Optimising **Gut Health** in **Long Covid**

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Heather Leeson DipNT

Hypothesized mechanisms in Long Covid

Positive nutrition

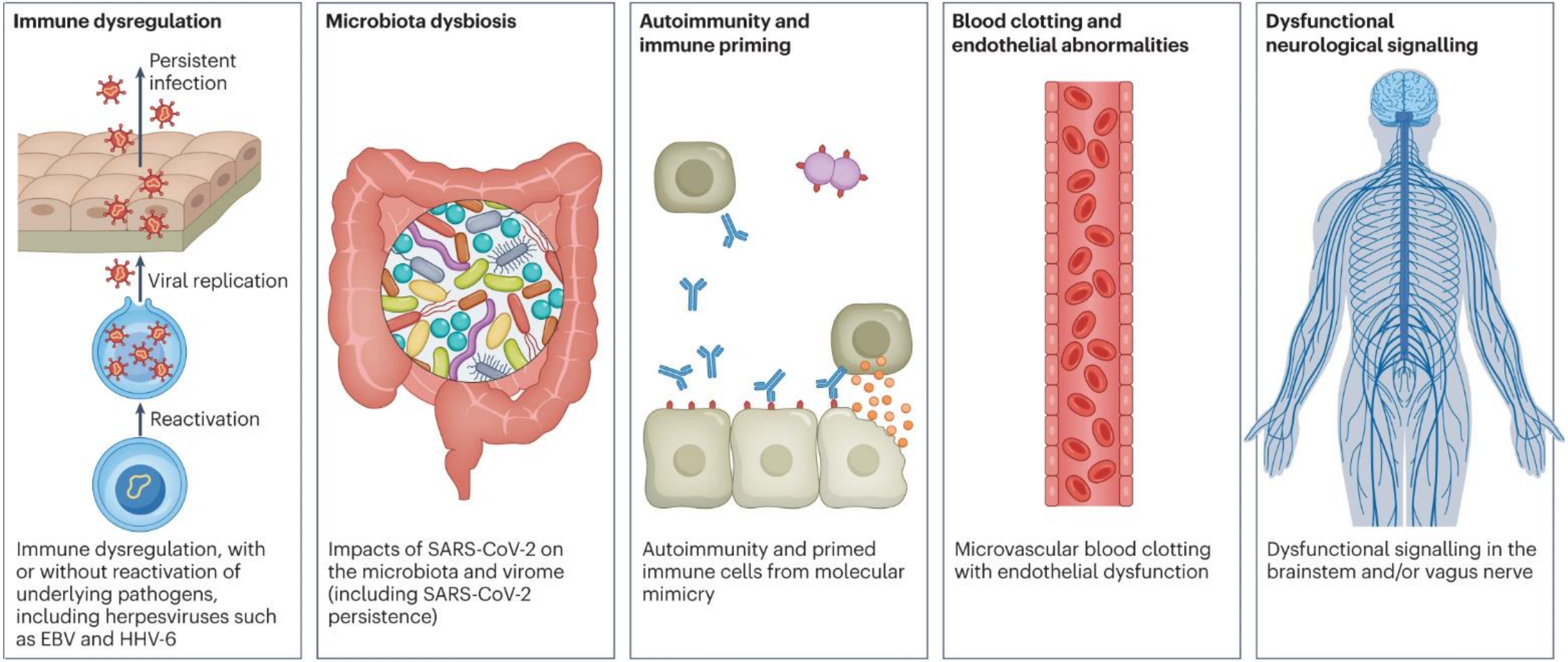
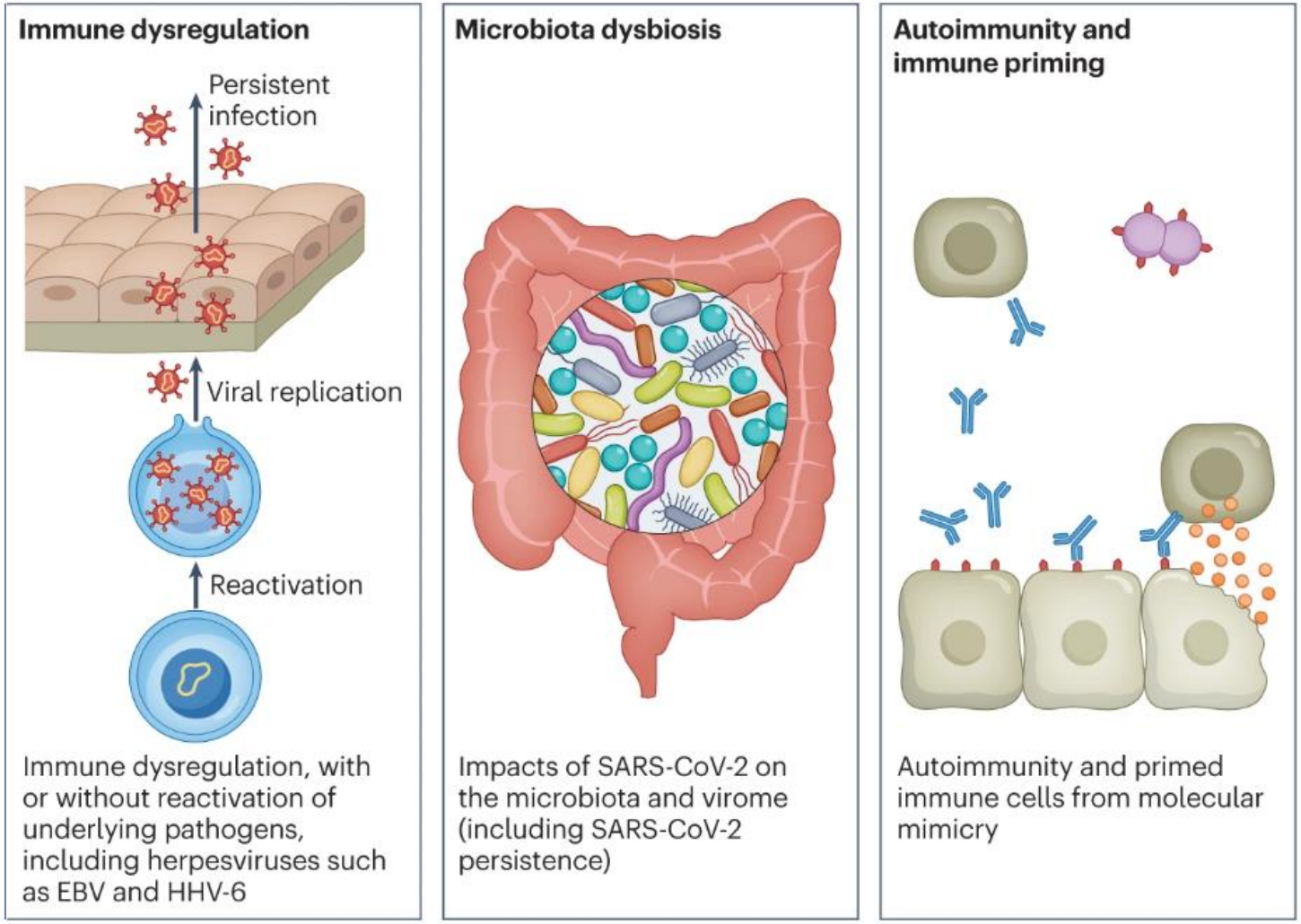


Fig. 3: Hypothesized mechanisms of long COVID pathogenesis. | Nature Reviews Microbiology

