

Lipopoly-what?!

LPS and the Gut Barrier

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Overview

- Meet the Team
- The LPS Story (Setting the Scene)
- Structure and function of LPS
- LPS and the Gut Barrier
- Metabolic Endotoxaemia & Systemic Effects
- Testing the Gut Barrier
- Special Offer
- Thank You!



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Meet the Team



Charlotte Hunter
Head of KBMO UK



Linette Petrillo
Customer Services



Kelly Hutson
Events & Sales



Clare Kennedy
Operations Manager



Natasha Khan
Sales



Emily Birch
Clinical Support & Communications



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The LPS Story Setting the Scene



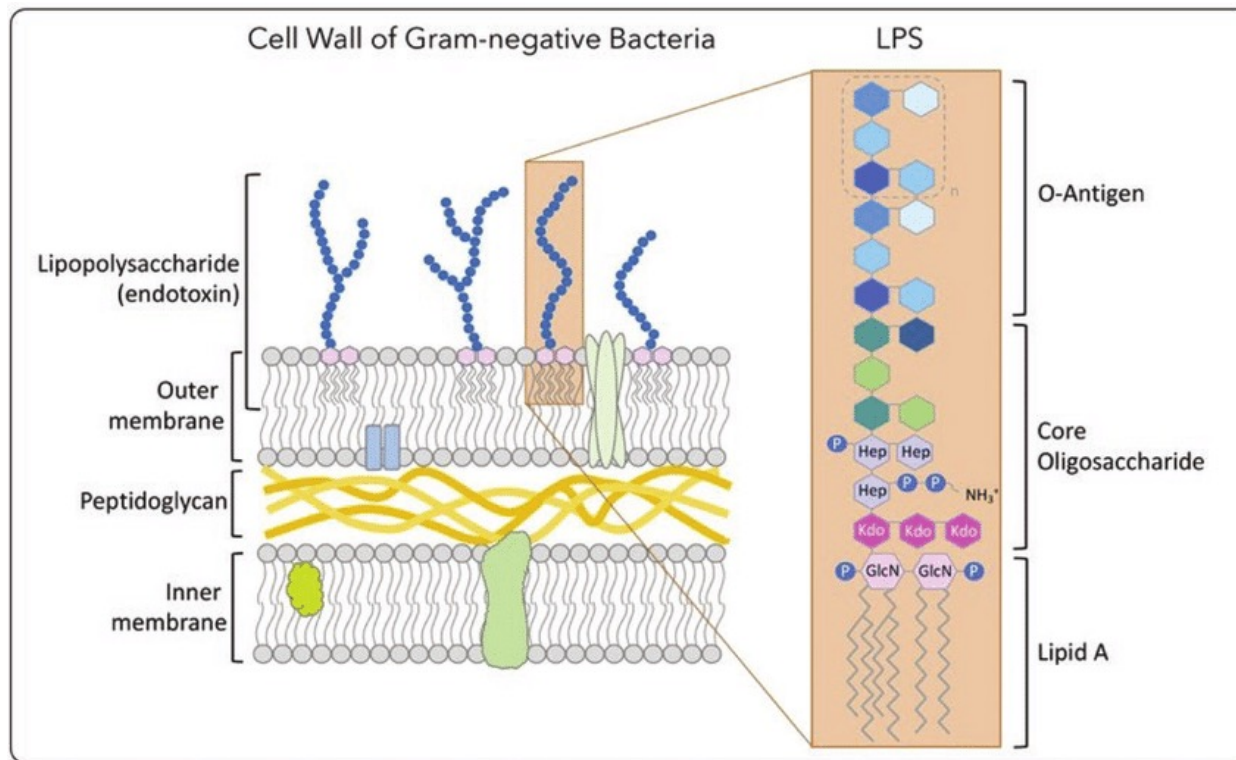
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A Brief History of LPS

- 1888: fever seen after injection of killed bacteria → a bacterial toxin suspected
- 1892: Richard Pfeiffer names it “endotoxin” (from *Vibrio cholerae*)
- Early 1900s: Centanni isolates it → heat-stable, not a protein
- 1930s-40s: Boivin & Mesrobianu show it is sugar + lipid → the term lipopolysaccharide (LPS)
- 1952: Westphal & Lüderitz develop extraction → opens the door to LPS research
- 1980s: Lipid A identified as the biologically active “endotoxic” part
- 1998: TLR4 recognised as the immune receptor for LPS



What are Lipopolysaccharides (LPS)?



- A large molecule made of fat + sugar
- Found on the outer membrane of Gram-negative bacteria
- 3 parts: Lipid A, Core oligosaccharide, O-antigen
- Lipid A is the toxic component recognised by the immune system
- Acts as both a structural shield for bacteria and an immune signal for the host

Why is LPS so Interesting?

- LPS plays a dual role → vital for bacteria, challenging for humans
- Acts as a Microbe-Associated Molecular Pattern (MAMP) triggering immunity
- Key to bacterial survival → gives structure, protection, and resistance
- In humans, it can drive inflammation or sepsis
- Still full of unknowns regarding structure, function, and host interaction

