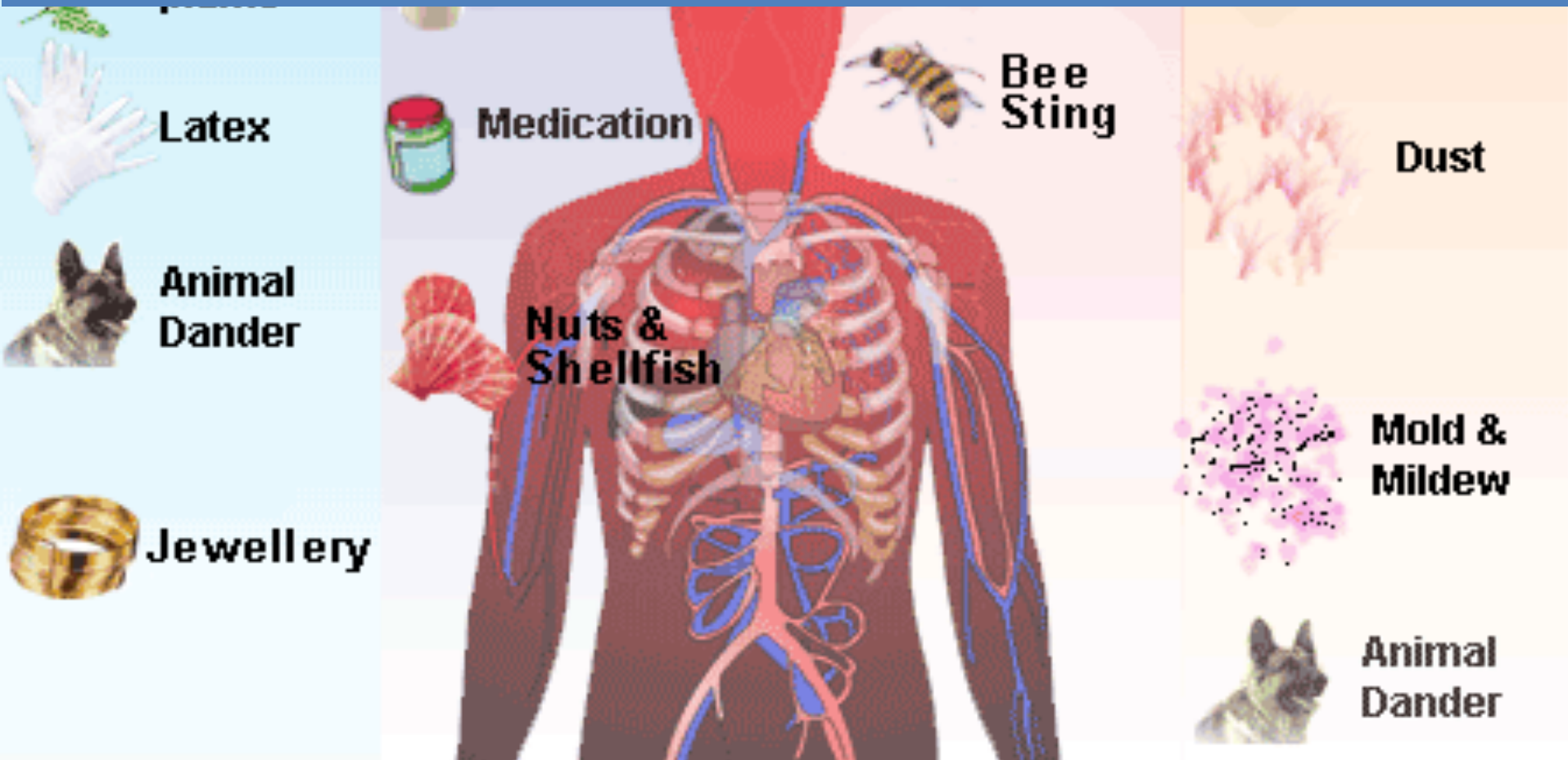


The Rise and Rise of Allergies



Presented by Daniel Baden ND

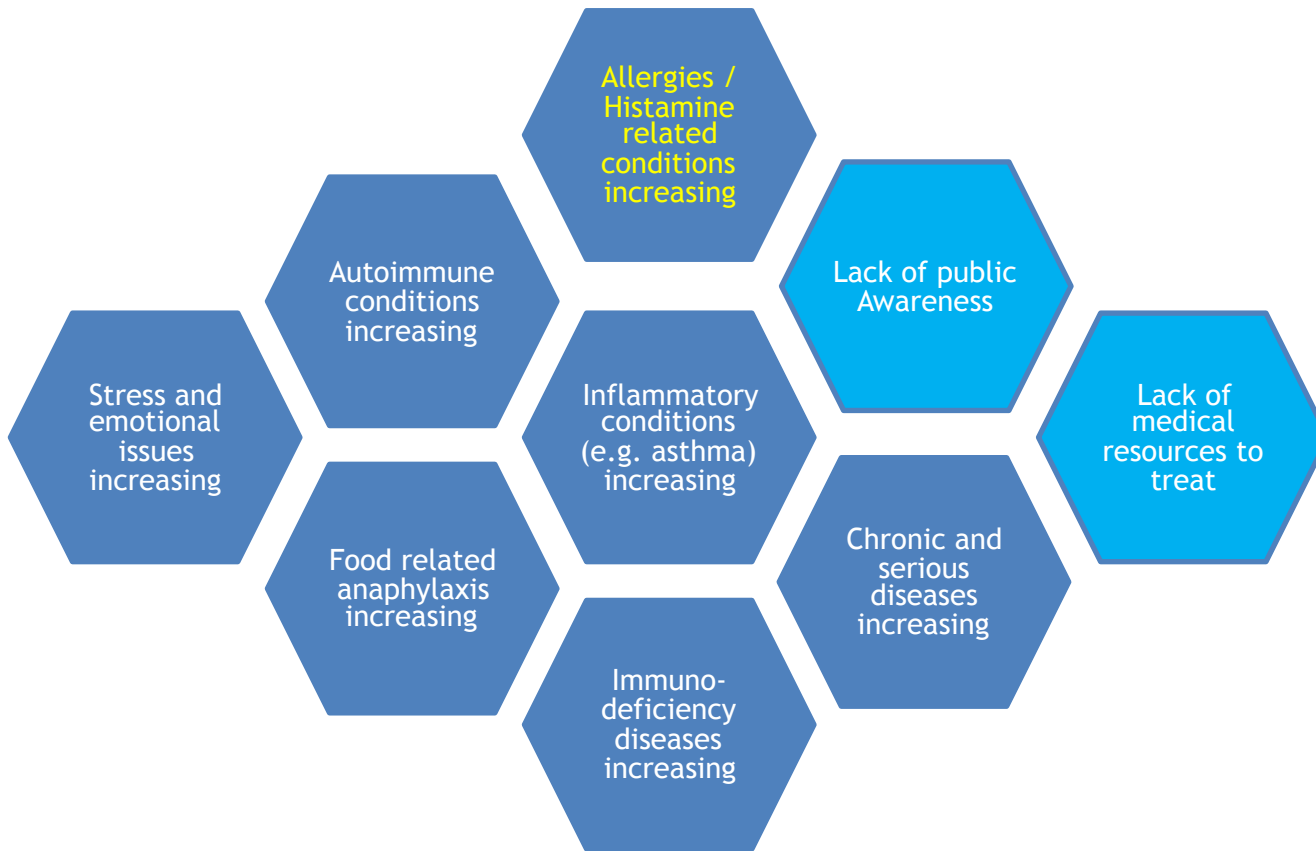
Allergies

- Allergic diseases share a common pathophysiology of immune dysregulation and inflammation
- Chronic allergies may be exacerbated or prolonged by chronic inflammation
- Allergies have a close relationship with histamine and its related disorders

Increasing Allergy Prevalence

- 30% world population *(Imm and Allergy Clinics of Nth Am Vol31, Iss.1, 2011)*
- Prevalence of food allergies increasing over last few decades; especially for migratory population *(Intern Med J. 2017 Mar;47(3):256-261)*
- 1998: 6.3 serious allergic reactions per 100,000;
2011: 17.7 serious allergic reactions per 100,000
(181% increase over 13 years)
- 7x increase in 5-14 age bracket

Part of a Group?



Why the Increase?

- Reduced immune challenges early in life
- Eradication of most parasitic infections
- Altered microbiome species due to low-fibre diets and widespread antibiotic usage ('old friends' hypothesis)
- Changes to home heating/ventilation
- Decline in physical activity
- Delayed introduction of allergenic foods (*NEJM 29.02.16*)
- Lifestyle induced dietary changes (e.g. different methods of preparing foods)
- Nutritional deficiencies (e.g. Zinc and Vitamin D)
- Ethnic translocation (can also decrease)