The gastrointestinal tract is a major interface with the immune system

70-80% of our immune system is located at the gut

Positive nutrition



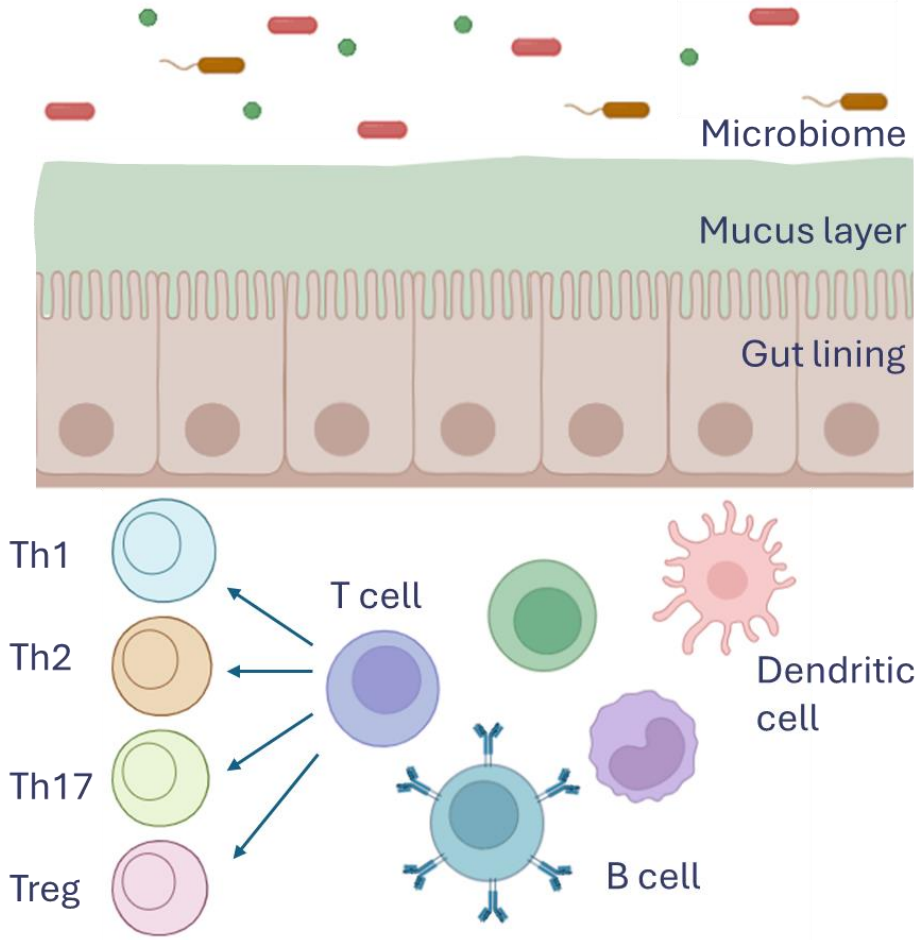


Fig. 3: Hypothesized mechanisms of long COVID pathogenesis. | Nature Reviews Microbiology

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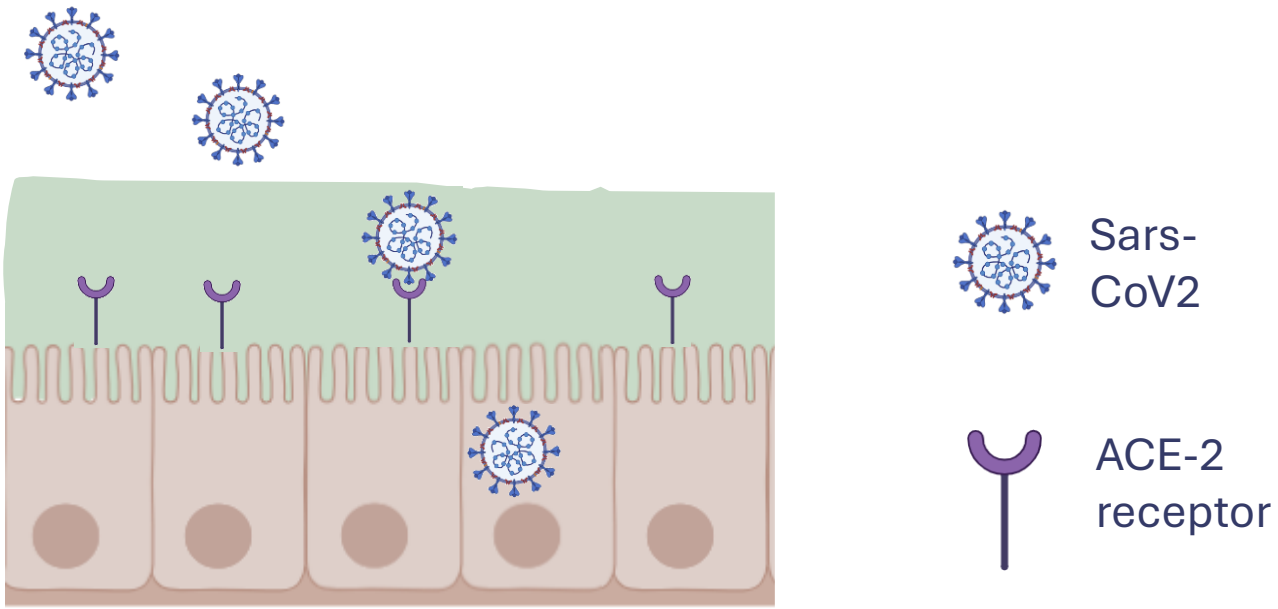
Viral infection and persistence in the gut:

ACE-2 receptor is highly expressed in the gut lining

Prolonged faecal shedding of viral RNA for up to 210 days post-infection

Long Covid is associated with inflammation at the gut – risk factor



Mechanisms of Gut-Related Viral Persistence in Long COVID - PMC

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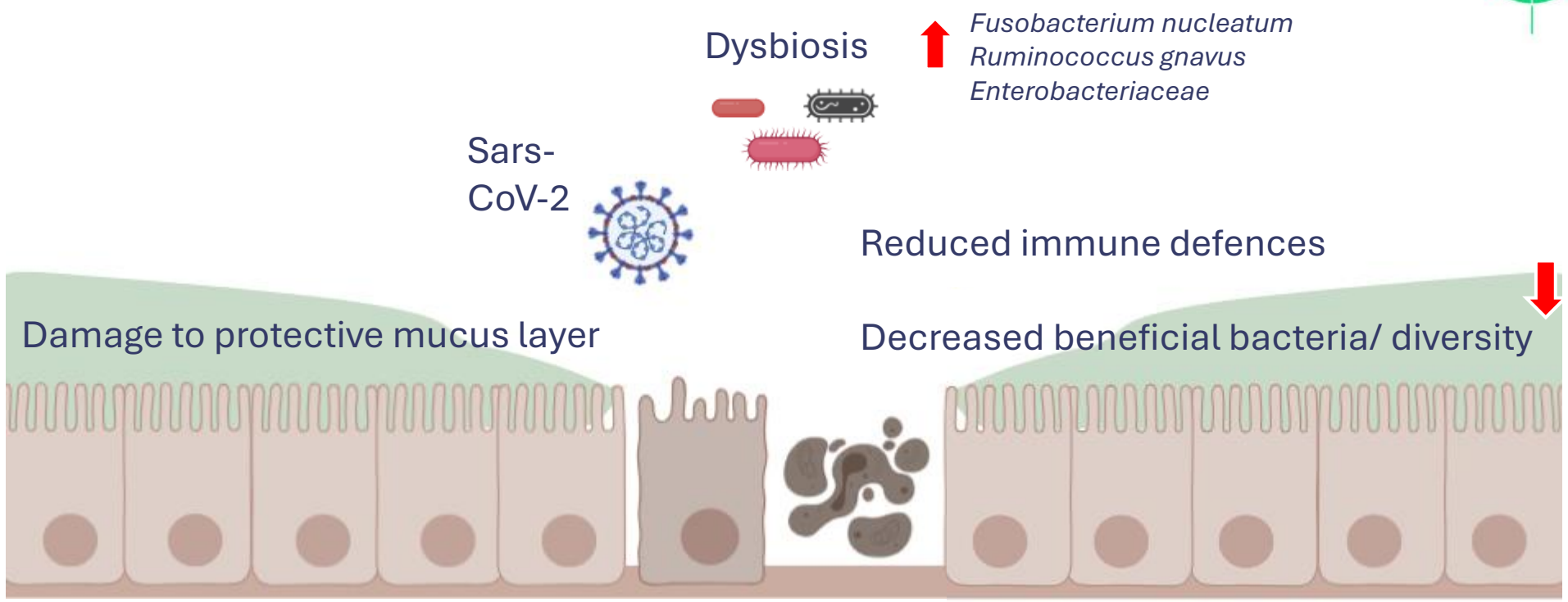
Inflammation, damage signals, leaky gut, dysbiosis



