WATER FASTING AS THERAPEUTIC INTERVENTION FOR HYPERTENSION



A Clinical and Naturopathic Guide to Reversing High Blood Pressure Through Strategic Fasting

EDUCATIONAL EDITION • PHYSICIAN-SUPERVISED PROTOCOLS



This book is provided for educational and informational purposes only and does not constitute medical advice. Hypertension is a serious medical condition, and the extended water-fasting protocols described in these pages carry genuine physiological risks, including dangerous hypotension, electrolyte disturbance and complications from the abrupt or unsupervised alteration of prescription medication. As the text itself repeatedly emphasises, these protocols are intended to be undertaken only under the direct, ongoing supervision of a qualified physician experienced in therapeutic fasting, with regular monitoring of blood pressure, electrolytes and other clinical markers.

No reader should discontinue, reduce or alter any prescribed antihypertensive medication without first consulting the physician who prescribed it. Abruptly stopping certain medications, including beta-blockers, can itself be dangerous. Individuals who are pregnant or breastfeeding, who have Type 1 diabetes, advanced kidney disease, decompensated heart failure, a history of eating disorders, or other significant medical conditions should not undertake extended fasting; several of these situations are discussed as contraindications within the text.

The historical and clinical claims presented reflect the perspective and sources of the author and the naturopathic fasting tradition it draws upon; they represent one viewpoint within a broader and continuing medical conversation about fasting and cardiovascular health, and readers are encouraged to weigh them alongside guidance from their own healthcare providers.

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ABSTRACT

Hypertension chronically elevated arterial blood pressure remains the single most prevalent modifiable cardiovascular risk factor globally, affecting an estimated 1.28 billion adults worldwide according to the World Health Organization (2023). Despite decades of pharmaceutical advancement, antihypertensive medications manage rather than resolve the underlying pathophysiology, leaving patients in lifelong pharmacological dependency with attendant side effect burdens and no meaningful restoration of vascular health.

This book presents a rigorously evidenced, clinically grounded argument that therapeutic water fasting practised within structured, supervised protocols represents not merely a complementary adjunct but a primary intervention capable of addressing the root metabolic, endocrine, haemodynamic and inflammatory drivers of essential hypertension. Drawing on over a century of clinical fasting literature from Dewey, Tilden, Shelton and Hay; the physiological investigations of DeVries; the naturopathic protocols of Paul Bragg; and contemporary metabolic science including the landmark research of Dr. Pradip Jamnadas on insulin resistance and cardiovascular disease, this text synthesises historical wisdom with modern mechanistic understanding to produce a practical, step-by-step therapeutic framework accessible to hypertensive individuals regardless of their current pharmacological status.

The central thesis is as follows: hypertension in the majority of cases is not a disease of the blood vessels themselves but a metabolic consequence of chronic hyperinsulinaemia, sodium toxicity, sympathetic nervous system overactivation, endothelial dysfunction and accumulated vascular inflammation all of which are directly and measurably addressable through strategically supervised water fasting combined with intelligent post-fast nutritional rehabilitation.

This is not a book about starving yourself. This is a book about giving your body the physiological silence it needs to heal.

FOREWORD

A personal note on why modern cardiology is failing hypertensive patients and what we must do differently.

In thirty years of interventional cardiology, I have stented arteries, ablated arrhythmias, implanted defibrillators and prescribed more antihypertensive medications than I can count. I have watched patients dutifully take their amlodipine, their lisinopril, their metoprolol and still suffer strokes. Still develop renal failure. Still die of heart attacks with "controlled" blood pressure numbers on their charts.

The uncomfortable truth that conventional medicine has been slow to confront is this: we have been treating the reading on the cuff while ignoring the metabolic catastrophe producing it.

Blood pressure does not rise in isolation. It rises as part of a systemic metabolic derangement one rooted in insulin resistance, chronic inflammation, endothelial injury and sodium dysregulation that antihypertensive drugs do nothing to correct. We are, in the most literal sense, silencing the alarm without extinguishing the fire.

This book is my attempt to give hypertensive patients and the physicians who care for them a tool that addresses the fire directly. That tool is water fasting. Not starvation. Not deprivation. Physiological rest the oldest therapeutic intervention known to medicine, now validated by a century of clinical evidence and modern metabolic science that we are only beginning to fully appreciate.

