Microbiome Center

Evidence-based, personalized precision medicine

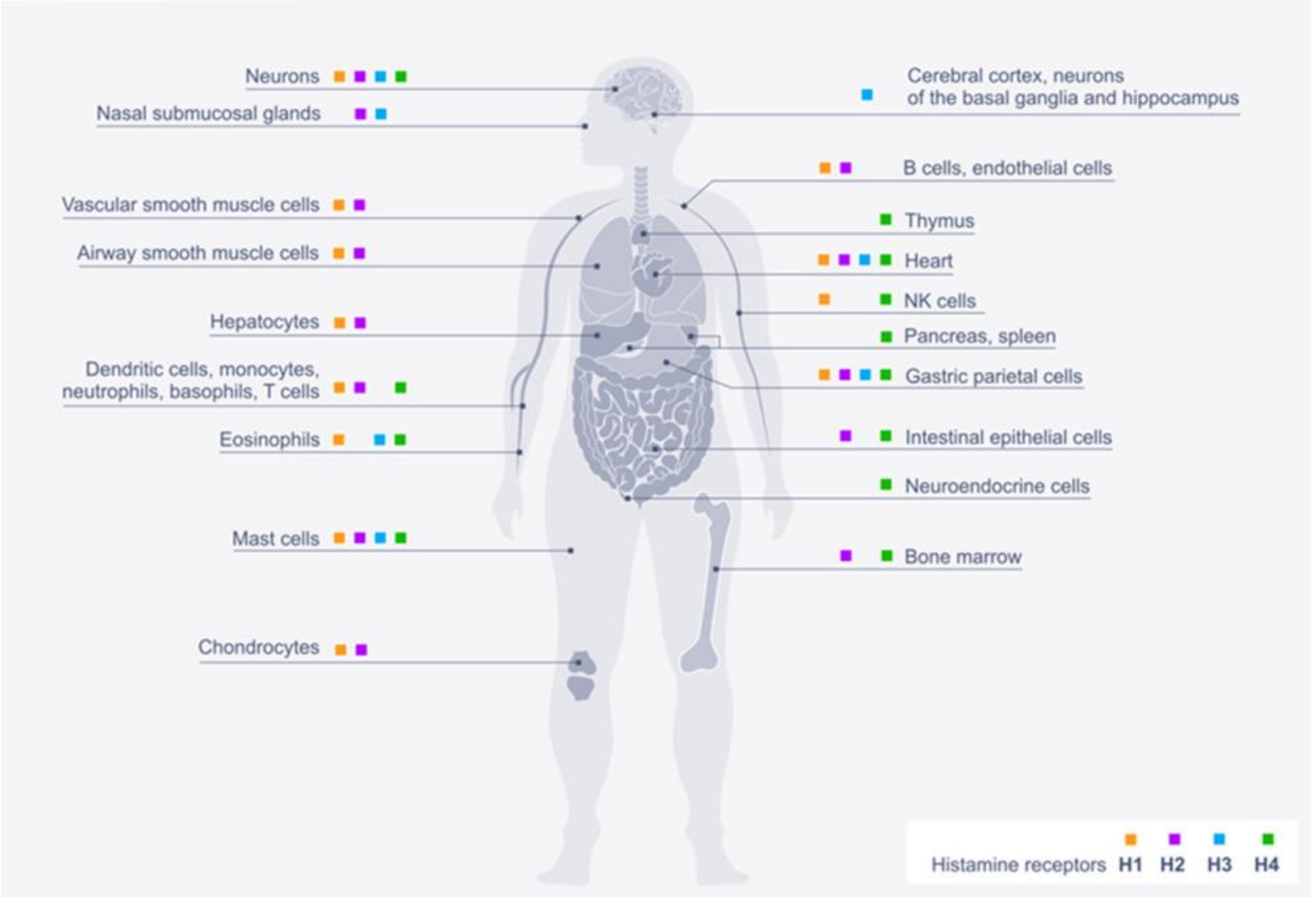
.... helping chronic patients more effectively, in less time.

Histamine

Karin Pijper, Dennis Zeilstra, Barbera Eijgel – 6 February 2025

What is histamine?

- Discovery[1]:
  - in 1932 discovered to play a major role in allergies
  - in 1940s first antihistamines
- Histamine is a biogenic amine[1]:
  - Amine: chemical compound that originates from an amino acid
  - Other amines: dopamine, noradrenaline, tyramine
- Presence:
  - In nature ubiquitously present[2]
  - Many functions in humans[2,3]: it is a **neuro-immuno-endocrine system mediator**



1. Lieberman, P.Annals of Allergy, Asthma & Immunology.106,.S2–S5.(2011)
2. Hrubisko, M. et al.Nutrients.13,.2228.(2021)
3. Smolinska, S. et al.Metabolites.12,.895.(2022)

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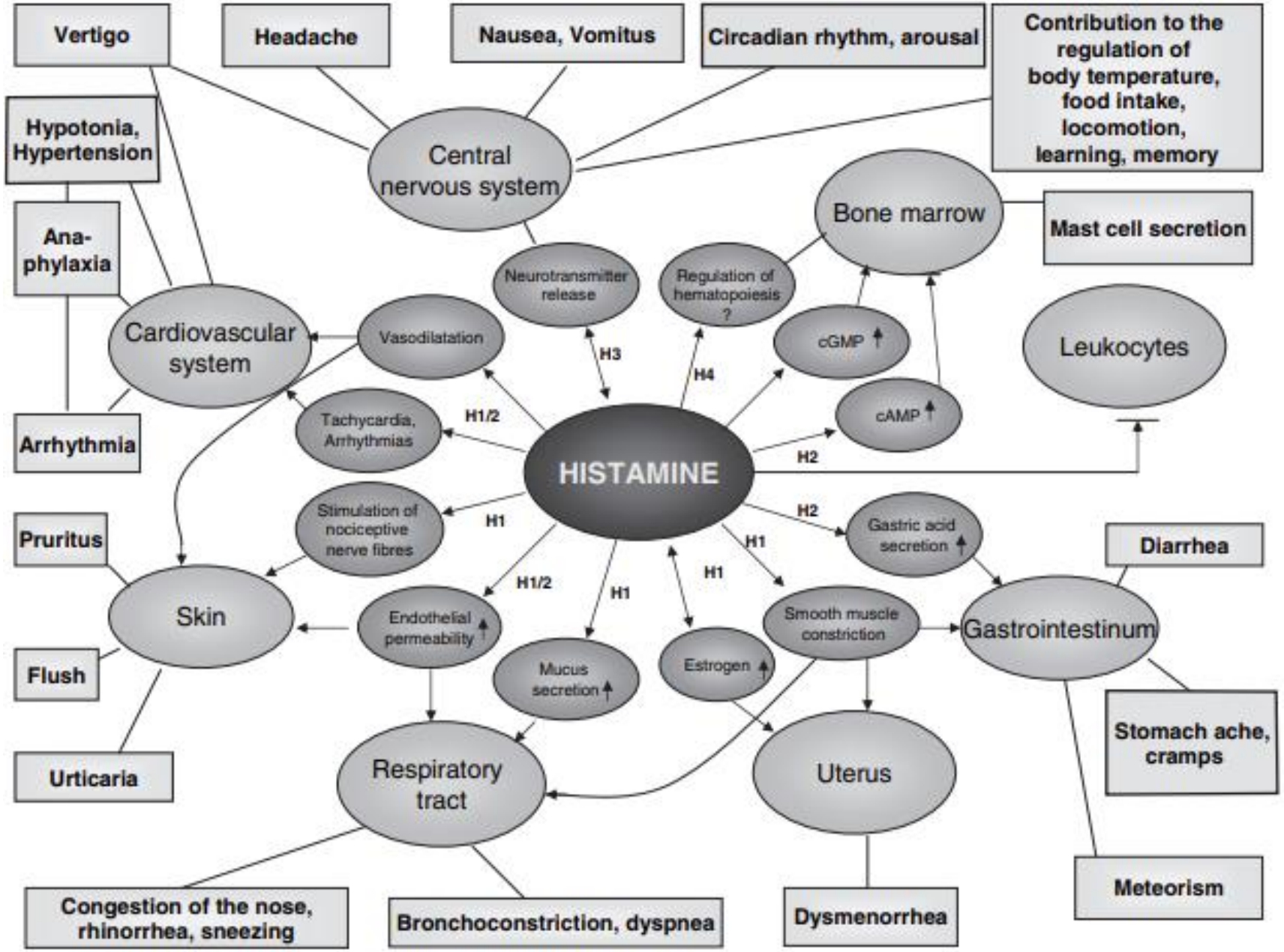

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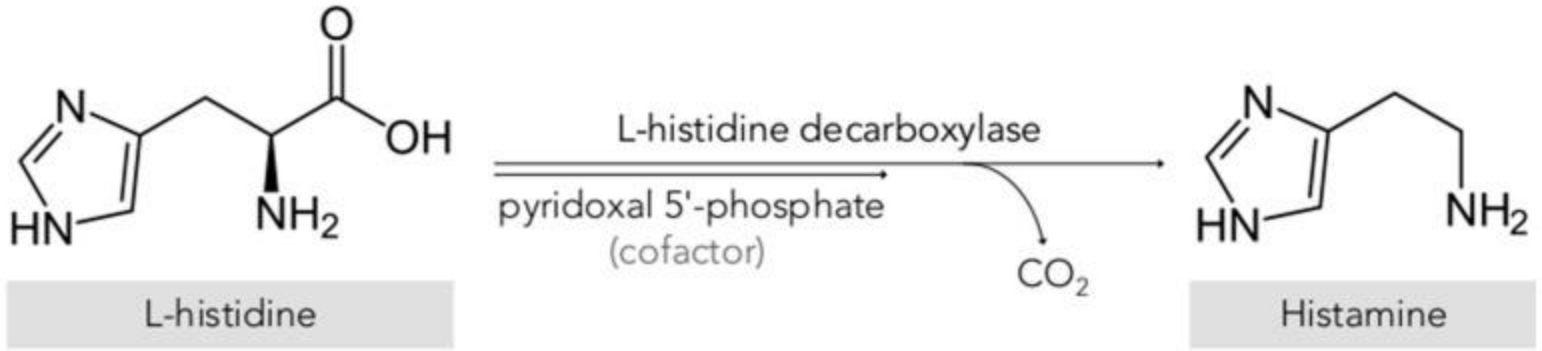
Biosynthesis

- Through decarboxylation from histidine (+ vit B6) -> histamine



- Short synthetic pathway in plants and animals: histamine is quickly available
- Histidine is found in almost all foods

1. Comas-Basté, O. et al. Biomolecules. 10, .1181. (2020)

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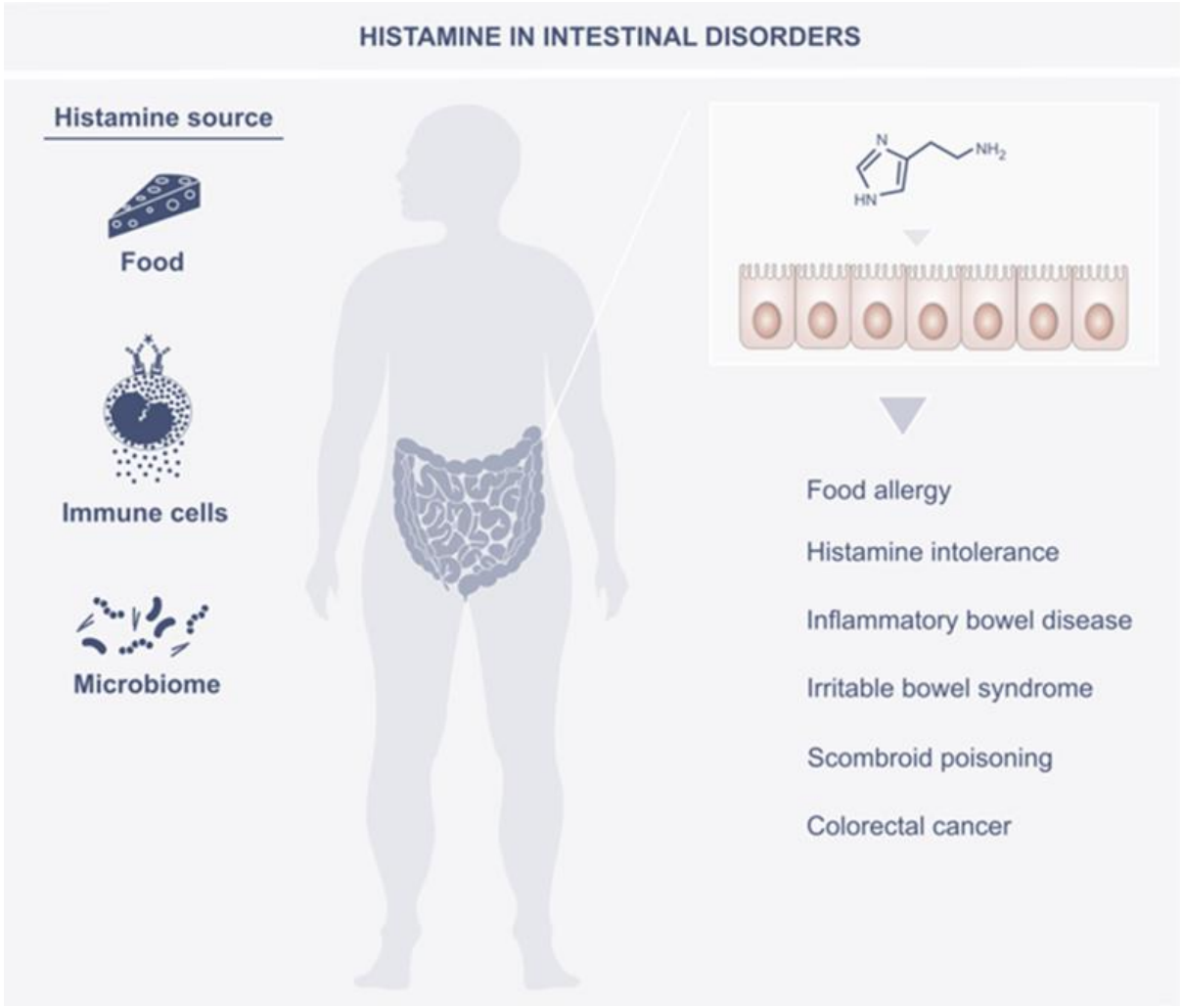
Sources of histamine

1) Food
2) Gut bacteria
3) Endogenous production:
   - Mast cells and other immune cells release histamine
   - Certain nerve cells



1. Smolinska, S. et al.Metabolites.12,.895.(2022)

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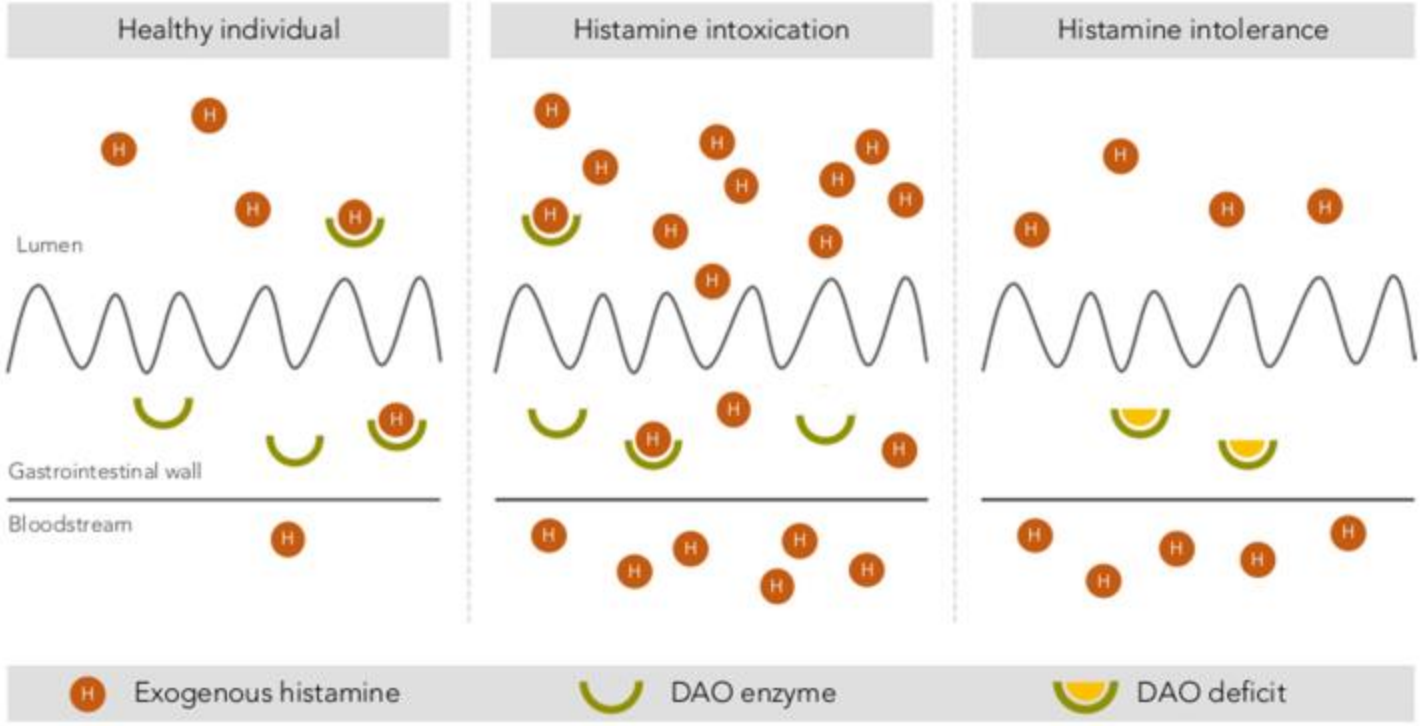
Histamine intolerance

- Initially, illness due to excessive histamine was termed **histamine intoxication**
  - Spoiled foods, especially fish
- Histamine loads leading to symptoms vary substantially: response of individual plays large role, changing the definition to **histamine intolerance**
  - Important role in response for DAO
  - HI also considered a disorder due to reduced histamine-degrading capacity or lack of DAO



1. Comas-Basté, O. et al. Biomolecules. 10, 1181. (2020)

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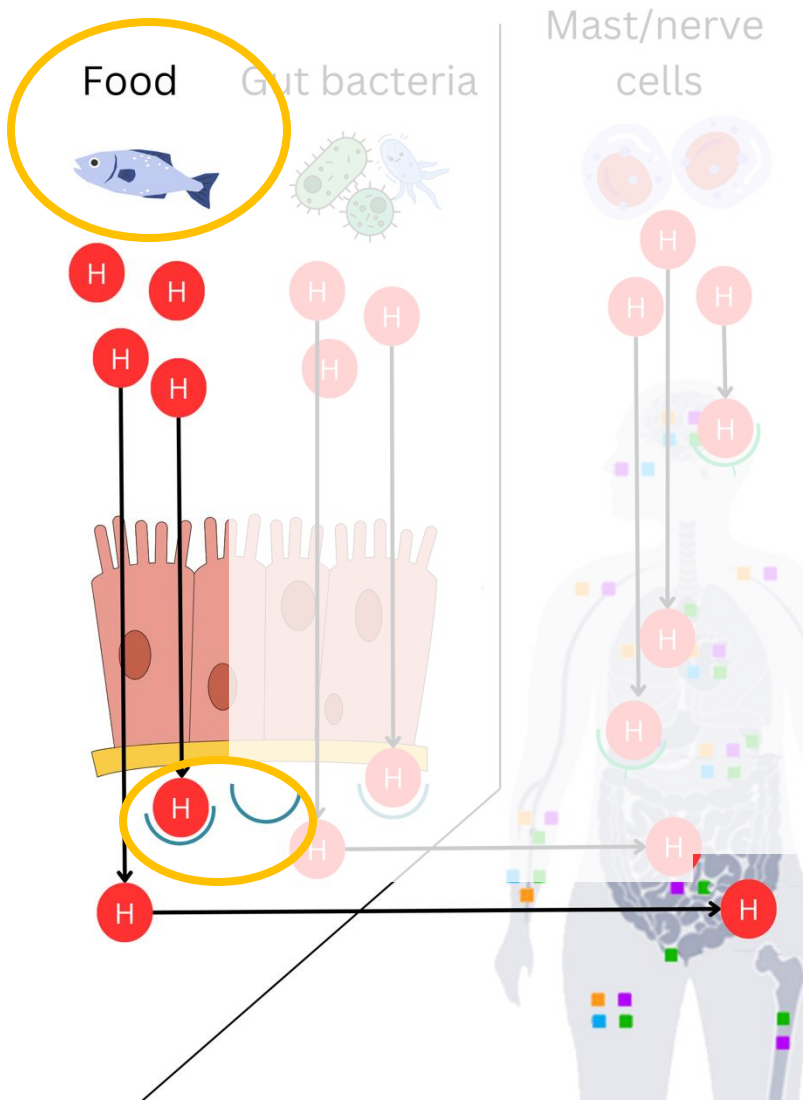
Histamine intolerance

- Originally, the diagnosis “histamine intolerance” thus focused on[1]:
  - Dietary histamine
  - Capacity to handle dietary histamine intake

- Typically, treatment for histamine intolerance consisted of[1]:
  - Limit food intake of histamine
  - supplement DAO



1. Comas-Basté, O. et al. Biomolecules. 10, .1181. (2020)

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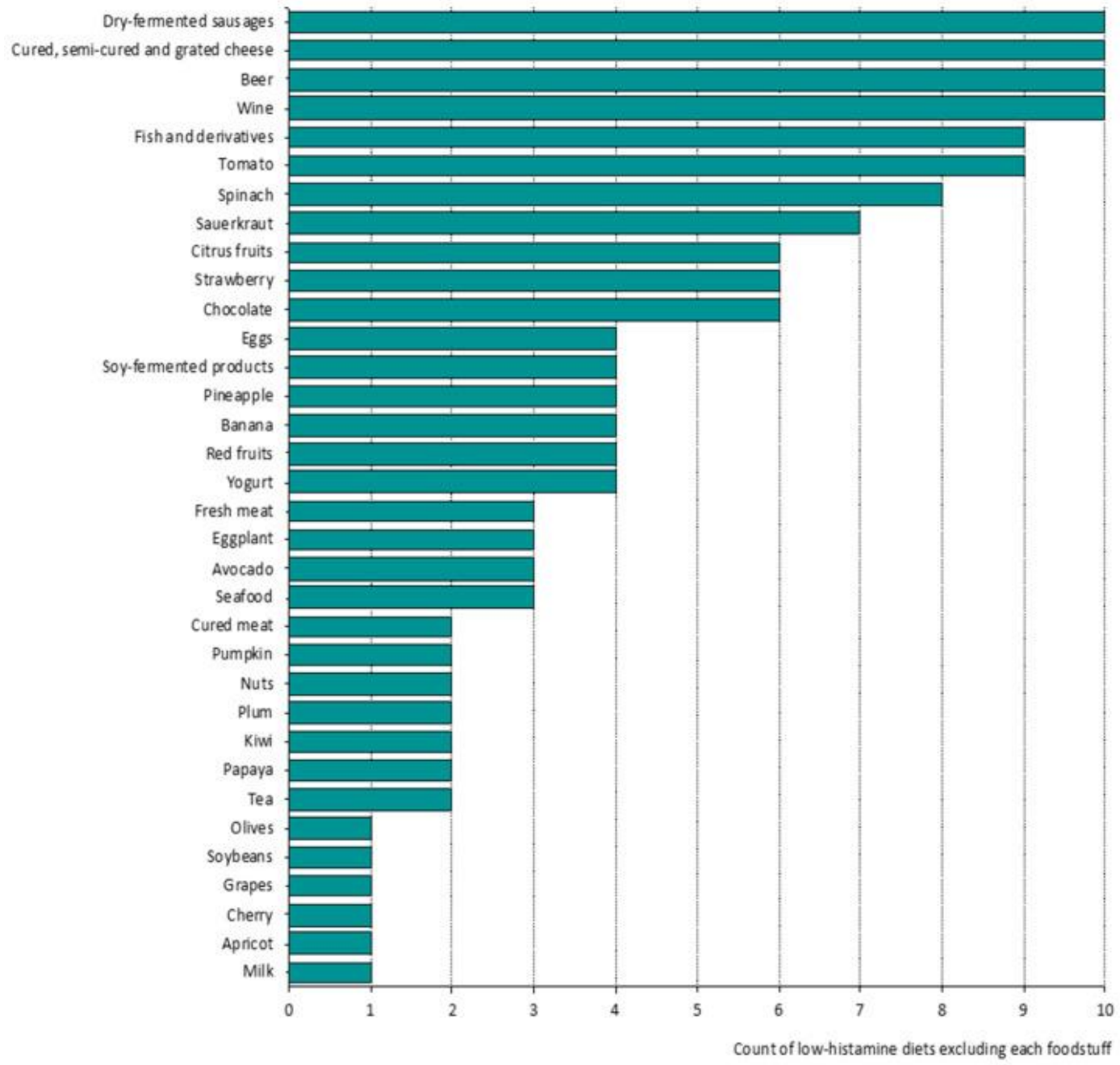
Histamine diet

- Various low-histamine diets are being used
- A review found 10 diets described in scientific literature
- Interestingly, the overlap between these 10 diets was very small, with only 4 food items occurring in all 10 diets