Gut microbiota dynamics in a prospective cohort of patients with post-acute COVID-19 syndrome | Gut

Gut Microbiota Dysbiosis Correlates With Long COVID-19 at One-Year After Discharge - PMC

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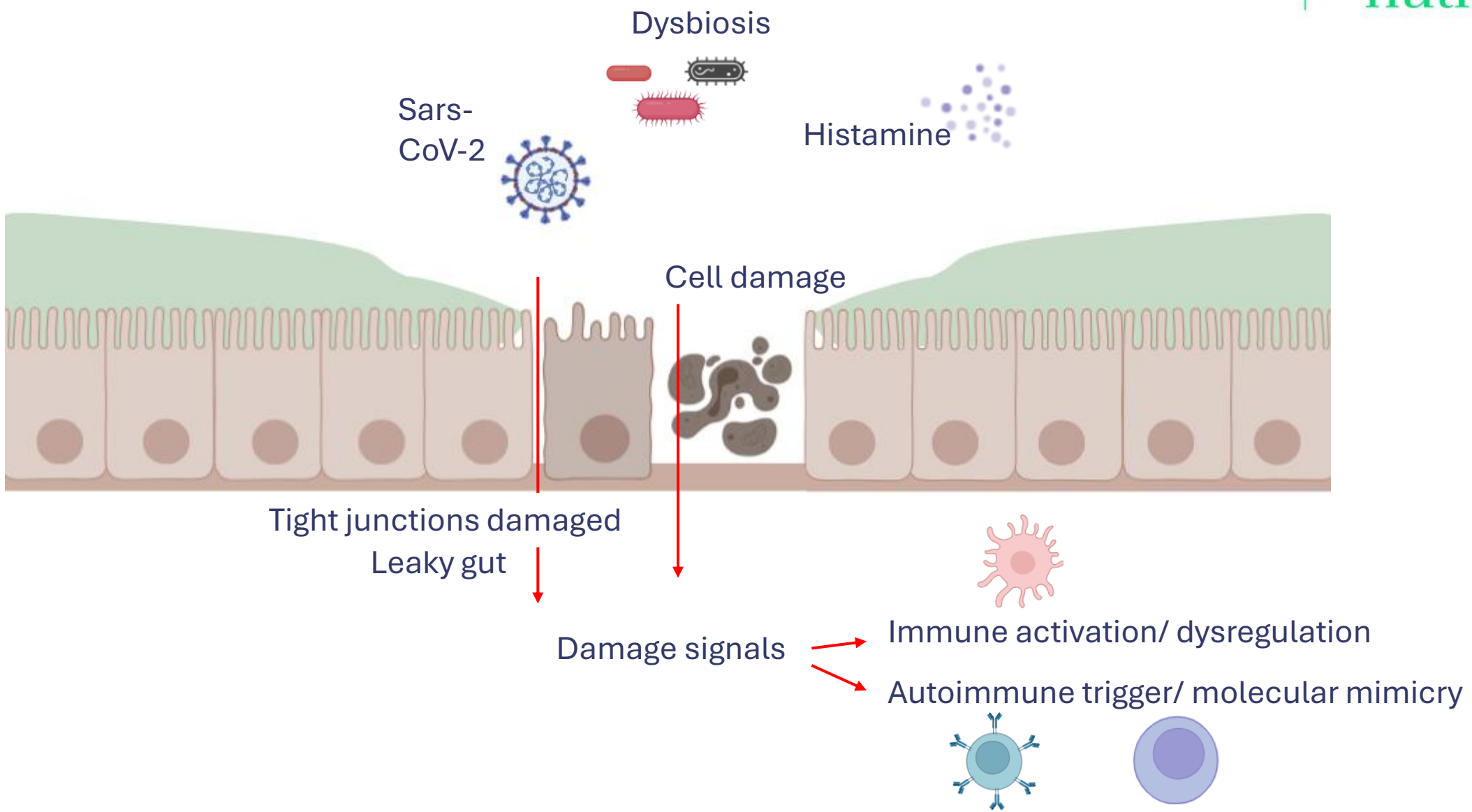
Inflammation, damage signals, leaky gut, dysbiosis



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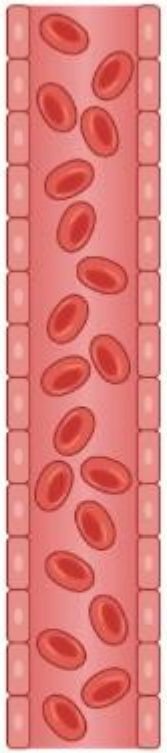
How does the gut influence blood clotting in Long Covid?

Positive nutrition

Blood clotting and endothelial abnormalities

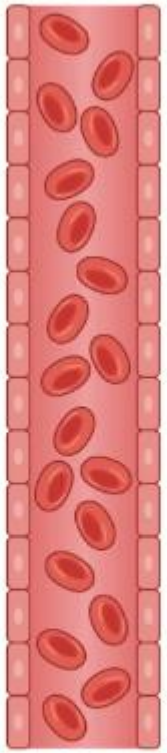


Microvascular blood clotting with endothelial dysfunction

How does the gut influence blood clotting in Long Covid?

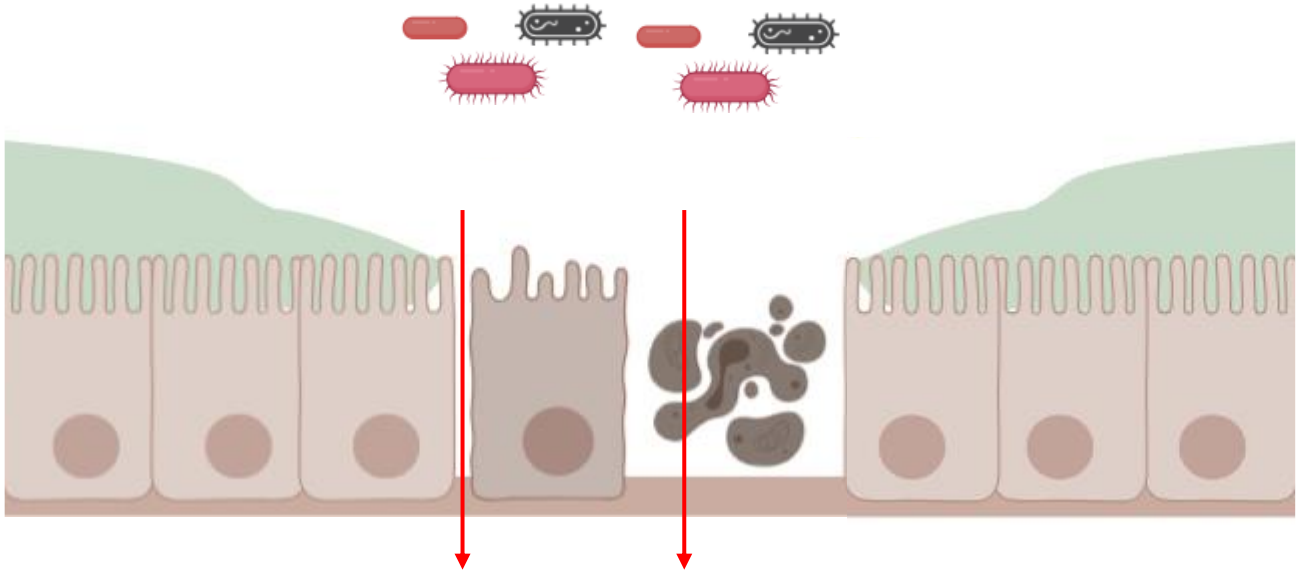
Positive nutrition

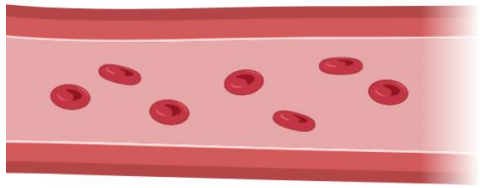
Blood clotting and endothelial abnormalities