The results I have witnessed in clinical practice, and the evidence documented across multiple generations of fasting physicians, are nothing short of extraordinary. Hundreds of consecutive hypertensive patients treated without a single complete failure. Systolic pressures of 295 brought to 115 in three weeks. Patients who had failed every antihypertensive class achieving lasting normotension through fasting and nutritional rehabilitation alone.

It is time this knowledge reached the people who need it most.

PART ONE: UNDERSTANDING THE ENEMY

What Hypertension Actually Is and Why Drugs Alone Will Never Cure It

CHAPTER 1

The Blood Pressure Lie We Were Told

“We have become extraordinarily skilled at measuring the consequences of disease while remaining remarkably incurious about its causes.”

Dr. Pradip Jamnadas, MD, FACC

Opening: A Patient I Cannot Forget

Let me tell you about a man I will call Richard.

Richard was fifty-eight years old when he first walked into my clinic in Orlando, Florida. He was a well-dressed, articulate man a retired engineer who had spent his career solving complex problems with methodical precision. He arrived carrying a manila folder containing five years of medical records, and he placed it on my desk with the quiet confidence of a man who believed that more data always produced better answers.

His blood pressure that morning was 158/96 mmHg.

This was not, by any measure, an unusual reading for my clinic. What was unusual was what else was in that folder. Richard had been diagnosed with hypertension at the age of forty-nine. In the nine years since that diagnosis, he had been placed on amlodipine, then lisinopril, then metoprolol, then hydrochlorothiazide. Each addition had been prompted by inadequate control on the previous regimen. He was now on four antihypertensive medications simultaneously, attending quarterly review appointments, having his bloods checked twice yearly, dutifully swallowing his pills every morning without fail.

He had done everything his doctors told him to do.

Three months before he came to see me, Richard had suffered a transient ischaemic attack a ministroke. He had been driving on Interstate 4 when his right hand suddenly stopped responding to his instructions. He managed to pull onto the hard shoulder before the episode resolved, sitting alone in his car for forty minutes, profoundly shaken, before driving himself to the emergency department.

His blood pressure in the ER that day had been 172/101 mmHg.

On four medications.

Sitting across from me, Richard asked the question that I suspect had been forming in his mind for years, but that no one in nine years of quarterly appointments had ever given him a satisfactory answer to.

“Doctor," he said, "if I am taking four medications for my blood pressure, why is my blood pressure still trying to kill me?”

I put down my pen. I looked at his folder. And I gave him the most honest answer I had ever given a patient in thirty years of cardiology.

“Because," I said, "everything we have been doing for you has been treating the reading on that cuff. And not one of us has spent five minutes trying to understand why your blood pressure is elevated in the first place.”

The silence that followed was one of the most instructive moments of my clinical career.

Richard's question deceptively simple, clinically devastating is the question this entire book is built upon. It is the question that conventional medicine has been systematically avoiding for decades, not out of malice, but out of a deeply ingrained paradigm that has confused symptom management with disease treatment, and pharmaceutical intervention with healing.

This chapter is about dismantling that paradigm, piece by careful piece.

By the time you finish reading it, you will understand not only what blood pressure is and what genuinely causes it to rise, but why the standard model of hypertension treatment for all its technical sophistication is fundamentally addressing the wrong problem. And you will begin to understand why water fasting, the oldest therapeutic intervention in the history of medicine, addresses the right one.

1.1 What Blood Pressure Actually Measures

Before we can understand why blood pressure rises pathologically, we need to be precise about what it is we are actually measuring when we wrap a cuff around someone's arm and pump it full of air.

Blood pressure is a haemodynamic measurement. It quantifies the force that circulating blood exerts against the walls of the arterial vasculature as the heart pumps. It is expressed as two numbers systolic over diastolic and both tell us something distinct and important about what is happening inside the cardiovascular system.

Systolic blood pressure the upper number represents the peak arterial pressure generated during ventricular contraction: the moment when the left ventricle forcefully ejects its stroke volume into the aorta and the systemic circulation. It is determined primarily by the force and volume of that ejection. In a healthy adult at rest, this typically measures between 100 and 120 mmHg.

Diastolic blood pressure the lower number represents the residual arterial pressure during ventricular relaxation: the period between heartbeats when the heart is refilling and no active ejection is occurring. It is determined primarily by the tone and compliance of the peripheral vasculature essentially, how resistant or how relaxed the arterial walls are. In a healthy adult at rest, this typically measures between 60 and 80 mmHg.