- Urbanisation

Growing Out of an Allergy?

- Approx. 26% of children in study of 40,000 “outgrew” their allergy
- The reality is it often doesn’t go away it ‘changes’ or ‘improves’

(New Scientist 8 August 2018)

Allergy (Mast Cell) Triggers

- Allergens (ingested/airborne)
- Drugs
- Alcohol
- Preservatives
- Stress
- Environmental toxins (organic/non-organic)
- Artificial colours and/or flavourings
- Temperature extremes

Allergies or Histamine Intolerance?

- Allergies are an IgE mediated, histamine response to an allergen
- Histamine Intolerance is a toxic response caused by excessive accumulation of endogenous or exogenous histamine, from an inability of the body to efficiently breakdown histamine, excessive mast cell storage and/or hypersensitivity of cell antigen receptors

IgE

- Different IgE antibodies detect different allergens
- Highly primed: 1000x more binding power to immune cells than any other class of antibody
- Thought to have evolved to protect from large now virtually redundant threats e.g. organisms burrowing into our skin, lungs or guts

Histamine Intolerance (HIT)

- High histamine and/or poor degradation
- Est. 1% of the population has histamine intolerance; 80% being middle-aged

(Am J Clin Nutr

2007;85(5))

- Effects 24% of patients presenting with food allergy symptoms

(Allergy.