Microvascular blood clotting with endothelial dysfunction

Dysbiosis





Portal vein → to the liver

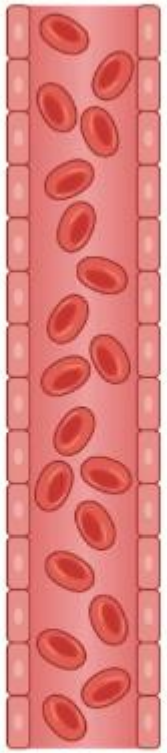
Coagulation proteins produced by the liver - impacted by bacterial products

The intestinal microbiome potentially affects thrombin generation in human subjects - PMC

How does the gut influence blood clotting in Long Covid?

Positive nutrition

Blood clotting and endothelial abnormalities



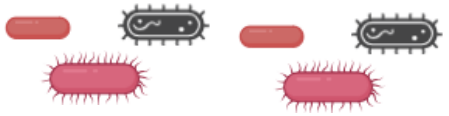
Microvascular blood clotting with endothelial dysfunction

Fusbacterium nucleatum

E coli

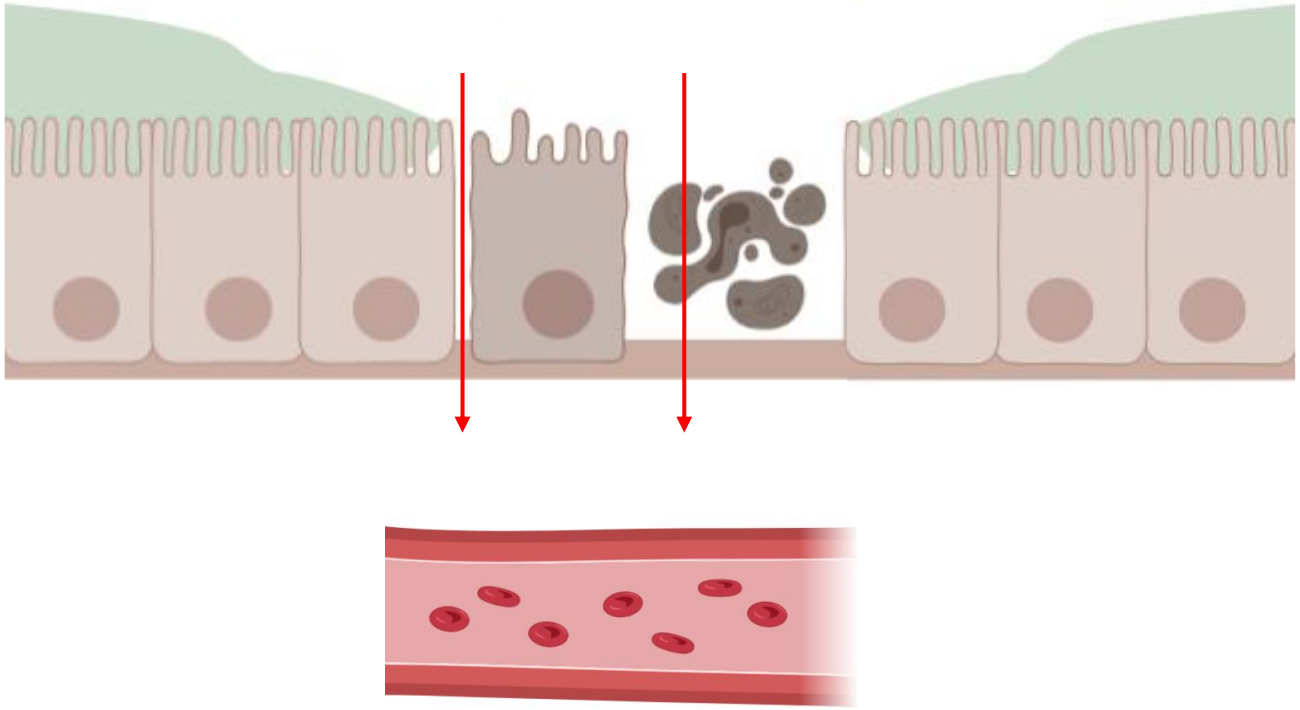
Ruminococcus gnavus

Dysbiosis



Enterococcus faecium, Streptococcus thermophilus **– association with platelet abnormalities**

Enterobacteriaceae, *Enterobacterales*, and *Gammaproteobacteria* - **association with abnormal clotting tests**



Portal vein → to the liver

Gut microbiome alterations in patients with COVID-19-related coagulopathy | Annals of Hematology

Gut-brain axis

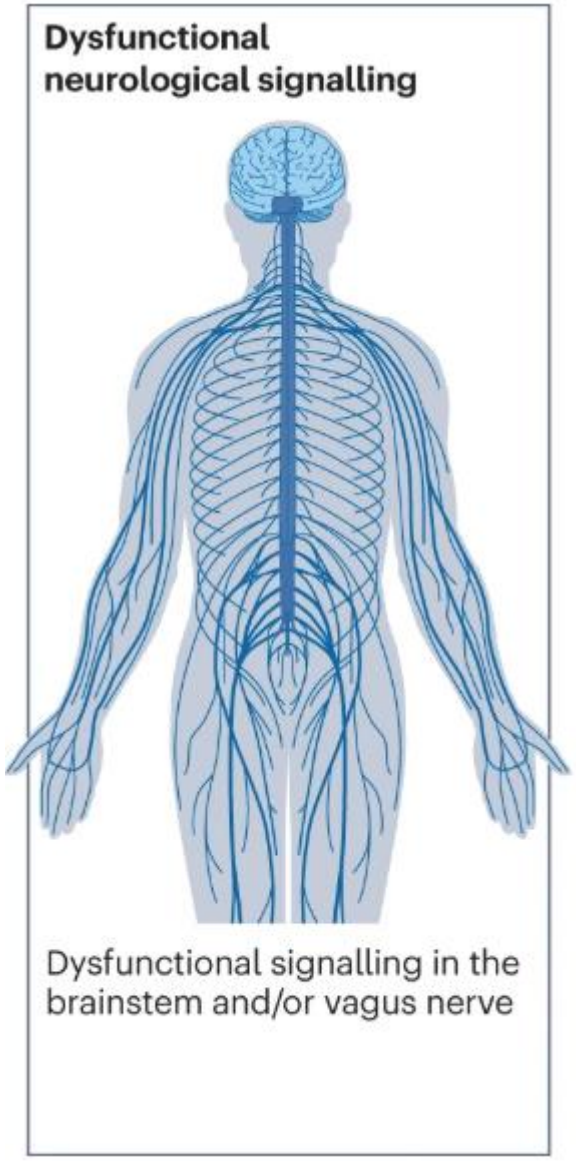
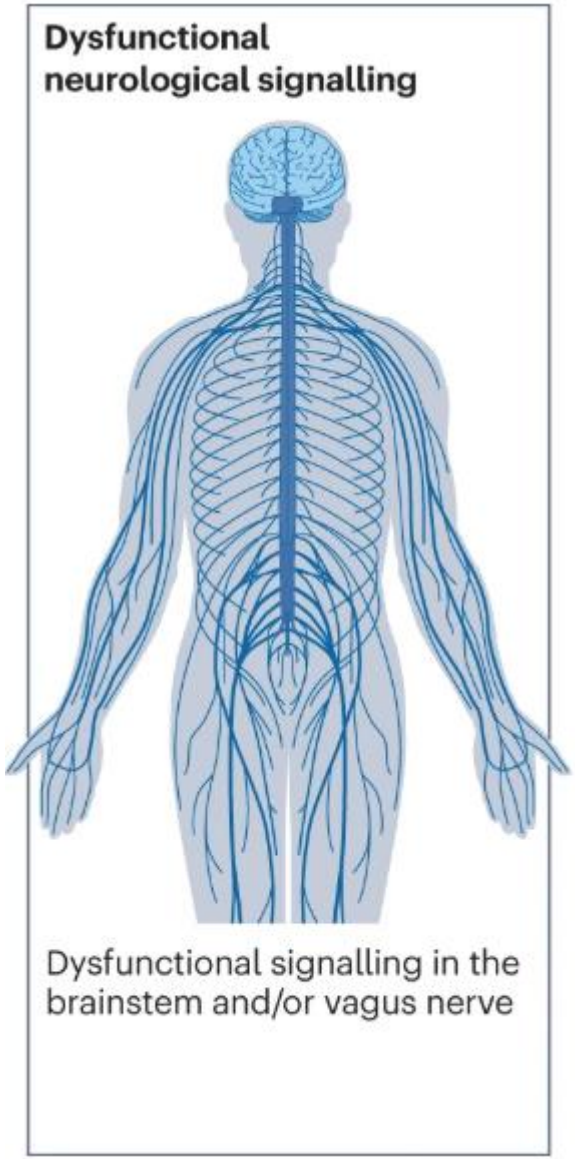