1. Sánchez-Pérez, S. et al.Nutrients.13,.1395.(2021)

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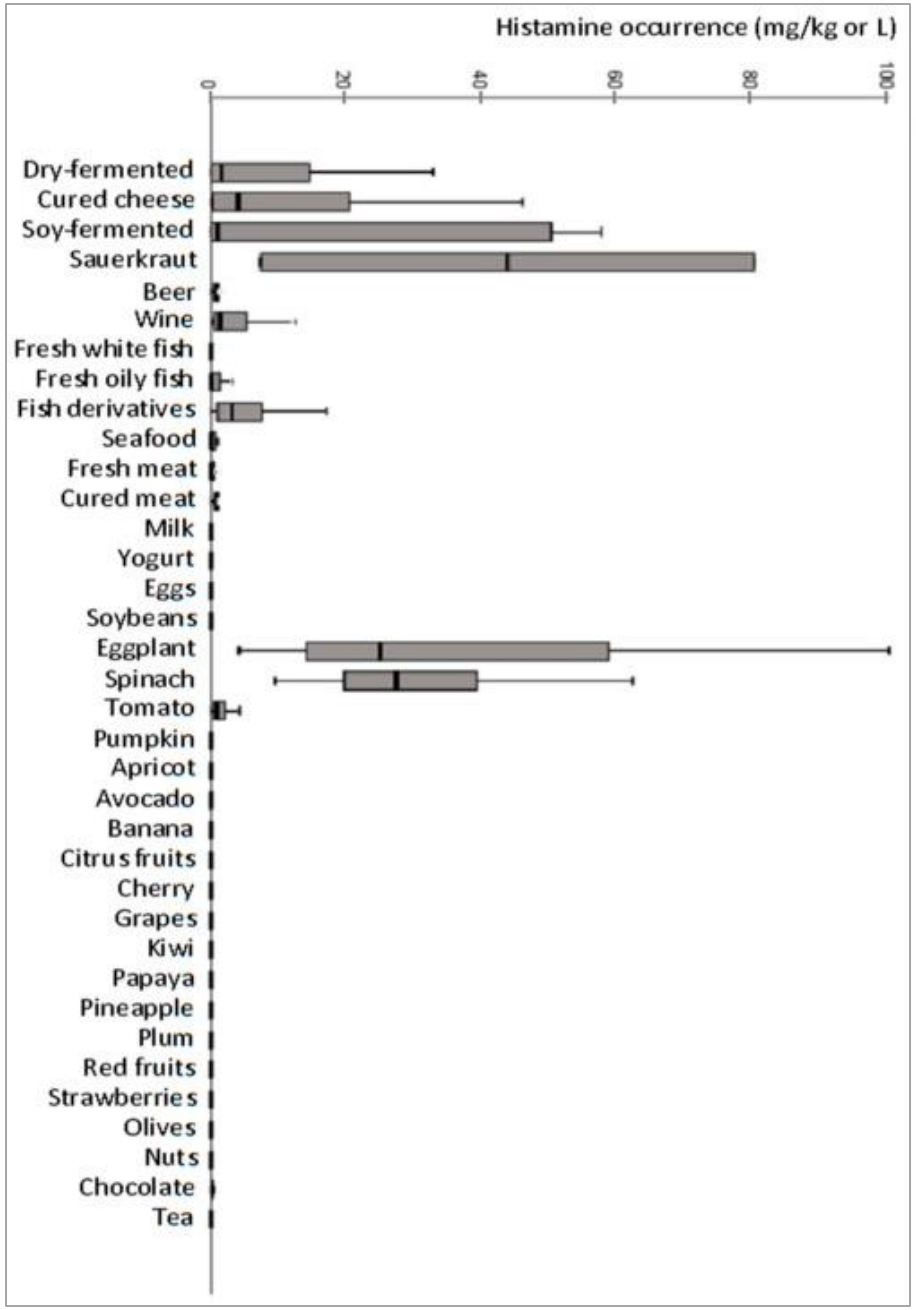
Histamine diet

- The researchers also analyzed the actual histamine content in these foods, as bought in Spain[1].
- The vast majority of the excluded food items (68%) did **not** have high levels of histamine.
- High levels of other biogenic amines were found too:
  - Especially tyramine (dry-fermented products, cheese, fermented soy).
  - Also putrescine and cadaverine
  - May compete for the available DAO.
- NB: some food are said to trigger release of endogenous histamine, but no evidence of this effect is found



1. Sánchez-Pérez, S. et al.Nutrients.13,.1395.(2021)

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Histamine intolerance - lack of reproducibility

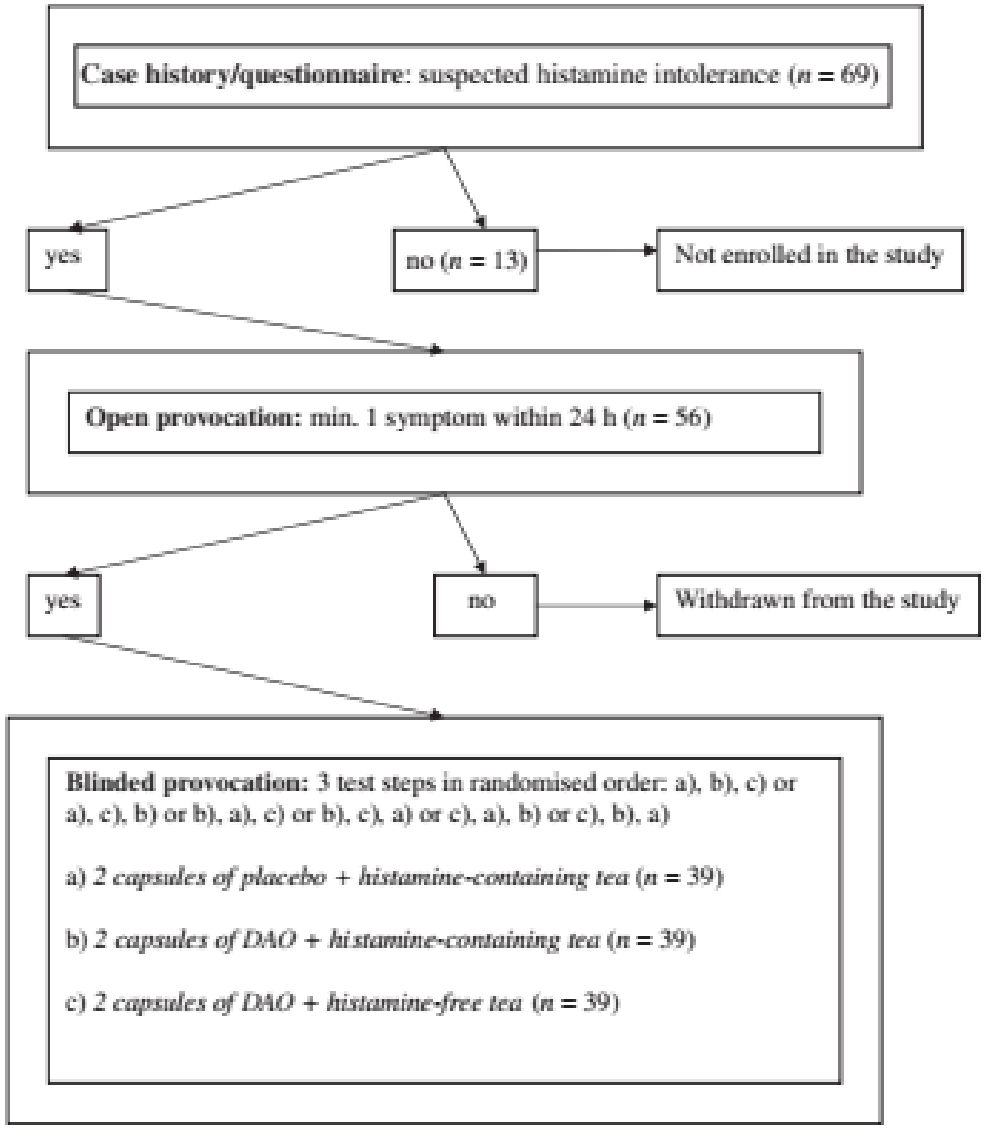

Table 2. Number (*n*) and percentage (%) of subjects with at least 1 positive reaction among blinded treatment groups

	n	*n* of positive reactions	% of positive reactions
DAO + histamine-containing tea	39	30	76.9
DAO + histamine-free tea	39	25	64.1
Placebo + histamine-containing tea	39	30	76.9

1. Komericki, P. et al.Wien Klin Wochenschr.123,.15–20.(2011)

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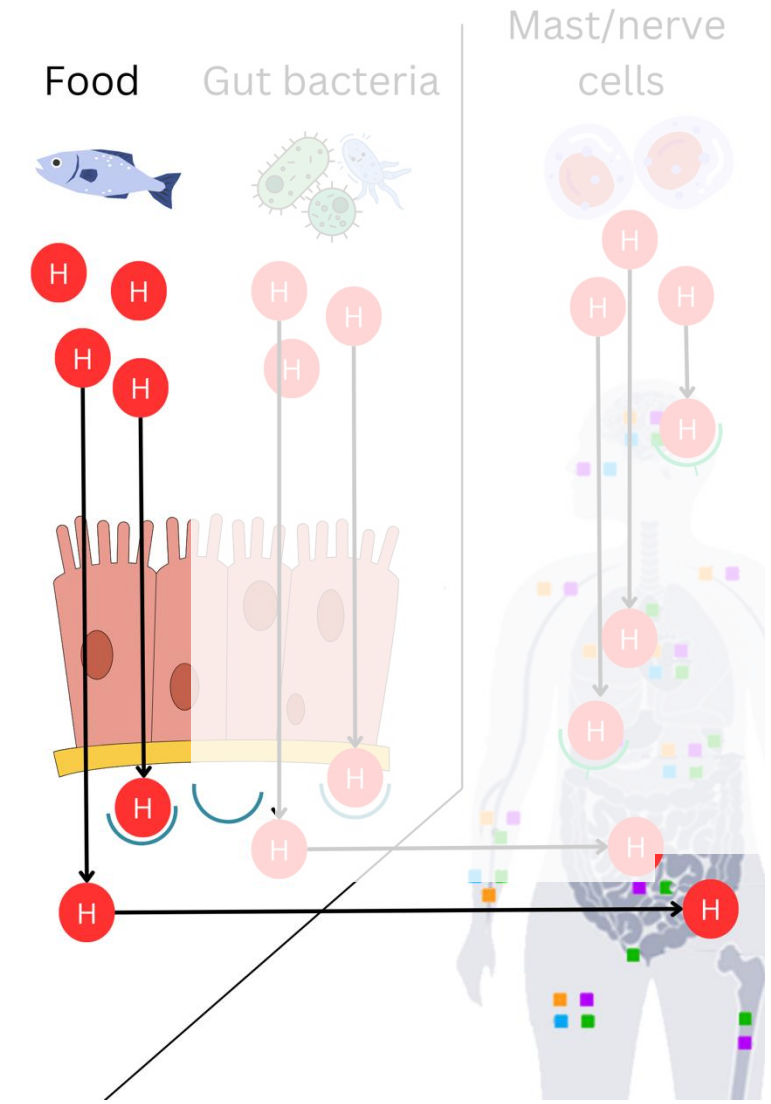
The term “histamine intolerance” is inaccurate

- Diet is not the only histamine source. Insufficient DAO cannot explain all symptoms
- Intolerance to a body’s own substance essential for survival, would be incompatible with life.
  - Ever heard of adrenaline or testosterone intolerance?
  - Fructose, lactose, gluten intolerance refer to substances foreign to the body
- The classical term histamine intolerance is a **misnomer** and an **oversimplification**



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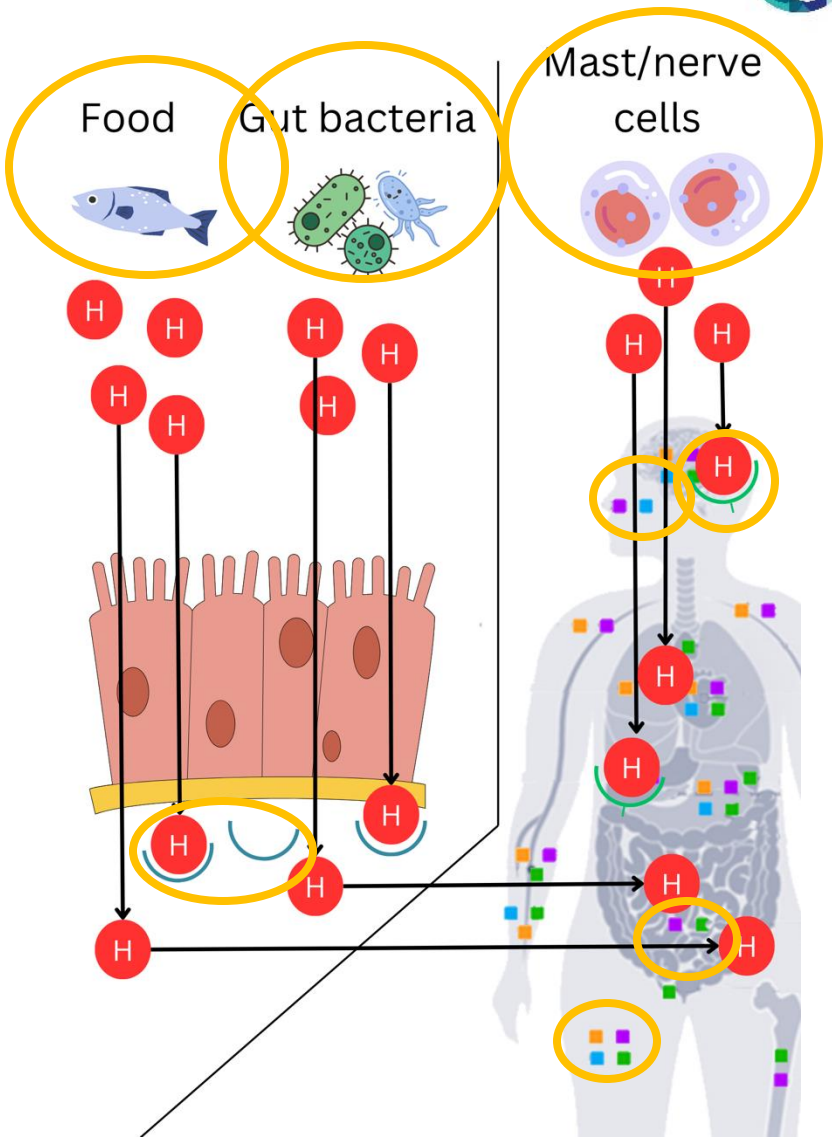
Factors playing a role

The overall response to histamine is determined by:

- Histamine exposure
  - Dietary histamine load
  - Bacterial production of histamine
  - Release of histamine by mast cells
  - Release of histamine by nerve cells
- Histamine action:
  - Expression of the four histamine receptor types (with different effects)
  - Blocking of specific receptor types
- Histamine breakdown:
  - Release of and breakdown by DAO
  - Breakdown by HNMT



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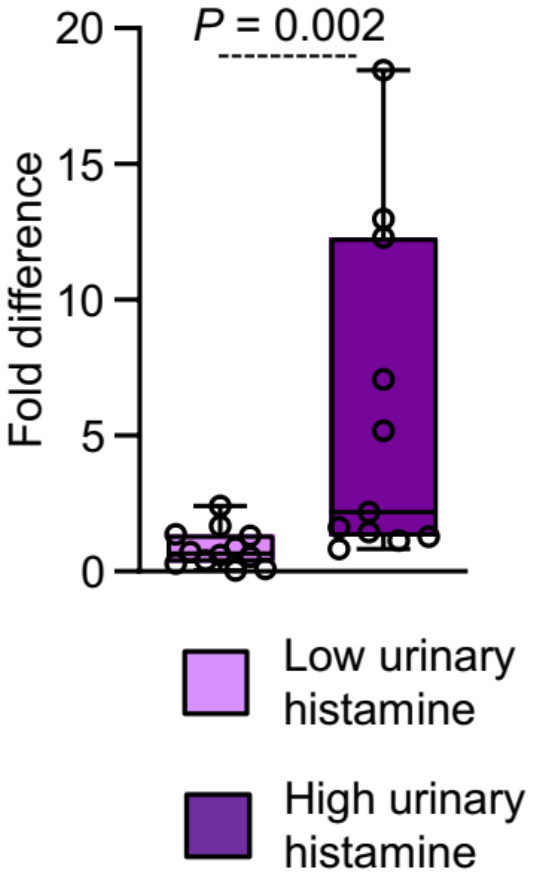
Typically, pathogenic bacteria are considered

- Histamine-producing bacteria can convert histidine into histamine, e.g.:
  1) Serratia spp.
  2) Morganella spp.
  3) Klebsiella spp.
  4) Citrobacter spp.

- Example: study found high levels of *Klebsiella aerogenes* in IBS patients



1. De Palma, G. et al.Science Translational Medicine.14,.eabj1895.(2022)

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But … various commensals can produce histamine

Almost 100 species out of 32,000 found to have histidine decarboxylase gene

1. Mou, Z. et al. BMC Genomics 22, 695 (2021)

Even if bacteria can produce histamine, that doesn't mean they will

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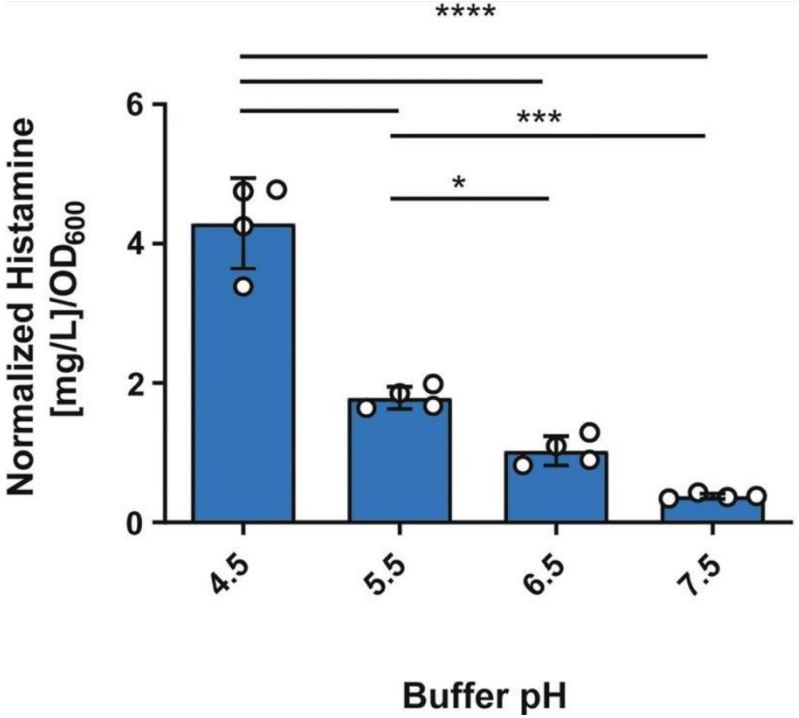
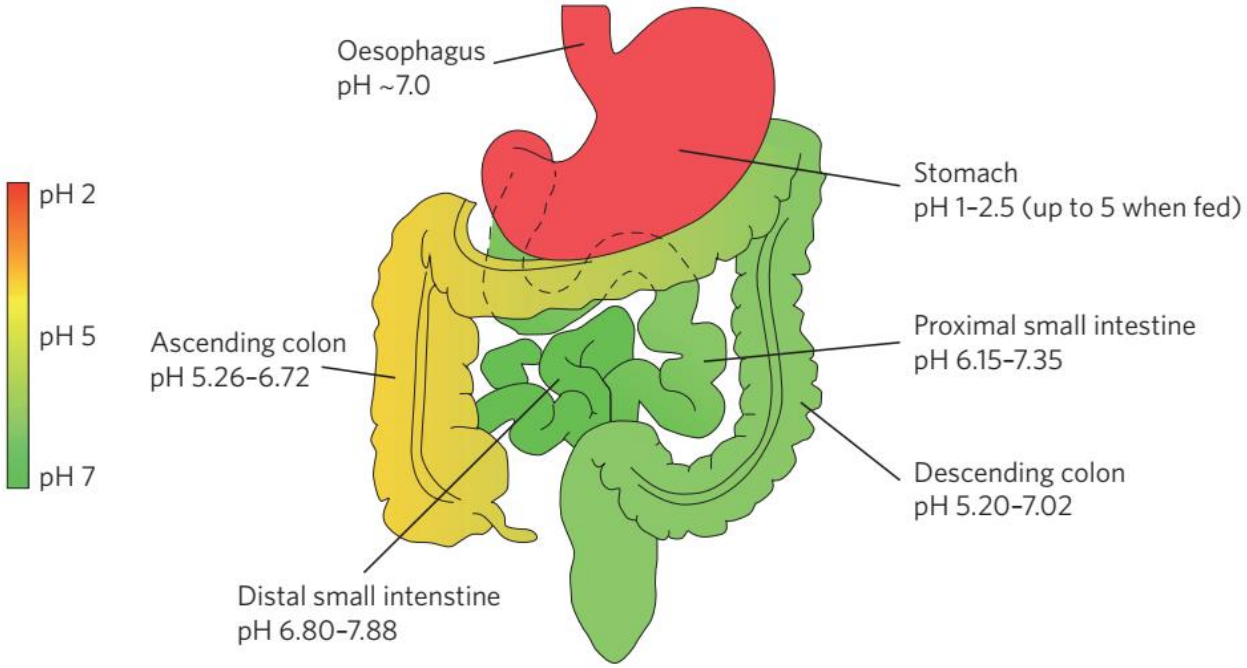
pH is an important factor



L. reuteri 6475 can produce histamine, but the amount depends heavily on the environment pH[1]

Conversion of amino acids is a protective mechanism for bacteria in acid environment[2]



1. Hall, A. E. et al. Microb Cell Fact 18, 212 (2019)
2. Wang, Y. et al. Front Bioeng Biotechnol 9, 612285 (2021)
3. Khutoryanskiy, V. V. Nature Mater 14, 963–964 (2015)

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Nutrient availability has large impact

TABLE 3. Influence of glucose concentration and growth rate on the production of organic acids and amines by *C. perfringens* grown in continuous culture

D (per h)	Culture conditions[a]	Fermentation products[b] (mmol/g [dry wt] of cells)													% Amines produced
		Organic acids					Amines								
		A	B	L	S	Total	Me	Di	Pr	Py	Bu	Pu	Ca	Total	
0.04	Glucose limited	29.7	6.7	1.1	2.4	39.9	0.5	0.6	1.5	0.4	0.5	0.8	1.1	5.4	12.1
	Amino acid limited	44.6	10.7	31.9	4.6	91.8	0.5	0.5	1.8	0.4	0.1	0.7	0.4	4.4	4.6
0.08	Glucose limited	25.1	2.3	0.8	ND	28.2	1.0	0.5	1.3	ND	0.9	0.8	0.8	5.3	15.8
	Amino acid limited	17.1	2.4	57.6	T	77.7	0.8	0.4	1.5	0.3	1.1	0.6	0.3	4.0	4.9
0.16	Glucose limited	14.2	1.4	2.1	T	17.7	1.2	0.3	3.1	0.3	0.2	1.3	1.3	7.7	30.3
	Amino acid limited	11.3	1.8	51.3	ND	64.4	0.7	0.3	1.3	0.3	0.4	ND	0.8	3.8	5.6

[a] Cultures were grown on a glucose-limited medium containing 5.0 g of peptone and glucose per liter and on an amino acid limited medium containing 5.0 g of peptone per liter and 15 g of glucose per liter.

