

NOTES OF A MASTER FORMULATOR

PRINCIPLES AND PROTOCOLS FOR DETOXIFICATION,
MICROBIOME, AND ENVIRONMENTAL MEDICINE

FOR
DOCTORS AND
THE PATIENTS
THEY CARE FOR

SPENCER FELDMAN

**Notes of a Master Formulator
Principles and Protocols for Detoxification, Microbiome, and Environmental
Medicine**

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Introduction

This book exists because doctors kept asking for it.

For nearly three decades I have designed supplements and protocols for alternative medical practitioners — naturopaths, functional medicine physicians, integrative MDs, chiropractors, and the occasional conventionally trained doctor whose curiosity pulled them past the edges of their training. Two patents came out of that work. More importantly, a body of formulations came out of it, each built to address a specific mechanism in a specific clinical context, each refined against practitioner feedback and patient outcomes over years.

What accumulated alongside the products was a body of clinical reasoning — a way of reading patients, a set of principles for when to push and when to wait, a framework for understanding why protocols fail and what to do about it. Practitioners I worked with kept asking me to teach it. For years I did that one conversation at a time — phone calls, conference talks, training sessions for doctors and labs. Eventually the requests outpaced what I could deliver in person. I am shifting into a mentorship role now, and this book is part of that shift. It lets me pass on what I have learned without the time demands of formal instruction, freeing me to continue to invent.

The book is written for practitioners. The language assumes clinical literacy. The mechanisms are explained in enough detail that the practitioner understands why a protocol works, not just what to do — because a practitioner who understands the why can adapt when the patient does not fit the standard picture, and in chronic illness, the patient rarely fits the standard picture.

That said, this book is not closed to the motivated layperson. If you are working to improve your own health or that of someone you love, and you are willing to do the work of understanding what you read, the clinical reasoning here is yours to use. Some terms and concepts will be unfamiliar — the book assumes its reader has a basic understanding what a cytokine is, how histamine functions, what short-chain fatty acids are. These are not difficult ideas, but they are not explained from scratch. A search engine and an evening of reading will close most gaps. The knowledge is worth acquiring regardless of this book, and once acquired, everything that follows will read clearly.

Part One maps what gets in the way — the financial structures that shape what practitioners see and don't see, the diagnostic blind spots built into conventional workups, the substrate burdens the modern patient carries, and the patient-side patterns that stall even good protocols. Part Two is the work itself — the biology, the protocols, and the clinical reasoning that connects them. It is denser, more technical, and less concerned with persuading the reader than with equipping them.

A note on the writing. I worked with Claude (Anthropic, Claude 4.6) in producing this manuscript. The clinical content — every mechanism, every protocol, every

recommendation, every product formulation — is mine, developed across nearly thirty years of work with practitioners and patients. The AI contributed prose. It did not contribute thought. A reader encountering a clinical claim in this book is encountering my clinical judgment, not a language model's.

A note on conflicts of interest. My interest has always been unsolved problems. As a child I loved riddles and logic puzzles. My degree in mathematics was really just a degree in puzzle solving. Eventually the puzzle of the body got my attention, and with it the unsolved riddles that are chronic diseases. Helping a person whose chronic illness was unsolved satisfied both my drive for meaning and my stubborn refusal to walk away from an unsolved puzzle. The protocols that came of this over the years usually required ingredients, formulations, and methods of administration that did not yet exist. So I built them. I designed and sell formulations built around many of the mechanisms discussed in this book. They are available at remedylink.com. That is a conflict of interest the reader is entitled to know about from the outset. The framework in this book stands on its own. The principles and protocols can be applied with my products or with alternatives a knowledgeable practitioner selects. The ideas are what matter.

Consolidated protocol flowcharts for the clinical frameworks taught in this book are available at remedylink.com/protocols. They map the clinical decision-making sequence, the microbiome restoration sequence, the metal and chemical detoxification chains, the sinus protocol, the bile restoration work, the home environment assessment, and the diagnostic signals taught across multiple chapters. They are updated as the protocols evolve. The reader who wants a single reference to consult alongside patient work will find it there. There are also a few charts that the reader may find helpful at remedylink.com/charts.

A Note on Citations and the Dagger (†) Symbol

This book includes numbered reference citations throughout, collected in a References section at the end of each chapter. These point the reader to published literature supporting the claims made. Where a claim is marked with a dagger, no published literature is known to the author that directly supports it. These are the author's observations drawn from thirty years of clinical work with practitioners and patients. They are offered as clinical judgment, not as established science. The reader is invited to test them against their own experience.

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Part One — The Landscape

Chapter 1 — Drugs demand precision; supplements are more forgiving

If you give the wrong drug to a patient, you will likely push them in a direction they don't need to go, and sometimes in the opposite direction entirely. The drug itself often has to be detoxified by a body that was already burdened. Side effects are common, too much of the wrong drug can mean a hospital visit or worse, and multiple drugs risk interactions, synergistic toxicities, and potentiations.¹ The clinical posture this requires is precision — right diagnosis, right drug, right dose, right duration, cross-referenced against every other drug the patient may be on. Get any of those wrong and you've added to the problem you were trying to solve.

This is why the drug model sometimes tells patients: come back when you're worse, so we can be sure what you have. The physician isn't being callous. They don't want to commit to a drug protocol until the diagnosis is clear enough to justify the risk of being wrong. So they wait. The patient waits with them. And in the meantime, the condition often becomes harder to treat than it would have been if intervention had started earlier.

Supplements behave differently. If you give the wrong supplement, the patient is usually still better off than they were. Supplements that aren't addressing the main issue often address something else useful in passing. The toxic profiles are generally low. Too much of a supplement is more likely to produce loose stools or mild discomfort than a hospital visit. The penalty for being wrong is small.

This asymmetry has a clinical consequence that practitioners trained in pharmaceutical thinking often miss: with supplements, you can and should experiment. You don't have to wait for diagnostic certainty before intervening because the cost of being wrong is bounded.

You can try something based on a reasonable clinical hypothesis, observe what happens, and adjust. The intervention itself becomes part of how you figure out what's going on. A good therapy is also diagnostic — when the patient responds, you've learned something about what was actually wrong. If they don't respond, you've learned something too. And if the supplement worsens symptoms, that is also telling — you've found the right lever, you just moved it in the wrong direction.

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Chapter 2 — The influence of financial models

The financial model behind drugs shapes what the practitioner sees in practice just as much as the pharmacology does. Developing a new drug costs somewhere between one and two billion dollars by the time you include failed candidates and the cost of capital.¹ A U.S. patent runs twenty years from the filing date, but the filing happens years before approval, so the effective commercial window after a drug reaches the market is typically seven to twelve years.² Everything downstream is shaped by that window.

The first consequence is that drug companies cannot profit from what they cannot patent. Off-patent drugs, unpatentable compounds, and natural substances are all outside the business model, regardless of how well they work. This isn't a conspiracy — it's arithmetic. A company with a billion-dollar development cost and a shrinking exclusivity window has to direct research toward patentable molecules with high projected sales. Compounds that are cheap, old, or found in nature get left behind even when the clinical evidence for them is strong.³ Companies are also competing against each other, so the drug with the fastest clinical response has a market advantage — but faster is not always safer in the long term.

Technology does move forward. New drugs are sometimes genuinely safer and more effective than the ones they replace. But many older drugs are more effective, safer, or both — yet they are no longer profitable, so they are no longer marketed, no longer taught, and in some cases no longer manufactured.⁴ The absence of a drug from current practice is often an economic signal, not a clinical one.

The second consequence is the marketing infrastructure. Drug companies fund medical education, both formal (residency programs, curricula, continuing education) and informal.⁵ They pay physicians as consultants, speakers, and advisors. For roughly two decades ending in the early 2010s, the dominant form of physician-industry relationship was the all-expenses-paid "educational" event — resort destinations, cruise ships, luxury hotels for a weekend of nominal lectures surrounded by golf, meals, and entertainment.⁶ The events were legal, widely attended, and rarely disclosed. A physician returning from such a trip with the company's drug fresh in mind was, predictably, more likely to prescribe it.⁷

That era has largely ended. The 2010 Physician Payments Sunshine Act required disclosure to CMS of any payment above ten dollars, and the data is now public on the Open Payments database.⁸ But the financial relationships did not end — they moved into forms harder to perceive as compensation: consulting contracts, speakers' bureaus, advisory board fees, research grants, institutional payments for clinical trial participation.⁹ A 2024 analysis found that nearly sixty percent of the reviewers for The BMJ, JAMA, The Lancet, and The New England Journal of Medicine had received industry payments during a recent three-year period, totaling over a billion dollars.¹⁰

Government participates in this system as well. Insurance companies, following federal quality measures, tie physician bonuses to specific medical decisions.¹¹ Pediatricians under certain Blue Cross Blue Shield contracts can earn substantial bonus payments for hitting childhood immunization thresholds — with the structure often designed so that falling below the threshold forfeits the entire bonus.¹² The same logic applies to statin prescribing rates, A1c targets, colonoscopy rates, and other HEDIS quality measures.¹³ Regardless of your stance on vaccines, we can all agree that rewarding a physician financially for performing any specific medical procedure creates a conflict of interest.

The third consequence is that peer review, the system physicians are trained to trust as the filter between truth and nonsense, has documented structural problems. Journals have retracted hundreds of papers after discovering fake peer-review rings.¹⁴ Paper mills sell authorship and arrange publication for payment.¹⁵ Editors have been caught accepting bribes.¹⁶ The major publishers — Elsevier, Wiley, Springer Nature, Sage, Taylor & Francis, Wolters Kluwer — are currently defendants in a federal antitrust lawsuit over their peer-review practices.¹⁷ None of this means individual studies cannot be trusted. It means that "peer-reviewed" is not the guarantee of reliability the word implies.

The net result is a system in which the financial interests of pharmaceutical companies, insurers, government programs, and journals are tightly coupled. Drugs save lives every day, and the pharmaceutical industry has produced extraordinary medicines. But the claim that drugs are developed, vetted, and prescribed solely on the basis of patient benefit does not survive contact with the financial structure.

Supplements have their own problems. Quality control in the supplement industry is poor. Independent testing routinely finds products that contain a fraction of the labeled active ingredient, or none of it.¹⁸ Herbs are frequently contaminated with mold, heavy metals, or solvent residues.^{19,20} Some companies are excellent; others are selling flour in capsules. The practitioner who chooses supplements is not escaping a quality problem — they are trading one quality problem for another, and must select sources with the same care a pharmacist brings to compounding.

What this means for the practitioner is this: when a physician says "if it worked, I'd have heard about it," that claim rests on an assumption about how information flows through medicine that does not match reality. Primary care physicians are seeing patients every fifteen minutes.²¹ They do not have time to read primary literature. The "research" most physicians encounter is curated by pharmaceutical representatives, reinforced by continuing-education programs funded by the same companies, and summarized in journals whose reviewers have financial relationships with those companies. An intervention that is cheap, off-patent, or derived from nature has no one with the budget to put it in front of the physician. Its absence from the physician's awareness is evidence of its economic profile, not its clinical value.

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Chapter 3 — Reference ranges are calibrated against a sick population

When a patient gets bloodwork back and the values fall within the reference range, the practitioner and the patient both exhale. The assumption is that "within range" means healthy. That assumption is wrong.

Reference ranges are statistical constructs. A lab draws blood from a large sample of the population, calculates the central distribution of values, and defines a reference range. Anything outside that band gets flagged. This wisdom-of-crowds approach works when the crowd is healthy. The problem is that the crowd isn't.

The modern American population is chronically ill. Rates of obesity, type 2 diabetes, autoimmune disease, cardiovascular disease, neurodegenerative disease, infertility, anxiety, depression, and chronic pain are all dramatically higher than they were a century ago.¹ When reference ranges are calibrated against this population, what gets called "normal" is the central tendency of a sick cohort. A patient whose values sit comfortably in the middle of the reference range is not healthy by any absolute standard — they are average within a population that is itself unwell.

Weston Price's work in the 1930s documented what a genuinely healthy population looks like.² He traveled to isolated communities that had not yet adopted industrial food — Swiss alpine villagers, coastal Gaelic islanders, Inuit hunters, Aboriginal Australians, Andean highlanders, Melanesians, African pastoralists — and found populations with nearly perfect dental arches, almost no caries, broad facial structure, minimal degenerative disease, minimal mental illness, and minimal crime. When those same populations adopted white flour, sugar, and refined vegetable oils, the next generation showed narrowed arches, crowded teeth, increased susceptibility to infection, and the emergence of chronic diseases the donor populations had never seen. This was not a hundred years of slow decline. It was one generation. Price's work is observational and cross-cultural rather than controlled — it cannot isolate specific dietary variables — but the pattern across fourteen geographically and genetically distinct populations is striking and consistent.

Francis Pottenger's cat studies demonstrated a similar pattern in controlled experiments.³ Cats fed cooked meat and pasteurized milk showed progressive degeneration across generations — skeletal abnormalities, behavioral changes, reproductive failure — while cats fed raw meat and raw milk remained healthy. The lesson is that inputs that a species is not adapted to will produce reference-range statistics that reflect disease rather than health.

The practitioner is working downstream of roughly a hundred and twenty years of this degradation. Soil depletion,⁴ industrial food, environmental toxin load, electromagnetic exposure, chronic sleep restriction,⁵ chronic stress, sedentary life, and ubiquitous pharmaceutical exposure have all compounded. The reference range is what you get when you average this population. It is not a description of health.

A patient with a fasting glucose of 95 mg/dL is within range. A patient with a fasting glucose of 75 mg/dL is also within range. These two patients are not equally healthy. A patient with a vitamin D of 32 ng/mL is within range. A patient with a vitamin D of 60 ng/mL is also within range. Again, not clinically equivalent. The reference range admits both because the range is wide enough to accommodate a population that includes many patients who are chronically inflamed, chronically deficient, and chronically underperforming biochemically.

The correct target is not the middle of the reference range. The correct target is the bloodwork of a twenty-five-year-old high-caliber athlete with a calm disposition and high cognitive function.† A practitioner working toward that target will find room to move in almost every patient's labs.

A second flaw compounds the first. Lab reports are binary — a value is either flagged or it isn't. But biology is continuous. A fasting glucose of 99 mg/dL is reported as normal. A fasting glucose of 100 mg/dL is reported as impaired. These two patients are clinically identical. The cutoff is a reporting convention, not a biological boundary.⁶

A third flaw compounds both. Individual values within range can hide ratio imbalances that are clinically significant. A lab test may define 30 to 60 as acceptable for two values that should normally move in proportion. A patient with 31 on one and 59 on the other has both values within range, nothing flags, but the ratio is roughly one-to-two when healthy would be one-to-one.

Some of these ratios are named and reported. BUN-to-creatinine gives kidney perfusion and hydration information that neither value does alone; a ratio above 20 suggests dehydration or reduced renal blood flow even when both values are in range.⁷ Albumin-to-globulin tracks protein synthesis, immune activation, and nutritional status; inverted ratios appear in chronic inflammation and certain cancers before either protein moves out of range.⁸ AST-to-ALT patterns distinguish viral hepatitis, alcoholic liver injury, and non-alcoholic fatty liver when both enzymes sit within normal limits.⁹ Triglyceride-to-HDL is one of the more reliable insulin-resistance markers; a ratio above 3.5 indicates metabolic dysfunction in patients whose individual values are unremarkable.¹⁰ Neutrophil-to-lymphocyte predicts cardiovascular and cancer mortality more reliably than either count alone.¹¹

The fourth distortion is that the goalposts move with age, and they move in the direction of accepting decline as normal. A healthy young adult has an eGFR of 90-120 (mL/min/1.73m²). An eGFR of 60 in a thirty-year-old triggers a chronic kidney disease workup. The same value in a seventy-five-year-old is routinely called "age-appropriate."¹² But a kidney filtering at half the rate of a healthy young kidney is not fine — it has accumulated damage over decades from medications, dehydration, blood pressure, blood sugar dysregulation, mineral accumulation, and toxin exposure.

The same pattern applies across most lab values. DHEA-S reference ranges drop by a factor of five to ten between age twenty-five and seventy-five.¹³ Growth hormone, IGF-1, free testosterone, and thyroid function all have age-adjusted ranges that permit substantial decline before flagging. In each case, "adjusted for age" actually means adjusted for the observed decline in the population — which is not the same as the decline that is biologically necessary.

Some decline with age is real. A seventy-five-year-old man will not have the testosterone levels of his twenty-five-year-old self without exogenous support. But this acknowledgment should be tightly scoped. The seventy-five-year-old can and should aim for the cardiovascular function, the liver function, the kidney function, the blood glucose regulation, the cognitive capacity, and the inflammatory profile of a healthy younger man. Not every system degrades at the same rate, and not every system needs to degrade at all. The current system lumps everything together and treats the aggregate decline as inevitable.

The result is that patients in their fifties, sixties, and seventies are routinely told their labs look "fine for their age" when what is actually true is that their labs look typical of a sick population at that age. Typical is not healthy. Age-adjusted is not optimal.

Patient symptoms can sometimes fill the gap the reference range leaves open, but patients with high pain tolerance will under-report, and patients with chronic conditions have often forgotten what normal feels like. Between a reference range that calls sick normal and a symptom report that may understate how sick the patient actually is, there is substantial room for a practitioner to miss what is there to find.

Clinical pearl- When you see someone who is an outlier for good health and slow aging, ask them if they know why. Sometimes it is constitutional genetics, but every once in a while they will teach you something like 'yes, I fast 2 weeks every year...'

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Chapter 4 — Financial distortions in hospitals and alternative medicine

This chapter examines the diagnostic step after bloodwork — imaging, biopsies, and procedural evaluations. The same pattern repeats: the institution doing the test has financial incentives that shape what gets ordered, and the practitioner who treats those recommendations as neutral clinical judgment is trusting a process that isn't what it appears to be. Alternative medicine is not exempt. It has its own parallel version.

Most American hospital care runs on fee-for-service reimbursement. Every test ordered is a billable unit. Estimates of low-value care — care where risks and costs exceed benefits — run between ten and thirty percent of total spending, roughly two to three hundred billion dollars per year.¹ Cedars-Sinai's vice chairman for surgery has said directly that there remains a continued financial incentive to do the test, do the procedure, do something more.²

Defensive medicine reinforces this. A physician who orders a test and finds nothing has protected themselves legally. A physician who declines a test and misses something faces malpractice exposure.³ The legal incentive and the financial incentive point in the same direction — more testing, more imaging, regardless of whether the test was likely to change management.

Diagnostic tests are not uniformly safe. CT scans involve ionizing radiation. The risk is small per scan and real across a lifetime of accumulated imaging.⁴

Gadolinium-based MRI contrast agents are a larger concern. Gadolinium is a heavy metal, highly toxic in its free ionic form, theoretically kept stable by chelating ligands.⁵ In patients with compromised kidney function, the chelate can fail before excretion, releasing free gadolinium and producing nephrogenic systemic fibrosis — a debilitating and sometimes fatal fibrosing disorder.⁶ Since 2006, the industry shifted to more stable macrocyclic agents and screened for kidney function, but newer data show gadolinium deposits in the brain, bone, and other tissues even in patients with normal renal function.⁷ There are now around four hundred and fifty million doses administered worldwide, and understanding of the toxicity is slowly being recognized.⁸

Biopsy introduces a different risk. When a needle is inserted into a tumor and withdrawn, the needle tract is a potential route for tumor cells to be displaced into surrounding tissue or circulation. A systematic review identified over eight thousand reported cases of iatrogenic tumor seeding, with rates varying by tumor type — roughly 2.7% in liver cancer biopsies, 3-5% in breast.⁹ Technical modifications can reduce but not eliminate the risk.

This is a perfect example of the benefits of immediate supplement intervention suggested in Chapter 1. Cancer is also on a spectrum. Some cells are abnormal, but not yet classified as cancer. If you even suspect a patient has cancer, why not begin a supplement program immediately? Waiting for positive confirmation is understandable if

your only tools are surgery, radiation, or chemo, but you lose valuable time by waiting and doing nothing.

None of this means hospitals should be avoided. Diagnostic testing saves lives. Cancer caught early is more treatable. The critique is that the fee-for-service system over-applies tools that are appropriate in some cases and inappropriate in others, and the patient arrives at the alternative practitioner's office with tests already performed, radiation already absorbed, contrast already retained, and possibly a biopsy tract already seeded.

Now the other side. Alternative medicine has its own diagnostic-for-profit problem. Many "energy scan" devices output results that are not reproducible.¹⁰ Change the name of a patient so that the machine cannot refer to a previous reading for 'continuity' and you can get two different very readings. The device generates a narrative — "your liver is toxic," "you have heavy metal burden" — that justifies an expensive protocol. The protocol is the point. The device is theater.

As for therapeutics, I was asked about the ion foot bath detoxification systems. I put my feet in, watched the water bubble and change color. I was told these were toxins leaving my system. I asked them to run the test without my feet in it. Same discolored water. It was oxidation of the metal plates. That's not to say the technology has no benefit — voltage in the body has effects, and people do claim benefits beyond placebo — but the color change is fraudulent, and the system is actually exposing you to metal toxins now in solution.†

Lab fraud exists in the alternative space as well.¹¹ Some labs are excellent. Others run inadequately trained technicians, process samples in ways that introduce artifact, use proprietary methods never independently validated, and produce reports with invented normal ranges calibrated to make everyone look sick enough to need treatment.

Live blood analysis illustrates the pattern clearly. Done properly, dark-field or phase contrast microscopy of a fresh blood drop can show real things standard lab work does not: white blood cell activity and morphology, platelet clumping, parasitized RBC, rouleaux formation, and fibrin crystallization speed.¹² Done improperly, poorly trained operators crush the slide or mash the objective, producing artifactual shapes described to the patient as parasites, yeast, or cellular damage. Blood improperly squeezed from the finger creates further artifact. Dirty glass slides have artifacts that are described as toxins in the patients blood. The patient sees something alarming on a monitor, accepts the interpretation, and an expensive protocol follows.

The principle across both systems is the same: any diagnostic system whose economic incentives reward finding something will tend to find something. The magnitude differs — a hospital runs millions of dollars of imaging per day; a bioenergetic practitioner charges a few hundred per scan — but the structural pattern is identical.

The practitioner's job is to read both systems with appropriate skepticism. Hospital imaging findings are real in the sense that what the scan shows is what the tissue looks like — but whether the finding needed to be looked for, needs to be acted on, and justified the potential harm, are separate questions. Alt-med device readings should be weighted according to reproducibility and the track record of the operator. The practitioner must develop the judgment to know which data is trustworthy, which is partially trustworthy, and which is theater.

Clinical pearl: If the patient is going to get an MRI, ask the radiologist whether the machine's resolution is high enough to make gadolinium contrast unnecessary. If contrast is required, use a macrocyclic (not linear) contrast agent and use a gadolinium chelator before, during, and after the injection. More on this in the metal detox chapter.

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Chapter 5 — Finding... and being a good doctor

This book is written for practitioners, but most readers will also eventually be patients, and will have family members who need care. The question of how to find a clinician you can work with is not separate from the clinical content that follows. It is the prerequisite.

One option is a traditionally trained physician whose curiosity has expanded their scope into integrative or functional medicine. This person has the diagnostic training, prescribing authority, hospital privileges, and credentialing to handle the acute and pharmaceutical side of care, and has done the additional work to understand what is available outside the pharmaceutical model. Physicians like this exist and their number is growing, but they are not evenly distributed geographically and often have waiting lists.

Another arrangement is two or more practitioners working in parallel — a traditionally trained MD or DO for diagnostic and pharmaceutical work, and alternative practitioners such as NDs, DCs, or L.Acs. This only functions if all are willing to coordinate, or at minimum to not undermine one another.

The single most important quality to look for is curiosity. A curious practitioner, like a fine wine, gets better with age. The accumulated experience of a clinician who has kept learning across decades is something no recent graduate can match, and something no closed-minded veteran ever develops.

A practitioner's response to a patient who brings them new information is the most reliable signal of how the relationship will function. When you bring a well-researched question, there are three responses that indicate a practitioner worth keeping:

The first: "Yes, I'm familiar with that. Here's how we're already using it, or here's why I don't think it applies to your case." This is a practitioner who is current and has a reasoned position.

The second: "No, I'm not familiar with that, but let me look at what you've brought and we'll see how it might apply." This is a practitioner secure enough to acknowledge a gap and curious enough to investigate.

The third: "I don't have time to properly research that, but if you want to try it, I'll take a supportive role. If I see you getting better or worse in ways you might not notice yourself, I'll tell you." This is often the most realistic arrangement with a busy conventional physician, and entirely workable as long as the practitioner follows through on monitoring.

All three responses share a common trait: they are non-defensive. The practitioner may agree, disagree, or defer, but they engage.

The response to watch for is any variation of dismissal. "There's no evidence for that." "If it worked, I'd have heard about it." "That's pseudoscience." "You're not the doctor, I am." The last is the most revealing — a practitioner who needs to remind the patient of the credential hierarchy has confused their training with infallibility. Training is the beginning of clinical judgment, not the end of it.

A few practical notes for patients. When you bring a question, bring it well-prepared. Respecting the practitioner's time by doing the reading yourself first is the price of admission. Do not bring ten questions at once. Bring one or two at a time, well-framed, with supporting material. A practitioner who gets a list of twenty interventions in one visit will default to refusing all of them — not because any one is necessarily wrong but because the volume is unmanageable. The relationship develops over multiple visits.

When you find a practitioner who engages well, protect the relationship. Be the patient who shows up informed, follows through, reports back honestly, pays bills on time, and does not waste clinical time with drama or anxiety. Good practitioners are scarce and selective about whom they invest their limited attention in. The patient who makes the relationship easy is the patient who gets deeper engagement when they need it.

If you are a practitioner reading this, the reverse applies. The patient who brings you well-documented information is an opportunity to learn. If they have a problem you see often but don't have a good protocol for, and they are willing to test a therapy on themselves, then — assuming you consider the protocol harmless — see what unfolds. Any benefit they receive is something you can mentally file away for future patients with a similar presentation.

Chapter 6 — Treat the symptoms and the test

There is a standing argument in clinical practice about which to trust when a patient's labs and symptoms tell different stories.

One camp leans toward the labs. Symptoms are subjective — they vary day to day, depend on the patient's reporting style, and two patients with the same pathology can describe their experiences in completely different terms. Labs offer apparent objectivity: same blood, same lab, same numbers. They can be compared against a reference range and tracked over time. For a physician seeing six patients an hour, labs offer stable substrate for clinical decisions.

The other camp leans toward the symptoms. Patients suffer in their bodies, not in their lab values. A patient with normal labs and persistent symptoms is still suffering, and the practitioner who tells them their labs are fine has not done their job.

Both camps are partially right. Labs and symptoms are two readings of the same underlying physiology, taken from different angles, each catching things the other misses. The practitioner who reads them as two information streams — and who pays particular attention to where they disagree — has access to diagnostic information that commitment to either stream alone cannot reach.

The case for labs

A practitioner working without labs is blind to a substantial portion of the patient's physiology. Glucose regulation, lipid metabolism, kidney filtration, liver enzyme activity, electrolyte status, thyroid function, inflammatory markers — none can be inferred from how the patient feels at the precision required to manage them clinically. A patient with a fasting glucose of 180 mg/dL may feel fine while slow vascular damage accumulates over years.¹ The lab makes silent pathology visible.

Labs also catch what symptoms underreport. A stoic patient minimizes pain and fatigue. A patient chronically ill for years has lost the reference point to notice slow decline. The CRP climbing for three years registers inflammation the patient has stopped feeling. The lab does not care how the patient reports.

Labs permit tracking that symptoms cannot match. A patient on a metals chelation protocol can report feeling better, but the urinary metals test tells the practitioner whether the protocol is mobilizing all the target metals or only a subset of them. The labs are the reproducible measurement that shows whether the protocol is doing what it was meant to do, independent of subjective experience.

Why symptoms have been triaged

The shift to lab-leaning is not because physicians stopped caring about symptoms. It is because the time required to take a thorough symptom history has been compressed.

Mid-twentieth-century primary care visits typically ran twenty to thirty minutes; current visits average closer to fifteen, with much consumed by electronic record documentation.²

The good news is that depth of symptom inquiry can be approximated by structured questionnaires. The patient fills out the form before the visit, arriving with the information already organized. The Standard Process Systems Survey is a particularly good example — roughly two hundred questions across fourteen sections covering autonomic balance, sugar handling, cardiovascular function, liver and gallbladder, digestion, endocrine subtypes, foundational vitamin status, and gender-specific patterns.

What labs miss

Some tests measure surrogates, not the underlying physiology. The standard kidney panel reports creatinine and BUN as markers of glomerular filtration. A patient with substantial tubular damage — where most reabsorption work happens — can have entirely normal creatinine and BUN. Tubular damage produces low molecular weight proteinuria (beta-2 microglobulin, retinol-binding protein, alpha-1 microglobulin, NAG) that requires specific tests to detect.³ None are on the standard panel. Microalbumin catches earlier glomerular damage than creatinine, but most panels do not include it.

Tests beyond the lab's capability: Many tests the chronic illness practitioner needs require specialty laboratories — mycotoxin panels, persistent organic pollutant panels, comprehensive heavy metal challenge testing, CIRS-associated inflammatory markers, comprehensive 24-hour hormone metabolite testing. These exist but are not available at the patient's local hospital lab.

Tests that aggregate what they should distinguish: Some lab tests combine elements that should be reported separately — the metals chapter (Chapter 32) addresses this in the context of f-block elements and chelation, where a lab failure to distinguish between gadolinium and uranium has direct clinical consequences for how the practitioner proceeds.

Labs offer only a snapshot: A lab draw captures the patient's chemistry at a single moment. A patient who develops a headache and tight jaw within an hour of eating at a Chinese restaurant has delivered diagnostic information no routine panel will catch — a glutamate response suggesting impaired glutamate clearance.⁴ That imbalance can have upstream causes the standard workup might not surface: chronic sinus inflammation disrupting local GABA precursor production, or a microbiome shift reducing GABA-producing bacterial populations.⁵ The chronic anxiety the patient has carried for years may be the third-order consequence of a pattern detectable only when a meal loads the glutamate system enough to produce a transient symptom.

A patient who reports a specific kind of headache after exposure to particular environmental conditions is mapping an environmental sensitivity in real time. A patient

who feels substantially worse after eating wheat is providing data the IgG panel may not show. A patient whose mood drops on certain medications is providing data about methylation the genetic panel only suggests indirectly. The practitioner who routinely asks about post-exposure symptoms gathers diagnostic data the snapshot approach cannot match.

Tests that do not exist yet: Glymphatic clearance rate has been studied with intrathecal contrast MRI in research settings but has no clinical test.⁶ Cribriform plate patency is in principle assessable but no standard workup combines the needed methods. Receptor-class activity for systems like histamine receptors is not testable at all — the receptor map is inferred from clinical pattern and response to receptor-selective interventions.

What symptoms miss

Stoic and chronic patients underreport. A patient with high pain tolerance describes dysfunction another patient would have presented with months earlier. A patient chronically ill long enough to forget normal reports their drifted baseline as their normal state.

Anxious patients overreport. A patient with low CO₂ † or low endorphins will describe symptoms more severe than the underlying pathology warrants. Their reports are not false — they are experiencing what they describe — but the experience is amplified by an upstream cause.

Patients have language for some symptoms and not others. A patient may describe headache, fatigue, and GI upset because they have words for those. The same patient may have substantial autonomic dysfunction they experience as "I feel weird," cognitive shifts they experience as "I'm just not myself," hormonal shifts they experience as "something's off."

Day-to-day variation obscures patterns. A snapshot taken on a good day misses the running pattern. A snapshot on a bad day exaggerates it. Given the variables in someone's life — diet, sleep, supplements and drugs started or stopped, weather including cloud cover, temperature, humidity, and barometric pressure — symptoms can be confusing. For this reason, a chronically sick patient should create a health diary. Knowing the timing of things helps identify patterns, especially in symptoms that wax and wane.

Disagreement is data

Normal labs, present symptoms: The conventional response is to reassure the patient and suggest the symptoms may be stress or in their head. This response is wrong twice — it tells the patient something untrue (labs being normal does not mean nothing is wrong; it means the tests run did not catch what is wrong), and it dismisses the diagnostic information the symptoms provide.

The correct response is to read the symptom pattern and ask what tests would surface the pathology the standard panel missed. The patient with fatigue, brain fog, joint pain, and skin changes whose standard labs are normal may have the gadolinium picture described above. The patient with recurrent angioedema and normal allergy testing may have hereditary angioedema with C1 esterase inhibitor not yet ordered.⁷ The patient with chronic kidney symptoms and normal creatinine may have tubular dysfunction with low molecular weight proteinuria markers not yet tested.

This pattern also catches subclinical pathology. Early kidney damage produces symptoms before creatinine moves.⁸ Early autoimmune disease produces symptoms before antibody levels rise to diagnostic thresholds.⁹ The patient who is symptomatic with normal labs is often the patient whose pathology is in the early stage where intervention is most effective.

Abnormal labs, absent symptoms: Sometimes more dangerous. Some pathologies produce abnormal labs long before symptoms, and the symptom-free interval is exactly when intervention works best.

Kidneys are the most notorious example — a patient with declining eGFR can be entirely symptom-free for years while damage progresses.¹⁰

Cardiovascular plaque has an additional misleading layer. Stress testing catches ischemia from fixed-stenosis lesions — plaques that have narrowed an artery roughly 70-85% before detection. A patient with 50-60% blockage at multiple sites can pass cleanly. But most acute heart attacks come from rupture of plaques that were less than 70% stenotic — vulnerable plaques characterized by inflammation, thin fibrous caps, and immune-cell infiltration rather than degree of stenosis.¹¹

Additionally, even a mildly blocked artery can become completely blocked if it spasms. Arterial smooth muscle contraction is modulated by magnesium and local inflammatory signaling,¹² and a magnesium-depleted, systemically inflamed patient carries a vasospasm risk no stress test will detect.

A clean stress test does not mean cardiovascular health. It means fixed-stenosis lesions, if present, have not yet reached the detection threshold. The inflammatory and immune workup addressing vulnerable plaque biology — H4-driven foam cell mechanism,† the inflammatory marker patterns, the lipid particle subfractions — is what serves the patient the negative stress test does not.

Both abnormal: When labs and symptoms agree, the practitioner has the easiest case. The labs identify the problem, the symptoms confirm clinical significance, and together they give direction and motivation. This is the case conventional medicine handles well.

When the test does not exist: If you suspect a mechanism on the basis of pattern and no test can confirm or rule it out, you can let the intervention answer the question. Give a test dose of a supplement you have experience with that addresses the suspected

mechanism. Watch the response window. If the patient improves, you have decent evidence the mechanism was contributing. If not, you have reason to suspect another driver. The intervention is itself the diagnostic. This works because of the asymmetry Chapter 1 named — supplements permit experimentation because the cost of being wrong is low.

Clinical pearl: Abnormal labs are not always bad news. A tumor that is dying will often swell before it resolves. Increased dimensions on ultrasound with labs that look worse might be tumor lysis syndrome and a sign that the protocol is working, though drainage and detox support may need a boost.

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Chapter 7 — Single-cause reasoning can leave gains on the table

A patient's presenting complaint is rarely the product of one cause. More commonly, there is a primary insult doing most of the work, with minor insults, second-order effects, and constitutional weaknesses filling out the rest. The primary insult is usually what the workup identifies first because it crosses the symptom threshold most obviously. The others sit below the threshold — not because they are trivial, but because biology runs on reserve. Redundant systems, overlapping pathways, and compensations absorb some load before anything is felt.¹ The minor contributors are consuming reserve, but the reserve is holding.

The patient has usually acclimatized to this state. Health that erodes gradually does not feel like erosion. It feels like aging, or like being busy, or like the way things are now. Patients who have lost twenty percent of their energy, ten percent of their cognitive clarity, a quarter of their sleep quality, and a meaningful fraction of their stress tolerance over ten or fifteen years may describe themselves as fine until something pushes them over an edge.

Take a patient presenting with persistent brain fog, difficulty concentrating, and low afternoon energy — a thin-framed woman with a history of running low on iron since adolescence and a family history of autonomic sensitivity. The workup identifies significant mold exposure — elevated mycotoxins on urine testing, clear history, classic presentation.² That is the primary insult. The workup also reveals mild sleep apnea, partial small intestinal dysbiosis, B12 and ferritin at the low end of the reference range, and a sympathetic-dominant autonomic pattern. Some of these are secondary to the mold — apnea can be exacerbated by mold-driven sinus inflammation,³ dysbiosis is common downstream of immune disruption,⁴ sympathetic dominance tracks with chronic immune activation.⁵ Others are constitutional — the patient has run low on iron since adolescence and has a family history of autonomic sensitivity.

A practitioner who addresses the mold will often see dramatic improvement. Mold was doing most of the damage. Removing it drops the load below the threshold, the fog lifts, the energy returns. The practitioner has done the hardest and most consequential piece of work.

The temptation at this point is to stop. The patient is satisfied. The remaining items look minor. This is the moment the chapter is about. Those items were minor in the context of the mold doing the heavy lifting. With the mold removed, their contribution to the patient's long-term resilience becomes the next piece of work. The apnea is still fragmenting sleep. The dysbiosis is still consuming micronutrients and generating toxins that translocate. The B12 and ferritin are still low-normal. The autonomic reserve is improved, but still shallow. The primary insult is gone, but the patient's baseline has not been fully restored.

Addressing these contributors will not necessarily produce symptomatic improvement the patient notices. A patient who feels fine may or may not have a strong sense of the

benefit from treating their apnea or bringing their B12 into the optimal range. The gains are not always felt, and if they are, may simply be a general feeling of mild improvement, but they are banked. They show up years later as the viral infection recovered from in three days rather than three weeks, the stressful period absorbed without a crash, the surgical recovery without complications, the cognitive decline that doesn't start when it otherwise would have.†

This is where the practitioner's job definition matters. If the job is to resolve the complaint, it ends when the complaint ends. If the job is to balance the system and build resilience, it ends when the system is balanced. The practitioner has to be clear about which they are doing.

The patient should be given the information to choose. The accurate statement is: the presenting symptoms have resolved, and stopping here is reasonable. It is also true that several other contributors were found, that they are not currently producing noticeable symptoms, and that addressing them would restore resilience you do not currently have. If you choose to continue, here is what that looks like. If you choose not to, here is what to watch for that would bring you back.

For the patient navigating their own care: when a symptom resolves, do not assume you are done. Ask what else was found. Ask what was not addressed. Ask what to watch for.

Clinical pearl: The symptom that brings a patient in isn't always the problem that is most in need of addressing, it may simply be the one most obvious to the patient.

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Chapter 8 — The substrate: what the modern patient carries

The contributors to chronic disease are not random. There is a common stack of burdens that shows up across patients regardless of what brought them in, and one or more items in that stack is often the primary cause itself. Even when the primary cause lies elsewhere, the stack is still present, draining reserves, and any intervention will work better with it addressed.

Microbiome disruption, chemical and metal toxicities, mold exposure, and sleep disorders are very common† and each will be addressed in later chapters in depth. The purpose here is to establish that these are not niche findings for specialized cases. They are the substrate on which the modern patient's biology is operating.

Microbiome disruption is the oldest and most universal of the substrate burdens. Antibiotics are probably the original driver.¹ Antibiotics are life-saving, but they are almost always given without support for the microbiome during treatment and without rebuilding during the critical post-antibiotic window when mucosal real estate has been vacated.² That window closes quickly. Without active rebuilding, the organisms that colonize the vacated space are often not the ones that were there before and can be difficult to evict.