Fig. 3: Hypothesized mechanisms of long COVID pathogenesis. | Nature Reviews Microbiology

Gut-brain axis



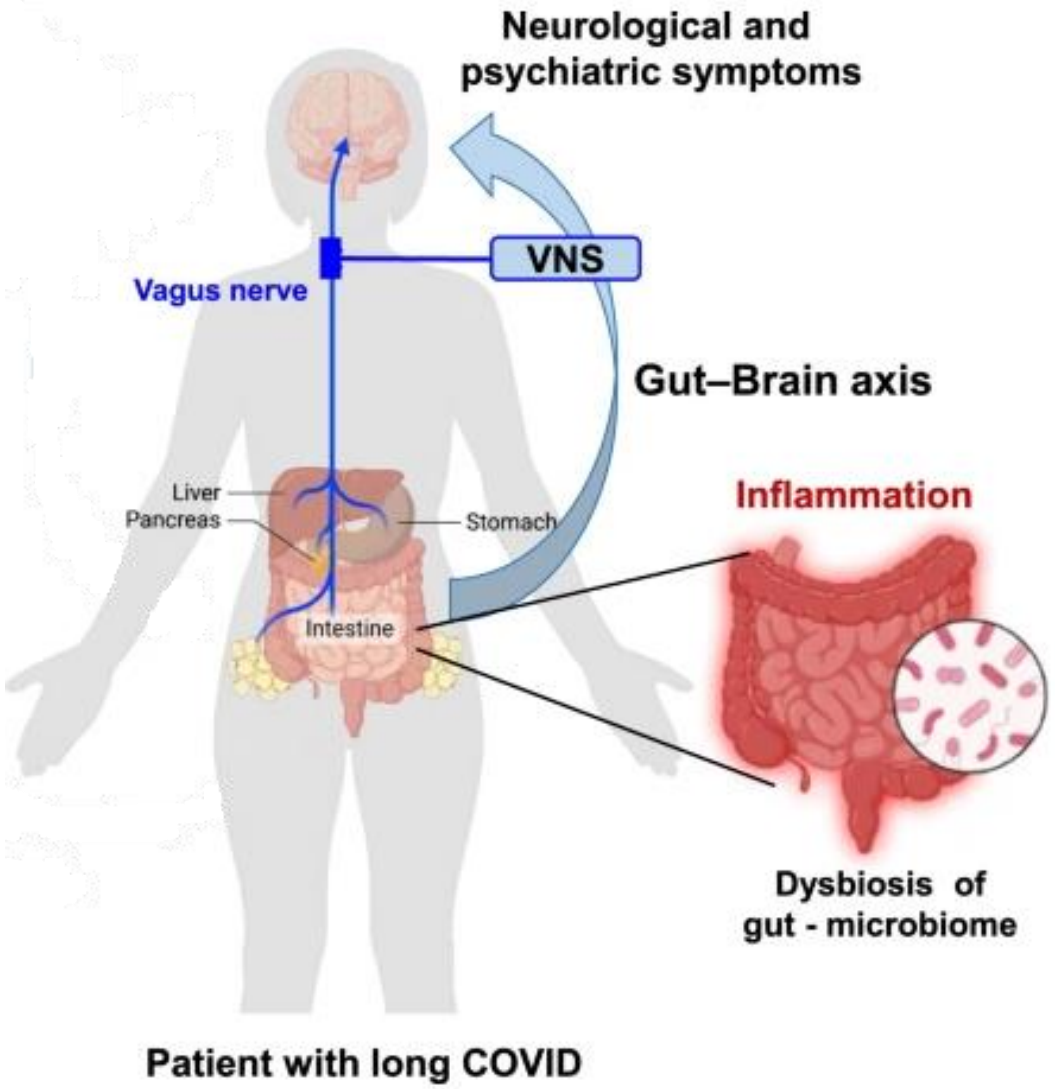


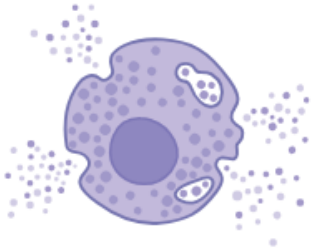
Image adapted from:
Detrimental effects of COVID-19 in the brain and therapeutic options for long COVID: The role of Epstein–Barr virus and the gut–brain axis | Molecular Psychiatry

