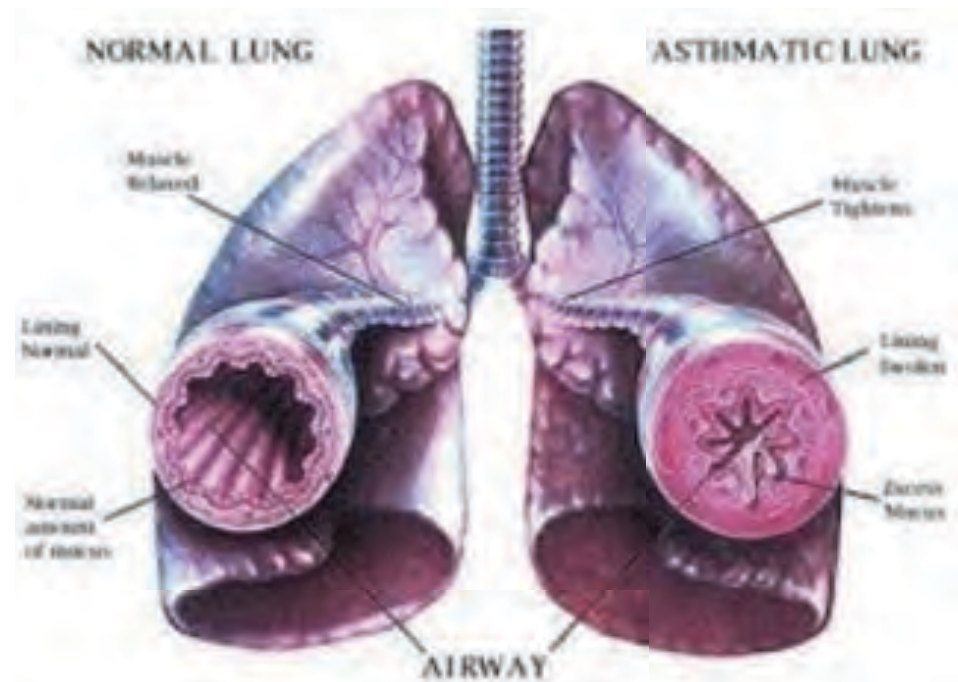
The studies of Zamel

- Dr Noe Zamel, Canadian respirologist was intrigued by the inhabitants of Tristan da Cunha (the most remote inhabited island in the world) where 50% of it's 261 residents suffer from chronic asthma
- No pollution, no industry, no processed food & air is pure.