A second consequence is less widely recognized. Antibiotics, by suppressing bacteria, indirectly support fungi. Bacteria and fungi are ancient enemies,³ and when the bacterial population is knocked down, the fungal population expands.⁴ The human immune system handles bacterial challenges better than fungal ones, which means the clinical trade on a course of antibiotics is often an acute bacterial problem swapped for a lower-grade chronic fungal one.† The bacteria-fungi war is treated in depth later; here it is enough to note that the antibiotic history of a patient is part of the substrate picture.

Chemical burden is the second item. The modern environment loads the patient with pesticides, herbicides, plasticizers, solvents, flame retardants, personal care product ingredients, and pharmaceutical residues.⁵ Most are fat-soluble, accumulating in tissue and clearing slowly. The clearance pathways require cofactors the diet must continually replenish,⁶ and pathways needed for other work — hormone metabolism, neurotransmitter processing — compete for the same cofactors.⁷

Toxic metal burden is the third. Lead from historical exposure,⁸ mercury from dental amalgams and seafood,⁹ aluminum from cookware and vaccines,¹⁰ cadmium from tobacco smoke and industrial exposure,¹¹ arsenic from groundwater and rice.¹² Metals differ from chemicals in that they cannot be broken down — they can only be bound and excreted, or moved to storage tissues where they do less immediate damage.

Mold is the fourth. A significant fraction of homes, workplaces, and schools have water damage and active mold growth, much of it hidden behind walls, in attics, crawl spaces and especially in HVAC systems.¹³ Mold produces mycotoxins that are themselves a chemical burden, but mold also actively suppresses the pathways the body would use

to clear it.¹⁴ A patient with chronic mold exposure is carrying a toxin that has altered their immune system to prevent its own removal.

Sleep disorders is the fifth. While not something literally carried in the body, it is a very common burden.¹⁵ A patient who is not sleeping well is a patient whose detox capacity is throttled. The glymphatic system operates almost exclusively during deep sleep.¹⁶ Liver detoxification follows circadian rhythms with peak activity overnight.¹⁷ Immune surveillance and repair cycling are sleep-dependent.¹⁸

These five burdens share a common effect: they drain the patient's capacity to heal. Healing requires energy in two senses.

The first is reserves — ATP for cellular work, minerals for enzyme function, cofactors for metabolic pathways. Each burden consumes these in its own way. Microbiome disruption through immune activation and nutrient competition. Chemical load through Phase I and Phase II cofactor consumption. Metal load through displacement of essential minerals at enzyme sites. Mold suppresses neuropeptide production. A patient carrying all four is running at a chronically depleted baseline that no amount of supplementation can fully correct until the underlying consumption is reduced.

The second is immune balance. Inflammation is not an error state — it is part of the healing cycle, designed to mobilize repair resources and resolve in a reasonable time frame.¹⁹ The problem is when the inflammatory cycle cannot complete. A stalled inflammatory state continues to consume resources without resolving, producing ongoing tissue damage and systemic immune activation.²⁰ Each burden drives this stall in its own way. The microbiome keeps presenting bacterial products. The chemical and metal loads produce ongoing tissue irritation. The mold actively prevents the immune response from resolving. The patient stays stuck in inflammation not because their immune system is misconfigured but because the inputs that trigger and sustain inflammation never stop coming.

Finally, sleep stitches all healing together. It is when tissue repairs and detoxification is done.

Clinical pearl: All five of these burdens should be suspected present to some degree until proven otherwise.

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Chapter 9 — Dose and response: The line, the curve and the step

Chapter 1 gave permission to experiment. Chapter 8 described what the patient is likely carrying when that experimentation begins. Neither addressed how hard to push, how fast, and at what dose. The practical habit most practitioners develop — start low, observe, increase incrementally — implicitly treats effect as proportional to dose across the titration range. This is appropriate for many substances. It fails, sometimes silently, for others. The dose-response relationship follows one of three shapes.

The first response is linear. Dose and effect scale roughly proportionally across the useful range. Double the dose, roughly double the effect. Many nutrient supplements behave this way.¹ A patient deficient in magnesium gets incremental benefit from each increment, up to the point where additional magnesium hits absorption limits or produces loose stools. The linear curve is what "start low and go slow" was designed for.

The second response is exponential. Below a certain threshold, the substance produces modest effect that scales roughly with dose. Above an inflection point, gains accelerate.

The sinuses illustrate this clearly. Healthy paranasal sinus epithelium produces nitric oxide continuously.² NO has potent vasodilating and antimicrobial activity.³ A patient with some degree of sinus compromise produces less NO. Improving the sinus condition incrementally improves local NO output — better sleep quality, local antimicrobial defense, nasal breathing. These are real benefits that scale roughly with improvement.

But past the inflection point, the improvements become obvious in unexpected ways. An older male patient may report morning erections he hadn't had since he was much younger.† The NO output has crossed a threshold where erectile function — dependent on NO-driven vasodilation⁴ — visibly improves.

The third response is stepwise — discrete rather than continuous. The substance either works or it doesn't, depending on whether a threshold is crossed, with no gradient in between.

A clear example is remediating a moldy house. A protocol that knocks the mold down 50% may not be enough for the patient's immune system to give the all-clear signal. Only at greater than 95% reduction does the immune system stop generating histamine and bradykinin, and the patient gets relief.†

Step responses are where conventional dosing strategy fails most visibly. A practitioner applying "start low and go slow" to a stepwise substance gives sub-threshold doses indefinitely, sees no effect, and concludes the intervention does not work — ruling out the very protocol the patient needed, not because it was wrong but because it was never given at a dose that could have worked.

Recognizing which curve a given substance follows is part of the clinical work. Antimicrobials tend toward stepwise. Nutrients tend toward linear. Interventions depending on systemic concentration thresholds tend toward exponential. But the shape can shift with the patient's condition — a substance that is linear in a healthy patient can become stepwise in one whose clearance pathways are overwhelmed, because the sub-threshold range widens.†

Interventions can also demonstrate all three response types. They may be linear for a certain percentage of accepted dose ranges, then exponential at the upper ranges, with an unexpected stepwise shift producing an entirely new benefit at only the highest doses.

This puts the practitioner in a tradeoff. Going slowly protects the patient from being overwhelmed. It also means the patient may suffer longer than necessary, and for stepwise substances, the practitioner may never find out whether the protocol would have worked. Going quickly reaches the thresholds where exponential and stepwise effects appear, but risks overtaxing a patient whose reserves are already depleted. The judgment is not a universal rule. It is a per-patient, per-substance calibration based on what the substance needs to do its work and what the patient can absorb while it does.

Clinical pearl: The optimal dose can vary dramatically between clients with the same presentation.

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Chapter 10 — Rate-limiting inputs

The best protocol in the world, missing a rate-limiting input, cannot be fixed by making the protocol more aggressive. If the patient does not have what the protocol requires to finish its work, adding more protocol does not add more completion. It adds more demand against the missing input, and the system stalls harder.

Rate-limiting is a concept from enzyme kinetics. A biochemical pathway runs at the speed of its slowest step.¹ Every other input can be abundant; if one is short, the pathway's output is capped at whatever the short input allows. Doubling the abundant inputs does nothing.

The same logic applies clinically. A protocol is a sequence of biological steps. Each step has its own requirements. When one is missing, the protocol's outcome is bounded by that absence, regardless of how well-chosen the rest of the intervention was.

Iodine is the clearest example. David Derry, a Canadian thyroid physician, published a 2009 case series in *Medical Hypotheses* on topical Lugol's iodine applied to four surgical scars.² One was fifty years old, on Derry's own face, from mole removal in childhood. Within three days of daily application, the scar began to regenerate — scar tissue was replaced by normal skin architecture including hair follicles and normal dermal structure. Stopping iodine halted the process. Resuming it restarted the process. The fifty-year-old scar regenerated completely over roughly two years. The study is a single case series in a hypothesis journal — suggestive but not definitive.

What this tells you is not simply that iodine is a scar remedy. It is something more fundamental. Adult human tissue, given the right input, some tissue can regenerate rather than scar.† Scar is a patch. Regeneration is a rebuild. The body defaults to the patch when the rebuild is not supported. This is not a failure of the body. It is a sensible allocation, but it is allocation under constraint, and the constraint is iodine. Supply the iodine and the choice the body would prefer becomes possible.

Iodine deficiency in the modern population is common.³ Soil depletion has reduced iodine in food crops. Bromide, fluoride, and chlorine — halogens that compete with iodine at the same receptor and transporter sites — are ubiquitous in the modern diet, water supply, and medication list, actively displacing what little iodine the patient takes in.⁴ U.S. data confirms the pattern: the proportion of women of reproductive age with inadequate iodine intake roughly doubled between 2001 and 2018, and nearly half of pregnant women now fall below the recommended threshold.⁵

Selenium operates on the same principle with different epidemiology. Selenium is required for thyroid hormone conversion — the deiodinases that convert T4 to active T3 are selenoproteins — and for glutathione peroxidase function.⁶ Where selenium is deficient, iodine work often cannot complete because the conversion step is bottlenecked. In parts of central Africa, China, New Zealand, and other regions with selenium-poor soils, iodine and selenium deficiencies co-occur and must be addressed

together.⁷ In the United States, national food distribution and naturally high selenium in several farming regions leave the population generally replete — the American patient is far more likely to be iodine-limited than selenium-limited. But patients on restricted diets, with compromised absorption, or from regions with genuine soil deficiency should be evaluated.

Zinc shows up most visibly as an artifact of chelation. Chelators bind zinc as readily as they bind toxic metals,⁸ so aggressive chelation on a patient with borderline zinc status produces rapid zinc depletion the practitioner may not have anticipated. The chelation becomes its own rate-limiter — the patient cannot continue because the zinc supporting immune function and wound healing has been stripped out. This is covered in the chelation teaching.

Protein and B12 are rate-limiters for patients on vegan and vegetarian diets. Plant protein is lower in bioavailable amino acid density than animal protein,⁹ and the sulfur-containing amino acids most useful for tissue repair are harder to assemble from plant sources alone. B12 is not produced in meaningful amounts by any plant.¹⁰ Fermented foods and algae often cited as vegan sources either contain B12 analogs that compete with true B12 at the receptor without providing its function, or contain true B12 in amounts too small to meet requirements.¹¹ A vegan patient whose healing is stalled, whose energy is low, whose cognitive function is drifting is often rate-limited by exactly these two inputs. No protocol aggressiveness will compensate.

Sleep belongs on this list though it is not a nutrient. Most tissue repair happens during sleep — growth hormone pulse,¹² glymphatic clearance,¹³ immune reset during slow-wave sleep.¹⁴ A patient sleeping four to five hours a night has repair capacity rate-limited by the hours not slept, regardless of protocol optimization.

These five are examples, not the full list. The practitioner will encounter patient-specific rate-limiters no general list can anticipate. The general habit to cultivate is to ask, before aggressive intervention: what does this protocol require that the patient may not have?

The patient populations where rate-limiters should be suspected by default are those whose intake is constrained or whose apparent reserves are thin. Patients on extreme diets have narrowed the nutrient inputs available. Patients who drink only distilled water have removed the trace mineral load that ordinary water provides — over time, a distilled-water habit strips minerals faster than most patients replace them. Patients with slight builds who appear malnourished often are.

The clinical posture this chapter argues for is boring compared to aggressive intervention, and that is the point. Before escalating dose, before adding the next tool, ask whether the current protocol is limited by what the patient can absorb, or by what the protocol is providing. If the rate-limiter is on the input side, more protocol does not help. Only the missing input does.

Clinical pearl: A sudden onset of giggling from taking (and sometimes even holding) the right supplement is a positive indication. This is one way the patient's body can communicate.

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Chapter 11 — Substances that stall healing

The previous chapter was about absence — when something the body needs is missing, healing stalls at the missing input. This chapter is about the opposite problem. Healing also stalls when something is present that shouldn't be.

Detoxification in common usage has been narrowed to mean a short-term cleanse. That is not what the word means here. Detoxification in the clinical sense is the removal of anything present in the body that does not belong there, with the recognition that the patient's symptoms, lack of progress, or inability to hold gains may be a direct consequence of what is still present.

What can be present that shouldn't be? More than most practitioners assume. Chemical burden — pesticides, herbicides, plasticizers, solvents, flame retardants, personal care product residues, pharmaceutical metabolites — accumulates in fat-soluble form and is cleared slowly when it is cleared at all.¹ Metal burden — lead, mercury, aluminum, cadmium, arsenic — sits in tissues and displaces essential minerals at enzyme sites.² Molds and their mycotoxins drive their own category of immune disruption, actively suppressing the clearance pathways the body would use to remove them.³ Stealth infections — chronic viruses, certain spirochetes, intracellular bacteria — persist by hiding from the immune system and consume host resources for years or decades.⁴ Thickened, stalled bile prevents conjugated fat-soluble toxins from leaving even though they have been correctly processed.⁵ Stones — gallstones, kidney stones, smaller microliths that don't show on imaging — are physical obstructions or irritants. Biofilm is a structured matrix that pathogens build to shield themselves from both the immune system and antimicrobial protocols.⁶ Retained cellular debris — dead cells, damaged proteins, oxidized lipids, the remains of unresolved inflammation — accumulates in tissues and lymphatics and continues to consume immune attention. Even EMF, for sensitive patients, acts like a toxin — the body cannot remove it, only be shielded from it⁷

The general principle: the body cannot fully heal around a persistent presence.

This produces the same trap described from the absence direction. A protocol that produces partial benefit looks like it needs more of itself. The temptation is to push harder. Sometimes the correct move is to stop pushing the current protocol entirely, identify what presence is capping the response, and address that first. The system that has been compensating around the presence will often do its own work once the presence is removed, without further intervention.

The chapters that follow do two pieces of work before the detox arc proper begins. The next chapter teaches the predictable failure modes that the supplement industry produces in clinical practice. The chapter after that synthesizes everything the first half has taught into a single diagnostic instinct: when something isn't working, stop pushing, figure out why, act on what you find. From there the book moves into the specific work of detoxification — water-soluble versus fat-soluble compounds, what can leave on its

own and what requires help, the operation chain that takes a toxin from storage to exit, and the tools for each part.

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Chapter 12 — The detox traps

Before we talk about the right way to do detoxification, we should understand how not to. There are several distinct ways a detox protocol can produce harm, and most are predictable consequences of how the supplement industry designs, manufactures, and markets its products. First, a piece of clinical machinery for reading what is happening when a patient feels worse on a protocol.

The goal of a well-designed detox is silence.† The patient never notices it is happening. The toxins move out, the burden decreases, the labs improve, and the patient gradually feels better. The cultural narrative that detox is supposed to feel bad — that suffering is part of the process, that "die-off" reactions are evidence the protocol is working — is not a clinical standard. It is a story that fills the gap left by protocols that produce reactions and practitioners who do not know how to read them.†

A second good outcome is immediate, even if minor, improvement. Some patients improve significantly within days once a protocol begins — most commonly when the blood compartment was carrying a meaningful share of the toxic load and the early phase clears it. This is real, but the practitioner must be mindful. Toxins also accumulate in tissue compartments — fat, bone, brain, organ tissue — and tissue stores release into circulation slowly.¹ If the protocol is stopped at the point of rapid improvement, the blood compartment will gradually re-accumulate from tissue stores, and symptoms will return. The timeline varies — days for some patients, months for lead stored in bone.²

The clinical practice that addresses this is to check in at one month and again at three months after apparent resolution.† If symptoms are returning, the tissue stores are still releasing, and the protocol needs to resume. For patients with deep-seated burden, a maintenance dose may be appropriate for many years, keeping the blood cleared as the body slowly turns over tissue stores.

In seriously toxic patients with high stored burden and limited reserve, silent detox is not always possible. Even with the best protocols, there is always some redistribution — no binder or chelator is perfect.³ A sensitive, highly toxic patient may feel the load passing through, especially in the first few days. The question is when a reaction crosses from acceptable into something requiring investigation. The criterion: each day should be less severe than the day before.† If the reaction stabilizes at a low but continual level, this may be acceptable, but consider lowering the dose.

This is the practitioner's tool for distinguishing between the side effects of detoxifying someone very toxic and the side effects of a problem with the protocol itself.

Trap one: The protocol was poorly designed

Examples: a Phase I inducer without Phase II support for chemical detox,⁴ or chelators that aren't appropriate for the metals present or are too weak — either can cause redistribution.

The corrective is to stop the protocol and identify the missing piece. More of the same product compounds the problem.

Trap two: The product itself is contaminated

Some of what the patient excretes during a "detox" is not their stored toxins leaving — it is the product's contaminants going in and coming back out.⁵ Low-quality zeolite frequently contains heavy metals.⁶ Low-quality chlorella can contain heavy metals from growing water and mold toxins from improper drying. Low-quality herbal products can carry pesticide residues, solvents and adulterants.⁷

The clinical recognition cue: urinary metals appearing during a detox protocol may be the patient's stored metals leaving (the desired outcome) or the product's metals entering through the supplement and leaving through urine. The same lab result can have either meaning.

The corrective is product audit, not dose adjustment. The supplement must be replaced with one whose sourcing and quality control can be verified.

Trap three: The patient is more burdened than the protocol's standard dose was designed for

The product is well-designed and uncontaminated. The patient simply has more total burden than the standard protocol was built for, and a dose appropriate for a typical patient overwhelms this one.

This is not the industry's fault. The corrective is lower dose, slower titration, longer cycles between rounds, and in extreme cases a stepped entry beginning at fractional doses. Some patients will need a permanently modified version.

These three traps produce similar surface presentations — the patient feels worse, the validity window is violated — and the corrective for each is different. Trap one needs the missing component added. Trap two needs the product replaced. Trap three needs the dose reduced. Reaching for the wrong corrective makes things worse.

A practical procedure for trap three: Depending on the patient and their presentation, drop to ten to twenty-five percent of the original dose. If the patient reports manageable discomfort that decreases day by day inside the validity window, the practitioner has confirmed both that the protocol is correct and that the patient can tolerate it at reduced dose, and can begin titrating up. If the reaction at ten percent is still outside the window, the patient is likely dealing with one of the first two detox traps.

The communication pattern that hides the traps

The hardest piece is not the traps themselves. It is the pattern that conceals them.

The patient starts a protocol. They feel worse. They report this. The practitioner, expecting a detox reaction, reassures: you're detoxing, stay with it, this is normal. The patient continues. They feel worse still. At some point they stop reporting, because reporting produces reassurance rather than action, and because feeling worse on a protocol they were told would help starts to feel like personal failure rather than clinical information. The patient either suffers through real damage in silence or quietly drops out.

This pattern fails in both directions. If the reaction was a trap, the reassurance was wrong and the patient was harmed. If it was a real detox response within the validity window, the reassurance was technically correct, but the relationship dynamic it produced — patient learns that reporting feels-worse is met with stay-the-course — means that next time, for any reason including a real trap, they might not report. The relationship may have been trained to suppress exactly the information the practitioner needs.

The way out is structural. The practitioner does not say "stay with it" without first checking the validity criteria. If within the five-day decreasing window, the practitioner supports the patient while explicitly inviting continued reporting: "tell me how each day compares to the one before, and if it isn't getting milder by day three, we stop and look." If outside the window, stop and investigate the three traps. The patient is never put in the position of deciding whether their reaction is "real" detox or something concerning. That judgment is the practitioner's job.

The supplement industry produces the conditions for these traps. Practitioner habits and patient communication patterns determine whether the conditions translate into real harm. The practitioner's job is to source carefully enough to minimize trap two, design protocols completely enough to minimize trap one, dose conservatively enough to minimize trap three, while maintaining the kind of patient relationship that surfaces problems early enough to address them before they become serious harm.

Clinical pearl: Consider keeping a small snow globe in your office. It is a wonderful tool to explain why the detox protocol you are suggesting is designed as it is. A shake of the snow globe creates a cloud of particles floating about. The lesson is, we never want to turn a patient into a snow globe. Mobilize only what you can capture and drain.

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Chapter 13 — Patient failures

The book has spent twelve chapters on systems and on practitioners. Completing the picture requires looking at the patient. Some protocols fail because the system failed them. Some fail because the practitioner missed something. And some fail because the patient is the failing system, and no amount of system reform or practitioner skill will produce a result the patient is not willing or able to participate in producing.

This chapter is harder to write because "patient noncompliance" is the alibi every failed practitioner reaches for. The book has been at pains to teach the practitioner to look at themselves first. This chapter is not a license to do otherwise. It is a description of a real category of failure that exists alongside the others.

There are three patterns.

Pattern one: The patient lacks the discipline to follow the protocol

They agree to it in the office, leave with the supplements, and then don't take them. Or take them inconsistently. Or skip the dietary or other lifestyle changes. The protocol fails not because it was wrong but because it was never run.

Before calling this a discipline failure, three things must be true.

1-The protocol must be achievable for this patient's life. A working adult with two children, a demanding job, and a long commute cannot run a fifteen-supplement, four-times-daily protocol that requires meal preparation and an exercise regimen no busy person actually does. The practitioner who designs an unworkable protocol and blames the patient for not maintaining it has the failure on the wrong side. Step one is asking whether what was prescribed is something this specific patient could actually do.

2-The patient must have the neurochemical capacity to follow through. Lack of motivation can be a clinical finding, not a character trait. Brain fog reduces the capacity to remember. Depression reduces the capacity to want to.¹ Dopamine dysregulation makes consistent action across days harder.² Sleep deprivation flattens executive function.³ A patient who cannot maintain a protocol may be carrying a substrate burden that is actively interfering with their ability to comply. The substrate work this book teaches often resolves the apparent noncompliance by addressing what was making compliance impossible.

3-The patient must be able to afford your protocol. The practitioner must have a real, if uncomfortable, conversation about the patient's budget. Suggesting an expensive protocol that is optimal, but one they cannot follow through on, is not helpful. The hard truth is that unless you set aside a discretionary fund for charitable cases, sometimes you must triage a protocol for a patient and choose what is most important yet within their budget to accomplish.

After all three qualifiers are honored, what remains is genuine discipline failure — patients who do not follow through despite a reasonable protocol and adequate capacity. That category is real. The honest move is to name what is happening, ask whether they want to continue, and if so, restructure the relationship with closer monitoring or a simpler protocol. If the patient does not want to do the work, the practitioner is better off knowing.

Pattern two: The patient is not actually there for treatment

They are in the office at the behest of a spouse, parent, adult child, court order, or employer. They show up, listen, take the bag of supplements, consent to the lifestyle changes. They never had any intention of running the protocol.

This is the easiest to misread because the surface looks like discipline failure. The recognition cue is that changes the practitioner makes do not produce changes in compliance. A patient who lacks discipline but wants the result improves when the protocol is simplified. A patient with neurochemical barriers improves when those are addressed. A patient who is not there for treatment does not improve under either intervention.

The honest move is to name the observation: "I notice that the changes we've made haven't shifted what you're actually doing. Sometimes this means the protocol still isn't right. Sometimes it means the work isn't work you've decided you want to do. I'd rather know which is true than keep trying to fix the wrong thing."

Pattern three: The patient has an addiction they cannot overcome

This is a specific subset that needs separate treatment because the mechanism is different. The patient is not failing because they are lazy or distracted. They are failing because they are physiologically pulled toward something the protocol asks them to give up, and the pull is stronger than their will.

Addiction here is broader than the usual usage. It includes substance addictions, but also patterns harder to recognize. There are at least three mechanisms worth knowing.

Addiction as energy-access workaround The body, when it has lost reliable access to physiological energy, learns to use alarm states as substitutes.† Allergens and reactive foods become addictive because the cortisol and adrenaline rush they trigger is the only way the patient knows how to feel awake.⁴ Patients listing their favorite foods sometimes list the foods they are highly reactive to.† The corrective is not simply to teach avoidance, but to also address the underlying energy depletion so the patient has another source before the alarm source is taken away.

Addiction as infection's reward-hijacking Many chronic infections actively manipulate the host's reward and punishment chemistry.† Parasitic infections can drive sugar and glutamate cravings because parasites use those substrates.⁵ Cancer's Warburg

metabolism requires sugar at rates that may drive the patient to eat in ways that feed the cancer.⁶ Bacterial overgrowths fermenting carbohydrate produce signals that increase carbohydrate craving.⁷ The patient experiences these as their own appetites. They are not — at least not entirely.

The push away from what hurts the organism is equally real. Bitter compounds are broadly antimicrobial,⁸ and bacterial endotoxin actually increases the host's sensitivity to bitter taste, making bitter foods more aversive.⁹ Candida colonization is associated with reduced sensitivity to bitter and sweet, meaning the patient does not register warning signals that would normally limit intake.¹⁰ Shifting to a higher sugar and lower bitter diet both feeds the Candida and applies a selectively biased pressure against the Candida's foe, bacteria.

The objection that microbes are too simple to manipulate sophisticated human neurochemistry rests on a backwards assumption — that humans invented this chemistry and microbes would have to learn it. The actual history is the opposite. Serotonin is present in bacteria, protozoa, fungi, and plants.¹¹ Gut bacteria produce serotonin directly.¹² Dopamine is produced by multiple bacterial genera.¹³ GABA is produced by Lactobacillus and Bifidobacterium and was used for bacterial signaling long before neural signaling.¹⁴ Toxoplasma gondii carries its own tyrosine hydroxylase gene and produces L-DOPA inside infected cells.¹⁵ Neurotransmitters are the ancient biochemical language. Humans are recent speakers of a dialect. The microbes are native speakers, and some of them are fluent enough to write.

Addiction as self-medication of a neurochemical deficit This is the third mechanism and it is important enough to warrant its own chapter, the one that follows.

Clinical pearl: The following reframe for the patient helpful: If stranded in a lifeboat, thirsty, would you drink the seawater? It is water. But it would only make you thirstier, only satisfy you for a moment, then make the thirst worse. That is what addictions are. The frame removes agency from the setup — a person in a lifeboat cannot be blamed for being thirsty. It lets the practitioner raise the topic without the patient having to defend themselves.

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Chapter 14 — The substance is the clue

Some addictions are self-medication of a neurochemical deficit the patient can feel but cannot name.† The deficit produces a chronic uncomfortable state, a background noise of anxiety or flatness or pain or inability to focus, and the patient discovers that a particular substance makes that noise stop. The first exposure is not recreational. It is closer to relief.

The deficit itself, however, can arrive through entirely different doors.

Some patients were born with it. A genetic polymorphism in a GABA-synthesizing enzyme, a variant in the dopamine D2 receptor, an inherited weakness in endorphin production. These patients have never known a normal baseline. They grew up with an undefined sense that something was wrong, that life required more effort than it seemed to require of the people around them, and when they encountered the substance that corrected the imbalance, the experience was not getting high. It was arriving at normal for the first time.

Other patients acquired the deficit through toxic exposure. A mold exposure that depleted glutathione and disrupted neurotransmitter precursor pathways. A chronic infection that diverted tryptophan toward the kynurenine pathway and away from serotonin synthesis. Heavy metal accumulation that impaired enzymatic function across multiple systems. Years of processed food that starved the cofactor pools the brain depends on. These patients had a functional baseline once and lost it, often so gradually they cannot point to when things changed. The substance they reach for is compensating for damage the environment inflicted.

Still others arrive at addiction through the medical system itself. The patient prescribed opioids after surgery for managing the post-operative pain, now cannot stop. The patient given benzodiazepines for anxiety who finds, when they try to discontinue, that their baseline anxiety without the drug is far worse than it was before they started. In these cases the medical intervention, through receptor downregulation and tolerance, has unmasked and activated a potential addiction that might otherwise have remained silent.

Three different origins. But in all three cases, the substance the patient gravitates toward is not chosen at random. It is chosen because its pharmacology matches the specific deficit the patient is carrying.† The drug of choice is diagnostic, regardless of how the deficit arose.

A related version of this idea has been in the psychiatric literature since 1985, when Edward Khantzian proposed what he called the self-medication hypothesis. Khantzian argued, based on clinical observation, that drug-dependent individuals are drawn to specific substances because of the match between the drug's pharmacological action and the individual's dominant painful emotional state. Opioid addicts were not seeking euphoria. They were muting an intolerable baseline of emotional pain. Cocaine users

were not chasing a high. They were treating depression, low energy, and an inability to feel engaged with ordinary life.

Khantzian's framework was built on affect, on emotional experience. What he did not do, and what matters for the practitioner reading this book, is trace those emotional states back to their biochemical substrates and then ask the functional question: why is that substrate depleted, and what would restore it? And he did not distinguish between the patient who was born depleted, the patient who was depleted by their environment, and the patient who was depleted by their treatment. These are different clinical situations with different intervention paths, even when the surface presentation looks the same.

Reading the substance

Start with the commonplace addictions, the ones practitioners see every day, and work through what each one suggests about the patient carrying it.

Sugar. The patient with the sugar habit is often treated as if they simply lack dietary discipline, but sugar triggers a substantial dopamine release in the nucleus accumbens through the same reward circuitry that responds to other addictive substances. Even modern foods considered healthy — fruits, grains — are extremely sweet, historically speaking (more on this in a future chapter). This has had an effect on our sugar homeostasis. It is also worth noting that sugar feeds many of the organisms discussed in the microbiome chapters that follow. The craving may not be entirely the patient's own.†

Caffeine. It is so ordinary that most people do not think of it as an addiction at all, but the patient who cannot function without morning coffee and crashes without it is telling you something specific. Caffeine blocks adenosine receptors, which reduces the sensation of fatigue, and it increases dopamine and norepinephrine activity in the prefrontal cortex. The person who depends on caffeine to think clearly, to feel motivated, to get through the afternoon is likely running low on baseline dopaminergic or norepinephrinergic tone. They may also be carrying adenosine buildup from chronically poor sleep, which is its own clinical finding. But there is another layer worth considering. Caffeine also inhibits phosphodiesterase, slowing the breakdown of cyclic AMP and effectively preserving ATP signaling. A patient whose mitochondrial function is compromised — whether from toxic burden, nutrient depletion, or chronic infection — is a patient whose ATP production is inadequate to meet demand. As ATP degrades to ADP and then AMP, adenosine accumulates, producing the fatigue signal that caffeine masks. The caffeine is not just patching a neurotransmitter deficit. It may be papering over an energy production problem at the mitochondrial level, which opens an entirely different line of clinical investigation.

Social media and phone scrolling. The patient who cannot stop checking their phone, who scrolls through social media for hours without intending to, who feels a compulsive pull toward notifications and feeds, is running the same dopaminergic deficit as the

sugar addict and the caffeine dependent. Every notification, every like, every new piece of content delivers a small dopamine pulse. The architecture of these platforms is designed to exploit exactly this: variable-ratio reinforcement, the same schedule that makes slot machines compelling, tuned to deliver unpredictable micro-rewards that keep the dopamine system engaged. The patient who is hooked on their phone is not simply weak-willed. They are a person with insufficient baseline dopaminergic tone who has found a source of dopamine that is free, legal, available twenty-four hours a day, and deliberately engineered to be difficult to stop. The practitioner who recognizes compulsive phone use as a dopamine-deficit signal has gained a piece of diagnostic information that the patient would never have thought to mention, because no one thinks of their phone as a drug. It is also worth noting that social media use often displaces the very activities that would restore healthy neurochemistry naturally: face-to-face social connection, physical movement, unstructured time outdoors, and sleep. The behavior that compensates for the deficit simultaneously deepens it.

Video games. The same variable-ratio reinforcement architecture that drives social media engagement was pioneered in game design. Loot boxes, leveling systems, achievement rewards, and multiplayer rankings all deliver dopamine through unpredictable reward schedules. But video games also recruit additional neurochemistry that social media does not. The sense of mastery and competence that comes from progressing through a game activates reward pathways tied to achievement and agency — feelings that a patient with low dopamine or low norepinephrine may not be generating from their actual life. The social component of online multiplayer games can provide oxytocin and belonging signals for a patient who is isolated. The immersive nature of gaming can quiet an anxious or racing mind in much the same way alcohol does for the GABA-deficient patient, by occupying attentional bandwidth so completely that the default mode network — the source of rumination — gets suppressed. The child or adult who cannot stop gaming may be self-medicating dopamine deficit, social isolation, anxiety, or all three. As with social media, the hours spent gaming displace the activities that would address the underlying deficits: physical movement, face-to-face relationships, sleep, and unstructured time that allows the brain to restore itself.

Pornography. This is the behavioral addiction most patients will never volunteer and most practitioners will never ask about. Sexual arousal and orgasm produce a surge across multiple neurotransmitter systems simultaneously: dopamine, oxytocin, vasopressin, and testosterone all spike. A patient with compulsive pornography use may be self-medicating any one of these deficits, and which one is dominant changes the clinical picture. A patient with low testosterone may be using arousal to generate the drive he is missing. A patient with low vasopressin may find that the behavior temporarily clears cognitive fog. A patient with depleted oxytocin gets a low-barrier bonding hit without the relational risk that real intimacy demands. A patient with low dopamine is running the same reward-seeking pattern as the sugar addict and the phone scroller, but through a more potent delivery mechanism. The complication is that every one of these molecules dysregulates with chronic overstimulation — vasopressin shifts toward anxiety and stress reactivity, oxytocin binds to images instead of relationships, dopamine receptors desensitize, and the deficit that started the cycle

deepens. Like social media, the behavior that compensates for the deficit simultaneously worsens it.

Alcohol. Alcohol enhances GABA-A receptor activity broadly while simultaneously suppressing glutamate, the brain's primary excitatory neurotransmitter. The patient is GABA-deficient, glutamate-dominant, or both.† This is why alcohol withdrawal is medically dangerous in a way that most other withdrawals are not. Remove the exogenous GABA enhancement from a system that was already running insufficient inhibitory tone and the excitatory system, now completely unbraked, can produce seizures.

Psychiatric medications. One in six American adults fills at least one psychiatric prescription per year. Antidepressant use alone runs above eleven percent of the adult population and climbing. Add benzodiazepines — over eighty million prescriptions dispensed annually in the United States — and stimulant prescriptions for ADHD — which nearly doubled from fifty million to over eighty million per year between 2012 and 2022 — and the numbers describe a population-level pattern of neurochemical supplementation that no one calls addiction but that functions identically to the mechanisms this chapter describes.

The model is familiar from other industries. The first prescription is easy to get. The prescriber is often a general practitioner, not a psychiatrist — over forty percent of all psychotropic medications are prescribed by GPs. The patient presents with anxiety, insomnia, low mood, or difficulty concentrating. The prescription provides relief. It works. The patient feels better. And then, when they try to stop, they discover that the drug has not corrected the underlying deficit. It has masked it while simultaneously downregulating the brain's own production of the neurotransmitter the drug was supplementing. The patient is now worse off than before they started: the original deficit remains, and the brain's compensatory response to the drug has deepened it.

SSRIs are the clearest example. The patient presents with low mood. The SSRI blocks serotonin reuptake, increasing synaptic serotonin availability. The patient feels better. But the brain, registering the increased serotonin signal, downregulates its own serotonin production and reduces receptor density. When the patient tries to discontinue, they experience withdrawal symptoms that are often indistinguishable from the original depression — and frequently worse. The prescriber interprets this as evidence that the patient "still needs the medication." The patient stays on. The cycle continues.

Benzodiazepines follow the same logic with GABA. The patient presents with anxiety. The benzodiazepine enhances GABA-A receptor sensitivity to endogenous GABA. The patient feels calm. But chronic use downregulates GABA receptor density, so that the patient's own GABA — which may have been marginal but functional before the prescription — is now insufficient to produce calm without the drug. Discontinuation produces rebound anxiety that exceeds the original complaint. The patient who entered

the system with a mild GABA deficit now has a severe one, maintained by the very drug that was prescribed to treat it.

Stimulant medications for ADHD complete the pattern with dopamine. Adderall, Ritalin, and Vyvanse work by increasing dopamine and norepinephrine availability in the prefrontal cortex — which is precisely the deficit the caffeine-dependent patient is self-medicating through less potent means. The child or adult diagnosed with ADHD and placed on stimulants often experiences genuine relief, because the medication is correcting a real dopaminergic deficit. But the same question applies: why is the dopamine low? Is it a genetic variant in dopamine receptor density? Is it iron deficiency limiting tyrosine hydroxylase? Is it chronic inflammation depleting BH4? Is it a gut dysbiosis reducing dopamine precursor availability? The stimulant prescription answers none of these questions. It patches the output without investigating the input, and in doing so it can become a permanent fixture in the patient's life — not because the patient is addicted in the conventional sense, but because the upstream deficit was never identified or addressed.

This is not an argument against all psychiatric medication. There are patients for whom these drugs are appropriate and necessary. It is an argument that the practitioner should understand what these drugs are doing neurochemically, should recognize that long-term use often converts a treatable deficit into a drug-maintained dependency, and should consider whether the upstream deficit — the reason the patient needed serotonin or GABA or dopamine support in the first place — could be addressed through the substrate and cofactor work this book teaches, either before the prescription is written or as a path toward eventual discontinuation.

Nicotine. Nicotine acts on nicotinic acetylcholine receptors and secondarily drives dopamine release in the nucleus accumbens. Insufficient cholinergic tone shows up as poor concentration, difficulty sustaining attention, and a feeling of cognitive sluggishness. Insufficient dopamine shows up as low motivation and an inability to find ordinary activities rewarding.

Cannabis. Clinical endocannabinoid deficiency has been proposed as a real syndrome, potentially underlying conditions like fibromyalgia, irritable bowel syndrome, and migraine. The chronic cannabis user may be patching a system that underproduces anandamide, the body's primary endocannabinoid. The result of that underproduction is poor stress buffering, heightened pain sensitivity, disrupted sleep, and emotional rigidity. The patient who uses cannabis to manage pain, anxiety, or insomnia and finds that nothing else works as well may be telling you that their endocannabinoid system is not producing what it should. THC is substituting for what anandamide is supposed to be doing.

Opioid pain medications. The patient who was prescribed opioids for a legitimate injury and cannot stop taking them long after the injury has healed is the most medically visible version of this pattern. Opioids bind to mu-opioid receptors, the same receptors

that respond to the body's endogenous opioid peptides: endorphins and enkephalins. Once the injury is healed, stopping creates a rebound they cannot endure.

What the pattern reveals

The conventional notion of an "addictive personality" suggests that some people are globally vulnerable to any substance they encounter. But if the mechanism is a deficit in a particular neurotransmitter system, the prediction is different. A patient with low GABA and normal endocannabinoid tone will find alcohol compelling and marijuana unremarkable. A patient who scrolls social media compulsively but has no interest in alcohol or cannabis is telling you the deficit is dopaminergic, not GABAergic, not endocannabinoid. The patient who smokes but has never been drawn to pornography or phone scrolling may have a cholinergic deficit more than a dopaminergic one. The substances the patient is not drawn to are as informative as the one they are. The specificity of the addiction reflects the specificity of the deficit.

It is also on a spectrum, and the practitioner who only looks for the severe end will miss the data that the mild end provides. The patient who drinks a bottle of vodka a day is obviously addicted. But the patient who has two glasses of wine every evening to unwind is also giving you information. They may not meet any clinical definition of addiction. They may not think of themselves as having a problem. But the fact that they have settled into a nightly pattern of exogenous GABA enhancement tells you that their own GABAergic system is not producing enough inhibitory tone to transition from the stress of the day into rest without help. That is a mild deficit, but it is still a deficit, and it still points the practitioner toward the same investigation: what is the GABA status, what are the cofactors doing, what is driving the excitatory tone that the wine is dampening? The same logic applies to the patient who needs coffee to function but would never call themselves an addict, or the patient who eats something sweet every afternoon and describes it as a treat rather than a dependency. The severity of the pattern tells you how deep the deficit runs. It does not change what the pattern means.

This reframe changes the clinical conversation. Instead of asking how do we stop the behavior, the practitioner asks what deficit is this behavior compensating for, and what would it take to restore the body's own production? That is a question this book's framework can answer.

Why the neurotransmitter is low

This is where the three doors matter clinically, because the investigation path differs for each.

