

Chapter 6: Fiber, Fatty Acids, and the Blood-Brain Barrier

Summary

The fiber in beans, grains, fruits, and vegetables passes through your small intestine without being digested. In the colon, gut bacteria ferment it and make short-chain fatty acids, mainly acetate, propionate, and butyrate. This chapter follows those molecules: butyrate fuels the cells that line your colon, all three act on receptors and even on how genes are switched on, and some travel in the blood. It then looks at the gut barrier, the real science of intestinal permeability, and why "leaky gut syndrome" is not a recognized diagnosis. Finally, it asks whether these microbial molecules reach the brain, where the best evidence (on microglia and the blood-brain barrier) still comes from mice.

Concepts Covered

1. Dietary Fiber
2. Fermentation
3. Short-Chain Fatty Acid
4. Butyrate
5. Propionate
6. Acetate
7. Colonocyte
8. Free Fatty Acid Receptor
9. Gene Regulation by Butyrate
10. Intestinal Permeability
11. Leaky Gut Claim
12. Zonulin
13. Lipopolysaccharide
14. Metabolic Endotoxemia
15. Microglia Maturation
16. BBB Permeability

Prerequisites

- [Chapter 3: Meet the Microbiome](#) (gut microbiota, microbial diversity, germ-free mice, correlation vs causation)
- [Chapter 4: The Immune System as a Sense Organ](#) (intestinal epithelium, tight junctions, regulatory T cells, microglia)
- [Chapter 5: Chemical Messengers and the Serotonin Myth](#) (the blood-brain barrier)

Following the leftovers



Some of the most interesting gut-brain science starts with the part of your food that you can't digest. In this chapter we'll follow fiber all the way from a pot of lentils to the cells of your colon, and then ask a harder question: does anything made from it reach the brain? Along the way you'll meet "leaky gut," one of the most popular claims online, and find out which parts of it are real.

6.1 What Happens to the Beans You Can't Digest?

On Sunday afternoons, Riya cooks with her grandmother. Today it's dal: yellow lentils simmered until soft, then finished with a sizzling spoonful of cumin, garlic, and chili in hot ghee. Her grandmother never measures anything. Riya, who has Crohn's disease and has spent two years learning more about her gut than she ever wanted to, stirs the pot and asks a question her grandmother can't answer: "Most of this gets digested, right? But what happens to the part that doesn't?" (Riya is a fictional student who appears throughout this book.)

It's a better question than it sounds. Your small intestine absorbs most of the starch, protein, and fat in that bowl of dal. But lentils also contain fiber, which your own body has no enzymes to break down. That fiber rides on into the colon, where trillions of microbes are waiting. They eat it, and in the process they make small molecules that soak into your colon wall, enter your blood, and, in mice at least, influence cells inside the brain. This chapter follows that journey step by step, and at each step it asks the Hype Meter question: is this shown in people, or only in mice?

6.2 Dietary Fiber: Food for Your Microbes

Imagine you and a roommate share a kitchen. You cook dinner, eat what you like, and leave the rest on the counter. Your roommate, who has tools you don't have, turns your leftovers into something new, and some of it comes back to you as a gift. Fiber works a bit like those leftovers. You can't use it yourself, but the microbes in your colon can, and they hand back some useful products.

Dietary fiber is the part of plant foods that human digestive enzymes can't break down, so it reaches the large intestine mostly intact. MedlinePlus, the US National Library of Medicine's health site, describes fiber as a type of carbohydrate found in fruits, vegetables, grains, and legumes (beans, lentils, and peas). Because it isn't fully digested, fiber provides only about half the calories per gram of other carbohydrates.

Not all fiber is the same. MedlinePlus sorts it into two broad forms:

Type	What it does in water	Where you find it	What it does in the gut
Soluble fiber	Attracts water and forms a gel	Oat bran, barley, nuts, seeds, beans, lentils, peas, some fruits and vegetables	Slows digestion
Insoluble fiber	Doesn't dissolve	Wheat bran, vegetables, whole grains	Adds bulk to stool and helps move contents along

Most high-fiber foods contain both kinds. Riya's lentils are rich in soluble fiber, while the whole-wheat roti her grandmother serves alongside adds insoluble fiber. Scientists also describe fibers by how *fermentable* they are, meaning how easily microbes can break them down, and fibers differ a lot in this. Starch that escapes digestion in the small intestine (called resistant starch) is also fermented in the colon. The two-column table is a useful start, but "fiber" is really a family of very different molecules.

How much fiber do people eat? According to [MedlinePlus](#), Americans average about 16 grams a day. The [2020 to 2025 Dietary Guidelines for Americans](#) suggested about 25 grams a day for girls aged 14 to 18 and about 31 grams for boys of the same age. The newer [Dietary Guidelines for Americans, 2025 to 2030](#) (released in January 2026) don't give a gram target; they encourage high-fiber and minimally processed foods instead.

Those are population guidelines, not personal prescriptions. People with some gut conditions get different advice from their care teams, and that's a conversation to have with a doctor or dietitian, not something to change on your own.

For families

Food carries love, culture, and memory, like Riya's Sunday dal. This chapter is about what microbes do with fiber, not about "good" or "bad" foods. If your teen has a gut condition, their care team may give them food advice that's different from general guidelines, and it helps to follow that plan without commenting on their plate. A useful question at dinner is "What would make eating easier for you right now?" rather than "Should you be eating that?"

6.3 Fermentation: Your Colon's Microbial Kitchen

When you hear "fermentation," you might picture yogurt, kimchi, or bread dough rising. Those all involve microbes breaking down sugars without much oxygen and making new products, like acids or gas. Your colon does the same thing every day, on a much larger scale.

Fermentation is the process in which microbes break down carbohydrates without oxygen, releasing energy for themselves and leaving behind products such as gases and short-chain fatty acids. The colon is a good place for it. It has very little oxygen, food moves slowly, and it is home to most of your gut microbes (you met them in [Chapter 3](#)).

Where exactly does it happen? A classic [1987 study by Cummings and colleagues](#) answered this in an unusual way. The team measured short-chain fatty acids in the intestines and blood of people who had died suddenly, sampled within four hours of death. The concentration was low at the end of the small intestine (about 13 mmol per kilogram of contents) but high throughout the colon, highest in the first part, the cecum (about 131), and lower farther along in the descending colon (about 80). The colon contents were also most acidic in the cecum (pH about 5.6) and less acidic farther down (about 6.6), because those acids pile up where fermentation is busiest. The authors concluded that most fermentation in people happens in the cecum and ascending colon, the first stretch of the large intestine.