Structure & Function of LPS

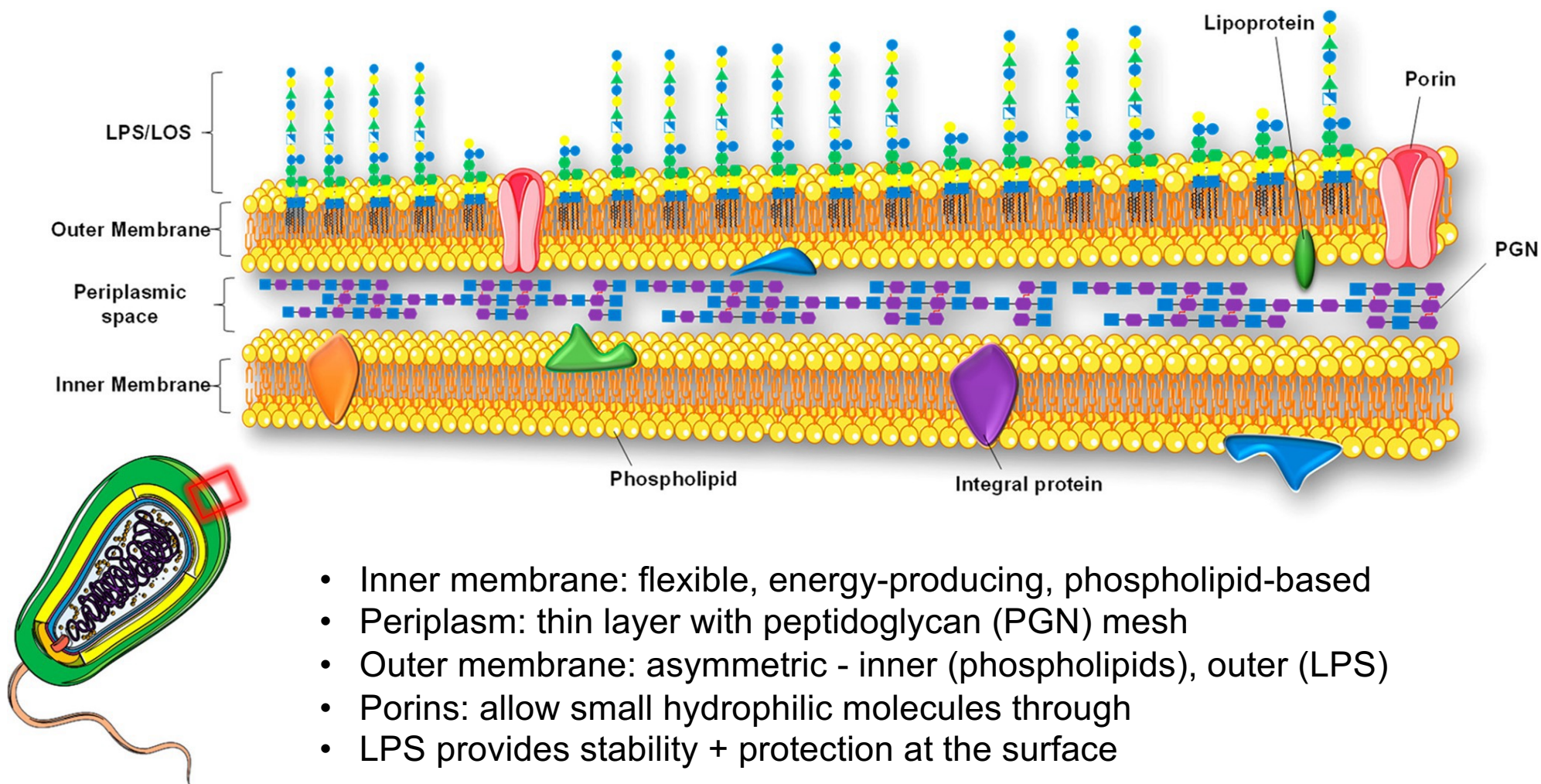


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LPS Acts as a Shield & a Signal

- LPS anchors into the outer membrane of Gram-negative bacteria
- Creates an asymmetric bilayer: inner side = flexible, outer = rigid
- Lipid A forms the anchor; sugars extend outward
- Ionic bonds between phosphate groups and divalent cations add strength
- This structure gives LPS its barrier and defence role





- Inner membrane: flexible, energy-producing, phospholipid-based
- Periplasm: thin layer with peptidoglycan (PGN) mesh
- Outer membrane: asymmetric - inner (phospholipids), outer (LPS)
- Porins: allow small hydrophilic molecules through
- LPS provides stability + protection at the surface

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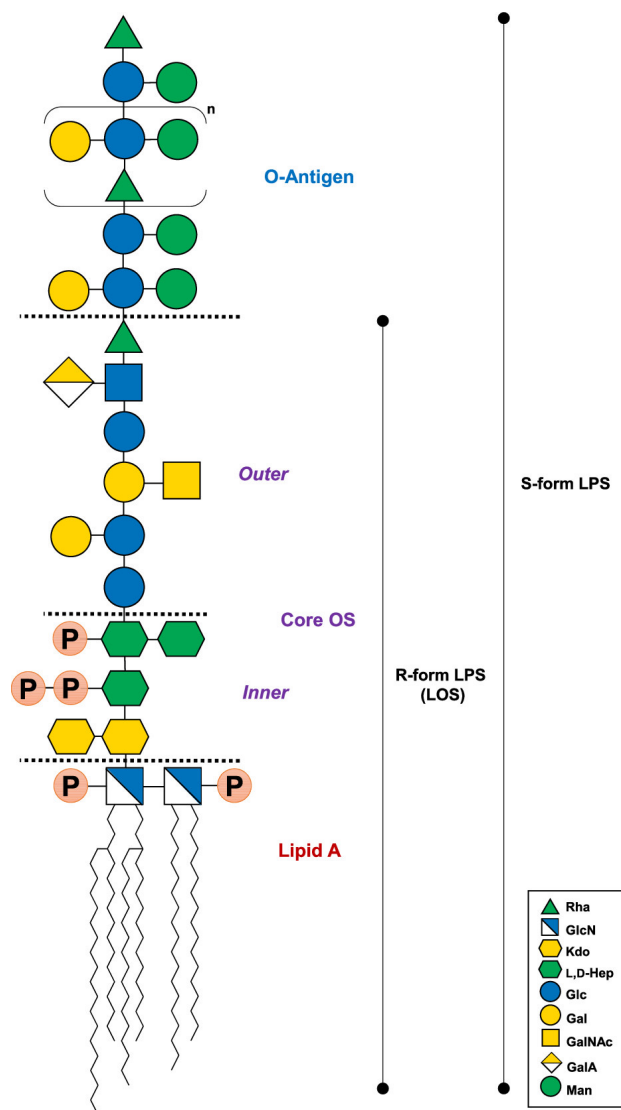


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Structure: Rough vs Smooth

- Gram-negative bacteria show smooth (S-form) or rough (R-form) LPS
- S-form LPS has three parts: (1) Lipid A (anchor, toxic centre), (2) Core oligosaccharide (links anchor to surface sugars), (3) O-antigen (outer polysaccharide chain)
- R-form (LOS) lacks the O-antigen and found in species like *Neisseria* and *Haemophilus*
- These structural differences affect bacterial appearance, immune recognition, and virulence