2017;00:1-9)

Causes of HIT

- Decreased enzymes (DAO and HNMT) that breakdown histamine
- Biogenic amines such as putrescine (protein rich and fermented foods, cheese) can release bound histamine into circulation
- Allergies, infection, GIT bleeding (Aspirin?)

Viral Changes to GIT

- Infection with common viruses can cause damage to gut wall
- Adenovirus (common cold); Rotavirus (diarrhoea); Hep C virus; reovirus (colds, gastritis)
- May cause inflammation; coeliacs; gluten sensitivity
- Virus changes immune responses and loss of tolerance to dietary antigens
- Children with intolerance found to have very high levels of “Interferon Regulatory factor 1” in gut wall

(Science DOI:1126/science.aah5298)

Common HIT Symptoms

- Acute or chronic gastrointestinal symptoms:
 - Irritable Bowel Syndrome
 - Digestive problems, flatulence, abdominal pain, intestinal cramps, frequent or chronic diarrhoea (histamine increases bowel motility), heart burn, acid reflux (increases HCl), nausea, vomiting
- Headache, itchy skin, oral allergy syndrome as well as red eyes and swollen eyelids

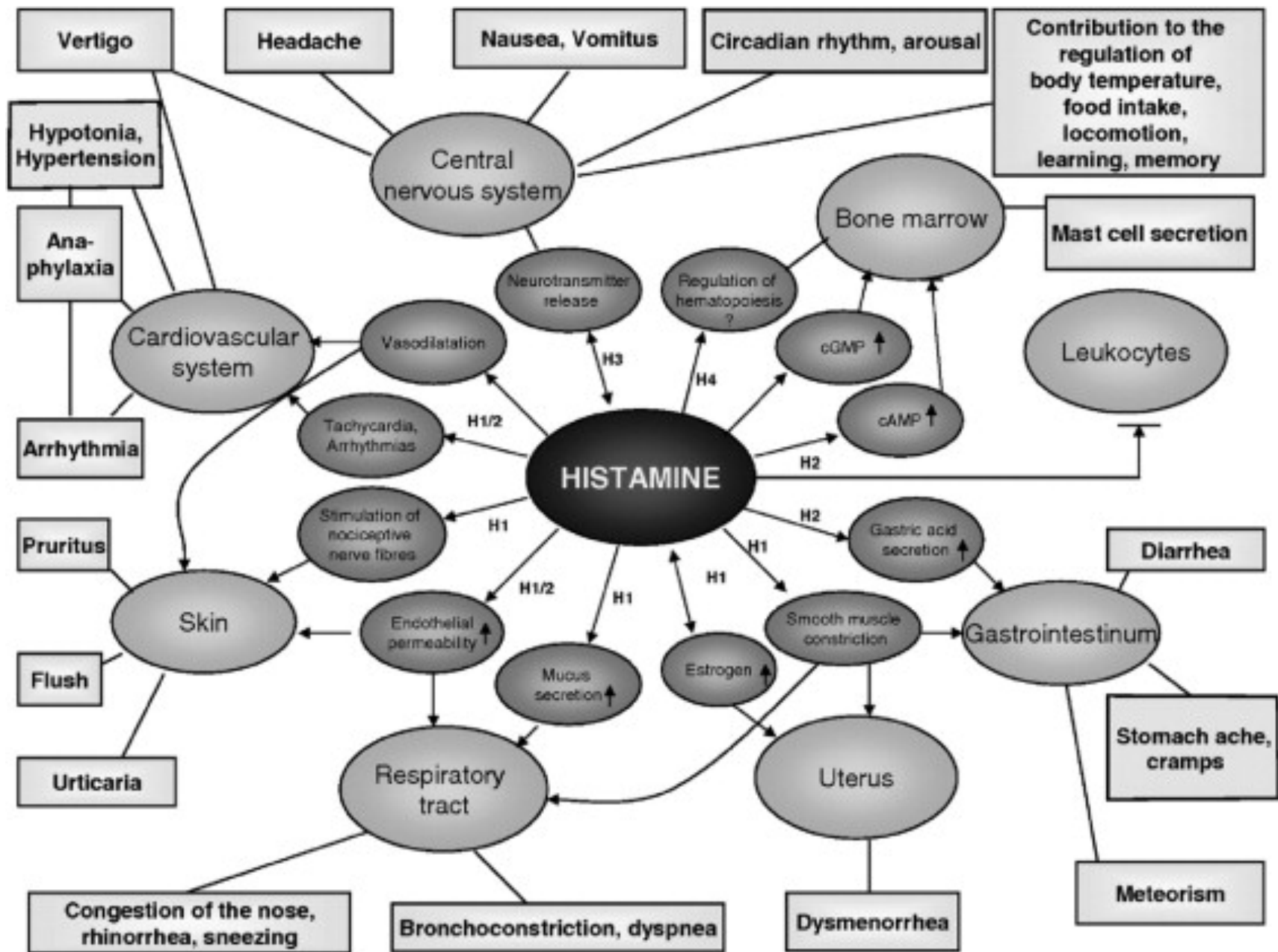
(Gut. 2006 Apr;55(4):445-7)