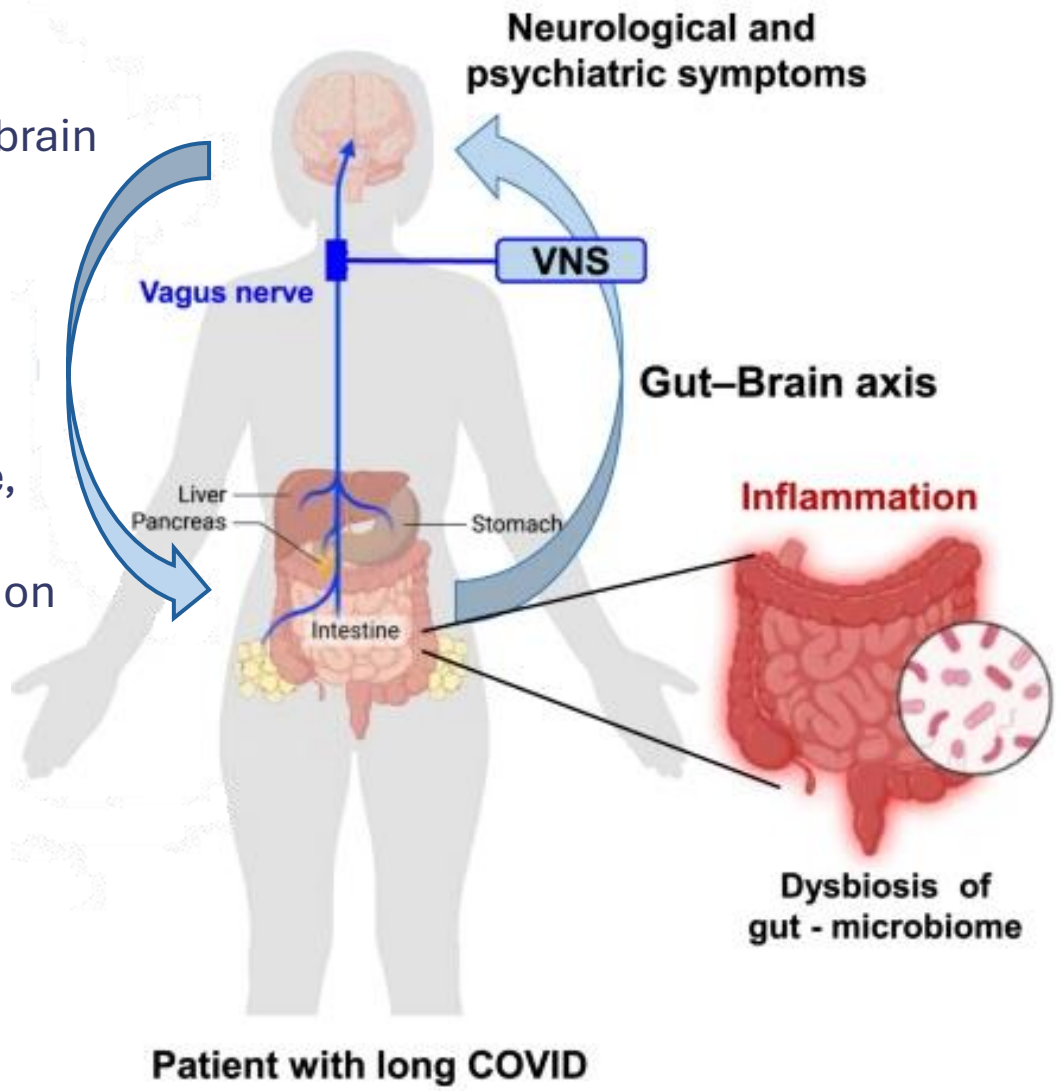
Gut-brain axis

Positive nutrition

Neuroinflammation, oxygen reduction in brain

Increased histamine, damage to gut and systemic inflammation



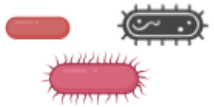


Stabilizing histamine release in gut mast cells mitigates peripheral and central inflammation after stroke | Journal of Neuroinflammation | Full Text

Aims of a gut repair protocol

Positive nutrition

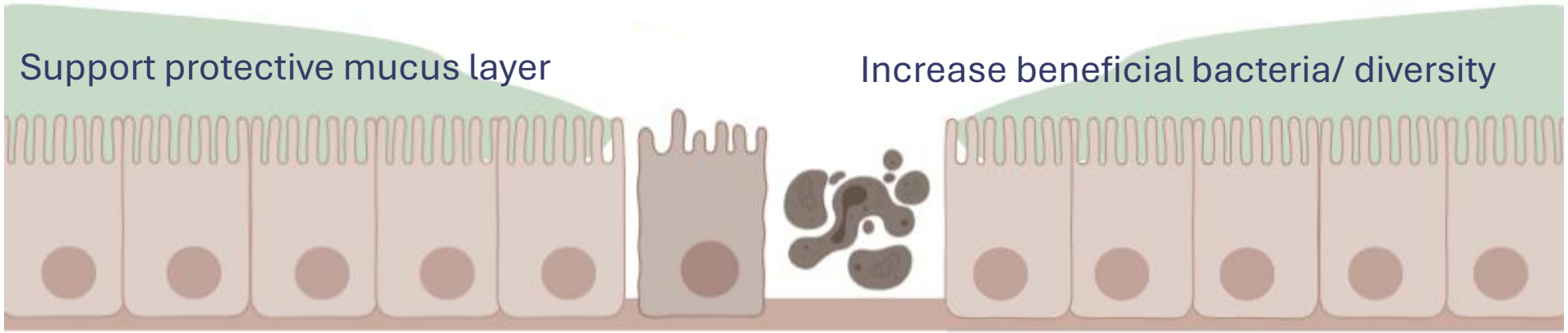
Decrease Dysbiosis



Improve immune defences and decrease inflammation

Support protective mucus layer

Increase beneficial bacteria/ diversity



Repair leaky gut

→ Reduce triggers for inflammation, immune dysfunction and/ or autoimmunity

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Stool Tests

Markers of gut health, inflammation and leaky gut

- Leaky gut marker e.g. zonulin
- Immune markers e.g. sIgA, bet defensin, lactoferrin, calprotectin

Microbiome

- Bacterial strains by PCR/ 16s analysis
- Also ideally including yeasts/ candida and parasites

Other

- Digestive markers e.g. reduced digestive enzyme production, bile acids
- SIBO by breath test

GI 360

Dietary Changes

Reduce	Increase	Tips and swaps
Inflammatory oils and fats	Omega-3	Tinned fish e.g. salmon, mackerel Reduce processed foods Avoiding cooking with seed oils
Sugar	Fibre and polyphenols	Swap white bread and pasta for wholegrain Reduce portions sizes Or avoid ‘carbs’ for some people Maintain vegetables, fruits, diversity Pulses as tolerated (histamine/ SIBO)
Gluten	Gluten free or Non-grain fibres	Buckwheat, quinoa Grains such as oats or rice

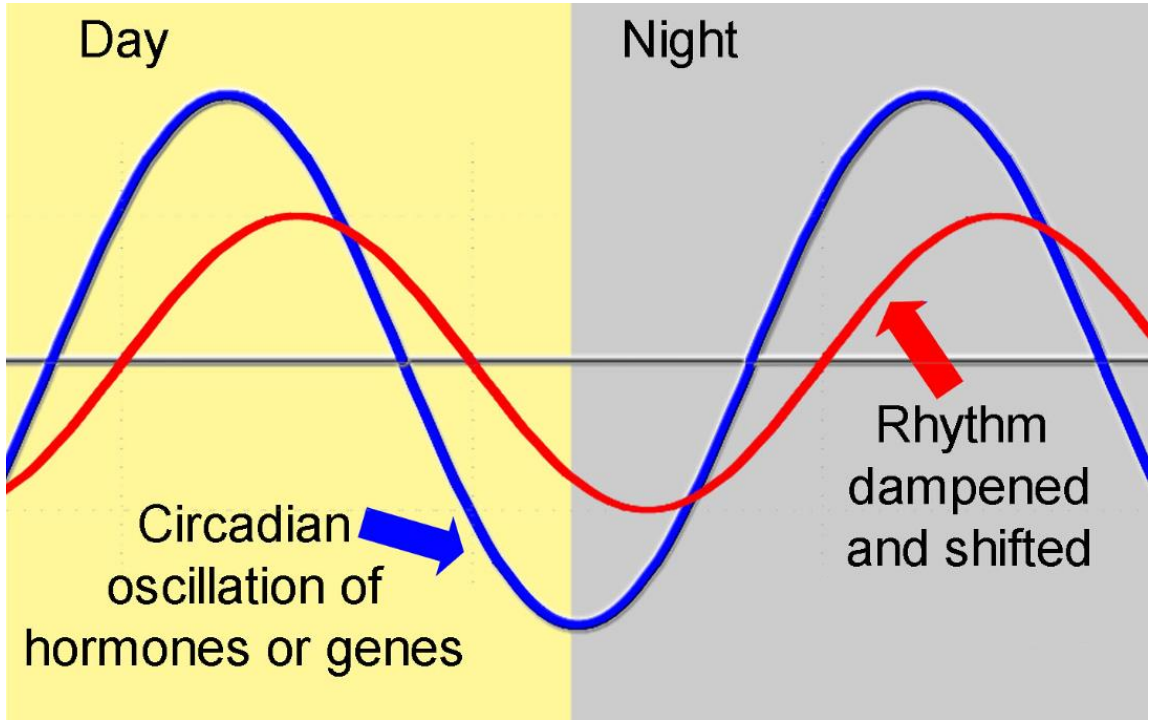
Trialling a low histamine diet

Positive nutrition

Avoid	Include	Tips and swaps
Aged or preserved or tinned meats, cheese and fish Avoid shellfish Most beans and pulses	Fresh meat, fish, chicken, eggs Fresh dairy products Most grains	Freeze cooked food immediately in small batches for defrosting on the day of eating Freeze meat and fish on day of purchase if not cooking straight away
High histamine fruits & vegetables: Strawberries, avocado, banana, spinach, aubergine, tomato Avoid pickled or fermented vegetables, dried fruit	Fresh fruit & vegetables	Swap spinach for kale Swap strawberries for any other berry Try sauces based on coconut milk as a base instead of tomato
Cacao, alcohol	Caffeine free herbal teas	If you are consuming alcohol (or other triggers) take charcoal alongside to absorb excess