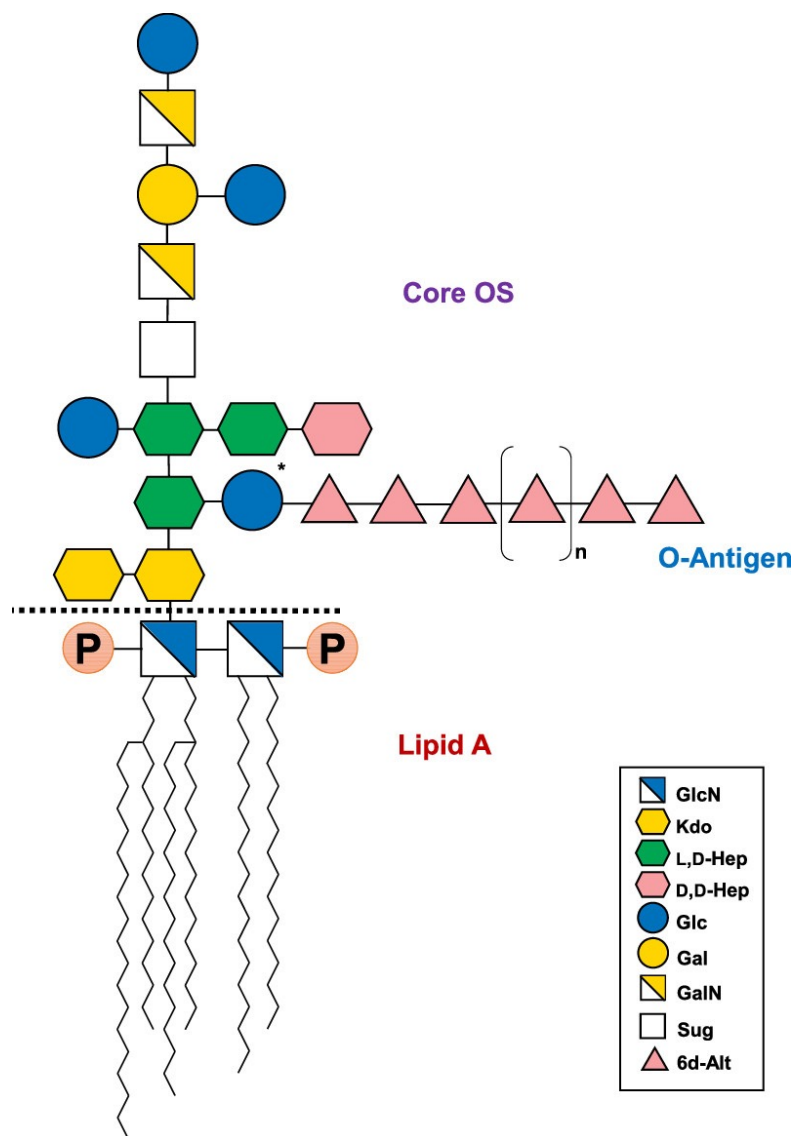


Schematic representation of an LPS molecule

Showing its three main regions.
 Structure depicted for illustration only.
 Zigzag lines represent fatty acid chains of Lipid A.

Variations & Expectations

- LPS structure varies widely between species and strains; some bacteria modify or replace parts of the core with other sugar polymers or capsules
- Others express enterobacterial common antigen (ECA) instead of standard outer sugars
- These variations alter toxicity, immune recognition, and serotype classification
- A few species can even survive without LPS (a surprising discovery!)



Example of an atypical LPS structure

E.g. in some Gram-negative bacteria (e.g. *Yersinia enterocolitica* serotypes O:3 and O:9) where the O-antigen attaches directly to the inner core.



LPS & the Gut Barrier

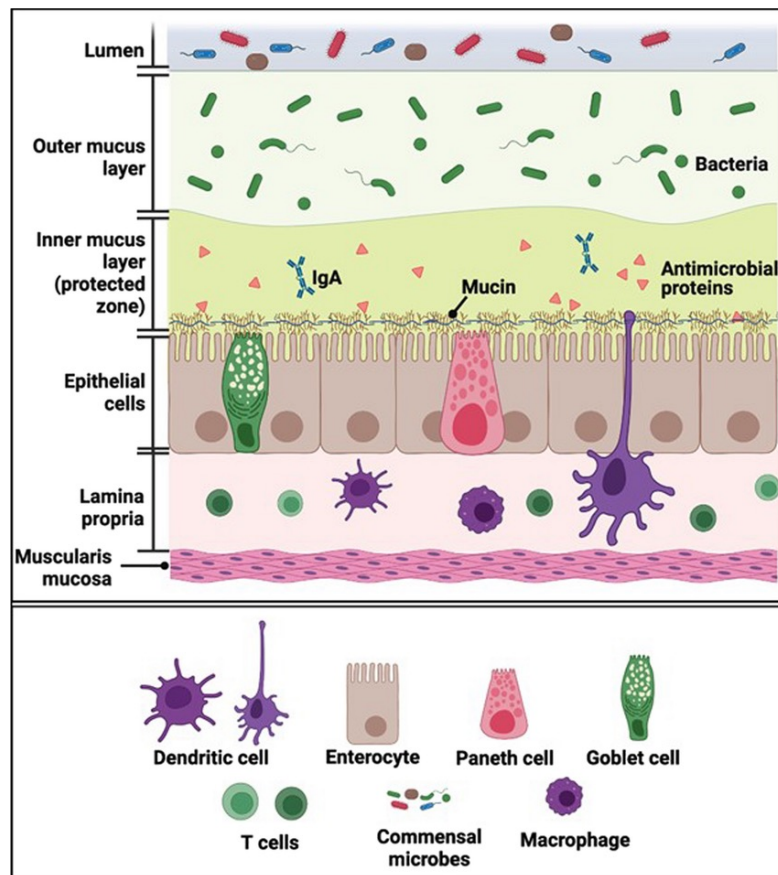


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When we talk about
the gut barrier, we're
not just talking about
one wall of cells, it's a
whole team.

What is the Gut Barrier?



- Three interactive layers protect the intestinal surface
- Luminal layer: commensal microbes block pathogen overgrowth
- Mucus layer: physical + chemical defence with antimicrobial proteins and IgA
- Epithelial layer: selectively permeable → allows nutrients, blocks toxins
- Together they maintain barrier integrity and keep LPS out

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LPS & the Gut Barrier?