	Histamine-intolerant patients	Food-hypersensitive patients	Food-allergic patients
Absolute and relative frequencies			
<u>Allergic rhinitis</u>			
Runny nose	37.50%	44%	47.60%
Stuffy nose	37.50%	28%	42.90%
Itchy nose	37.50%	24%	42.90%
Red eyes and swollen eyelids	50%	36%	38.10%
Watery eyes	37.50%	16%	28.60%
Sneezing	37.50%	28%	47.60%
Swollen airways	37.50%	20%	42.90%
Oral allergy syndrome	50%	40%	61.90%
<u>Skin changes</u>			
Itchy skin	62.50%	52%	33.30%
Urticaria	37.50%	20%	19.10%
Skin rash	37.50%	40%	33.30%
<u>Gastrointestinal alterations</u>			
Nausea and vomiting	62.50%	48%	42.90%
Stomach pain	37.50%	72%	52.40%
Diarrhoea	50%	72%	76.20%
<u>Asthmatic symptoms</u>			
Cough	0	16%	23.80%
Shortness of breath	25%	24%	23.80%
Wheezing	0	4%	19.10%
Headache	50%	56%	47.60%

Histamine Receptors

Four types of receptors found in different parts of the body and having distinctly different effects when activated

Receptor Type	Major Tissue Locations	Major Biological Effects
H ₁	smooth muscle, endothelial cells	acute allergic responses
H ₂	gastric parietal cells	secretion of gastric acid
H ₃	central nervous system	Modulating neurotransmission
H ₄	mast cells, eosinophils, T cells, dendritic cells	regulating immune and inflammatory responses



Diamine Oxidase (DAO)

- Low DAO generally = high histamine
- May be transient suppression (e.g. blocking drugs)

Or

- Long term suppression (eg inflammation)

(Histamine and histamine intolerance; Maintz and Novak, SpringMed Pub. 2004:43-52)

(Curr Opin Clin Nutr Metab Care. 2011 Jul; 14(4))

Potential Causes of Low DAO

- Known food sensitivities
- DAO-blocking foods: alcohol, energy drinks, and tea
- Genetics
- Inflammation of GIT
- Non-steroidal anti-inflammatory drugs (ibuprofen, aspirin)
- Antidepressants (Cymbalta, Effexor, Prozac, Zoloft)
- Immune modulators (Humira, Enbrel, Plaquenil)
- Anti-arrhythmics (Propranolol, Metoprolol, Cardizem, Norvasc)
- Antihistamines (Allegra, Zyrtec, Benadryl)
- Histamine (H2) blockers (Tagamet, Pepcid, Zantac)

Microbiome (Gut bacteria)

- Some gut bacteria convert histidine in food to histamine
- Bad bacteria can cause inflammation in the GIT
- Inflammation reduces DAO production
- Inflammation increases mast cell degranulation leading to excessive production of histamine

(Allergy Clin Immun 2013;69(3):273-281)

Microbiome: Balance

“Homeostatic interactions between innate immune cell populations and the intestinal epithelium are strictly regulated; however, once the regulatory axis between the innate mucosal and epithelial cells is disrupted, intestinal inflammation is inevitable”

(Eur Jnl Immunology Vol 43, Issue 12 2013)

Microbiome: Balance

- 22 human faecal samples were cultured with **gluten** as the principal nitrogen source; 144 strains belonging to 35 bacterial species involved in gluten metabolism in the human gut were isolated:
 - 94 strains were able to metabolise gluten
 - 61 strains showed an extracellular proteolytic activity against gluten proteins
 - several strains showed a peptidasic activity towards the immunogenic 33-mer gliadin peptides
- Most of the strains were classified within the phyla Firmicutes and Actinobacteria, mainly from the genera Lactobacillus, Streptococcus, Staphylococcus, Clostridium and Bifidobacterium
- *A broad complement is required to fully metabolise gluten*

(FEMS Microbiol Ecol. 2014 May;88(2))

Microbiome: Balance

Children who developed allergy were significantly less often colonized with lactobacilli group I (*Lactobacillus (L.) rhamnosus*, *L. casei*, *L. paracasei*), *Bifidobacterium adolescentis* and *C. difficile* during their first 2 months.