For the patient born with the deficit, the question is genetic and constitutional. Polymorphisms in GAD enzymes that synthesize GABA, variants in the DRD2 receptor that reduce dopamine sensitivity, inherited differences in endorphin production. These patients have always been this way. Their history will reflect it: early-onset anxiety, childhood difficulty with focus or mood regulation, a sense of being different that

predates any substance exposure. The practitioner cannot change the genetics, but they can support the compromised pathway epigenetically with the cofactors and precursors it needs to function as well as it can.

For the patient whose deficit was acquired through toxic or environmental exposure, the detoxification teachings that will be explained in this book are uniquely appropriate.

For the patient whose deficit was created or revealed by medical treatment, the picture is different again. The post-surgical patient prescribed opioids who cannot discontinue them may have had marginal endorphin production before the surgery, masked by the ordinary demands of daily life, and the opioid simply showed them what adequate opioid-receptor activation felt like. Or the opioid itself, through prolonged receptor occupation, may have downregulated the patient's endogenous production, creating a deficit that did not exist before treatment began. The patient maintained on SSRIs for years faces the same situation with serotonin: the drug has been doing the work the brain should be doing, and the brain has reduced its own capacity accordingly. In these cases the practitioner is dealing with iatrogenic neurochemistry, and the intervention path must account for receptor recovery timelines that do not apply to the other two categories.

Three different origins, three different clinical investigations. But in all three cases the substance the patient chose tells you which system to look at. The drug of choice is diagnostic regardless of how the deficit arose. Correcting the upstream condition does not guarantee that the addiction resolves. But attempting to treat addiction without investigating the upstream condition is like treating a fever without looking for the infection.

The rat park lesson

In 1978, a Canadian psychologist named Bruce Alexander asked a question that challenged the prevailing model of addiction research. For decades, the standard experimental setup involved placing a rat alone in a small cage with two water bottles, one plain and one laced with morphine. The isolated rats reliably chose the morphine water, often to the point of self-destruction. The conclusion seemed clear: the drug itself was irresistibly addictive, and exposure led inevitably to dependence.

Alexander was not convinced. He noticed something the other researchers had overlooked, or at least had not considered important. The rats in these experiments were isolated, confined, unstimulated, and alone. They were living in conditions of profound social and environmental deprivation. What if the addiction was not purely a response to the drug but a response to the conditions?

To test this, Alexander built what he called Rat Park, a large enclosure with toys, tunnels, running wheels, nesting material, and a colony of rats of both sexes who could socialize, play, mate, and live something closer to a normal rat life. He gave the Rat Park rats the same two-bottle choice: plain water or morphine water.

The results were striking. The rats in Rat Park overwhelmingly preferred plain water. Even rats that had consumed morphine for weeks before being placed in Rat Park reduced their morphine consumption dramatically once they had access to a rich social and physical environment. The isolated rats in standard cages, meanwhile, continued drinking the morphine water at high rates.

Alexander's experiment has been debated, partially replicated, and critiqued in the decades since. Some replication attempts have produced mixed results, and the relationship between environment and drug consumption turns out to be more complex than the original study suggested. But the core finding has held up in a broader sense. Dozens of subsequent studies using enriched-environment designs have found that social connection, physical stimulation, and environmental complexity reduce drug self-administration in rodents. The effect is robust enough that it has changed how many researchers think about the relative contributions of pharmacology and environment to addictive behavior.

This does not mean that pharmacology is irrelevant, or that sufficiently enriched environments prevent all addiction, or that the patient's social circumstances are the practitioner's responsibility to fix. It means that the practitioner assessing a patient with an addiction — and by our expanded definitions, that is now the majority of the population† — is looking at a system with at least two layers of cause. The first layer is biochemical: the cofactor depletions, metabolic bottlenecks, and substrate burdens that compromise neurotransmitter production. The second layer is environmental: the degree to which the patient's life provides the natural stimulation, social connection, and engagement that healthy neurochemistry requires. Both layers matter. Addressing only the biochemistry while ignoring the environment, or addressing only the environment while ignoring the biochemistry, leaves half the problem untreated.

What this looks like in practice

The practitioner who absorbs this chapter does not become an addiction specialist. They become a practitioner who, upon encountering a patient with an addiction, asks a different set of questions.

Instead of asking how much do you drink, the practitioner asks what does alcohol do for you that nothing else does? The answer, whether the patient frames it as relaxation, stress relief, shutting off racing thoughts, or being able to sleep, tells the practitioner which neurotransmitter system is likely running short.

Instead of telling the patient to quit smoking, the practitioner asks what happens to your thinking and your focus when you go without cigarettes for a day? The answer tells the practitioner whether acetylcholine, dopamine, or both are part of the picture.

Instead of judging the patient who cannot stop eating sugar, the practitioner asks what the sugar is doing for the patient's energy, mood, and motivation, and begins to

investigate the dopaminergic system upstream, and looks at their diet, even if they assure the practitioner it is "healthy."

And instead of assuming the patient on long-term SSRIs has a settled psychiatric condition, the practitioner asks what the serotonin status was before the prescription, what upstream factors might have driven it low, and whether the drug is now maintaining a dependency it was supposed to resolve.

The opioid crisis was not an accident of pharmacology. It was a sales strategy. Purdue Pharma marketed OxyContin to physicians with the explicit message that the drug was safe for long-term use and that addiction risk was minimal — claims they made while holding internal data that contradicted both. They knew the first prescription would produce relief. They knew receptor downregulation would make discontinuation difficult. They knew the patient would stay on. The business model depended on it.

Social media companies employ operant conditioning experts — behavioral psychologists trained in the same reinforcement schedules B.F. Skinner used to shape behavior in laboratory animals† — to engineer platforms that maximize engagement. The pull-to-refresh gesture is mechanically identical to pulling a slot machine lever. The notification badge is a variable-interval trigger designed to produce compulsive checking. These are not accidents of design. They are features, built by people who understand exactly what they are doing to the dopamine systems of their users, because engagement is the product they sell to advertisers. Video game studios employ the same expertise, engineering loot box mechanics, leveling rewards, and achievement systems specifically to exploit variable-ratio reinforcement and keep players engaged past the point of benefit. The goal is not to harm the user. The goal is revenue. The harm is what happens when the brain's reward circuitry is treated as a resource to be extracted from.

The practitioner reading this chapter is looking at patients who are caught in systems designed to create and maintain the very deficits those systems then profit from. The drug that creates the dependency it was prescribed to treat. The platform that depletes the dopamine it was designed to temporarily supply. The game that displaces the real-world engagement the player's brain needs to function. These are not separate problems. They are the same economic model applied through different delivery mechanisms, and the patient sitting across from the practitioner is often caught in more than one of them simultaneously.

The practitioner who learns to read these signals does not need to become an addiction specialist or a psychiatrist. They need to become a practitioner who understands that when a patient cannot stop reaching for something, the reaching itself is data — and the question worth asking is not how do we stop the reach, but what is the hand looking for.

Humility and hope

Sometimes a patient does everything right and still does not recover. The protocol is sound. The compliance is complete. The substrate has been addressed, the rate-limiters supplied, the presence categories worked through. The patient runs the work the practitioner designed, and it does not produce the result. This happens. It is uncommon enough that it should not be the practitioner's first explanation, and common enough that any practitioner who does this work long enough will encounter it.

When it happens, the practitioner has to be careful with what they say. There are such things as incurable patients, but that is not for the practitioner to judge. The patient may be beyond what this practitioner knows how to fix, while another practitioner might have the answer. The patient may be beyond what exists in today's medicine, while tomorrow's discovery might change what is possible. The patient may be beyond all human help, seemingly at death's door, and even then, miracles do happen. None of these possibilities is something the practitioner can rule out.

The honest statement is much smaller. "I am sorry. This is beyond my ability." That is the entire defensible message. It preserves the patient's standing in the world of possibility. It tells the truth about the practitioner's limits without overstating them into limits on everyone and everything else.

The next chapter closes Part One by naming the limits of what has been taught so far. Everything up to this point has been landscape, the way the terrain is shaped. What follows is the terrain itself.

Clinical pearl: Loneliness is a neurochemical deficit that no supplement will fully correct. Oxytocin nasal spray can serve as a temporary measure, but real connection is the goal. This is especially important with elderly patients, but do not assume — isolation shows up at every age.

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Part Two - Principles and Protocols

Chapter 15 — Technology changes both treatments... and symptoms

Medicine moves with its tools. The practitioner working in any given decade inherits diagnostic and therapeutic capabilities from the decade before, extends them, and hands them forward. What is worth examining is that the same technological acceleration driving better diagnostics and more powerful therapies is also producing new categories of disease. The practitioner must be fluent in both sides.

On the diagnostic side: radiology can now see into the body at resolutions that would have been science fiction thirty years ago, using a fraction of earlier radiation doses.¹ Functional imaging — fMRI, PET, continuous glucose monitoring — lets the practitioner observe physiological processes as they happen. Lab work has become both more sensitive and broader. Our understanding of metabolic and immune pathways has deepened to the point where the practitioner can intervene at specific nodes rather than at the coarser level of "support the organ." Genomics and pharmacogenomics have made visible a layer of patient variation — GSTM1 deletions, DAO variants, MTHFR polymorphisms — that was entirely hidden before.² Microbiome sequencing has made the microbiome itself a clinically tractable target.³

But technology is a double-edged sword. The same civilization produces more chemicals entering air, food, and water at rates outstripping safety testing.⁴ Electromagnetic radiation from electronics whose safety testing was rushed by decades. Ultra-processed food with extrusion, emulsification, industrial seed oils, and flavor chemistry producing metabolically novel inputs.⁵ Pharmaceutical loads in patients over sixty competing for the same clearance pathways as environmental chemicals. Light pollution and screen exposure disrupting circadian rhythms.⁶ Microplastics now present in human blood, placental tissue, and brain.⁷

Technology impacting health is not a new phenomena. Over the roughly ten thousand years since the agricultural revolution, we have been breeding plants to be ever sweeter, less fibrous, and less bitter.⁸ I call this process the 'Candification' of food.†

Now the pace has become exponential, and the gap between the introduction of a new technology and our understanding of what it does to us has widened.

The practical consequence is that new disease manifestations are not simply a matter of better diagnostics finding what was always there. Real new patterns of dysfunction are emerging that may not have even existed when the doctor was in residency. The doctors of today face symptoms and causes that a generation ago did not exist, and this trend shows no sign of slowing.

A modern practitioner must have working knowledge of at least four domains not part of traditional training:

Microbiology — specifically, the resident microbiomes of the gut, sinuses, mouth, skin, and urogenital tract, and how they shape immune function, metabolism, neurotransmitter production, and detoxification capacity.⁹ Not the microbiology of infectious disease, which the conventional curriculum covers, but the microbiology of the populations that live in and on us.

Toxicology — both metals and chemicals. Not the toxicology of acute poisoning, which is also covered in conventional training, but the toxicology of chronic low-dose exposure, which is a different science with different implications.¹⁰

Building science — water damage and mold growth hidden behind walls or in HVAC systems, poor ventilation trapping contaminants, building materials off-gassing VOCs, electromagnetic field exposures.¹¹ A practitioner who cannot ask the right questions about the patient's home and workplace is missing a major source of chronic exposure.

Molecular biology — specifically, how modified RNA platforms behave once inside the body. Not the molecular biology of normal cellular processes, which the conventional curriculum covers, but the biology of synthetic genetic material engineered for stability — how it interacts with ribosomes, how long it persists, what proteins it produces, and what immune consequences follow.†

Most of what follows in this book is that teaching. We begin with the microbiomes, move through toxicology and building science. The molecular biology of modified RNA platforms is beyond the scope of this volume, but the practitioner must understand that this domain exists, when patients are presenting with consequences from it, and that the tools to recognize and address those consequences are available.

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Chapter 16 — The costs of cooking and how to hack your diet

The previous chapter named the candification of food as one of the challenges facing every patient's microbiome -- the breeding of ever sweeter, less fibrous crops across a hundred generations of agriculture. But agriculture was the second simplification. The first one happened roughly two million years earlier, when our ancestors learned to cook.

Cooking made us human.¹ It also set in motion the colonic and metabolic patterns that the agricultural candification would later compound. Understanding what cooking actually does -- to plant cell walls, to starch, to protein -- is necessary before the microbiome chapters that follow. Those chapters will teach the practitioner how to rebuild colonic ecology. This chapter explains one of the first stresses we as a species applied to it. The issue is not just what modern patients eat. It is how they prepare it.

The benefits of cooking were immediate and enormous. Heat gelatinizes starch, denatures protein, and breaks down plant cell walls.² More calories become available from the same food. Chewing time drops. The gut shrinks. The colon of a modern human is less than sixty percent the mass expected for a primate our size.³ That freed-up metabolic energy went somewhere specific: the brain. Our ancestors traded gut for cortex, digestion for cognition. The anthropologist Richard Wrangham has argued convincingly that this trade is what separated *Homo erectus* from everything that came before.¹ We have become, physiologically, a cooked-food species.

But the trade came with a cost. Cooked starches and sugars injure the colon and exhaust the pancreas. Cooked protein burdens the liver. Then there are the 2nd and 3rd order effects from these injuries. Each path has its own mechanism, its own timeline, and its own clinical consequences.

What cooking does to plants

A raw plant cell is a fortress. The cell wall is a layered composite of cellulose, hemicellulose, and pectin, cemented together by the middle lamella. Nutrients and fermentable polysaccharides are locked inside this architecture. When this structure arrives intact in the colon, bacteria must dismantle it from the outside in, layer by layer, releasing substrate gradually along the full length of the large intestine. The ascending colon gets the fastest-fermenting fragments. The transverse gets the next layer. The descending colon and sigmoid get the slowest-releasing material -- the structural polysaccharides that take hours of microbial enzymatic work to access. This progressive release is how the microbiome stayed fed from cecum to rectum.

Cooking changes this in three ways

First, heat solubilizes pectin. The polymer backbone breaks through a reaction called beta-elimination, and what was insoluble structural cement becomes soluble, rapidly fermentable fragments. Second, hemicellulose partially solubilizes. Third, starch

gelatinizes -- the crystalline amylose structure unwinds into an amorphous gel that human pancreatic amylase can now digest completely in the small intestine. Very little reaches the colon. The pancreas must produce the insulin to handle the resulting glucose spike -- the same spike, three meals a day, decade after decade, that drives the trajectory toward insulin resistance.

The result in the colon: the ascending colon receives a burst of rapidly available substrate -- solubilized pectin and hemicellulose fragments -- and ferments them quickly. The saccharolytic relay works. Short-chain fatty acids are produced. pH drops. Everything looks fine in the first third of the colon.

But the substrate is consumed too quickly. By the transverse colon, fermentable carbohydrate is diminished. By the descending colon and sigmoid, there is little left. Without carbohydrate to ferment, the microbial community shifts proportionally toward proteolytic metabolism - fermenting whatever protein, amino acids, and endogenous materials are available^{10,11}. This produces ammonia, indoles, phenols, hydrogen sulfide, and the toxic branched-chain fatty acids. The pH rises. Butyrate production drops. The colonocytes of the sigmoid and rectum receive less of the fuel they depend on.

This is not a minor detail. Butyrate is not just one short-chain fatty acid among three. It is the primary energy source for colonocytes, the signal that maintains epithelial hypoxia, the inducer of antimicrobial peptide production, the stabilizer of tight junctions, and the driver of mucus secretion. It is also a histone deacetylase inhibitor -- a direct regulator of gene expression in the colonic epithelium. When butyrate production drops in the distal colon, the cells that line the sigmoid and rectum lose their preferred fuel, their barrier maintenance signal, and their epigenetic brake on uncontrolled proliferation. This is one mechanism -- not the only one, but a significant one -- linking distal colonic substrate deprivation to the elevated cancer risk that is known for that part of the colon.

And the barrier erodes from both directions. The Bacteroidetes -- the bacterial population that specializes in degrading complex polysaccharides -- do not disappear when dietary substrate runs out distally. They switch to the next available polysaccharide: the mucus layer itself.⁹ The colonic epithelium continuously secretes a gel of mucin glycoproteins decorated with complex sugar chains, and the Bacteroidetes have the enzymatic machinery to dismantle every one of those chains. When dietary polysaccharide is exhausted, the Bacteroidetes begin foraging on the host's own protective barrier. The mucus layer thins. The inner dense layer -- which is supposed to be sterile and directly protects the epithelium -- loses thickness. More bacteria contact the epithelial surface. More antigen translocation. More immune activation. And because butyrate is the primary signal driving colonocytes to secrete more mucin, the mucus is being consumed faster and replenished slower at the same time.

The degree of this effect depends on cooking intensity. Lightly steamed vegetables retain more cell wall structure than vegetables boiled to mush. But the direction is

always the same: cooking front-loads fermentation into the proximal colon and leaves the distal colon progressively deprived.

What cooking does to protein

Cooking denatures protein. The three-dimensional structure unfolds, exposing cleavage sites to digestive enzymes. In the small intestine, this means faster absorption -- amino acids appear in the portal blood sooner and at higher concentration than they would from raw or less-denatured protein.⁴ The total amount absorbed does not change much. True ileal digestibility of cooked meat averages around ninety-five percent regardless of cooking temperature.⁵ What changes is the speed.

This matters more than it sounds. When amino acids flood into the liver rapidly, the liver and gut wall take a larger share before releasing the remainder to the rest of the body.⁷ (In medical terminology, this first-pass extraction by the gut and liver is called splanchnic sequestration, but the concept is simple: the liver eats first.) The liver sees a surge it cannot fully direct into protein synthesis, so it shunts the excess toward oxidation.⁶ The amino acids are deaminated, the carbon skeletons are burned as fuel, and the nitrogen enters the urea cycle for disposal. The liver does gain energy from burning those carbon skeletons -- this is not a net energy loss. The issue is the increase in ammonia formed and the extra work load to the liver.

Cooking also liberates free glutamate from protein. Raw meat has its glutamic acid bound within the protein structure. Heat breaks those bonds and releases free glutamate -- the same molecule as MSG. This is why cooked meat tastes more savory than raw. Every cooked meal delivers a dose of free glutamic acid that the equivalent raw meal does not. The implications extend beyond excitatory neurotransmission. Glutamic acid + Ammonia (both elevated now) = Glutamine, a preferred fuel source for cancer cells -- a metabolic dependency so consistent it has been termed "glutamine addiction" in the oncology literature.¹² Parasites exploit the same fuel. *Toxoplasma gondii* uses glutamine as one of its two major energy substrates, and either glucose or glutamine alone is sufficient for the parasite's survival and replication.¹³ *Trypanosoma cruzi* switches to glutamine-based metabolism when glucose is exhausted.¹⁴ *Leishmania donovani* requires glutamine synthetase for its survival and infectivity.¹⁵

The parallel to carbohydrate metabolism is direct. Refined carbohydrates overwhelm the system with a glucose spike -- the excess is stored as fat or causes glycation damage. Cooked protein creates the amino acid equivalent -- a spike that overwhelms the liver's synthetic capacity, with the excess oxidized and the nitrogen disposed of as urea.

Any form of protein denaturation produces this effect. Jerky, which is dried at temperatures that denature protein and then further broken down by prolonged heat exposure, creates the same fast-protein pattern as freshly cooked meat. The dense dried matrix may slow gastric emptying slightly, but the protein arriving in the small

intestine is fully denatured and rapidly digestible. If it was cooked or heat-processed, it spikes.

The problem compounds with age. The liver's first-pass extraction of dietary amino acids increases as we get older -- in old rats, it roughly doubles.⁸ Why this happens is not fully understood.

Over years, the cumulative hepatic workload from processing repeated high-bolus amino acid meals contributes to the trajectory from healthy liver to fatty liver to compromised liver.†

There is no blood test equivalent to glycated hemoglobin (HbA1c) that specifically tracks the cumulative burden of amino acid spikes. However, fructosamine and glycated albumin measure the Maillard reaction happening in the blood -- glucose binding to the free amino groups on circulating proteins. The rate of this reaction depends on both glucose concentration and the availability of free amino groups. It is the author's position that postprandial amino acid spikes from cooked protein may meaningfully increase the substrate available for glycation beyond what chronic hyperglycemia alone produces, compounding the AGE burden. When rapid amino acid absorption is combined with high blood glucose -- the standard postprandial state of the modern diet -- both reactants for the Maillard reaction are present at high concentration simultaneously.†

The similarity between ammonia neurotoxicity and the clinical presentation of Parkinson's disease deserves attention. Patients with hyperammonemia from liver disease frequently exhibit motor symptoms that closely resemble Parkinson's -- bradykinesia, rigidity, tremor, and parkinsonian gait. In documented cases of portal vein thrombosis with hyperammonemia, the parkinsonism was reversible: when ammonia levels normalized with treatment, the motor symptoms resolved completely within a week.¹⁶ Recent research has identified urea cycle dysregulation and nitrogen overload in Parkinson's disease models, with ammonia proposed as a direct regulator of alpha-synuclein aggregation -- the hallmark protein of Parkinson's pathology.^{17,18} The author believes that chronic, subclinical ammonia burden -- below the threshold of frank hyperammonemia but above the level our ancestors experienced on slower-absorbed protein -- may be a contributing factor in neurodegenerative disease that has not been adequately investigated.†

Carbonic anhydrase inhibitors are used in the treatment of Parkinson's disease and other neurodegenerative conditions. Methazolamide has demonstrated neuroprotective effects in models of Huntington's disease, Alzheimer's disease, and ischemic brain injury.¹⁹ The published explanation is that methazolamide inhibits cytochrome c release from mitochondria. But this is a description of what it does, not a mechanistic explanation of why inhibiting an enzyme that interconverts carbon dioxide and bicarbonate should protect neurons from degeneration. The published literature does not provide a satisfying causal chain connecting carbonic anhydrase inhibition to mitochondrial stability.²⁰ The author's position: carbonic anhydrase inhibitors raise tissue carbon dioxide levels. Elevated CO₂ facilitates ammonia clearance. The

neuroprotective effect is not a mysterious mitochondrial side benefit -- it is the expected result of reducing the ammonia burden on neural tissue.

The hacks

This chapter does not argue for a raw food diet. Raw food diets often produce an initial period of benefit -- likely from increased fiber, polyphenol intake, and reduced processed food -- but they lead to caloric insufficiency and nutritional compromise over time.† We are a cooked-food species. Our anatomy has adapted to it. The point is not to abandon cooking but to mitigate its colonic and metabolic costs.

For starches: a Paleo food hack

A paleolithic diet would have included substantial quantities of wild tubers, which were fibrous, starchy, and far less sweet than their modern counterparts. Modern potatoes, sweet potatoes, and yams have been bred for sweetness and soft texture, part of the 'Candification' pattern described earlier. The starch in a cooked modern potato is predominantly rapidly digestible starch, which breaks down to glucose in the small intestine almost as fast as table sugar. Very little reaches the colon to feed the microbiome and can cause blood sugar spikes which have consequences of their own. The same is true of modern grains. Ancestral grains were small, tough, and high in fiber. Modern wheat, rice, and corn have been bred for yield and palatability, which in practice means softer, starchier, and faster to digest. A bowl of freshly cooked white rice delivers its glucose payload almost entirely in the small intestine. The colon, and the microbial ecosystem that depends on fermentable substrate reaching it, gets nearly nothing.

But there is a simple preparation method, supported by a growing body of research, that partially reverses this. It does not require removing starches from the diet. It requires cooking and preparing them differently.

Boil the grains, beans (preferably whole) or tubers (potato, etc...) with a small amount of oil or fat in the water. This is not the same as adding oil after cooking. During cooking, the starch granules swell open, and the lipid molecules enter the granule and form complexes with the amylose chains inside. These amylose-lipid complexes resist enzymatic digestion and serve as scaffolding that encourages more resistant starch to form during the cooling step that follows. Oil added after cooking merely coats the surface and slows gastric emptying, which helps, but it cannot penetrate the already-closed granule to form the internal complexes that do the heavier work.

After cooking, refrigerate the starch for twenty-four hours. During cooling, the gelatinized starch retrogrades, meaning the amylose chains recrystallize into structures that digestive enzymes cannot easily break apart.

The food can be reheated gently with minimal loss of the effect. Do not boil it again in water or bake it at high temperature. A gentle reheat preserves the crystalline structures formed during cooling. The patient does not need to eat cold rice or cold potatoes.

When serving, add vinegar or another acid, which independently slows amylase activity and gastric emptying. Serve the starch alongside protein and fat, both of which further blunt the glucose spike. And if it is practical, eat the starch with the protein and fat, or at the end of the meal rather than the beginning.

Each of these steps layers on the one before it. Taken together, they can reduce the glycemic impact of starched ~50% †, without removing a single food from the patient's diet. More of the starch reaches the colon intact, where it feeds the bacteria the microbiome chapters describe. The patient gets to keep eating rice and potatoes. The microbiome gets fed. The blood sugar stays flatter. That is closer to how a paleolithic body would have experienced a tuber or a handful of wild grain, not because the food is ancestral, but because the preparation has restored something the modern food lost. Among carb sources more readily available, consider purple sweet potatoes. They are lower in glycemic index than many common starches and have a longer shelf life than potatoes which sprout (if organic and not sprayed with toxic sprout inhibitors).

A chart showing the effects of these food preparation hacks on G.I. (glycemic index) and blood sugar can be found at www.remedylink.com/charts.

The other side of the equation is insulin resistance. Even if we lower the sugar reaching the bloodstream, we still need insulin to bring it into the cells. Interestingly, some patients report that going gluten free improves insulin resistance.

For protein: eat it raw or rare

Consider eating protein raw or rare when the source is safe. This is not as exotic as it sounds. Sushi and ceviche are raw fish. Steak tartare and carpaccio are raw beef. The author has eaten raw ground beef regularly for years without incident. Cooking temperature of 75 degrees Celsius produces the fastest protein digestion; temperatures below 60 produce meaningfully slower absorption⁵ -- closer to the "slow protein" pattern that results in less liver extraction, less oxidation, less urea production, less free glutamate release, and better net amino acid balance.⁴ Rare meat is a practical middle ground for those not ready for raw.

The goal is not to undo two million years of adaptation to cooked food. It is to recognize that the adaptation came with a cost, that the cost compounds with the agricultural candification that followed, and that simple preparation adjustments can offset the most significant consequences without requiring anyone to eat like an australopithecine.

Clinical pearl: Anatomically speaking, the human digestive system is somewhere between that of a wolf and a pig. We are designed to be part carnivore, part omnivore.†

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Chapter 17 — Microbiome as ally and mentor

Much of what is taken for granted as the patient's own — the architecture of the nervous system, the immune system's capacity to recognize friend from foe, the cognitive substrate the patient has been working with their whole life — was built in partnership with microorganisms.

The microbiome chapters ahead will teach how to examine, measure, and restore the microbiome. The reader does not need the depth of what follows for the protocol to make sense. What follows is meant to demonstrate the value of this underappreciated system — what the microbiome has been doing for the patient since before they were born, and why the practitioner's work with it reaches further than the patient in the room.

This is a synthesis rather than a standard developmental biology framework. The individual mechanisms referenced are documented in the literature; the organization into four stages is the author's.

Initiation one — neural architecture in utero

The fetus develops inside a body colonized by trillions of microorganisms. The maternal microbiome produces metabolites continuously — short-chain fatty acids, neurotransmitter precursors, B vitamins, bile acid derivatives, tryptophan metabolites — a subset of which cross the placenta during the entire period the fetal neural architecture is being laid down.¹

Maternal SCFAs reach fetal circulation and influence neural progenitor cell proliferation and differentiation.² Maternal inflammatory state — strongly regulated by microbiome composition — affects fetal brain development through cytokine signaling.³ Maternal tryptophan metabolism, which the microbiome heavily shapes, affects serotonin availability during fetal neurodevelopment.⁴ Mode of delivery has been correlated with subsequent cognitive outcomes.⁵

The synthesis: a fetus's neural architecture — neuron number and organization, synaptic density and pattern — is shaped in part by the metabolic environment the maternal microbiome produces. † Intelligence and neural complexity are partly a gift of the maternal microbiome. † A mother arriving at pregnancy with an impaired microbiome passes a different starting substrate to her child.

The clinical implication is immediate. When the practitioner works with a woman or girl who will one day be fertile, the microbiome work is not only restoration for the patient in the room. It is preparation for any future pregnancy.

Initiation two — self-recognition via IgA in colostrum

At birth, the infant's gut is close to sterile. In vaginal delivery, the infant is seeded by the maternal vaginal and fecal microbiome.⁶ In cesarean delivery, the infant bypasses this

transfer and is colonized primarily by skin organisms from the mother, medical staff, and the hospital environment.⁷ Skin organisms are not gut organisms.

Roughly a third of U.S. infants are now born by cesarean.⁸ These children have measurably higher rates of allergies, asthma, eczema, and other immune-mediated conditions.⁹

The infant's immune system must decide almost from first breath which organisms are permitted residents and which are invaders. This decision is taught by the mother in the first milk. Colostrum contains an extraordinary concentration of secretory IgA antibodies shaped by the mother's lifetime of immune experience.¹⁰ The IgA coats newly colonizing bacteria and effectively tags them: these are known, these are tolerated, these are not to be attacked.

An infant who receives no colostrum, or colostrum from a mother whose microbiome and immune system are compromised, does not receive this training in full.† Many patients who develop autoimmune presentations later in life turn out, on careful intake, to have missed this initiation.† This is not a claim that autoimmunity is simply caused by formula feeding. It is a claim that one foundational layer of immune self-recognition comes from colostrum IgA, and patients who missed it are working without a foundation others have.

Initiation three — postnatal myelination and cognitive development

Most mammals are born with largely complete nervous systems. Humans are born radically underdeveloped — the birth canal is too narrow to pass a fully developed brain. Myelination continues through infancy and into early childhood.¹¹ The prefrontal cortex and hippocampus undergo substantial postnatal development.

The substrate comes significantly from breast milk. Nervonic acid, concentrated in myelin, is present in human milk.¹² Sphingomyelin contributes similarly.¹³ Human milk oligosaccharides shape the infant microbiome, which produces metabolites that reach the developing brain.¹⁴

An infant not breastfed develops with different substrates available — different lipid profile, different microbial-metabolite-precursor profile, a different gut microbiome producing different circulating metabolites during the window when the brain is being built. Nervonic acid is only created in the body in very small amounts for nerve and brain repair. Fortunately, supplemental nervonic acid is available.

Initiation four — other-recognition and immune education

After colostrum IgA tags the commensal populations, the maturing immune system continues to encounter new organisms. The established microbiome teaches pathogen recognition — commensals occupy niches, produce signals that train T-cell and B-cell

development, and regulate the balance between inflammatory and regulatory immune programs.¹⁵

An infant with a robust, diverse microbiome develops an immune system that recognizes pathogens efficiently and tolerates commensals reliably. An infant whose microbiome was disrupted develops a less well-trained immune system.¹⁶ Patients with recurrent infections, unusual susceptibility to pathogens, and chronically elevated inflammatory markers may present with the developmental consequences of incomplete fourth initiation.†

Clinical pearl: When you repair the microbiome of a woman, you also improve the developmental environment any of her future children will be born into. Since microbiomes are passed on mother to child, the work you do with one woman can echo for generations.†

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Chapter 18 — Four insults to the microbiome

The previous chapter laid out what the microbiome builds during developmental windows we do not yet know how to reopen. This chapter lays out what modernity does to that system.

Many modern patients were born to mothers whose own microbiomes were already compromised, and with each generation the partnership has grown more fragile. The damage compounds across lineages — a mother whose Initiations were incomplete passes an impaired environment to her fetus and impaired colostrum to her newborn.† That child grows into a mother who passes an even more impaired environment forward.

Against that background, four categories of modern pressure act on every individual patient. Two are optional in principle — avoidable for some patients. Two are not.

Insult one — disrupted birth and infancy

Cesarean delivery bypasses the vaginal and maternal fecal colonization that would normally seed the infant gut.¹ Formula feeding removes the colostrum IgA that tags commensals as self, and removes the breast milk substrates the developing brain evolved to use.² Heavy antibiotic exposure in infancy strips the microbiome during the window when it was supposed to be establishing.³

The disruptions reinforce each other. An infant born by cesarean is more often formula-fed, for practical reasons. An infant bottle-fed from the start is more often exposed to early antibiotics, because the protective microbiome is not there to hold against early infection (and receives no nervonic acid for nerve and brain growth).

This danger is not universal. Many patients were born vaginally, breastfed fully, and kept off antibiotics in infancy. The intake establishes what actually happened. And the practitioner is not the patient's conscience — some cesareans saved lives, some mothers could not breastfeed, some infant antibiotics were genuinely indicated.

Insult two — a food supply that no longer feeds the microbiome

This is ubiquitous. The human microbiome evolved alongside a food supply rich in complex carbohydrates and structurally intact fiber.⁴ The modern food supply has these substrates in drastically reduced quantity and variety. Plants have been selectively bred toward sweetness, yield, and shelf life, and away from the fiber and oligosaccharide content that characterized their wild ancestors.⁵ Industrial processing removes further fiber. This was referred to earlier as the 'Candification†' of our food supply.

Even patients with good eating habits — whole foods, home cooking, avoidance of processed products — are eating varieties bred away from what the microbiome

evolved on.† The danger is not dietary mistakes by the individual. It is the food supply itself.

Insult three — chronic antibiotic-like exposures

Also ubiquitous. Compounds and conditions that are not antibiotics by classification but exert antibiotic-like pressure on the microbiome continuously.

Glyphosate inhibits microbial biosynthesis pathways at concentrations encountered in the food supply.^{6,14} Artificial sweeteners — sucralose, saccharin, aspartame — alter microbiome composition at dietary doses.⁷ Emulsifiers in processed foods disrupt the mucus layer the microbiome sits in.⁸ Pharmaceutical residues pass through wastewater treatment into drinking water in low but continuous concentrations.⁹ Chlorinated water is designed to kill bacteria and does not stop when it reaches the gut. Factory-farm meat carries residual antibiotics from feedlot dosing.¹⁰

Individually, each exposure is below antibiotic-treatment level. Collectively and continuously across years, they constitute a background antibiotic load every patient in the industrialized world carries.† This cannot be entirely avoided — a patient who filters water, eats organic, and avoids processed food can reduce but not eliminate it.

Insult four — acute antibiotics

The clinical antibiotics prescribed for diagnosed infections. These are acute, high-dose, and intentional. They save lives but are prescribed far more than indicated — often for viral infections, often prophylactically for minor dental work, often in broad-spectrum forms when narrow-spectrum would suffice.¹¹ Each course wipes large portions of the microbiome. Diversity recovers partially over months to years and does not always recover fully.¹²

Fluoroquinolones — Cipro, Levaquin — deserve specific naming. They can wipe more than half the species diversity of the gut in a single course,¹³ and the damage is disproportionately persistent. A patient who has taken fluoroquinolones, even once, may never fully recover without targeted restoration.† Intake should flag fluoroquinolone history specifically.

The clinical picture

Two of these four dangers — the food supply and chronic antibiotic-like exposures — are present in every modern patient's life at every moment. The other two — disrupted birth and acute antibiotics — are distributed unevenly. The intake establishes which.

Across generations, the damage compounds. The modern microbiome is not a neutral starting point the following chapters will optimize. It is a depleted and pressured system under attack from multiple directions since before the patient was born.

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Chapter 19 — The microbiome is a garden

The microbiome is a living symbiotic system — trillions of organisms with their own metabolism, signaling, and responses. It cannot be forced the way a chemical reaction can. The practitioner who reaches for the microbiome with the same mental model they bring to other clinical work produces worse results than the one who sets conditions and lets the microbiome do its own work.

The useful frame is gardening. A gardener does not grow a plant by dictat. The gardener sets conditions — soil, water, light, temperature, adjacent plantings, timing — and the plant grows. The precision is in the conditions, not in forcing the target.

Microbiome intervention is much like the garden analogy. The practitioner works on terrain — pH, bile flow, transit time, available substrates. Works on diet — fiber, bitters, less-bred plants, adequate protein, removal of foods feeding wrong populations. Works on lifestyle — hydration, movement, sleep, stress. The microbiome attempts its own restoration once conditions allow.

Gardening is not passive. Setting conditions correctly requires precise understanding of what the microbiome needs and cannot tolerate.

Weeding is part of gardening

In a natural state — unprocessed food, clean water, no antibiotic exposure — the human microbiome assembles and maintains itself without intervention.¹ The practitioner's work is corrective of what modernity has done.

But we are not in the default state. The modern patient's microbiome has been overrun with populations that took advantage of altered terrain. These populations will not leave on their own and actively hold the terrain they created. The practitioner is reclaiming a garden that has been invaded.

That reclamation includes weeding. When pathogenic populations are entrenched — producing ammonia and alkalinizing the colon, forming biofilm matrices, colonizing territory they shouldn't be in — those populations do not always shift passively when terrain is corrected. Some are actively degrading the terrain, creating global or at least micro-conditions they thrive in. They have to be removed.

Weeding in the microbiome is real force. Targeted antimicrobials, biofilm-penetrating agents, negative high voltage/low amperage applications†, and in some cases focused antibiotic use are all forms of weeding. A practitioner who refuses to weed on the grounds that "we cooperate with the microbiome" may end up with a patient whose terrain never clears.

But weeding alone does not make a garden. Bare dirt with weeds pulled needs fertilizer and seed. In microbiome work: prebiotics feed the populations that belong, and probiotics add seed where the seed bank is genuinely missing.

A microbiome with a balanced terrain can repopulate species from very small numbers of surviving organisms — even a single bacterium, given the right conditions, is enough.² Most of the time, what the patient needs is terrain and fuel for organisms already present, not the introduction of new ones. Probiotics are genuinely indicated when specific populations have been driven so deep into dormancy they will not recover in useful timeframe, or have been fully eradicated, but this is more rare than you might think.†

The sequence matters. Fertilizing weedy ground feeds the weeds. Adding seed to hostile terrain produces seed that doesn't germinate.† Probiotic flooding into a dysbiotic gut is one of the most common ways practitioners waste their patients' money — the probiotic passes through, nothing takes, and the practitioner concludes the product doesn't work when the garden wasn't ready for seed.

Antibiotics as herbicides

A broad-spectrum antibiotic is the microbiome's equivalent of spraying herbicides and pesticides across the garden. It kills some bad players and many good ones.³ The visible problem resolves and the garden is left as scorched earth.

This is sometimes correct. For a patient with a bacterial infection they cannot clear, the ongoing damage of the infection can be worse than the temporary damage to the microbiome, but then we must make sure that the damage to the microbiome is indeed temporary by repopulating quickly. The assumption that a garden or a microbiome will self-assemble after scorched-earth intervention is often incorrect. What grows back is whatever happens to be present and whatever the now-dysfunctional terrain favors — rarely the populations that were there before. Antibiotic-associated diarrhea, post-antibiotic yeast overgrowth, post-antibiotic *C. difficile* colonization — all expressions of what grows back when the garden was not supported after intervention.⁴

What this means for the chapters that follow

The chapters treating specific microbiome work — large intestine, small intestine, sinuses — all operate inside the gardening frame. Each teaches a terrain to create, weeds to manage, fertilizers to add, and selectively, seeds to introduce. The specific organisms, terrain parameters, and weeds differ, but the structure is the same: set conditions, manage the populations degrading those conditions, feed what you want to grow, add seed where genuinely missing.

We begin with the large intestine.

You are not simply acting on a target. You are tending a system that has its own life, its own agenda, and its own capacity to heal once the conditions are right.

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Chapter 20 — We can't fix what we choose not to examine

The large intestine is the most information-dense output the body produces. It is the largest microbiome, the terminal step of the digestive tract, where everything upstream — stomach acid, biliary function, pancreatic output, small intestinal transit, fermentation dynamics, hydration, diet — produces a visible, measurable output. Every day, a functioning colon delivers a free report on digestion, fermentation, transit, microbiome balance, and bile flow. Almost no one reads it.