Source: histamineintolerance.org.uk

Lifestyle – the circadian rhythm



Sleep disruption ↓ *Diversity*
Lactobacillus, Bifidobacteria, Akkermansia, Faecilabacterium

Sleep Deprivation and Gut Microbiota Dysbiosis: Current Understandings and Implications - PMC

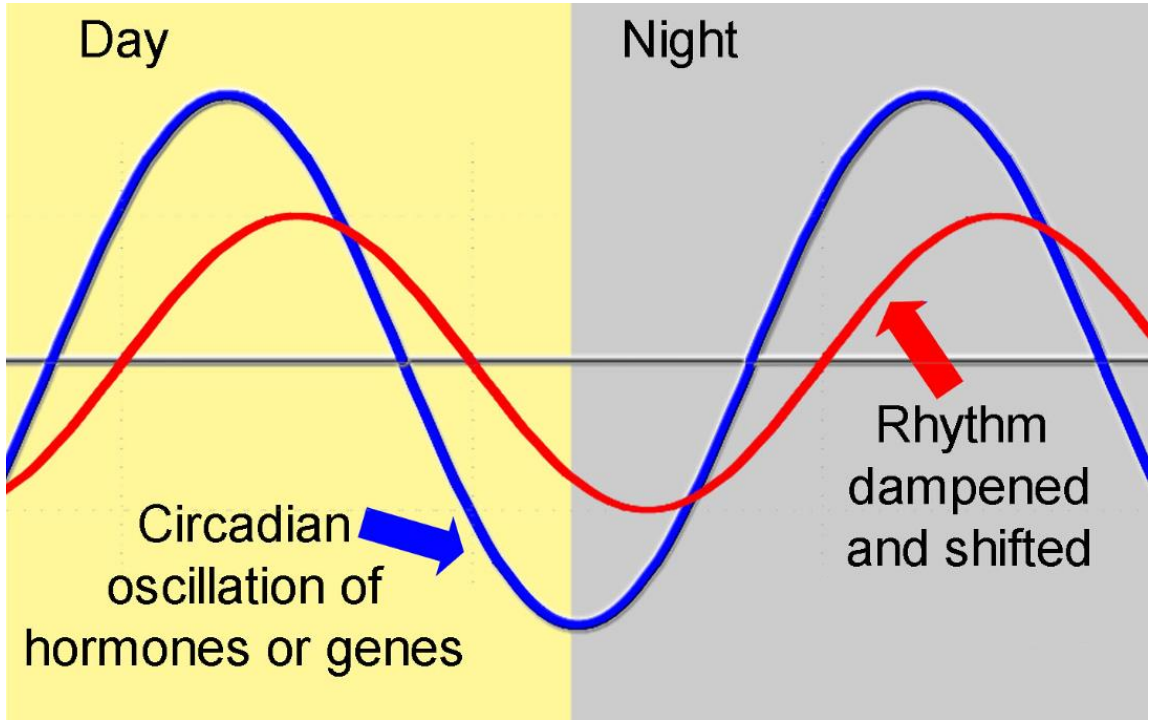
Stress ↑ *Mast cell activation*
Leaky gut

Psychological stress and corticotropin-releasing hormone increase intestinal permeability in humans by a mast cell-dependent mechanism - PubMed

The possibility of circadian rhythm disruption in long COVID – PMC

Circadian rhythm disruption in Myalgic Encephalomyelitis/Chronic Fatigue Syndrome: Implications for the post-acute sequelae of COVID-19 - PMC

Lifestyle – the circadian rhythm



Maintain day/ night rhythm

- Early morning light to help phase shift
- Any daylight exposure vs darkness at night
- Limit screens and blue light 2 hours before bed

- Regular eating pattern

- Meditation, yoga nidra
- Nerva App

Possible Roles of Cyclic Meditation in Regulation of the Gut-Brain Axis – PMC

Smartphone app-delivered gut-directed hypnotherapy improves symptoms of self-reported irritable bowel syndrome: A retrospective evaluation - PubMed

Supplements – with caution

Positive nutrition

Supplement	Examples	Diet
Probiotics	VSL#3 Biokult multi strains L reuteri, L Rhamnosus GG	Fermented foods e.g. kefir, sauerkraut, kimchi (stronger) miso and kombucha (milder) *caution* with histamine issues/ MACS
Prebiotics	PHGG GOS FOS Inulin	Wholegrains, buckwheat, pulses, flaxseeds as tolerated Onions, garlic (high FODMAP) Apples, pears (stewed) Resistant starches (re-heated potato, rice, pasta)
Polyphenols	Curcumin Resveratrol EGCG Pomegranate extract Grape seed extract	Brightly coloured foods and lots of spices Berries, pomegranate, acai Dark greens Walnuts Green tea, Extra virgin olive oil

Supplements – with caution

Supplement	Examples	Diet
Anti-inflammatory	Reishi, Lion's mane etc Vitamin D Omega-3 Lactoferrin Curcumin Boswellia	Oily fish Turmeric, ginger, garlic Mushrooms – whatever us available
Leaky gut	Zinc carnosine L-glutamine (can be trigger) Marshmallow, slippery elm NAG	Protein Bone broth (short stew if reducing histamine)
Anti-microbials	Allicin Oregano oil, thyme, clove Grapefruit seed extract Caprylic acid Artemisia Berberine (strong)	Garlic, ginger, thyme, oregano

Sample Case

Patient Background

Long Covid 1.5yrs - extreme fatigue, cognitive dysfunction, PEM, ‘moderate’ i.e. housebound

POTS diagnosis

Histamine – caused issues with thermoregulation, heart rate spikes, sleep disruption, cognitive dysfunction, greater sensitivity to noise/ light and headaches

<u>History of gut issues:</u>

Mild autoimmune activity – mild psoriasis

Gut issues e.g. bloating, reflux, likely gluten intolerance

Sample Case

Beta Defensin 2	4ng/g	NORMAL	<68ng/g
Secretory IgA	11ug/g	NORMAL	<188ug/g

Low immune defences

Inflammation	**RESULTS:**		**RANGE:**
Calprotectin	43.0ug/g	NORMAL	<100ug/g

Mild inflammation

Digestion	**RESULTS:**		**RANGE:**
Bile Acids	425umol/L	NORMAL	<3477umol/L
Pancreatic Elastase	245ug/g	NORMAL	>200ug/g

Reduced digestive capacity

Other	**RESULTS:**		**RANGE:**
FIT (Occult Blood)	0.0ug/g	NORMAL	<10ug/g
Zonulin	17ng/g	NORMAL	<100ng/g

Zonulin detected

Sample Case

Commensal Bacteria	RESULTS:		0 - 4 / 5 - 8 / 9 - 12 / 13 - 16 / 17 - 20	RANGE:
Akkermansia muciniphila	11.6	HIGH		1.7-7.1
Anaerostipes caccae	6.0			3.0-7.3
Bacteroides spp.	16.3			14.8-17.5
Bifidobacterium spp.	11.0			7.3-16.3
Blautia obeum	15.9			15.5-17.9
Coprococcus eutactus	<DL	LOW		10.4-16.5
Escherichia coli	12.9	HIGH		4.5-12.0
Eubacterium rectale	10.8			7.7-14.8
Faecalibacterium prausnitzii	14.4			14.2-18.3
Lactobacillus spp.	12.9	HIGH		2.7-8.9
Roseburia homini	13.9	HIGH		5.7-10.2
Ruminococcus bromii	14.5			14.2-17.7
Subdoligranulum variabile	8.9			6.3-12.5