(Clinical and Experimental Allergy Vol 39, Issue 4, 2009)

Intestinal Balance: Parasites

“possible treatment for inflammatory disorders like celiac disease due to the changing of immune responses such as cytokine production. Various surveys showed the therapeutic effects of a controlled parasitic infection on autoimmune disorders. Some studies reported that hookworm infection decrease gluten sensitivity and can employ to treat celiac disease. It is suggested that rising prevalence of inflammatory bowel disorders such as IBD could be associated with the decreased prevalence of intestinal helminthes”

(Gastroenterol Hepatol Bed Bench. 2015; 8(2))

Histamine and Circadian Rhythms

- Histaminergic activity shows a clear circadian rhythm-



day :

during sleep

- Imbalance effects sleep quality, quantity and timing

(Behavioural Brain Research 124(2):129-352001)

Genetic Influence

- Cellular changes lead to chronic allergic inflammation in sinuses
- Genes determine thickness of mucous lining
- Patients with nasal polyps have this gene 'turned on'

(Nature 2018)

Immune exhaustion

- Chronic immune challenges decrease activity of T-cells in some patients

For example:

- may worsens bowel symptoms
- Potentially perpetuates vicious cycle of gut immunity/allergy/inflammation

(Gut, June 2017)

Mood and Allergies

Research Results:

- Flare reaction during happiness and are smaller than flare reactions during sadness
- Replication with hypnotic manipulation
- Conclusions: mood is a predictor of histamine related skin hypersensitivity reactions

(EJACI Vol 56, Iss 8 2001)

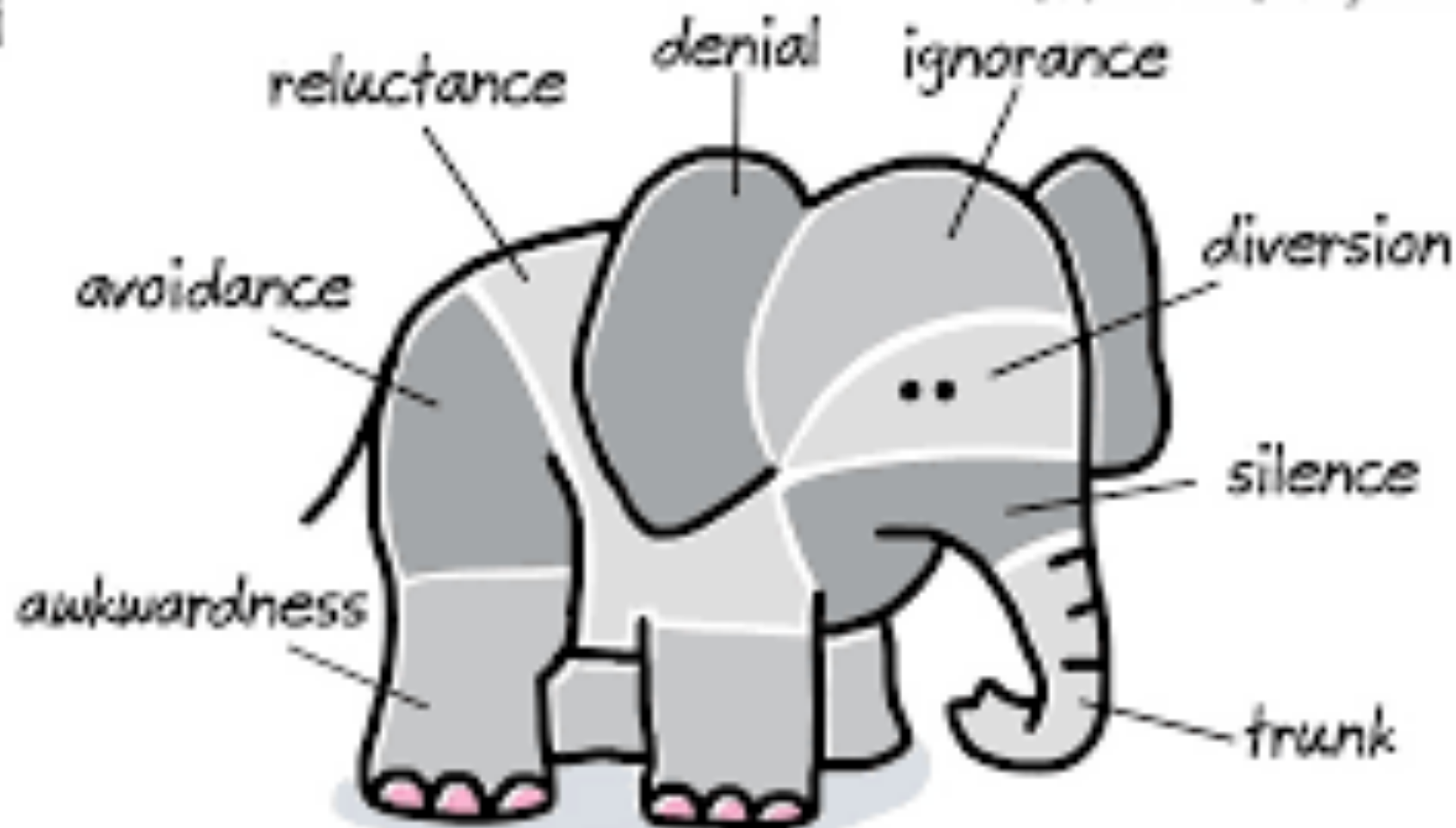
Stress and Allergy

- Histamine is an inflammatory molecule
- Cortisol is an anti-inflammatory compound
- High histamine levels increase adrenal activity