Fermentation also makes gas, which is why a big, sudden jump in fiber can cause gas, bloating, and cramps. MedlinePlus notes that these problems often settle as the gut's bacteria adjust, which is one reason dietitians suggest adding fiber gradually. Gas from fermentation is a normal sign that your microbes are working, not a sign of damage.

Same fiber, different kitchens



I find it amazing that two people can eat the same bowl of dal and make different amounts of each fermentation product. What gets made depends on which microbes are in your kitchen, and that's one reason diet studies in people give such mixed results.

6.4 Three Short-Chain Fatty Acids

Fermentation produces many things, but three molecules get the most attention. A **short-chain fatty acid** (SCFA) is a small fatty acid, with a chain of no more than six carbon atoms, made mainly when gut microbes ferment fiber and resistant starch. A 2016 review in the journal *Cell* by [Koh and colleagues](#) calls SCFAs a major class of bacterial products that can act on receptors, change how genes are switched on, and serve as fuel. The big three are:

- **Acetate** is the two-carbon SCFA and usually the most abundant. It travels the farthest, passing through the liver and reaching the rest of the body in the blood.
- **Propionate** is the three-carbon SCFA. Much of it is taken up by the liver before it can reach the rest of the body.
- **Butyrate** is the four-carbon SCFA. Most of it never leaves the gut wall, because the cells lining the colon use it as fuel.

You may see a fixed ratio of these three quoted online. The amounts actually vary from person to person and from one part of the colon to another, so this book just says that acetate is usually the most plentiful.

The Cummings study showed where each one goes in the human body. The researchers measured SCFAs in three kinds of blood: the portal vein (which carries blood from the gut straight to the liver), the hepatic vein (blood leaving the liver), and ordinary blood in the arm (peripheral blood).

Where the sample came from	Total SCFAs (micromoles per liter)
Portal vein (gut to liver)	about 375
Hepatic vein (leaving the liver)	about 148
Peripheral blood (rest of body)	about 79

Total SCFAs drop at each step, because cells keep using them. The mix also shifted along the way: the colon lining took up more butyrate, the liver took up more propionate, and acetate was the main SCFA in every sample. So the gut wall gets most of the butyrate, the liver gets much of the propionate, and the rest of the body, including the brain's blood supply, sees mostly acetate.

SCFA	Carbon atoms	Main destination	Example roles in research
Acetate	2	Rest of the body via blood	Most abundant in blood; used as fuel by many tissues
Propionate	3	Liver	Mostly removed by the liver; also signals through receptors
Butyrate	4	Colon-lining cells	Main fuel for colonocytes; affects gene activity and immune cells

6.5 Butyrate and the Colonocyte

Most cells in your body get their energy from fuels delivered by the blood, such as glucose and fats. The cells lining your colon are unusual: they get much of their energy from the colon's contents, delivered by microbes.

A **colonocyte** is one of the epithelial cells that line the inside of the colon. Colonocytes absorb water and salts and help form the barrier between the gut contents and the body. (The barrier itself, with its mucus and tight junctions, was introduced in [Chapter 4](#).)

The clearest experiment on colonocyte fuel comes from mice. In 2011, [Donohoe and colleagues](#) compared colonocytes from germ-free mice (raised with no microbes at all) with those from normal mice. The germ-free colonocytes were in an energy-starved state: their power plants (mitochondria) were making less energy, and the cells had started breaking down their own parts to survive, a process called autophagy. When the researchers added butyrate, the starved cells recovered. The team concluded that in mice, colonocytes use bacterial butyrate as their primary energy source. The human autopsy data fit this picture, since the human colon lining took up butyrate more than the other SCFAs. So do lab studies of human cells.

In 1980, Roediger tested colonocytes taken from 14 surgery specimens of human colon: when butyrate was the only fuel offered, about three-quarters of the cells' oxygen use went to burning it, and butyrate stayed a major fuel even when glucose was also available ([Roediger 1980](#)).

Germ-free mice are an extreme case, though. They show what happens when microbes are completely missing, not what happens when a person eats a little less fiber one week.

Butyrate also appears to do more than feed cells. In mice, SCFAs, and butyrate in particular, help the colon build up regulatory T cells, the immune cells that calm inflammation. Two 2013 papers showed this: [Smith and colleagues](#) in *Science* found that SCFAs regulated the size and function of the colon's regulatory T cell population and protected mice against colitis (colon inflammation), and [Furusawa and colleagues](#) in *Nature* found that butyrate drove immature T cells to become regulatory T cells and reduced colitis in a mouse model. These are mouse findings. They help explain why scientists are interested in butyrate for inflammatory bowel disease, but they don't show that eating more fiber treats Crohn's disease or ulcerative colitis in people.

Hype Meter: "Butyrate helps protect the gut lining"

Strong

Moderate

Preliminary

Hype

Verdict: Moderate. In mice, butyrate is the main fuel for colonocytes (Donohoe 2011) and helps build calming regulatory T cells that protect against colitis (Smith 2013; Furusawa 2013). In people, the evidence is real but small: the colon lining takes up butyrate preferentially (Cummings 1987, autopsy data), colon cells from surgery specimens burn it as a main fuel (Roediger 1980, lab study), and in 4 patients with diversion colitis (inflammation in a stretch of colon cut off from the stool stream after surgery) rinsing that stretch with SCFAs cleared the inflammation over four to six weeks ([Harig 1989](#)). But a later double-blind trial in 13 patients found that two weeks of SCFA rinses worked no better than salt water ([Guillemot 1991](#)). What's missing is strong evidence from larger human trials that raising butyrate improves the gut lining or prevents disease. **What would change the grade:** Randomized trials in people showing that raising colon butyrate (through diet or another route) improves measured barrier function or disease outcomes would move this up. Trials showing no effect would move it down.

6.6 How SCFAs Send Messages: Receptors and Genes

Fuel is only part of the story. SCFAs also work as signals, and they do it in two different ways. Think of a building with a doorbell and a dimmer switch. A visitor can ring the doorbell from outside, or someone inside can turn the lights up or down. SCFAs can do both.

The doorbell: receptors. A **free fatty acid receptor** is a protein on the surface of a cell that detects fatty acids outside the cell and passes a signal inside. Two of them respond to SCFAs. They were first called GPR43 and GPR41, and were later renamed free fatty acid receptor 2 (FFAR2) and free fatty acid receptor 3 (FFAR3), according to a 2020 review by [Silva, Bernardi, and Frozza](#) in *Frontiers in Endocrinology*. These receptors sit on many cell types, from the gut lining to immune cells and nerve cells. When SCFAs bind them on enteroendocrine cells (the hormone-making cells of the gut lining you met in [Chapter 2](#)), the cells release gut hormones such as GLP-1 and peptide YY. Those hormones can then signal through the blood or the vagus nerve. FFAR2 shows up again and again in this chapter: the mouse studies on regulatory T cells and on brain immune cells both found that the receptor was needed for the effects.