[b] A, Acetate; B, butyrate; L, lactate; S, succinate; Me, methylamine; Di, dimethylamine; Pr, propylamine; Py, pyrrolidine; Bu, butylamine; Pu, putrescine; Ca, cadaverine. ND, Not detected; T, trace (<0.1 mmol/g [dry weight] of cells)

1. Allison, C. et al. Applied and Environmental Microbiology 55, 2894–2898 (1989)

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Beneficial species (e.g. Lactos) inhibit biogenic amine-producing pathogens

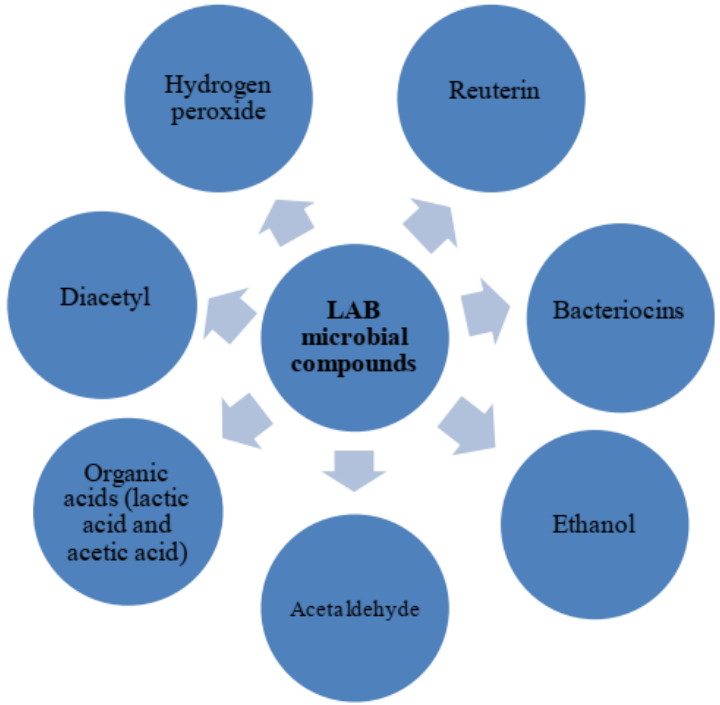

Table 4: Effect of lactic acid bacteria on the production of biogenic amines by foodborne pathogens

LAB	HIS	TYR	PUT	CAD	Unit	Pathogens	Broth/Food	References
Control	20.32	2167.25	638.68	48.37	mg/L	*E. coli*	Tyrosine decarboxylase broth	Toy et al., 2015
Pediococcus acidophilus	11.16^{I}	351.13^{S}	192.07^{I}	27.12^{I}				
Control	177.4	502.8	563.3	644.1	mg/kg	pathogen	Fermented sausages	Xie et al., 2015
Lactobacillus plantarum	28.93^{I}	268.1^{I}	70.03^{I}	252.6^{I}				
Control	0.00	0.82	35.33	185.87	mg/L	*S.* Paratyphi A	Lysine decarboxylase broth	Kuley et al., 2012
Lactobacillus plantarum	1.10^{S}	8.02^{S}	31.10^{I}	433.98^{S}				
Control	673.9	7.5	-	-	mg/L	*L. monocytogenes*	Ornithine decarboxylase broth	Özogul et al., 2015
Streptococcus thermophilus	37.8^{I}	93.9^{S}	-	-				
Control	0.90	-	-	-	mg/100g	pathogen	Tuna (*Euthinus affinis*)	Thiruneelakandan et al., 2013
Lactobacillus plantarum	0.60^{I}	-	-	-				
Control	0.57	2.52	10.05	0.78	mg/L	*S. aureus*	Histidine decarboxylase broth	Özogul, 2011
Lactococcus lactis	5.79^{S}	41.13^{S}	61.95^{S}	7.60^{S}				
Control	-	-	207.3	228.2	mg/ml	*E. faecium*	Traditional Chinese sausage	Xie et al., 2016
Lactobacillus plantarum	-	-	147.9^{I}	197.9^{I}				
Control	-	-	138.59	235.95	mg/kg	pathogen	Fermented pork sausage	Limsuwan et al., 2007
Lactobacillus sakei	-	-	82.23^{I}	224.74^{I}				
Control	1.00	18.6	11.6	7.59	mg/kg	pathogen	Spanish Type Culture Collection (CECT, Valencia, Spain)	Peñas et al., 2010
Leuconostoc mesenteroides	2.14^{S}	26.4^{S}	32.1^{S}	19.1^{S}				

^{S}: stimulation effect of LAB on pathogenic bacteria

^{I}: Inhibition effect of LAB on pathogenic bacteria

1. Özogul, F. et al. Critical Reviews in Food Science and Nutrition 58, 1660–1670 (2018)

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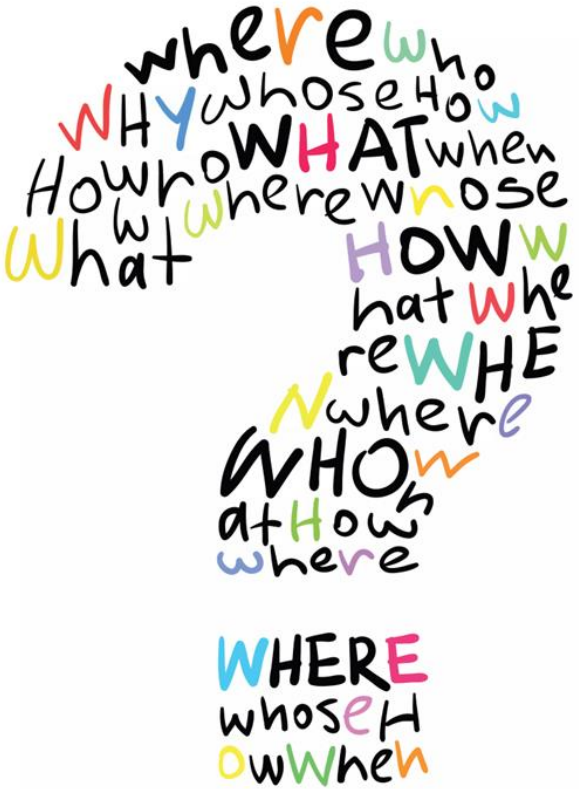
Questions



Factors playing a role

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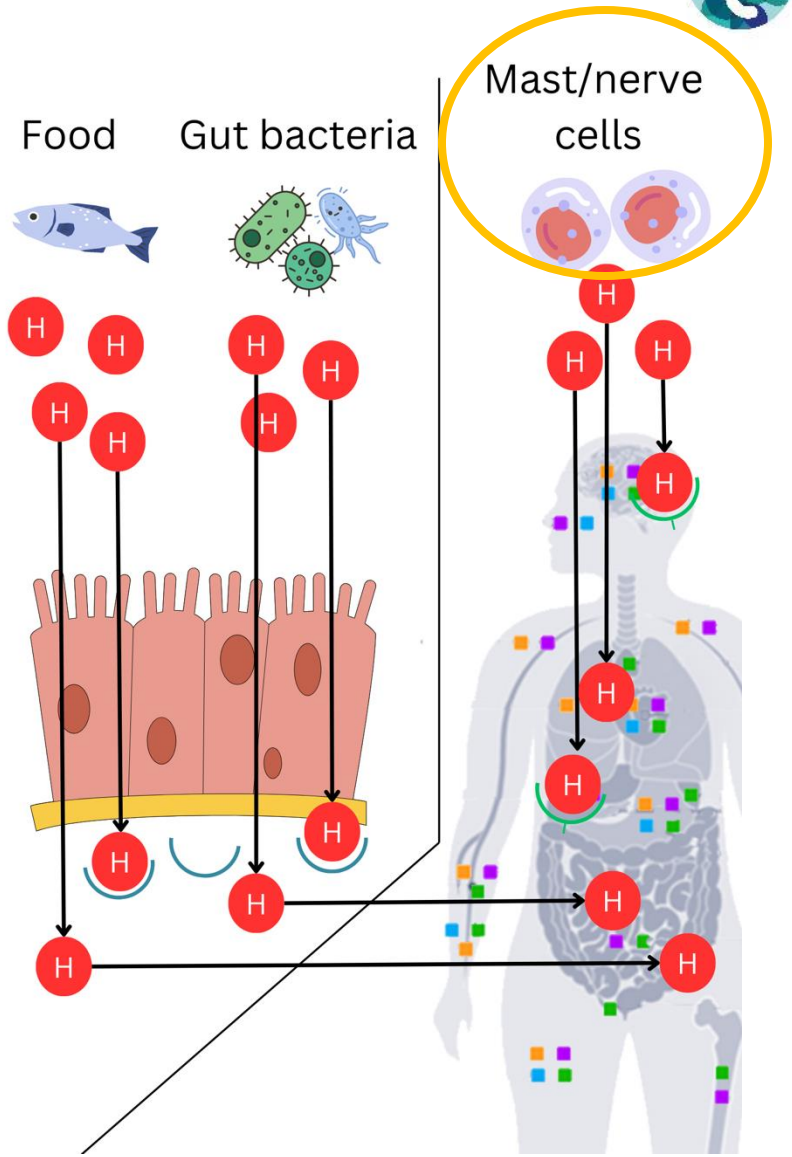

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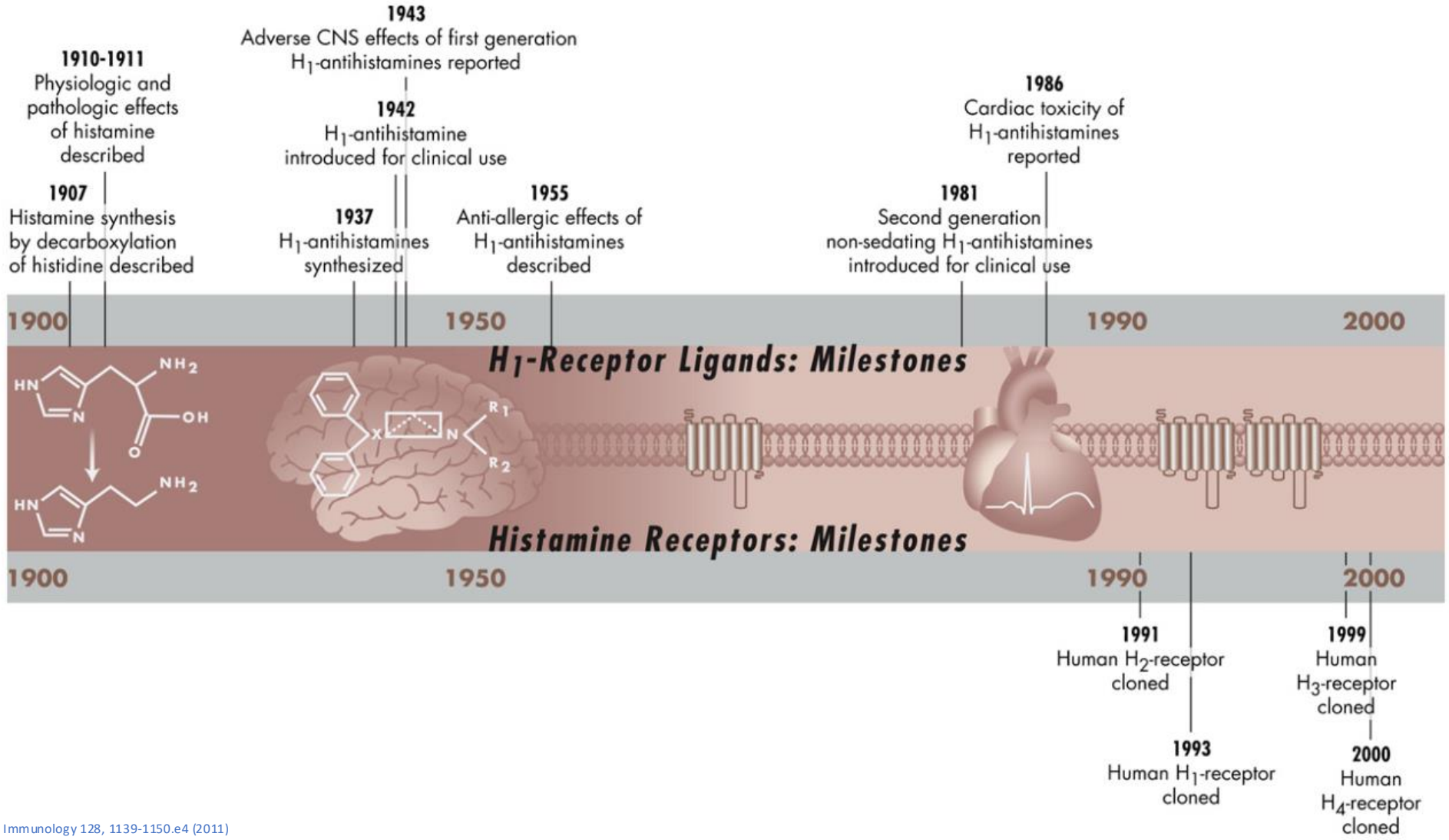
Antihistamines' long history of use in allergic diseases



1. Simons, F. E. R. et al. Journal of Allergy and Clinical Immunology 128, 1139-1150.e4 (2011)

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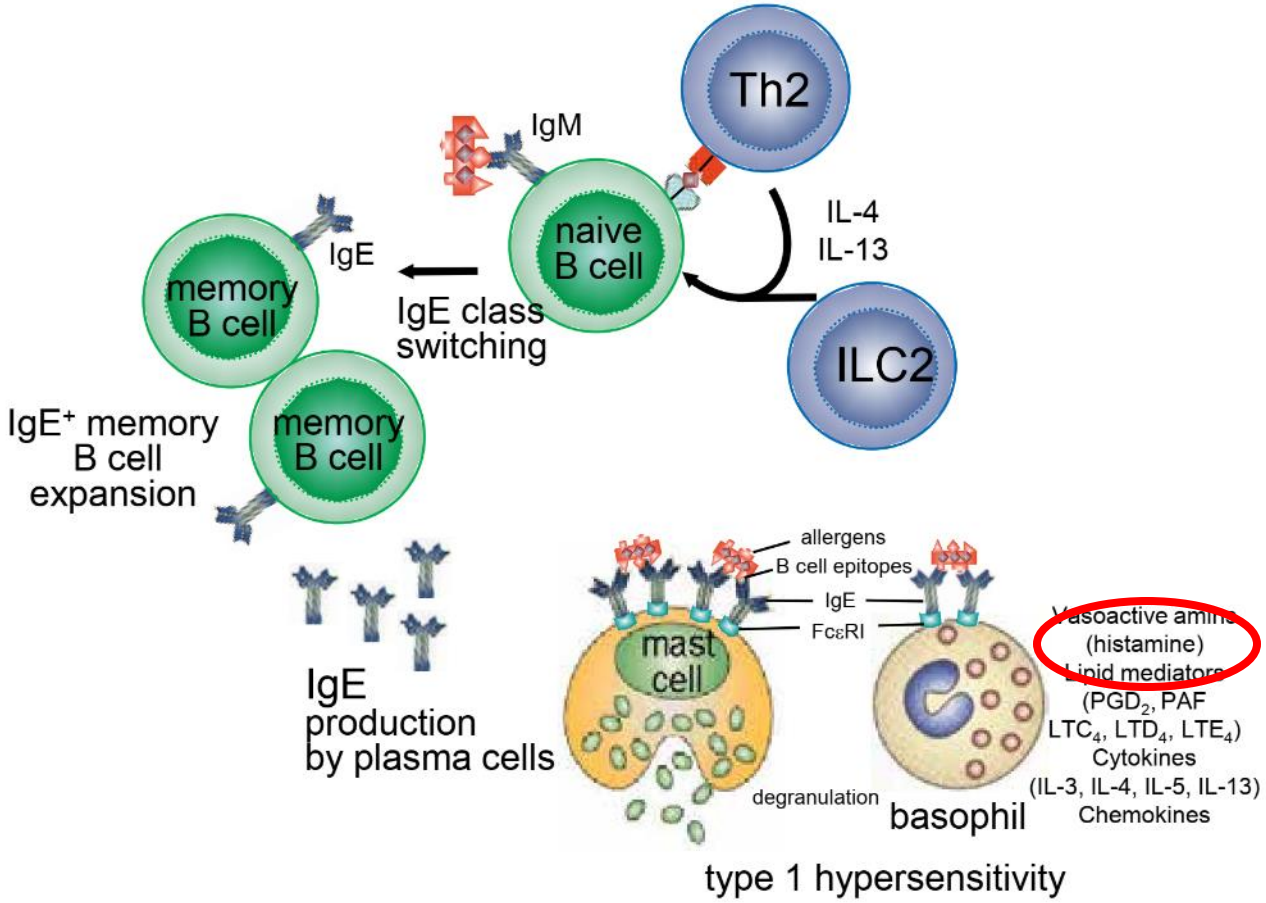
Role of histamine in allergic responses



type 1 hypersensitivity

- The immunologic basis of allergic diseases has two phases[1]:
  - **Sensitization phase**: sensitization and development of memory T and B cell responses and IgE production
  - **Effector phase**: new encounter with allergen causes cross-linking of IgE-FcεRI complexes on sensitized basophils and mast cells → activated and release anaphylactogenic mediators responsible for the immediate hypersensitivity reaction.

1. Akdis, C. A. et al. (European Academy of Allergy and Clinical Immunology, 2014)

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Probiotics beneficial in allergies

Meta-analyses show benefits of probiotics in:

- Prevention and treatment of atopic dermatitis in children[1]
- Treatment of atopic dermatitis in adults on short and long term[2]
- Treatment of cow-milk allergy in children[3]
- Prevention of atopy and food hypersensitivity in children[4]
- Etc.

1. Jiang, W. et al. Paediatr Drugs 22, 535–549 (2020)
2. Li, Y. et al. Journal of Dermatological Treatment 0, 1–10 (2022)
3. Qamer, S. et al. Eur J Pediatr 178, 1139–1149 (2019)
4. Zhang, G.-Q. et al. Medicine (Baltimore) 95, e2562 (2016)

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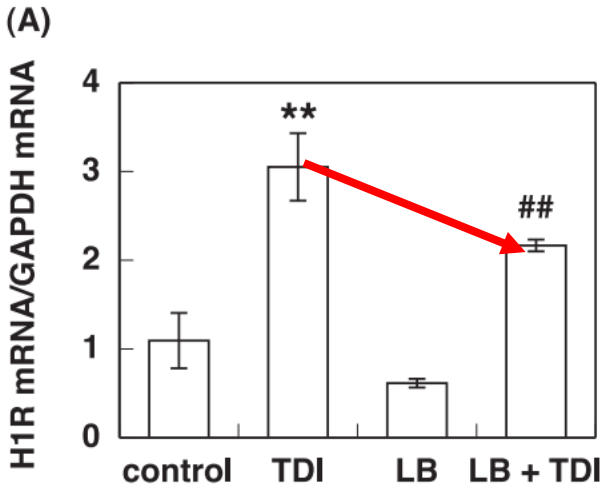
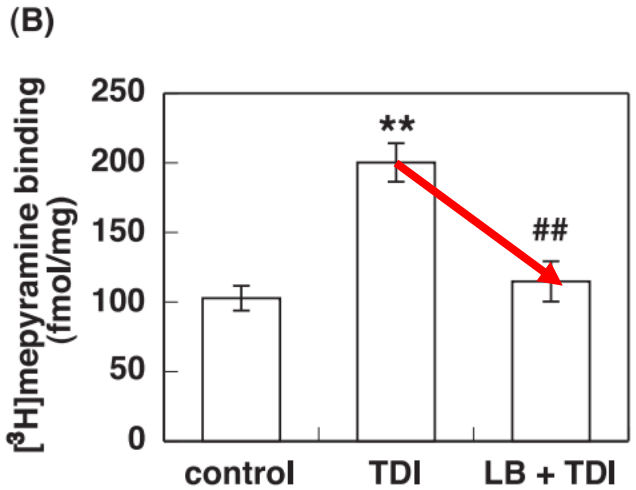
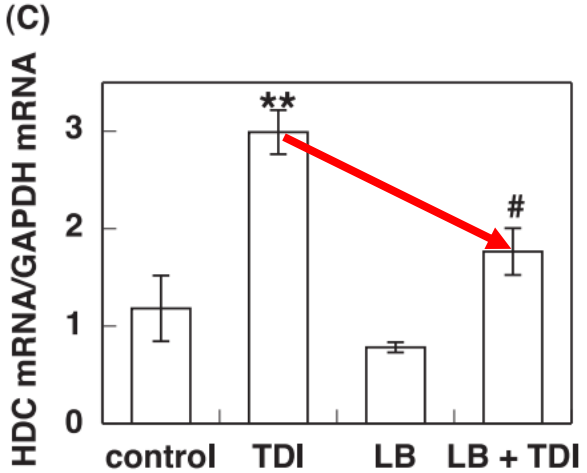
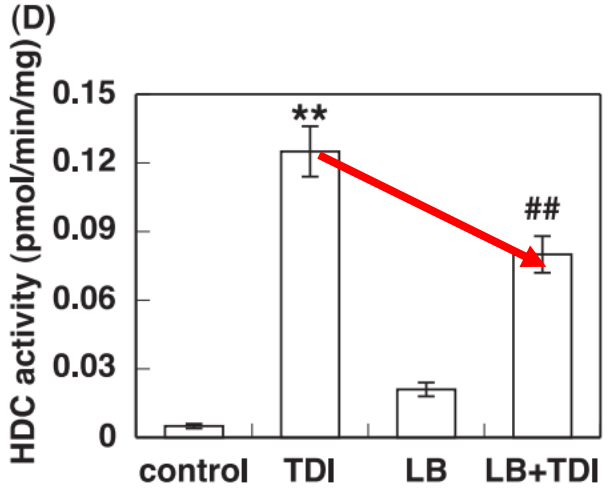
Specific probiotics lower histamine expression

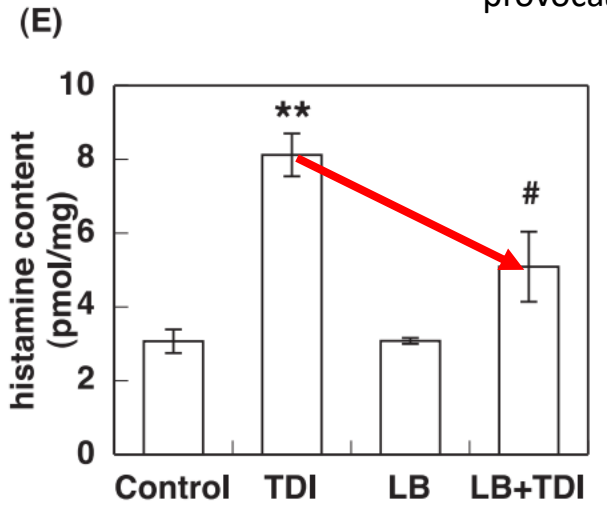




TDI: toluene 2,4-diisocyanate (used for sensitization and provocation of allergy)







1. Dev, S. et al. Journal of Pharmacological Sciences 107, 159–166 (2008)

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Link between allergies and SIBO

- Small intestinal bacterial overgrowth (SIBO) has a direct effect on the microbial interaction with the immune system.
- Microbiome Center suspects mechanistic link between SIBO and allergies:
  - Both SIBO and allergies show low levels immunogenic bacteria in fecal analyses.
  - Patients with SIBO more often have allergies.
  - Indeed, a small study found a high level of comorbidity[1].
- One cause of SIBO is failure of the forward barrier: the acidic stomach.
  - Less acidic stomach environment prevents adequate denaturing of folded proteins, associated with increased risk of food allergies[2,3].
  - PPI use in children is associated with increased prevalence of asthma[4,5] or food allergies[5].

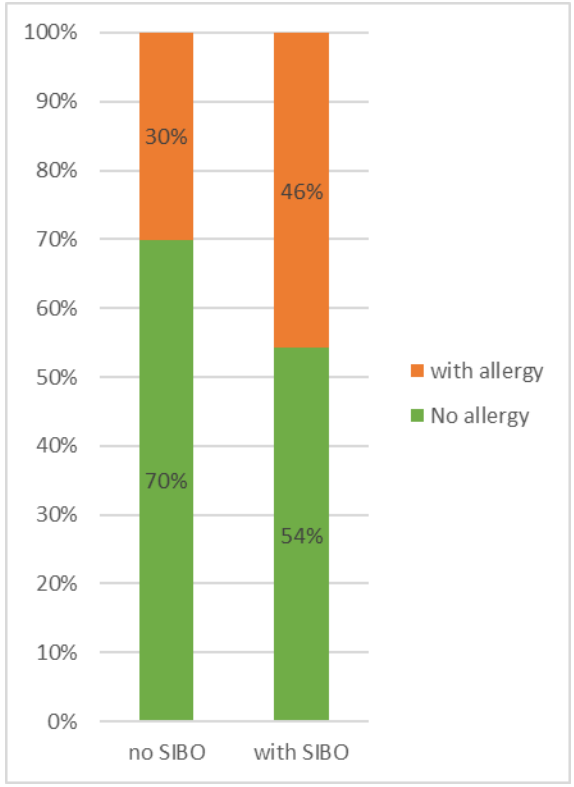

Table 2. *Frequency of allergies in subjects with and without SIBO and the odds ratio of allergic disease in patients with CAP for SIBO*

Allergy	SIBO				
	Negative n = 35	Positive n = 35	OR	95% IC	p-value
Any allergy	10 (28.6%)	25 (71.4%)	5.45	1.96-15.17	0.001
CMPA	0	9 (25.7%)	1.34	1.10-1.63	0.001
Food allergy	2 (5.7%)	7 (20%)	1.12	0.79-21.48	0.07
Rhinitis	8 (22%)	18 (51.4%)	3.57	1.27-10.01	0.01
Asthma	0	5 (14.3%)	1.16	1.01-1.36	0.02
Urticaria	1 (2.9%)	1 (2.9%)	1	0.06-16.64	0.75
Atopic dermatitis	3 (8.6%)	7 (20%)	2.66	0.62-11.30	0.15

SIBO: small intestinal bacterial overgrowth; CAP: chronic abdominal pain; CMPA: cow's milk protein allergy. Chi-squared test was performed.

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2. T. G. Guilliams, L. E. Drake, Integr Med (Encinitas). 19, 32–36 (2020).
3. Untersmayr, E. et al. J Allergy Clin Immunol 121, 1301–1308; quiz 1309–1310 (2008)
4. Wang, Y.-H. et al. JAMA Pediatr 175, 394–403 (2021)
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Link between allergies and SIBO

- The backward barrier may fail due to **constipation** leading to SIBO[1].
- Interestingly, food allergies, such as cows' milk allergy, are associated with constipation[2,3].
- Chicken or the egg:
  1. Does allergy lead to constipation?
  2. Does constipation lead to (SIBO leading to) allergy?
- Option 2 more likely:
  - Even non GI allergies such as atopic dermatitis[4], asthma[5] and allergic rhinitis[6] are associated with constipation.