(Clin Exp Allergy ;38(1); 2008)

PARTS OF THE ELEPHANT IN THE ROOM

© John Atkinson, Wrong Hands



Pilot comparative study on the health of vaccinated and unvaccinated 6-to 12-year-old US children. J. Transl. Sci,

In summary (in relation to allergy):

*Vaccinated children were **30-fold more likely to be diagnosed with allergic rhinitis (hay fever)** than non-vaccinated children

* Vaccinated children were **22-fold more likely to require an allergy medication** than unvaccinated children

*Vaccinated children were **3.8-fold more likely to be diagnosed with middle ear infection (otitis media)** than unvaccinated children (OR 3.8)

Chronic Illness Diagnosis	% Vaccinated Children Diagnosed	% Unvaccinated Children Diagnosed
Allergic Rhinitis	10.4%	0.4%
Other allergies	22.2%	6.9%
Eczema/atopic dermatitis	9.5%	3.6%
Learning disability	5.7%	1.2%
ADHD	4.7%	1.0%
Any neurodevelopmental disorder	10.5%	3.1%
Any chronic illness	44.0%	25.0%

The relationship between vaccine refusal and self-report of atopic disease in children. Jnl of allergy and clinical immunology, 115(4), 737-744. (2005)

Study of 1,177 children (515 never vaccinated, 423 partially vaccinated and 239 completely vaccinated).

Parents who chose not to vaccinate their children were significantly less likely to report asthma only when they also reported no family history of asthma or exposure to antibiotics during infancy. Likewise, children of parents who refused vaccines were less likely to report hay fever only when there was no family history of allergies. All children of vaccine abstainers were less likely to have eczema or current wheeze. These associations persisted after controlling for measured confounders (age, sex, source of medical care, antibiotic exposure, and familial clustering). There were dose-response relationships; asthma, hay fever, eczema and wheeze were reported most frequently among completely vaccinated children and somewhat less frequently among partially vaccinated children. |

Hormones?

- 4.2% females vs 2.9% males have food allergies or intolerances
- Before puberty the rate is double for males
- High histamine potentiates oestrogen increasing menstrual pain
- In pregnancy, DAO production increases by 500x by the placenta

Psychiatric Drugs and Histamine

- SSRI's selectively require histamine to work

(Int J Neuropsychopharmacol. 2015 Sep;

18(10)

- Antipsychotics (e.g. Risperidone and Seroquel) are both potent anti-histamines due to their variable affinity for H1 receptors)

(Prim Care Companion J Clin Psychiatry. 2004; 6(suppl

2): 3-7)

- Beware of rebound effects associated with discontinuation

Antipsychotic Medications and the Microbiome

- 24% of 1000 tested drugs impact the microbiome negatively
- Anti-psychotics are over represented in this group

(Nature, Vol 555, March 2018)

Increasing Incidence of Allergy in Aging

- Immunosenescence
- Concurrent diseases
- Drug poly-therapy
- Adverse drug reactions
- Accumulation of metabolic toxins
- Nutritional deficiencies (Zinc)
- Physiological changes to gut, neurons, lungs
- Reduced gut enzymes
- *Good case history very relevant*

(Aging Dis. 2017 Apr; 8(2))

The Pursuit of Pleasure

1. Some foods contain exorphins (e.g. gluten, milk protein, cafestrol from coffee, chocolate)
2. Allergens create a stress response increasing opiates
3. Mast cells contain dopamine. Rapid rise and decrease matches food cravings and post-ingestive (of allergen) hangover

Diagnostic question:

What food can you absolutely not do without?

Low Histamine Diets

- Few studies demonstrating a direct link between eating histamine foods and adverse reactions (excluding known allergens)
- Available research suggests between 50-75% success rate by limiting histamine foods

High Histamine Containing Foods

- Microbial fermented foods
- Cheese
- Alcoholic beverages (Red Wine)
- Vinegar
- Processed meats
- Fish/seafood (esp. canned)
- Most citrus fruit, grapes and berries
- Solanaceae family vegetables
- Pumpkin, avocado
- Cocoa, chocolate, cola

Histamine 'Releasing' Foods

Whilst not necessarily high in histamine, consumption of certain foods/additives result in elevated serum histamine levels mainly via bacterial or chemical conversion.

Foods:

Egg whites, strawberries, raspberries, shellfish

Chemicals:

Tartrazines, benzoates etc.