The dimmer switch: genes. Inside every cell nucleus, DNA is wrapped around spool-like proteins called histones. When DNA is wound tightly, genes in that stretch are harder to read; when it's loosened, they're easier to switch on. Cells use small chemical tags called acetyl groups to loosen the wrapping, and they use enzymes called histone deacetylases (HDACs) to remove those tags again. **Gene regulation by butyrate** is butyrate's ability to block histone deacetylases, which leaves more acetyl tags on histones and changes which genes a cell turns on. Koh and colleagues list HDAC inhibition as one of the three main ways SCFAs act.

Here's a concrete example from mice. In the Furusawa study, butyrate increased acetyl tags on histones at the *Foxp3* gene, the master switch that makes a T cell become a regulatory T cell. That suggests a chain: microbes ferment fiber, butyrate is made, butyrate loosens the DNA at *Foxp3*, and more calming immune cells develop. In colonocytes, though, the Donohoe team found that butyrate's rescue effect worked mainly through fuel, not through HDAC blocking. The same molecule can act differently in different cells.

Two jobs, one molecule



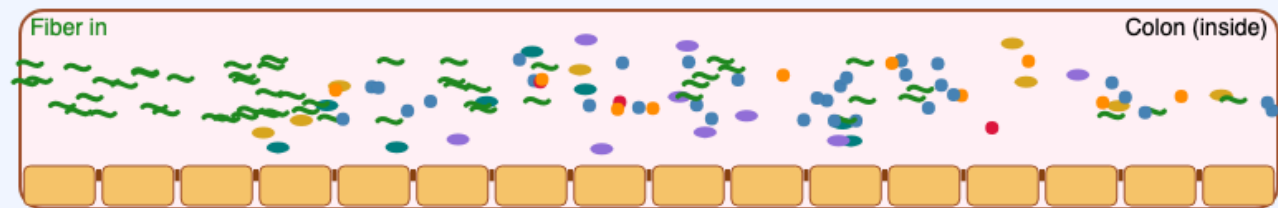
If histones and HDACs feel like a lot, hang in there: you only need the big idea. Butyrate can ring a doorbell on the outside of a cell (a receptor) or reach inside and turn a dimmer switch on genes (HDAC blocking), and different cells listen in different ways.

Now you can follow the whole path in a model. Use the MicroSim below to trace fiber from the moment it enters the colon to the cells of the colon wall.

Diagram: Fiber to Butyrate

Fiber to Butyrate

Set fiber and microbe diversity, press Start, and follow the fiber into the colon wall.



Colon-lining cells (colonocytes) and tight junctions

● Acetate ● Propionate ● Butyrate

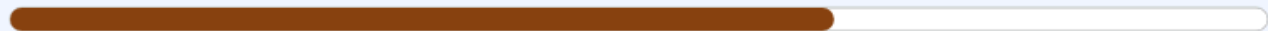
Fermentation into SCFAs (relative)



Colonocyte fuel from butyrate (relative)



Tight junction seal (relative)



Moderate fermentation. Acetate is the most plentiful SCFA; butyrate mostly stays to fuel the lining.

MOUSE STUDIES ONLY: germ-free mice, not shown in humans

Microglia maturity (line = germ-free)



BBB tightness (line = germ-free)



Bars: mice with normal microbes. Black lines: germ-free mice (no microbes). Adding microbes, or SCFAs, partly reversed the germ-free changes. Fixed panel: these studies did not test fiber amounts.

Start

Reset

☒ Show mouse-only panel

Fiber: 16 g/day



Diversity: medium



US average about 16 g a day. 2020 to 2025 guidelines: about 25 g (girls 14 to 18), 31 g (boys 14 to 18).

[Back to Fiber to Butyrate Lesson Plan](#)

Interactive simulation: <https://aaryavvatts-lab.github.io/gut-brain-textbook/sims/ch06-fiber-to-butyrate/main.html>

Open the Fiber to Butyrate fullscreen



MicroSim specification: Fiber to Butyrate



Type: microsim **sim-id:** ch06-fiber-to-butyrate

Library: p5.js

Status: Implemented

Bloom Level: Understand

Bloom Verb: trace

Learning Objective: The learner will trace dietary fiber through bacterial fermentation to acetate, propionate, and butyrate and their effects on colonocytes and tight junctions, and distinguish these from brain effects shown only in mice.

Canvas: 570 px drawing area plus 140 px controls (iframe 712 px); responsive to about 380 px wide.

Controls: Start/Pause, Reset, Show mouse-only panel (checkbox, default on); Fiber slider (0 to 40 g/day, step 1, default 16); Microbe diversity slider (5 steps from very low to very high, default medium).

Rules: Fermentation rises with fiber and levels off at high intakes; more microbe diversity raises fermentation capacity and the share of butyrate. Acetate is always the most plentiful SCFA drawn; butyrate particles move into the colon wall. Colonocyte fuel follows butyrate; tight junction seal rises with fuel but never drops to zero, because other factors also maintain it. The mouse-only panel is fixed: bars show microglia maturity and blood-brain barrier tightness in mice with normal microbes, and black lines show germ-free mice; it does not respond to the sliders, because those studies compared microbes with no microbes rather than testing fiber amounts. All values are relative and illustrative.

Feedback: A status line describes the fermentation level and where each SCFA goes. Reference marks under the fiber slider show the US average (about 16 g a day) and the 2020 to 2025 guideline values for ages 14 to 18.

Provenance: Sections 6.2 to 6.6 and 6.10 (MedlinePlus fiber page; Cummings 1987; Donohoe 2011; Erny 2015; Braniste 2014). All model numbers are illustrative.

Start at the default of 16 grams a day, about the US average, and press Start. Watch green fiber strands enter on the left and turn into blue acetate, orange propionate, and red butyrate as the bacteria work on them. Notice that only the red butyrate dots drift down into the colon wall, and that the colonocytes glow brighter and the gaps between them narrow as butyrate fuel rises. Now drag the fiber slider to 0, then to 30. Then try the diversity slider: with very low diversity, the same fiber makes less of everything, and especially less butyrate.

Finally, look at the purple dashed panel. It shows two brain effects that have been found **only in germ-free mouse studies**: more mature microglia and a tighter blood-brain barrier when microbes are present (the bars) than when they are absent (the black lines). Move the fiber slider and notice that this panel doesn't change, because those studies compared mice with and without microbes, not different amounts of fiber. Turn the panel off and on, and notice that nothing in the human part of the model depends on it. That separation is the point. Sections 6.7 to 6.10 explain why the boundary matters.