Most Western patients do not look at their stool. Most practitioners do not ask detailed questions about it. The practitioner's comfort with this topic sets the room. Directness, not jokes or indirection, makes the conversation easy. There is nothing funny or shameful about digestion. Treat it that way and the patient will too.

The three pass/fail tests

Stool pH between 5.7 and 6.2. Healthy colonic fermentation produces short-chain fatty acids that acidify stool¹ into this range.† This target is tighter and lower than mainstream references. The tighter target reflects what stool pH looks like in pre-antibiotic-era populations and in hunter-gatherer groups outside the industrialized food supply.² A pH above 7.0 indicates pathogenic or proteolytic populations outcompeting the saccharolytic commensals, or urease-expressing organisms actively alkalinizing the colon.†

How to measure

Expensive pH meters exist that can measure semi-solids like stool, but we do not need that degree of accuracy. All you need is some pH Hydrion paper in the 6-8 range. Keep the paper dry when not in use.

Methods:

- Press pH paper against stool on toilet paper after wiping. Works well early in protocol when residue is present; harder as microbiome heals as toilet paper becomes unnecessary.
- Defecate onto newspaper laid on the floor and sample directly. Cleanest reading.
- If stool smears on paper, leave in contact for three seconds, then wipe the smear off with fresh toilet paper. The embedded color reads clearly.†

pH paper registers only on damp material. If the stool is dry on the surface, break the stool and sample from the inside. Take the most alkaline reading produced. Do not test stool that has gone into toilet water.

One qualifier: a patient already showing pH 5.7-6.2 without microbiome work is either genuinely healthy† (rare) or producing that pH for the wrong reason. Carbohydrate malabsorption and short bowel syndrome drive undigested carbohydrates into the

colon, where aggressive fermentation produces acidic readings that are not healthy. Ask whether the patient has been diagnosed with carbohydrate malabsorption, short bowel syndrome, celiac disease, fructose intolerance, or lactose intolerance. If no, the reading is genuine. If yes, it is a false signal.

No toilet paper needed

No healthy animal soils itself.† When animal traders examined livestock for health, they would lift the tail to see if feces were present — if so, the animal was deemed sick.† A fully formed, well-evacuated stool with adequate fiber and normal mucus leaves essentially nothing behind. The patient does not need to wipe, or needs only a cursory check. A patient requiring extensive wiping is soiling themselves the way a sick animal does, pointing to an upstream issue.†

At least one bowel movement per day

This is the floor. Below this, transit time extends into the range where conjugated toxins get cleaved by colonic bacteria and reabsorbed into portal circulation,³ and the colon functions more as storage than exit route.

The four optimal markers

A bowel movement for every meal eaten.† Three meals should produce three or four BMs per day, including the waking BM that clears overnight accumulation.† This reflects healthy gastrocolic reflex function.⁴

BM on waking plus shortly after each meal.† The timing pattern behind the count.

The stool sinks. Floating usually indicates gas entrapment — excess fermentation, carbohydrate malabsorption, or SIBO.⁵ It can also indicate fat malabsorption, requiring follow-up questions about oily appearance and pale or clay-colored stool.

Mild smell. A carnivore's stool will always have some smell, but truly overwhelming odor reflects protein putrefaction, H₂S production, and unfavorable fermentation patterns.⁶ Inadequate stomach acid allowing protein to pass into the colon undigested, sulfur metabolism pushed toward H₂S, or proteolytic-dominant microbiome.

A note on gas

Gas is normal output of healthy fermentation. What matters is excessive gas or foul-smelling gas. Gas should be mostly odorless.†

Excessive gas can come from hydrogen overproduction relative to consuming populations. It can be CO₂, generally less concerning, or methane, which has its own issues.⁷ Methane is produced by methanogens and causes spasm and partial paralysis of intestinal smooth muscle, producing the constipation pattern characteristic of

methane-dominant SIBO. Patients who present with chronic constipation that does not respond to fiber or hydration often have methane-producing organisms. Beyond methane, gram-negative populations and methanogens produce hydrogen sulfide, dimethyl sulfide, mercaptans, and ammonia in varying combinations.

The pressure contributes to colonic distension, and any toxic gases cross into the bloodstream — the intestinal wall is not a barrier to small-molecule gases.⁸ Gas volume can also apply pressure to the heart and organs above the colonic arch, which is why some patients describe cardiac-area discomfort that is actually digestive.†

Fecal-smelling stool and gas — the classic indole and skatole signature — points toward distal carbohydrate depletion, meaning, not enough slow fermenting fiber, and saccharolytic populations in the descending colon have simply run out of substrate and switched to fermenting amino acids as a fallback. Sulfurous, putrid, or death-like smell — hydrogen sulfide, putrescine, cadaverine, ammonia — points toward a globally alkaline colon where dedicated proteolytic organisms like Klebsiella, Proteus, Fusobacterium, and pathogenic Clostridium have taken over, producing a different and more toxic metabolite profile.

Transit time Measurement

The easiest way to test is to take a tsp of chlorophyllin. The interval is transit time is how long it takes for the stool to turn bright green.

Eighteen to twenty-four hour transit time is optimal.⁹ Transit under sixteen hours suggests a toxin burden the body is clearing quickly, acute infection, malabsorption, hyperthyroidism, certain medications, or high stress.

Thirty-six is acceptable. Beyond thirty-six, investigate.† Transit longer than thirty-six hours is where the deconjugation problem becomes serious.³ Toxins the liver conjugated for excretion sit long enough for bacterial enzymes to cleave the conjugation, releasing the free toxin back into circulation. Fix the transit and the burden often decreases without any other intervention.†

If the patient has done everything right and has dry pebbly stools, it's likely constipation. Getting a patient to drink water can be difficult. As we age, osmoreceptors become desensitized and people simply do not feel thirsty when they should. The body then goes to one of the only places it can pull water from — the feces, and the outcome... dry stools and constipation.

Explaining to patients that dry stool means the body was so thirsty it was pulling water from fecal matter to drink can be the reframe that gets them drinking. A good rule of thumb is the mouth should always be moist.

Clinical pearl: Weak kidney tubules that do not optimally reabsorb electrolytes can make drinking water feel uncomfortable. In this case, offer electrolyte-rich water and work on kidney repair.

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Chapter 21 — Gram positive vs. Gram negative

Every bacterium in the colon wears one of two kinds of armor, and the distinction matters more than most practitioners realize. Gram-positive organisms have a thick, single-layered peptidoglycan wall. Gram-negative organisms have a thinner peptidoglycan layer wrapped in a second outer membrane — and embedded in that outer membrane is lipopolysaccharide. LPS. Endotoxin. One of the most inflammatory substances known to man.

Not all Gram-negative bacteria are the same, and not all LPS is the same. The variable that determines whether LPS triggers inflammation or promotes immune tolerance is a structural component called lipid A. The lipid A from commensal Bacteroidetes — the ancestral Gram-negative populations the human gut evolved alongside binds TLR4 weakly or acts as a competitive antagonist. It occupies the receptor without triggering the full inflammatory cascade. Some commensal LPS actively dampens immune activation.¹ A gut dominated by these organisms has LPS that is training the immune system toward tolerance.

The lipid A from Proteobacteria and pathobiont strains — the populations that expand in a dysbiotic modern gut fits the TLR4/MD-2 receptor complex tightly and triggers a strong NF- κ B-driven inflammatory response. This is the LPS most immunology textbooks describe, and it is the LPS the modern gut is increasingly producing.

The modern gut has traded one for the other. And the trade is not limited to the LPS itself. The same commensal Bacteroidetes that produce tolerogenic LPS are primarily saccharolytic — they ferment complex carbohydrates and produce the protective short-chain fatty acids. When those populations are displaced by the inflammatory Gram-negative strains, the patient loses the tolerogenic LPS and the protective SCFA production simultaneously. What replaces them runs proteolytic fermentation when fiber is scarce, generating toxic metabolites and consuming protective intestinal mucin. One ecological shift produces both outcomes at once.

The problem is not that Gram-negative bacteria exist in the colon. They are supposed to be there. The problem is which ones, in what ratio, and what happens when intestinal permeability is compromised and the more inflammatory LPS translocates to other locations in the body.

When the wrong Gram-negative populations dominate — we will refer to them as Toxic Gram Negative, or TGN bacteria† — the damage comes from three mechanisms. Each produces a distinct clinical picture the practitioner needs to recognize.

The first mechanism is endotoxin translocation. In a compromised gut, LPS from TGN bacteria crosses the epithelium into the portal and then systemic circulation. This is metabolic endotoxemia — not sepsis, but persistent low-grade TLR4 activation driving insulin resistance, atherosclerosis, neuroinflammation, and fatty liver disease.² The patient presents with systemic inflammation that does not resolve. The practitioner looks for autoimmune disease, food sensitivities, hidden infections — all reasonable — but

never considers that the inflammation is being fed continuously by bacterial wall fragments leaking from the gut. And because the tolerogenic commensal LPS has been replaced by inflammatory TGN LPS, the immune system has lost the signal that would otherwise be training it to stand down.

Dehydration compounds this problem through a mechanism most practitioners never consider. When the body is short on water, the colon reclaims more of it from the fecal stream. That is its job. But increased water reabsorption does not happen selectively. As the colon pulls water across the epithelium, dissolved and suspended material in the lumen concentrates against the mucosal surface. LPS, which was already present at some baseline level, is now present at a higher effective concentration per unit of mucosal contact area.

Transit slows simultaneously. A dehydrated fecal mass moves more slowly through the colon, extending the contact time between concentrated luminal contents and the epithelial barrier. Higher concentration and longer exposure are independently sufficient to increase translocation. Together they are multiplicative.

There is also a direct transport mechanism. When water moves across the colonic epithelium via the paracellular route, it carries dissolved solutes with it — a process called solvent drag. In vivo perfusion studies have consistently shown the colon to be more permeable to paracellular markers than the small intestine, a finding that initially surprised researchers given that colonic tight junctions measure as tighter in isolated tissue preparations. The explanation is solvent drag: the volume of water moving paracellularly through the colon is large enough to carry molecules that would not otherwise cross the barrier on concentration gradient alone. LPS fragments and micelles small enough to fit the paracellular pathway get swept along with the water the body is trying to reclaim.

The mucus layer takes damage as well. Adequate hydration is required to maintain the gel phase of the colonic mucus barrier. A compacted, dehydrated fecal mass physically abrades the mucus layer and the epithelium beneath it, creating micro-disruptions that allow passage of molecules too large for intact paracellular transport.

The clinical consequence is that a chronically underhydrated patient will be running a low-grade endotoxemia.†

The second mechanism is toxic short-chain fatty acids. Acetate, propionate, and butyrate are protective — produced primarily by Gram-positive Firmicutes fermenting dietary fiber.³ Lactate and succinate play intermediary roles depending on context. But the putrefactive SCFAs — valerate, isovalerate, isobutyrate — are produced by protein fermentation in TGN organisms like certain Bacteroides, Clostridium, and Fusobacterium species.⁴ When fiber drops and protein rises without fermentable substrate, the balance shifts from saccharolytic to proteolytic fermentation, and the putrefactive SCFAs accumulate.

Formic acid illustrates the principle clearly. Formate is a normal metabolic intermediate — an electron shuttle between organisms, a currency of interspecies cooperation.⁵ In a diverse ecosystem it does not accumulate. In a depleted ecosystem where the cross-feeding partners have been lost, it does. And accumulated formate is cytotoxic — it disrupts intracellular pH and inhibits mitochondrial respiration. The molecule is not the problem. The loss of the infrastructure that was supposed to handle it is.

The third mechanism is putrefying amines. TGN bacteria produce biogenic amines — putrescine, cadaverine — at disproportionately higher rates than Gram-positive bacteria.⁶ But the amines that matter most clinically are the ones the body converts into something worse. Trimethylamine, produced from dietary choline and carnitine, is oxidized hepatically to TMAO — a promoter of atherosclerotic plaque formation, endothelial dysfunction, and platelet hyperreactivity.⁷ A patient with TGN-dominant flora eating a steak is running a different metabolic program than a patient with a healthy microbiome eating the same steak.

The three mechanisms are different in their specifics but share a single upstream cause: the replacement of ancestral Gram-negative populations with TGN populations. That one shift produces inflammatory LPS where tolerogenic LPS used to be, proteolytic fermentation where saccharolytic fermentation used to be, and amine metabolites the body converts into cardiovascular and other toxins. The same patient eating the same diet gets a different metabolic result depending on which Gram-negative populations are doing the processing.

A practitioner managing chronic inflammation, cardiovascular risk, or gut dysfunction without addressing the TGN ecology of the colon is working downstream of the problem. No amount of anti-inflammatory supplementation will outpace a gut that is continuously producing the inflammatory inputs that translocate throughout the body.

Mildly acidic colonic pH selectively suppresses TGN populations while favoring the Gram-positive butyrate producers that maintain barrier integrity.⁸ At pH 5.5, *Bacteroides* species grow poorly and butyrate-producing Firmicutes dominate; at pH 6.7, the ratio inverts almost completely.⁹ The loop is self-reinforcing in both directions. More fiber, more SCFAs, lower pH, more Gram-positive dominance. Or: less fiber, higher pH, more TGN expansion, more toxic output. The protocols that follow break the second loop and initiate the first.

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Chapter 22 — Stool pH controls microbiome content

Stool pH is the selection pressure that determines which populations grow in the colon and which do not. Shift the pH and the microbiome shifts with it. Fail to shift the pH and no amount of probiotic supplementation, dietary intention, or clinical effort will produce durable change.

The pH of the colonic environment is itself the cause of population composition. Different populations have different pH preferences¹, and each actively reshapes pH toward the range it prefers. Acid-producing populations lower pH. Alkali-producing populations raise it. The dynamic is self-reinforcing in both directions — that is why pH works as a clinical lever.

This chapter teaches the mechanism behind that lever — what generates colonic pH, which populations compete across the pH landscape, how pH governs the antimicrobial system that holds the ecosystem together, and what the practitioner can do when the system has tipped the wrong way.

The gradient from right to left

The colon is not a single uniform environment²¹. The ascending colon, where nutrients from the small intestine first arrive, is the most acidic of part of the healthy colon. Short-chain fatty acid concentrations here are the highest in the large intestine¹⁰. This is where the bulk of carbohydrate fermentation occurs.

The pH rises slightly (but still acidic) as we move to the transverse and descending colon. Fermentable substrate is partially depleted. Short-chain fatty acid concentrations decline. The community balance begins to shift: gram-negative polysaccharide degraders that produce acetate and propionate but not butyrate start to dominate.

Without slow to ferment fibers, the descending colon and sigmoid can shift alkaline. Short-chain fatty acid production drops and instead we get products of protein fermentation — ammonia, branched-chain fatty acids, phenolic compounds — progressively increase from proximal to distal¹¹. While there are always protein sources for this to happen (desquamated epithelial cells, mucins, pancreatic secretions, bacterial cell turnover) if an alkaline pH favors it, consuming more protein than we can absorb in the small intestine exacerbates this problem.†

Note: Stool pH reflects the distal end of this gradient. It is always more alkaline than the proximal colon. The practitioner reading a stool pH is looking through a window into the descending colon, not the ascending. A stool reading of 6.0 likely reflects a proximal colon at approximately 5.5 to 5.7.

In the colon, pH is not an independent variable. It is a consequence of microbial metabolism. When saccharolytic bacteria ferment carbohydrate, they produce short-chain fatty acids — acetate, propionate, and butyrate. These acids lower the pH. When proteolytic bacteria ferment protein and amino acids, they produce ammonia, indoles, phenols, and branched-chain fatty acids. Ammonia raises the pH. The number on the

pH strip is the net result of these two opposing forces. A low pH means saccharolytic fermentation is winning. A high pH means it is losing. This is why pH is more useful than any single metabolite measurement. It integrates everything happening in the microbial ecosystem into one readable output.

The four populations

Beyond the conventional teaching on gram-positive and gram-negative bacteria, the colonic microbiome also divides into four functional groups that compete across this pH landscape. Their order from the most acid-tolerant to the most alkaline-favored defines the ecological succession that pH encodes. A chart showing these populations and their metabolic outputs plotted against pH is available at remedylink.com/charts

First: the lactic acid bacteria (LAB) and Actinobacteria. *Lactobacillus* (a Firmicute) and *Bifidobacterium* (an Actinobacterium, not a Firmicute, though functionally grouped here as a saccharolytic lactate producer). These are the most acid-tolerant organisms in the colon. They ferment prebiotic oligosaccharides — FOS, GOS, inulin, XOS — to lactate. Their substrates are heat-stable and arrive in the colon regardless of how the food was cooked. They are proximal fermenters by nature. They are also the population that human milk oligosaccharides selectively feed — a point that matters when intervention is discussed later in this chapter.

Second: the Bacteroidetes. Bacteroides and Prevotella. These are the generalist polysaccharide degraders. They carry enormous arsenals of polysaccharide utilization loci — fifty to a hundred per species — each dedicated to a specific complex carbohydrate. They degrade plant cell wall polysaccharides, resistant starch, and mucin glycans through extracellular enzymatic machinery, and they produce acetate and propionate via the succinate pathway. They do not produce butyrate. Their LPS is tolerogenic — it does not trigger inflammatory signaling. *Bacteroides* grow poorly at pH 5.5 but dominate at pH 6.7, but hunter gatherer *Prevotella* prefer the lower pH.†

Third: the saccharolytic Firmicutes. *Faecalibacterium prausnitzii*, *Roseburia*, *Eubacterium rectale*, *Clostridium* clusters IV and XIVa, and the cross-feeders *Eubacterium hallii* and *Anaerostipes*. These are the butyrate producers². They cross-feed on lactate plus acetate, converting it to butyrate — the lactate-to-butyrate relay. They also ferment resistant starch and specific fibers directly. They peak at a slightly higher pH than the lactic acid bacteria, around 5.7 to 6.2.⁸

Fourth: the toxic gram-negative Enterobacteriaceae and urease producers. *Klebsiella*, *Proteus*, *Morganella*, pathogenic *E. coli* strains, *Enterobacter*. These organisms tolerate a broad pH range — they grow fine at pH 5.75 in pure culture. Their competitive disadvantage in a healthy colon is not pH sensitivity. It is the short-chain fatty acid antimicrobial mechanism described in the next section. The competitive advantage of these organisms is not that they grow better at high pH. It is that their competitors grow worse.

Two mechanisms within this group drive the alkaline shift. The first is urease activity. Urease cleaves blood-derived urea into ammonia and CO₂, directly alkalinizing the lumen. This is the primary pH-engineering weapon — the enzyme that actively pushes the environment in their favor. The second is proteolytic fermentation. When carbohydrate substrate is depleted, these organisms and other proteolytic fermenters produce ammonia, hydrogen sulfide, indoles, phenols, and biogenic amines from amino acid fermentation. The substrates for urease are undigested protein reaching the colon and blood-derived urea diffusing into the lumen. The outputs are ammonia (from urease activity), inflammatory LPS, and the toxic branched-chain fatty acids — isobutyrate, isovalerate.

Many products of this group are directly toxic. Ammonia is CNS-toxic and drives liver work. Hydrogen sulfide is genotoxic at chronic low-level exposure¹⁰. The biogenic amines are histamine-class compounds driving systemic symptoms. The urease producers and the proteolytic fermenters are not always the same organisms, but they reinforce each other: urease raises pH, which favors the proteolytic fermenters, whose ammonia output raises pH further.

The SCFA antimicrobial mechanism

This is the mechanism that holds the entire ecosystem together, and it depends on pH. Short-chain fatty acids are weak acids with a pKa around 4.8. At the pH of a healthy proximal colon — around 5.5 to 6.0 — a substantial fraction of SCFAs exists in the protonated, undissociated form. This protonated form is membrane-permeable. It freely crosses the gram-negative outer membrane⁹, enters the bacterial cytoplasm (which is maintained at roughly pH 7.2), and dissociates inside the cell, releasing protons. This overwhelms the cell's acid tolerance systems, disrupts the proton motive force, and inhibits replication.

The critical finding: neither pH alone nor SCFAs alone are sufficient. Enterobacteriaceae grow perfectly well at pH 5.75 in the absence of SCFAs. They are also unaffected by SCFAs at pH 7.0. Suppression requires both conditions simultaneously — physiological SCFA concentrations at acidic pH. The protonated form of SCFA that does the damage only exists in sufficient quantity when the pH is low enough to keep the acids undissociated. As pH rises, SCFAs deprotonate, lose their membrane-penetrating ability, and the antimicrobial pressure lifts.

This is not how antibiotics work. Antibiotics kill on contact within hours. SCFA suppression works over days and weeks, exhausting the target organisms' ability to maintain themselves. The cell must expend energy pumping protons back out. Many pathogenic organisms can do this for a while. None can do it indefinitely. Patients often see pH shifts within one to two weeks of effective intervention, but the alkalinizing populations will not be gone on day three — but in time, with low pH, SCFA accumulation can drive them to dormancy or death.

Both outcomes are clinical wins. Dormancy is not death, but a dormant organism is not producing harmful metabolites or maintaining alkaline pH. If terrain is maintained, it stays dormant. If terrain is lost, it can reactivate — which is why maintenance matters even after acute success.

The gram-positive Firmicutes and Bifidobacteria tolerate their own metabolites because they have evolved efflux pumps and cytoplasmic buffering systems specifically adapted to SCFA exposure. The Bacteroidetes show some sensitivity to the most acidic conditions but tolerate the moderate acid range. The Enterobacteriaceae have no such adaptation. Inhibition also increases with SCFA chain length — butyrate suppresses Enterobacteriaceae more effectively than propionate, and propionate more than acetate²². This is another reason butyrate loss matters beyond its role as colonocyte fuel.

The positive feedback loop

Above approximately pH 6.5, the system begins to destabilize. SCFA protonation drops. The antimicrobial pressure on Enterobacteriaceae weakens. Urease output from these organisms rises — the enzyme's optimum is around pH 7.4, and the organisms are freed from SCFA-mediated membrane stress. Ammonia production increases. The ammonia raises pH further. More SCFA deprotonates. More suppression lifts. More Enterobacteriaceae grow. More urease is produced. More ammonia.

This is a self-accelerating positive feedback loop. Once it starts, the transition from acceptable to dysbiotic can happen rapidly because each step reinforces every other step. Population expansion of the inflammatory Enterobacteriaceae follows the urease-driven pH shift — their inflammatory LPS activates mucosal immune signaling, damages the epithelial barrier, and recruits neutrophils. The toxic branched-chain fatty acids — isobutyrate, isovalerate — appear as proteolytic fermentation displaces saccharolytic. Butyrate production collapses.

Breaking an established feedback loop requires intervention at multiple points simultaneously. This is why single interventions — just probiotics, just fiber, just pH correction — often fail in established dysbiosis. The loop re-establishes itself unless several legs are knocked out at once.

The lactate-to-butyrate relay

The two most acid-tolerant populations — the lactic acid bacteria and the saccharolytic Firmicutes — operate an internal relay. The lactic acid bacteria ferment prebiotic oligosaccharides to lactate. The Firmicutes cross-feeders (*Eubacterium hallii*, *Anaerostipes*) convert that lactate plus acetate into butyrate²³. When the relay is intact, lactate does not accumulate — it is consumed as fast as it is produced. The butyrate output is the clinically important endpoint.

When the relay breaks — typically because antibiotics have depleted the Firmicutes cross-feeders while leaving the lactic acid bacteria partially intact — lactate accumulates. Lactic acid has a pKa of 3.86, which makes it a substantially stronger acid than the SCFAs. Lactate accumulation drives pH below 6.0 through a different mechanism than healthy SCFA acidification. This produces the acidic pathology seen in critically ill patients — not a sign of a healthy ecosystem but of a relay that has failed at the receiving end.

Feeding prebiotic oligosaccharides to lactic acid bacteria only works if the cross-feeding Firmicutes are present to complete the relay. If they are not — if *Faecalibacterium prausnitzii*, *Roseburia*, *Eubacterium rectale*, *Eubacterium hallii*, and *Anaerostipes* are depleted — then lactate accumulates without converting to butyrate. The pH drops, because lactate is an acid, but the ecosystem has not recovered. The colonocytes are still starving for butyrate. The mucosal barrier is still unsupported. Lactate accumulation in the adult colon is not a sign of health — it is a marker of microbiota perturbation. In inflammatory bowel disease, elevated fecal lactate correlates with disease severity and with reduced butyrate-producing species. The clinical signs of this relay gap are a patient whose stool pH drops in response to prebiotic intervention but whose symptoms do not improve — or worsen. Bloating, gas, and osmotic loose stools with acidic pH but without clinical improvement suggest that the first tier of the relay is active but the second tier is missing. The organisms needed to complete the relay — the obligate anaerobic butyrate-producing Firmicutes — cannot currently be delivered as conventional probiotics. They die within minutes of oxygen exposure, cannot survive encapsulation or shelf storage, and early clinical trials of next-generation probiotic formulations have failed to raise fecal butyrate levels reliably. The one intervention that can deliver a complete anaerobic community, including these organisms, is fecal microbiota transplant. FMT has demonstrated engraftment of *Faecalibacterium* and *Roseburia* in recipients, with transient restoration of butyrate synthesis. The limitation is durability — without concurrent substrate support, engraftment fades. Until shelf-stable formulations of strict anaerobes solve the delivery problem, FMT combined with sustained prebiotic feeding remains the most direct way to rebuild a broken relay.† Finding a suitable healthy donor can be a challenge.

What butyrate does

Butyrate deserves special attention because it is not interchangeable with the other short-chain fatty acids.

It is the preferred fuel for colonic epithelium³ and supports membrane integrity throughout the body, not just the gut.† It maintains epithelial hypoxia via PPAR-gamma activation⁶, which limits oxygen availability to facultative anaerobes. It stabilizes tight junctions. It drives mucus secretion. It induces antimicrobial peptide production. And it is a histone deacetylase inhibitor — a direct regulator of gene expression in the colonic epithelium that serves as an epigenetic brake on uncontrolled proliferation.

Propionate reaches the liver and contributes to glucose and lipid regulation⁴. Acetate does varied systemic work including contributing to the suppression of alkaline-loving pathogenic bacteria. All three short-chain fatty acids modulate regulatory T cells⁵,

tighten the gut barrier, cross the blood-brain barrier in small amounts, and influence microglial activation⁷ and neurotransmitter production and can have positive effects on mood.†

But when the Firmicutes-to-Bacteroidetes transition occurs as pH rises — the shift from butyrate producers to acetate and propionate producers — the colonocytes lose their preferred fuel, their barrier maintenance signal, their hypoxia signal, and their proliferation brake simultaneously. This is why the practitioner must read pH as a story about which bacteria are dominant, not just whether acids are present.

What ammonia does

Ammonia is both a marker and a mechanism.

As a marker, rising ammonia signals that proteolytic fermentation is gaining ground — that carbohydrate substrate has been depleted and the microbial community is fermenting protein and amino acids instead. As a mechanism, ammonia is directly toxic to colonocytes. It disrupts tight junctions, increases mucosal permeability, promotes inflammatory signaling, and is the alkalinizing agent that drives the positive feedback loop.

The urea that urease cleaves does not come from the diet. It diffuses into the colonic lumen from the blood. This means ammonia production in the colon is not entirely dependent on what the patient eats — it is partly driven by the systemic urea pool, which reflects whole-body protein metabolism. A patient with elevated blood urea nitrogen is delivering more substrate to colonic urease producers regardless of dietary changes. This is one reason why colonic dysbiosis can be stubbornly resistant to dietary intervention alone in patients with impaired renal function or high protein turnover.

Taking a stool pH

You'll need some 6-8 Hydrion pH paper. If the client has fecal matter on their toilet paper (likely with most microbiomes), press the moist stool into the pH paper, wait 5 seconds, then wipe off stool with fresh toilet paper.

If the stool is too dry to get a reading, they will need to defecate on a piece of paper, then take a piece of stool, break it in half and take a reading from the center.

In both cases, use the most alkaline color reading you see.

Reading a stool pH

Stool pH is the cheapest, fastest window into colonic ecology available to the practitioner. It is also the most commonly misinterpreted. pH is a better clinical target than tracking specific organisms. Specific organisms come and go with diet, seasons, stress, travel. What stays stable is which metabolic mode the colon is operating in, and stool pH is the single best readout of that mode.

A stool pH of approximately 5.7 to 6.2 is optimal.† It is consistent with saccharolytic dominance, adequate short-chain fatty acid production, sufficient protonation for Enterobacteriaceae suppression, and baseline levels of ammonia and toxic metabolites. In most patients, a pH in this range means the ecosystem is working. But as described

earlier, pH alone cannot distinguish a completed relay from a stalled one. It is a screening tool, not a confirmation.†

A stool reading of 6.0 likely reflects a proximal colon at approximately 5.5 to 5.7 — the zone of peak Firmicutes dominance and maximum butyrate production.

A stool pH of 6.5 to 6.8 suggests the community has shifted toward Bacteroidetes dominance. Butyrate production is declining. The SCFA antimicrobial mechanism is weakening. The system is still saccharolytic but losing ground. Intervention at this stage is easier than after the feedback loop engages.

A stool pH above 7.0 suggests the positive feedback loop is likely active. Ammonia is accumulating. Enterobacteriaceae are expanding. Butyrate production has dropped substantially. Proteolytic metabolites are rising. The practitioner should not expect a single intervention to reverse this.

A stool pH below 5.5 in a sick patient does not mean the colon is healthy. In critically ill patients, acidic stool reflects pathological fermentation — D-lactic acid, succinic acid, and formic acid from a disrupted ecosystem, not healthy short-chain fatty acid production. The relay has broken at the receiving end. Lactate is accumulating because the Firmicutes cross-feeders are gone. Propionic acid is markedly decreased. The number looks like a well-fed colon. It is not. This is the same-number-different-pathology pattern this book returns to repeatedly: a lab value only means something when the practitioner knows what is generating it.

The mortality data

One study links stool pH directly to survival. Osuka and colleagues measured fecal pH in 138 critically ill patients^{19,20} with systemic inflammatory response syndrome. They found a U-shaped relationship: both acidic feces (below pH 6.0) and alkaline feces (above pH 7.2) were significantly associated with increased mortality and bacteremia. A chart plotting the survival curve derived from this data is available at remedylink.com/charts

The two extremes represent different pathologies. The alkaline extreme means SCFA production has collapsed, Enterobacteriaceae dominate, ammonia is accumulating, and the colon has shifted to proteolytic metabolism. The acidic extreme, in these critically ill patients, meant pathological fermentation: the acids present were D-lactic acid, succinic acid, and formic acid — markers of ecosystem collapse, not healthy butyrate and propionate. Propionic acid was markedly decreased in both the acidic and alkaline groups compared to the normal range.

This data comes from the sickest possible population — ICU patients with SIRS. The practitioner should not extrapolate these ranges directly to outpatient practice. A healthy person with stool pH of 5.8 who is eating abundant fiber and producing butyrate is in a completely different metabolic state from an ICU patient with stool pH of 5.8 who is

producing D-lactate from a collapsed ecosystem. The number is identical. The clinical meaning is opposite.

A note on extensive stool testing

Comprehensive stool panels — reporting dozens of species, yeast, parasites, SCFAs, inflammation markers — are genuinely useful in complex cases. They are not the first move. pH paper costs a few cents per reading and tells the practitioner which metabolic mode the colon is running. The panel confirms in more detail what pH paper has already shown for free, and for patients who respond to standard interventions, the panel is information after the fact rather than something that changed what was done. Stool testing earns its cost in patients who do not respond to standard protocols, who have specific parasite suspicions, or whose symptoms do not track cleanly to pH.

What shifts the pH

Dysbiotic stool pH is entrenched. A practitioner who tells a patient with alkaline pH to eat more fiber and drink more water will usually find nothing has changed. Diet alone will not move established pH. The system is self-reinforcing: dietary fiber that in a healthy colon would feed saccharolytic fermentation gets consumed by whatever is dominant, which in a dysbiotic state is often not the pH-lowering populations.

This is where the teaching departs from what most practitioners want to believe about diet. Diet matters — a patient who restores pH and returns to low-fiber, high-processed food may not hold gains. Diet determines whether a healthy microbiome stays healthy¹⁶. But diet is generally not what restores a dysbiotic microbiome.

Diet will help, and could work in theory, especially for those with only mild dysbioses, but even those eating ‘healthy’ diets are still limited to modern crops. Finding paleolithic tubers is difficult and because we lack the ancestral bacteria needed to ferment them properly, those that are authentic, like sunchoke, will generate gas to the point of non-compliance. Exceptions exist like Taro root, but they are hard to find.

Restoration often requires direct intervention, and one of the best interventions is human milk oligosaccharide prebiotics (HMOs)[†], which selectively feed the lactic acid bacteria^{17,18} that produce the SCFAs that lower pH.

HMOs pass through the small intestine intact and arrive in the colon as selective food for LAB populations. Patients with these populations present, even in small numbers, often see pH shift within one to two weeks. Patients whose LAB populations have been driven further down may need LAB probiotic seeding alongside. The stepped protocol is the subject of the next chapter.

When HMOs are not enough

We already discussed how lack of cross feeding Firmicutes can derail a microbiome recovery. Another issue to contend with, and far more common, is patients who have urease-producing populations (typically Enterobacteriaceae like Klebsiella and Proteus) dominant enough that feeding LAB is insufficient to outcompete them. The LAB grow, produce some acid, and the urease organisms continue producing ammonia and bicarbonate faster than the LAB can keep up.

These patients need direct antimicrobial pressure on urease-producing populations. The next chapter teaches the stepped protocol.

Clinical pearl: Once gluten, oxalates, lectins, histamine reactivity, and any individual intolerances are accounted for, the final test for a food's inclusion in the diet is healthy stool formation.

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Chapter 23 — The Firmicutes:Bacteroidetes ratio controversy

The practitioner reading stool panels will encounter the Firmicutes-to-Bacteroidetes ratio — the F/B ratio — presented as a meaningful biomarker. A higher ratio is said to correlate with obesity. A lower ratio is said to correlate with inflammatory bowel disease. The implication is that the number itself tells the practitioner something actionable. It does not, and the reason it does not goes directly to the argument of the previous chapter.

The F/B ratio treats two enormous phyla as if each were a single organism. Firmicutes includes *Lactobacillus*, *Faecalibacterium*, *Roseburia*, *Eubacterium*, *Clostridium* clusters IV and XIVa, *Enterococcus*, and *Ruminococcus* — organisms with radically different metabolic outputs and clinical significance. Bacteroidetes includes both *Prevotella* and *Bacteroides* — two genera that share a phylum but occupy different ecological niches and respond to different substrates.

This is where the hunter-gatherer data becomes instructive and where the apparent contradictions in the literature resolve.

What traditional populations actually show

The Hadza of Tanzania, one of the last remaining foraging populations, show higher Bacteroidetes and lower Firmicutes than Italian urban controls¹ at the phylum level. But the Bacteroidetes enrichment is driven almost entirely by *Prevotella* — not *Bacteroides*.

The Hadza are depleted in *Bacteroides*, *Roseburia*, and *Faecalibacterium* relative to Western populations, yet enriched in *Prevotella*, *Eubacterium*, and *Treponema*. The Yanomami of the Amazon show a similar pattern: higher Bacteroidetes over Firmicutes, again driven by *Prevotella*⁶. In both populations, overall microbial diversity is substantially higher than in industrialized cohorts.

The Ju/'hoansi of the Kalahari, studied with shotgun metagenomics in 2024, show the opposite phylum-level ratio — Firmicutes at 47.5 percent, Bacteroidota at 39.8 percent⁵. Yet the Bacteroidetes present are again dominated by *Prevotella* and *Cryptobacteroides*, not by *Bacteroides*.

The BaAka Pygmies of Cameroon show *Prevotella* and *Treponema* enrichment³; neighboring Bantu populations transitioning to modern diets show an increased F/B ratio driven by gains in *Faecalibacterium* and lactic acid bacteria.

The consistent signal across all these populations is not the phylum-level ratio. It is three things. First: *Prevotella* dominance within Bacteroidetes, driven by high-fiber plant-based substrates and reflecting the enormous polysaccharide-utilization capacity these organisms bring to complex carbohydrate degradation. Second: high overall microbial diversity, with many organisms occupying many niches rather than a few organisms dominating. Third: robust fiber-degrading capacity across both phyla — Clostridiales from the Firmicutes side, Prevotellaceae from the Bacteroidetes side, working in parallel⁴.

What industrialized populations show

Industrialized populations show the reverse: Bacteroides dominance within Bacteroidetes (associated with animal fat and protein substrates, not plant polysaccharides), lower overall diversity, and reduced fiber-degrading capacity. Bacteroides and Prevotella are both gram-negative, both produce acetate and propionate, and both carry large polysaccharide-utilization loci — but they are not the same organism doing the same work. Prevotella is the plant-fiber specialist. Bacteroides is more metabolically generalist and associated with Western dietary patterns.

The distinction matters beyond substrate preference. The LPS from commensal Prevotella species carries a lipid A structure that binds TLR4 weakly or acts as a competitive antagonist — the tolerogenic pattern described in Chapter 21. The LPS from certain Bacteroides species, while also broadly tolerogenic, varies more across strains. The practitioner cannot assume that all Bacteroidetes LPS is equivalent. The ancestral Prevotella-dominant ecology and the modern Bacteroides-dominant ecology present different immune signatures even though both fall under the same phylum.

Why the F/B ratio fails

The F/B ratio collapses this distinction. A patient with high Prevotella-driven Bacteroidetes on a traditional diet and a patient with high Bacteroides-driven Bacteroidetes on a Western diet both show a low F/B ratio. The clinical meaning is opposite. This is the same-number-different-pathology pattern this book returns to repeatedly: a ratio only means something when the practitioner knows what is generating it.

The literature itself is contradictory because the ratio is too blunt to capture what is happening. Some studies find high F/B ratio in obesity. Others find no difference. Others find the reverse. The contradictions dissolve when the analysis moves to the genus level — what matters is which Firmicutes and which Bacteroidetes, not how much of each phylum is present. A patient whose Firmicutes are dominated by butyrate-producing Clostridiales⁷ and whose Bacteroidetes are dominated by Prevotella is in a fundamentally different ecological state from a patient whose Firmicutes are dominated by Enterococcus and whose Bacteroidetes are dominated by Bacteroides⁸. The phylum-level ratio cannot tell the difference.

The seasonal instability of the ratio

The seasonal cycling data from the Hadza adds a further caution. Bacteroidetes OTUs — primarily Prevotellaceae — fluctuate dramatically with seasons, disappearing in the wet season and reappearing in the dry season². Firmicutes composition remains relatively stable across seasons. The F/B ratio in these individuals swings substantially within a single year in response to normal dietary variation. Any biomarker that swings

that widely with seasonal food availability in healthy foragers is not measuring a stable pathological state. It is measuring what the person has been eating.

The practical teaching

When a stool panel reports the F/B ratio, the practitioner should look past the ratio to the genus-level composition underneath it. Prevotella dominance alongside high diversity is not dysbiosis. Bacteroides dominance alongside low diversity and depleted butyrate producers is dysbiosis, regardless of what the F/B ratio says. And pH paper, which costs a few cents, tells the practitioner whether the butyrate-producing Firmicutes are active — which is the clinical question the F/B ratio was never designed to answer.

Clinical pearl: Even with complex evaluations available, stool pH remains the single most informative laboratory finding for the gut.

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Chapter 24 —Lactic Acid Bacteria (LAB) are the foundation of the microbiome

Why LAB are the foundation

The lactic acid bacteria are the initiators of the entire colonic acidification succession.¹ Lactate is the first acid produced from saccharolytic fermentation, and once present in adequate quantity, other populations convert it to acetate, then propionate, then butyrate.² None of the downstream populations work without lactate as their substrate. A colon without LAB is a colon where the acidification succession never starts.†

The Bifidus LAB are highly vulnerable to antibiotics — they die off faster than most gut populations and recover more slowly.³ A patient with heavy antibiotic history may have lost some of their LAB, and the cascade follows: lower LAB, lower lactate; lower lactate, lower downstream acids; less acids, pH stays in the neutral to mildly alkaline state it arrived in from the small intestine. This favors the toxin forming neutral and alkaline loving bacteria.