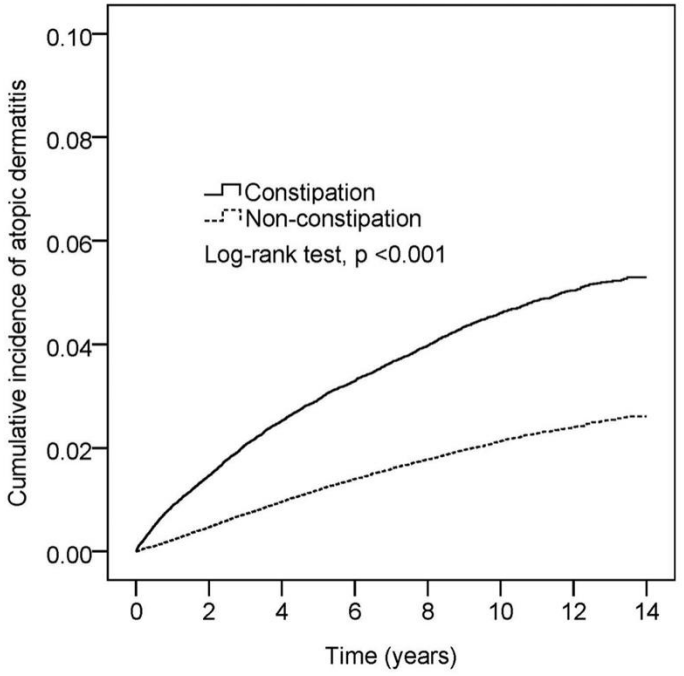

FIGURE 2 Kaplan–Meier curve of cumulative incidence proportion of atopic demattits in constipation group and non-constipation group

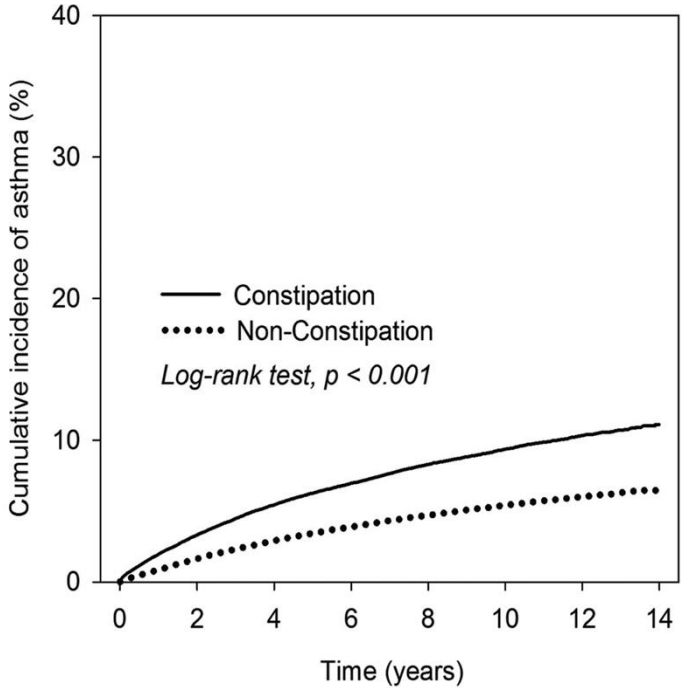

FIGURE 2 Kaplan-Meier curve of cumulative incidence proportion of asthma in constipation and non-constipation groups

1. F. R. Ponziani, V. Gerardi, A. Gasbarrini, Expert Review of Gastroenterology & Hepatology. 10, 215–227 (2016).
2. Connor, F. et al. Nutrients 14, 1317 (2022)
3. Miceli Sopo, S. et al. Int Arch Allergy Immunol 164, 40–45 (2014)
4. Huang, Y.-C. et al. Int J Clin Pract 75, e13691 (2021)
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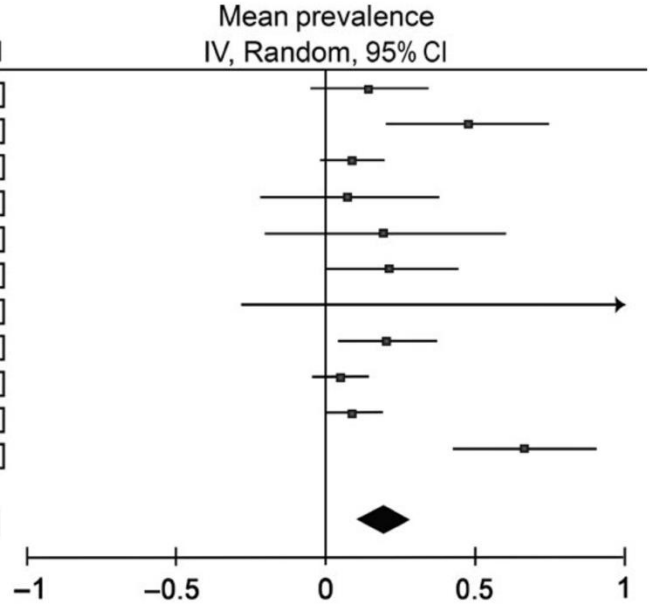
Link between allergies and SIBO

Study or Subgroup	Mean prevalence	SE	Weight	Mean prevalence IV, Random, 95%CI
Abdulkarim 2002	0.1428	0.09796	10.1%	0.14 [–0.05, 0.33]
Chang 2011	0.48	0.1385	7.3%	0.48 [0.21, 0.75]
Dewar 2012	0.09	0.0561	13.5%	0.09 [–0.02, 0.20]
Ghoshal 2004	0.08333	0.1563	6.4%	0.08 [–0,22, 0.39]
Lasa 2015	0.2	0.20242	4.5%	0.20 [–0.20, 0.60]
Mooney 2014	0.2157	0.11288	9.0%	0.22 [–0.01, 0.44]
Prizont 1970	0.5	0.4	1.5%	0.50 [–0.28, 1.28]
Rana 2007	0.2069	0.08512	11.1%	0.21 [0.04, 0.37]
Rana 2008	0.05	0.04775	14.2%	0.05 [–0.04, 0.14]
Rubio Tapia 2009	0.09395	0.04685	14.2%	0.09 [0.00, 0.19]
Tursi 2003	0.6666	0.1217	8.4%	0.67 [0.43, 0.91]
Total (95% CI)			100.0%	0.20 [0.10, 0.30]

Heterogeneity: Tau² = 0.02; Chi² = 32.14, df = 10 (*P* = 0.0004); I² = 69%

Test for overall effect: Z = 3.99 (*P* < 0.0001)



- From doctors in the Microbiome Center network we often hear comorbidity between food intolerances/allergies and SIBO.
  - Indeed, associations are found:
    - Lactose intolerance[1].
    - Celiac disease[2,3] (figure).
  - There is some evidence that suggest that celiac disease patients who do not respond to gluten-free diet more often have SIBO[4].

1. **In patients with allergies, be aware of SIBO and vice versa.**
2. **The MC knowledge network helps to rapidly gain new insights**

1. Zhao, J. et al. Aliment Pharmacol Ther 31, 892–900 (2010)
2. Losurdo, G. et al. Neurogastroenterol Motil 29, (2017)
3. Shah, A. et al. Journal of Gastroenterology and Hepatology n/a,
4. Safi, M.-A. A. et al. Turk J Gastroenterol 31, 767–774 (2020)

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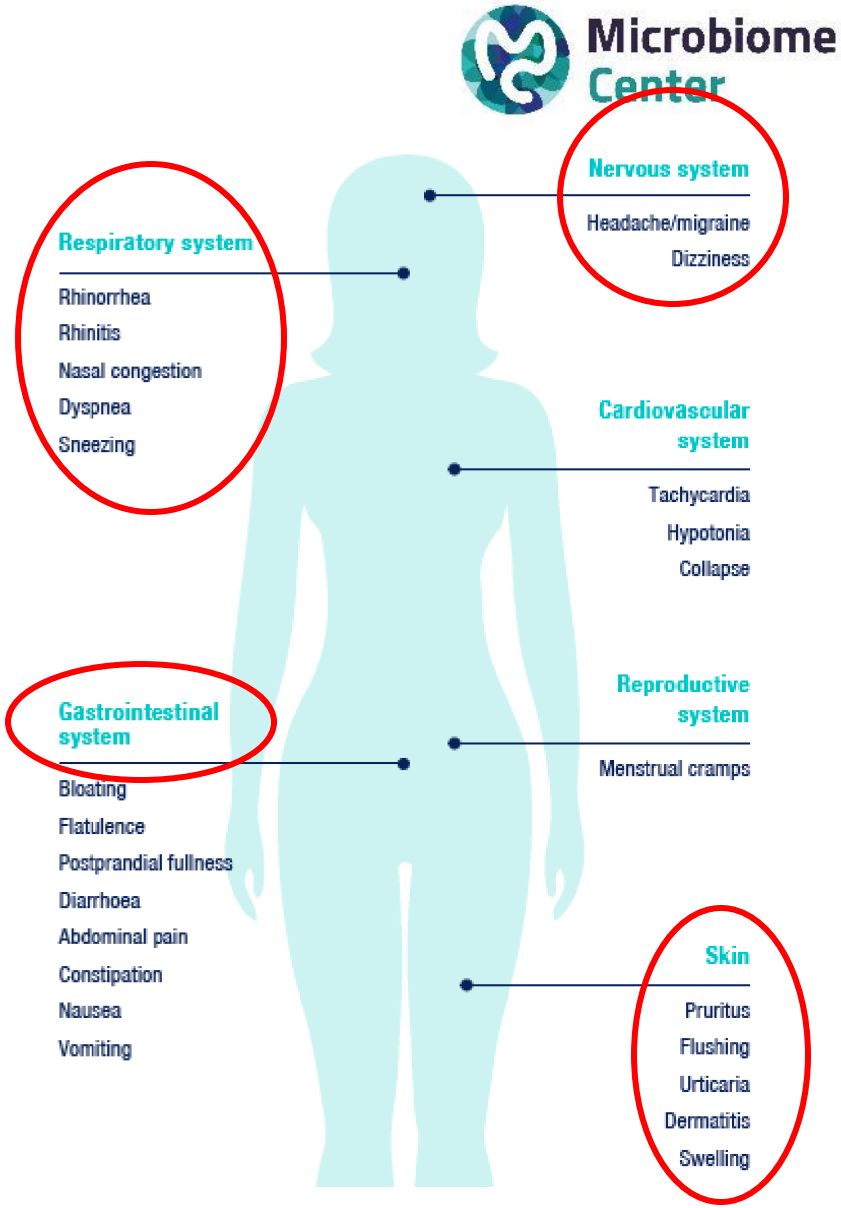
Case Histamin

Patient: 39-year-old male

Symptoms:

- **Chronic abdominal issues** since childhood
- Constantly **swollen nasal mucosa**, leading to restricted airflow
- Obstructive sleep apnea (OSAS)
- Chronic **fatigue** and reduced vitality
- Overweight (BMI 31)
- Increased muscle tension, especially in the neck (leading to headaches)
- Occasional **itching** on the back
- Moderate **mental health issues**, concentration problems, easily overstimulated



1. . Hrubisko, M. et al. Nutrients. 13, .2228. (2021)

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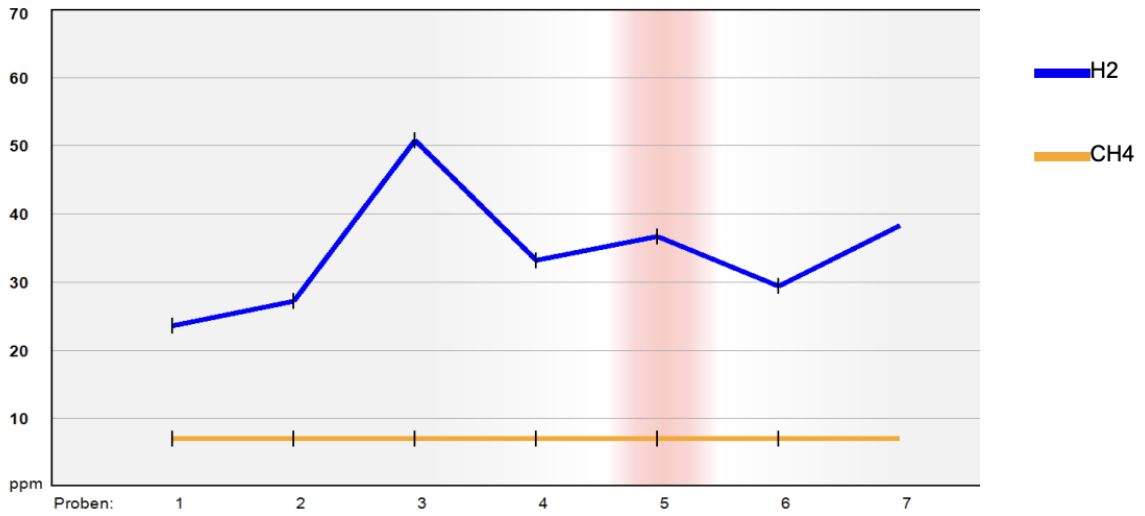
Case Histamin

Breath Test Results:

Hydrogen SIBO

SIBO test

SIBO test SIBO



SIBO test (waterstof)

Ademgasanalyse 1	23,6	ppm	AT NA) GC
Ademgasanalyse 2	27,2	ppm	AT NA) GC
Ademgasanalyse 3	50,8	ppm	AT NA) GC
Ademgasanalyse 4	33,2	ppm	AT NA) GC
Ademgasanalyse 5	36,7	ppm	AT NA) GC
Ademgasanalyse 6	29,4	ppm	AT NA) GC
Ademgasanalyse 7	38,3	ppm	AT NA) GC

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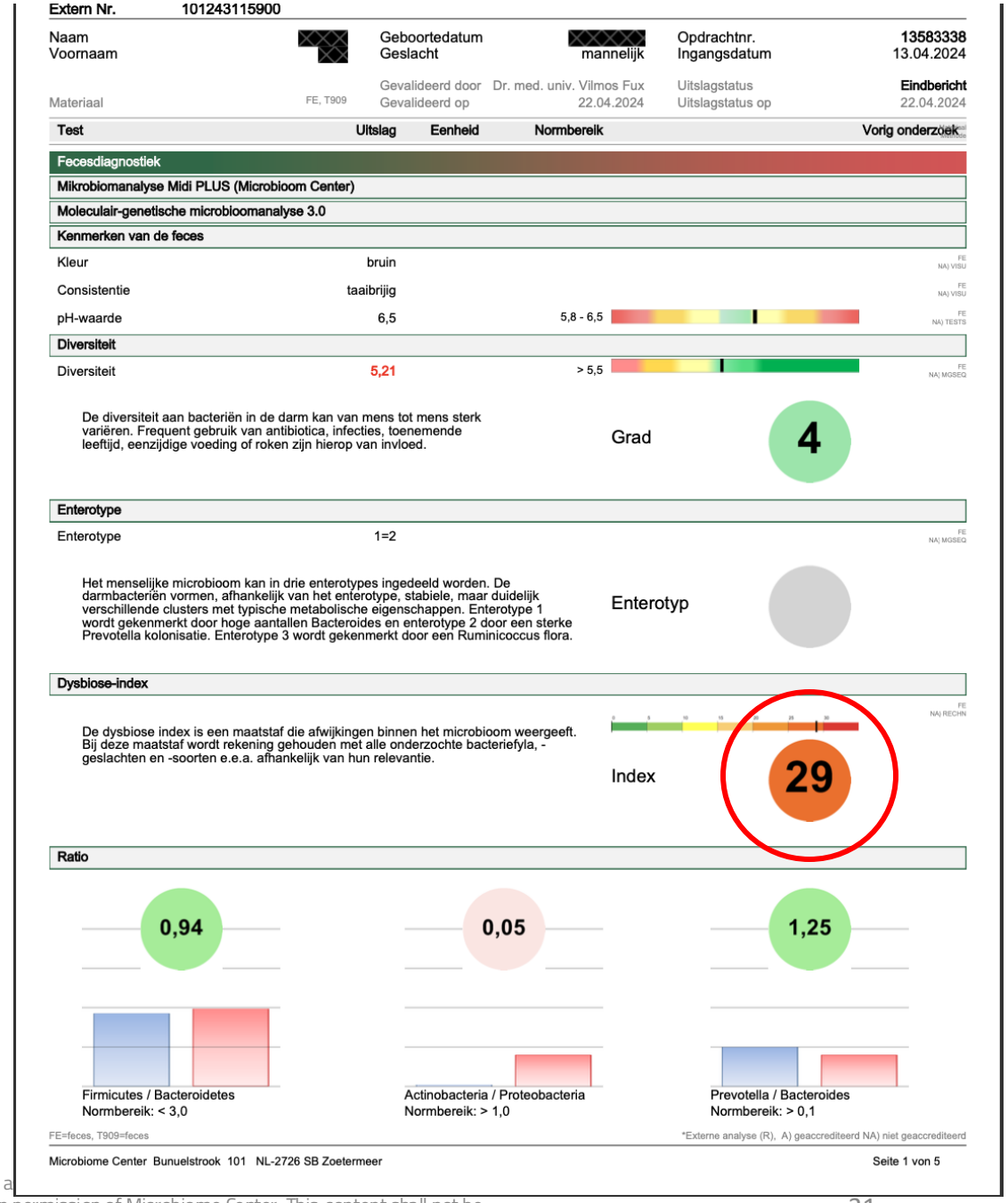
Case Histamin

Microbiome results:

- Leaky gut
- Poor fat digestion
- Elevated inflammatory markers
- Unmeasurable high histamine
- Increased antigliadin antibodies



Extern Nr. 101243115900

Naam [redacted] Geboortedatum [redacted] Opdrachtnr. 13583338
Voornaam Geslacht mannelijk Ingangsdatum 13.04.2024

Materiaal FE, T909 Gevalideerd door Dr. med. univ. Vilmos Fux Uitslagstatus Eindbericht
Gevalideerd op 22.04.2024 Uitslagstatus op 22.04.2024

Test	Uitslag	Eenheid	Normbereik	Vorig onderzoek
Fecesdiagnostiek				
Mikrobiomanalyse Midi PLUS (Microbioom Center)				
Moleculair-genetische microbioomanalyse 3.0				
Kenmerken van de feces				
Kleur	bruin			
Consistentie	taaibrijig			
pH-waarde	6,5		5,8 - 6,5	
Diversiteit				
Diversiteit	5,21		> 5,5	

De diversiteit aan bacteriën in de darm kan van mens tot mens sterk variëren. Frequent gebruik van antibiotica, infecties, toenemende leeftijd, eenzijdige voeding of roken zijn hierop van invloed.

Grad 4

Enterotype

Enterotype 1=2

Het menselijke microbioom kan in drie enterotypes ingedeeld worden. De darmbacteriën vormen, afhankelijk van het enterotype, stabiele, maar duidelijk verschillende clusters met typische metabolische eigenschappen. Enterotype 1 wordt gekenmerkt door hoge aantallen Bacteroides en enterotype 2 door een sterke Prevotella kolonisatie. Enterotype 3 wordt gekenmerkt door een Ruminicoccus flora.

Enterotyp

Dysbiose-index

De dysbiose index is een maatstaf die afwijkingen binnen het microbioom weergeeft. Bij deze maatstaf wordt rekening gehouden met alle onderzochte bacteriefyla, -geslachten en -soorten e.e.a. afhankelijk van hun relevantie.

Index 29

Ratio

0,94 — Firmicutes / Bacteroidetes
Normbereik: < 3,0

0,05 — Actinobacteria / Proteobacteria
Normbereik: > 1,0

1,25 — Prevotella / Bacteroides
Normbereik: > 0,1

FE=feces, T909=feces

*Externe analyse (R), A) geaccrediteerd NA) niet geaccrediteerd

Microbiome Center Bunuelstrook 101 NL-2726 SB Zoetermeer

Seite 1 von 5

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Naam [redacted] Opdrachtnr. 13583338

[redacted] Geslacht mannelijk Ingangsdatum 13.04.2024

Test	Uitslag	Eenheid	Normbereik	Vorig onderzoek
Indeling van bacteriën naar fylum				
Actinobacteria	0,2	%	1,5 - 7	
Bacteroidetes	49,4	%	20 - 45	
Firmicutes	46,4	%	50 - 75	
Fusobacteria	0,0	%	0,0 - 1,0	
Proteobacteria	4,0	%	1,0 - 3,5	
Verrucomicrobia	0,0	%	1,5 - 5,0	
Overige	0,0	%		
Metaboloom (stofwisselingsactieve bacteriegroepen)				
Secundaire galzuren	21,9	%		
TMA / TMAO	-41,5	%		
Indoxylsulfaat	-50,0	%		
Fenolen	-45,5	%		
Ammoniak	66,2	%		
Histamine	-50,0	%		
Equol	-48,0	%		
Beta-glucuronidasen	-49,4	%		
Indeling van bacteriën naar fylum met de belangrijkste bacteriegeslachten en -soorten				
Actinobacteria				
Bifidobacterium	1,4 x 10^9	KVE/g feces	> 1,0 x 10^10	
Bacteroidetes				
Bacteroides	2,0 x 10^11	KVE/g feces	> 5,0 x10^10	
Prevotella	2,5 x 10^11	KVE/g feces	> 1,0 x 10^10	
Prevotella copri	24	%		
Firmicutes				
Butyraatproducerende bacteriën				
Totaal kiemgetal	1,6 x 10^11	KVE/g feces	> 2,4 x 10^11	
Faecalibacterium prausnitzii	7,6 x 10^10	KVE/g feces	>1,0 x10^11	
Eubacterium rectale	1,5 x 10^10	KVE/g feces	> 2,0 x 10^10	
Eubacterium hallii	7,4 x 10^9	KVE/g feces	> 1,5 x 10^10	
Roseburia spp.	4,6 x 10^10	KVE/g feces	> 3,0 x10^10	
Ruminococcus spp.	3,2 x 10^9	KVE/g feces	> 5,0 x 10^10	
Coprococcus spp.	9,5 x 10^9	KVE/g feces	> 5,0 x 10^10	
Butyrivibrio spp.	4,9 x 10^8	KVE/g feces	>1,5 x 10^10	
Clostridia				
Totaal kiemgetal	3,3 x 10^8	KVE/g feces	< 4,0 x 10^9	
Clostridia Cluster I	1,0 x 10^5	KVE/g feces	< 2,0 x 10^9	
Fusobacteria				
Fusobacterium	1,9 x 10^7	KVE/g feces	< 1,0 x 10^7	
Verrucomicrobia				
Akkermansia muciniphila	1,0 x 10^7	KVE/g feces	> 5,0 x 10^9	
Proteobacteria				
Pathogene of potentieel pathogene bacteriën				
Haemophilus spp.	1,9 x 10^7	KVE/g feces	< 5,0 x 10^8	

FE=feces, T909=feces

*Externe analyse (R), A) geaccrediteerd NA) niet geaccrediteerd

Naam [redacted] Opdrachtnr. 13583338

[redacted] Geslacht mannelijk Ingangsdatum 13.04.2024

Test	Uitslag	Eenheid	Normbereik	Vorig onderzoek
Acinetobacter spp.	< 1,0 x 10^5	KVE/g feces	< 1,0 x 10^6	
Proteus spp.	< 1,0 x 10^5	KVE/g feces	< 1,0 x 10^6	
Klebsiella spp.	2,9 x 10^7	KVE/g feces	< 1,0 x 10^7	
Enterobacter spp.	< 1,0 x 10^5	KVE/g feces	< 1,0 x 10^6	
Serratia spp.	< 1,0 x 10^5	KVE/g feces	< 1,0 x 10^7	
Hafnia spp.	< 1,0 x 10^5	KVE/g feces	< 1,0 x 10^6	
Morganella spp.	< 1,0 x 10^5	KVE/g feces	< 1,0 x 10^6	
Citrobacter spp.	4,8 x 10^6	KVE/g feces	< 5,0 x 10^8	
Pseudomonas spp.	< 1,0 x 10^5	KVE/g feces	< 5,0 x 10^7	
Providencia spp.	< 1,0 x 10^5	KVE/g feces	< 5,0 x 10^7	
H2S-vorming				
Sulfaatreducerende bacteriën (SRB)	4,9 x 10^9	KVE/g feces	< 2,5 x 10^9	
Desulfovibrio piger	< 1,0 x 10^5	KVE/g feces	< 1,0 x 10^9	
Desulfomonas pigra	< 1,0 x 10^5	KVE/g feces	< 1,0 x 10^9	
Bilophila wadsworthii	< 1,0 x 10^5	KVE/g feces	< 2,0 x 10^9	
Immunogeniciteit / mucine vorming				
Immunogeen werkende bacteriën				
Escherichia coli	8,6 x 10^5	KVE/g feces	10^6 - 10^7	
Enterococcus spp.	1,43 x 10^6	KVE/g feces	10^6 - 10^7	
Lactobacillus spp.	4,8 x 10^4	KVE/g feces	10^5 - 10^7	
Mucine vorming / slijmvliesbarrière				
Akkermansia muciniphila	1,0 x 10^7	KVE/g feces	> 5,0 x 10^9	
Faecalibacterium prausnitzii	7,6 x 10^10	KVE/g feces	>1,0 x10^11	
Archaea				
Methanogenen				
Methanobrevibacter spp.	< 1,0 x 10^5	KVE/g feces	< 5,0 x 10^8	

Opmerking: Het nieuwe OmicSnap-buisje en de daarin aanwezige matrix maken een nog effectievere monsteranalyse mogelijk, vooral bij grampositieve bacteriën. Dit resulteert in lichte verschuivingen in de normbereiken. We vragen u hier rekening mee te houden.