What this model leaves out

- Real fiber is many different molecules, fermented at different speeds by different microbes; the sim treats all fiber as one thing.
- It shows no gas, no protein fermentation, and no other microbial products, and it skips the liver and blood steps that sort acetate and propionate.
- The tight junction seal depends on many things besides butyrate, including the mucus layer, immune cells, inflammation, and medicines; the sim links it only to butyrate, and that link comes mostly from cell and mouse studies.
- The levels are relative teaching numbers, not measurements. Real SCFA amounts vary widely between people and from day to day.
- The mouse panel compares mice with and without microbes. It does not mean that eating more fiber changes a person's microglia or blood-brain barrier.

6.7 The Gut Barrier and Intestinal Permeability

Picture a city with a wall around it. The wall has gates that let in food and trade, and guards who keep out invaders. A wall with no gates would starve the city. A wall with too many holes would let in danger. The gut lining is like that wall. It must let nutrients and water through while keeping microbes and their products out.

A 2017 review by [Odenwald and Turner](#) explains that the barrier needs two things: an unbroken layer of epithelial cells, and junctions that seal the narrow spaces between those cells. A 2019 review in *Gut* by [Camilleri](#) adds that the full barrier also includes the surface mucus and immune defenses beneath the lining. You met each of those parts in Chapter 4.

Intestinal permeability is how easily substances pass across the gut lining from the inside of the intestine into the body, either through the cells or through the gaps between them. Some permeability is normal and necessary. The question doctors and scientists ask is whether permeability is higher than usual, and whether that matters.

How do you measure something so small? The most common method in people is a sugar test. A person drinks a solution containing two sugars that the body doesn't use, often lactulose (a large sugar that slips through mainly by the gaps) and mannitol (a smaller one that passes more easily). Over the next few hours, both come out in the urine. If the ratio of lactulose to mannitol in the urine rises, more is getting through the gaps, which means permeability is higher. Researchers can also study small tissue samples (biopsies) taken during a scope test.

Camilleri lists several things that increase permeability in people for a while: endurance exercise, common pain relievers called NSAIDs (such as ibuprofen), pregnancy, and some food additives called emulsifiers. Inflammatory diseases that damage the lining, such as Crohn's disease, also increase it. The exercise finding surprises some readers. Sam, Riya's best friend, runs cross-country, and long hard runs can temporarily make

his gut more permeable. That doesn't make running harmful. It shows that permeability goes up and down with normal life, and that a single high measurement isn't a disease. (Sam is a fictional student who appears throughout this book.)

The important limits come from the same reviews. Odenwald and Turner write that most clinical data on barrier loss are correlative, which makes it hard to tell whether a leaky barrier causes a disease or is caused by it. Camilleri adds that inflammatory and ulcerating diseases make the gut leaky, but no such disease can be cured just by normalizing the barrier, and it is still unproven that restoring barrier function improves symptoms. Hold on to that idea. It's the key to the next section.

6.8 "Leaky Gut": Real Measurement, Overblown Claim

Search "leaky gut" online and you'll find thousands of posts. They often go something like this: your gut lining has holes, toxins pour into your blood, and that causes fatigue, brain fog, anxiety, autism, acne, and autoimmune disease. Luckily, the post continues, this powder or test kit can fix it.

The **leaky gut claim** is the popular idea that a condition called "leaky gut syndrome" is a common hidden cause of many symptoms and diseases throughout the body, and that it can be diagnosed with consumer tests and cured with diets or supplements. It mixes a real, measurable thing (intestinal permeability) with a chain of claims that the evidence doesn't support. "Leaky gut syndrome" is not a recognized medical diagnosis.

Let's separate the pieces:

Piece of the claim	What the evidence says	Grade
The gut barrier exists and can become more permeable	True and measurable in people (sugar tests, biopsies)	Strong
Permeability is higher in some diseases, like Crohn's	Yes, but mostly correlation; the disease can cause the leakiness	Strong (link); unclear (cause)
Leaky gut causes autism, depression, and most chronic illness	Not supported by human evidence	Hype
A supplement or diet can "heal" a leaky gut and cure symptoms	No disease has been cured by fixing permeability; diet claims need confirmation	Hype
A blood test for zonulin tells you if your gut is leaky	Common kits don't measure zonulin (see below)	Hype

One molecule appears in many leaky gut ads. **Zonulin** is a protein that some researchers, including the group of Fasano and colleagues, propose loosens tight junctions in the small intestine; it has been reported to be the same molecule as a blood protein called pre-haptoglobin 2. In a [2020 review](#), Fasano and coauthors present a "structured hypothesis" that a zonulin-driven leaky barrier contributes to autoimmune diseases like celiac disease and type 1 diabetes in genetically at-risk people. A hypothesis is a reasonable idea to test, not a settled fact. (That review discloses that Fasano holds stock in a company and consults for a diagnostics company, which a careful reader notes.)

The bigger problem is the test. In 2018, [Scheffler and colleagues](#) measured "zonulin" with a widely used commercial test kit in 376 people. The results didn't match the people's haptoglobin genes, which they should have if the kit measured pre-haptoglobin 2. When the team checked what the kit actually grabbed, it wasn't pre-haptoglobin 2 at all; it detected related proteins instead, most likely one called properdin. In 2019, a separate team in Australia, [Ajamian and colleagues](#), tested two other commercial kits and found they mostly detected haptoglobin and complement C3, other blood proteins. They advised caution about using serum zonulin as a marker of gut barrier health until the tests improve. So a teen who gets a "high zonulin" result from a consumer test may not have learned anything about their gut.

Hype Meter: "Leaky gut causes autism, depression, and everything else"

Strong

Moderate

Preliminary

Hype

Verdict: Hype. Intestinal permeability is real and can be measured, and it rises in some diseases and stressful states. But reviews describe the human data as mostly correlative, no disease has been cured by fixing permeability, and "leaky gut syndrome" is not a recognized diagnosis. Popular zonulin blood tests don't reliably measure zonulin. **What would change the grade:** Large human studies showing that increased permeability comes before a specific condition, plus randomized trials showing that repairing the barrier prevents or improves that condition, could move a narrow version of the claim (one condition, not "everything") toward Preliminary.

6.9 Lipopolysaccharide and Metabolic Endotoxemia

If something does cross a more permeable barrier, what is it? One candidate has been studied closely. Many gut bacteria, the kind called gram-negative bacteria, have an outer coat built partly from a molecule that the immune system recognizes instantly as "bacteria are here."

Lipopolysaccharide (LPS) is a large molecule made of fat and sugar parts that forms much of the outer membrane of gram-negative bacteria; immune cells detect it through pattern recognition receptors (from [Chapter 4](#)) and respond with inflammation. Scientists also call LPS endotoxin. In a serious infection, large amounts of LPS in the blood can trigger a dangerous body-wide reaction. But tiny amounts can also show up in the blood normally; in mice, the level rises a bit after meals and falls during fasting.