LAB are seeded by the mother during vaginal birth.⁴ HMOs do not put LAB into the infant — they selectively feed LAB once present. This selectivity is key: HMOs are structured so LAB can metabolize them and most other organisms cannot, giving LAB dominance during the window when colonic terrain is being set.⁵

This is why HMO supplementation is the right tool for restoring adult patients whose stool pH is neutral or alkaline.† The adult colon shares with the infant colon the narrower problem that LAB need selective food. HMOs feed LAB and largely nothing else. Generic fiber feeds many populations including the wrong ones.

Step 1 — HMO supplementation

An HMO-based prebiotic formulated for selective LAB feeding is the starting intervention. HMOs reach the colon undigested, where they selectively feed remaining LAB populations. LAB grow on the HMO substrate, produce lactate, and the acidification succession begins.

Watch stool pH. Movement downward week by week is the signal of response. Continue until pH stabilizes in the healthy range or until two weeks pass without movement.†

Two weeks without movement triggers escalation. A common reason: urease-producing populations are dominant enough to maintain alkaline pH against whatever lactate the LAB are producing.†

Step 2 — Targeted antimicrobial pressure on urease organisms

The mechanism: urease-producing organisms (Klebsiella, Proteus, Morganella, certain Candida species) carry the urease enzyme, cleaving urea into two molecules of ammonia and one of CO₂.⁶ The ammonia hydrates to produce hydroxide, which directly

alkalinizes stool. The CO_2 equilibrates to bicarbonate and proton in equal amounts — pH-neutral on net, but the bicarbonate creates a buffer that resists acidification from LAB lactate.⁶ So urease organisms both raise pH directly and make it harder to push back down.† This is why feeding LAB harder does not break the loop — direct antimicrobial pressure is required.

Consider ingredients such as pomegranate rind,⁷ geranium flower, pine bark extract,⁸ persimmon tannins, hibiscus flower,⁹ and cranberry extract,¹⁰† The goal is to relieve the buffering pressure so LAB-driven acidification can succeed.

Watch pH through this step. A patient whose pH starts moving on addition of these ingredients has the urease-driven pattern. Maintenance dosing may continue past pH stabilization, as urease populations driven dormant can reactivate if pressure is removed too quickly.†

If pH still has not moved after two more weeks, escalate.

Step 3 — Escalated antimicrobial pressure

Ellagitannins are broader-spectrum than the urease-suppressing ingredients, operating through several mechanisms simultaneously.¹¹ Ellagitannins also are prebiotic for certain good bacteria. Run alongside both HMOs and urease-suppressive ingredients.

Same monitoring rhythm. Movement is response; lack of movement triggers the next escalation.

Step 4 — LAB probiotic seeding when the seed bank is empty

If two weeks pass on step 3 without pH movement, it is possible that there is no LAB seed left for the HMO to feed — possibly as a result of very heavy antibiotic histories, particularly fluoroquinolone exposure.†

LAB probiotic seeding introduces the populations directly.¹² With antimicrobial pressure from steps 2 and 3 already in place and HMO substrate available, the introduced LAB have a chance to take. This is not the probiotic flooding the previous chapter warned against — the terrain has been worked on for weeks, and seeding is into prepared ground.†

Step 5 — Voltage, bacteriophages, essential oils, and bitters

If after two weeks on the full step 4 protocol pH has still not moved, additional tools are warranted.

Bitters and essential oils — berberine,¹³ gentian, oregano,¹⁴ thyme,¹⁵ ginger, pine — provide multi-mechanism antimicrobial action through biofilm penetration, quorum

sensing disruption, and differential susceptibility of pathogens compared to commensals.

Bacteriophage therapy targets specific bacterial populations using phages that kill the target without affecting non-target populations.¹⁶ Response is binary — the target is either present or it is not. For patients with a history of sore throats, or suspected PANDAS (including adults that may have had it as children), consider the Sextaphage bacteriophage for Streptococcus.

Low amperage, high negative voltage operates differently from chemical antimicrobials. Adequate tissue voltage maintains dormancy; supra-physiological voltage actively repels certain populations, particularly parasites.†

These tools are not a fixed sequence at step 5. The practitioner judges which to add based on the patient.

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Chapter 25 — Strength in Diversity

The microbiome is valuable for the real estate it colonizes (thus denying the same for toxic species), but also what it makes. Postbiotics are the compounds bacteria produce. The most clinically important are the short-chain fatty acids: acetic acid, propionic acid, and butyric acid.¹ There are others — bacteriocins, neurotransmitter precursors, vitamins, signaling molecules — but the SCFAs do the bulk of the work for colonic restoration. They feed colonic epithelium, lower pH, regulate the immune system, and suppress or kill bacteria thriving at higher pH. SCFAs also exert powerful effects on mood, each acting differently.†

The bacteria that produce these compounds need food. That is what oligosaccharides (prebiotics) do. The previous chapter covered HMO-based selective feeding while the colon is still alkaline. Once the colon reaches pH 6.5, the terrain has shifted enough to begin feeding more broadly.†

Why diversity matters

A healthy colon hosts many kinds of bacteria. Different species produce different SCFAs, ferment different substrates, and occupy different sections of the colon.² Different bacteria need different oligosaccharide categories to thrive, and without more expensive testing, practitioners cannot predict which population is missing in which patient. Broad coverage ensures whichever populations are missing can find what they need.

Broad oligosaccharide coverage does a second job: different oligosaccharides act as decoy molecules at the gut wall, blocking pathogen attachment at different receptor types.³ Broad coverage means broad pathogen interference.

Sourcing diversity

Oligosaccharides come from many food categories:

- Tubers: galacto-oligosaccharides
- Fruits and vegetables: xylo-, pectin-, and fructan-oligosaccharides
- Wild game: connective tissue oligosaccharides
- Mushrooms: chitin-oligosaccharides
- Seaweeds: fuco-dan-oligosaccharides
- Honey and traditional fermented foods (miso, kimchi): isomalto-oligosaccharides

A patient eating a traditional varied diet would consume this diversity as a matter of course. A patient on a modern industrial diet will likely fall short in many categories.

Direct oligosaccharide supplementation is one way to close the gap. A multi-category formulation drawing from all these sources can deliver coverage the modern diet rarely provides. The seaweed-derived oligosaccharide Fuco-dan is expensive enough that

most products skips it — its inclusion is a marker of whether a formulation is priced for quality or cost.†

When to introduce diversity

Above pH 6.8, SCFA concentrations are not yet sufficient to suppress the wrong populations. Broad feeding would expand bad bacteria along with good.† This is why HMO-based selective feeding was the only reasonable move while pH was high. At pH 6.5 and below, most bad populations are no longer in the dominant position and the good are producing acid — broad feeding now reinforces the good more than the bad.† The protocol order is non-negotiable: pH first, diversity second.†

Direct postbiotic supplementation

Feeding good bacteria is one path to better postbiotic output. Supplementing postbiotics directly is another — faster, but without building production capacity. Practitioners can use sodium acetate, sodium propionate, and sodium butyrate.⁴ The SCFA ratio should approximate that found in healthy hunter-gatherer microbiomes.† As microbiome restoration progresses, patient-side production rises and direct supplementation becomes less necessary, but remember, this too requires an acidic pH. SCFA do their work when protonated and this requires an acidic pH.

Fermented foods

Sauerkraut, kimchi, miso, kefir, traditional yogurt, fermented vegetables — these contain bacterial postbiotics and live organisms.⁵ and contribute postbiotic input at the dietary level.

Some patients do not tolerate fermented foods. Histamine-sensitive patients may react.⁶ Fermented foods also commonly contain both L and D lactic acid — the D form is mildly neurotoxic.⁷ For most patients this is a non-issue, but for patients who are neurologically reactive or fatigued in unusual patterns, fermented foods may be worth avoiding temporarily.† Direct SCFA supplementation are tolerated when fermented foods are not.

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Chapter 26 — You are what you eat, your microbiome is what you don't digest

When digestion is intact, the small intestine extracts most of what the patient eats, and only indigestible residue — fiber and oligosaccharides — reaches the colon.¹ The microbiome thrives on this residue because it evolved to. A truly symbiotic arrangement. We do not compete for the same fuel.

When digestion fails, undigested or under-digested food spills over into the colon. The colon's microbiome was never built to ferment whole proteins, fats, or starches. Spillover changes the substrate, and the microbiome's output changes accordingly.²

The core principle: a patient is what they eat. Their microbiome is what they cannot digest. † When nutrients meant for the small intestine spillover into colon, this causes dysbiosis. A reverse form of spillover is when bacteria meant for the colon colonize the small intestine.

Five causes of spillover

1. Insufficient chewing. Larger food particles overwhelm the small intestine's capacity.
2. Poor digestive capacity. Age-related decline, proton pump inhibitors,³ bile flow obstruction, and pancreatic insufficiency all reduce chemical breakdown.
3. Poor absorption. Inflammation, villus damage, or mucosal compromise reduces uptake even when food is broken down adequately.⁴
4. Overeating. The small intestine has finite throughput. Excess passes through. †
5. Weak ileocecal valve, sometimes from surgical adhesions — allows retrograde movement of colonic bacteria into the small intestine. †

Three macronutrient pathways

In addition to the production of ammonia and other toxins from proteolytic fermentation mentioned in an earlier chapter, protein spillover also produces putrescine and cadaverine — toxic amines that signal danger at a deep biological level⁵, and can trigger fear, aggression or disgust towards the person whose microbiome makes them. †

Fat spillover produces reuterin (a broad antimicrobial — the patient is essentially self-dosing a microbiome-disruptive antibiotic from their own undigested fat),⁶ acrolein (a genotoxin),⁷ and trimethylamine (converted to TMAO, an arterial plaque precursor).⁸ The cardiovascular literature is catching up to what fat spillover does to the vascular system — the underlying issue is digestive failure, not dietary fat itself. †

Carbohydrate spillover produces gas and feeds Candida overgrowth.⁹ The patient experiences bloating, distention, and gas.

The four-gas framework

Hydrogen — normal in moderation. Some acts as antioxidant¹²; some is converted to acetate by good bacteria.¹⁴ Excess produces loose stools and provides substrate for H₂S and methane producers.

Hydrogen sulfide — beneficial in moderation (prevents bacterial translocation, supports mucosa, helps stabilize plaque).¹³ In excess, damages cells, promotes leaky gut, and contributes to neurological pathology.¹¹ The rotten-egg smell is the diagnostic.

Carbon dioxide — normal. Contributes to colonic buffering chemistry.

Methane — produced by methanogens. Causes spasm and partial paralysis of intestinal smooth muscle, producing the constipation pattern characteristic of methane-dominant SIBO.¹⁰ Chronic constipation not responding to fiber or hydration is often a methane problem.

For practitioners with budget, breath gas testing makes the profile visible.¹⁴

Constipation

Constipation is a global contraindication during active metal and especially chemical detox (more on this in upcoming chapters). Constipation generally leads to a more alkaline (higher) stool pH, which leads to deconjugation. This happens for three reasons.

Protein putrefaction increases. As fermentable carbohydrates get used up, bacteria shift toward breaking down proteins and amino acids. This produces alkaline byproducts like ammonia, amines, and indoles, which raise stool pH.

Short-chain fatty acid (SCFA) production declines. SCFAs — acetate, propionate, and butyrate — are the main acidifying compounds in stool and are produced by bacterial fermentation of dietary fiber and resistant starch. With prolonged transit, the fermentable substrate gets depleted, so SCFA output drops and the acidifying effect is lost.

Water reabsorption concentrates alkaline compounds. The colon continues absorbing water from stool during slow transit, which can concentrate the remaining alkaline metabolites.

Slowed transit also gives intestinal bacteria more time to produce TMAO and elevate LPS load. A patient who takes cholestyramine to lower cholesterol but becomes constipated is increasing TMAO and LPS — the upstream drivers of the inflammatory cholesterol elevation the binder was prescribed to address. The marker improves while the cause worsens.

Clinical pearl: Dysbiosis creates odors that the practitioner can recognize.

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Chapter 27 — Your genetics are not your destiny

A patient walks in with a genetic test report. They have been told they carry a variant for a methylation gene, or a detoxification gene, or are at a higher risk for a specific type of cancer. They have read about what it means. They feel broken — that something fundamental has been decided about them.

Genetic variants are real. They affect how the body handles certain inputs. But what the test does not tell the patient is that their human genome is not the only genome operating in their body. The microbiome carries metabolic pathways the human genome does not encode, produces compounds the body cannot make on its own, and performs detoxification, vitamin synthesis, immune regulation, and neurotransmitter precursor generation.¹ The patient's biology is a partnership between their human genome and their microbial genome.

What the patient was told their genes condemned them to is, in many cases, what their human genes alone would produce in the absence of microbial support.† With a healthy microbiome, the picture is different.

What genetic variants actually mean

Some variants reduce the patient's capacity to run a particular enzymatic step efficiently. The MTHFR variant is one — the enzyme still functions, but at a fraction of normal speed.² The patient is not making zero. They are making less. Lifestyle determines how much demand they put on that pathway. A patient whose toxin load is low, diet clean, digestion intact, and microbiome healthy may never feel the limitation. A patient overwhelming the same pathway will feel it strongly.

The library

Think of the genome as a library. Each gene is a cookbook on the shelf. Some contain recipes for healthy food. Others contain recipes that should never reach the table. Every patient has both kinds.

It matters little which cookbooks are in the library if no one takes them off the shelf. A book never opened changes nothing. A book used every day shapes everything.

Epigenetics is the study of which books come off the shelf.³ Lifestyle decisions — diet, sleep, stress, microbiome — determine which books get pulled down and which stay gathering dust.

The genetic test tells the patient which books they have. It does not tell them which books are being read.

What this means for the patient

The variants are real but not the whole story. Variants that reduce a specific pathway describe a limitation, not an absence — lifestyle determines how heavily the patient leans on that limited pathway. Variants marking increased disease risk are warnings, not sentences — what determines whether vulnerable books come off the shelf is epigenetics, and lifestyle is the largest input the patient controls.

The microbiome is one of the most powerful epigenetic levers we have and is highly consequential for how variants express.† Restoring the microbiome is, in a real sense, genetic work — not changing DNA, but changing which genes pull in the patient's favor.

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Chapter 28— Parasites: don't always kill them... sometimes just show them the door

Parasites are an interesting case. Traditional doctors believe that they are mostly absent from the general population and people wanting a 'parasite cleanse' are ignorant at best and delusional at worst. On the other side, some alternative practitioners believe that parasites are endemic in even 1st world patients and a contributor to virtually all diseases. Where is the truth? Likely in the middle. Parasites are common, they contribute to a great deal of disease even in first-world countries,¹ but the correct strategy for addressing them is not the strategy most practitioners reach for first.

For this chapter, parasites means helminths — roundworms, tapeworms, hookworms, flukes — and protozoa including *Toxoplasma*, *Trypanosoma*, *Giardia*, and *Entamoeba*. Bacterial and fungal overgrowths are addressed in other chapters.

Why kill-based protocols aren't always best

The instinct on encountering a parasite is to kill it. This can produce problems varying by parasite size and location.

Small parasites dissolved in place release their contents. Many protozoa and small helminth larvae, when killed chemically, dissolve in host tissue, releasing metabolic byproducts and any organisms the parasite carried.² The patient may experience a worse burden after the kill than with the parasite alive.

Large parasites encapsulated produce chronic irritation Larger parasites the body cannot dissolve are walled off in granulomatous capsules.³ Killing the parasite inside does not remove the capsule. The encapsulated material continues to irritate surrounding tissue, sometimes for life.

Chemical irritation drives burrowing or resistance Helminths that can migrate through tissue respond to chemical attack by burrowing deeper, where concentration is lower.⁴ Sub-lethal doses produce parasites in less accessible tissue. Over time, repeated sub-lethal pressure may also produce resistance.

The toxicity ceiling on herbal antiparasitics

Most antiparasitic herbs are toxic by design — they kill the parasite by chemistry the host handles less well. Wormwood contains neurotoxic thujone at sustained doses.⁵ Clove (eugenol) is hepatotoxic at elevated doses.⁶ Black walnut and juglone-containing herbs have their own profiles. Berberine at antiparasitic doses places significant hepatic load.⁷

Don't always kill them. Sometimes, show them the door

One strategy is non-kill expulsion: make the host tissue inhospitable so the parasite leaves,† and an excellent tool for this is negative high voltage applied externally over the affected region.†

Two mechanisms

Stun effect High voltage - Low amperage can stun parasites and disrupt the parasite's nervous system and mobility without killing it in place, causing them to dislodge from tissue walls.†

Counter-attractant signal Healthy tissue carries a baseline negative charge that parasites orient toward. Inadequate tissue voltage produces an attractive signal. Supra-physiological negative voltage reverses this — the parasite receives a repellent signal and is driven to leave.†

Unlike chemical antiparasitics, voltage at therapeutic settings has no toxicity ceiling and can be repeated as often as warranted.

Practitioners and patients applying negative high voltage over the abdomen routinely report finding living parasites in the toilet afterward — alive because they were driven out, not killed in place.†

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Chapter 29— The body's many gardens

The word microbiome, in common usage, refers almost exclusively to the colon. The body hosts many distinct microbiomes, each with its own ecology tuned to the specific work that section needs done. This chapter is about the small intestine. Unlike the large intestine, feeding diversity and building dense populations would harm the small intestine. The small intestine wants the opposite.

What the small intestine is for

The small intestine is the digestive and absorptive corridor. Food passes through approximately twenty feet of jejunum and ileum, acted on by bile, pancreatic enzymes, and brush-border enzymes.¹ Breakdown products are absorbed into the bloodstream and lymphatics. By the time what remains reaches the ileocecal valve, the host has extracted most of what was nutritionally available.

This work depends on the small intestine having a being relatively low microbial population. A dense microbial population would compete with the host for nutrients, produce gas and acid before absorption, consume bile acids and interfere with fat digestion.²

The colon wants high microbial density. The small intestine wants low. Same gut, same continuous tube, two completely different ecologies.

The eight protections of the small intestine

Adequate chewing matters as a precondition. Saliva contains lysozyme,³ and chewing triggers the cephalic phase of digestion. Food chewed thoroughly arrives pre-treated with antimicrobial saliva and meets a prepared digestive system.

Stomach acid Parietal cells produce HCl bringing pH below 2.⁴ Few microbes survive. Stomach acid declines with age, PPI use, and chronic stress — delivering food to the small intestine still carrying a microbial load.

Bile as detergent Bile acids disrupt lipid membranes of bacteria and fungi.⁵ A patient with poor bile flow — from gallbladder removal, bile stasis, chronic biliary dysfunction — has lost a major antimicrobial layer.

Pancreatic enzymes Trypsin and chymotrypsin cleave bacterial proteins. Lipase disrupts microbial membranes. Amylase reduces substrate for microbial fermentation.⁶ Pancreatic insufficiency delivers undigested food that becomes microbial substrate.

FXR-triggered antimicrobials As bile acids reach the terminal ileum, they activate FXR, triggering local antimicrobial peptide production — a sentinel system at the ileal-colonic boundary.⁷ When bile flow fails, this signaling fails too.

The migrating motor complex (MMC). The cleaning rhythm between meals — a wave of contraction sweeping from duodenum to ileocecal valve roughly every ninety minutes during fasting, physically removing accumulated microbes.⁸ The MMC requires fasting to fire. A patient who eats continuously suppresses it for most of their waking hours.

The fasting window The MMC needs at least three to four hours between meals, and the most important activity happens during overnight sleep. A twelve-to-fourteen-hour overnight fast gives the MMC its most thorough window. The difference between a clean and colonized small intestine often comes down to this.†

Immune function Peyer's patches and lamina propria immune cells patrol the mucosal surface, identifying microbes and producing secretory IgA.⁹ When systemic immune function is compromised, this patrol weakens.

The ileocecal valve The one-way boundary keeping colonic contents from refluxing into the terminal ileum.¹⁰ When incompetent — most often from surgical adhesions — dense colonic populations colonize the small intestine in retrograde. One of the most common origins of SIBO.

SIBO and SIFO

When protections fail, bacteria (SIBO) and/or fungi (SIFO) proliferate where they should not.¹¹ The picture is toxic fermentation in the small intestine — bloating shortly after meals, gas profiles varying by dominant organism (hydrogen, methane/constipation, hydrogen sulfide/rotten egg), wall damage contributing to leaky gut and systemic inflammation, and nutrient deficiencies despite adequate intake.

The conventional approach — repeated antimicrobial courses — treats the symptom without restoring the failed protections.† The overgrowth recurs because the defense system is still broken. Each antibiotic round further damages the microbiome.

Spore-formers and the soil-plant-gut cycle

The healthy small intestine hosts predominantly transient, spore-forming bacteria from the genus *Bacillus*.¹² Soil contains many thousands of microbial species, but only a small fraction survive cooking and human digestion. The *Bacillus* species — perhaps five percent of soil microbes — are the fraction that became our digestive symbionts once humans mastered fire.†

Their life cycle fits the small intestine's needs. They exist in soil as dormant spores — metabolically inactive, resistant to heat and acid.¹³ Spores enter the body on plant matter and from soil contact. They survive the stomach because spores are not metabolizing. When they reach the small intestine, bile triggers germination.¹⁴ The active cell produces antimicrobial compounds, regulates local immunity, and supports digestion. The sickest colons (highest pH) provide the optimal environment for these beneficial bacteria to exert their healing effects most powerfully. A proper *Bacillus*

formulation is most active where it's most needed † - in compromised, dysbiotic environments with elevated pH, settling to a more background protective posture as the gut pH returns to health. A graph plotting pH against Bacillus activity can be seen at remedylink.com/charts.

Antibiotics affect the spore population differently from resident colonic populations. Because spores are transient and not metabolizing while in spore form, they are not susceptible to antibiotics the way colonized bacteria are.¹³ This makes the spore protocol usable during and after antibiotic courses — a significant advantage when antibiotics are clinically necessary.

The loss of the spore bacteria

In soil, the spores participate in the plant-root symbiosis — plants exude sugars to feed soil microbes, which in return solubilize minerals, fix nitrogen, and protect root zones.¹⁵ Soil to plant to gut to soil. Modern farming has broken that connection.

Fertilizer Synthetic NPK feeds plants directly, bypassing the symbiotic exchange.¹⁶ Plants stop feeding soil microbes, and spore populations decline around root zones.

Agricultural chemicals Pesticides, herbicides, and fungicides damage the broader soil microbiome including spore populations.

Human hygiene Paved surfaces, indoor environments, antimicrobial hand products minimize soil contact.

The kitchen Peeling and thoroughly washing vegetables removes the spores that remain. The skin of root vegetables is where most soil-derived microbial content sits.

The combined effect: modern patients receive a vanishingly small fraction of the spore exposure human biology evolved to receive daily. The small intestine loses the population that was doing several protective jobs — Bacillus species secrete antimicrobial peptides (surfactin, iturin, fengycin, bacillomycin),¹⁷ modulate local immunity,¹⁸ and contribute enzymatic digestive activity.

The seven strains

There are at least 7 Bacillus spore bacteria that should be included in the human diet to recreate a paleolithic exposure. † Some can be found in common spore based supplements, a few are more rare.

Commonly available Bacillus strains

Bacillus subtilis — The foundational immunoregulator. Produces iturin and fengycin (antifungal).¹⁷ Contributes diamine oxidase activity (degrades dietary histamine).¹⁸ Digests biofilm matrices.¹⁹

Bacillus coagulans — Produces L-form lactic acid, contributing to pH regulation in the proximal colon.²⁰

Bacillus clausii — Contributes antibiotic resilience and immune modulation. Tolerates concurrent antibiotic exposure, making it useful during and after courses.²¹

Bacillus licheniformis — protein specialist. Produces proteases reducing protein spillover into the colon.²² May help with anxiety.

Specialty Bacillus strains - useful, not commonly available

Bacillus velezensis — The antifungal and biofilm-disruptor. Produces polyketide compounds and proteases.²³

Bacillus megaterium — The largest Bacillus species, most varied output. Contributes chelation activity, B12 production, phosphate solubilization.²⁴

Bacillus amyloliquefaciens — The starch specialist. Produces amylase and bacillomycin (antifungal targeting ergosterol).²³

Bile and the spore protocol

Spores require bile to germinate.¹⁴ A patient with adequate bile flow takes spores and they activate in the duodenum. A patient with compromised bile flow — gallbladder removed, chronic biliary stasis — does not produce enough bile for reliable germination. The spores pass through poorly activated.†

The workaround: bile salts taken with spore supplementation provide the germination trigger, but for long term success, the gall bladder must be addressed directly.

When and how

Spore supplementation operates in the small intestine — not gated by colonic stool pH.† A patient still working on stool pH can begin spore work simultaneously, as the two act in different compartments.

Take with food, when bile flow is most active. Because Bacillus spores are transient, they must be a daily part of the diet.

Intestinal Microbiome flowchart

This concludes the teachings on the large and small intestine microbiomes. For complete protocols, visit remedylink.com/protocols

Clinical pearl: The grumbling sounds a patient may start to hear are not a bad sign. That is the migrating motor complex coming online. It means the gut is cleaning house between meals the way it is supposed to.

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Chapter 30: The Sinuses — Where the Brain, Immune System, Lungs, and Circulation Converge

The paranasal cavities — frontal, maxillary, ethmoid, sphenoid — together hold a volume the size of a couple of golf balls. By every measure of size, the sinus is a minor system. By every measure of consequence, it is one of the most important in the body, because of what it connects to.† The brain sits directly above it. The immune system runs through the lymphoid tissue in and around the sinus walls. The lungs receive the air the sinus conditions. The circulation receives the nitric oxide the sinus produces continuously.¹

The brain

The cribriform plate is a thin, perforated bone separating the upper sinus cavity from the underside of the brain. The name comes from the Latin for "sieve" — the bone is riddled with openings through which olfactory nerves descend from the brain into the sinus mucosa.²

The cribriform plate also carries the brain's waste. The glymphatic system — lymphatic-like clearance run by glial cells — is most active during sleep, when cerebrospinal fluid flows through perivascular spaces, picks up metabolic waste, and exits the brain.³ The majority of that exit happens through the cribriform plate, where waste-laden fluid drains into the sinus cavity and is cleared by mucociliary flow toward the throat.⁴ The cribriform plate is a brain drain.

Two failure modes follow. A congested or biofilm-coated sinus cannot accept drainage at the rate the brain produces it.† The waste backs up and goes retrograde into the brain, creating symptoms such as brain fog, dulled cognition, low-grade headache and many forms of senility.†

The cribriform plate is two-way. Whatever can leave through it can enter.⁵ A sinus containing mycotoxins, bacterial toxins, or VOCs delivers those compounds through the cribriform plate into the brain — specifically into the olfactory bulb, adjacent to the amygdala, hippocampus, and near the hypothalamus and pituitary.⁶ A toxic sinus delivers its toxins preferentially to the parts of the brain governing fear, memory, mood, and hormonal regulation.† This is the structural reason sinus dysfunction so often co-presents as cognitive difficulty or mood disorder.

A practical note: raising the head of the bed four to eight inches above the foot supports both sinus and glymphatic drainage. Risers under the bed frame or a wedge under the mattress.

One more consequence: amyloid plaque appears to function in part as a binder, capturing toxins and microbial fragments entering the brain across the cribriform plate.†^{7,27,28} In this framing, amyloid is not the primary disease but a downstream response. Removing amyloid without addressing the upstream toxic input releases what

it was holding — consistent with the disappointing outcomes of major anti-amyloid drug trials.^{8,26} Sinus restoration is upstream work in the most literal sense.†

The immune system

The sinus mucosa hosts a small consortium of organisms that occupy niches otherwise available to pathogens, calibrate local immune response, and produce neuroactive metabolites that reach the brain via the cribriform plate.⁹

Three organisms do most of this work. The following is not a complete list of the postbiotics they make, but is included to show the complexity of their output.

Corynebacterium pseudodiphtheriticum — Synthesizes glutamate and tryptophan precursors the other members use as raw material.¹⁰

Dolosigranulum pigrum — Produces GABA, which crosses the cribriform plate and dampens amygdala activation.¹¹ A patient with a healthy Dolosigranulum population is getting continuous low-dose GABA delivery to the fear-response center.

Commensal Staphylococcus epidermidis — carries the enzyme SadA, converting precursors from Corynebacterium into phenylethylamine, dopamine, serotonin, and tryptamine.¹² These also cross the cribriform plate.

Together they produce a continuous stream of neuroactive compounds that calm the amygdala and support mood and cognition.†

Two regulatory peptides are characteristically depleted in patients with chronic sinus and mold illness.

Melanocyte-stimulating hormone (MSH) — produced by the pituitary, with roles far beyond the name. MSH regulates inflammation, mucosal immunity, sleep cycle, leptin signaling, and pain modulation.¹³ Depleted MSH produces chronic mucosal inflammation, disrupted sleep, leptin resistance, increased pain sensitivity. Mold-toxin exposure reliably depletes MSH by disrupting hypothalamic signaling.¹⁴

Vasoactive intestinal peptide (VIP) — produced throughout the body, with roles in vascular tone, immune regulation, circadian rhythm, and pulmonary function.¹⁵ Depleted VIP produces shortness of breath on exertion that does not match cardiovascular workup, exercise intolerance, dysregulated immune response. Also depleted by mold exposure.¹⁴

Sinus restoration removes the suppression of MSH and VIP at its source.† If needed to accelerate recovery, nasal delivery of these peptides may be helpful.

The lungs and circulation

The sinuses produce NO continuously, in concentrations far higher than the rest of the airway.¹ NO is released into air passing through the sinus during nasal breathing and carried into the lungs, where it dilates pulmonary blood vessels, improves ventilation-perfusion matching, relaxes bronchial smooth muscle, and exerts antimicrobial activity.¹⁶ NO reaching the bloodstream contributes to systemic vasodilation.

This is why nasal breathing matters. Mouth breathing bypasses the sinus entirely. No NO delivery.

What displaces the consortium

Antibiotics clear the sinus along with everything else. A patient with multi-decade antibiotic history has likely lost the consortium decades ago. The sinus has no microbial reservoir analogous to the appendix.† When the healthy sinus microbiome is displaced, its return is slow and rarely complete.

Water-damaged building exposure carries both mold and toxic bacteria together.¹⁷ *Aspergillus*, *Stachybotrys*, *Penicillium* produce mycotoxins. *Actinomyces*, certain pathogenic *Bacillus* species, and *Mycobacteria* produce endotoxins and exotoxins. These are ancient enemies. Mold and bacteria in the sinus enter active chemical combat — both sides escalating output, the patient caught in the crossfire of mycotoxins, the cribriform plate, exotoxins, and endotoxins.¹⁹

Bacteria under this attack form biofilms — defensive matrices that resist antibiotics, ordinary antimicrobials, and persist years after the patient has left the moldy environment.²¹ MARCoNS — multiple-antibiotic-resistant coagulase-negative staphylococcus — has been documented in sinuses of chronic mold patients.²⁰

The arrival of these organisms reverses the consortium's signaling through three mechanisms.

Tryptophan theft. Sinus inflammation activates IDO, shunting tryptophan from serotonin into the kynurenine pathway, terminating in quinolinic acid — an excitotoxin that crosses the cribriform plate and activates the amygdala.²¹

GABA blockade. Mycotoxins act as GABA receptor antagonists, removing the brake on amygdala activation at the receptor level.²²

Hormonal predation. Pathogenic *S. aureus* strains carry Hsd12, which may degrade testosterone and estradiol locally in nasal mucosa.†²³ This local hormone degradation is not detected by conventional serum testing — the destruction happens at the tissue level while circulating levels appear adequate. Practitioners running standard hormone panels miss it.

The patient is losing inhibitory signals and gaining excitatory and damaging ones while MSH and VIP are simultaneously suppressed. Chronic sinusitis is associated with

elevated rates of depression and anxiety.²⁴ Any patient with treatment-resistant psychiatric symptoms deserves a sinus workup.

Restoration

Two sinus sprays run in parallel from the start. They do different and synergistic work.

The first addresses the biofilm matrix that protects the toxic infections and binds to the fat soluble toxins, — mycotoxins, bacterial lipid toxins, retained inflammatory lipids — that ordinary water-based washes cannot solubilize.

Hydroxypropyl beta-cyclodextrin, N-acetylcysteine²⁵, magnesium di-potassium EDTA, and bicarbonates may address these issues. The cyclodextrins are molecular cages with hydrophobic interiors — they encapsulate fat-soluble compounds and may support their removal from sinus tissue. More on cyclodextrins in an upcoming chapter. NAC may support the dissolution of disulfide bonds in biofilm matrices, exposing what was hiding inside. EDTA may support localized chelation at the tissue interface. Bicarbonate fluffs the mucin layer and supports ciliary clearance.

The second sinus spray provides the postbiotics a healthy sinus microbiome would normally produce both to suppress intruders, as well as regulate the neuro-immune axis and mood.

The labyrinthine architecture of the sinuses means stubborn pockets can take time to fully clear. Patients with continuous re-exposure — those still living or working in water-damaged buildings — may prefer maintenance use.

After two weeks of using the first two sprays, or once the sinuses are clear, you can repopulate *Corynebacterium pseudodiphtheriticum*, *Dolosigranulum pigrum* and Commensal *Staphylococcus epidermidis*.

The mouth

The mouth has its own microbiome, and its own failure modes. Dead teeth, root canals, and cavitations can become focal infections — chronic, low-grade, often asymptomatic at the dental site itself. The problems they create appear elsewhere in the body, along predictable pathways mapped by the tooth meridian system (available at remedylink.com/charts). A dead upper bicuspid and a chronic lung problem. A failed root canal on a lower molar and a recurring gut or heart problem. The connections are not random.

If a patient developed a persistent problem after a root canal, extraction, cavitation, or tooth death, check whether the affected organ or tissue falls on the same meridian as the tooth. For cancer, the time delay is usually about five years.† A biological dentist — one trained in the systemic consequences of dental focal infections — may be required for evaluation and treatment.

Clinical pearl: A custom dental tray — or even an over-the-counter mouth guard — filled with hydrogen peroxide gel and worn for 15 minutes once or twice a day provides oxidative challenge to anaerobic organisms that accumulate along the gumline and in periodontal pockets, without disrupting the aerobic commensal population. Inexpensive, low-risk, and something the patient can do at home indefinitely.

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Chapter 31: The Sinus and Genital connection

The previous chapter established that the sinuses are the body's primary nitric oxide factory and that restoring sinus function can improve systemic NO. This chapter explains what NO deficiency costs.

The costs are not subtle. Nitric oxide relaxes vascular smooth muscle — without it, blood pressure rises.¹ It inhibits platelet activation, adhesion, and aggregation — without it, clotting risk increases and atherosclerotic plaque progresses.² It mediates bronchodilation — without it, airways constrict.³ It modulates immune surveillance — without it, pathogen clearance slows and wound healing slow down.⁴ It supports mitochondrial function — without it, energy production falls.⁵ Every one of these consequences is documented. Every one of them is downstream of the same molecule. And every one of them improves when NO is restored.

The practitioner managing hypertension, clotting risk, exercise intolerance, asthma, slow wound healing, or chronic fatigue may be managing five separate diagnoses that share a single upstream cause, compromised sinuses.

But NO deficiency has one consequence that most practitioners never discuss and that the patient can observe every morning without a lab draw.

Nocturnal penile tumescence

Every healthy male gets erections during sleep. Three to five per night, totaling ninety minutes to three hours, occurring during REM. The clinical term is nocturnal penile tumescence — NPT. It is not driven by arousal. The erection is not sexual. It is vascular maintenance.

The oxygenation is not about continuous flow. During erection, NO relaxes the trabecular smooth muscle, arterial inflow surges, the expanding sinusoids compress the subtunical venules against the tunica albuginea, and venous outflow is occluded. Blood is trapped — but it is arterial blood, fully oxygenated. The tissue soaks in it for the duration of each episode. In the flaccid state, oxygen tension in the cavernosum is closer to venous levels. The erection is the only time the tissue receives a full arterial oxygen load.

Each episode floods the corpus cavernosum with oxygenated blood. The flaccid penis exists in a low-oxygen state. Without periodic erections, oxygen tension in the cavernosal tissue drops, and two things happen. Nitric oxide synthase — the enzyme that produces NO locally — requires oxygen as a substrate. Low oxygen means less NO. And cavernosal hypoxia drives collagen synthesis. Smooth muscle is replaced by collagen. Elastic tissue becomes fibrotic tissue.⁶

The penis shrinks. This is structural, not functional. Smooth muscle cells undergo apoptosis. Collagen is deposited. Adipocytes accumulate in the subtunical region.⁷ The tissue becomes less distensible. Erect volume decreases. The loss is measurable.

The cycle is degenerative. Less NO means fewer erections. Fewer erections means less oxygenation. Less oxygenation means more fibrosis and further suppression of NO synthase. Which means even fewer erections. Each year without adequate NPT advances the remodeling.

The timeline

NPT is present from birth. Frequency peaks at 13-14 as the hypothalamic-pituitary-testicular axis matures.⁸ During puberty, total tumescence time per night runs about 159 minutes.⁹ Peak frequency and rigidity hold through the late twenties. Total tumescence time begins declining after 30. By 55, both maximum circumference change and rate of change are significantly reduced. The majority of men over 60 do not achieve full rigidity during sleep even when they report normal waking intercourse.¹⁰

The conventional framing attributes this to aging. The mechanism says otherwise. The decline after 30 correlates with falling androgens — testosterone modulates central arousal pathways and NO synthase expression. But the decline after 55 reflects organic changes in the corpus cavernosum and penile vascular system.¹¹ That is fibrosis. That is the accumulated consequence of decades of declining oxygenation cycles.

The practitioner who reaches for testosterone replacement in a patient with declining morning erections without assessing endothelial function may be working downstream.

What NPT measures

NPT is the only biomarker that simultaneously reads endothelial function, NO bioavailability, autonomic balance, sleep architecture, and hormonal status. It requires no lab, no device, no appointment.

Absent or declining NPT tells the practitioner that the endothelium is not producing adequate NO, or the autonomic nervous system is not releasing parasympathetic control during REM, or sleep architecture is disrupted, or testosterone has dropped below the permissive threshold. The penile arteries are smaller than coronary arteries. They show dysfunction first. Erectile dysfunction precedes cardiovascular events by an average of three to five years.¹²

The same physiology in women

The clitoris is not a small external structure. It is a substantial erectile organ — two crura extending along the pubic rami, two vestibular bulbs flanking the vaginal canal, and a

visible glans that represents a fraction of the total mass. The erectile tissue is homologous to the corpus cavernosum. It develops from the same embryological precursor. It engorges by the same mechanism: nitric oxide relaxes trabecular smooth muscle, arterial inflow increases, and the tissue fills with oxygenated blood.¹³

Women experience nocturnal genital engorgement during REM on the same schedule — three to five episodes per night, driven by the same parasympathetic outflow, independent of erotic content. Sleep lab studies using vaginal photoplethysmography have documented this since the 1970s.¹⁴ The clitoral crura engorge. The vestibular bulbs swell. Vaginal transudation increases. The entire vascular bed receives its arterial oxygen load.