Mycobioom: relevante gisten				
Candida albicans (CA)	<1,0 x 10^3	KVE/g feces	<1,0 x 10^3	
Candida krusei (CK)	<1,0 x 10^3	KVE/g feces	< 1,0 x 10^3	
Candida glabrata (CG)	<1,0 x 10^3	KVE/g feces	< 1,0 x 10^3	
Candida dubliniensis (CD)	<1,0 x 10^3	KVE/g feces	< 1,0 x 10^3	
Candida parapsilosis (CP)	<1,0 x 10^3	KVE/g feces	< 1,0 x 10^3	
Candida tropicalis (CTp)	<1,0 x 10^3	KVE/g feces	< 1,0 x 10^3	
Candida lusitaniae (CL)	<1,0 x 10^3	KVE/g feces	< 1,0 x 10^3	
Parasieten				
Pathobionten				
Blastocystis hominis	negatief		negatief	
Dientamoeba fragilis	negatief		negatief	
Pathogene darmprotozoa				
Giardia lamblia	negatief		negatief	
Entamoeba histolytica	negatief		negatief	

FE=feces, T909=feces

*Externe analyse (R), A) geaccrediteerd NA) niet geaccrediteerd

Microbiome Center

Naam	[redacted]		[redacted]	Opdrachtnr.	13583338
[redacted]	Geslacht		mannelijk	Ingangsdatum	13.04.2024

Test	Uitslag	Eenheid	Normbereik	Vorig onderzoek
Cryptosporidium spp.	negatief		negatief	FE A) MOLEK
Cyclospora cayetanensis	negatief		negatief	FE A) MOLEK
Vertering				
Vetgehalte	5,60	g/100g	< 3,5	FE NA) PHOT
Stikstofgehalte	0,90	g/100g	< 1,0	FE NA) PHOT
Suikergehalte	3,00	g/100g	< 2,5	FE NA) PHOT
Watergehalte	72,80	g/100g	75 - 85	FE NA) PHOT
Extra parameter(s)				
Calprotectine	27,70	mg/l	< 50	FE A) ELISA
Alfa-1-antitripsine	85,6	mg/dl	< 27,5	FE A) ELISA
Secretoir Immunoglobuline A	>7500,0	µg/ml	510 - 2040	FE A) ELISA
Zonuline	80,75	ng/ml	< 55	FE A) ELISA
Histamine in feces	>24000,0	ng/ml	< 959	T909 A) ELISA
Speciale gastro-enterologische diagnostiek				
Gluten-sensitieve enteropathie / coeliakie				
Anti-gliadine antilichamen in feces	146,13	U/l	< 100	FE A) ELISA
Anti-transglutaminase antistoffen in feces	<50,00	U/l	< 100	FE A) ELISA

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Case Histamin

Treatment:

- **Dietary Adjustments:**
  - Remove gluten and sugars, increase protein intake
- **2-week Elemental Diet**, followed by:
- **Interventions:**
  - MyOwnBlend
  - Metadigest Lipid (enzymes)
  - 2-Prepare, borage oil, and A-mulsion (for gut healing)

Element	Dagdosering	Bedrag	Type	Link
MyOwnBlend, magistrale bereiding 2 maanden (oraal)		€ 275,00	Persoonlijke Bereiding	
PHGG	4		Magistral compound	
Bacillus clausii UBBC-07	1		Magistral compound	
2'-Fucosyllactose	3		Magistral compound	
Enterococcus faecium + Bacillus subtilis	2		Magistral compound	
Lactiplantibacillus plantarum DR7	1		Magistral compound	
Akkermansia muciniphila, gepasteuriseerd	2		Magistral compound	
S. Boulardii	2		Magistral compound	

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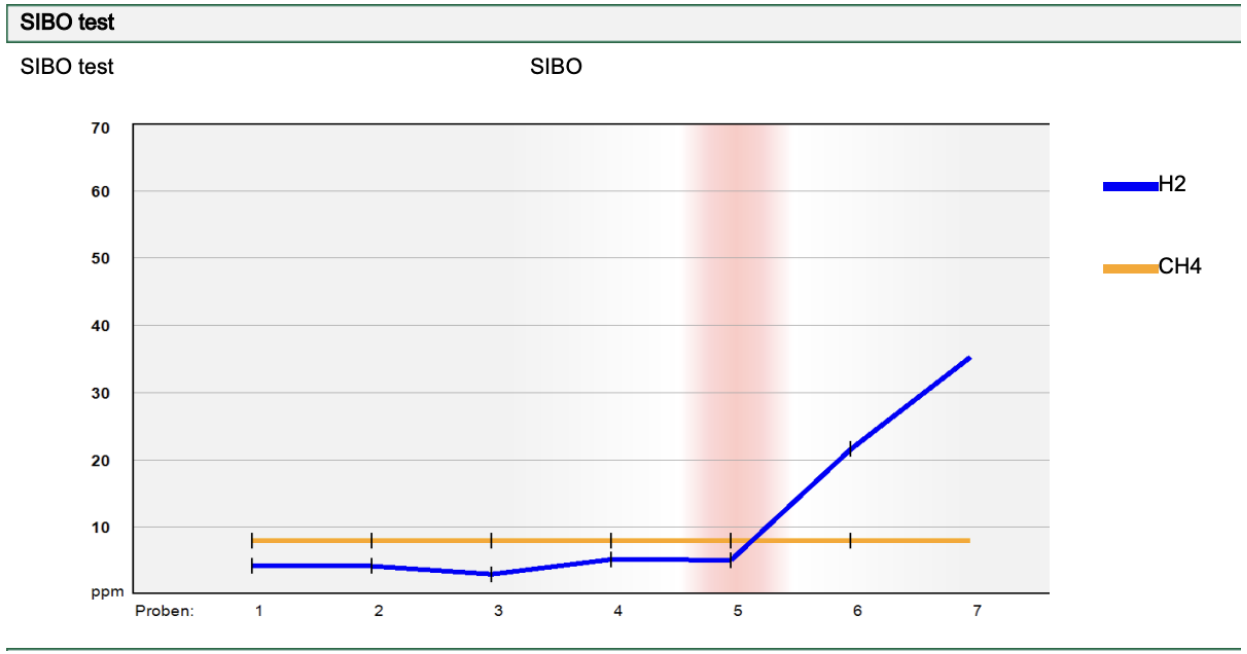
Case Histamin

Results:

- Hydrogen SIBO resolved
- Histamine fully normalized
- Most symptoms (nasal mucosa issues, fatigue, headaches, and abdominal pain) largely disappeared
- Lost over 10 kg

01-07-2024



01-07-2024

Test	Uitslag	Eenheid	Normbereik	Vorig onderzoek
Fecesdiagnostiek				
Extra parameter(s)				
Histamine in feces	<200,0	ng/ml	< 959	>24000,0

T909
A) ELISA

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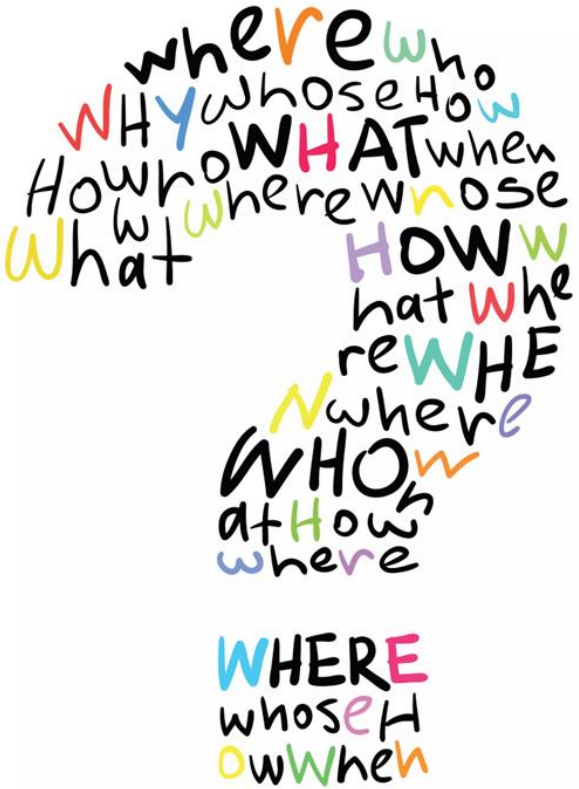
Microbiome Center

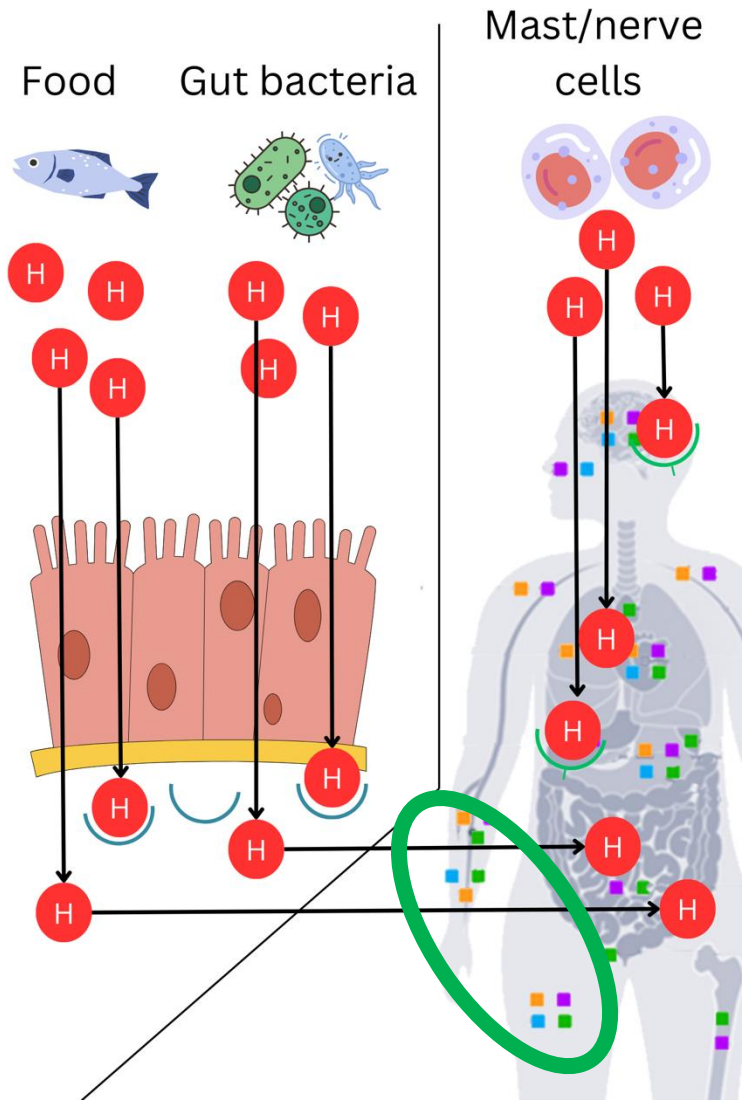
Questions



Factors playing a role

The overall response to histamine is determined by:

- Histamine exposure
  - Dietary histamine load
  - Bacterial production of histamine
  - Release of histamine by mast cells
  - Release of histamine by nerve cells
- Histamine action:
  - Expression of the four histamine receptor types (with different effects)
  - Blocking of specific receptor types
- Histamine breakdown:
  - Release of and breakdown by DAO
  - Breakdown by HNMT



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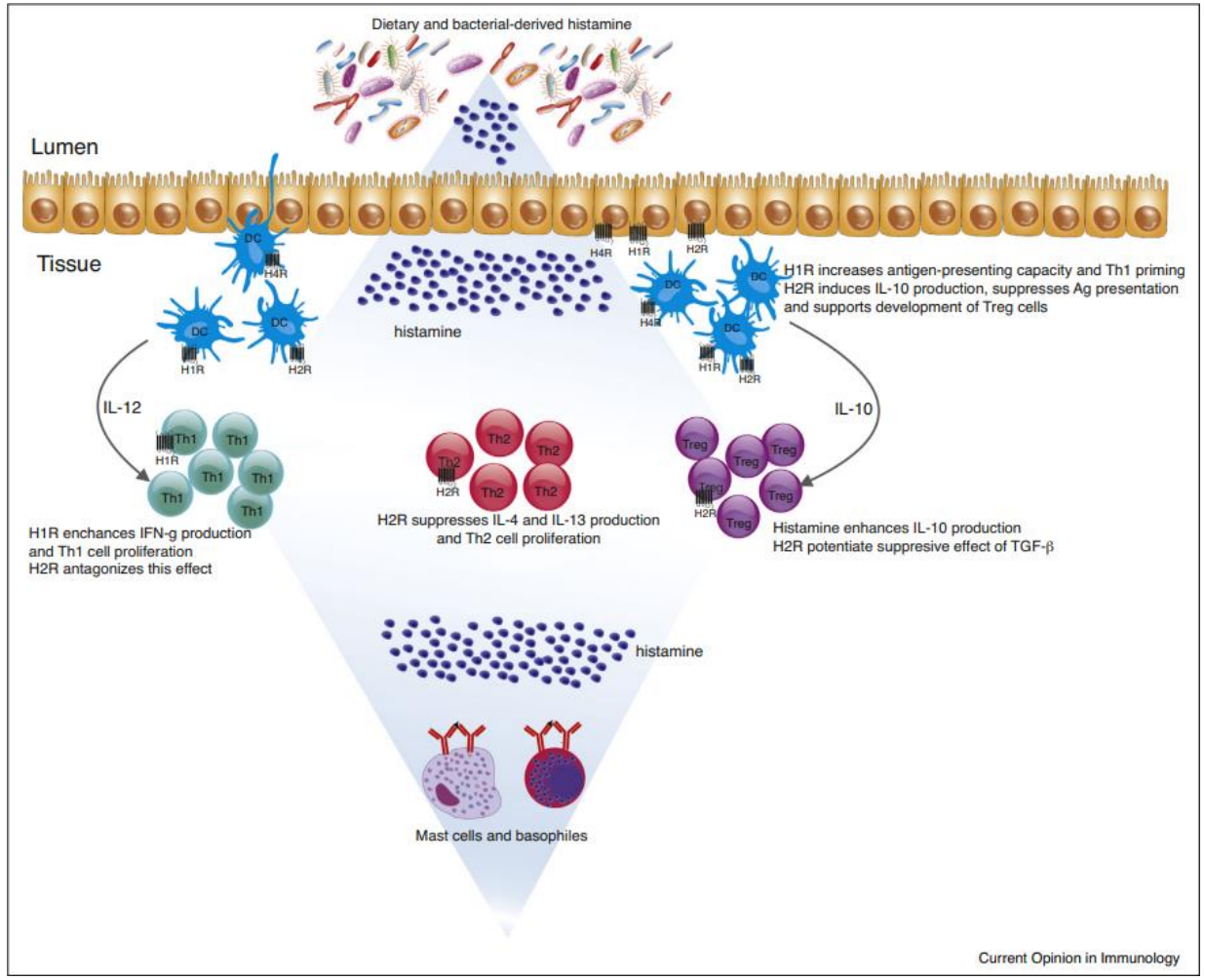
Histamine is not only pro-inflammatory
Effects are regulated by receptor expression

- H1R: classical immediate hypersensitivity responses:
  - smooth muscle cell contraction
  - increased vascular endothelial cell permeability
  - synthesis of platelet activating factor
  - release of von Willebrand factor and nitric oxide.
- H2R: antagonizes H1R effects:
  - relaxation of smooth muscle cells
  - anti-inflammatory

Overview of histamine receptors.

	H1R	H2R	H3R	H4R
Chromosomal location	3q25	5q35.2	20q13.33	18q11.2
G protein coupling	Gαq	Gαs	Gαi/0	Gαi/0
Intracellular signal transduction	Activates PLC, PKC and calcium release	Increases cAMP and activates PKA	Inhibits cAMP, activates MAPK, PKB and calcium release	Inhibits cAMP, activates MAPK, PKB and calcium release
Tissue location	Ubiquitous	Ubiquitous	Neurons	Bone marrow, hematopoietic cells, keratinocytes



1. Barcik, W. et al. Current Opinion in Immunology 48, 108–113 (2017)

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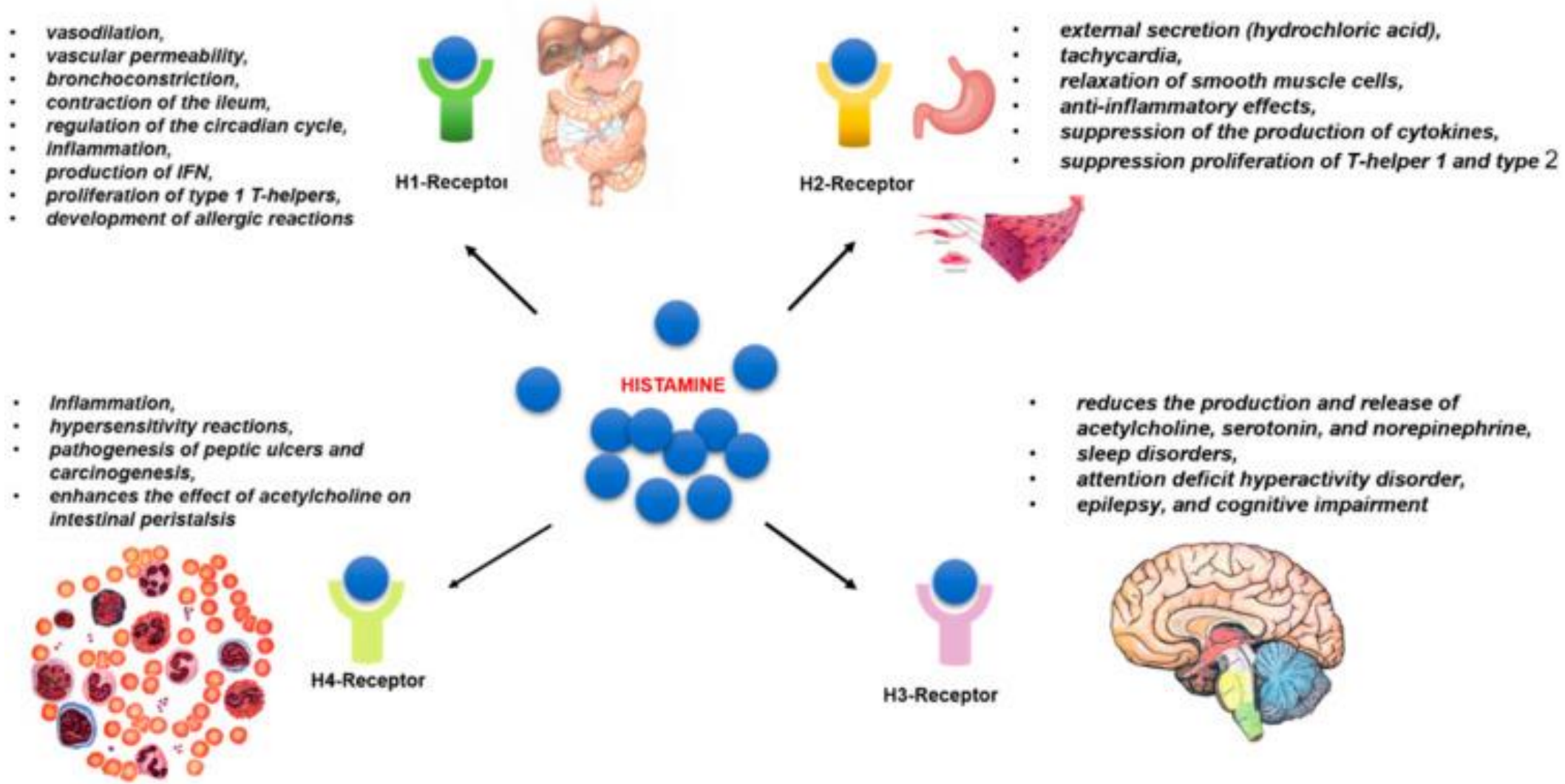

1. Shulpekova, Y. O. et al.Nutrients.13,.3207.(2021)

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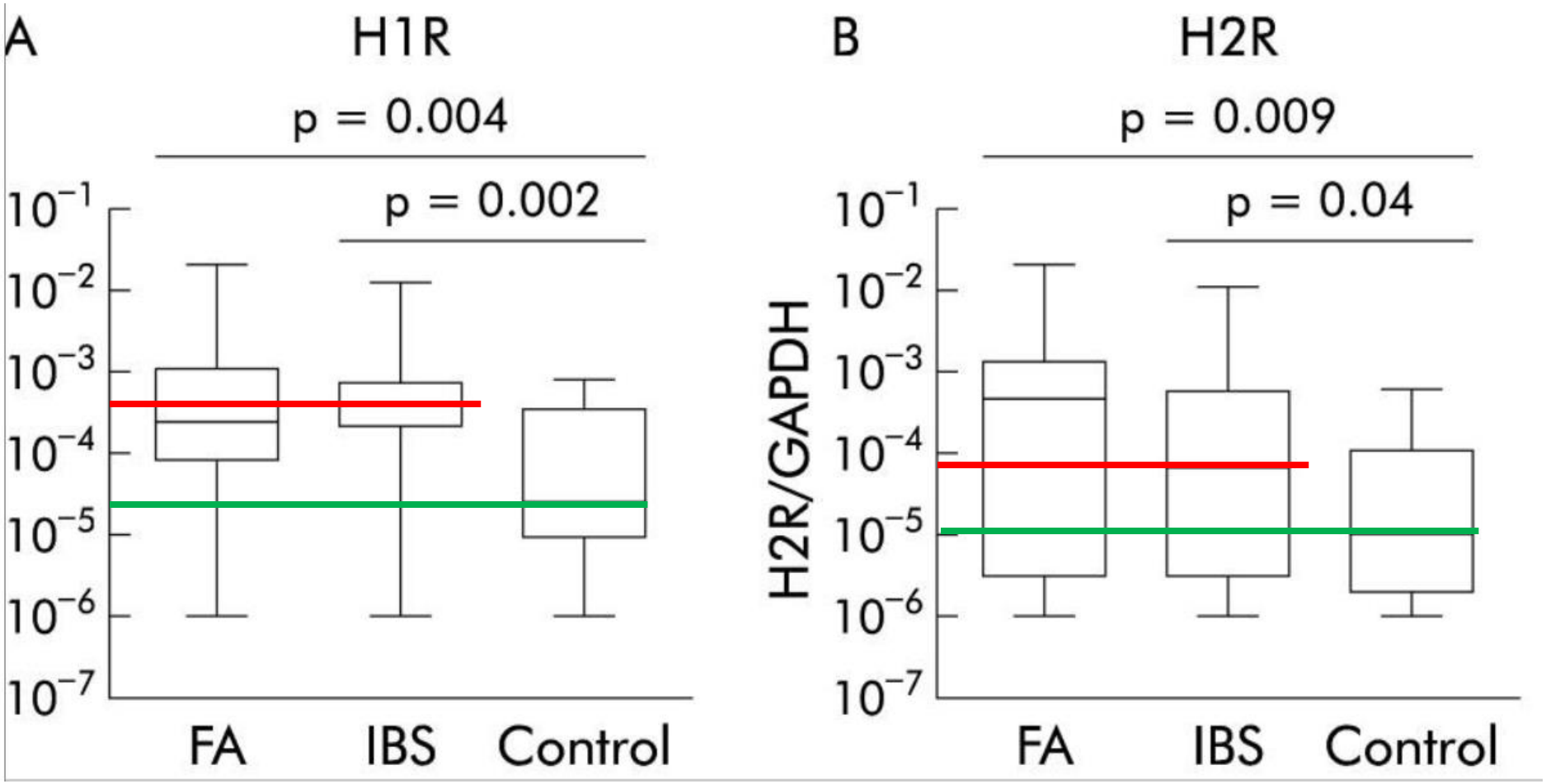
Increased H1R and H2R expression in IBS pts