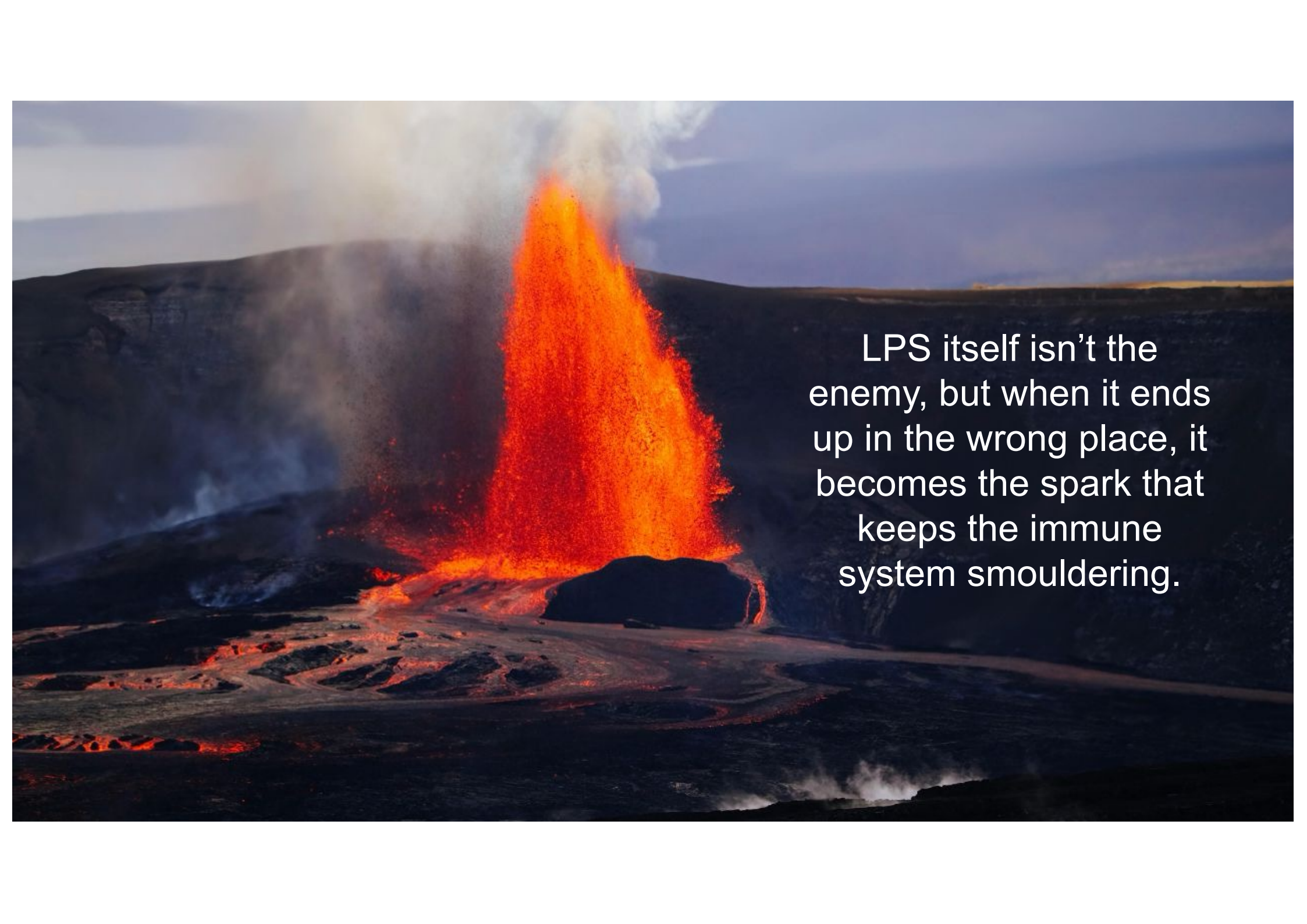
- LPS is meant to stay inside the gut lumen
- A healthy gut barrier keeps it out of circulation
- Stress, infection, dysbiosis, or diet can loosen tight junctions
- LPS can then “translocate” across the barrier
- Triggers immune activation + low-grade inflammation



What Happens When LPS Enters Circulation?

- When LPS crosses the barrier, it enters circulation
- Recognised by immune receptors (mainly TLR4)
- Triggers inflammatory signalling → cytokines, acute-phase response
- Leads to low-grade systemic inflammation
- Chronic exposure linked to metabolic and inflammatory conditions



A dramatic photograph of a volcanic eruption. A massive, bright orange and red plume of lava is being ejected from a dark, rocky crater. The lava flows are visible on the ground around the base of the eruption. The sky is dark and cloudy, with some smoke or ash rising from the crater. The overall scene is one of intense natural power and heat.

LPS itself isn't the enemy, but when it ends up in the wrong place, it becomes the spark that keeps the immune system smouldering.



Endotoxaemia & Systemic Effects



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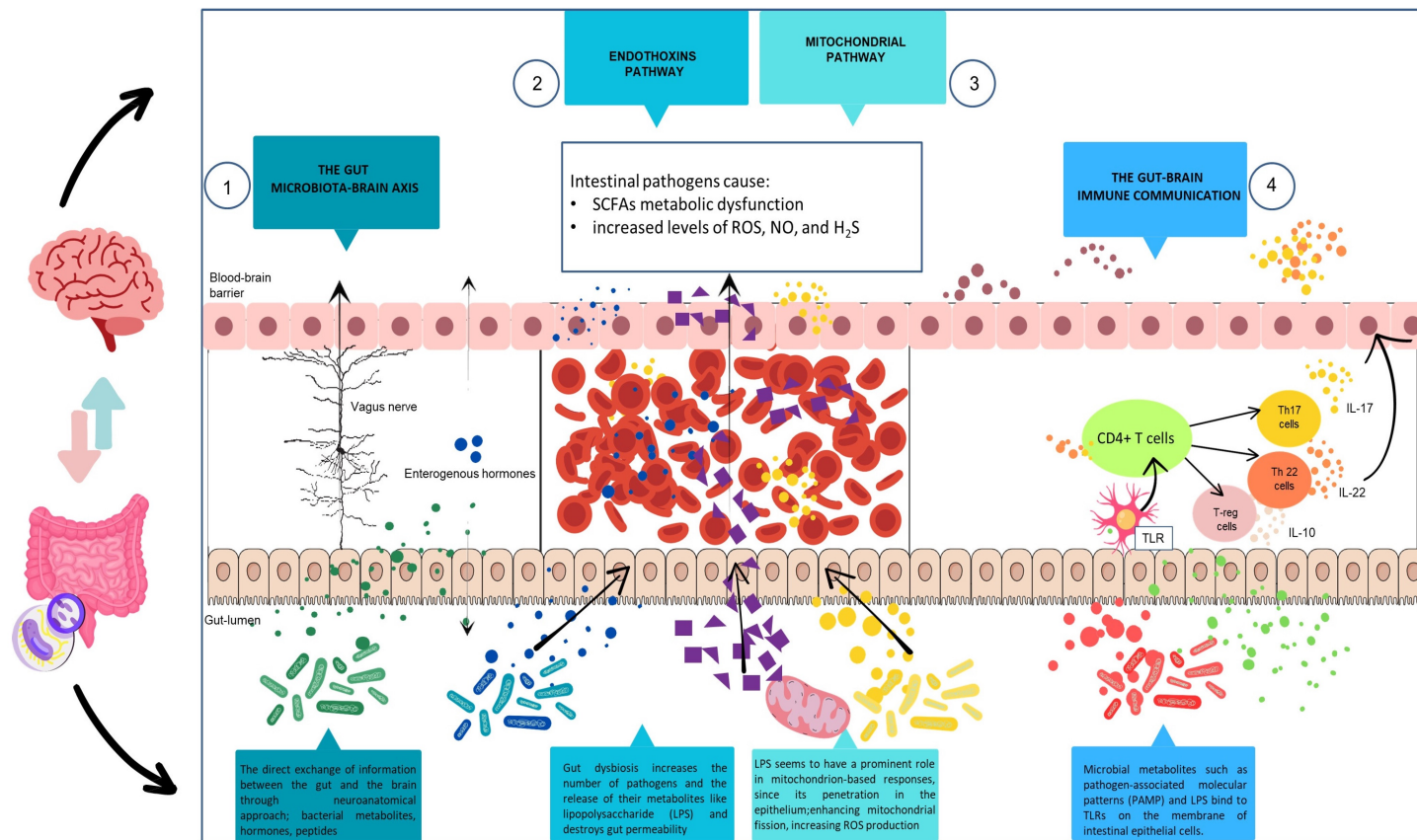
What is Endotoxaemia?