The tissue-maintenance logic is identical. Clitoral erectile tissue is smooth muscle. Without periodic oxygenation, the same cascade applies: oxygen tension drops, NOS activity falls, TGF-beta1 drives collagen deposition, and smooth muscle is replaced by fibrotic tissue. The clinical consequence is well documented in another context — postmenopausal vulvovaginal atrophy. When estrogen declines, blood flow to genital tissue falls, and the result is thinning, loss of elasticity, dryness, and diminished sensation. The conventional framing treats this as hormonal. The mechanism is vascular. Estrogen supports NO synthase expression.¹⁵ Less estrogen means less NO. Less NO means less engorgement. Less engorgement means less oxygenation. The downstream tissue changes are the same ischemia-fibrosis pathway operating in the male cavernosum.†

The biomarker is less visually obvious but it is self-observable. Women who are paying attention notice the sensation of increased fullness or blood flow in the genital region on waking — their version of morning tumescence. When that sensation is absent or has faded over years, the same vascular and autonomic questions apply. Is NO production adequate? Is sinus function intact? Is sleep architecture preserved? Is the autonomic nervous system achieving parasympathetic dominance during REM?

The connection

Chronic low-grade endotoxemia — the first toxic output described in the Gram-negative chapter — impairs endothelial function systemically. The sinus chapter established that restoring sinus function restores systemic NO. This chapter establishes what that restoration accomplishes at the tissue level: it interrupts the ischemia-fibrosis cycle in both sexes. Erections return. Genital engorgement normalizes. Oxygenation cycles resume. Smooth muscle is maintained. The fibrotic remodeling slows or reverses — consistent with data showing that PDE5 inhibitors, which sustain the NO/cGMP signal, increase the smooth muscle-to-collagen ratio in aging cavernosal tissue.¹⁶

Clinical pearl: If asking about morning erections or morning genital sensation feels awkward in conversation, put it on the intake form. Patients who would hesitate to answer out loud may answer on paper. The data is too important to lose to discomfort.

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Chapter 32: Sleep Apnea - The Condition We Sleep Through

What apnea is

During an apnea event, the airway closes completely. Breathing stops. Oxygen saturation drops. The brain, registering the threat, triggers a sympathetic surge — heart rate spikes, blood pressure spikes, cortisol and catecholamines flood the system. The patient takes a few recovery breaths, drifts back toward sleep, and the cycle repeats. A patient with severe apnea goes through this cycle hundreds of times in a single night.

Hypopnea is the partial version — the airway narrows but does not fully close. Airflow is reduced, oxygen drops partially, and the brain responds with a lighter version of the same alarm. The distinction matters clinically because apnea and hypopnea produce different dream signatures, which becomes a diagnostic tool later in this chapter.†

The deep sleep bargain

The body faces a dilemma it cannot solve. As sleep deepens, muscle tone drops throughout the body — including the muscles that hold the airway open. The deeper the sleep, the more the throat relaxes, the more vulnerable the airway becomes. The body has two choices, and both are bad.

The first choice: prevent deep sleep from happening. The brain keeps sleep shallow enough that the airway muscles retain enough tone to stay open. The patient breathes adequately all night but never reaches the deep slow-wave and REM stages where tissue repair, growth hormone secretion, memory consolidation, and immune reconstitution occur. The patient sleeps eight hours and wakes exhausted, because the sleep that happened was not the sleep the body needed.

The second choice: allow deep sleep. The muscles relax fully, the airway collapses, oxygen drops, the brain fires a sympathetic alarm, the patient is yanked back to shallow sleep or waking, recovers, drifts deep again, collapses again, and cycles in and out of deep sleep all night — choking their way through the restorative stages in fragments too short to do their work. Again, the patient wakes exhausted.

Patients with apnea can alternate between both strategies across the night. The body oscillating between protecting the airway and protecting sleep depth, succeeding fully at neither. The result is a patient who is both oxygen-deprived and sleep-deprived simultaneously.

The mammalian hibernation reflex

The body interprets repeated overnight oxygen drops as a life-threatening situation. Mammalian biology has a response pattern for this — the hibernation reflex†, an ancient program designed to slow metabolism and conserve resources during periods

when oxygen availability is unreliable.¹ The reflex was useful when the threat was a long winter. It is not useful when the threat is the patient's own airway, repeating the same false signal every night for years.²

Testosterone drops in men^{3,4}. Thyroid output drops — reverse T3 rises, active T3 falls, the body deliberately slowing metabolism.⁵ Body fat accumulates and resists the patient's efforts to lose it. Libido reduces. Morning erections fail. Women develop severe PMS and menstrual cramping. Both sexes experience persistent fatigue that does not respond to rest, because the rest itself is being fragmented by events the patient is not aware of. Cognitive function dulls. Mood drops. Anxiety patterns establish around the chronic sympathetic activation. Cardiovascular risk rises substantially over years of untreated apnea^{6,7} — the repeated overnight blood pressure spikes are real cardiovascular events even though the patient is asleep through them.^{8,9,10,11,12}

A patient presenting with low testosterone, weight gain unresponsive to diet, fatigue, mood disturbance, and reduced libido is presenting with the classic downstream profile of untreated apnea. The conventional approach addresses each symptom separately — testosterone replacement, thyroid support, diet plans, antidepressants. None approaches the upstream cause. The apnea continues to fire its cycle every night, and the symptoms are regenerated faster than they can be addressed downstream.

The cascade is self-reinforcing. Weight gain narrows the airway, increasing apnea severity, increasing metabolic suppression, increasing weight gain.†

The moving goalposts

Conventional medicine measures apnea severity using the apnea-hypopnea index — the number of apnea or hypopnea events per hour of sleep. The AHI cutoffs for what counts as a clinical problem have drifted over the decades, and the drift has gone in one direction: the threshold for "normal" has been raised.

The current convention treats up to five events per hour as normal — meaning a patient who stops breathing four times per hour, every hour, for the entire night, is considered apnea-free by the standard scoring. Five to fifteen is mild, often considered subclinical. Fifteen to thirty is moderate. Above thirty is severe. A healthy patient has zero events per hour.† The body is not designed to stop breathing during sleep at any rate.

Three anatomical failure locations

The airway can fail at three locations, each with its own drivers and interventions.

The sinuses A patient whose sinuses are chronically inflamed, congested, or colonized by pathogenic organisms breathes through the mouth during sleep. Mouth breathing collapses the soft palate and narrows the pharyngeal airway — the mechanical prerequisite for obstruction.^{13,14} Beyond the mechanical effect, toxins and inflammatory

products draining from the sinuses into the throat cause or add to airway inflammation directly.

The tongue The genioglossus — the muscle that holds the tongue forward — can fail through age-related loss of tone or through innervation damage. Mold exposure deserves specific mention here. Mycotoxins reaching peripheral nerves disrupt the signaling that maintains airway tone, producing an apnea component that is downstream of neurological compromise rather than structural tissue. The tongue can also swell from inflammation or grow too large for the oral cavity from fat deposits.

The soft palate This structure vibrates against partially obstructed airflow, which is the sound of snoring. Snoring is not early-stage apnea, it is a location signal. A patient with tongue-driven or sinus-driven apnea may not snore at all. The absence of snoring does not rule out apnea.

A patient may have failure at one location, two, or all three simultaneously.

Four upstream causes

The gift of speech

The human larynx sits lower in the throat than the larynx of any other mammal — the anatomical accommodation that makes human speech possible. The trade-off is a more collapsible airway. Other mammals do not have apnea the way humans do. We pay for language with a baseline airway vulnerability that the other upstream causes amplify. This is the one we cannot fix.

Congenital deformity

Narrow palate, deviated septum, enlarged tonsils or adenoids, structural narrowing at any point. These patients may have had apnea since childhood without diagnosis. For some, palate expansion through dental orthotics widens the upper palate over time, expanding the nasal airway and improving upper airway geometry. The intervention is real and can be substantial for the right patient. It also has to be done correctly — an experienced practitioner is essential. Done wrong, it produces dental problems, jaw discomfort, or asymmetric expansion. The process moves teeth with some discomfort during the active phase.

Weak muscles

Age and innervation damage. Tongue exercises — protocols exist for strengthening the genioglossal muscle through targeted daily work — and electrical stimulation via TENS or EMS units applied to the relevant muscle groups can both support tone. But the first move is not muscle-strengthening. The first move is addressing inflammation. A patient exercising the genioglossus while inflammation continues to compromise the airway is

doing real work against an ongoing insult. Reduce the inflammation first. The order matters.

Inflammation

Inflammation in airway tissue — sinus, throat, palate — narrows the airway by adding swelling to whatever the baseline anatomy already is. Sources: mold and bacterial exposure, food sensitivities, alcohol close to bedtime, environmental irritants, chronic infection. This is the first move in nearly every apnea workup because it touches all three anatomical locations and because it overlaps substantially with the sinus restoration work of the previous chapter.

Dream analysis as your personal sleep lab

The diagnostic tool the practitioner has — given that the patient cannot witness their own apnea — is dream content. Dreams reflect the physiological state of the brain during sleep, and apnea events produce characteristic signatures.

Violent and suffocation dreams point to apnea.† A patient who reports recurring dreams of being attacked, fighting, drowning, being buried alive, or smothered is reporting the dream signature of frank apnea events.† The brain, registering the airway closure and oxygen drop, generates dream content matching the physiological reality.† The patient is in literal respiratory danger, and the dreaming mind produces imagery that reflects it.

Frustrating dreams point to hypopnea.† The patient who dreams of running, climbing, being stuck, searching for something that cannot be found, dialing a phone that will not connect — these are the dream signatures of partial airway compromise. The brain is registering effort without adequate result, and the dream content mirrors it.

Pounding heart on waking points to apnea — the sympathetic surge from an oxygen desaturation event that broke through to waking. Sweat-soaked sheets point to apnea — the sympathetic activation produces night sweats independent of hormonal status. Choking or gasping awakening is severe apnea breaking through. Waking unrefreshed after adequate sleep hours. Morning headaches from overnight CO₂ retention.

The wrong question is "how do you sleep?" The patient does not know. The right questions are about things the patient can answer — dream content, morning symptoms, daytime patterns. A patient who falls asleep while driving has a problem that transcends willpower.

The sinus connection

CPAP addresses the downstream obstruction. It does not address the upstream cause. Sinus restoration has reduced or eliminated apnea without CPAP in cases I have observed, by restoring nasal airflow and removing the mouth-breathing trigger.† The observation base is small but the mechanical logic is direct.

The practitioner evaluating a patient with fatigue, weight gain, low testosterone, and poor sleep should consider apnea early — and should evaluate the sinuses as part of the apnea workup. If the answer is sinus dysfunction, CPAP is a workaround, not a solution. CPAP also carries low compliance — many patients find it intolerable and abandon it. An upstream intervention that removes the need for the device is preferable to a downstream device the patient will not use.

Severe obstructive sleep apnea can drive oxygen saturation (SpO₂) down significantly. In clinical practice, desaturations into the **70s and 80s percent** are commonly seen during severe apnea events. This is an enormous amount of stress on the heart and brain that can be happening many times a night.

Clinical pearl: If the patient shares a bed with their partner, they may be able to confirm snoring or apnea.

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Chapter 33: The Order of Operations

Detoxification is a complex event. The framework taught here is a simplification, but it is a useful framework for clinical interventions.

The first steps of detoxification happen inside the cell. Phase 1 modifies the toxin molecule, exposing or adding a reactive chemical handle. Phase 2 attaches a water-soluble tag to that handle, usually glucuronic acid, glutathione, or sulfate. Phase 3 pumps the tagged molecule out of the cell through ATP-powered transporter proteins in the cell membrane. Liver hepatocytes also conjugate bile acids with glycine or taurine through a separate pathway that bypasses Phase 1 but shares the same Phase 3 exit.

What happens after the conjugated toxin exits the cell differs depending on whether it exits through bile or urine, and each route has its own failure modes. A more complete exposition on these later aspects will follow in subsequent chapters.

These phases must be operational in reverse order. Phase 3 before Phase 2. Phase 2 before Phase 1. Each phase creates a product that the next phase must handle, and if the next phase cannot handle it, the product accumulates inside the cell. The accumulation is often more dangerous than the original toxin.

Why Phase 3 must come first

Phase 3 is the exit door of the cell. The ABC transporter proteins, including P-glycoprotein and the MRP family, use ATP to pump conjugated toxins out of the cell. Without functional Phase 3, conjugated metabolites have no way to leave. They are water-soluble, bulky molecules that cannot passively diffuse back through the lipid membrane the way the original fat-soluble toxin entered.

This is well documented. Reduced P-glycoprotein expression in the brain has been directly linked to Alzheimer's disease.¹ In the gut, impaired P-glycoprotein function is associated with inflammatory bowel disease.² When MRP1 function is inhibited experimentally, intracellular glutathione export fails and toxic substrates build up inside the cell.³

Phase 3 is the only phase with a direct per-molecule energy cost. Phase 1 and Phase 2 are enzymatic reactions driven by electron donors and conjugation substrates. Phase 3 physically pumps molecules against a concentration gradient. Every molecule it moves costs one unit of ATP. When cellular ATP production is compromised, Phase 3 is the first detoxification phase to fail.

It is important to at least estimate the patient's status of their Phase 3 pumps before increasing Phase 1 and 2.† A practical screening indicator for cellular ATP status is serum CO₂ on a standard metabolic panel.† CO₂ is a byproduct of the Krebs cycle, the same cycle that generates the electron carriers driving mitochondrial ATP synthesis. When mitochondrial output drops, CO₂ production drops with it. A serum CO₂ below 27

suggests underperforming mitochondria.† This is not a precise laboratory measurement of ATP, but it is a clinically useful signal that a practitioner can read off a basic blood panel.

Why Phase 2 must come before Phase 1

Phase 1 enzymes, primarily the cytochrome P450 family, convert a stable toxin into a reactive intermediate that is often more toxic than the parent compound.⁴ This intermediate now has a chemical handle that Phase 2 can grab to attach the conjugation tag. But if Phase 2 cannot keep pace, those electrophilic intermediates accumulate and attack DNA, cell membranes, and proteins. This can drive multiple chemical sensitivities (MCS).†

The body is designed to prevent this. The aryl hydrocarbon receptor, which activates many Phase 1 enzymes, also activates the Nrf2 pathway, which upregulates Phase 2.^{5,8} The system is meant to run as a coordinated unit. But coordination fails when Phase 2 substrates are depleted. Glucuronic acid, glutathione, and sulfate are all consumed by the conjugation reaction.^{6, 7} Under heavy toxic load, the cell runs out of conjugation substrate before it runs out of Phase 1 capacity and the cell fills with more reactive toxins than it started with and these can be genotoxic.

Phase 2 failure also disables Phase 3 indirectly. The MRP transporters strongly prefer conjugated substrates, particularly glutathione conjugates and glucuronide conjugates. They have limited ability to recognize and move the unconjugated intermediates that Phase 1 produces. So when Phase 2 fails, Phase 3 sits idle even if its transporters are intact, because the cargo is in the wrong format. Phase 2 is the gatekeeper between activation and efflux. Its failure creates both problems at once: reactive intermediates accumulating upstream, and export capacity going unused downstream.

Bile acid conjugation: a parallel system using the same exit door

The liver performs another conjugation that is not part of Phase 1 or Phase 2 but shares the same dependence on Phase 3 transport. Before bile acids are secreted into bile, hepatocytes conjugate them with the amino acids glycine or taurine. This conjugation does not require Phase 1 activation. The bile acid is synthesized from cholesterol inside the hepatocyte, conjugated by the enzyme bile acid-CoA:amino acid N-acyltransferase, and then pumped out of the cell by the bile salt export pump, an ABC transporter in the same family as the Phase 3 pumps. Bile acid conjugation makes the bile acid more water-soluble and less toxic to the cells lining the biliary tract.

Intracellular toxification

When Phase 1 outruns Phase 2 and Phase 2 outruns Phase 3, the cell accumulates two categories of toxic material simultaneously. Reactive intermediates that were never

conjugated are attacking internal structures. Conjugated metabolites that were successfully tagged have no exit and are consuming space and resources. The cell is being poisoned by its own detoxification machinery.

Persistent toxins are the clearest example of this pattern. Dioxins, PCBs, DDT, and mycotoxins actively overdrive Phase 1 through the aryl hydrocarbon receptor while suppressing Phases 2 and 3.⁵ The toxin genetically reprograms the detoxification machinery to favor the one phase that generates dangerous intermediates while shutting down the two phases that would eliminate them. The toxin creates the imbalance that prevents its own removal.

The two prerequisites for chemical detox

Metal toxicity is a common reason for compromised mitochondrial ATP production in these patient populations. Mercury, lead, cadmium, arsenic, and gadolinium displace iron-sulfur clusters in the electron transport chain, bind thiol groups on the enzymes of Complexes I through IV, and uncouple oxidative phosphorylation so that mitochondria consume oxygen without producing proportional ATP.^{9,10} The downstream consequence is predictable: low ATP disables Phase 3 transporters and disabled Phase 3 traps conjugated and unconjugated toxins inside cells.

The second prerequisite operates at the gut level. Phase 2 conjugation attaches a tag to a toxin -- glucuronide, sulfate, or glutathione -- and the liver excretes it into bile for intestinal elimination. But dysbiotic gut bacteria produce enzymes that cleave these tags: beta-glucuronidase strips glucuronide conjugates, sulfatases strip sulfate conjugates, and peptidases and transpeptidases dismantle glutathione conjugates.¹¹ The toxin reverts to its fat-soluble form, is reabsorbed through the intestinal wall, and returns to the liver via the portal circulation. This is enterohepatic recirculation. The body did all the work of Phase 1 activation, Phase 2 conjugation, and biliary excretion, only to have a gut bacterium undo the Phase 2 conjugation stage and send the toxin back to the liver for conjugation again. Each pass consumes conjugation substrates and can generate another round of reactive intermediates. The same problem extends beyond Phase 2. Bacterial bile salt hydrolases deconjugate the glycine and taurine tags the liver attached to bile acids, undoing that conjugation as well.

Bacteria do all this for their own metabolic benefit. Some use the released conjugant as a nutrient source. Others use it in their energy metabolism. Others deconjugate bile compounds as a form of self-protection. The reason varies, but the result is the same: the conjugation work gets undone and the patient becomes more toxic while losing energy to feeding the bacteria.

Intracellular metal detoxification improves mitochondrial ATP, which can often be seen as a rise in CO₂ in bloodwork. Improved ATP improves Phase 3. Outside the cell in the gut, microbiome management reduces bacterial deconjugation activity, which prevents toxic bacteria from undoing the liver's conjugation work. Both should be in place before

chemical detoxification begins. Phase 3 capacity must be equal to or greater than Phase 2 output, and Phase 2 capacity must be equal to or greater than Phase 1 output. The practitioner who understands this will never start a detox protocol with Phase 1 stimulation.

Why the microbiome comes first in practice

The biochemical logic argues for metals first. Metal burden suppresses the mitochondrial energy production that Phase 3 depends on, and without Phase 3, nothing downstream works. But the clinical reality argues for beginning with the microbiome.

Microbiome restoration produces visible results quickly. A patient watching their stool pH drop from 7.5 to 6.2 over two to three weeks and whose digestion improves has evidence the work is real. That early win builds the trust and buy-in that carries the patient through what may be months of chelation, which produces less visible feedback and requires more patience from everyone involved.

The microbiome work also establishes one of the two prerequisites for chemical detox while the metals work establishes the other. By the time chelation has sufficiently restored mitochondrial ATP production, the gut is already prepared. The patient does not face a second waiting period before chemical detox can begin. The two prerequisites were built in parallel, with the faster one started first.

Clinical pearl. Always stagger multiple protocols by a few days. Let any immediate improvements or discomforts show up before adding a second set of variables confounds the picture and complicates your diagnostics.

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Chapter 34: Lymphatics — The forgotten circulation

Before we get to the teachings that will start mobilizing chelated metals and conjugated chemicals, we must also address the body's drainage system — the lymphatic circulation. The body has two circulatory systems. The one most people know about has a pump. The heart moves blood through arteries and veins in a continuous loop, and that loop runs whether you are sprinting or sleeping. The second system has no pump. The lymphatic system carries waste, dead cells, immune complexes, metabolic byproducts, and toxins conjugated for removal, and it moves only when the body moves. This creates a problem that most detoxification protocols ignore entirely.

A practitioner can design the right protocol. The patient can take the right products at the right doses in the right sequence. The mobilization chemistry can be working exactly as intended. But if the transport system that carries mobilized material from tissue to exit is static, the material has nowhere to go. It sits. It recirculates. It deposits somewhere else. The patient feels worse, the practitioner adjusts the protocol, and neither one identifies the actual bottleneck, which is not chemical but mechanical.

The lymphatic system depends on skeletal muscle contraction against lymphatic vessels, respiratory pressure changes from breathing, and the one-way valves inside lymphatic vessels that prevent backflow. Without regular muscle contraction, lymphatic fluid accumulates. Proteins that should have been cleared remain in the interstitial space. Immune cells that finished their work sit in nodes that become congested rather than active. The system designed to remove what does not belong begins to hold what does not belong.

What does lymphatic congestion look like in a patient? Puffiness, especially in the morning, that improves with movement. Fluid retention that does not fully respond to dietary changes. Stiffness on waking that loosens within the first hour of activity. Chronic sinus congestion that does not resolve with antimicrobials. Symptoms that reliably improve with exercise and reliably return with sedentary periods. Tender or swollen lymph nodes that persist without acute infection. A general heaviness that lifts when the patient is physically active and settles back when they stop.

The storage battery

The connective tissue that surrounds every organ, fills the spaces between cells, and forms the structural matrix of the body is not inert scaffolding. It is a reservoir.^{1,2} The extracellular matrix and the interstitial fluid it holds function as a storage and exchange medium³ for nutrients, signaling molecules, and waste products. Think of it as a storage battery. When conditions are right, this battery holds nutrients. Minerals, amino acids, signaling molecules, and growth factors are stored in the matrix and drawn upon by cells as needed. The connective tissue functions as a second liver in this sense, a distributed storage organ that buffers the body's supply lines.

But a battery that can hold nutrients can also hold toxins. When lymphatic flow through the connective tissue is adequate, the interstitial fluid turns over. Waste products are flushed into the lymphatic system and carried away. Nutrients are delivered, used, and replenished in a continuous cycle. The storage capacity of the matrix stays available for what the body needs.

When lymphatic flow stagnates, the flushing stops. Toxins that should have been cleared remain in the matrix.⁴ Heavy metals, chemical metabolites, inflammatory byproducts, and cellular debris accumulate in the same tissue that is supposed to be storing nutrients. As the toxin load in the connective tissue rises, the storage capacity available for nutrients falls. The storage battery is full of the wrong thing, toxin rather than nutrients.

This means that lymphatic stagnation does not just slow the removal of waste. It actively degrades the body's nutrient reserves. A patient with chronically stagnant lymphatics may show signs of nutrient insufficiency even with adequate intake and supplementation, because the storage medium that should be holding and delivering those nutrients is occupied by what was not flushed out. Restoring lymphatic flow does two things at once. It clears the toxin burden from the connective tissue, and it restores the storage capacity that allows nutrients to be held and used properly.

The lost sleep

Before the electric lightbulb, most people in temperate climates did not sleep the way we sleep now. The dominant pattern was segmented sleep. People went to bed when it got dark, slept for roughly four hours, woke for one to two hours, then slept again until morning. During the waking interval they got up, tended fires, prayed, talked, did small tasks, checked on animals, visited neighbors. Then they went back to sleep.

This pattern is documented extensively in pre-industrial European records. It was so ordinary that it had its own vocabulary. First sleep and second sleep were common terms.⁵

What this meant for the lymphatic system is something nobody talks about. A person sleeping in two segments was never horizontal and immobile for more than four hours at a stretch. The waking period in between involved getting up, moving, walking, standing. The lymphatic system got a mid-night pumping cycle built into the structure of sleep itself.

Consolidated eight-hour sleep is a product of artificial lighting. Once people could cheaply illuminate their evenings, they stayed up later and compressed their sleep into a single block. That single block is the longest period of lymphatic stasis in a modern person's day. For someone who also sits at a desk for eight or ten hours, the lymphatic system may be effectively static for the majority of every twenty-four-hour cycle.

The patient did not create this problem. The structure of modern life created it. Artificial lighting eliminated segmented sleep. Sedentary work eliminated daytime movement. The lymphatic system that evolved to be pumped by a body that walked, lifted, climbed, squatted, and woke in the night now sits in a body that barely moves.

Putting the pump back

The first intervention is movement. Nothing else discussed in this chapter matters if the patient is not moving.

This does not require a gym membership or an exercise program. For the patient who sits at a desk all day, an under-desk pedal device changes the equation. The legs are contracting against lymphatic vessels for hours instead of being static for hours. It is the lowest-effort, highest-yield change a sedentary patient can make because it runs in the background while they work.

For the patient who cannot exercise conventionally, a mini trampoline provides lymphatic pumping through vertical oscillation. The repeated small bounce loads and unloads lymphatic valves throughout the body. It requires two to five minutes, it can be done in a living room.

Sequential compression devices that mechanically inflate and deflate around the limbs in a wave pattern are highly effective.⁶ These are the pneumatic sleeves used in clinical and post-surgical settings to prevent blood clots, but their effect on lymphatic flow is equally significant. The segmental compression milks lymph through the vessels in the direction of flow, doing mechanically what muscle contraction does physiologically. Home units are available and are particularly useful for patients who are immobile, post-surgical, or too deconditioned for even minimal exercise.

Local congestion

Systemic movement solves the systemic problem. But regional lymphatic centers can become local bottlenecks even in a patient who exercises regularly. The cervical nodes draining the sinuses, the axillary nodes, the inguinal nodes, the mesenteric nodes serving the gut. When a regional lymphatic problem is sustaining a clinical picture, systemic movement alone will not resolve it.

Cupping over lymphatic regions provides direct mechanical mobilization. The vacuum effect pulls fluid toward the surface, decompresses the tissue, and physically moves lymph through nodes that have become static. This is not a new idea. Cupping traditions across multiple cultures have been applied over lymph node regions for centuries.

A note on cancer. The question of whether mechanical lymphatic mobilization can promote metastatic spread has been debated extensively. The current clinical evidence

does not support the claim that gentle lymphatic drainage spreads cancer.⁷ Studies of manual lymphatic drainage in breast cancer patients have not shown increased recurrence rates, and oncology centers routinely use lymphatic drainage therapy for cancer-related lymphedema. However, direct vigorous mechanical pressure on a known tumor is a different matter. Animal studies have demonstrated increased tumor cell fragments in lymphatic vessels when heavy pressure is applied directly to tumor tissue. The prudent clinical position is this: gentle systemic lymphatic support is not contraindicated in cancer patients, but aggressive mechanical manipulation directly over a known tumor site should be avoided. The practitioner should know the difference between mobilizing the lymphatic system and compressing a tumor.

Ultraviolet A light, applied to the skin during cupping, adds a second dimension. UVA reaches the papillary dermis where capillary blood is being drawn toward the surface by suction. At specific wavelengths it has documented local immunomodulatory effects, suppressing overactive local immune responses and promoting regulatory immune activity.⁸ When regional lymphatic congestion is being sustained not just by physical stasis but by a local immune response that has become self-perpetuating, the combination of mechanical mobilization and local UV immunomodulation can break the cycle from both directions at once.

A device combining both cupping and UVA is available at our website.

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Chapter 35: Nature uses relay races, so should we

Early humans had exposure to metals, the mineral content of water, the metals in soil and plants and animal tissue — all of this was part of the diet biology evolved alongside, and the body has dedicated handling systems for small amounts of them. What has changed in the modern environment is the amounts. The body's regulatory systems for iron, copper, zinc, manganese, magnesium and the others were calibrated for the small natural quantities.¹ Industrial activity has pushed exposure to those metals well past what the calibration can handle.

Some chemical detox pathways handle both metals and chemicals — glutathione is the obvious example, since it conjugates many chemical electrophiles and also binds soft metals through its sulfur² — but the same pathway is rarely equally good at both. When one pathway gets exhausted by heavy load of one type, capacity for the other type drops along with it. A patient saturating their glutathione system on chronic chemical exposure has less glutathione available to bind incoming mercury, which means more of the mercury reaches storage rather than being escorted out. The same patient with a heavy mercury burden has less glutathione available for chemical conjugation, which means more chemical exposure reaches the activation step without adequate downstream conjugation, producing the multiple-chemical-sensitivity pattern the previous arc described.

What makes metals categorically different

Metals persist

Many synthetic chemicals can be broken down by Phase I enzymes, conjugated by Phase II enzymes, and the original molecule no longer exists in the form it entered the body. The patient's burden goes down by one molecule for each successful pass through the chain.

Metals persist as elements. While the body can modify metals (they can be oxidized, reduced, methylated, demethylated, and bound to organic carriers), what no modification does is destroy the metal. Iron in either valence state is still iron. Mercury bound to glutathione is still mercury. The atom persists through every transformation. And some modifications make the metal more toxic, not less — oxidized iron (Fe^{3+}) is more catalytically dangerous than reduced iron (Fe^{2+}), which is one of the reasons free iron in tissue is so destructive.³ The body can shuffle metals between forms, between carriers, and between compartments, but the only way to reduce the patient's metal burden is to escort the metal out of the body intact or render it inert, crystallizing it in the tissue, but this has unknown long term effects.

The body has native mechanisms for this movement. Metallothionein sequesters soft metals. Glutathione conjugates mercury and moves it into bile.² Ferritin cages iron.⁴ The

kidney excretes some metal complexes at baseline. Hair, nails, sweat, and breast milk are all excretion routes for certain metals.⁵ But these native systems are slow, limited in capacity, and easily overwhelmed — they sequester and manage metals more than they eliminate them. A patient whose exposure exceeds the capacity of those native systems accumulates a burden that the body cannot clear on its own timeline. Chelation accelerates and extends what the body can do natively, moving quantities that the native systems cannot handle at the pace the clinical situation requires.⁶

Metals are catalytic

A metal atom does its damage and is not consumed. Mercury catalyzes the formation of free radicals.⁷ It does this again and again. One atom of mercury can catalyze thousands of oxidative events over its residence time in the body. The same atom keeps catalyzing the same destructive chemistry indefinitely, until it is bound by something that holds it tightly enough to stop the catalysis. One milligram of free mercury sitting in tissue will go on producing damage for as long as it stays unbound there. The damage is not a one-time event. It is a low-level continuous process whose rate is set by how much metal is present and where it is sitting.

Metals enable body-temperature reactions that should not be possible. The body's chemistry is calibrated to its native temperature. The reactions that should happen at that temperature, happen; the reactions that should not happen at that temperature, do not happen, because the activation energy is too high for the molecules involved to find each other and react. Metals are catalysts that lower activation energy.⁸ Metals make certain reactions accessible at body temperature that would otherwise require heat, pH and or pressures the body does not have. Some of those reactions are useful — this is why the body uses essential metals as enzyme cofactors. Reactions the body wants to run, run on essential metals at controlled doses in controlled positions. Reactions the body does not want to run, run anyway when toxic metals occupy the wrong positions or when essential metals end up in the wrong concentrations.

This makes metals are disproportionate per mass and is why metal poisoning produces severe disease at exposures that would be inconsequential for most chemicals.⁷ The mass is not the right unit for measuring the burden. The catalytic load is.

Structural damage from metals persists after the metal is removed. When a metal is cleared, the patient's chemistry returns toward normal in the metal's ongoing role — the catalytic damage stops, the displaced enzymes can repopulate with their native cofactors, the Fenton chemistry quiets — but the structural damage the metal produced does not undo itself. Demyelination does not spontaneously remyelinate just because the mercury that drove the demyelination is gone. Oxidized membranes do not spontaneously reduce. Denatured proteins do not automatically refold.⁹

Where metals are in the body

The frame of "metal storage" undersells where metals actually sit in a chronically exposed patient. Yes, some of the metal burden is in long-term storage — bone for hard

metals like lead and aluminum, fat tissue and the lipid-rich brain compartment for soft metals like mercury and cadmium. But a fraction of the metal a patient is carrying is not in storage at all. It is bound to plasma proteins and circulating in blood. It is occupying transporter molecules in cell membranes. It is sitting in enzyme active sites where the enzyme thinks it has the right cofactor but in fact has a toxic substitute. It is in the extracellular fluid throughout the body. It is in active metabolic positions, often displacing the essential metal that should have been there.¹⁰

The chelation protocol is not just unloading bone and fat. It is also stripping toxic metals off plasma proteins, displacing them from transporters and enzyme sites, and pulling them out of the extracellular spaces where they have accumulated. Each of these requires a chelator that can reach the location and bind the metal more tightly than whatever is currently holding it.

Storage compartments deserve their own attention because they are the slowest part of the burden to clear. Bone is the long-term reservoir that practitioners most often underestimate. Lead in particular partitions into bone over years of exposure and stays there for decades.¹¹ The bone turnover that releases stored lead back into circulation is slow — it happens steadily through life as bone remodels, faster during periods of active bone metabolism like pregnancy, lactation, menopause, and immobilization-related bone loss; slower otherwise.¹² A patient with significant historical lead exposure will continue to release lead from bone into blood for the rest of their life, regardless of whether the original exposure source is still present. The blood-lead level a clinician measures captures the current circulating fraction; the bone-lead store the patient is sitting on does not show up on the same test.

Fat tissue serves the same role for soft metals and for fat-soluble organomercurials. Mercury that has been in the body for years has had time to partition into adipose tissue and into the lipid-rich brain compartment.¹³ Like bone-stored lead, fat-stored mercury releases slowly back into circulation as fat tissue turns over, with the rate accelerating during weight loss, fasting, and any other process that mobilizes fat stores faster than baseline.

Connective tissue is also a storage site that is often overlooked. While fat is a calorie storage depot, connective tissue can store both nutrients and toxins, and the more toxins it holds, the less nutrients it can store for us.

The protocol that clears the circulating fraction without staying the course and also working through the storage fraction will produce rapid initial improvement followed by gradual return of symptoms over months as the storage compartment refills the blood compartment. The work is not finished when the blood normalizes. The work is finished when the storage compartments have been substantially worked through and the blood is staying clean without continuing intervention.

Testing and its limits

Blood metals testing captures what is in active circulation — recent exposure, mobilization in progress, the fraction the body is actively trying to move.¹⁴ It does not capture what is in storage. A patient with a lifetime of lead accumulation may have a normal blood lead level and a substantial bone burden simultaneously. The blood test is doing what the blood test does; it is not designed to measure storage compartments.

Urine challenge testing, the practice of administering a chelator and then measuring metals in the urine that follows, has its own limitations. Most labs challenge with a single chelator — typically a soft-metal chelator like DMSA, or EDTA, a hard/borderline metal chelator. DMSA will underreport hard metals and EDTA will underreport soft metals.¹⁵ This produces an imbalanced reading that can lead the practitioner to chase one metal class while missing another. Optimally you combine them.

Another issue is that the lab reports total metal output, but it cannot distinguish between metals the chelator successfully bound and is excreting (the desired clinical outcome) and metals that were mobilized from storage but redistributed rather than being captured (an iatrogenic outcome). The same urine test result can have either meaning, and the lab cannot tell which it is. Comparing a provoked result to a non-provoked reference range — which some labs encourage — may overstate the burden.¹⁶

The most stable chelators — the macrocyclic class described later in this chapter — may not be fully detected by standard lab assays, because the very stability that makes them clinically valuable obscures the chelated complex from the detection method. This is a potential issue with adding a stable terminal chelator to a diagnostic challenge in an attempt to make the challenge "safer" — doing so confounds the test in ways the lab will not flag and may produce false-negative readings on metals that are actually present.

Hair testing has a specific gap. Hair detects organic mercury (methylmercury, the form found in seafood) and inorganic mercury salts. It does not reliably detect elemental mercury vapor — the form most commonly released from amalgam fillings and from some occupational exposures.¹⁷ A patient with a substantial elemental mercury burden from amalgams or occupational vapor exposure can show a clean hair test and still be carrying significant mercury.

ICP-MS panels for heavy metals report individual elements. But f-block elements — lanthanides and actinides — are typically batched together by the lab and reported as uranium.¹⁸ Gadolinium from retained MRI contrast, cerium from industrial catalysts or cigarette lighter flints, lanthanum and neodymium from supplements or occupational exposure — all of it lands in the uranium column. The practitioner sees elevated uranium and assumes the patient's well water is contaminated. The actual burden may be gadolinium from a prior MRI with contrast, which requires a different chelation approach entirely. This is a real and underappreciated source of misdiagnosis in heavy metal testing, and the practitioner who does not ask about prior MRI history when seeing elevated uranium on a panel is working from a false premise.

Gadolinium retention specifically deserves attention. Gadolinium-based contrast agents were long considered safe and fully excreted. Evidence now shows retention in brain, bone, and skin tissue, particularly after repeated administrations and particularly with linear (non-macrocyclic) agents.¹⁹ Patients presenting with symptoms after MRI with contrast — pain, cognitive changes, skin changes — may have legitimate gadolinium retention.²⁰ Chelation with DTPA has been used in case reports, though no standardized protocol exists.²¹

Testing is data, but understand the limits of each test.

Nature, when it has to move something challenging from one place to another, often uses relay races. Hand-offs between specialists, each adapted to one stage of the journey, with the next runner ready before the previous one lets go. This is how the body moves oxygen from lungs to mitochondria. It is how the immune system passes a pathogen from innate first responders to adaptive specialists. It is how electrons move through the respiratory chain. And it is especially true for metals — iron is the marquee example. Dietary iron is taken up by enterocytes, handed to ferroportin for export across the basolateral membrane, handed to transferrin in plasma, transferred to transferrin receptors at target cells, escorted to ferritin for storage, and released by ferritin to whatever enzyme needs the iron at the moment it needs it.⁶ Five distinct carriers. Each one binds iron more or less tightly than the others, and the iron moves toward whichever carrier holds it appropriately for the next stage of the journey. The body tries to never let iron travel as a free ion. It hands the iron from carrier to carrier the entire way, because a free iron ion in tissue is catalytically destructive, and free transit is exactly what the relay structure is designed to prevent. The body's own metal handling is the model that a good chelation protocol should imitate. The protocols that fail almost always fail because they tried to make a single chelator do all the legs of the race.

The relay race

Chelation protocols should be designed as a relay race with 3 kinds of runners.† The runners in the race all do the same job - solubilizes the metal by binding it into a complex the body can carry. Where the tiers differ is in the speed and stability of that solubilization, and in the size of the spaces the chelator can reach.

Tier 1 chelators are small molecules with one or two donor groups capable of binding a metal ion. Citrate, and malate for those with histamine issues, are good examples of a hard-metal Tier 1 chelators — they carry carboxylate groups that bind hard metal cations and can dissolve the crystalline mineral deposits where hard metals are sequestered, displace hard metals from binding pockets in proteins, and reach into small spaces a larger chelator cannot enter.

Alpha-lipoic acid would be considered a soft-metal Tier 1 chelator— it carries two sulfhydryl groups close enough together to grip a soft metal atom from both sides, and it is fat-soluble enough to reach into lipid compartments.²²

Tier 1 chelators solubilize quickly and they reach the smallest spaces. The tradeoff is that the same low molecular weight that lets them reach into small spaces also gives them low binding affinity. They form complexes quickly, and they release them quickly. For this reason, Tier 1 chelators are never used alone. Used alone, they solubilize a metal at one location and then release it again somewhere else, depositing the metal in a new location instead of escorting it out. They are used inside a relay where more stable chelators are present to receive what the Tier 1 hands off.

Tier 2 chelators are larger molecules — multiple donor groups linked together in a linear or branched backbone. Each Tier 2 can be understood as a chain or net of Tier 1s, with the multiple donors gripping the metal from multiple angles at once. This makes Tier 2 chelators more stable than Tier 1 chelators, while their flexible backbone still lets them adapt to metals of varying ion sizes. EDTA is an example of a Tier 2 hard-metal chelator²³ and MiaDMSA is an example of a Tier 2 soft-metal chelator²⁴.