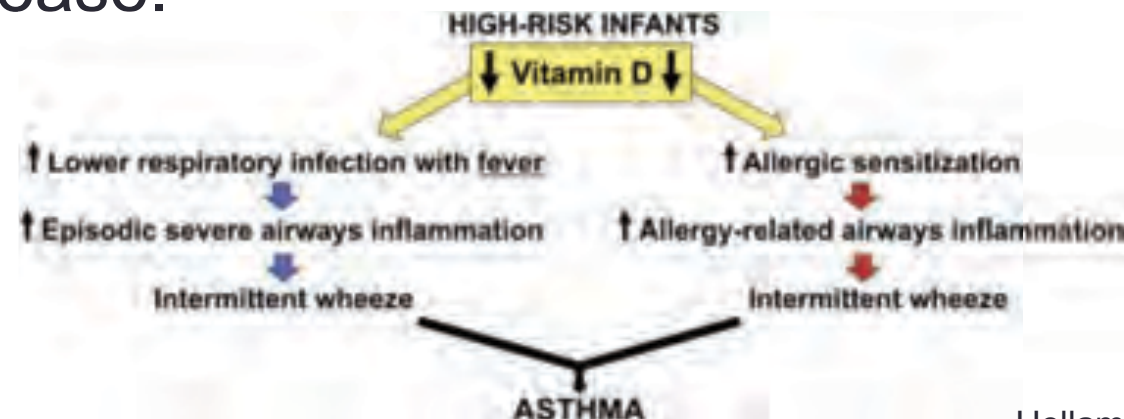
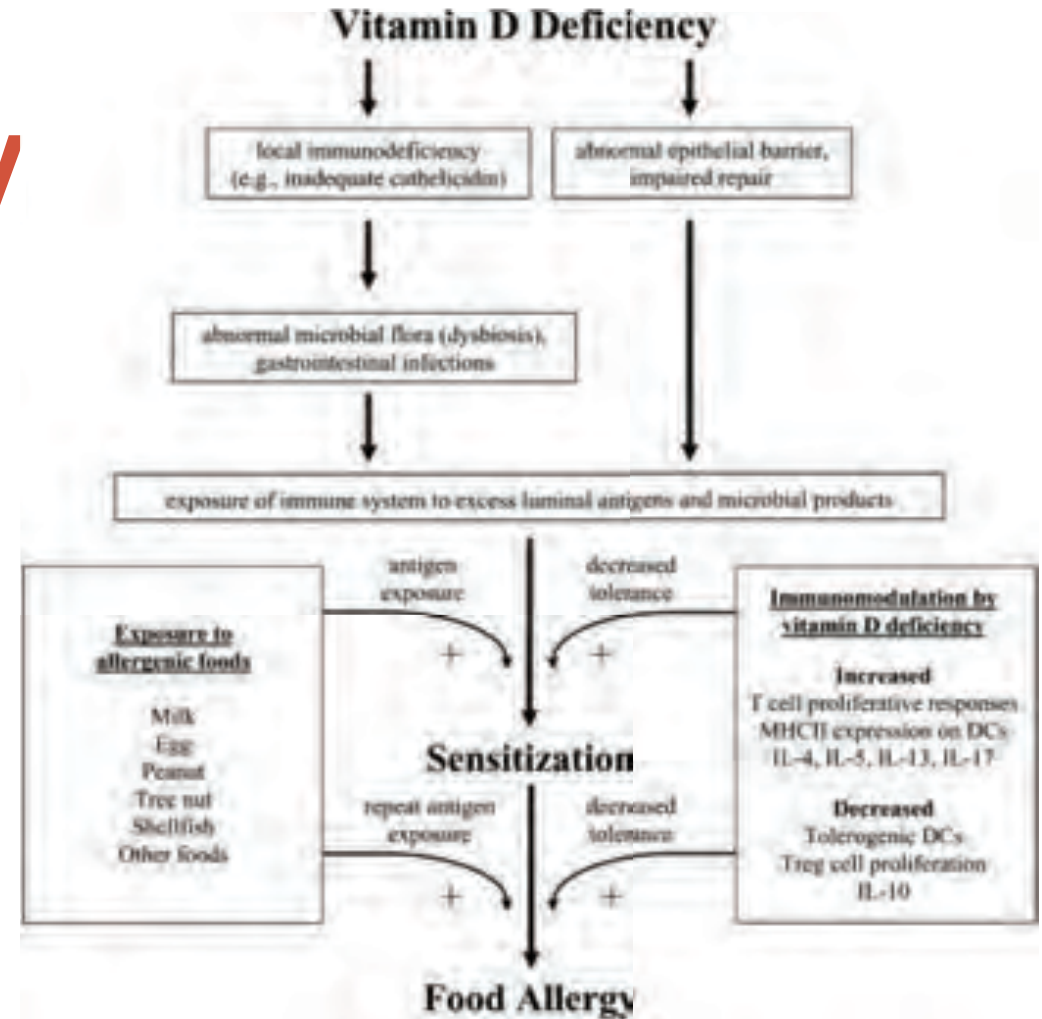
The studies of Zamel

- Zamel postulated a genetic link
- He identified a gene common to all located on chromosome 11 called ESE-3.
- ESE-3 causes collagen deposition in the lungs
- Only one of many genes.
- Also possible link to lack of vitamin D as only ave. of 4.05 sun hours per day?



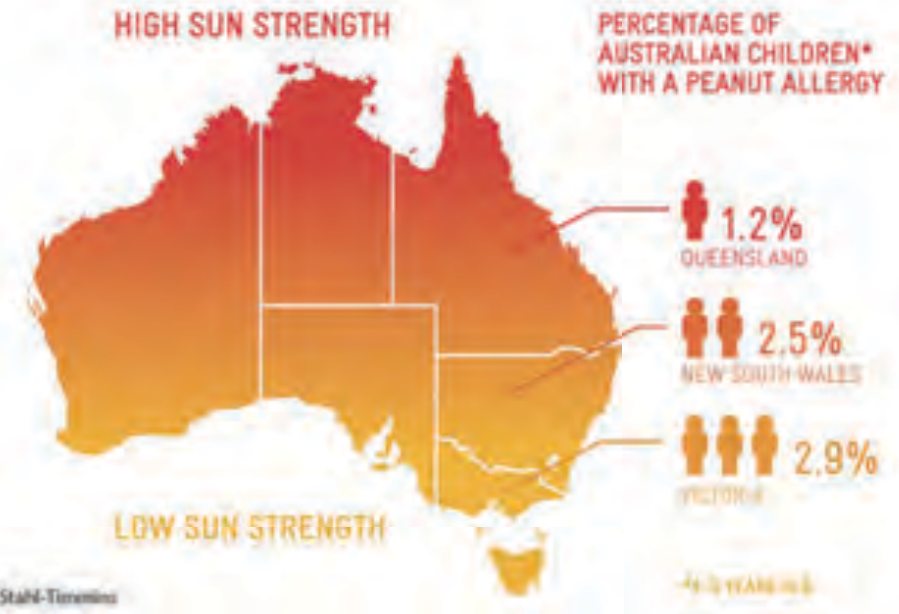
Vitamin D & allergy

- Vitamin D is an anti-inflammatory
- Studies have shown the association with lack of Vitamin D and allergic disease development i.e. peanut & food allergy, asthma, and other atopic disease.