- Endotoxemia = low-grade presence of bacterial LPS in the bloodstream
- Caused by barrier leakage → LPS moves from gut to blood
- Triggers systemic inflammation even without infection
- Linked to metabolic, cardiovascular, skin, and neurodegenerative conditions
- But small, transient rises (e.g. after high-fat meals) are normal



Gut–Brain Communication and Endotoxemia

- LPS and cytokines can influence the brain via multiple routes
- Vagus nerve signalling connects gut and brain directly
- Bloodstream carries inflammatory mediators and LPS
- Blood–brain barrier (BBB) integrity determines CNS exposure
- Chronic endotoxemia may contribute to microglial activation and neurodegeneration

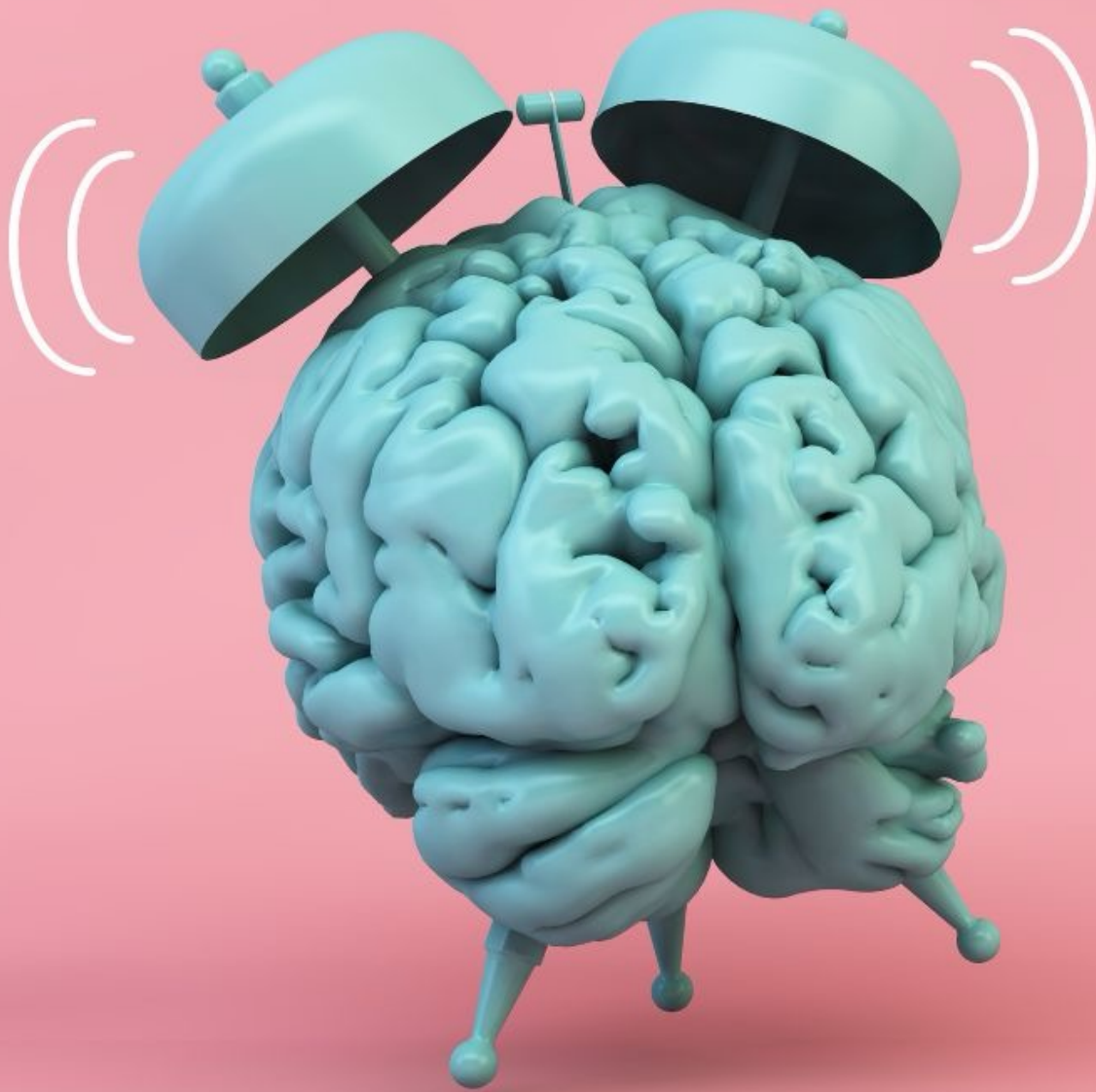


Two-way communication between the gut microbiota and the brain. Dysbiosis and barrier disruption allow bacterial metabolites and endotoxin (LPS) to enter circulation, influencing immune signalling and brain function.