Anti-inflammatory diet

- Benefit supported by strong evidence
- Inflammatory foods (eg High meat consumption/low fruit and veg; fried foods) change microbiome that modulate immune system

Testing

- Serum histamine is very labile
- Skin prick test for allergic rhinitis has mixed results (50-60% accuracy)
- IgE (RAST) and Eosinophil counts are less accurate

(Allergy, Asthma & Clinical Immunology 2016;12:20)
(Australian Society of Clinical Immunology and Allergy)

Non-standard tests:

- ELISA-ACT test no independent data

Oral Food Challenge Testing

- Cumbersome but most accurate and reliable
- Considered safe (2% anaphylaxis)
- Free and non-invasive
- Detailed reaction diary important (physical and emotional manifestations)

(Annals of Allergy, Asthma and Immunology 2017)
(Allergology International Vol 63, Issue 3, 2014)

What can you
do?

Reduce risk early: train the immune system

- In utero benefit of allergen intake
- Exclusive breastfeeding for first 4 months (WHO 6m)
- Breast milk contains allergens and aeroallergens
- Exposure through breast feeding increases tolerance and reduces allergies
- Breast milk contains IgA's, Antigens, gut growth factors, microbiome influencing factors
- Modulation of immunity and inflammation
- Offer 'risk' foods to children in risk group early. Introduction to peanuts between 4-11 months saw 81% decrease in peanut allergy

Nigella sativa (Black Cumin)

TRADITIONAL USE:

**bronchial asthma,
allergies, headache,
infections, dysentery,
obesity**

KEY ACTIONS:

- ✓ Antihistamine
- ✓ H1 receptor antagonist
- ✓ Intestinal mast cell inhibitor
- ✓ Antioxidant
- ✓ Anti-inflammatory
- ✓ Antimicrobial (bacterial, fungal, parasitic, viral)
- ✓ Immune-modulating
- ✓ Protects GIT



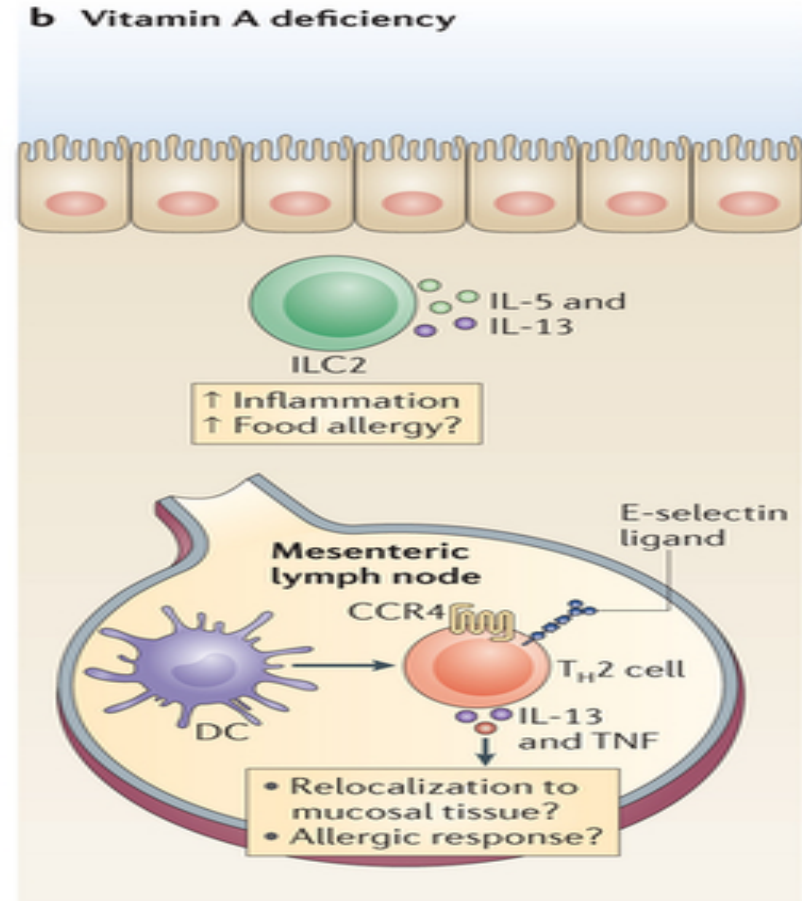
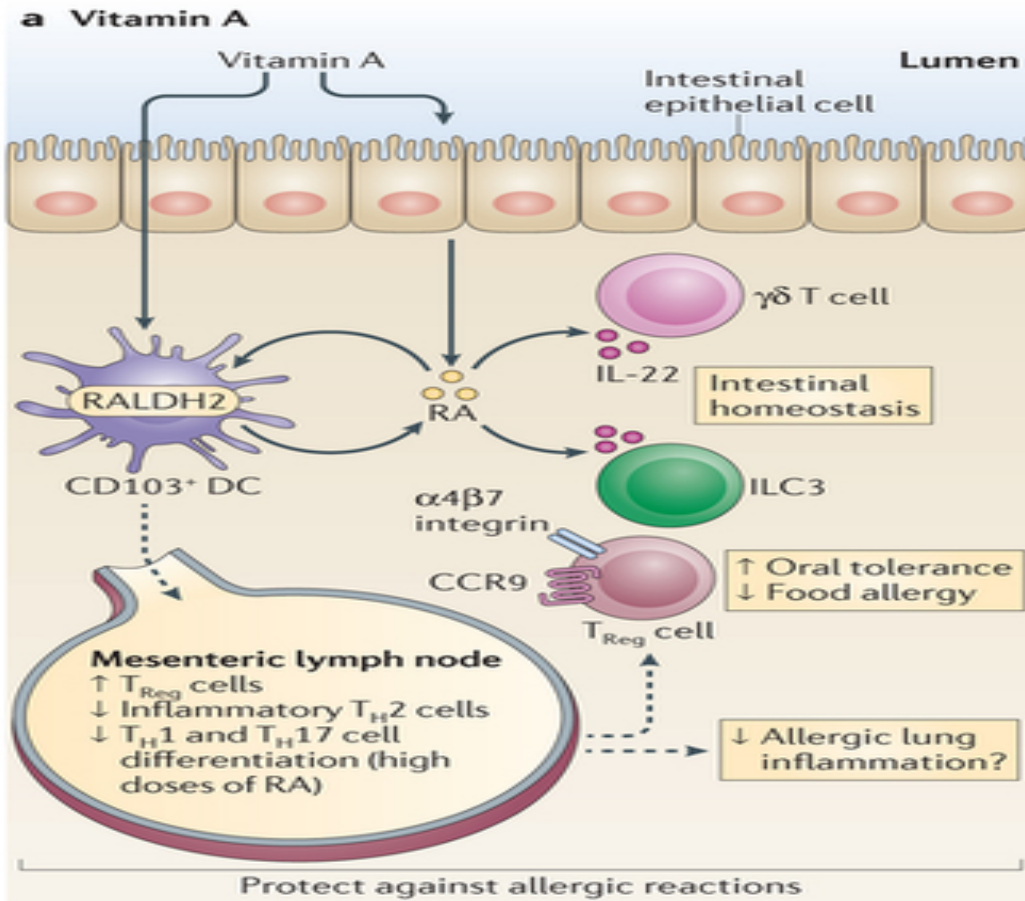
Vitamin A: enhances resistance to allergens