In 2007, [Cani and colleagues](#) studied those tiny amounts in mice. They found that a high-fat diet for four weeks raised the level of LPS in the blood by about two to three times. They named this low but chronic rise **metabolic endotoxemia**: a small, long-lasting increase in blood LPS, linked to diet and gut microbes, that may promote low-grade inflammation and metabolic problems such as insulin resistance. When the researchers infused LPS under the skin of mice for four weeks to copy that rise, the mice developed higher blood sugar and insulin and signs of inflammation in fat tissue, much like the high-fat-fed mice. Mice lacking an LPS-sensing protein called CD14 were protected from most of these changes.

This is strong mouse evidence that small amounts of LPS can drive inflammation and metabolic changes. In people, the picture is less clear. Human studies of blood LPS, diet, and metabolic health are mostly observational, and links like these don't show which came first. For this book's purposes, metabolic endotoxemia is a promising idea with a strong mouse base and still-developing human evidence. It is one reason scientists care about the barrier, not a reason to fear food.

If you're going through this

If you have Crohn's disease, ulcerative colitis, or IBS, you may see posts claiming your illness is "just leaky gut" that a powder can fix. Your condition is real, it's more complicated than that, and your care team treats it with approaches tested in people. Advice about fiber and food can also be different for you than for the general public, so check with your doctor or dietitian before changing what you eat or adding a supplement, even one that sounds harmless.

6.10 From Gut to Brain? Microglia and the Blood-Brain Barrier

Now for the question that put "brain" in this chapter's title. Do SCFAs, or other microbial molecules, change the brain? To answer it, recall two things from earlier chapters. **Microglia** are the brain's resident immune cells ([Chapter 4](#)). The **blood-brain barrier** (BBB) is the tightly sealed lining of the brain's blood vessels that controls what passes from the blood into the brain ([Chapter 5](#)). For a refresher on glia, see [From Neuron to Bedside, Chapter 1](#).

The BBB works a lot like the gut barrier you just studied, with cells sealed together by tight junction proteins. A 2020 review by Silva and colleagues notes that SCFAs can cross the BBB using transporter proteins, based mostly on animal studies, so they are at least able to reach the brain in small amounts. Two well-known mouse studies looked at what happens when microbes are missing entirely.

Microglia. Microglia maturation is the process by which young microglia develop into fully functional immune cells that can watch over brain tissue and respond to infection or injury. In 2015, [Erny, Prinz, and colleagues](#) reported in *Nature Neuroscience* that germ-free mice had widespread microglia defects: their microglia looked and behaved immature, and their innate immune responses were impaired. Giving the mice a complex mix of microbes partly restored the microglia. The team found that SCFAs helped regulate microglia, and mice lacking the SCFA receptor FFAR2 had microglia that looked like those of germ-free mice. According to the

Silva review, giving germ-free mice a mixture of acetate, propionate, and butyrate was enough to drive microglia toward maturity. All of this is in mice.

The blood-brain barrier. BBB permeability is how easily substances can pass from the blood into the brain across the blood-brain barrier; when it's higher, the barrier is "leakier." In 2014, [Viorica Braniste, Sven Pettersson, and colleagues](#) reported in *Science Translational Medicine* that germ-free mice had a leakier BBB than normal mice, starting before birth and lasting into adulthood. Their brain blood vessels had less of two tight junction proteins, occludin and claudin-5. When the team gave adult germ-free mice normal gut microbes, the barrier tightened. In follow-up experiments described in the full paper, giving germ-free mice a single butyrate-producing bacterium, or butyrate itself, also reduced leakage, and butyrate raised occludin levels in parts of the brain.

What about people? Here the evidence becomes thin. No study has shown that gut bacteria change BBB permeability in humans, and the microglia work has no direct human version. The closest human experiment tested SCFAs and stress hormones.

In a 2020 triple-blind trial, [Dalile and colleagues](#) gave 66 healthy men either a placebo or a supplement designed to release an SCFA mixture in the colon, for one week. Both SCFA doses reduced the rise in the stress hormone cortisol when the men faced a stressful public task, but they didn't change the men's mood ratings. That's one small, short study in men only, measuring a hormone rather than the brain directly. A 2019 review by the same group concluded that research on whether SCFAs explain microbial effects on mood and thinking is sparse, especially in humans. You'll learn much more about cortisol in [Chapter 7](#).

A germ-free mouse is not a person who skipped vegetables



Germ-free mice have zero microbes from birth, which no human ever has. When you read "gut bacteria protect the blood-brain barrier," check whether the study compared mice with no microbes to mice with normal ones, because that's a big difference that doesn't translate directly to fiber on your plate.

Hype Meter: "Short-chain fatty acids protect the human blood-brain barrier"

Strong

Moderate

Preliminary

Hype

Verdict: Preliminary. In germ-free mice, the BBB is leakier and microglia are immature, and adding microbes or butyrate partly reverses this (Braniste 2014; Erny 2015). But no human study has shown that gut microbes or SCFAs change BBB permeability. The one small human trial of colon-delivered SCFAs (66 men, one week) found a lower cortisol response to stress, not a change in the brain barrier or mood.

What would change the grade: Human studies that measure BBB permeability directly (for example, with brain imaging) before and after changes in gut SCFAs, repeated in larger and more varied groups, would be needed to move it up. Animal research in general has a mixed record: only about one in three highly cited animal studies were later tested successfully in human trials.

Let's apply the six questions from [Chapter 1](#) to the blood-brain barrier study, since it's the one behind many "your gut bacteria protect your brain" headlines.

How to read a gut-brain claim: the 2014 germ-free mouse BBB study

Question	This study
Mouse or human?	Mouse only. Germ-free mice were compared with mice that had normal microbes. No human data were collected.
Correlation or cause?	Closer to cause, in mice. The researchers changed the microbes (adding them to germ-free mice, or giving butyrate) and measured the barrier change. But germ-free mice differ from normal mice in many ways at once.
How many?	Small groups. One key adult experiment used 3 mice per group, which is common in this kind of lab work but limits confidence.
How long?	From before birth (embryonic days 13.5 to 18.5) to adulthood (8 to 10 weeks old), with recolonization experiments lasting days to weeks.
Who paid for it?	Public and nonprofit funders in Sweden, Singapore, the European Union, and the US, including the Swedish Research Council, the Swedish Brain Foundation, and the NIH, as listed in the paper.
Is something being sold?	No product. The paper states that the authors have no competing interests.