1. Sander, L. E. et al. Gut 55, 498–504 (2006)

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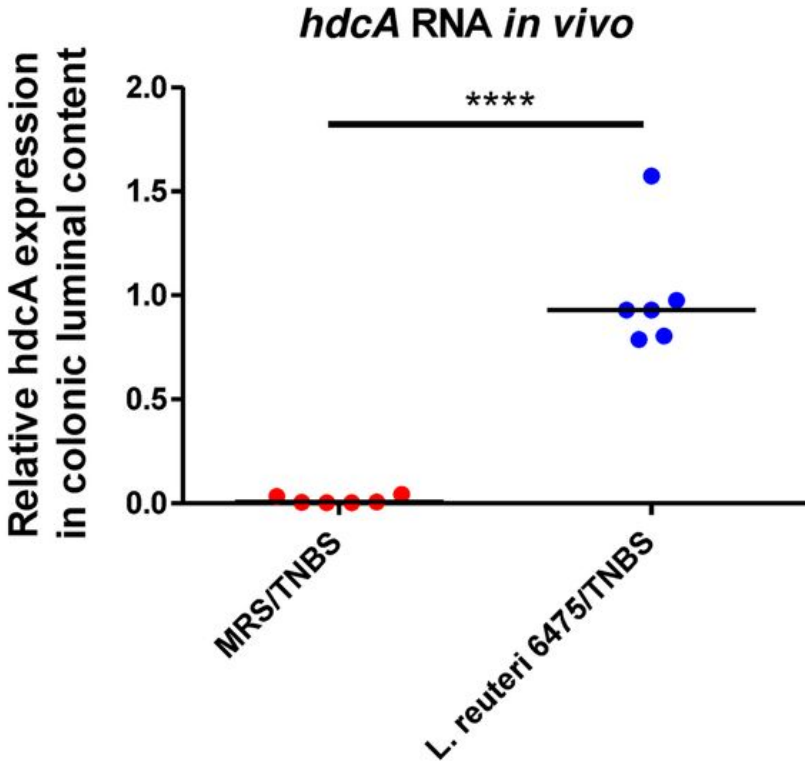
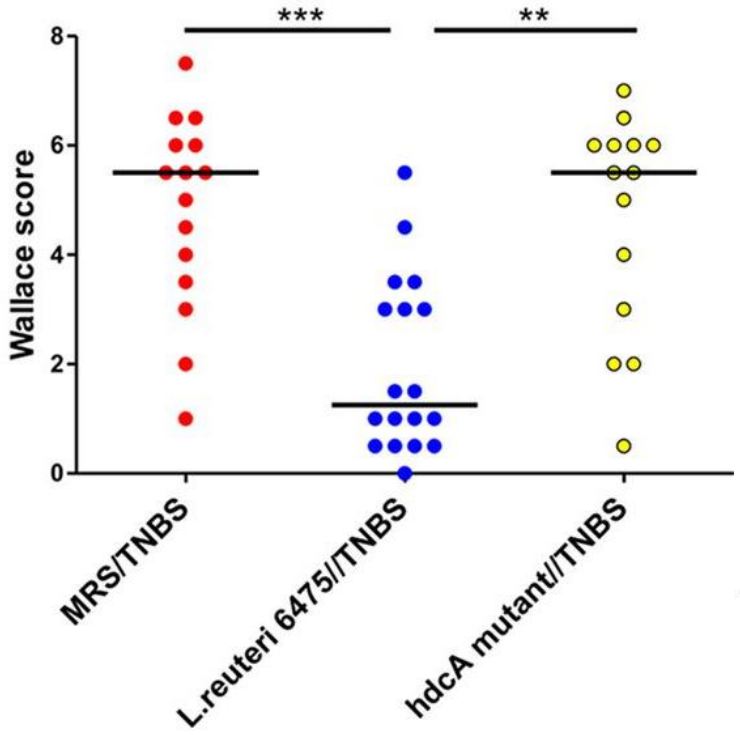
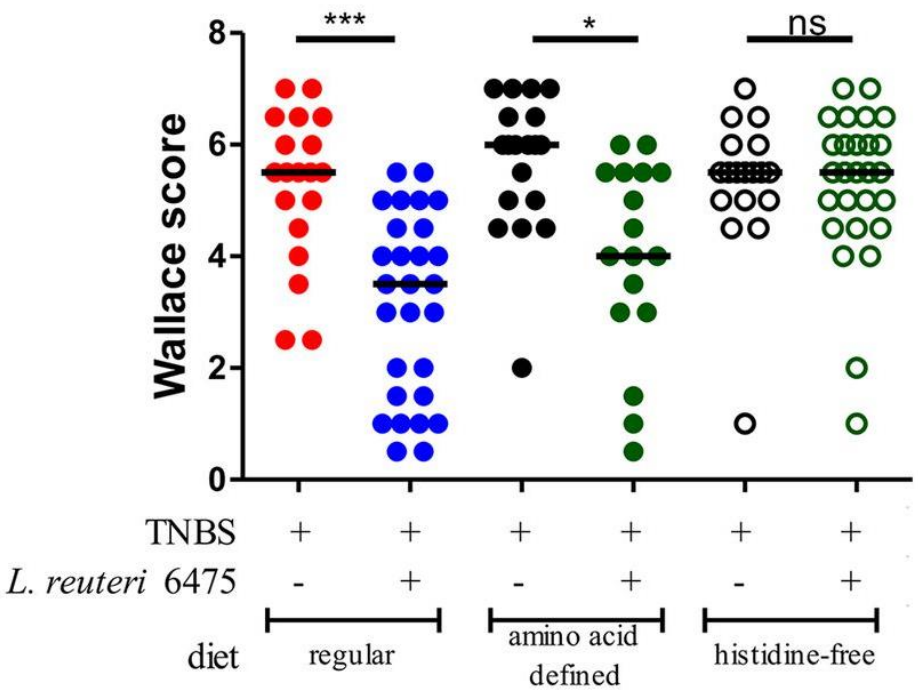
Probiotic histamine can lower inflammation







- Mouse model of colitis
- *L. reuteri* 6475 induces histidine decarboxylase expression
- *L. reuteri* 6475 lower inflammation (Wallace score), but mutants do not
- Histidine must be present in diet for the effect
- Effect due to binding to H2R
- Also involved: compounds suppressing H1R pathway

1. Gao, C. et al. mBio 6, 10.1128/mbio.01358-15 (2015)
2. Ganesh, B. P. et al. Mucosal Immunology 11, 380–393 (2018)

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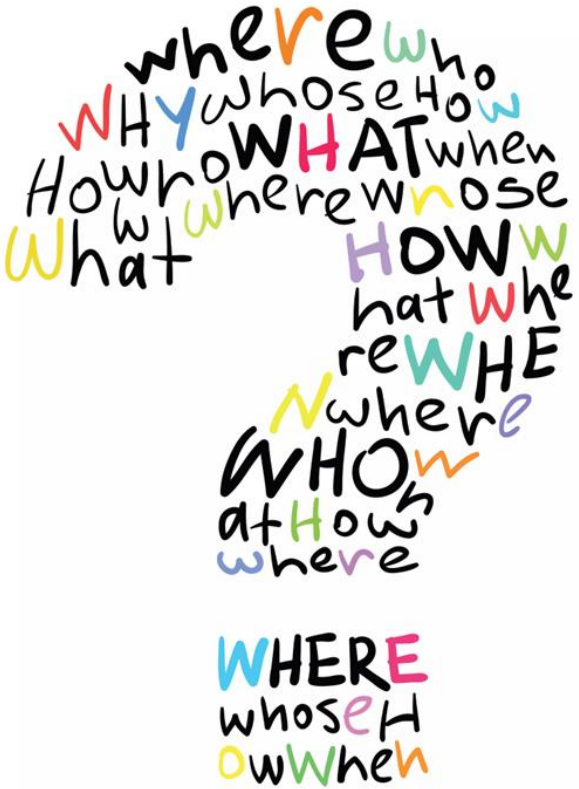

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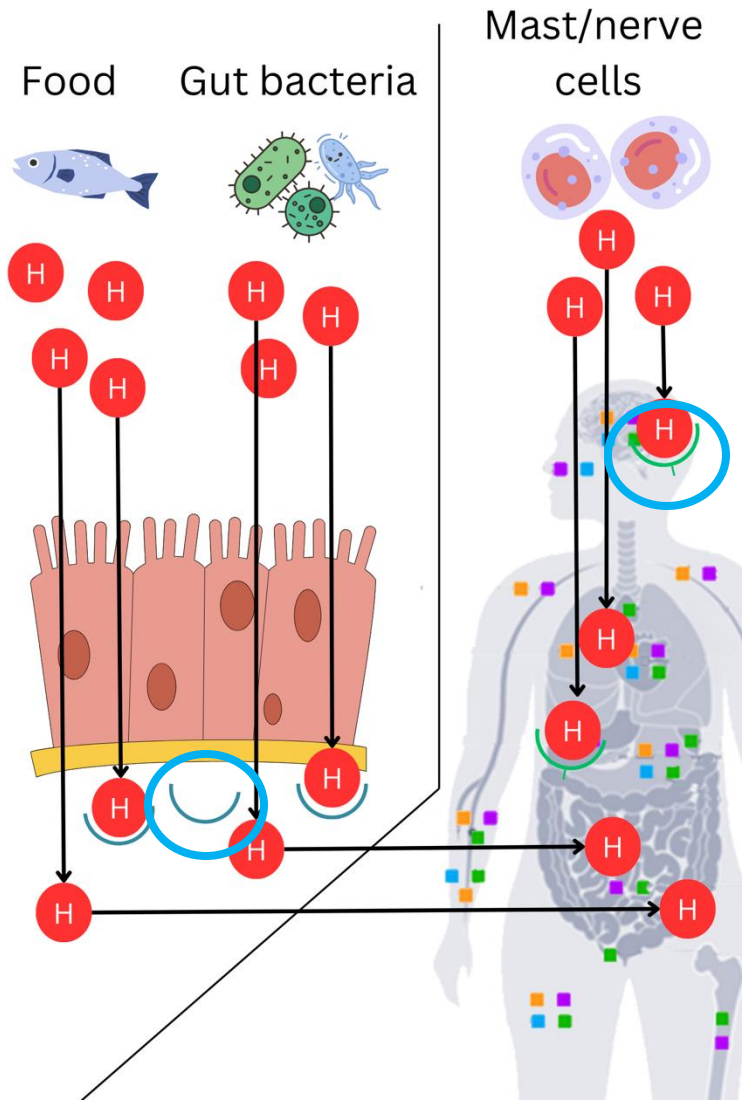

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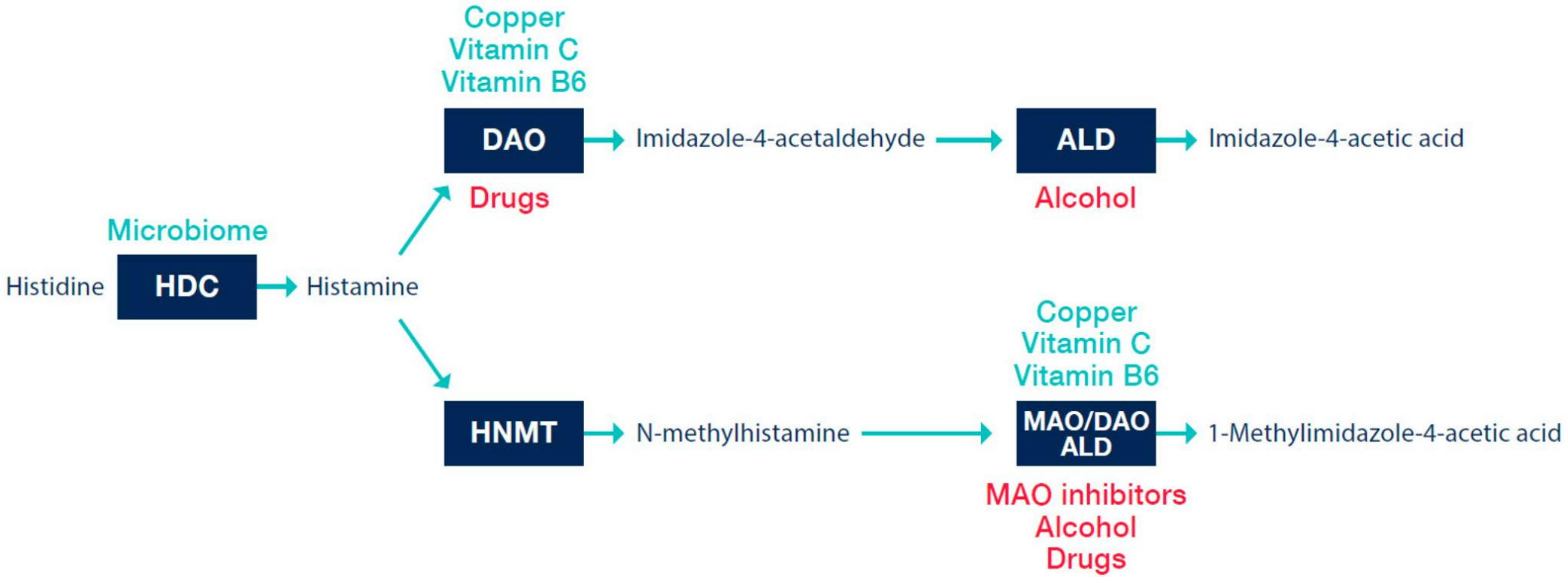
Histamine breakdown

Two degradation pathways[1,2]:

- Diamine oxidase (DAO) → **excreted (extracellular);** gut, placenta, kidney, thymus, seminal plasma
- histamine-N-methyltransferase (HNMT) → **intracellular;** brain, liver, spleen, respiratory, etc.



1. Hrubisko, M. et al. Nutrients.13,.2228.(2021)
2. Comas-Basté, O. et al. Biomolecules.10,.E1181.(2020)

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Histamine breakdown

- DAO needs copper, Vit B6, Vit C, zinc, manganese
- HNMT requires: methionine, magnesium, manganese, iron, coenzyme Q10, vit B2, vit B6, vit B12, folate, vit B3

- Without these substances, sufficient histamine degradation cannot take place.

- ***Many patients have a deficiency of at least 2 cofactors***

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Histamine breakdown

Drugs that block DAO:

- N-Acetylcysteine (cough expectorant)
- Amitryptiline (antidepressant)
- ASS (aspirine)
- Metamizole (analgesic and antipyretic)
- Diazepam (benzodiazepine)
- Prilocaine (local anaesthetics)

Drugs that block HNMT:

- Chloroquin (antimalarial-drug)
- Tacrine (Alzheimer's disease)
- Diphenhydramin (H1-blocker)

Other:

- Alcohol

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DAO and histamine intolerance diagnosis

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Diagnosis of histamine intolerance: solution is sought in the wrong place

- **Classic diagnosis:**
  - Diamine oxidase normal value: >10 unit/ml (U/ml)
  - Histamine intolerance : <10 U/ml
    (10-15 U/ml: consider clinical signs)

- **But:**
  - Detection of high histamine levels in the gut, blood or urine do not always correlate with low DAO activity
  - Patients with low DAO activity do not always automatically have symptoms of histamine intolerance

- **Determination of DAO activity alone is not sufficient**

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Diagnosis of histamine intolerance: solution is sought in the wrong place

- **….and:**
  - High histamine levels in stool/blood can have multiple causes
  - Especially inflammation of gut epithelium is problematic
    - Inflammation is accompanied by endogenous histamine release
    - Leads to less DAO release, which in turn leads to food intolerances (e.g. lactose intolerance)

The longer intestinal mucosa is inflamed, the less DAO can be produced. As a result, more histamine enters the bloodstream.

A low DAO level is almost always the result of chronic intestinal inflammation and not the primary problem.

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Diagnostic pathway

- **1st: Perform a microbiome test to rule out gut dysbiosis**
  - Optionally: screen for histamine in the stool

- 2nd: Test for histamine in heparin blood, histamine in 2nd morning urine or 24-hour collection urine, methylhistamine in 2nd morning urine or 24-hour collection urine.
- If one of these is conspicuous, an extended diagnosis could follow: DAO, HNMT

Determining the DAO as the first parameter often leads in the wrong direction

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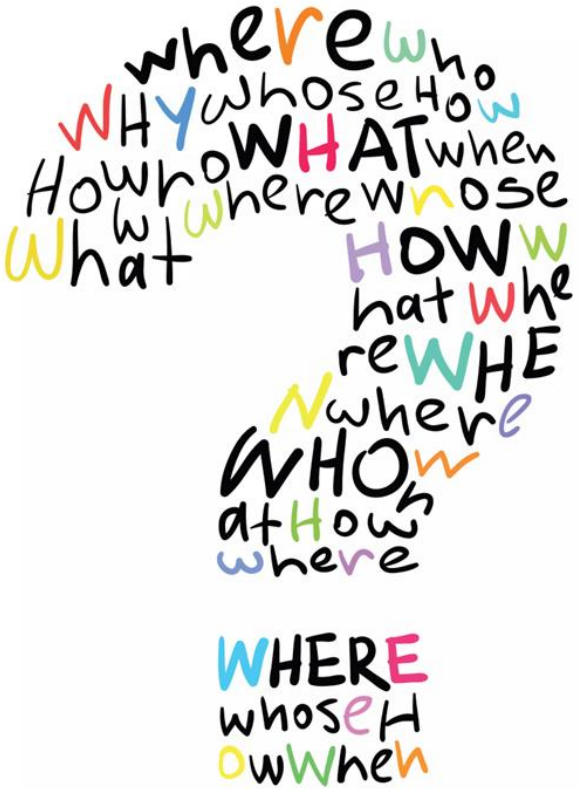
Questions



Histamine and probiotics: is it about histamine-producing capability?

- Many brands advertise with probiotics for histamine intolerance
- Often only about absence of histamine-producing capability

- But should we focus on that?
  1. Various commensals can produce histamine
  2. Histamine can have anti-inflammatory effects
  3. Even if bacteria can produce histamine, that doesn't mean they will
  4. Microbes can induce or suppress endogenous histamine release

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So it is complex, how to treat then?

It’s impossible to know source of histamine (food, bacteria, mast cells), or to know source of complaints (H1R vs H2R, impaired DAO, excessive histamine). How to treat then?

Step 1: Treat the gut ecology as a whole via personalized microbiome treatment

- Solves leaky gut
- Reduces inflammation
- Lowers expression of HDC/histamine production of pathogens/commensals
- Modulates expression of histamine 1 and 2 receptors
- Removes causes like SIBO

1. Sánchez-Pérez, S. et al.Nutrients.13,.1395.(2021)

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Step 2: take diet into account

- Use unprocessed whole foods:
  - Vegetables, fresh fish, meat, fruit, nuts, seeds, herbs, water, tea, coffee
- Optimize the gut environment by making it less proteolytic:
  - Sufficient fibers, carbs, and fats
  - Promote lactate, acetate, butyrate, and other (fatty) acid production by stimulating lactobacilli, SCFA generators
- Temporarily avoid foods that trigger symptoms (e.g. lactose, fructose, gluten, etc.)
- Limit eating moments (e.g. intermittent fasting)
- Sufficient DAO cofactors (copper, B6, C, etc.)

(Optional step 3: if very severe)

- **Temporarily** avoid top 7 histamine-containing foods (study[1]):
  1. Sauerkraut
  2. Eggplant
  3. Spinach
  4. Fermented soy
  5. Cured cheese
  6. Dry fermented sausages
  7. Fish derivates
- **Temporarily** avoid DAO scavengers:
  - Alcohol, aspirin, NAC
  - Specific prescription drugs
- **Temporarily** suppletion of DAO

1. Sánchez-Pérez, S. et al.Nutrients.13,.1395.(2021)

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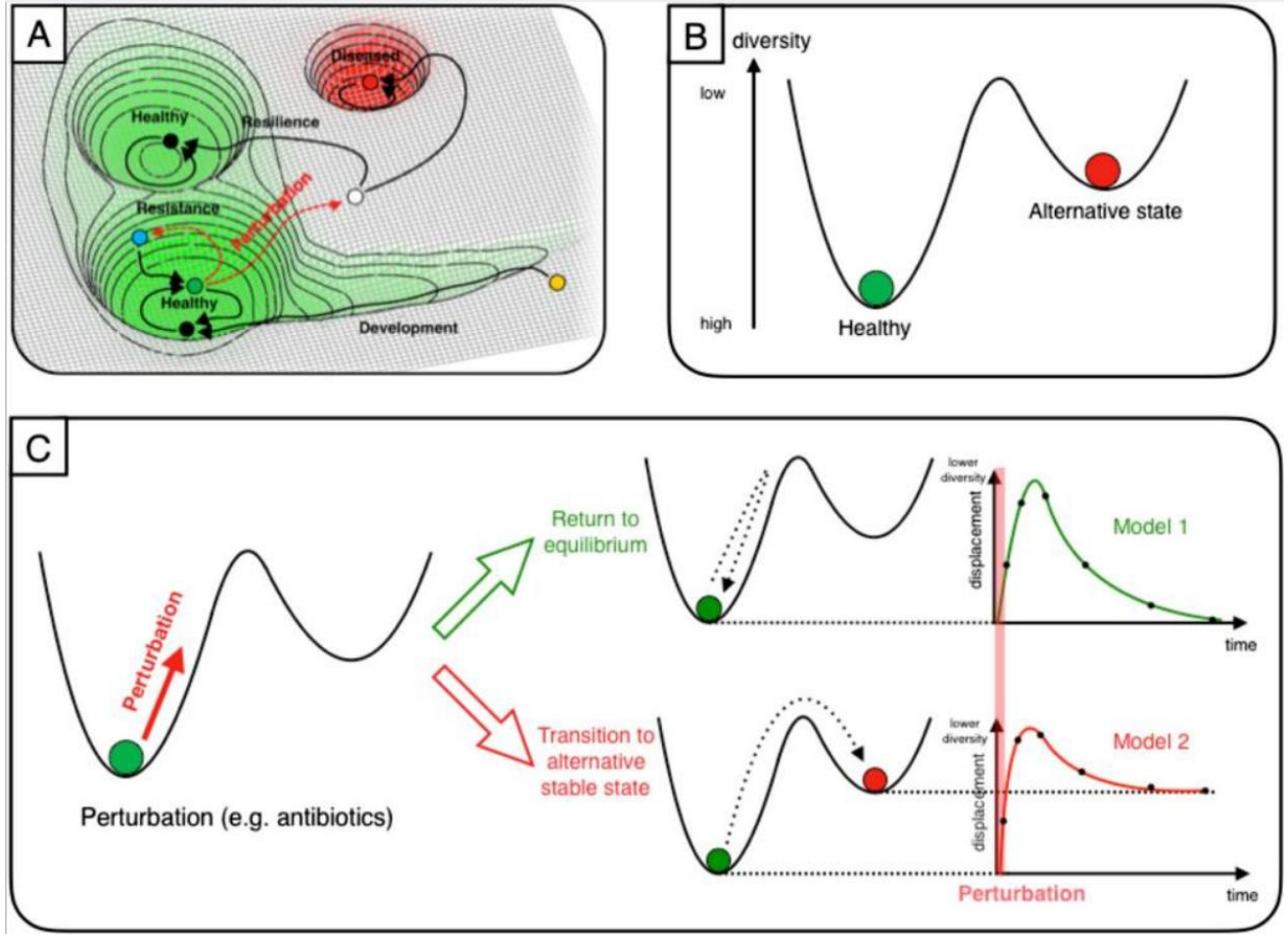
The microbiome is an ecology: balance is key

- From an ecology perspective, it is about balance points.
- This can be illustrated with a ball in a stability landscape[1].
  - Disturbances of the microbiome can be considered forces that push the ball from its balance point.
- A healthy ecosystem has ‘resilience’: resistance against change.
- In a disturbed microbiome, the goal is to modulate it back into a desired stable state.
  - This is done by treating disturbing factors such as pathogens, inflammation, permeability, etc.