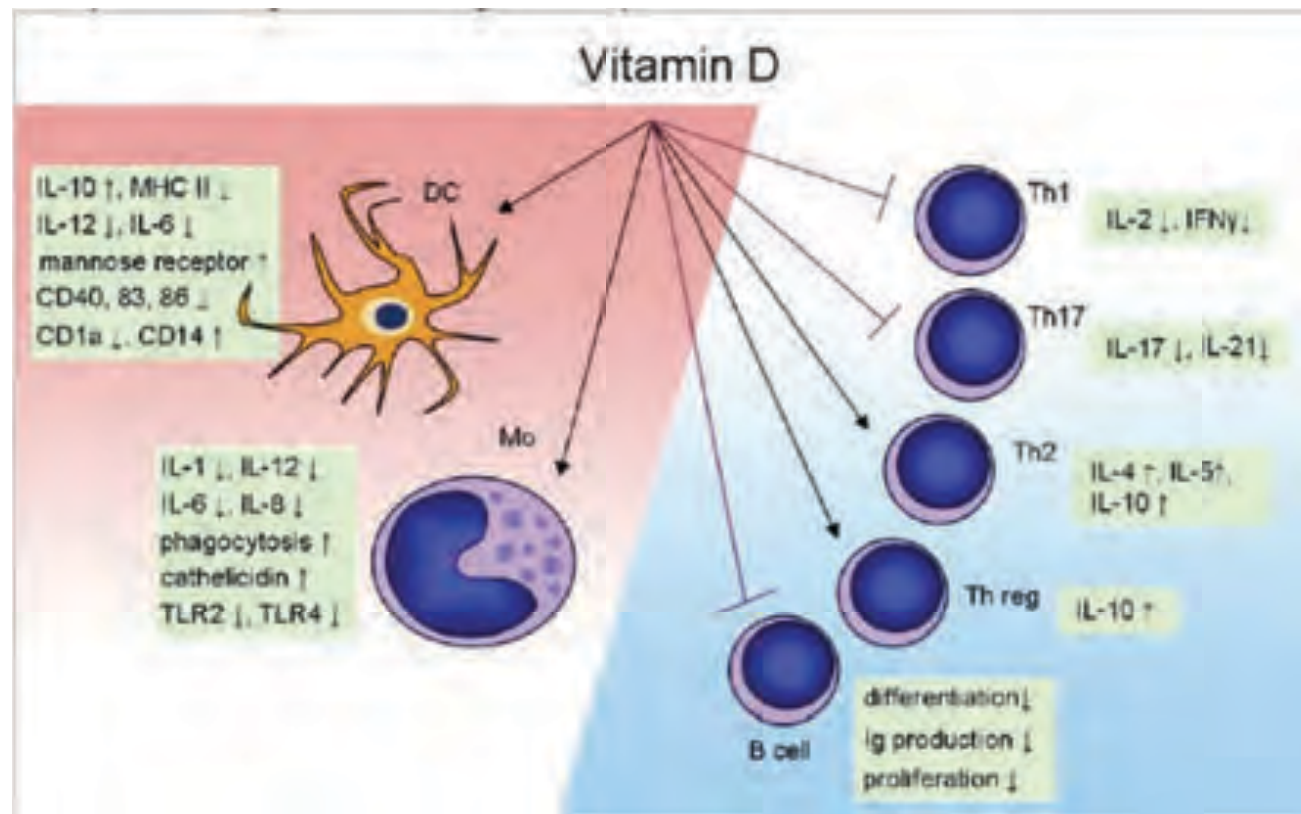


Vitamin D & allergy

- Australian study compared peanut allergy in North vs South- HIGHER in South due to fewer sun hours!



- Vitamin D has immunomodulatory function i.e. T cell production
- Potential therapy especially in early childhood.
- Food fortification esp. in processed foods.



Food processing and allergy

Allergies were relatively non-existent pre 1980.

Recession in Ireland 1980-87, demand for cheap convenience foods
Highly processed

What does food processing do to food?
Reduces nutritional content

Effects the allergenicity of food proteins

Preservatives i.e. sulphites, tartrazine, MSG are irritants



Yellow Dye Allergy Symptoms

- Migraine headache
- hives
- itchy skin
- swelling of the face
- tightness in the chest
- asthma
- wheezing
- dizziness or fainting
- fast heartbeat
- low blood pressure and
- tightness in your throat

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