Tier 3 chelators are macrocyclic — four or more donor groups closed into a rigid ring with the metal trapped at the center. DOTA is the canonical Tier 3.²⁵ DOTA's rigid ring geometry makes it slow at both binding and releasing — once a metal is inside the DOTA cage, it stays there. This is what makes Tier 3 the most stable form of solubilization in the relay. The same property that makes DOTA slow to release also makes it slow to bind: it does not reach into small spaces the way Tier 1 does, and it does not have the same geometric flexibility that Tier 2 does, making it unsuitable for certain very large atoms. Methyl DOTA is the same macrocycle modified for fat solubility — methyl groups added to the structure let the molecule cross cell membranes, where it then demethylates back to the active DOTA form intracellularly.†

How the relay actually works

The donor-chemistry axis follows what chemistry calls the HSAB principle — Hard-Soft Acid-Base theory.²⁶ See chart at remedylink.com/charts. Hard metals prefer hard donors: carboxylate groups (COOH), oxygen-based coordination. Soft metals prefer soft donors: thiol groups (SH), sulfur-based coordination. Borderline metals — lead is the most clinically important — respond to both, and nitrogen donors (NH₂, amine groups) sit in the borderline category, appearing in the backbone of EDTA, DTPA, and the macrocyclic chelators where they contribute binding strength without determining hard-soft selectivity on their own. Getting the match wrong means the chelator reaches the metal but cannot bind it effectively, or binds it weakly enough that the metal is mobilized but not captured — the worst possible outcome.

This explains the successes of EDTA²⁷. It can bind to hard, soft metals and borderline metals, and as a Tier 2 chelator, it shares some aspects of Tier 1 and Tier 3. It is a good all purpose general chelator, but we can do better by incorporating it in a relay protocol.

The relay works through affinity gradients. When a Tier 1 chelator carrying a metal encounters a Tier 2 chelator, the metal preferentially transfers to the Tier 2, because the

Tier 2 binds it more tightly. When a Tier 2 carrying a metal encounters a Tier 3, the metal preferentially transfers again. While a Tier 3 chelate and its metal can disassociate, it is the least likely to of all chelator Tiers to do this.

Every tier used alone has a cost. A Tier 1 chelator alone solubilizes metal but is prone to releasing it somewhere along the route to excretion — redistribution, not removal. A Tier 2 alone carries the same risk at a lower rate. A Tier 3 alone is the safest single agent — it rarely drops its cargo when urine is properly alkalized (more on this later) — but it is unnecessarily slow and cannot access metals locked in crystalline deposits or small binding pockets that only the smaller chelators can penetrate. The full relay is what gets the metal out from where it actually is, at a pace that matters clinically, with minimal redistribution.†

A patient with mixed metal burden — most patients, in practice — needs both donor chemistries represented in the protocol. The hard side of the relay is Tier 1a citrate or malate salt, Tier 2 EDTA, Tier 3 DOTA. The soft side of the relay would be Tier 1b alpha-lipoic acid, Tier 2 MiaDMSA — DOTA also serves as the Tier 3 chelator for most soft metals. Despite its O/N donor chemistry, DOTA's macrocyclic cage geometry produces stability constants with soft metals (Hg log K = 26.4) that exceed those of sulfur-donor chelators (DMSA Hg log K = 16.5). The textbook prediction that soft metals require soft donors is overridden by the macrocyclic stability advantage. The exception is arsenic, where MiaDMSA (log K = 19.5) is the strongest available holder and functions as the de facto Tier 3.

Compounds like emeramide have been proposed as soft-metal terminal chelators. According to the inventors, Emeramide renders mercury inert due to its very high stability constant. According to the inventors, Emeramide renders mercury inert due to its very high stability constant. This means that Emeramide isn't a chelator, but a precipitator. The bound metal is not soluble. It is instead rendered inert and remains in the body. Insoluble particulate matter in tissue is recognized by the innate immune system as foreign. Macrophages attempt phagocytosis. If the particle is too large or too insoluble to digest, you get frustrated phagocytosis — chronic inflammatory signaling, NF-κB activation, cytokine release, potentially fibrosis. This is the mechanism behind asbestosis, silicosis, and gout (urate crystals). Metal precipitates are conceptually in the same category — indigestible crystalline particles in soft tissue. This is not a criticism of Emeramide, but more an open question regarding Precipitators versus Chelators.

A clinical observation confirmed by the stability data: in practice, DOTA, the macrocyclic Tier 3 chelator, has served as a useful rescue when a soft-metal protocol produced unexpected reactions. The stability constants explain why — DOTA binds mercury at log K 26.4, substantially higher than DMSA's 16.5. The macrocyclic cage geometry overrides the donor-chemistry mismatch that textbook HSAB would predict. DOTA is not merely rescuing — it is the stronger holder.

Counterions

A chelator can only bind a target with stronger affinity than the counterion it arrived with. If the counterion is held loosely, the chelator drops it readily and binds the toxic metal. If the counterion is held tightly, the chelator may not let go of the counterion in time to bind the target, and it passes through the patient without doing the work it was sent to do.

For EDTA, the counterions the author prefers are magnesium and potassium. Magnesium-and-potassium-bonded EDTA releases its counterions readily because EDTA binds toxic metals more tightly than it binds magnesium or potassium. This produces several useful things at once. The EDTA becomes available to bind the metal it was sent for. The released magnesium and potassium contribute to mineral status in a patient population that is broadly deficient in both. And the magnesium released into circulation slightly increases the solubility of the crystalline mineral deposits where hard metals are stored, which makes those deposits incrementally more accessible to the relay's smaller runners. Calcium-bonded EDTA holds calcium more tightly, which makes the EDTA less available, but more importantly, means the EDTA cannot bind to more calcium. The removal of dystrophic calcium deposits, especially from the arteries, is one of the many benefits of EDTA chelation, but this only happens with a calcium free EDTA.

Delivery routes

Oral delivery works for some chelators and fails for others. Citrate and malate absorb orally and reach hard-metal compartments. Alpha-lipoic acid absorbs orally and reaches lipid compartments. EDTA absorbs poorly when taken orally — roughly 5-18% bioavailability²⁸ — which is why oral EDTA products produce limited clinical effect. Most of an oral EDTA dose chelates metals in the gut lumen, which can be useful for dietary metal exposure and enterohepatic recirculation of biliary metal, but never reaches systemic circulation.

The delivery routes that work for poorly-absorbed substances are intravenous, suppository, and liposomal. Intravenous delivery puts the chelator directly into plasma at full dose but requires clinical infrastructure. Suppository delivery routes the chelator through rectal veins into systemic circulation, bypassing both stomach acid and intestinal absorption.²⁹ Liposomal delivery encapsulates the substance in phospholipid vesicles — useful for substances that survive digestion intact but absorb poorly across the intestinal wall, which is EDTA's specific limitation. Recent clinical practice has moved toward liposomal EDTA as a primary delivery route — it preserves the bioavailability that intravenous and suppository routes provided, while removing the infrastructure and convenience barriers that limited those older routes.

Readiness gates

Metal work carries readiness gates that have to be confirmed before the protocol begins. These are not suggestions. They are preconditions. If any one of these gates is not met, you do not chelate yet. You fix the missing gate first.

The first gate is urine pH. Chelate-metal complexes are maximally stable within a pH range, and acidic urine can destabilize them. Protons compete for the coordination sites on the chelator molecule. Remember, protons are basically hydrogen and hydrogen is, chemically speaking, another metal. If urine pH drops low enough, the acid displaces the metal from the chelator in the renal tubule. The metal is now free and sitting in kidney tissue. That is redistribution injury, and the kidney is silent — the patient may or may not feel it happening. The target during active chelation is a urine pH of 7.5 or higher. This is not a rate optimization; it is a stability threshold. Below it, the chelator may deliver its metal cargo to the kidney rather than out of the body.

Achieving this requires loading a mineral cation paired with a metabolizable anion — potassium citrate, magnesium citrate, sodium citrate. The mechanism: the liver oxidizes citrate through the TCA cycle, generating three bicarbonate equivalents per molecule, while the mineral cation remains in circulation to carry the alkaline load forward. It is the cation plus the bicarbonate yield that drives urine pH up. Citric acid alone — lemon juice, bulk citric acid powder — does not work. The citrate still oxidizes to bicarbonate, but the three protons that came with the acid form offset the alkaline yield, netting roughly zero pH change. The patient squeezing lemons into water thinking they are alkalinizing is not reaching the target. The patient taking potassium citrate is, because the potassium carries the bicarbonate's alkaline effect into the urine. If the patient is histamine-reactive and citrate is contraindicated, malate is the substitute — same logic, the mineral-bonded form is what matters. Slightly higher doses may be needed, but most patients reach 7.5 within a day or two either way. Alkalinization should begin one to two days before the active chelation dose, verified with urine pH paper, and maintained throughout the chelation cycle. Patients with systemic acidosis will reach alkaline pH temporarily and then drift back — the chelation dose must be timed to coincide with the alkaline window.

The second gate is functional liver and gallbladder. The lipid-soluble chelate complexes leave through the bile route, and that route requires bile flow to be working.

The third gate is kidney function. The kidney is silent and slow to heal; damage to it does not announce itself the way damage to many other organs does.³⁰ Lower back pain during chelation is a signal to stop and allow recovery for one to three months. In some cases, recovery takes longer, or does not fully occur. Do not push past warning signs assuming the kidney will bounce back quickly. The corollary: properly paced chelation can actually improve kidney function over time, by removing the metal burden that has been compromising the kidney's enzymatic machinery.³¹ The same intervention that damages a kidney when run aggressively can support a kidney when run patiently. The variable is pace. Kidney function should be assessed before chelation.

The fourth gate is mineral status — magnesium and potassium specifically, which are depleted in most modern adult patients at baseline and which chelators continue to deplete during active use.³² The replenishment runs alongside the chelation continuously.

Mineral replenishment serves a second purpose beyond preventing deficiency. When the chelator removes a toxic metal from an enzyme active site or transport protein, that binding site is now empty. If a beneficial mineral is available to occupy the site, the site is more resistant to re-occupation by another toxic metal. If the site is left empty, the next toxic metal that passes by sits right back down. Repletion is to chelation what potassium iodide is to radiation exposure: prophylactic occupation of binding sites that would otherwise be vulnerable.

How the protocol unfolds

For sensitive patients, the practitioner begins with the most stable runner — the Tier 3 macrocyclic chelator DOTA — at low dose, alone, and observes response. The Tier 3 on its own produces relatively little redistribution risk, because its stability profile keeps it from dropping cargo back into circulation, which makes it the safest single agent to start with. Some patients respond strongly to the Tier 3 alone, which means the protocol is getting useful work done at this minimal level

When the Tier 3 at gradually increasing doses (up to 300 mg) produces neither further clinical movement nor adverse symptoms, the practitioner adds the Tier 2 — EDTA for hard-metal coverage and/or MiaDMSA for soft-metal coverage. For sensitive patients, the molar dose of a Tier 2 should always be lower than that of a Tier 3.

When the combined Tier 3 and Tier 2 effect plateaus, the practitioner can add the Tier 1 — citrate and malate for hard metals, alpha-lipoic acid for soft metals. Again, by the same principle, for sensitive patients, Tier 1 should amounts should never exceed the molar dose of either Tier 2 or Tier 3. The Tier 1 reaches into the small spaces the larger chelators cannot enter — protein binding pockets, crystal interstices, enzyme active sites where the metal is occupying the position of the missing essential cofactor.

Adding Tier 1 is the most risky part as it has the greatest chance for redistribution. For patients with Gadolinium symptoms, Tier 1 should be held back for at least 6 months.

Remember, for sensitive patients, by molar measurements, Tier 3>Tier 2>Tier 1. For most patients, this level of control is unnecessary.

For most patients (those without Gadolinium or high levels of Mercury), Tiers 1, 2 and 3 are done at the same time and the citrates are dosed primarily by how much it takes to alkalize the urine.

The alkalizing of the sensitive patient may have to be accomplished by sodium bicarbonate baths if Tier 1 citrates are contraindicated.

When the three-tier protocol plateaus, the practitioner then moves to the fat-soluble form of the Tier 3 — Methyl DOTA — to reach intracellular compartments. This is the most aggressive level of the standard protocol, and the risk of mineral stripping is very

real. Magnesium and zinc levels must be brought up to normal levels before using Methyl DOTA and should be replenished on the off cycle (3-5 days on, 2 days off). Complete protocol instructions are available at remedylink.com/protocols.

Post-Chelation Tissue Repair

When the active metal protocol has done its work, the patient will still be carrying the consequences of the years the metal was present. Scarred kidneys. Demyelination in the central or peripheral nervous system. Oxidative damage to mitochondrial membranes. Denatured proteins in long-lived tissue.

Amentoflavone has been shown to prevent and, to a degree, reverse organ fibrosis, particularly in the kidneys.^{33,34}

Nervonic acid is often a rate-limiting factor in nerve repair, and supplementation can accelerate remyelination when the underlying toxic burden has been addressed.

Many peptides have global healing effects and can be taken nasally or orally. BPC-157 is the most widely known, but KPV and Thymosin Beta-4 also deserve the clinician's attention.

Injectable porcine brain peptides — Cerebrolysin and Cerebroneurogen — can be self-administered with a syringe pump and a subcutaneous infusion set for brain and nerve repair.

Finally, water fasting to trigger autophagy of dead, damaged, and senescent cells. In my experience, the water fast only truly begins on day four, after glycogen stores are diminished. Toxins begin dumping typically on or about day seven. When the tongue becomes clear again and the body is no longer releasing the odors of toxic autophagy — roughly days ten through fourteen — it is time to break the fast with meat and vegetable broth.

Clinical pearl: Chelating a patient with gadolinium poisoning is like disarming a bomb. Do not rush this protocol.

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Chapter 36: Chemicals - The load the body did not evolve to carry

The human body did not evolve alongside synthetic chemicals. There were no plasticizers in the ancestral environment. There were no pesticides, no flame retardants, no perfluorinated compounds, no industrial solvents. The molecules the modern patient encounters every day, by the thousands, did not exist when human biology was being shaped, and the body has no purpose-built systems for handling most of them. What it has instead are general-purpose detoxification pathways — built originally to handle plant toxins, bacterial metabolites, and the body's own waste — that are now being asked to handle a chemical load they were never designed for.

Some of these chemicals the body manages adequately, given enough support. Others it manages poorly. A few it cannot manage at all, and those simply accumulate. The patient's chemical burden is the running balance of what came in versus what got out, and for most modern patients that balance has been net positive — meaning chemicals coming in faster than going out — for their entire lives. The accumulated load contributes to inflammation, hormonal disruption, neurological problems, immune dysregulation, and the broader pattern of chronic illness that has become the dominant clinical picture in industrialized populations.

What modern patients are exposed to

The list of chemicals a modern patient encounters across an ordinary day is long enough that no chapter can name them all. What follows is a working sketch of the major categories, organized roughly by where the exposure happens.

Mycotoxins Toxic secondary metabolites produced by mold species. The primary route of clinical concern is inhalation. Water-damaged buildings produce airborne mycotoxins carried on spores, hyphal fragments, and fine particulate. Inhaled mycotoxins bypass first-pass liver metabolism entirely, entering the bloodstream through the pulmonary vasculature and reaching the brain and systemic circulation before the liver has any opportunity to conjugate them.

Agricultural chemicals Pesticides applied to crops in the field. Herbicides applied to soil before planting and to crops during growth. Fungicides applied to fruits, vegetables, and grain to prevent spoilage between harvest and consumption. Most of the conventional produce in the modern food supply carries residues of one or more of these compounds, and the residues are present at levels that have been deemed acceptable by regulatory agencies but that the body still has to clear.

Glyphosate deserves specific naming. The world's most widely used herbicide, glyphosate is sprayed on conventional crops at scale, applied as a pre-harvest desiccant on grains and legumes (which means the timing of application puts the residue into the food directly), and is detectable in the bodies of essentially every patient in the industrialized world. Beyond its direct toxicity, glyphosate damages the gut microbiome — earlier chapters introduced the mechanism — and disrupts mineral

availability by binding metals into unavailable forms. Glyphosate is not the only agricultural chemical that matters, but it is the one with the broadest exposure footprint and the one that compounds with the gut microbiome work that the previous chapters have addressed.

Plasticizers and food contaminants Bisphenol A and its substitutes, phthalates, and the broader family of plastics-derived endocrine disruptors leach from food packaging, water bottles, can linings, plastic cookware, and most prepared foods that have touched plastic during processing. These compounds mimic estrogen at the receptor level, disrupting hormonal signaling at concentrations far below what older toxicology models considered relevant.

Persistent organic pollutants PCBs from older industrial processes, dioxins from combustion and incineration, organochlorine pesticides like DDT that were banned decades ago but persist in soil and food chains. These compounds are fat-soluble and resist degradation. They accumulate in fat tissue, bioaccumulate up food chains, and remain detectable in the bodies of patients born long after the original sources of exposure were curtailed.

PFAS — per- and polyfluoroalkyl substances — deserves its own naming alongside glyphosate. PFAS are the "forever chemicals" — synthetic compounds engineered for water and oil resistance, used in non-stick cookware, water-resistant clothing, food packaging, firefighting foam, carpet treatments, and a wide range of consumer products. The carbon-fluorine bonds that give PFAS their useful properties also make them extraordinarily resistant to breakdown. The body has no efficient pathway to clear them. PFAS exposure is essentially universal in the modern population. The compounds disrupt hormonal signaling, contribute to immune dysfunction, and have been associated with elevated rates of several cancers in epidemiological studies.

Flame retardants Polybrominated diphenyl ethers and similar compounds applied to furniture foam, electronics, building materials, and children's products. These compounds outgas slowly across the lifetime of the products they treat, contaminating indoor air and household dust. They accumulate in fat tissue and disrupt thyroid function.

Personal care products Cosmetics, lotions, shampoos, deodorants, sunscreens, fragrances. The skin is permeable to many of the compounds in these products, and daily use across the body's surface produces a substantial cumulative absorption that most patients do not account for.

Pharmaceutical residues Both the medications a patient takes themselves and the residues that pass through municipal water supplies from population-level pharmaceutical use. Most municipal water systems do not remove pharmaceutical compounds, and trace concentrations of antibiotics, hormones, antidepressants, and other widely used drugs are routinely detectable in tap water.

Indoor air Most modern patients spend more than ninety percent of their time indoors, and indoor air typically carries higher concentrations of volatile organic compounds, particulates, and biological contaminants than outdoor air. Building materials, furnishings, cleaning products, and personal care products all contribute. The healthy buildings chapter later in the book takes this up at length.

Water contaminants Beyond pharmaceutical residues, municipal water often contains chlorination byproducts, fluoride, heavy metals leached from aging pipes, agricultural runoff, and the broader range of compounds that conventional water treatment was not designed to remove.

This list is not exhaustive. New compounds enter commercial use faster than regulatory science can evaluate them. The biomonitoring data are unambiguous: phthalates, bisphenols, perfluorinated compounds, organophosphates, polybrominated diphenyl ethers, and hundreds of other synthetic chemicals are detectable in cord blood. The patient arrives already loaded.

How the body processes chemicals

Detoxification is fundamentally a solubility problem. If a toxin is water soluble, it can leave by the kidneys or bile without any further processes. Fat-soluble toxins are another matter. They cross cell membranes, accumulate in fat tissue, and reach the brain and other lipid-rich compartments. The body excretes waste through water-based systems: urine, bile, sweat. A fat-soluble molecule cannot leave through a water-based exit. It has to be converted from fat-soluble to water-soluble before excretion can happen. The analogy is a greasy dish in a water-only sink — without soap, the grease does not wash off. So, detoxification is often about finding the right "soap" for the chemical burden in question, except in the body, the "soap" is not always a single compound. Often it is a series of bio-transformative steps, each with its own requirements.

The body's detoxification system accomplishes this conversion in four steps, each of which can fail independently.

Phase I — activation The cytochrome P450 enzyme family modifies the chemical — typically by oxidation, reduction, or hydrolysis — adding or unmasking a reactive functional group. This is the first thing that happens. The chemical sitting in tissue gets acted on by CYP450 enzymes. The result is an intermediate that is chemically activated and often more reactive — more toxic — than the parent compound. Phase I is preparation: it creates the molecular handle that Phase II will use.

Phase II — conjugation The intermediate that Phase I produces is more reactive than what it started with — the molecular handle that was added or unmasked will bind to whatever it touches. If it binds a protein, the protein is damaged. If it binds a cell membrane, the membrane is damaged. If it binds DNA, the result is a mutation. Phase I has added genotoxicity to a compound that was already harmful. Under normal

conditions, this is not a problem — Phase I and Phase II enzymes sit side by side in the endoplasmic reticulum, and the reactive intermediate is conjugated within milliseconds of being produced. It is not supposed to exist as a free molecule for longer than a fraction of a second. But this rapid handoff depends entirely on Phase II having adequate raw materials — glutathione, glucuronic acid, sulfate, glycine. When those substrates are depleted, the handoff stalls. The intermediate that was supposed to exist for milliseconds now circulates, binding DNA, damaging proteins, disrupting membranes. Phase II couples the reactive intermediate to one of these water-soluble molecules, quenching the reactive site and making the molecule water-soluble enough to be transported out. If Phase II cannot keep pace with Phase I, the reactive intermediates accumulate. This is the biochemical basis of the first Detox Trap discussed earlier in the book and multiple chemical sensitivities (MCS) — the machinery that generates toxic intermediates is running ahead of the machinery that neutralizes them.† The patient feels worse and concludes that detox "doesn't work" or is harmful. What failed was the pacing, not the principle.

Phase III — cellular efflux The conjugated, now water-soluble molecule must be pumped out of the cell. This is accomplished by ATP-binding cassette (ABC) transporter proteins — molecular pumps embedded in cell membranes that actively push the conjugated toxin from the inside of the cell to the outside. Without functional Phase III, the toxin is solubilized but trapped inside the cell. Different interventions apply here than in Phases I and II — this is a transporter and energy problem, not a conjugation problem. Mitochondrial support matters because the pumps require ATP.

Terminal excretion — kidneys or liver-bile-colon The conjugated, effluxed toxin is now water-soluble and in the circulation. It leaves the body through one of two routes: the kidneys filter it into urine, or the liver secretes it into bile, bile delivers it to the small intestine, and it transits the colon to stool. The bile route is the primary exit for most conjugated chemicals, particularly larger molecules. The next chapter develops bile as a system — not just a toxin export route, but a river that performs six distinct functions in the body, all of which degrade when flow is compromised.

Here is where the microbiome work from earlier chapters connects directly to chemical detox. Conjugated toxins delivered to the colon via bile can be deconjugated by gut bacteria — which use our Phase 2 conjugates as their food. Enzymes like beta-glucuronidase cleave the conjugation tag that Phase II attached. But deconjugation does not reverse Phase I. The functional group that was added or unmasked is still there. What reabsorbs through the intestinal wall is not the original parent compound — it is the Phase I intermediate, still carrying the reactive handle, without the Phase II conjugation that was neutralizing it.

Deconjugation creates a toxin that is worse than what the patient started with. The liver will re-conjugate it — spending another round of glucuronic acid, sulfate, or glycine to do so — and export it into bile, where it is delivered back to the same dysbiotic gut, where it is deconjugated again, and reabsorbed again. Liver conjugates, gut deconjugates. Liver conjugates, gut deconjugates. The cycle repeats indefinitely. On every pass the

Phase I intermediate circulates through the body in its most reactive form, binding proteins, damaging membranes, reaching DNA.

And on every pass the liver loses. The conjugation tags it attached — glucuronic acid, sulfate, glycine — are stripped off and consumed by the bacteria that cleaved them. Beta-glucuronidase is not an accidental byproduct of bacterial metabolism. It is a feeding strategy. Glucuronic acid is a sugar acid, and the bacteria that produce beta-glucuronidase are harvesting it as a carbon and energy source. Every conjugated molecule the liver exports is a meal that selectively feeds the deconjugating population. The loop does not just repeat — it strengthens the bacteria that drive it while depleting the substrates the liver needs to keep conjugating.

The bacteria responsible are predominantly gram-negative anaerobes — *E. coli*, *Bacteroides*, *Clostridium* — flourishing in the higher-pH environment of a dysbiotic colon, where SCFA-driven suppression is absent. Sulfatases that cleave sulfate conjugates follow the same pattern: *Bacteroides*, *Prevotella*, gram-negative organisms favored by alkaline colonic conditions. A healthy colon dominated by gram-positive fermenters produces short-chain fatty acids that lower pH and suppress beta-glucuronidase activity. A dysbiotic colon dominated by gram-negatives does the opposite — higher pH, higher beta-glucuronidase, more deconjugation, more reabsorption, more feeding of the organisms that cause the problem.

The patient's detoxification system is not failing to work. It is working, and the work is being undone, and the undoing is producing something more dangerous than the original chemical while systematically stripping the liver of the substrates it needs to continue.

This is why chemical detox must happen after the microbiome is repaired, or at least reaches a stool pH ≤ 6.8 .† If the gut flora are in disarray, the bacteria that deconjugate toxins are overrepresented, and every chemical the liver conjugates and exports gets stripped and sent back in its most reactive form. The microbiome chapters came first in the book for this reason. Attempting chemical detox with a broken microbiome is working against active sabotage.

The four classes of chemical removability

Not all chemicals are equally difficult for the body to process. The practical distinction is a spectrum of removability.

Mild

The body handles these adequately given no continual high exposure. Cooking byproducts — heterocyclic amides, acrylamides, methylfurans — fall here. Phase I and II capacity is sufficient under normal conditions.

Moderate

A healthy body handles these, but exposure can exceed capacity. Some pesticides and food preservatives. Accumulation occurs when intake is sustained or when Phase I/II capacity is compromised by other burdens.

Persistent

The body can remove these, but slowly, with some having half-lives measured in years. Accumulation is typical without active intervention. Mycotoxins, DDT, dioxins, PCBs. These compounds are extremely fat-soluble — they reach everywhere, including the brain, intracellular compartments, and cell membranes. Worse, persistent toxins tilt the Phase I/Phase II balance against the patient. They activate the aryl hydrocarbon receptor, which induces Phase I enzymes dramatically — but while Phase II enzymes are also induced, the induction cannot keep pace. Phase I outstrips Phase II capacity. At the same time, the oxidative stress these toxins generate depletes glutathione — the primary Phase II substrate — faster than the body can replenish it. The enzymes are being told to work, but the raw materials are being consumed. The result is functionally identical to Phase II suppression: reactive intermediates accumulate because conjugation cannot keep up with activation. The toxin creates its own version of multiple chemical sensitivity.

The intervention principle for persistent toxins is modulate, not necessarily accelerate. If Phase I needs to be slowed and Phases II and III need support, consider Urolithin A (UA). UA modulates Phase I downward when excessive while upregulating Phases II and III and can be created internally by ingesting ellagitannins.

Certain supplements that are otherwise beneficial must be avoided during persistent toxin detox because they suppress Phase III: quercetin, resveratrol, curcumin, green tea extract, propolis, chili spices, black pepper (piperine). These are not harmful in general — they are specifically counterproductive when the clinical goal is moving persistent toxins through the efflux pumps.

Forever chemicals

PFAS represent the extreme end — carbon-fluorine bonds that resist all biological degradation. The body has essentially no pathway for clearing them. These require different strategies entirely, and the honest clinical reality is that current tools are limited.

Saunas — can't we just sweat it out?

Sweat contains measurable concentrations of heavy metals, phthalates, bisphenols, and other environmental chemicals^{1,2,3}. Infrared and Finnish sauna both produce adequate sweat volume for clinical purposes. Chemicals stored in subcutaneous fat are mobilized by heat and excreted through sweat glands, bypassing the liver-kidney pathway entirely. Infrared sauna produces sweat that is roughly eighty-two percent water compared to ninety-six percent for conventional heat sauna⁴ — the difference is

sebaceous gland activation, which delivers more lipophilic compounds per volume of sweat.

But sauna is not sufficient as a standalone intervention. Toxins mobilized by heat (lipolysis) that are not excreted through sweat enter the circulation, are filtered by the liver, conjugated (if the machinery is intact), and excreted into bile. From bile they reach the gut, where deconjugation and reabsorption become the dominant failure mode. Sauna should be added only after the practitioner determines the patient can handle additional detoxification load and the stool pH is ≤ 6.8 . It is an adjunct, not a starting point.†

A properly designed chemical detox manages all phases of detox, not just one or two.

Clinical Pearl: If the acupuncture point Liver 3 is tender on firm palpation, this is a 'liver stress / time for a detox' sign. Resolution of this tenderness is a positive indication.

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Chapter 37: Bile - The Body's Soap

Bile is produced continuously in the liver, collected and concentrated in the gallbladder, released into the small intestine in response to the arrival of food, and carried through the gut to its eventual exit. Bile exists on a continuum, with gallstones at one end, bile sludge in the middle, and bile that moves freely at the other.

When food arrives in the duodenum — particularly food containing fat — the gallbladder contracts, releasing concentrated bile into the small intestine where it does six distinct jobs.

Acid neutralization Bile arrives at a pH around 9.5. The chyme arriving from the stomach is at a pH around 2. Bile neutralizes the acid and brings the small intestine to roughly pH 8, where enzymes work and the mucosal lining is not corroded. A patient with poor bile flow delivers acidic chyme into a small intestine that cannot neutralize it, producing chronic low-grade acid burns along thirty feet of tissue — indigestion, heartburn, ulcer-like symptoms that conventional medicine treats with acid-suppression drugs without addressing the bile-flow problem that produced them.¹

Fat emulsification Bile acids are detergents — molecules with a water-soluble end and a fat-soluble end that break fat droplets into sizes pancreatic lipase can act on. Without adequate bile, fat absorption drops, and with it the fat-soluble vitamins A, D, E, and K. A patient with poor bile flow may be eating a nutrient-dense diet and still showing fat-soluble vitamin deficiencies.³

Peristalsis stimulation Bile arriving in the duodenum signals the gut to move its contents forward. Constipation that does not respond to fiber is often a bile-flow problem. The alternating constipation and diarrhea pattern — long stretches of slow transit followed by sudden urgent movement — is one expression: contents accumulate without adequate motility signal, eventually trigger irritation-driven diarrhea, then the cycle resets.⁴

Immune regulation Bile contributes to the calibration of immune response in the gut wall. Poor bile flow produces dysregulated mucosal immunity in the small intestine, with elevated risk of intestinal autoimmunity and inappropriate inflammatory response to ordinary food contents.

Parasite and Candida suppression Bile acids at meal-stimulated concentrations disrupt the membranes of organisms that would otherwise colonize the small intestine — one of the eight protections taught earlier. A patient with poor bile flow loses this protection.

Fat-soluble toxin excretion The conjugates produced by Phase II are excreted into bile for transport through the gut and out of the body — the biliary branch of terminal excretion. A patient with poor bile flow has a bottleneck at this step: conjugates back up, recirculate, and the clinical picture looks like detox failure when it is actually an excretion failure.^{3,5}

Three problem categories when bile flow is compromised. The consequences of biliary obstruction — whether from stones, sludge, sphincter dysfunction, or substrate deficiency — fall into three categories.

Intestinal consequences. All six functions degrade. The cluster of fat intolerance, fiber-unresponsive constipation, and fat-soluble vitamin deficiency in a patient eating well points to bile flow as the system that needs attention.

Systemic toxin accumulation. Cholesterol's primary excretion route is through bile — obstructed flow produces rising cholesterol because the molecule has nowhere to go. Bilirubin accumulates, producing jaundice in severe cases.² Thousands of other compounds the liver was trying to excrete also back up. Bile acids themselves, when retained in the bloodstream, are immunosuppressive — they inhibit chemotaxis and phagocytosis.⁶

Retrograde damage to liver and pancreas. When stones lodge in the valves controlling bile flow, gallbladder contraction forces bile backward into the liver and pancreas. Bile at pH 9.5 causes alkaline chemical burns in tissues not designed to encounter it. Chronic retrograde exposure to the pancreas contributes to pancreatitis and the inflammatory environment preceding pancreatic cancer. Chronic retrograde exposure to the liver contributes to hepatitis and progressive liver damage.

Bile is location-dependent

Bile's effects depend entirely on where it is. In the intestines: beneficial. In the bloodstream from obstruction: immunosuppressive. In the pancreas and liver from retrograde flow: caustic.

The practitioner who understands this principle will not treat bile as simply good or simply bad. The clinical question is always: where is it, and is it flowing where it should?

Two conventional approaches and their limits

Cholecystectomy. The house plumbing metaphor captures the problem. Imagine the plumber has removed all the faucets in your house — pipes now stick out of the walls, dripping continuously. After gallbladder removal, bile drips continuously into the small intestine rather than being released in concentrated boluses with meals. Between meals, bile irritates the mucosa and contributes to bile-acid diarrhea. With meals, the patient does not get the concentrated release needed, and fat absorption drops permanently.

The surgery does not address the cause of the stones, the quality of the bile, or the possibility of stones elsewhere in the biliary system. Stones form because the bile substrate balance was wrong — typically depleted phosphatidylcholine, glycine, and taurine. Cholecystectomy removes the container the stones collected in. It does nothing about the composition of bile that produced them. With those substrates still depleted, the bile the liver produces is still lithogenic — still wanting to crystallize — and stones

now form in the hepatic ducts and liver tissue itself. Many post-cholecystectomy patients return with the same symptoms, now from stones in tissues harder to address. The surgery solved nothing upstream.⁷

The standard liver-gallbladder flush. The recipe — Epsom salts, olive oil, lemon juice — forces a strong gallbladder contraction. The green objects that appear in the stool are often not gallstones but saponified compounds produced by olive oil and bile mixing in the gut. † Actual gallstones sink in water; these objects float.⁷

The flush does sometimes pass real stones, but it does not address why they formed. Substrate deficiencies are now worse as so much bile has been lost. † New stones begin forming. By two weeks after the flush the gallbladder typically contains as many stones as before, leading to protocols recommending up to twelve flushes. The procedure addresses output rather than input.

A modern interpretation

A modern approach would address the substrate deficiencies that produce the wrong bile composition, dissolve stones rather than expelling them, target the liver directly, and provide the work continuously.

The best delivered would be as a rectal. The suppository route — rectal vein to portal circulation to liver — provides first-pass hepatic delivery at higher concentration than oral delivery. The ingredients can be taken orally if cost is a constraint, but the suppository route is meaningfully superior for liver access.

Ingredients to consider

Chanca piedra — stone dissolution and prevention. The name translates from Spanish as "stone breaker." The active compounds dissolve uric acid and oxalate crystallizations and prevent their formation — effective on gallstones, kidney stones, and liver stones, since all form through similar crystallization processes.⁸

Phosphatidylcholine is one of the major substrates the liver uses to produce bile that stays liquid⁹, but modern chronic stress depletes phosphatidylcholine continuously — the synthesis of adrenaline and noradrenaline consumes methyl groups that would otherwise have gone to phosphatidylcholine production.

Glycine and taurine. They conjugate with bile acids to form taurocholate, taurochenodeoxycholate, glycocholate, and glycochenodeoxycholate¹⁰. Both react directly with hypochlorous acid — the active disinfectant in chlorinated water — and are consumed in the process. Patients with regular chlorine exposure (swimming pools, hot tubs, unfiltered shower water) are depleting the same amino acid pools that bile acid conjugation depends on.

Clinical use

The third case is post-cholecystectomy. Removal of the gallbladder does not resolve the issue of bile viscosity, does not improve bile composition, and does not prevent stone formation in the liver itself. The same formulation that dissolves gallbladder stones works on hepatic stones.

Warning sign: a dry, cramping, or hot sensation in the gallbladder area signals the work is mobilizing material faster than the gallbladder can handle. Pause for a few days, then resume at lower frequency.

Clinical Pearls: If the acupuncture point Gallbladder 41 is tender on firm palpation, this is a gallbladder stress sign. Resolution of this tenderness is a positive indication.

For patients with substantial stone burden, therapeutic ultrasound — distinct from diagnostic ultrasound — can be added applied externally over the right upper quadrant. It mechanically disrupts stones and sludge that the formulation is dissolving.

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Chapter 38: Binders - When the Gut Isn't Ready

The previous chapters established the sequence: the liver conjugates toxins, exports them into bile, bile delivers them to the gut, and the gut is supposed to let them leave. When the microbiome is intact — gram-positive fermenters dominant, short-chain fatty acid production high, colonic pH low — the conjugation tags stay on, and the toxin exits in stool. The system works.

When the microbiome is not intact, the system works against itself. Beta-glucuronidase and sulfatase activity climb, conjugation tags are stripped⁵, and the freed toxin — now carrying the reactive Phase I handle without the Phase II neutralization — reabsorbs across the colonic wall and returns to the liver for another round. The liver spends another unit of glucuronic acid, sulfate, or glycine to re-conjugate it. The gut strips it again. The loop depletes the liver while feeding the organisms that drive the problem.

The clinical threshold for chemical detox is a stool pH ≤ 6.8 . Below those marks, beta-glucuronidase activity is likely suppressed enough that the liver's conjugation work holds, and excretion proceeds without significant reabsorption. The binder conversation becomes less relevant.†

But not every patient can wait. Some patients present with active mycotoxin or chemical burden that requires intervention before the microbiome work is finished, while other are so sensitive that binders are still indicated.

Cholestyramine and bile acid sequestrants Cholestyramine, colestipol, and colesevelam bind bile acids and capture fat-soluble toxins⁴ riding in bile — including deconjugated mycotoxins that would otherwise reabsorb. Ritchie Shoemaker adopted cholestyramine as the standard binder for mycotoxins in mold-illness work¹. The limitation: most patients develop constipation, which raises colonic pH, increases beta-glucuronidase activity, and worsens the very deconjugation cycle the binder is trying to compensate for. A second limitation in the mycotoxin context — oral binders work on mycotoxins in the gut but do not reach mycotoxins that entered through inhalation and colonized in the sinuses. The sinus protocol addresses that compartment. Both routes must be worked.

Fiber binders Psyllium binds toxins, usually supports transit⁶ (the opposite of cholestyramine), and serves as a prebiotic that feeds the short-chain fatty acid-producing bacteria that lower colonic pH and suppress beta-glucuronidase. Always taken in powder form mixed with water, never capsules — capsules risk intestinal blockage if they lodge without adequate hydration. Sourcing caveat: psyllium falls into a regulatory category allowing higher pesticide residue, and many brands are contaminated with lead. A reputable source is clinically critical.

Charcoal Broad nonspecific binder useful for acute exposures². Binds nutrients and medications, so timing matters. Not a daily detox binder.

Bentonite and zeolite bind metals and some organic compounds³. The metals chapter develops this further.

Clinical pearl: All oral binders pull fat-soluble vitamins alongside toxins. Supplement fat-soluble vitamins and time binders away from nutritional supplements by at least two hours. Titrate to avoid constipation above all else — constipation defeats the purpose of the binder by creating the conditions that drive deconjugation and reabsorption.

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Chapter 39 — A soap for all seasons

Soap dissolves things water alone cannot. A drop of oil on water sits on the surface and does not mix. A drop of oil in soapy water dissolves and washes away, because the soap molecule has one end that likes water and one end that likes oil, bridging between the two. The cyclodextrin family works on the same principle with more specific geometry. Instead of an end that likes oil, the cyclodextrin has a closed cage¹ with an oil-friendly interior. Fat-soluble toxins enter the cage. The cage's exterior is water-soluble, so it carries the toxin out through any water-based exit route the body has.

What cyclodextrins are

A cyclodextrin is a ring-shaped molecule made of glucose units linked together to form a closed cage — hydrophilic on the outside, hydrophobic on the inside. The interior is the right size to hold a small fat-soluble molecule, and when such a molecule encounters the ring in an aqueous environment, it slides into the interior and stays there. The complex is now water-soluble and can be carried out of the body through routes that pure fat-soluble compounds cannot use.