1. Shaw, L.P., et al, 2019. ISME J 13, 1845–1856

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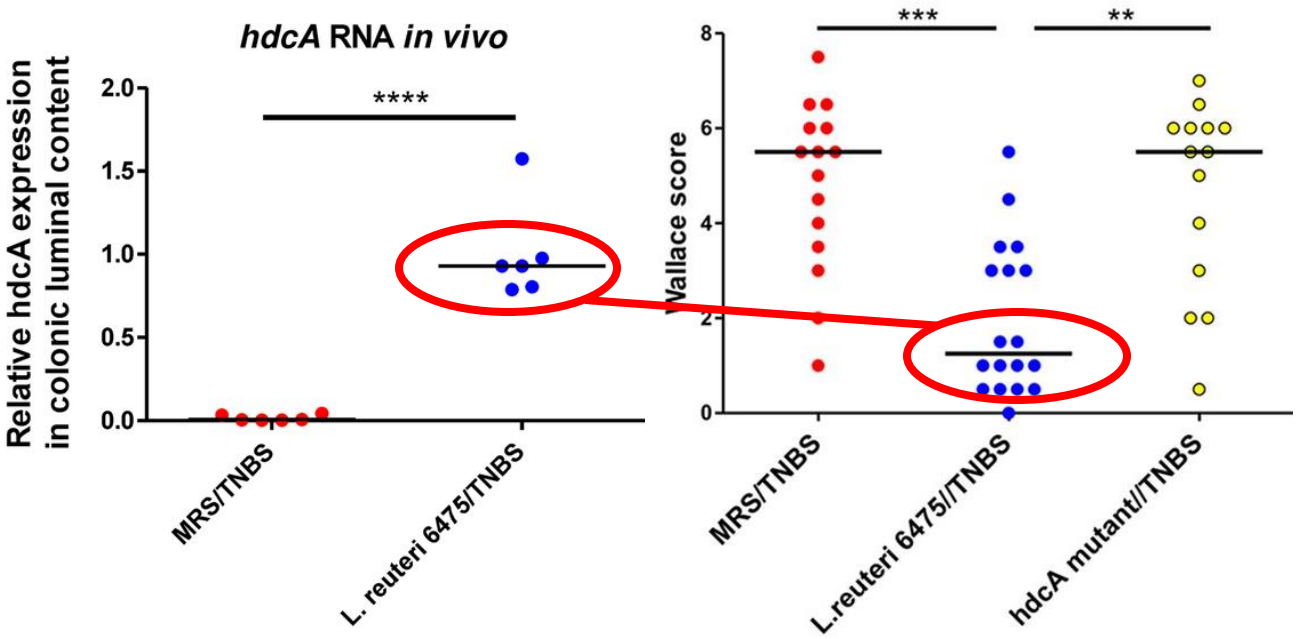

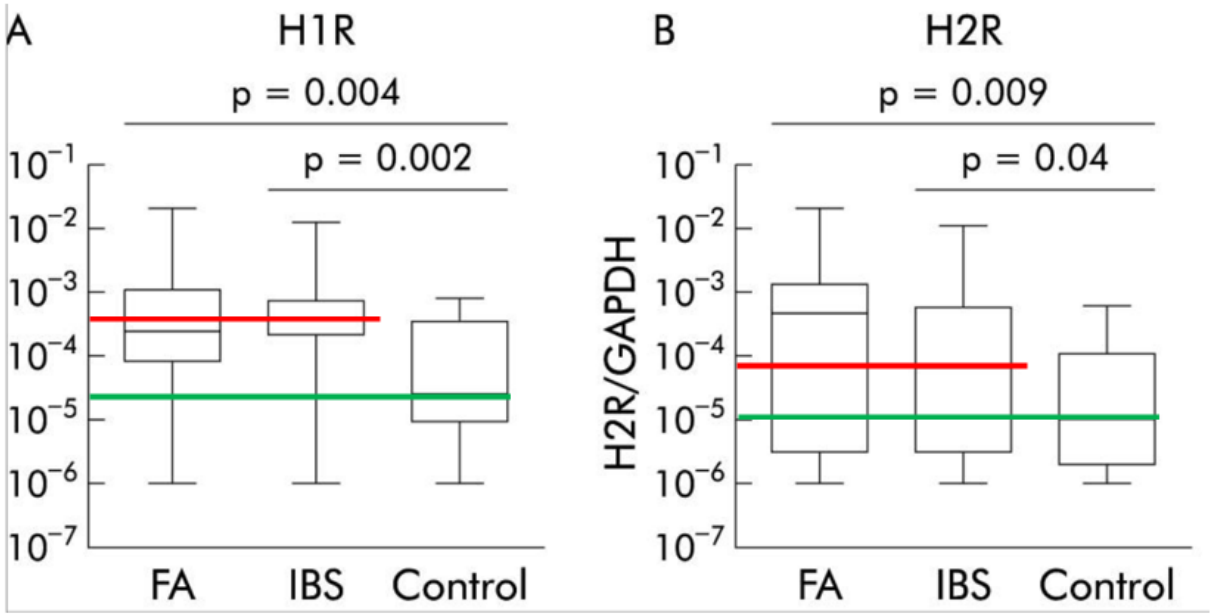

L. reuteri: anti-inflammatory **because** histamine-production

Total effect: balance between H1R and H2R

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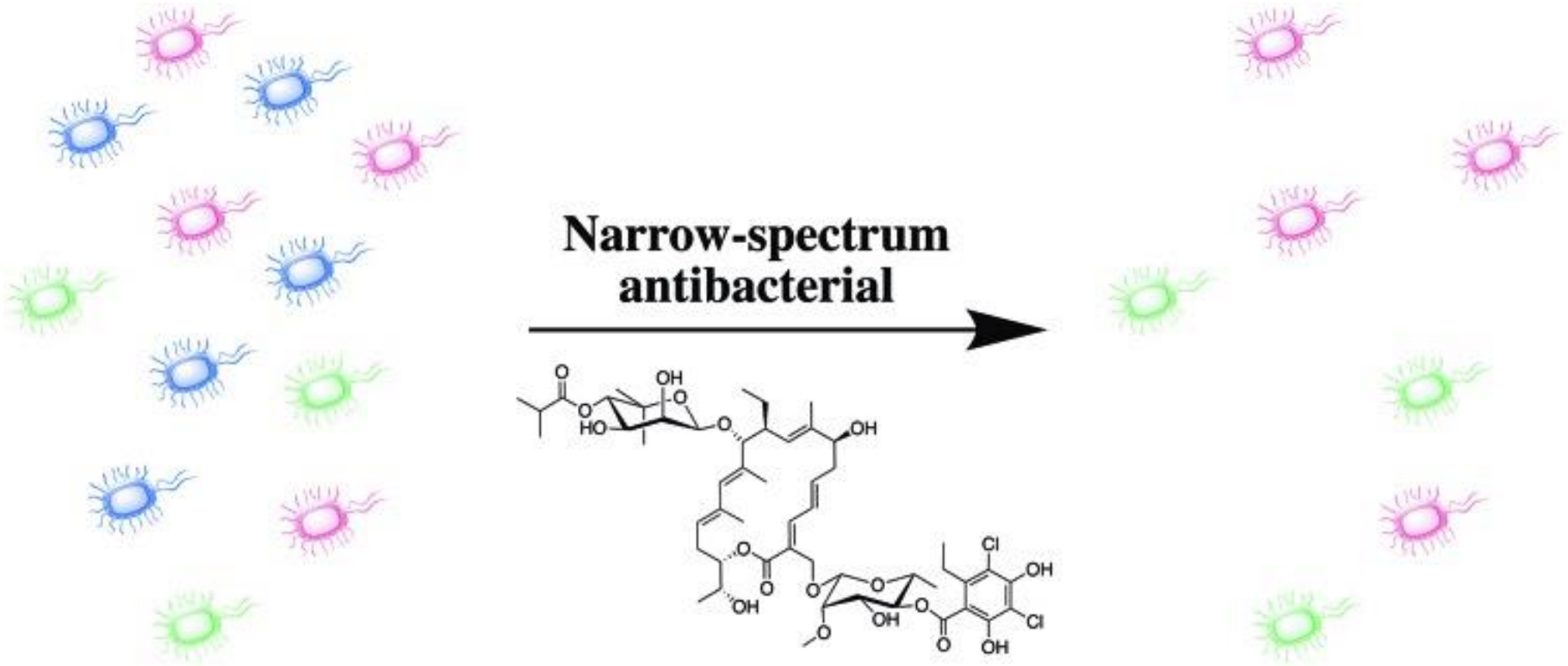
In an ecosystem, reductionistic cause-effect does not apply

Classic view on narrow-spectrum antibiotics:



1. Melander, R. J. et al. MedChemComm. 9,.12. (2017)

In an ecosystem, reductionistic cause-effect does not apply

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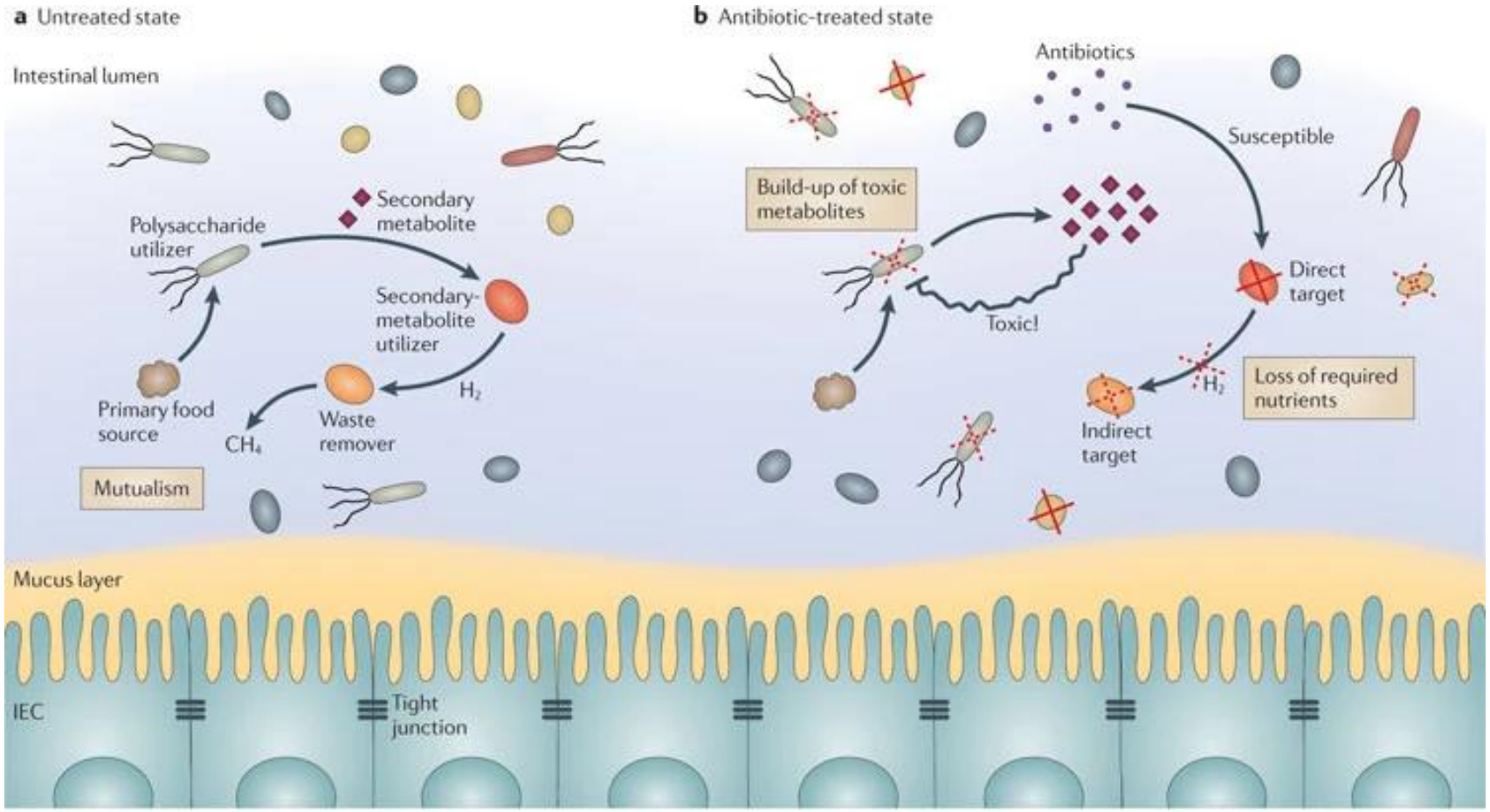
The ecological reality:



1. Willing, B. P. et al.Nat Rev Microbiol.9,.233–243.(2011)

Nature Reviews | Microbiology

In an ecosystem, everything happens at the same time

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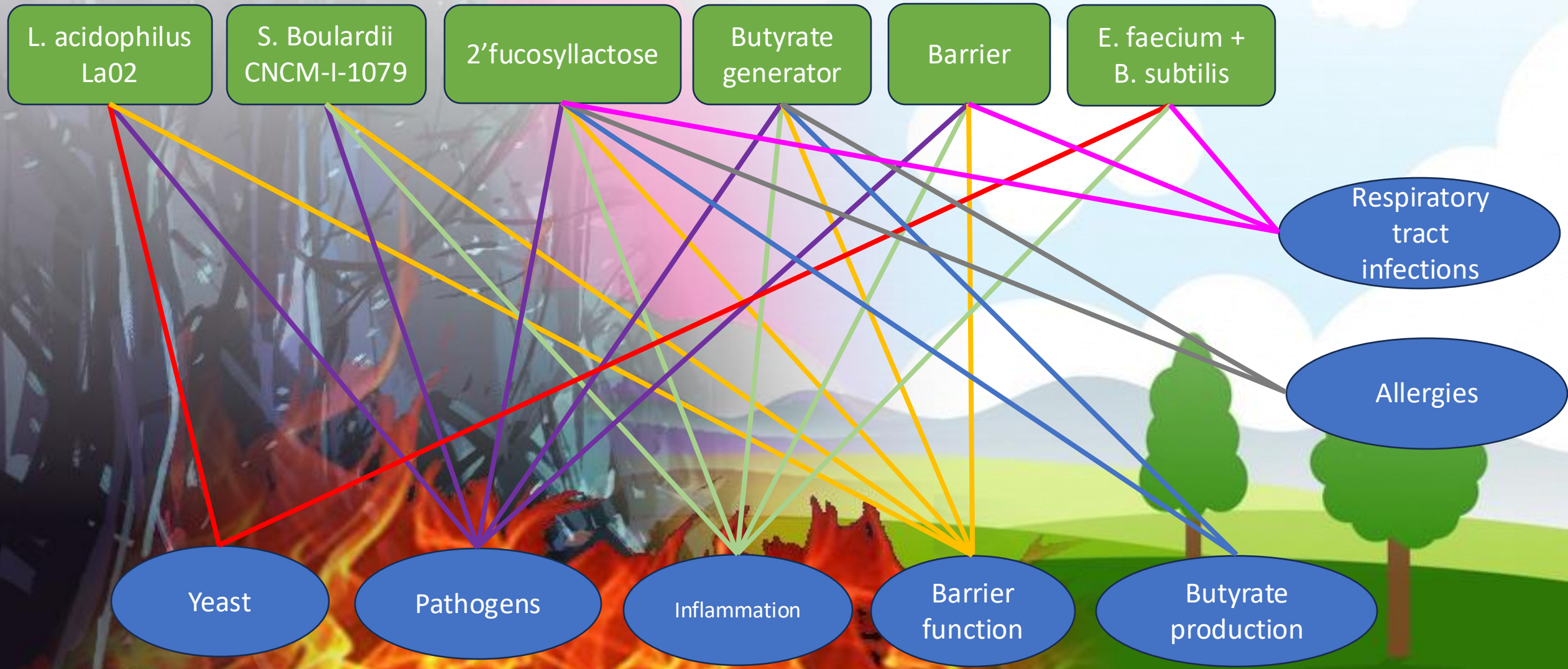
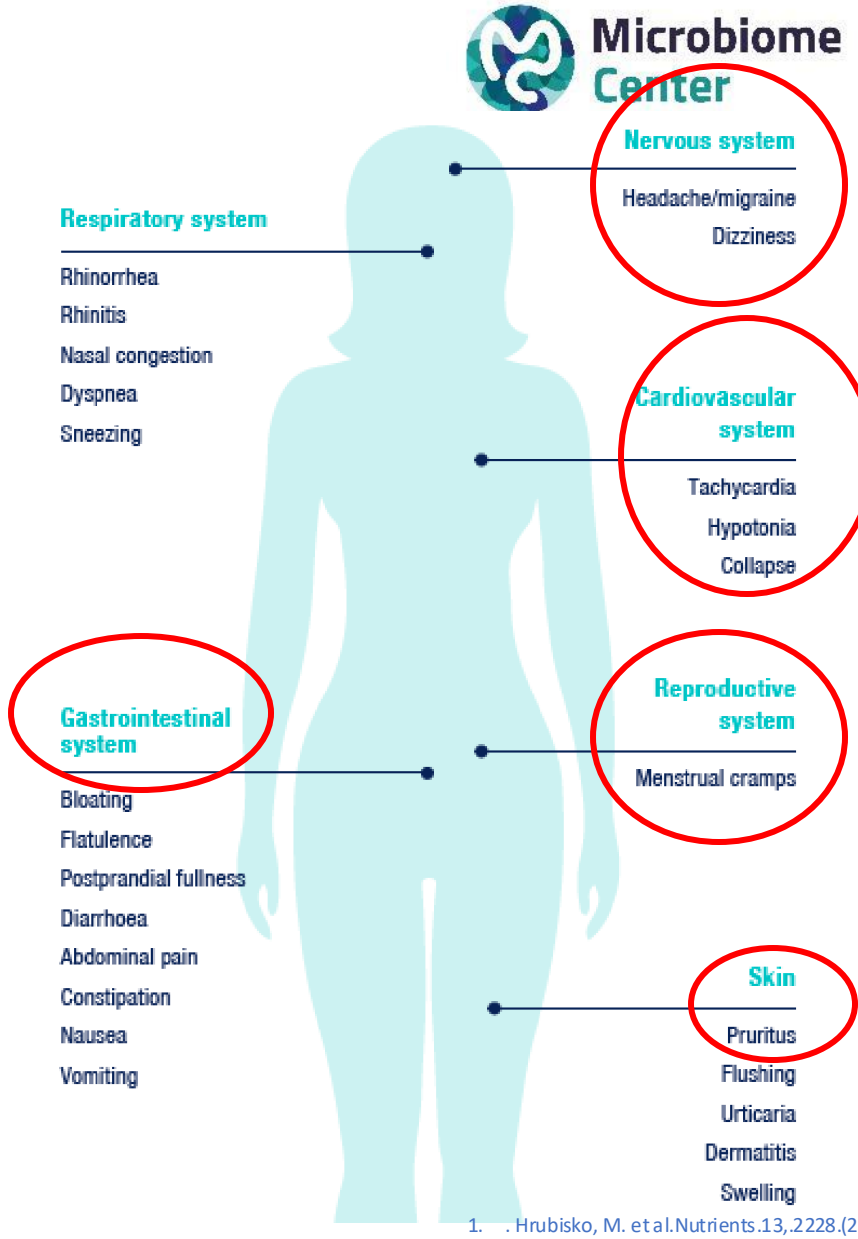


Case 2 Histamine

Patient: 46-year-old female

Symptoms:

- **Mood Swings** (since approx. age 16)
  - Diagnosed with depression / bipolar disorder.
- **Gastrointestinal Issues & Food Allergies** (since approx. age 8)
  - Symptoms: bloating, gas, fluctuating stools, abdominal pain.
  - Reactions to gluten, egg yolk, and tomatoes.
- **Mastocytosis with Anaphylactic Attacks** (since approx. age 8)
  - Triggers: food, stress, physical exertion (high intensity), hormonal changes (menstruation).
  - Uses **Epi-pen** approximately **once a month** and has had multiple ER visits due to mastocytosis anaphylaxis.
- Chronic stress, tension, fatigue, low energy
- Dizziness, weakness, light-headedness, tachycardia
- Mastocytosis skin spots



1. . Hrubisko, M. et al. Nutrients. 13, .2228. (2021)

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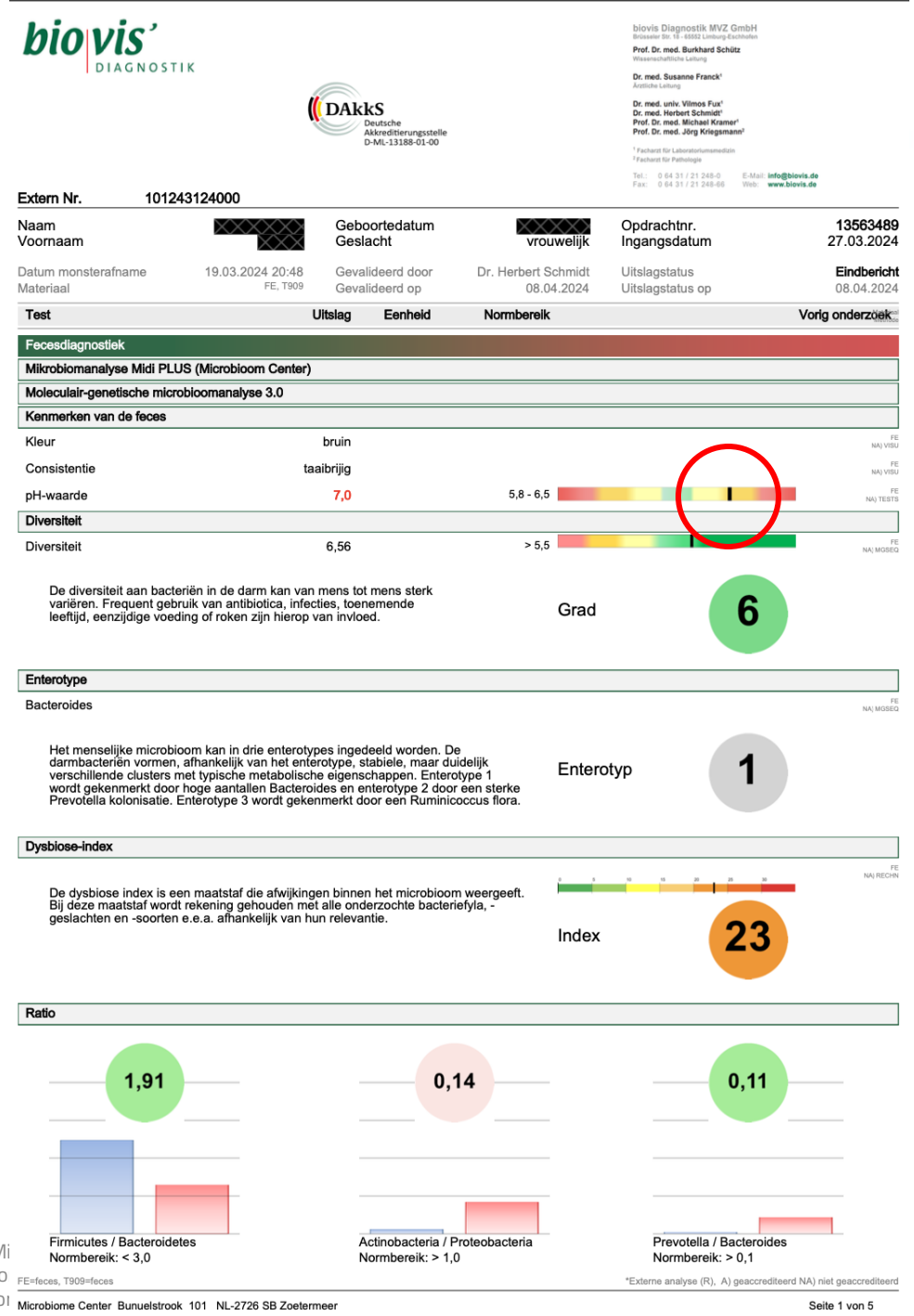
Case 2 Histamin

- **Microbiome results April'24:**
  - Dysbiosis
  - Low Akkermansia Levels
  - High Fat Content
  - Elevated Zonulin



bio|vis' DIAGNOSTIK

DAkkS Deutsche Akkreditierungsstelle D-ML-13188-01-00

biovis Diagnostik MVZ GmbH
Prof. Dr. med. Burkhard Schütz
Dr. med. Susanne Franck
Dr. med. univ. Vilmos Fux
Dr. med. Herbert Schmidt
Prof. Dr. med. Michael Kramer
Prof. Dr. med. Jörg Kriegsmann

Extern Nr. 101243124000

Naam	[redacted]	Geboortedatum	[redacted]	Opdrachtnr.	13563489
Voornaam		Geslacht	vrouwelijk	Ingangsdatum	27.03.2024
Datum monsterafname	19.03.2024 20:48	Gevalideerd door	Dr. Herbert Schmidt	Uitslagstatus	Eindbericht
Materiaal	FE, T909	Gevalideerd op	08.04.2024	Uitslagstatus op	08.04.2024

Test	Uitslag	Eenheid	Normbereik	Vorig onderzoek
Fecesdiagnostiek				
Mikrobiomanalyse Midi PLUS (Microbioom Center)				
Moleculair-genetische microbioomanalyse 3.0				
Kenmerken van de feces				
Kleur	bruin			
Consistentie	taaibrijig			
pH-waarde	7,0		5,8 - 6,5	
Diversiteit				
Diversiteit	6,56		> 5,5	

De diversiteit aan bacteriën in de darm kan van mens tot mens sterk variëren. Frequent gebruik van antibiotica, infecties, toenemende leeftijd, eenzijdige voeding of roken zijn hierop van invloed.

Grad 6

Enterotype

Bacteroides

Het menselijke microbioom kan in drie enterotypes ingedeeld worden. De darmbacteriën vormen, afhankelijk van het enterotype, stabiele, maar duidelijk verschillende clusters met typische metabolische eigenschappen. Enterotype 1 wordt gekenmerkt door hoge aantallen Bacteroides en enterotype 2 door een sterke Prevotella kolonisatie. Enterotype 3 wordt gekenmerkt door een Ruminicoccus flora.

Enterotyp 1

Dysbiose-index

De dysbiose index is een maatstaf die afwijkingen binnen het microbioom weergeeft. Bij deze maatstaf wordt rekening gehouden met alle onderzochte bacteriefyla, -geslachten en -soorten e.e.a. afhankelijk van hun relevantie.