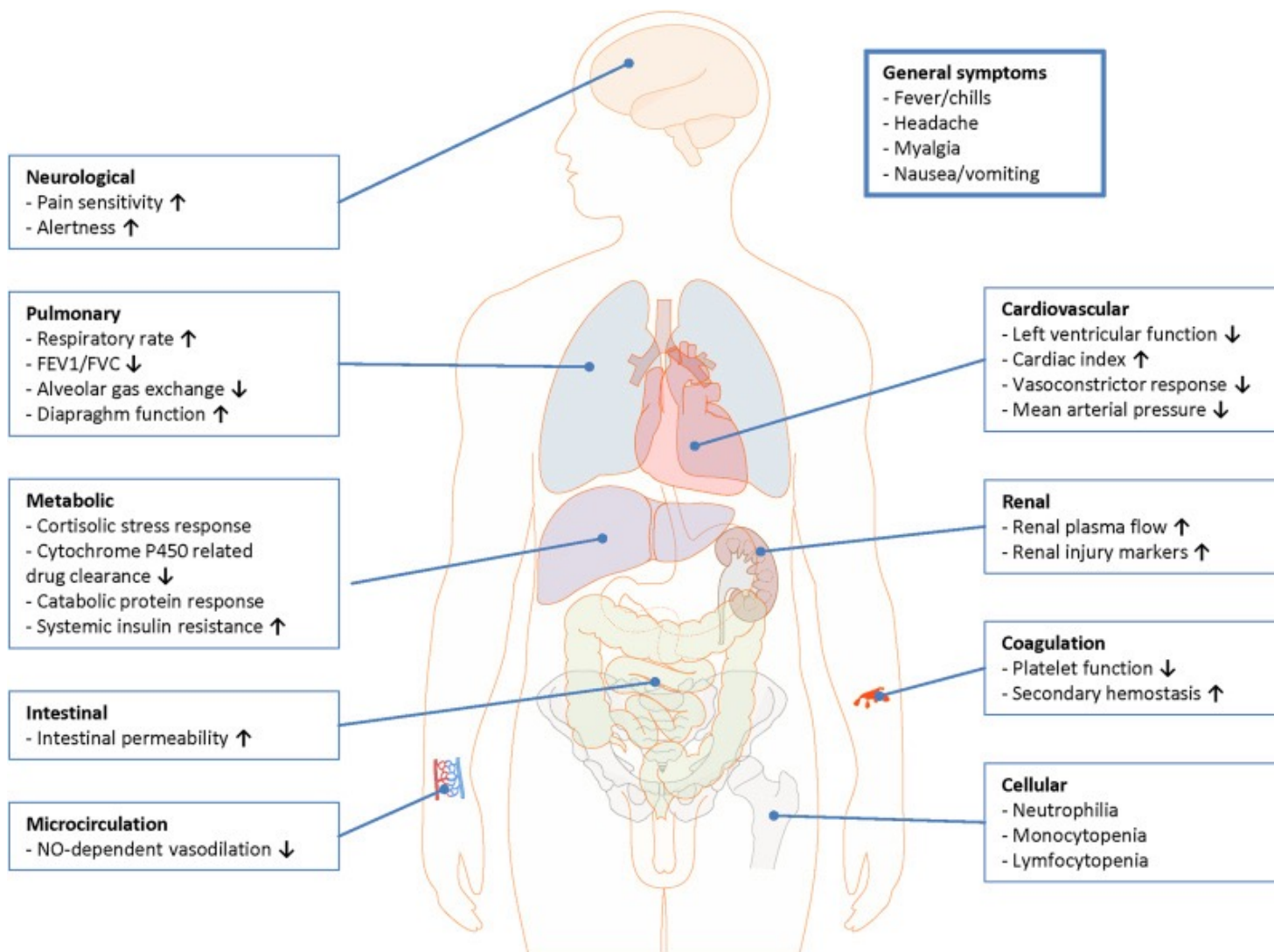
DOI: (10.1016/j.biochi.2018.06.014)



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**When the gut barrier
“leaks” the brain hears
the message loud and
clear!**

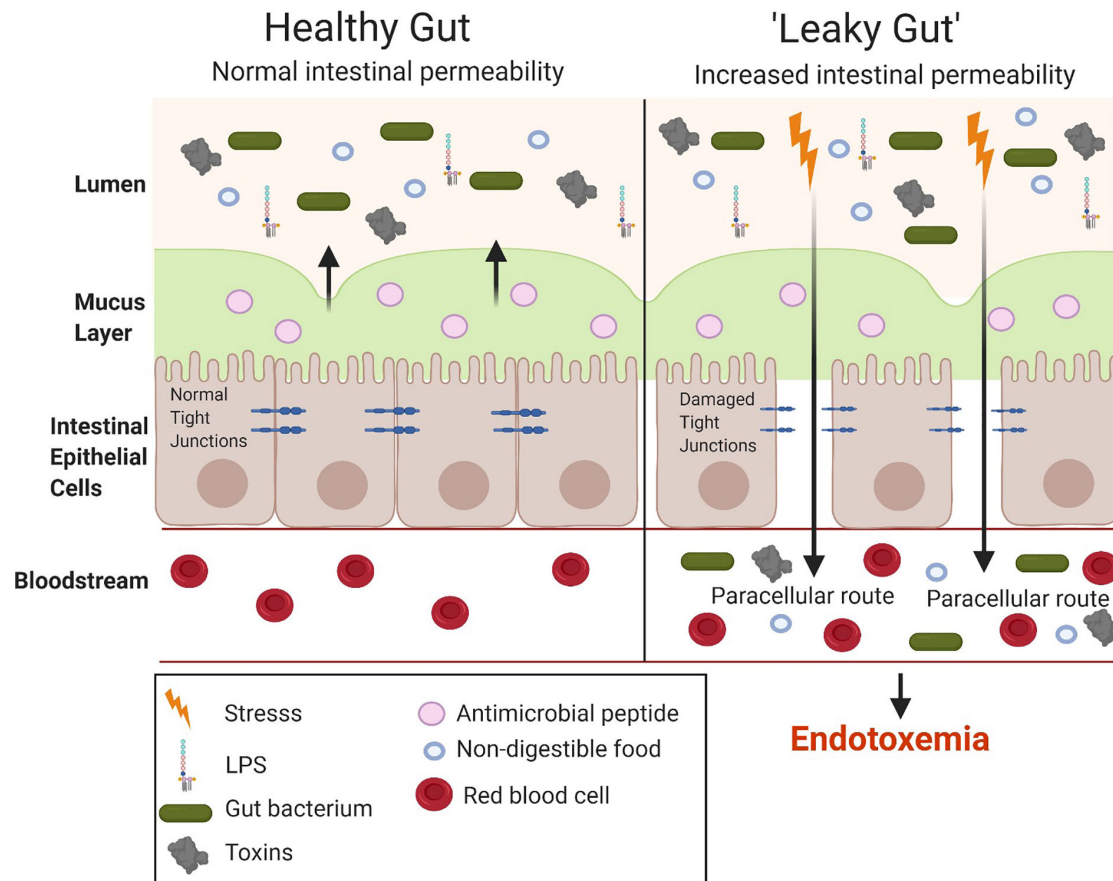


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Why Endotoxaemia Matters in Clinical Practice