Three sizes exist, named alpha, beta, and gamma², each with a different interior cavity diameter capturing different ranges of guest molecules. Beta-cyclodextrin in its hydroxypropyl form (HPBCD)³ has the cavity size that matches the largest range of clinically relevant fat-soluble toxins, and it is the cyclodextrin that does most of the work in the formulations taught here.

The mechanism is fundamentally different from surface adsorption. A cholestyramine molecule binds toxins by attracting them to its surface with relatively weak forces, and the binding is competitive — anything that binds well to the same surface, including nutrients and fat-soluble vitamins, displaces some of the toxin. A cyclodextrin holds its guest molecule inside a closed ring. The guest is physically encapsulated, not stuck to a surface, and the binding is more selective: only molecules of the right size and lipophilicity fit into the cage. This produces less competition with nutrients than surface binders create.

Cyclodextrins are not alternative medicine. They are FDA-approved drug delivery vehicles used in over forty pharmaceutical products⁶. Sugammadex, a modified gamma-cyclodextrin, is injected intravenously after surgery to encapsulate rocuronium⁷ and instantly reverse neuromuscular paralysis. HPBCD mobilizes cholesterol from lysosomes in Niemann-Pick Type C disease⁸, where a genetic defect traps cholesterol inside the cell.

The technology is genuinely modern. Cyclodextrins were discovered in the late nineteenth century but were not characterized or made commercially available until the 1970s. Their therapeutic application as a binder in their own right — capturing the hydrophobic toxins the modern environment produces — is more recent still.

How should cyclodextrins be delivered?

Cyclodextrins are best absorbed by IV, rectally, or via the sinuses. Rectal cyclodextrin routes the active compounds through the rectal veins into hepatic portal circulation, delivering them to the liver. Cyclodextrins taken orally are partially absorbed but limited by osmotic effects on the intestines — take more than a certain amount and it causes the runs — and cyclodextrins are among the types of supplements that exhibit stepwise dose effects.

It is important to note that only the hydroxypropyl forms should be used, as other types do not have good safety profiles⁴.

In circulation, HPBCD can serve as a surrogate albumin for patients whose albumin levels are low and whose carrier capacity for fat-soluble toxins is therefore reduced.† A patient with low albumin has toxins that would otherwise be moved out efficiently sitting in tissue longer. HPBCD provides additional carrier capacity and supports the transport step of the detox chain. This matters particularly for patients with chronic illness, where albumin is often depleted as part of the broader illness pattern.

HPBCD also captures persistent toxins that the conjugation step has not fully processed. Some toxins the modern environment delivers are difficult substrates for the body's conjugation pathways — they sit in fat tissue for years and the conjugation system processes them inefficiently when they do reach the liver. HPBCD can encapsulate some of these compounds directly, providing an exit route that does not depend on the conjugation pathway being adequate for that specific substrate.

Cyclodextrins and heart health

The cholesterol that ends up in an arterial plaque is not the cholesterol on the bloodwork report. The bloodwork measures cholesterol dissolved in lipoproteins, circulating in plasma — soluble, mobile, available for reverse transport back to the liver. The cholesterol in a mature plaque has stopped circulating. It has been deposited in the arterial wall, taken up by macrophages that came to clean up the deposit, oxidized into forms the macrophage cannot process, and eventually crystallized into solid cholesterol monohydrate. The conventional reverse-cholesterol-transport pathway cannot reach it.

Macrophages arrive to clean up the crystallized cholesterol. They engulf it but cannot process it — cholesterol crystals damage the lysosomal membranes inside the macrophage, the cell cannot digest what it took in, it dies, and its lipid-laden corpse becomes a foam cell. The foam cell's contents — unprocessed cholesterol, inflammatory signals, cellular debris — add to the plaque volume and inflammatory environment, which recruits more macrophages, which die the same way. The plaque grows from the cleanup attempt itself.

This is the situation cyclodextrin enters. The hydrophobic interior of the ring matches the cholesterol molecule, and cholesterol slides in. What is true at the level of a single molecule is also true at the level of a crystal surface: the ring binds cholesterol at the crystal face, lifts it off, and carries it into the aqueous phase. The crystal dissolves from

its surface inward, dose by dose. In aqueous solution, cyclodextrin can raise the solubility of cholesterol by a factor of up to one hundred and fifty thousand⁵.

The reverse cholesterol transport pathway, which could not reach the crystal, can reach the molecule the cyclodextrin has just liberated. Free cholesterol mobilized from the plaque enters the macrophage, exits by the conventional efflux transporters, joins HDL, returns to the liver, and leaves the body as bile acid. The cyclodextrin does not replace reverse cholesterol transport. It restarts it, by moving the substrate out of a phase where the transport machinery has no access and into a phase where it does. In this way the cyclodextrin can have an enzymatic effect.

There is a second mechanism that compounds the first. Cyclodextrin entering a foam cell triggers a transcriptional shift in the macrophage itself. The liver X receptor gets activated by the oxysterols cyclodextrin produces inside the cell, and the activated receptor turns on the genes that code for the efflux transporters. The macrophage that was a passive storage container becomes an active exporter again. The cell that was part of the plaque becomes part of the cleanup. This effect has been demonstrated in animal models and in human carotid endarterectomy specimens incubated with cyclodextrin.

The clinical implication is that arterial plaque is not, mechanistically, a permanent deposit. It became permanent under the conditions the body had available — no way to dissolve crystals, no way to restart transport from a foam cell. Cyclodextrin changes the conditions. The deposit was permanent only because the tools were missing.

Three notes belong with this teaching. First, the work is slow. A mature plaque represents years to decades of deposition, and dissolving happens dose by dose at the crystal surface. Expect months of consistent use to see measurable change, not weeks. Second, calcifications are not the same thing as foam cells. For calcified plaque, chelation should be considered. Most atherosclerosis has both soft and hard aspects, and fortunately HPBCD and chelators work well together. Third, the plasma cholesterol number on standard bloodwork is the wrong place to look for evidence. The cyclodextrin's effect is on tissue cholesterol — what is in the wall, in the foam cell, in the crystal — and tissue cholesterol does not show up on a lipid panel. The right monitoring tool is imaging of the arterial wall itself such as carotid ultrasound.

Cyclodextrins, the spike protein and prions

A properly folded protein keeps its fat-soluble amino acids tucked on the inside of the fold, with water-soluble amino acids on the outside. This is what allows the body's water-based machinery — proteases, chaperones, transport proteins — to grab, process, and clear it. A misfolded protein has at least one fat-soluble amino acid on the outside. The body's water-soluble handling systems cannot get hold of it. It lodges in fat-rich compartments — cell membranes, brain tissue, lipid stores — resists breakdown, and accumulates. It is a fat-soluble toxin. Those that propagate, that is, cause other proteins near them to misfold in the same manner are called prions.

Prions are associated with nearly every neurodegenerative condition known⁹. This is where cyclodextrin connects. The same cage geometry that encapsulates fat-soluble chemical toxins encapsulates the fat-soluble amino acids on the outside of a misfolded protein, prion or not. The ring surrounds them, renders the entire complex water-soluble, and allows the body to excrete it. The tool that addresses mycotoxins and persistent organic pollutants addresses misfolded proteins (including prions) by the same mechanism.

Spike proteins from certain viral exposures and certain pharmaceutical interventions contain prion domains. When spike protein is broken down by proteolytic enzymes (a common alternative medical intervention), some research suggests that the spike protein fragments into approximately seven prion fragments.† Each templates neighboring proteins into misfolded configurations. The cleavage that was supposed to solve the problem has produced seven new ones.

This is why breaking down spike protein without simultaneously capturing the fragments is dangerous. You solve one problem — the intact spike protein — and create another — seven prions accumulating in fat tissue, particularly the brain. We must not trade heart disease for dementia.

The clinical rule is simple: never cleave spike protein without binding the fragments.† The proteolytic enzymes that break down spike protein must be paired with cyclodextrin to capture what the cleavage releases .†

Lysosomes

The Niemann-Pick application named earlier is not limited to a rare genetic disease. It is a general mechanism. Any cell whose lysosomes are engorged with material the cell cannot digest is in the same situation — toxic waxes, crystallized compounds, prions, oxidized fats accumulate, the lysosome swells, and the cell's housekeeping stalls. Water fasting upregulates autophagy, but fasting cannot solve what the enzymes cannot digest. Cyclodextrin bypasses the limitation entirely — it encapsulates the material, renders it water-soluble, and allows the cell to export it. The lysosome shrinks. The cell resumes normal function. Lipofuscin — the yellowish-brown pigment granules that accumulate in lysosomes with age^{10,11,12} — is a visible marker of this failure. It is the residue of incomplete lysosomal digestion, largely composed of oxidized lipids and cross-linked proteins that lysosomal enzymes cannot break down further. Its accumulation correlates with cellular aging and neurodegeneration, and it occupies lysosomal volume that would otherwise be available for functional housekeeping.

Reactivating paralyzed immune cells

Macrophages and neutrophils that engulf material they cannot digest become immobilized — alive but paralyzed, unable to perform immune function. Eventually they rupture, releasing their toxic contents and triggering inflammation. A white blood cell count can look adequate on paper while the actual working immune force is a fraction of the number. Cyclodextrin clears the contents that paralyzed them and returns the cells

to active duty — immune restoration not by producing more cells but by reactivating the ones already there.

Phospholipid and vitamin replacement

Cyclodextrins extract not only toxins but also membrane phospholipids and fat soluble vitamins. Consider supplementing with fish oil — one teaspoon, twice per week — taken at least 12 hours separated from the cyclodextrin dose. The separation matters: taking fish oil alongside the cyclodextrin would simply have the cyclodextrin encapsulate the fish oil and remove it.

The nasal application

The cyclodextrin spray as part of the sinus restoration protocol uses the same active compounds applied through a different route for a different indication.

As taught earlier, cyclodextrins can be delivered via a nasal spray. The same cyclodextrins applied to the nasal cavity reach the brain at concentrations no systemic route can match. The mechanism is the cribriform plate fast-track — the same anatomy that allows toxins in a compromised sinus to flow upward into brain tissue also allows therapeutic compounds to reach the brain directly, bypassing the blood-brain barrier entirely.

The numbers are striking. Cyclodextrin administered intravenously reaches the brain at very low rates — only about three-hundredths of one percent of the administered dose, because the blood-brain barrier excludes cyclodextrins effectively and an active efflux system pumps out what does cross. The nasal route delivers roughly thirty to forty times more to the brain than IV, with only about three percent entering systemic circulation. Most of what is sprayed stays local to the nasal cavity and goes to the brain via the direct nose-to-brain pathway.

The clinical implication is that the nasal cyclodextrin spray, beyond its sinus-restoration role, is a brain-targeted intervention. Patients with brain fog that does not resolve with systemic detox work, neurological symptoms following mold exposure, post-viral cognitive symptoms, or persistent symptoms after spike-protein exposure may benefit from the nasal spray as the only route by which cyclodextrins reach the brain at therapeutically useful concentrations.

The same active compound, in two formulations and two routes, addresses two anatomical compartments — the liver and general circulation through the rectal gel, the brain through the nasal spray. Patients with both systemic and brain-resident toxin burdens use both routes.

Clinical pearl: When a patient with a compromised liver begins rectal cyclodextrin administration, liver enzymes may rise for up to six weeks. This is not damage. The cyclodextrins are mobilizing fat-soluble compounds the liver now has to process.

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Chapter 40: Treat the patient... and their home

The practitioner reading this may be thinking: I am a clinician, not a building contractor. The building science in this chapter is not complex. The practitioner already understands substrates, colonization, moisture-dependent growth, and selection pressure. A building is just another body to diagnose and treat. The practitioner who gains this literacy will find it changes outcomes in ways that body-only protocols cannot.

We spend most of our lives inside buildings. The building is the largest single ongoing exposure in our lives — larger than diet, larger than work, larger than anything the patient might think to identify when asked what they have been exposed to. The home is not a neutral container. It is a participant in the patient's biology.

Why water-damaged buildings matter so much

The fungi that colonize damp building materials are familiar to anyone who has read about mold illness. *Aspergillus*, *Stachybotrys* and others establish themselves on wet drywall, on damp wood, in HVAC systems, and in any indoor location where moisture has accumulated long enough for spores to germinate. Each produces its own characteristic mycotoxins — aflatoxins from *Aspergillus*, trichothecenes from *Stachybotrys*, ochratoxin from *Penicillium* — that aerosolize into the indoor air. The mycotoxin load from a substantially water-damaged building is large, continuous, and composed of compounds that are among the more biologically active toxins in the natural world.¹

But the same conditions that grow mold also grow bacteria. *Actinomyces*, certain *Bacillus* species, *Mycobacteria*, and other bacterial groups colonize the same wet building materials, and produce their own endotoxins and exotoxins that aerosolize alongside the mycotoxins.²

What makes the combined exposure worse is the layered combat happening in the building materials. Bacteria and fungi are ancient enemies; when they share territory, they fight. Bacteria also fight other bacteria for the same niche, and molds fight other molds. The patient is breathing the byproducts of all three wars simultaneously. Each organism escalates its chemical output in response to attack, and the patient is caught in the crossfire.³

Both bacteria and fungi form biofilms — structured matrices that physically shield the cells inside from antimicrobial compounds and from the patient's own immune system. A patient who left a water-damaged building years ago can still be carrying biofilm-protected populations in their sinuses from that exposure. Both populations continue to produce their toxins as long as their biofilms hold.⁴

What mold does that other toxins do not

Mycotoxins damage cells, disrupt mitochondrial function, displace enzyme cofactors, interfere with neurotransmitters, drive chronic inflammation... the list goes on. If that were all mold did, the protocols of the previous chapters would be adequate to clear it. Mold does something more pernicious. It actively suppresses the pathways the body would use to clear it.

Mycotoxins shift the immune system toward a TH2-dominant pattern — well-suited to extracellular parasites and allergic responses but poorly suited to clearing fungal exposures, which require TH1 and TH17 responses.⁵ Mycotoxins drive indoleamine 2,3-dioxygenase (IDO) activity, depleting tryptophan and producing quinolinic acid — an excitotoxin that contributes to neurological symptoms while simultaneously starving serotonin and melatonin production.⁶ They block GABA receptors, contributing to anxiety, sleep disruption, and sympathetic dominance.⁷ They deplete melanocyte-stimulating hormone (MSH) and vasoactive intestinal peptide (VIP), both regulatory peptides whose deficits drive broader hormonal and immune dysregulation.⁸

Several mycotoxin classes — aflatoxins and trichothecenes among them — are directly cytotoxic to adrenal cortex cells and disrupt steroidogenesis at multiple levels of the HPA axis.⁹ The mold patient who reports that they cannot handle stresses they used to handle easily is often describing adrenal compromise.

Why every modern home is at risk

Modern framing uses oriented strand board (OSB) for sheathing — pressed wood flakes glued together.¹⁰ The broken cellulose surfaces of OSB give mold easy access to wood fiber that whole wood would not present. During construction, OSB is typically left exposed to weather for weeks before the building is dried in, absorbing moisture and inoculating with airborne spores.¹¹ The sheathing then gets wrapped with house wrap that blocks bulk water but also slows vapor outflow, creating a moisture trap. The interior is finished with drywall whose paper backing is a second cellulose food source, and if the cavity is filled with cellulose insulation — a third.

The vulnerability comes down to lignin — the complex phenolic polymer that encases cellulose fibers in intact wood like armor. Lignin is hydrophobic, chemically resistant, and so difficult to degrade that only a narrow group of fungi have evolved the machinery to do it. In solid timber, the lignin matrix limits fungal access to the digestible cellulose underneath. When wood is mechanically processed into OSB, the lignin structure is disrupted and far more cellulose surface is exposed. The resins in OSB provide some moisture resistance but do not replicate the biological armor that lignin provided.¹²

Blown cellulose insulation takes the processing one step further — the lignin is essentially gone. Manufacturers treat it with borates for fire and mold resistance, and the borates work, but if they leach from sustained moisture exposure or were unevenly applied, what remains in the wall cavity is finely divided, maximally digestible organic material. From the mold's perspective, it is cotton candy.

Roof penetrations compound the problem. Solar panel mounting bolts, plumbing vents, electrical service masts, and satellite mounts are all potential leak paths. The penetration that leaks slowly produces water intrusion the homeowner does not see, where mold grows unobserved for years. Attics carry condensation risk when warm interior air meets cold roof decking. Crawlspace carry the risk of ground moisture wicking up into the substructure. Both are spaces the occupants do not enter and do not inspect. The practitioner should assume a patient's home has mold at some level, until proven otherwise.

Detection

The first question with any mold-suspected patient is whether the building is contributing to their symptoms now, or whether the load is from a past exposure. The distinction determines the order of interventions.

A few signs from the patient carry diagnostic weight. Tenderness on the midsternal acupuncture point CV17, palpated with the practitioner's thumb, signals bradykinin elevation — a downstream marker of kinin-kallikrein activation from fungal exposure. A globus sensation — a feeling of a lump in the throat, often noticed during eating or swallowing — carries similar weight. Either sign is sufficient to flag the mold workup.

The building itself can be assessed with inexpensive tools. A moisture meter measures water content in walls, floors, and building materials. Elevated readings where things should be dry — below windows, around plumbing penetrations, in basements, behind kitchen and bathroom fixtures — identify likely growth sites. A particle counter measures airborne particulates including mold spores and fragments; indoor 10-micron particle counts more than twice outdoor values suggest mold is growing inside the home (assuming no cooking, smoking or use of hair sprays or talc powder has occurred that day which can give false high readings). A UV flashlight illuminates the fluorescent compounds many mycotoxins produce — useful for spot-checking pantries, refrigerators, and food storage areas if you can lower ambient light sufficiently for the test.

For airborne sampling, settled-petri-dish methods preferentially capture heavier spores, air-sample methods capture lighter spores but can miss intermittent contamination, and real-time particle counting tracks cumulative load but does not identify species. A combination of several test methods is optimal if affordable.

Urine mycotoxin testing identifies which mycotoxins the patient is actively excreting. The test is informative when positive but carries a false-negative risk that parallels the metals testing limitation from the previous chapter. A patient with mycotoxins stored in fatty tissue and depleted clearance pathways can test negative while carrying significant burden. The principle of challenge testing applies here as it did with metals.

Remediation

A patient with a confirmed mold problem has three paths: remediate the building, leave it, or maintain an indefinite protocol to manage the ongoing exposure.

Remediation begins with finding and removing the contaminated materials. Fogging, air filtration, and the interventions below address airborne and surface contamination, but none of them can fix colonized OSB, wet drywall behind a wall, or saturated insulation. The source materials have to come out.

HVAC Ductwork moves air throughout the home continuously, distributing whatever contamination it contains to every room. Every person living in a home sheds approximately two pounds of skin per year, and this accumulates in the HVAC as a continuous food substrate for whatever organisms have established in the ductwork. The HVAC is not a passive distribution system. It is a selection chamber in which the organisms most adapted to digesting the occupants are the ones that flourish.

Two HVAC upgrades matter. First, a dehumidifier downstream of the AC coil. The AC dehumidifies the air at the room scale, but water condensing on the cold coil creates a localized wet zone inside the system — exactly where mold and bacteria would most welcome a water source. A downstream dehumidifier eliminates this. Second, a blower upgrade that supports HEPA filtration inside the system. Stock blowers cannot generate adequate flow through a HEPA filter. An upgraded blower turns the home's air handler into a continuous air-cleaning system.

Metal ductwork can be professionally cleaned. Flex duct and internally lined duct can be damaged by aggressive cleaning and may need replacement. Like the protocols for proper mercury removal from a tooth, HVAC cleaning must vent the removed dust outside the home, not through a filter that may fail.

Standalone air filtration units in bedrooms and main living areas are high-leverage regardless of the broader remediation plan. Most consumer HEPA units do not address mycotoxins — the toxins themselves are smaller and gas-phase or fragment-bound, and pass through HEPA. An effective unit requires several pounds of activated carbon in addition to the HEPA stage.

If remediation is out of the question due to cost, or your status as a renter, consider this as a minimum.

Turn off the HVAC system and open windows.

Place a high quality air filter, at the very least, in your bedroom.

Wash all your bedding with enzymes designed for mycotoxin degradation and seal your mattress and pillows in a vapor barrier system.

Fog the house monthly, and your bedroom every 2 weeks.

Fogging

Fogging — dispersing antimicrobial solutions as a fine mist — is the most practical intervention for ongoing reduction of airborne and surface mold and bacterial loads. A fogger directly attacks organisms and their biofilms on every surface the mist reaches, including inside the HVAC, behind furniture, and in corners that surface cleaning cannot address. The temporary humidity also can cause the airborne particles to fall to the floor where they can be vacuumed with a HEPA vacuum.

Equipment matters. A properly designed fogger delivers a near-invisible mist — a visible cloud means the particles are too large and will deposit moisture rather than a thin antimicrobial film. The fogger should not heat the solution, since many fogging solutions degrade with heat. It must be built from acid-compatible materials, since most metals corrode under acid exposure.¹³

Sanidate (peracetic acid and hydrogen peroxide) is the more potent antimicrobial. Peracetic acid (think vinegar) is broadly sporicidal and fungicidal, effective against resistant ascospore-forming molds that weaker agents leave behind.¹⁴ It breaks down to water, oxygen, and acetic acid. For heavy-duty remediation — first-pass treatment of a contaminated structure, fogging attics and crawlspaces, addressing established biofilms — Sanidate is the stronger tool. It is mildly corrosive to certain metals at fogging concentrations; sensitive electronics should be covered or removed.¹⁵

Hypochlorous acid (HOCl) is the same compound human neutrophils produce to kill pathogens. It is effective against common household molds and bacteria, non-toxic at fogging concentrations, and breaks down without residue.¹⁶ Its advantage over Sanidate is greater electronics safety — research on HOCl dry fog has shown no changes in performance parameters of exposed circuit boards and medical devices.¹⁷ HOCl can also be generated at home with an electrolysis device from salt water, giving the patient an indefinitely sustainable tool with no ongoing supply cost.

The practical approach is to use both: Sanidate for initial heavy remediation and periodic deep treatments, HOCl for ongoing maintenance fogging in living spaces with electronics in place.

Both solutions are non-toxic with adequate ventilation. The patient should be out of the building during fogging and can reoccupy within an hour of ventilating. Monthly fogging is often sufficient in moderate cases; weekly may be needed in severe cases until the source is addressed. The pattern to watch for is the patient who feels well after fogging and progressively worse before the next one — that means the interval is too long.

A note on HVAC fogging. The EPA considers HVAC ductwork a distinct use site under FIFRA. Neither Sanidate nor home-generated HOCl is currently registered for HVAC duct treatment. Fogging living spaces is straightforward; directing fog into ductwork is a different regulatory question, and practitioners should advise patients accordingly.

Porous surfaces

The soft contents of the home accumulate mycotoxins and continue to release them long after the source contamination is addressed.

Clothing is usually recoverable with multiple wash cycles using mycotoxin-degrading enzyme additives. Patients should test tolerance to a recovered garment before reintegrating their full wardrobe.

Carpets and upholstery may not be recoverable. The porous structure makes it difficult to verify whether cleaning has reduced the load.

Hard surfaces clean readily. The line falls at porosity.

Why some people get sick and others do not

Two people in the same moldy building can have radically different responses. The unaffected person often becomes a source of social pressure on the affected one, dismissing their symptoms as imagined. This damages relationships and delays intervention.

Part of the difference is genetic. Approximately 25% of the population carries HLA-DR haplotypes that predispose them to chronic inflammatory response to mold exposure, and these haplotypes appear in roughly 90% of patients seeking specialty evaluation for mold illness.¹⁸ But substrate burden also matters — a patient already carrying chemical and metal loads with depleted glutathione has less reserve to handle additional mold exposure. And total exposure history matters — a patient previously in a different moldy environment may carry residual biofilm-protected populations that lower their threshold and be sensitized to even the smallest exposures.

The unaffected occupant is not evidence that the affected occupant is imagining things. The two bodies are bringing different vulnerabilities to the same exposure. The teaching the practitioner offers is that the symptoms are real and that the path forward depends on what the patient can change about their situation, not on convincing the unaffected occupants.

Beyond mold

Highly sensitized people are likely already aware about Volatile organic compounds (VOCs) from new building materials, furniture, carpeting, paints, and adhesives. What they may not know about is:

Gas stoves produce nitrogen oxides and ultrafine particulates that have neurologic effects.† If a patient cannot switch to an electric stove, a range hood venting to outside during cooking can help.

Wood stoves must be used in a positive pressure environment, otherwise combustion toxins can be pulled into the living space through the chimney when not being used. Flues are designed not to fully seal for safety reasons.

What all this means for the practitioner

Ask about the building in every workup. Housing history — where, how long, whether water damage was present — is part of the clinical intake. So is workplace history. Schools are common exposure sites for children.

One mold assessment company reported a school heavily contaminated with mold whose students and teachers were constantly getting sick. The school said they could not afford to remediate and would not publicly acknowledge the problem for fear of lawsuit. Their solution was to bring in air filtration units each evening and remove them before students arrived each morning. The filtration did not fix the problem. It improved it somewhat. The home is not the only building to check. If a patient's symptoms worsen at work or a child declines during the school year, the exposure may be coming from a building the practitioner never thought to ask about.

Clinical pearl: If nothing is working with a highly sensitive patient, have them spend a week somewhere mold-free. Travel and novelty produce their own dopamine lift, but if symptoms meaningfully decrease within a week, you have your smoking gun. The building is the problem.

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Chapter 41: Trial by fire

The principle from Chapter 1 was that supplements are forgiving in a way drugs are not. Get the drug wrong and you have made the patient worse, sometimes substantially. Get the supplement wrong and the worst likely outcome is mild discomfort, an intervention that did nothing, or information about what the actual problem is not. The asymmetry permits a clinical posture that drug practice cannot allow. You can experiment. The intervention itself becomes part of how you figure out what is going on.

This chapter is the worked example of that principle. The condition the chapter addresses — histamine dysregulation — is uniquely suited to the trial-by-fire approach because it is uniquely difficult to diagnose by any other route. Most practitioners know histamine as the molecule of allergy, which means hives and hay fever, which means H1 receptors on skin and respiratory mucosa. Those are real. They are also only a small part of what histamine actually does in the body, and the symptoms produced by the other receptors are routinely missed because the practitioner is not looking for them.

A patient walks into the office with fibromyalgia, or with POTS, or with treatment-resistant depression, or with mid-cycle anxiety that resolves at menstruation, or with a heart that races without explanation, or with brain fog that began after a concussion eighteen months ago and never lifted. The conventional workup for each of these takes a different path. Rheumatology for the fibromyalgia. Cardiology for the POTS. Psychiatry for the depression. Gynecology for the cycle-correlated symptoms. None of those workups is likely to reach histamine, because none of those specialists is trained to see histamine as a candidate for the presentation in front of them.

The trial-by-fire posture is the answer. You suspect histamine on the basis of pattern, you give a single dose of liposomal DAO, and you watch what happens in the next hour. If the symptoms improve, you have your answer. If the symptoms do not improve, you have learned something equally useful: histamine was not a driver, and your differential moves elsewhere. The dose was harmless. The information is what you came for.

Before the histamine protocol, the receptor map. Without it, the practitioner does not know what they are looking for, and the trial becomes harder to design and harder to read.

H1 and H2 — Far Beyond Skin and Lungs

In skin, H1 and H2 produce the classical itch, hives, urticaria, and allergic dermatitis the textbook describes. In sinuses, they produce rhinitis, sinusitis, and congestion. In lungs, they produce asthma and bronchospasm. So far, this is the conventional picture.

In gut tissue, the same receptors produce food allergy and gut hypersensitivity — which the patient often experiences as IBS-like symptoms without the classical IgE-driven presentation. In muscles, H1 and H2 activation contributes to fibromyalgia. In joints, it contributes to arthritis and joint pain. In cardiovascular tissue, it produces hypertension

or hypotension depending on the receptor balance, dizziness, arrhythmias, and the orthostatic intolerance pattern conventional medicine calls POTS.^{3 4} In peripheral nerves, it contributes to chronic pain and neuropathy. In the prostate, it contributes to benign prostatic hyperplasia. In uterine tissue, it contributes to PMS, menstrual cramping, miscarriage, and difficulty conceiving. In bladder tissue, it produces interstitial cystitis and the burning urination that is not from infection.

The reframe this list represents deserves to be named directly. The fibromyalgia patient, the POTS patient, the interstitial cystitis patient — in each case, the histamine pathway is one of several contributors, sometimes the dominant one, and the patient who responds to a histamine intervention has had the dominant driver finally addressed after years of treatment that worked on other contributors.

The clinical posture the practitioner takes from this is that any chronic condition involving inflammation, smooth muscle dysregulation, or unexplained hypersensitivity is a candidate for the histamine workup. The list above is not exhaustive. The principle is that H1 and H2 receptors are far more widely distributed than the classical teaching emphasizes, and the symptom patterns they produce in the underemphasized tissues are easy to miss unless the practitioner is looking for them.

H3 — The Allergic Brain

H3 receptors live in the central nervous system, primarily on histaminergic neurons in the brainstem region called the tuberomammillary nucleus.⁵ Their function is regulatory. They sense the level of histamine in the brain and adjust histamine release in response. When brain histamine is high, H3 reduces release. When brain histamine is low, H3 permits more.

This is the protective mechanism the brain uses to keep histamine from rising too high in a closed compartment where swelling can be fatal.

The system has a vulnerability. Some H3 receptors carry constitutive activity — they are partially active without any histamine present, due to genetic variation or to chronic inflammation that has shifted the receptor's baseline.^{6 7} A patient with H3 constitutive activity has chronically suppressed brain histamine even when blood histamine is normal, because the H3 receptors are sending a constant suppression signal regardless of what the histamine level actually is.

Brain histamine is not just a signaling molecule for inflammation. It is a regulator of release for several other neurotransmitters the brain depends on for ordinary function. Acetylcholine, dopamine, serotonin, norepinephrine, and GABA release all respond to brain histamine signaling.^{5 8 9} When brain histamine is suppressed, the release of these neurotransmitters falls below the level the patient's nervous system needs.

The symptom pattern that follows is what I call the allergic brain. Low acetylcholine produces learning and memory difficulty. Low dopamine produces motivational loss and

the cluster of symptoms that resembles the pre-clinical phase of Parkinson's. Low serotonin produces depression. Low norepinephrine produces focus problems and presentations that look like ADHD. Low GABA produces inability to relax, poor deep sleep, and chronic anxiety. On top of these specific neurotransmitter deficits, the broader H3 syndrome includes headaches, brain fog, difficulty waking, temperature dysregulation, vertigo, and nausea.

This patient does not look allergic. They do not have hives or hay fever. They have psychiatric symptoms, and the standard differential for psychiatric symptoms does not include H3 dysregulation. This is one of the categories of patient where the trial-by-fire approach pays off most dramatically — a mechanism identified that years of psychiatric workup did not surface, opening a protocol that can do work no combination of psychiatric medications could do.

In this case, liposomal DAO can make the patient feel better or worse depending on BBB patency. If liposomal DAO makes the condition worse, that is valuable information. Right lever, wrong direction. Try histidine supplementation.

H4 — The Immune Cycle and the Cardiovascular Reframe

H4 receptors live on immune cells — mast cells primarily, also macrophages, eosinophils, T cells, and other lineages.¹⁰ The H4 mechanism is what makes histamine reactions self-reinforcing rather than self-limiting.

When mast cells encounter a trigger, they degranulate and release histamine into the surrounding tissue. Some of that histamine reaches H4 receptors on nearby mast cells, on macrophages migrating through the tissue, and on circulating immune cells in adjacent vasculature. H4 activation recruits more mast cells to the tissue, activates the cells that arrive, and promotes histamine production by the recruited cells — because mast cells and certain macrophages express histidine decarboxylase and synthesize their own histamine from dietary histidine.^{10 11} The result is a positive feedback loop: histamine begets more mast cells, more mast cells produce more histamine, more histamine activates more H4 receptors. The tissue becomes progressively more populated with histamine-producing cells, and the local histamine load rises over time even when the original trigger is no longer present.

The macrophage version of this story produces the cardiovascular reframe. Macrophages activated through H4 in the arterial wall accumulate cholesterol — they take up oxidized LDL and other lipid particles at rates that exceed their ability to process them.^{12 13} The cell continues producing its own histamine, which continues to activate H4 in the surrounding tissue, which continues to recruit more macrophages, which continue to accumulate cholesterol. Eventually the cholesterol-laden macrophages die, leaving their lipid contents behind in the arterial wall. These dead, cholesterol-engorged macrophages are foam cells, and accumulations of foam cells are the cellular substance of atherosclerotic plaque.^{14 15}

Atherosclerosis is not exclusively an allergic phenomenon, and the histamine pathway is not the whole explanation. Cholesterol metabolism, oxidative damage, endothelial injury, and a number of other contributors all participate in plaque formation. But the histamine-driven foam cell mechanism is one of the major pathways,¹² and it is essentially absent from the conventional cardiovascular treatment model. Adding histamine intervention to a cardiovascular protocol opens a treatment axis that conventional cardiology does not work on, and patients with significant histamine drivers may show cardiovascular improvement that statin therapy alone never produced.

The same mechanism in liver tissue may produce fatty liver. Macrophages in the hepatic sinusoids, activated through H4, accumulate fat in the same pattern. The patient with non-alcoholic fatty liver disease is not commonly understood as having a histamine-mediated condition, and the conventional approaches to NAFLD do not typically include histamine intervention. The mechanism suggests they should.

The broader principle from H4 is that histamine reactions are not events. They are processes, and the processes self-amplify without a clear end point if the conditions permit. † Tissue that has been hosting an H4-driven inflammatory cycle for years has accumulated structural change — more mast cells than it started with, more macrophages, more local histamine production capacity, and a lower threshold for activation than the same tissue had before the cycle began.

Mast Cells as Ancient Parasite Defense

A question worth pausing on. Why does the body produce all of these reactions in the first place? Itching, sneezing, coughing, diarrhea, vasodilation, vascular permeability, smooth muscle contraction — these are profoundly disruptive. What evolutionary pressure produced a system that does this?

The answer is parasites. Mast cells predate antibody-mediated immunity in evolutionary history. They evolved to handle parasitic worms — organisms too large for white blood cells to phagocytose. The defense strategy is mechanical expulsion.^{16 17 18}

Itch on skin causes scratching, which physically dislodges parasites embedded in or crossing the skin. Diarrhea in the gut flushes out parasites that have established themselves in the intestinal lumen. Cough in the lungs ejects parasitic larvae that have migrated through the airways. Sneezing in the sinuses expels parasites that have entered the nasal passages. Tearing and rubbing in the eyes wash and dislodge organisms that have reached the conjunctiva. Each of the symptoms patients call allergic is, in evolutionary terms, a precisely engineered parasite expulsion mechanism.

The clinical implication is significant. The mast cells producing modern allergy symptoms are not malfunctioning. They are correctly executing a defense program in response to a signal they have misinterpreted. The pollen, food protein or mold spore looks enough like a parasite to trigger the response.

This reframe matters for two reasons. First, it changes how the practitioner thinks about the patient's symptoms — not pathology, but normal physiology operating against the wrong target. Second, when the histamine workup does not resolve a hypersensitivity presentation that looks histamine-driven, the practitioner should consider that the mast cells may not be misfiring — they may be responding correctly to an actual parasitic infection the patient has not been diagnosed with. A persistent histamine picture that does not settle on protocol warrants a parasite workup, and the antiparasitic interventions discussed earlier become part of the differential rather than something separate.

Immunologic Scar

The H4 self-reinforcing cycle has a specific consequence in tissue that has been injured. When tissue is damaged — by physical trauma, by surgical incision, by burn, by significant infection, by repeated micro-injury — mast cells are part of the normal healing response.^{19 20 21} They enter the injured tissue, participate in the wound-edge approximation phase, and contribute to the inflammatory signaling that initiates repair. In clean healing, the mast cells leave as the tissue resolves, and the area returns to its baseline mast cell density.

In derailed healing, they do not leave. Healing can derail for many reasons — chronic systemic inflammation, ongoing toxin exposure, inadequate substrate for repair, repetitive re-injury, or a substrate burden that prevents the body from completing the resolution phase. When the resolution does not complete, the mast cells that came in for the acute phase persist.²² Once they persist, the H4 cycle takes over: the resident mast cells produce histamine, more mast cells are recruited, and the tissue becomes progressively more populated with histamine-producing cells. The threshold for symptomatic activation falls. The tissue becomes locally allergic and locally inflammatory long after the original injury has structurally healed.

This is what I call immunologic scar.† The framing is precise. There is a parallel to physical scar — tissue that has been changed by injury and that does not return to its original configuration — but the alteration is at the immune-cell population level rather than the structural level. The skin over a healed concussion may look normal. The brain tissue underneath, if the concussion produced a derailed inflammatory resolution, may carry an immunologic scar that lowers the threshold for inflammatory response indefinitely.

A useful way to describe what immunologic scar does to the patient is post-traumatic stress disorder at the tissue level. The tissue, like a traumatized nervous system, has been changed by the original event and remains permanently more reactive to subsequent stimuli. A small trigger that the original tissue would have handled without difficulty produces a disproportionate inflammatory response, because the local mast cell population is primed and waiting.

The list of triggers that produce immunologic scar is broad. Concussion is one of the most common and most under-recognized^{23 24} — the patient who had a concussion years ago and has carried a vague cluster of symptoms ever since (headaches, sleep changes, mood shifts, sensitivity to sensory input) is often a patient with cerebral immunologic scar. Research in TBI models shows that concussive head injury evokes persistent dural mast cell degranulation lasting at least thirty days, and that mast cells are the first responders — before microglia — in brain injuries.^{24 25} Injuries to the brain that happen while the brain is still recovering from an earlier injury are particularly susceptible. Whiplash from car accidents produces the same pattern in the cervical region, with downstream effects on autonomic function and headache patterns. Surgical trauma can produce immunologic scar at the surgical site, particularly for surgeries that involved significant tissue manipulation or complications. Significant burns leave immunologic scar in the affected skin and sometimes in deeper tissue. Repeated minor injuries — the athlete with chronic micro-trauma to a particular joint, the worker with repetitive strain — produce immunologic scar at the site of repeated insult.

The clinical implication is that previous injury history is a meaningful intake question for any patient with localized chronic inflammatory or hypersensitivity presentations. The connection between an old injury and current symptoms is not always obvious to the patient, and is rarely surfaced in conventional workups.

The intervention for immunologic scar is the same four-step protocol described below, but applied with the understanding that the work has to continue long enough to break the H4 cycle. Mast cells that have established residence in tissue do not leave quickly. The protocol has to lower the histamine load, stabilize the resident mast cells, and maintain that lowered state long enough for the cells to exit the tissue and for the tissue to return to its baseline mast cell density. This is months of work, not days.

Clinical pearl: On the topic of scars. Neural Therapy — the injection of a procaine solution under and along the length of a scar — can produce instant results on seemingly unrelated issues. If a problem appears chronologically after a surgical scar, consider it.

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Conclusion

I received a phone call many years ago from a woman to thank me. "My headache is gone," the elderly woman said. "Oh, that's nice," I replied. "No, you don't understand... my headache... it's gone," she insisted. "Ma'am, it sounds like you had a really bad headache. How long have you had it?" I asked. "Sixty years," she replied.

This is the advantage of working with first-cause principles — you get unexpected benefits.

The patient we see in front of us is likely carrying the combined weight of a dysbiotic microbiome, years of accumulated chemicals and metals in their tissues and wakes up every morning from a sleep stressed by a degree of mold that has colonized their HVAC system. These changes have been so gradual that they assume many of them are just aging. The symptoms they are presenting with are only part of the picture.

The body wants to heal. Given the right conditions — the right inputs supplied, the wrong presences removed, the right sequence respected — the body's own repair systems can do amazing things. Our job is to set the conditions. Miracles happen, and we are in the business of delivering them.

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