The conclusion: this is careful mouse work showing that, in mice, having microbes affects the BBB from early in life. It does **not** show that a particular food, supplement, or probiotic protects a person's brain barrier. A headline that skips from "germ-free mice" to "your brain" has jumped over the hardest part.

At the Bedside: The Leaky Gut Test



Meet the patient (fictional)

Tessa is a 15-year-old sophomore who spends a lot of time on social media. A wellness influencer she follows posted that bloating, tiredness, and "brain fog" are signs of leaky gut. Tessa bought an at-home "zonulin" test, which came back "high," and a "gut repair" powder. She also started eating much more fiber all at once. Now she's more bloated than before, has more gas, and is worried something is seriously wrong. Her mom brings her to her pediatrician.

What the doctor checks: The pediatrician asks about Tessa's symptoms, sleep, school stress, periods, family history of gut disease, and what she has been eating and taking. She asks about warning signs such as weight loss, blood in the stool, diarrhea that wakes her at night, or fevers; Tessa has none. The exam is normal. Because tiredness and bloating can have many causes, the doctor orders a few basic blood tests, including a blood count and a screening test for celiac disease. All are normal.

Connecting the signals: Tessa's symptoms got worse after she sharply increased her fiber. That fits normal fermentation: more fiber reaching the colon means more gas from microbes, which can cause bloating and cramps until the gut adjusts. The zonulin result doesn't change the picture. Research shows that widely used commercial zonulin tests detect other blood proteins, not zonulin, so a "high" result doesn't show that her gut is leaky.

Diagnosis: No sign of gut disease. Bloating and gas related to a fast increase in fiber. "Leaky gut syndrome" is not a recognized diagnosis, and her test result is not meaningful.

Why it happens: Fermentation by colon microbes makes short-chain fatty acids and gas (Section 6.3). Intestinal permeability is real and measurable in research, but consumer tests and the "leaky gut" label don't measure it reliably or explain everyday symptoms (Sections 6.7 and 6.8).

The mind-body side: Tessa has been checking her stomach constantly and reading about rare diseases at night, which keeps her anxious and makes her notice every gurgle. Worry about health can make normal body sensations feel louder and more alarming, a link you'll study in [Chapter 8](#). The pediatrician takes Tessa's symptoms seriously, explains what the tests do and don't show, and suggests ways to step back from content that frightens her. If the worry keeps interfering with school or sleep, the care team can connect her with a counselor who works with health anxiety.

Treatment today: The main treatment is clear information and reassurance, along with a follow-up visit. The doctor recommends that Tessa talk with a registered dietitian about how to adjust her eating in a way that suits her, rather than making big changes based on social media. She asks Tessa to check with her before taking any supplement, since "gut repair" products are not tested or approved to treat any disease, and their contents can vary.

What's new in research: Researchers are trying to develop drugs that tighten the gut barrier. The most advanced, larazotide acetate, is an eight-amino-acid peptide thought to block zonulin signaling ([Slifer and colleagues, 2021](#)). It was tested in a phase 3 trial in adults with celiac disease, but the sponsor ended that trial in 2022, according to its ClinicalTrials.gov record ([NCT03569007](#)). It is not approved, and Odenwald and

Turner's 2017 review noted that no FDA-approved drugs targeted the gut barrier. **Evidence grade: Preliminary.** Barrier repair as a treatment for any disease remains unproven.

 Your turn: reason through a variation

Tessa's friend Leo, also 15, has had diarrhea for three months, has lost weight without trying, and sometimes sees blood in his stool. His cousin says, "It's just leaky gut. Try the powder." How should you reason about this?

Answer: Leo's story is different. Weight loss, blood in the stool, and months of diarrhea are warning signs that need a doctor's evaluation, because they can point to conditions like inflammatory bowel disease, which you'll study in [Chapter 9](#). Increased permeability does happen in Crohn's disease, but there it's a result of inflammation, and treating the inflammation is what matters. Calling it "leaky gut" and trying a powder could delay real diagnosis and care.

This is a fictional teaching case. It is not medical advice. If you or someone you know has symptoms like these, talk to a doctor.

Common Misconceptions

Myth: All fiber is the same, so any fiber does the same thing in your gut.

Reality: Fiber is a family of different molecules. Soluble fibers form gels, insoluble fibers add bulk, and they differ in how easily microbes ferment them. Different fibers, and different microbes, produce different amounts of each short-chain fatty acid.

Myth: "Leaky gut" is a diagnosis doctors can confirm with a zonulin test.

Reality: Intestinal permeability is real and can be measured in research, mostly with sugar tests. But "leaky gut syndrome" isn't a recognized diagnosis, and two independent research teams found that common commercial zonulin kits measure other proteins instead.

Myth: The blood-brain barrier is a solid wall that nothing can cross.

Reality: The BBB is a selective filter made of sealed blood-vessel cells. Some substances, like the amino acid tryptophan and, according to animal research, SCFAs, cross with the help of transporter proteins. Others, like gut serotonin, don't.

Myth: If gut bacteria tighten the blood-brain barrier in mice, the same must be true in people.

Reality: The BBB and microglia results come from germ-free mice, which have no microbes at all. No human study has shown that gut bacteria change BBB permeability. Many results from mice don't hold up when tested in people.

Your Gut Check

Test yourself. Try each one before you open the answer.

? 1. Claim Check: "Your brain fog is caused by a leaky gut. Toxins are leaking into your blood and crossing into your brain. My gut-sealing powder fixes both barriers in 30 days!" ✓

Grade: Hype. Intestinal permeability is real, and the BBB is real, but this post chains together claims the evidence doesn't support. "Leaky gut syndrome" isn't a recognized diagnosis, no disease has been cured by fixing gut permeability, and no human study shows that gut changes alter the BBB. Someone is also selling a product with a promised timeline. A careful version would say: "The gut lining's permeability can change, and scientists are studying whether that matters for some diseases, but it isn't a proven cause of brain fog."

? 2. Predict: Riya's family switches from white rice to a mix of rice and lentils at most meals. Assuming her care team agrees with the change, what would you predict happens to fermentation in her colon over the next few weeks, and which SCFA would her colon lining use most? ✓

More fermentable fiber would reach her colon, so her microbes would likely ferment more and make more short-chain fatty acids, along with more gas at first while her gut adjusts. Acetate would probably still be the most plentiful SCFA overall, but her colonocytes would take up and use butyrate most. How much changes depends on which microbes she has, and in Crohn's disease the inflamed or scarred parts of the gut can behave differently, which is why her care team should guide any change.