Index 23

Ratio

1,91	0,14	0,11
Firmicutes / Bacteroidetes	Actinobacteria / Proteobacteria	Prevotella / Bacteroides
Normbereik: < 3,0	Normbereik: > 1,0	Normbereik: > 0,1

FE=feces, T909=feces

*Externe analyse (R), A) geaccrediteerd NA) niet geaccrediteerd

Microbiome Center Bunuelstrook 101 NL-2726 SB Zoetermeer

Seite 1 von 5

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Naam [redacted] Opdrachtnr. 13563489

[redacted] Geslacht vrouwelijk Ingangsdatum 27.03.2024

Test	Uitslag	Eenheid	Normbereik	Vorig onderzoek
Indeling van bacteriën naar fylum				
Actinobacteria	0,6	%	1,5 - 7	
Bacteroidetes	32,4	%	20 - 45	
Firmicutes	62,0	%	50 - 75	
Fusobacteria	0,0	%	0,0 - 1,0	
Proteobacteria	4,2	%	1,0 - 3,5	
Verrucomicrobia	0,0	%	1,5 - 5,0	
Overige	0,7	%		
Metaboloom (stofwisselingsactieve bacteriegroepen)				
Secundaire galzuren	-17,5	%		
TMA / TMAO	876,6	%		
Indoxylsulfaat	-50,0	%		
Fenolen	120,5	%		
Ammoniak	12,6	%		
Histamine	-50,0	%		
Equol	137,0	%		
Beta-glucuronidasen	-31,6	%		
Indeling van bacteriën naar fylum met de belangrijkste bacteriegeslachten en -soorten				
Actinobacteria				
Bifidobacterium	1,2 x 10^9	KVE/g feces	> 1,0 x 10^10	
Bacteroidetes				
Bacteroides	1,1 x 10^11	KVE/g feces	> 5,0 x10^10	
Prevotella	1,2 x 10^10	KVE/g feces	> 1,0 x 10^10	
Firmicutes				
Butyraatproducerende bacteriën				
Totaal kiemgetal	2,1 x 10^11	KVE/g feces	> 2,4 x 10^11	
Faecalibacterium prausnitzii	6,6 x 10^10	KVE/g feces	>1,0 x10^11	
Eubacterium rectale	3,2 x 10^9	KVE/g feces	> 2,0 x 10^10	
Eubacterium hallii	2,6 x 10^10	KVE/g feces	> 1,5 x 10^10	
Roseburia spp.	7,9 x 10^9	KVE/g feces	> 3,0 x10^10	
Ruminococcus spp.	3,8 x 10^10	KVE/g feces	> 5,0 x 10^10	
Coprococcus spp.	3,0 x 10^10	KVE/g feces	> 5,0 x 10^10	
Butyrivibrio spp.	3,5 x 10^10	KVE/g feces	>1,5 x 10^10	
Clostridia				
Totaal kiemgetal	8,3 x 10^9	KVE/g feces	< 4,0 x 10^9	
Clostridia Cluster I	3,3 x 10^7	KVE/g feces	< 2,0 x 10^9	
Fusobacteria				
Fusobacterium	1,9 x 10^7	KVE/g feces	< 1,0 x 10^7	
Verrucomicrobia				
Akkermansia muciniphila	1,0 x 10^5	KVE/g feces	> 5,0 x 10^9	
Proteobacteria				
Pathogene of potentieel pathogene bacteriën				
Haemophilus spp.	5,8 x 10^8	KVE/g feces	< 5,0 x 10^8	
Acinetobacter spp.	< 1,0 x 10^5	KVE/g feces	< 1,0 x 10^6	

FE=feces, T909=feces

*Externe analyse (R), A) geaccrediteerd NA) niet geaccrediteerd

Naam [redacted] Opdrachtnr. 13563489

[redacted] Geslacht vrouwelijk Ingangsdatum 27.03.2024

Test	Uitslag	Eenheid	Normbereik	Vorig onderzoek
Proteus spp.	< 1,0 x 10^5	KVE/g feces	< 1,0 x 10^6	
Klebsiella spp.	1,1 x 10^8	KVE/g feces	< 1,0 x 10^7	
Enterobacter spp.	2,2 x 10^7	KVE/g feces	< 1,0 x 10^6	
Serratia spp.	2,8 x 10^6	KVE/g feces	< 1,0 x 10^7	
Hafnia spp.	< 1,0 x 10^5	KVE/g feces	< 1,0 x 10^6	
Morganella spp.	< 1,0 x 10^5	KVE/g feces	< 1,0 x 10^6	
Citrobacter spp.	1,4 x 10^7	KVE/g feces	< 5,0 x 10^8	
Pseudomonas spp.	8,3 x 10^6	KVE/g feces	< 5,0 x 10^7	
Providencia spp.	< 1,0 x 10^5	KVE/g feces	< 5,0 x 10^7	
H2S-vorming				
Sulfaatreducerende bacteriën (SRB)	1,8 x 10^10	KVE/g feces	< 2,5 x 10^9	
Desulfovibrio piger	< 1,0 x 10^5	KVE/g feces	< 1,0 x 10^9	
Desulfomonas pigra	< 1,0 x 10^5	KVE/g feces	< 1,0 x 10^9	
Bilophila wadsworthii	< 1,0 x 10^5	KVE/g feces	< 2,0 x 10^9	
Immunogeniciteit / mucine vorming				
Immunogeen werkende bacteriën				
Escherichia coli	3,5 x 10^7	KVE/g feces	10^6 - 10^7	
Enterococcus spp.	2,78 x 10^5	KVE/g feces	10^6 - 10^7	
Lactobacillus spp.	< 1,0 x 10^5	KVE/g feces	10^5 - 10^7	
Mucine vorming / slijmvliesbarrière				
Akkermansia muciniphila	1,0 x 10^5	KVE/g feces	> 5,0 x 10^9	
Faecalibacterium prausnitzii	6,6 x 10^10	KVE/g feces	>1,0 x10^11	
Archaea				
Methanogenen				
Methanobrevibacter spp.	1,5 x 10^9	KVE/g feces	< 5,0 x 10^8	

Opmerking: Het nieuwe OmicSnap buisje en de daarin aanwezige matrix maken een nog effectievere microbiomanalyse mogelijk, vooral bij grampositieve bacteriën.
Dit resulteert in lichte verschuivingen in de normbereiken.
We vragen u hier rekening mee te houden.

Test	Uitslag	Eenheid	Normbereik	Vorig onderzoek
Mycobioom: relevante gisten				
Candida albicans (CA)	<1,0 x 10^3	KVE/g feces	<1,0 x 10^3	
Candida krusei (CK)	<1,0 x 10^3	KVE/g feces	< 1,0 x 10^3	
Candida glabrata (CG)	<1,0 x 10^3	KVE/g feces	< 1,0 x 10^3	
Candida dubliniensis (CD)	<1,0 x 10^3	KVE/g feces	< 1,0 x 10^3	
Candida parapsilosis (CP)	<1,0 x 10^3	KVE/g feces	< 1,0 x 10^3	
Candida tropicalis (CTp)	<1,0 x 10^3	KVE/g feces	< 1,0 x 10^3	
Candida lusitaniae (CL)	<1,0 x 10^3	KVE/g feces	< 1,0 x 10^3	
Parasieten				
Pathobionten				
Blastocystis hominis	positief		negatief	
Dientamoeba fragilis	grenswaarde		negatief	
Pathogene darmprotozoa				
Giardia lamblia	negatief		negatief	
Entamoeba histolytica	negatief		negatief	
Cryptosporidium spp.	negatief		negatief	

FE=feces, T909=feces

*Externe analyse (R), A) geaccrediteerd NA) niet geaccrediteerd

Microbiome Center

Naam	[redacted]	[redacted]	Opdrachtnr.	13563489
[redacted]	Geslacht	vrouwelijk	Ingangsdatum	27.03.2024

Test	Uitslag	Eenheid	Normbereik	Vorig onderzoek
Cyclospora cayetanensis	negatief		negatief	FE A) MOLEK
Vertering				
Vetgehalte	8,99	g/100g	< 3,5	FE NA) PHOT
Stikstofgehalte	0,90	g/100g	< 1,0	FE NA) PHOT
Suikergehalte	2,50	g/100g	< 2,5	FE NA) PHOT
Watergehalte	70,62	g/100g	75 - 85	FE NA) PHOT
Extra parameter(s)				
Calprotectine	<17,90	mg/l	< 50	FE A) ELISA
Alfa-1-antitripsine	<1,8	mg/dl	< 27,5	FE A) ELISA
Secretoir Immunoglobuline A	484,0	µg/ml	510 - 2040	FE A) ELISA
Zonuline	73,47	ng/ml	< 55	FE A) ELISA
Histamine in feces	<200,0	ng/ml	< 959	T909 A) ELISA
Secretoir Immunoglobuline A	484,0	µg/ml	510 - 2040	FE A) ELISA

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Case 2 Histamine

Treatment:

MyOwnBlend

Results:

- Reduced abdominal pain
- Better, firmer stool
- **Fewer mastocytosis attacks (no use of epi-pen since starting MOB - 6 months)**
- Reduced allergic reactions to foods such as gluten
- Increased energy
- Better sleep
- Less muscle & joint pain
- Fewer mastocytosis skin spots
- Less dizziness and weakness
- Weight gain (as if nutrients are being better absorbed)

MC ID	Element	Dagdosering
M002	MyOwnBlend, magistrale bereiding 2 maanden (oraal)	
BB058	S. Boulardii	2
BB044	L. sakei probio65	2
BB028	L. plantarum P-8	2
BB027	L. rhamnosus SP1	1
BB021	Bacillus coagulans Unique IS-2	2
BB023	2'-Fucosyllactose	4
BB011	Butyraat generator	2

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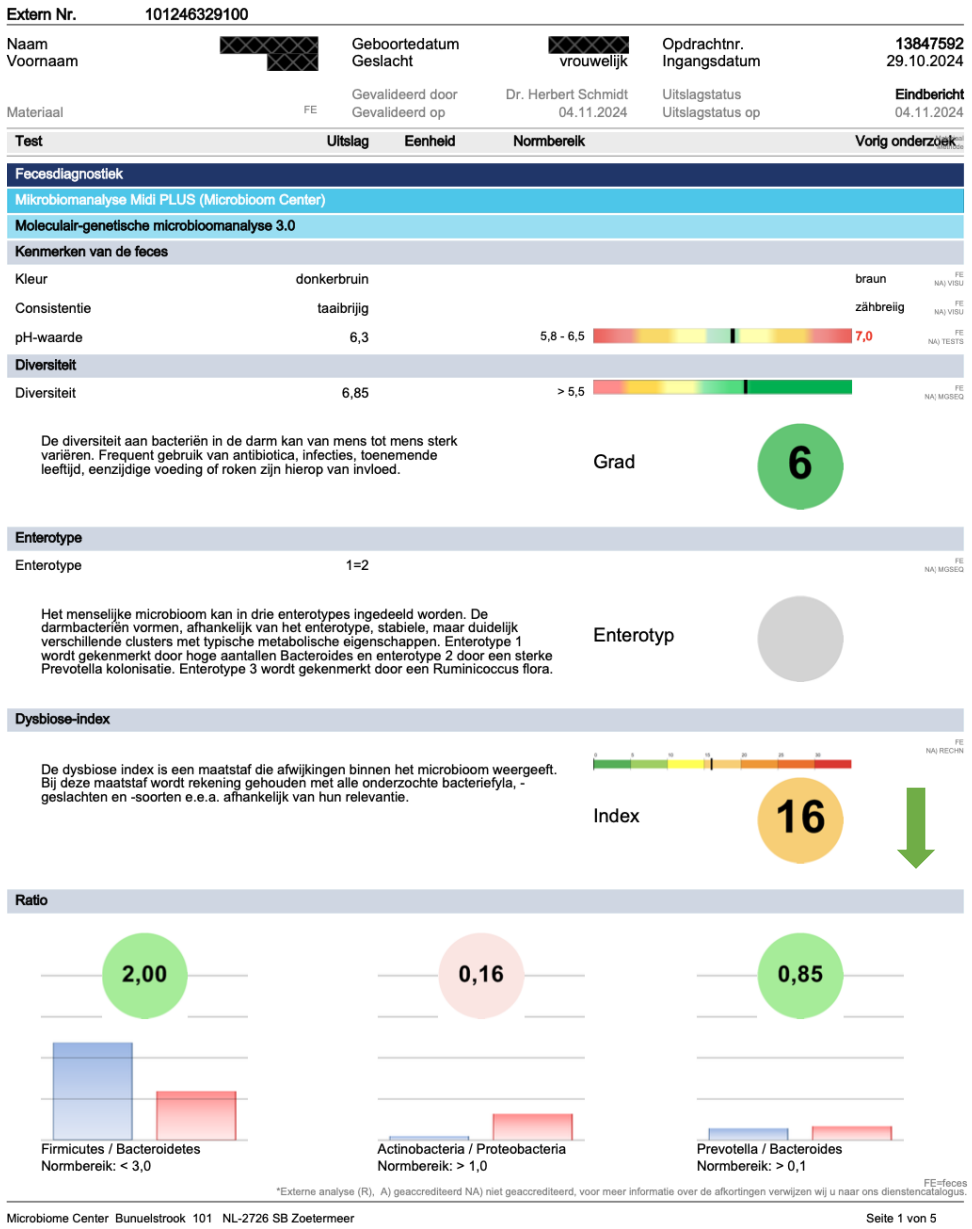
Case 2 Histamine

- Second microbiome analysis November'24:



Extern Nr. 101246329100

Naam [redacted] Geboortedatum [redacted] Opdrachtnr. 13847592
Voornaam Geslacht vrouwelijk Ingangsdatum 29.10.2024

Materiaal FE Gevalideerd door Dr. Herbert Schmidt Uitslagstatus Eindbericht
Gevalideerd op 04.11.2024 Uitslagstatus op 04.11.2024

Test	Uitslag	Eenheid	Normbereik	Vorig onderzoek
Fecesdiagnostiek				
Mikrobiomanalyse Midi PLUS (Microbioom Center)				
Moleculair-genetische microbioomanalyse 3.0				
Kenmerken van de feces				
Kleur	donkerbruin			braun
Consistentie	taaibrijig			zähbreiig
pH-waarde	6,3		5,8 - 6,5	7,0
Diversiteit				
Diversiteit	6,85		> 5,5	

De diversiteit aan bacteriën in de darm kan van mens tot mens sterk variëren. Frequent gebruik van antibiotica, infecties, toenemende leeftijd, eenzijdige voeding of roken zijn hierop van invloed.

Grad 6

Enterotype

Enterotype	1=2			

Het menselijke microbioom kan in drie enterotypes ingedeeld worden. De darmbacteriën vormen, afhankelijk van het enterotype, stabiele, maar duidelijk verschillende clusters met typische metabolische eigenschappen. Enterotype 1 wordt gekenmerkt door hoge aantallen Bacteroides en enterotype 2 door een sterke Prevotella kolonisatie. Enterotype 3 wordt gekenmerkt door een Ruminicoccus flora.

Enterotyp

Dysbiose-index

De dysbiose index is een maatstaf die afwijkingen binnen het microbioom weergeeft. Bij deze maatstaf wordt rekening gehouden met alle onderzochte bacteriefyla, -geslachten en -soorten e.e.a. afhankelijk van hun relevantie.

Index 16

Ratio

2,00 Firmicutes / Bacteroidetes Normbereik: < 3,0

0,16 Actinobacteria / Proteobacteria Normbereik: > 1,0

0,85 Prevotella / Bacteroides Normbereik: > 0,1

FE=feces

*Externe analyse (R), A) geaccrediteerd NA) niet geaccrediteerd, voor meer informatie over de afkortingen verwijzen wij u naar ons dienstencatalogus.

Microbiome Center Bunuelstrook 101 NL-2726 SB Zoetermeer Seite 1 von 5

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Naam [redacted] Opdrachtnr. 13847592

[redacted] Geslacht vrouwelijk Ingangsdatum 29.10.2024

Test	Uitslag	Eenheid	Normbereik	Vorig onderzoek
Indeling van bacteriën naar fylum				
Actinobacteria	0,5	%	1,5 - 7	
Bacteroidetes	29,7	%	20 - 45	
Firmicutes	59,3	%	50 - 75	
Fusobacteria	0,0	%	0,0 - 1,0	
Proteobacteria	3,2	%	1,0 - 3,5	
Verrucomicrobia	2,3	%	1,5 - 5,0	
Overige	5,1	%		
Metaboloom (stofwisselingsactieve bacteriegroepen)				
Secundaire galzuren	-28,7	%		
TMA / TMAO	564,1	%		
Indoxylsulfaat	-50,0	%		
Fenolen	67,8	%		
Ammoniak	16,5	%		
Histamine	-50,0	%		
Equol	-5,0	%		
Beta-glucuronidasen	-46,3	%		
Indeling van bacteriën naar fylum met de belangrijkste bacteriegeslachten en -soorten				
Actinobacteria				
Bifidobacterium	8,7 x 10^8	KVE/g feces	> 1,0 x 10^10	
Bacteroidetes				
Bacteroides	8,5 x 10^10	KVE/g feces	> 5,0 x10^10	
Prevotella	7,2 x 10^10	KVE/g feces	> 1,0 x 10^10	
Prevotella copri	6	%		
Firmicutes				
Butyraatproducerende bacteriën				
Totaal kiemgetal	3,3 x 10^11	KVE/g feces	> 2,4 x 10^11	
Faecalibacterium prausnitzii	6,9 x 10^10	KVE/g feces	>1,0 x10^11	
Eubacterium rectale	1,1 x 10^10	KVE/g feces	> 2,0 x 10^10	
Eubacterium hallii	3,2 x 10^10	KVE/g feces	> 1,5 x 10^10	
Roseburia spp.	3,3 x 10^10	KVE/g feces	> 3,0 x10^10	
Ruminococcus spp.	3,5 x 10^10	KVE/g feces	> 5,0 x 10^10	
Coprococcus spp.	3,3 x 10^10	KVE/g feces	> 5,0 x 10^10	
Butyrivibrio spp.	1,2 x 10^11	KVE/g feces	>1,5 x 10^10	
Clostridia				
Totaal kiemgetal	9,0 x 10^9	KVE/g feces	< 4,0 x 10^9	
Clostridia Cluster I	1,0 x 10^5	KVE/g feces	< 2,0 x 10^9	
Fusobacteria				
Fusobacterium	< 1,0 x 10^5	KVE/g feces	< 1,0 x 10^7	
Verrucomicrobia				
Akkermansia muciniphila	6,8 x 10^9	KVE/g feces	> 5,0 x 10^9	
Proteobacteria				
Pathogene of potentieel pathogene bacteriën				
Haemophilus spp.	2,2 x 10^8	KVE/g feces	< 5,0 x 10^8	

FE=feces

*Externe analyse (R), A) geaccrediteerd NA) niet geaccrediteerd, voor meer informatie over de afkortingen verwijzen wij u naar ons dienstencatalogus.

Naam [redacted] Opdrachtnr. 13847592

[redacted] Geslacht vrouwelijk Ingangsdatum 29.10.2024

Test	Uitslag	Eenheid	Normbereik	Vorig onderzoek
Acinetobacter spp.	< 1,0 x 10^5	KVE/g feces	< 1,0 x 10^6	
Proteus spp.	< 1,0 x 10^5	KVE/g feces	< 1,0 x 10^6	
Klebsiella spp.	1,0 x 10^7	KVE/g feces	< 1,0 x 10^7	
Enterobacter spp.	< 1,0 x 10^5	KVE/g feces	< 1,0 x 10^6	
Serratia spp.	1,0 x 10^7	KVE/g feces	< 1,0 x 10^7	
Hafnia spp.	< 1,0 x 10^5	KVE/g feces	< 1,0 x 10^6	
Morganella spp.	< 1,0 x 10^5	KVE/g feces	< 1,0 x 10^6	
Citrobacter spp.	5,2 x 10^7	KVE/g feces	< 5,0 x 10^8	
Pseudomonas spp.	< 1,0 x 10^5	KVE/g feces	< 5,0 x 10^7	
Providencia spp.	< 1,0 x 10^5	KVE/g feces	< 5,0 x 10^7	
H2S-vorming				
Sulfaatreducerende bacteriën (SRB)	9,4 x 10^9	KVE/g feces	< 2,5 x 10^9	
Desulfovibrio piger	< 1,0 x 10^5	KVE/g feces	< 1,0 x 10^9	
Desulfomonas pigra	< 1,0 x 10^5	KVE/g feces	< 1,0 x 10^9	
Bilophila wadsworthii	< 1,0 x 10^5	KVE/g feces	< 2,0 x 10^9	
Immunogeniciteit / mucine vorming				
Immunogeen werkende bacteriën				
Escherichia coli	6,7 x 10^6	KVE/g feces	10^6 - 10^7	
Enterococcus spp.	1,03 x 10^6	KVE/g feces	10^6 - 10^7	
Lactobacillus spp.	< 1,0 x 10^5	KVE/g feces	10^5 - 10^7	
Mucine vorming / slijmvliesbarrière				
Akkermansia muciniphila	6,8 x 10^9	KVE/g feces	> 5,0 x 10^9	
Faecalibacterium prausnitzii	6,9 x 10^10	KVE/g feces	>1,0 x10^11	
Archaea				
Methanogenen				
Methanobrevibacter spp.	1,2 x 10^9	KVE/g feces	< 5,0 x 10^8	

**Opmerking: Het nieuwe OmicSnap-buisje en de daarin aanwezige matrix maken een nog effectievere monsteranalyse mogelijk, vooral bij grampositieve bacteriën.
Dit resulteert in lichte verschuivingen in de normbereiken.
We vragen u hier rekening mee te houden.**

Test	Uitslag	Eenheid	Normbereik	Vorig onderzoek
Mycobioom: relevante gisten				
Candida albicans (CA)	<1,0 x 10^3	KVE/g feces	<1,0 x 10^3	
Candida krusei (CK)	<1,0 x 10^3	KVE/g feces	< 1,0 x 10^3	
Candida glabrata (CG)	<1,0 x 10^3	KVE/g feces	< 1,0 x 10^3	
Candida dubliniensis (CD)	<1,0 x 10^3	KVE/g feces	< 1,0 x 10^3	
Candida parapsilosis (CP)	<1,0 x 10^3	KVE/g feces	< 1,0 x 10^3	
Candida tropicalis (CTp)	<1,0 x 10^3	KVE/g feces	< 1,0 x 10^3	
Candida lusitaniae (CL)	<1,0 x 10^3	KVE/g feces	< 1,0 x 10^3	
Parasieten				
Pathobionten				
Blastocystis hominis	positief		negatief	positiv
Dientamoeba fragilis	positief		negatief	grenzwertig
Pathogene darmprotozoa				
Giardia lamblia	negatief		negatief	negativ
Entamoeba histolytica	negatief		negatief	negativ

FE=feces

*Externe analyse (R), A) geaccrediteerd NA) niet geaccrediteerd, voor meer informatie over de afkortingen verwijzen wij u naar ons dienstencatalogus.

Microbiome Center

Naam	[redacted]	Opdrachtnr.	13847592
[redacted]	Geslacht vrouwelijk	Ingangsdatum	29.10.2024

Test	Uitslag	Eenheid	Normbereik	Vorig onderzoek
Cryptosporidium spp.	negatief		negatief	negativ
Cyclospora cayetanensis	negatief		negatief	negativ
Vertering				
Vetgehalte	8,80	g/100g	< 3,5	8,99
Stikstofgehalte	0,89	g/100g	< 1,0	0,90
Suikergehalte	2,62	g/100g	< 2,5	2,50
Watergehalte	71,57	g/100g	75 - 85	70,62
Extra parameter(s)				
Calprotectine	<17,90	mg/l	< 50	<17,90
Alfa-1-antitripsine	<1,8	mg/dl	< 27,5	<1,8
Secretoir Immunoglobuline A	540,2	µg/ml	510 - 2040	484,0
Zonuline	45,28	ng/ml	< 55	73,47

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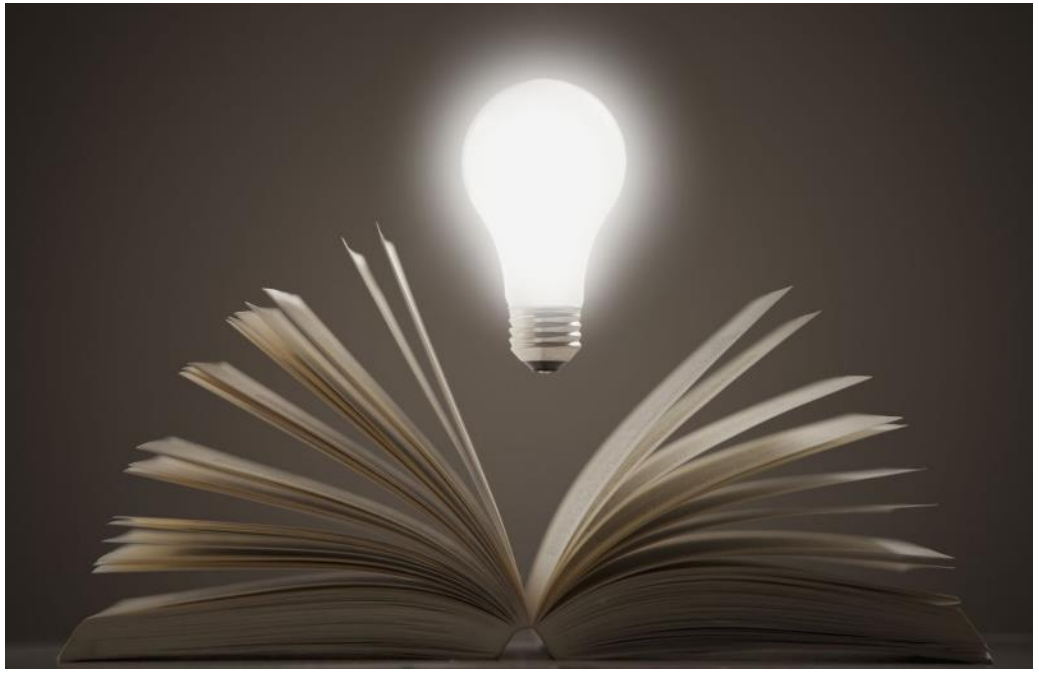
Take-home messages

- Histamine has important physiological roles! You cannot live without it.
- Histamine sensitivity has multiple potential causes
- In many cases low levels of the histamine-degrading enzyme DAO is the consequence rather than cause of inflammation rather

- Whether or not probiotic bacteria can produce histamine is of minor importance.
- In microbiome treatments it is all about balance.
- It is impossible for a doctor to know whether histamine sensitivity is cause of consequence, is endogenous or external.
- In case there are gut problems: start treating the microbiome.
  - Optimize diet for gut health, take into acount histamine content for severe cases.



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Webinar calendar

Intervisions/Arbeitskreisen

- February 12th: Arbeitskreis 2: discuss cases
- February 13th: Starter meeting (NL)
- February 18th: Arbeitskreis 1: starters (DE)
- March 19th: Arbeitskreis 2: discuss cases (DE)
- April 1st: Arbeitskreis 2: discuss cases (DE)
- April 3rd: Intervision: discuss cases (NL)
- April 8th: Starter meeting (NL)
- April 10th: Arbeitskreis 1: starters (DE)
- May 19th: Starter meeting (NL)
- May 21st: Arbeitskreis 2: discuss cases (DE)
- June 3rd: Arbeitskreis 1: starters (DE)
- June 5th: Intervision: discuss cases (NL)
- June 26th: Arbeitskreis 2: discuss cases (DE)

Thematic webinars:

- March 17th: Autism (EN)
- April 1st: Autism (DE)
- April 14th: Microbiome as ecosystem (NL)
- April 17th: Microbiome as ecosystem (DE)
- May 13th: Allergies (DE)

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