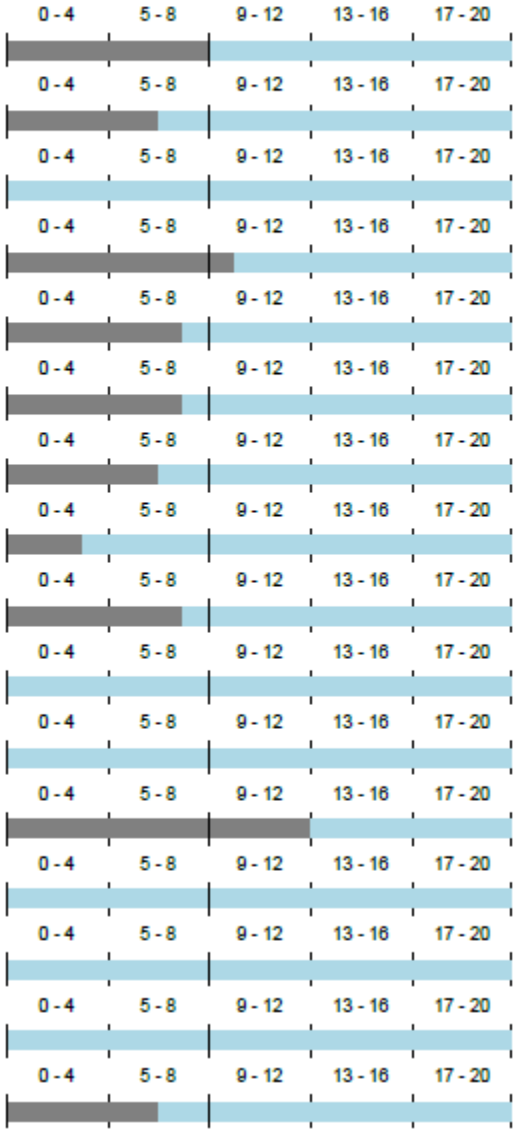
Positive nutrition

High levels of beneficial bacteria

Elevated Akkermansia, Lactobacillus

Sample Case

Gram Negative (-) Bacteria	RESULTS:		RANGE:
Bilophila wadsworthia	8.4		2.4-9.5
Citrobacter freundii	6.3	HIGH	<1.0
Citrobacter koseri	<DL		<DL
Desulfovibrio spp.	9.1	HIGH	<6.9
Enterobacter cloacae	7	HIGH	<2.8
Fusobacterium nucleatum	7.3	HIGH	<2.8
Hafnia alvei	6		0.8-9.0
Klebsiella oxytoca	3.1	HIGH	<1.5
Klebsiella pneumoniae	7.1	HIGH	<2.5
Morganella morganii	<DL		<0.5
Oxalobacter formigenes	<DL		<1.6
Prevotella copri	12.5	HIGH	<11.4
Proteus mirabilis	<DL		<0.4
Pseudomonas aeruginosa	<DL		<0.7
Serratia marcescens	<DL		<0.4
Veillonella spp.	6		4.0-10.0



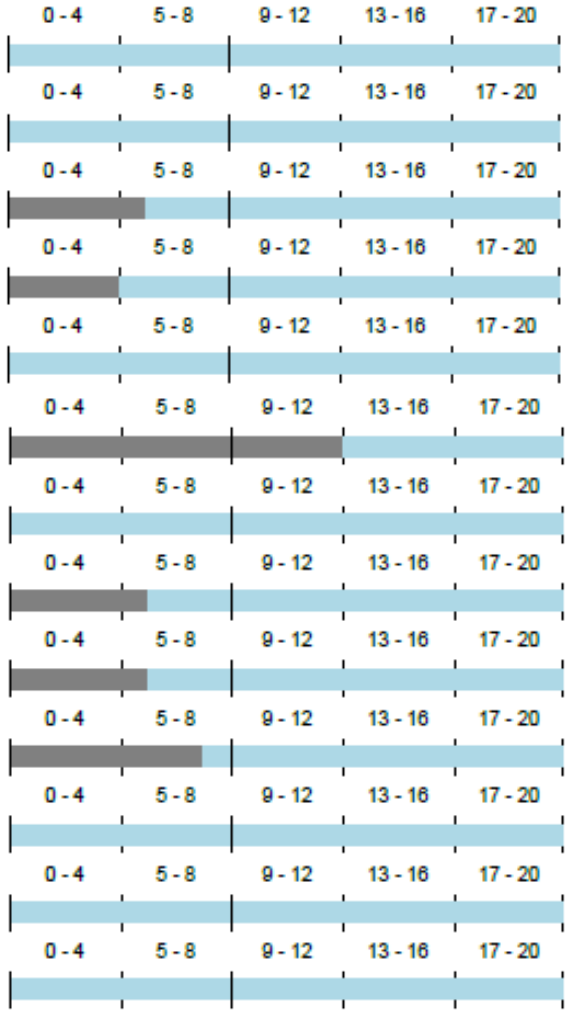
Positive nutrition

Significant dysbiosis and overgrowth

Enterobacter
Fusobacterium nucleatum
Autoimmune triggers
Histamine producing strains

Sample Case

Gram Positive (+) Bacteria	RESULTS:		RANGE:
Clostridium perfringens	<DL		<4.0
Clostridium sporogenes	<DL		<DL
Enterococcus faecalis	5.1	HIGH	<3.0
Enterococcus faecium	3.5	HIGH	<2.6
Enterococcus gallinarum	<DL		<0.9
Methanobrevibacter smithii	12.3	HIGH	<8.3
Mycobacterium avium	<DL		<0.2
Ruminococcus gnavus	5.0		4.1-10.7
Ruminococcus torques	5.4	HIGH	<2.3
Staphylococcus aureus	7.2	HIGH	<3.5
Streptococcus agalactiae	<DL		<0.9
Streptococcus pneumoniae	<DL		<0.1
Streptococcus pyogenes	<DL		<DL



Positive nutrition

Significant dysbiosis and overgrowth

Entercoccus
Ruminococcus
Damaging to mucus layer

Sample Case

Positive nutrition

Protocol

Diet - lower histamine, gluten free (provided by carer, limited changes)

More reliance on supplements - digestive enzymes, leaky gut repair, anti-inflammatory, anti-microbial

Medications - Nasal sodium cromolyn

Sample Case

Positive nutrition

Protocol

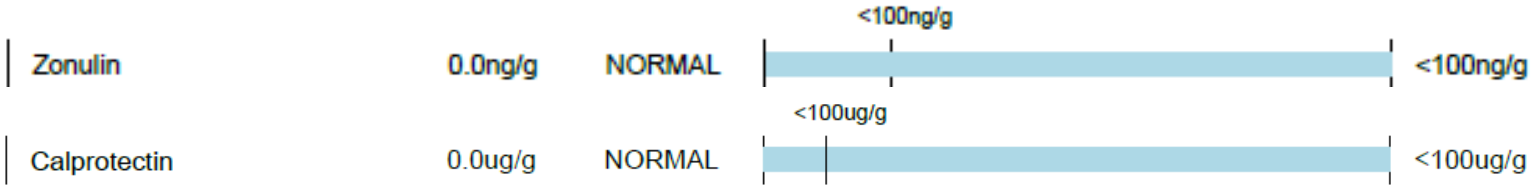
Diet – lower histamine, gluten free (provided by carer, limited changes)

More reliance on supplements - digestive enzymes, leaky gut repair, anti-inflammatory, stronger anti-microbial

Medications - Nasal sodium cromolyn

Outcome

Repeat test showed much improved markers and much improved microbiome



Patient symptoms - Much reduced food/ histamine reactions and sensitivities, safe re-introduction of foods

Positive nutrition

www.positivenutrition.ie

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