- “Leaky gut” (increased permeability → barrier no longer selective)
- Allows passage of LPS, food antigens, toxins, and immune triggers
- Drives low-grade inflammation and immune activation throughout the body
- Often linked with symptoms we see → bloating, fatigue, skin issues, weight changes, brain fog
- Restoring barrier integrity helps reduce systemic inflammation at its source

DOI: (10.3389/fimmu.2020.594150)



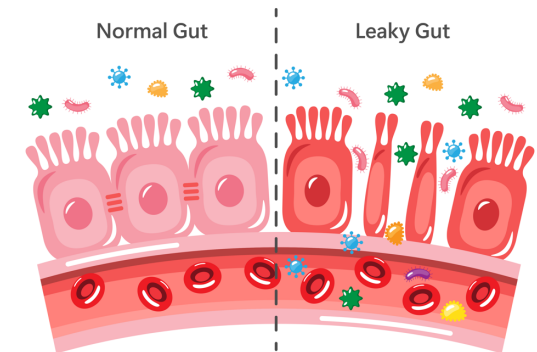
Testing the Gut Barrier



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The Gut Barrier Panel

Gut Barrier Panel						
	IgG1-4+C3d			IgA1-2		
		Cut off			Cut off	
Candida	Negative			Positive		
Zonulin	Negative			Positive		
Occludin	Negative			Negative		
LPS	Negative			Positive		



Our unique Gut Barrier Panel acknowledges that leaky gut occurs across a spectrum and includes the gatekeeper markers: Candida, Zonulin, Occludin and LPS.

For each marker we measure IgG 1-4 / C3d, + IgA 1-2.

Candida

Naturally occurring yeast, residing in the GI tract as part of the normal microbiome. Overgrowth is problematic.

We measure and use any candida overgrowth in the stomach/dysbiosis as a precursor to leaky gut occurrence

Zonulin

A marker of intestinal permeability. We use unique next generation Zonulin IgG antibody screening – a more stable and specific marker, exclusive to KBMO.

Developed by Dr Alessio Fasano & Dr Brent Dorval

Occludin

A marker of intestinal tight junction stabilization and optimal barrier function.

Elevated occludin indicates that the tight junctions between intestinal epithelial cells are breaking down

Lipopolysaccharide (LPS)

Potent endotoxin, present in outer surface membrane of gram-negative bacteria - many of which are pathogenic.

Major inducer of inflammatory response - triggers inflammatory cytokine release, can create direct epithelial damage in the gut, crosses the blood brain barrier.



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Zonulin

- Format: ELISA assay (serum or blood spot), same method used in Dr Fasano's studies.
- Measures: antibodies to zonulin, not stool protein
- Partnership: Dr Alessio Fasano (discovered zonulin) collaborated with KBMO
- Developer: Dr Brent Dorval, creator of the first rapid HIV diagnostic

A metal bucket with a handle is shown against a bright blue sky with wispy white clouds. The bucket has several small holes near its base, from which multiple streams of water are leaking out, creating a spray. The bucket is positioned on the left side of the frame.

“All disease begins in the
(leaky) gut”

Dr Alessio Fasano, MD



The FIT Test



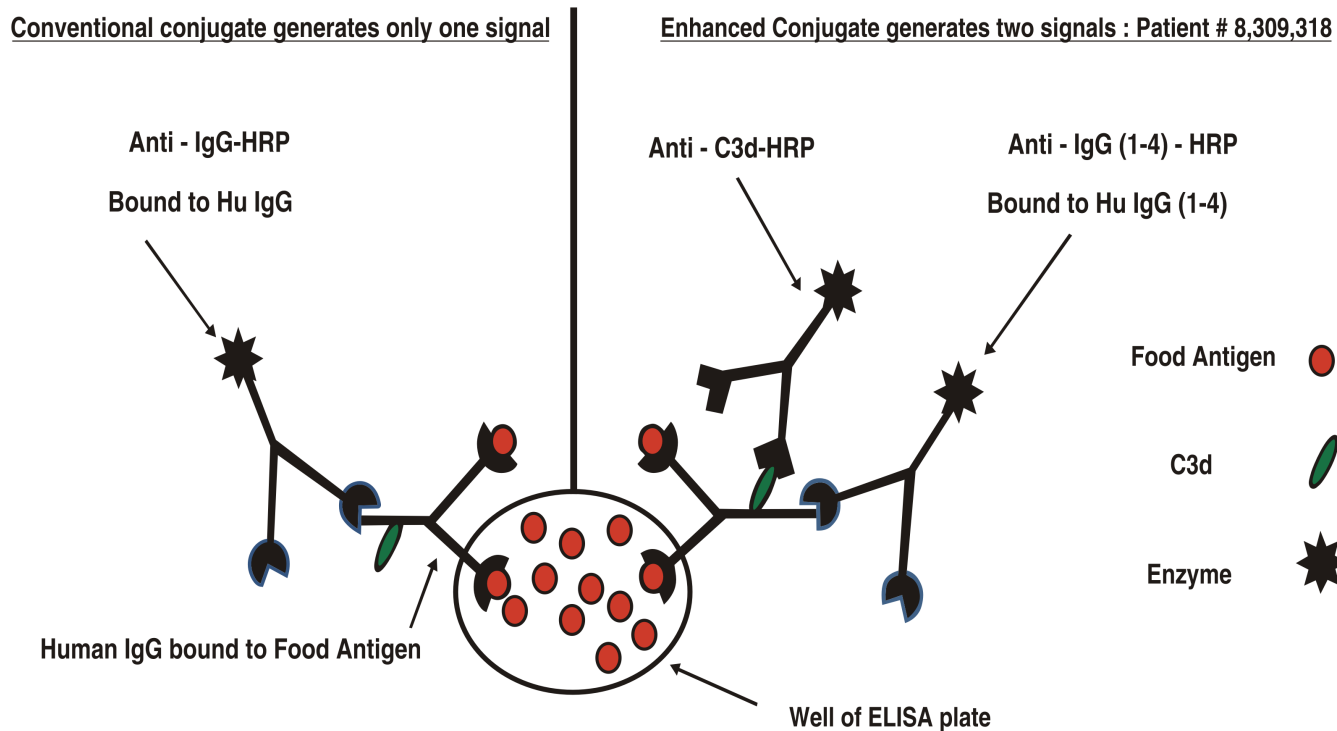
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The Food Inflammation Test (FIT)