? 3. Explain: In the 1987 autopsy study, total SCFAs were about 375 micromoles per liter in the portal vein but only about 79 in peripheral blood. Explain the drop. ✓

The portal vein carries blood directly from the gut to the liver, so it holds SCFAs fresh from the colon. On the way, the colon lining uses much of the butyrate, and then the liver takes up much of the propionate (and some acetate). By the time blood reaches the rest of the body, mostly acetate is left, at a much lower concentration.

? 4. Apply: A news story says, "Study finds mice without gut bacteria have leaky blood-brain barriers, so probiotics could protect your brain." Use the six questions to identify the two biggest problems. ✓

First, mouse or human: the study is in mice, so it can't show what happens in people. Second, the comparison: germ-free mice have no microbes at all, while a person taking a probiotic already has trillions of microbes. The study tested having microbes versus having none, not adding one product to a normal gut. The headline also skips the question of whether the probiotic in question even makes the relevant molecules.

5. Read the data. In the 1987 study by Cummings and colleagues, researchers measured total SCFAs in intestinal contents from people who had died suddenly:

Location	Total SCFAs (mmol per kg of contents)	pH
End of small intestine (terminal ileum)	about 13	not reported here

Location	Total SCFAs (mmol per kg of contents)	pH
Cecum (start of colon)	about 131	about 5.6
Descending colon (later colon)	about 80	about 6.6

? 5. What does this data show, and what can't it show? ✓

It shows that SCFAs are about ten times more concentrated at the start of the colon than at the end of the small intestine, and that they fall farther along the colon. That supports the idea that most fermentation happens in the first part of the colon, and the lower pH where SCFAs are highest fits acid build-up. It can't show what happens in living, healthy teens, since the samples came from adults after sudden death, and it can't show how diet changes these numbers, since diets weren't controlled. A helpful follow-up would measure SCFAs in living volunteers before and after a controlled change in fiber.

Exercises

Remember

1. Name the three main short-chain fatty acids and give the number of carbon atoms in each.

Answer ✓

Acetate (2 carbons), propionate (3 carbons), and butyrate (4 carbons).

1. What is a colonocyte, and what is its main fuel according to the mouse research in this chapter?

Answer ✓

A colonocyte is a cell that lines the inside of the colon. In mice, colonocytes use bacterial butyrate as their primary energy source.

Understand

1. Explain why dietary fiber reaches the colon while most starch from the same meal doesn't.



Answer



Human digestive enzymes break down most starch in the small intestine, where it's absorbed as sugar. We don't have enzymes that break down fiber, so it passes through the small intestine mostly intact and reaches the colon, where microbes can ferment it.

1. Explain the difference between how butyrate acts through a free fatty acid receptor and how it acts through gene regulation.



Answer



Through a receptor, butyrate binds a protein on the outside of a cell (like FFAR2) and triggers a signal inside, such as hormone release. Through gene regulation, butyrate enters the cell and blocks histone deacetylases, which leaves DNA more loosely wrapped and changes which genes are switched on.

Apply

1. Use the MicroSim to compare a fiber intake of 8 grams a day with 30 grams a day, at medium and at very low diversity. Record the fermentation and colonocyte fuel meters for all four combinations, then explain which change mattered more in the model and why the real answer might differ.
2. Sam reads that endurance exercise increases intestinal permeability and worries that cross-country is "giving him leaky gut." Using Section 6.7, write a short, accurate reply to Sam that explains what the research does and does not mean.

Analyze

1. Compare the evidence behind two statements: "Butyrate fuels colonocytes" and "SCFAs mature microglia." For each, identify whether the evidence comes from mice or humans, whether it shows cause or correlation, and which statement is closer to being true in people. Explain your reasoning.
2. The leaky gut claim combines several smaller claims. Break the claim "Leaky gut lets LPS into your blood, which causes depression" into at least three separate links, and analyze the evidence for each link using Sections 6.7 to 6.9.

Evaluate

1. A company sells an at-home zonulin test for teens "to check gut health." Evaluate whether the test is useful, citing at least two specific findings from this chapter, and decide what grade the product's claim deserves.

2. Some scientists argue that mouse studies of the BBB are valuable even though they don't prove anything about humans. Others say they create more hype than knowledge. Write a paragraph judging which view is more convincing, using the Braniste 2014 claim box as evidence.

Create

1. Design a study in human volunteers that could test whether a high-fiber diet changes intestinal permeability. Describe your groups, how long the study would last, what you would measure (and how), and one result that would support the hypothesis and one that wouldn't.
2. Create a short infographic script (five panels or fewer) that follows a lentil's fiber from Riya's grandmother's pot to the colon wall, labeling which steps are shown in humans and which only in mice.

Key Takeaways

- Dietary fiber is the part of plant foods that human enzymes can't digest. It reaches the colon, where microbes ferment it, mostly in the cecum and ascending colon.
- Fermentation produces gas and short-chain fatty acids, mainly acetate (usually the most abundant), propionate, and butyrate. In people, the colon lining takes up butyrate, the liver takes up propionate, and acetate reaches the rest of the body.
- In mice, butyrate is the main fuel for colonocytes and helps build calming regulatory T cells. SCFAs signal through free fatty acid receptors (FFAR2 and FFAR3) and, especially butyrate, by blocking histone deacetylases to change gene activity.
- Intestinal permeability is real and measurable, for example with sugar tests, and it rises with things like endurance exercise, NSAIDs, and gut inflammation. Most human data are correlative.
- "Leaky gut syndrome" is not a recognized diagnosis, commercial zonulin tests don't reliably measure zonulin, and no disease has been cured by fixing permeability.
- In mice, LPS from gut bacteria rises in the blood on a high-fat diet (metabolic endotoxemia) and can drive inflammation; human evidence is still developing.
- In germ-free mice, microglia stay immature and the blood-brain barrier is leakier; microbes and SCFAs partly reverse this. No human study has shown the same, so this remains Preliminary.

You followed fiber all the way!



You traced a lentil from the pot to the colon wall and learned to stop exactly where the human evidence stops. Next, in Chapter 7, we'll see what happens when stress hormones like cortisol enter the conversation, and why Sam's stomach knows when a big race is coming.

Quiz: Fiber, Fatty Acids, and the Blood-Brain Barrier

Test your understanding of Chapter 6. Choose the best answer, then click **Show Answer** to check.

Question 1

Which short-chain fatty acid is usually the most abundant, in both the colon and the blood?

- A. Acetate
- B. Butyrate
- C. Propionate
- D. Lactate

 **Show Answer**



The correct answer is **A**. In the 1987 human study by Cummings and colleagues, acetate was the main SCFA in every sample, from colon contents to peripheral blood. Butyrate (B) gets a lot of attention, but most of it is used up by the colon lining, so much less of it reaches the blood.

Concept Tested: Acetate **Bloom's Level:** Remember

Question 2

Where in the human digestive tract does most fiber fermentation take place?