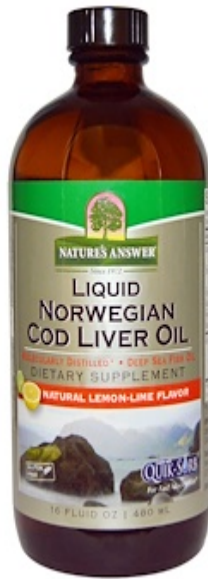
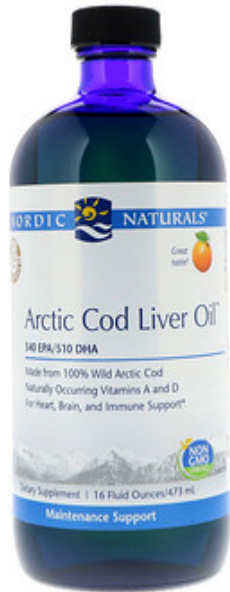
✓ Mucosal Health

✓ Secretory IgA

✓ Epithelial barrier

✓ GIT microbiota





Zinc

- Involved in controlling mast cell activation
- Positively controls inflammatory cytokine gene induction

(Yakugaku Zasshi. 2017;137(5))

- Zinc transporters are responsible for the intestinal epithelial homeostasis

(PLoS Genet. 2016 Oct 13;12(10))

Fish Oils

Prevention: Meta-analysis confirms that taking fish oils and probiotics during pregnancy significantly reduces allergy symptoms in offspring

(A systematic review and meta-analysis. PLoS Med 15(2): e1002507. Feb 2018)

Diet

- Anti-inflammatory
- Sugar
- FODMAP
- Exposure

Microbiome

- Hygiene hypothesis
- Age suitable
- Vaccination
- Balanced

Lifestyle

- Movement
- Nature

Toxins

- Chemicals
- Plastics

Stress

- Meditation
- Sleep
- Happiness

Balance

- Immunity
- Appropriate herbs and supplements

Environmental biodiversity, human microbiota, and allergy are interrelated

- By 2050 2/3'rds of us will live in urban environments with reduced green exposure
- All chronic inflammatory diseases and allergies are expected to increase
- Interactions with nature enhances wellbeing in urban areas; enriches the commensal microbiota and enhance its interaction with the immune system with far-reaching consequences

(Proceedings of the National Academy of Sciences (US) May 2012, 109 (21))

**THANK
YOU**