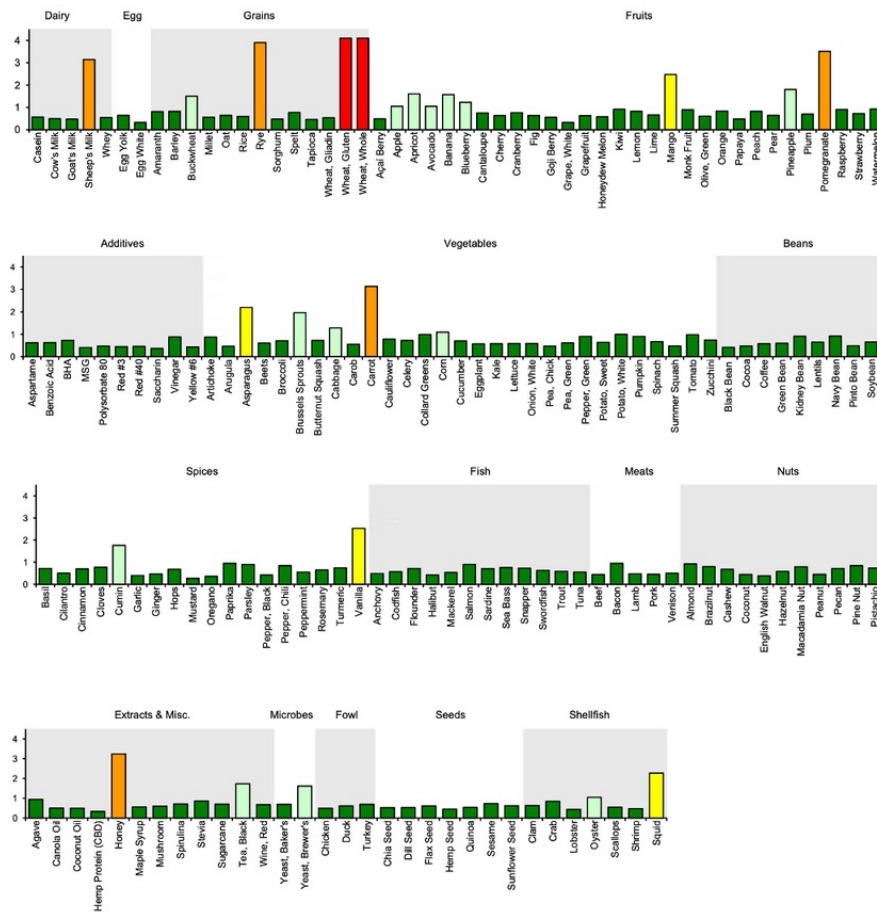
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Technology for Enhanced Sensitivity

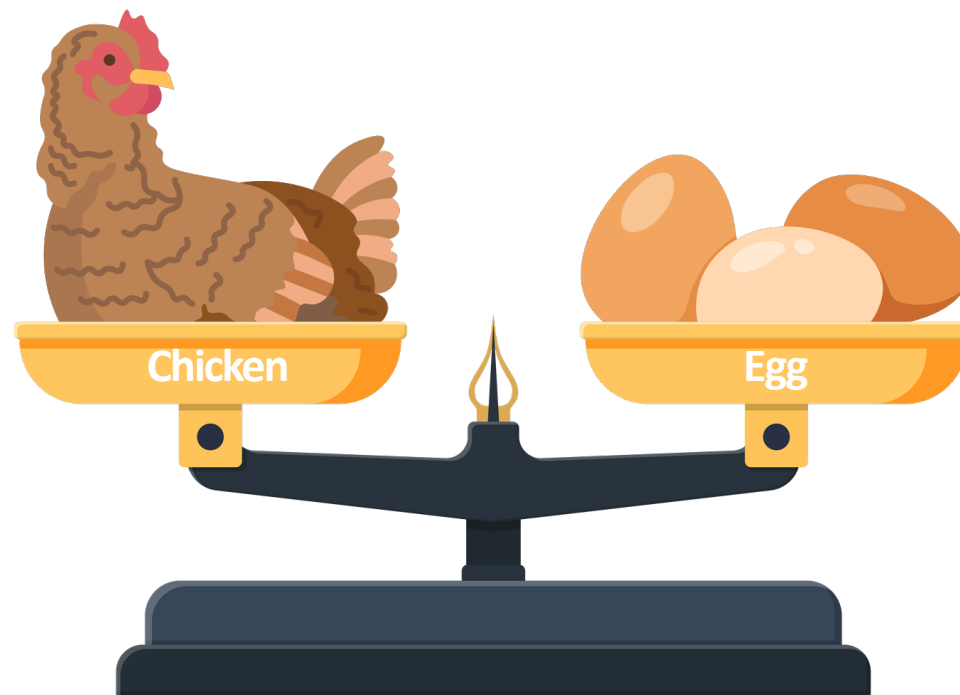


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The FIT Test Report



Food Sensitivity or Leaky Gut Which came first?



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Testing and Retesting



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Retesting the Gut Barrier

- The gut barrier is dynamic, not static, it can heal or regress over time
- Reassessment confirms progress after interventions (diet, stress, infection, medication etc)
- Helps distinguish true improvements from short-term fluctuations
- Identifies persistent barrier stress that may keep driving inflammation or symptoms
- Supports client motivation (visible data reinforces behaviour change), provides clinical accountability, and tracks long-term gut-immune health



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Special Offer

FIT176 (including the Gut Barrier Panel) for £180
instead of £300.

This is your opportunity to experience the test firsthand, explore the results, and see how it can transform your practice

Must be redeemed by Thursday 23rd October 2025



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Thank You



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