- A. In the stomach, where acid breaks fiber apart
- B. Throughout the small intestine, evenly from start to end
- C. In the first part of the colon, the cecum and ascending colon
- D. Only in the rectum, just before stool leaves the body

 Show Answer 

The correct answer is **C**. SCFA levels were low at the end of the small intestine and highest in the cecum, so most fermentation happens at the start of the colon. Option B is a common mix-up: the small intestine absorbs most digestible food, but fiber passes through it largely intact.

Concept Tested: Fermentation **Bloom's Level:** Remember

Question 3

What is a colonocyte?

- A. A type of bacterium that ferments fiber in the colon
- B. An epithelial cell that lines the inside of the colon
- C. An immune cell in the brain that responds to SCFAs
- D. A hormone released when fiber reaches the colon

 Show Answer 

The correct answer is **B**. Colonocytes are the cells lining the colon, and in mice they use bacterial butyrate as their primary fuel. Option A confuses the cell that uses butyrate with the microbes that make it.

Concept Tested: Colonocyte **Bloom's Level:** Remember

Question 4

In the 1987 autopsy study, total SCFAs fell from about 375 micromoles per liter in the portal vein to about 79 in peripheral blood. What best explains this drop?

- A. SCFAs break down on their own within seconds of leaving the colon.
- B. The kidneys filter SCFAs out before blood reaches the liver.
- C. The blood-brain barrier absorbs most SCFAs from the blood.
- D. The colon lining uses much of the butyrate and the liver takes up much of the propionate, so less is left for the rest of the body.

? Show Answer



The correct answer is **D**. The changing mix of SCFAs from colon to portal blood to hepatic vein showed greater uptake of butyrate by the colon lining and propionate by the liver. Option C is wrong because the brain receives only a small share of blood SCFAs; the big drops happen in the gut wall and liver.

Concept Tested: Short-Chain Fatty Acid **Bloom's Level:** Understand

Question 5

How does butyrate change which genes a cell switches on?

- A. It cuts DNA at specific genes, like a pair of scissors.
- B. It blocks histone deacetylases, leaving DNA more loosely wrapped and some genes easier to switch on.
- C. It replaces the cell's DNA with bacterial genes.
- D. It binds to the outside of the cell and stays there, never entering.

? Show Answer



The correct answer is **B**. By blocking HDACs, butyrate leaves more acetyl tags on histones, loosening the DNA so some genes are easier to read. In mice, this happened at the *Foxp3* gene that makes T cells become regulatory T cells. Option D describes receptor signaling, which is a separate way SCFAs act.

Concept Tested: Gene Regulation by Butyrate **Bloom's Level:** Understand

Question 6

Why do scientists say a "high" result on a common commercial zonulin blood test does not show that someone has a leaky gut?

- A. Independent studies found that widely used kits detect other blood proteins, not zonulin itself.
- B. Zonulin is only found in mice, so it can't be measured in people.
- C. Zonulin levels are always high in healthy people.
- D. The test measures stomach acid instead of blood proteins.

 Show Answer



The correct answer is **A**. Scheffler and colleagues (2018) and Ajamian and colleagues (2019) found that commercial kits picked up proteins like properdin, haptoglobin, and complement C3 instead of zonulin. Option B is wrong: zonulin is studied in people, but the popular tests don't measure it reliably.

Concept Tested: Zonulin **Bloom's Level:** Understand

Question 7

Sam runs a hard 10-mile training run, and the next day a research team measures his small intestine permeability with a sugar test. Based on this chapter, what result is most likely, and what does it mean?

- A. Permeability will be zero, because exercise seals tight junctions completely.
- B. Permeability will be higher, which proves he has leaky gut syndrome and needs a supplement.
- C. The sugar test can't be used on athletes.
- D. Permeability may be higher than usual, but this is a normal response to endurance exercise, not a disease.

 Show Answer



The correct answer is **D**. Camilleri's review lists endurance exercise as one of several stressors that increase intestinal permeability in people. Option B makes the leap the chapter warns against: a raised measurement isn't a diagnosis, and "leaky gut syndrome" isn't a recognized condition.

Concept Tested: Intestinal Permeability **Bloom's Level:** Apply

Question 8

A student uses the Fiber to Butyrate MicroSim. At 30 grams of fiber a day with very low microbe diversity, the colonocyte fuel meter is lower than at 20 grams with high diversity. Which real-world idea is the model illustrating?

- A. Fiber has no effect on SCFA production.
- B. Only the amount of fiber matters; microbes are all the same.
- C. How much butyrate is made depends on both the fiber eaten and which microbes are present to ferment it.
- D. High microbe diversity causes the blood-brain barrier to tighten in people.

? Show Answer



The correct answer is **C**. Fermentation needs both the fiber and the microbes that can ferment it, which is why the same meal can produce different amounts of SCFAs in different people. Option D is wrong because the blood-brain barrier effect has been shown only in germ-free mice, and the sim labels it that way.

Concept Tested: Butyrate **Bloom's Level:** Apply

Question 9

A headline says, "Gut bacteria keep your brain's barrier sealed." It is based on Braniste and colleagues (2014). Which statement best analyzes the gap between the study and the headline?

- A. The study compared germ-free mice with normal mice, so it can't show what happens in people, who always have microbes.
- B. The study was done in people, so the headline is accurate.
- C. The study found no difference between germ-free and normal mice.
- D. The study proved that a specific probiotic seals the human blood-brain barrier.

? Show Answer



The correct answer is **A**. The study found a leakier BBB in germ-free mice and tighter barriers after adding microbes, but no human data were collected, and the comparison was between no microbes and normal microbes. Option D overstates it: no probiotic product was tested in people.

Concept Tested: BBB Permeability **Bloom's Level:** Analyze

Question 10

Cani and colleagues (2007) found that a high-fat diet raised blood LPS two to three times in mice, which they called metabolic endotoxemia. A wellness site says, "This proves fatty food leaks bacterial toxins into your blood and makes you sick." What is the strongest criticism of this claim?

- A. LPS is not made by bacteria, so the study was mislabeled.
- B. The study was in mice, and human studies on blood LPS are mostly observational, so it doesn't prove the same effect in people.
- C. The study found that LPS lowers inflammation.
- D. Metabolic endotoxemia means a large, deadly LPS level, which the mice did not have.



Show Answer



The correct answer is **B**. The 2007 findings are strong mouse evidence, but human links between diet, blood LPS, and health are mostly correlations that can't show which came first. Option D gets the definition backward: metabolic endotoxemia means a small, chronic rise in LPS, not a severe infection-level spike.

Concept Tested: Metabolic Endotoxemia **Bloom's Level:** Analyze