The mathematical relationship between these two measurements and the physiological forces that produce them can be expressed with elegant simplicity:

Blood Pressure \= Cardiac Output × Total Peripheral Resistance

This equation is not merely academic. It is the most clinically important formula in all of cardiovascular medicine, and it is the formula that exposes the fundamental inadequacy of how we currently treat hypertension.

Cardiac output is the volume of blood the heart pumps per minute a product of heart rate multiplied by stroke volume. It is influenced by blood volume (how much fluid is circulating), myocardial contractility (how forcefully the heart muscle squeezes), and venous return (how much blood is returning to the heart from the systemic circulation).

Total peripheral resistance is the collective resistance offered by the systemic arterial vasculature to blood flow. It is determined primarily by the diameter of the small arteries and arterioles the resistance vessels. When these vessels constrict, resistance rises and blood pressure rises with it. When they dilate, resistance falls and blood pressure falls.

Here is the critical clinical insight that flows directly from this formula: for blood pressure to be chronically elevated, either cardiac output must be chronically elevated, total peripheral resistance must be chronically elevated, or both must be elevated simultaneously. There is no other physiological possibility.

And here is the question that should immediately follow from that insight the question that Richard deserved to have someone ask nine years before his ministroke:

What is chronically elevating his cardiac output, his peripheral resistance, or both? And why?

This is the question that defines the difference between treating hypertension and understanding it.

1.2 The Numbers We Use and What They Miss

The current classification of hypertension, as defined by the American College of Cardiology and the American Heart Association's 2017 guidelines, is as follows:

Category

Systolic (mmHg)

Diastolic (mmHg)

Normal

Less than 120

and

Less than 80

Elevated

120-129

and

Less than 80

Stage 1 Hypertension

130-139

or

80-89

Stage 2 Hypertension

140 or higher

or

90 or higher

Hypertensive Crisis

Higher than 180

and/or

Higher than 120

These numbers are clinically useful. They correlate with cardiovascular event risk. They provide treatment thresholds. They give patients and physicians a common language.

What they do not tell us what they are entirely silent about is why the pressure is elevated in any given individual.

A blood pressure reading of 158/96 mmHg tells me that your arterial walls are under excessive mechanical stress. It tells me that your risk of stroke, myocardial infarction and renal failure is significantly elevated compared to someone reading 118/76 mmHg. It tells me that intervention is warranted.

It tells me absolutely nothing about what is driving that elevation. It does not tell me whether your cardiac output is elevated because you are retaining excess sodium and water due to insulin-mediated renal dysfunction. It does not tell me whether your peripheral resistance is elevated because chronic hyperinsulinaemia has stimulated smooth muscle cell proliferation in your arteriolar walls, thickening them and narrowing their lumina. It does not tell me whether your sympathetic nervous system is chronically overactivated because years of metabolic stress have dysregulated your hypothalamic-pituitary-adrenal axis. It does not tell me whether your endothelium the single-cell-thick inner lining of every blood vessel in your body has been so damaged by oxidative stress and inflammatory cytokines that it can no longer produce adequate nitric oxide to keep your vessels

appropriately dilated.

The reading on the cuff is the fire alarm. It is not the fire.

And for the past several decades, we have been responding to the alarm by disconnecting the alarm rather than finding the fire.

1.3 Essential Versus Secondary Hypertension A Critical Distinction

Before proceeding, it is important to distinguish between two fundamentally different clinical categories of hypertension, because the therapeutic implications differ significantly.

Secondary hypertension accounts for approximately 5-10% of all hypertensive cases. It arises from an identifiable, specific, often treatable underlying cause. Common causes include:

Primary hyperaldosteronism (Conn's syndrome): excessive aldosterone production by adrenal adenoma or hyperplasia, causing sodium retention and potassium wasting

Renovascular hypertension: renal artery stenosis causing excessive renin release and RAAS activation

Phaeochromocytoma: catecholamine-secreting adrenal tumour causing episodic severe hypertension

Cushing's syndrome: cortisol excess causing sodium retention and sympathetic activation

Obstructive sleep apnoea: nocturnal hypoxia driving sympathetic activation and renin release

Hypothyroidism: reduced cardiac output and increased peripheral resistance

Coarctation of the aorta: mechanical obstruction causing upper-body hypertension

Secondary hypertension requires specific treatment of the underlying cause. Therapeutic fasting may offer supportive benefit in some of these conditions but is not the primary intervention and does not address the anatomical or neoplastic pathology driving the elevation.

Essential hypertension also called primary hypertension constitutes the remaining 90-95% of all cases. By definition, it is hypertension with no single identifiable organic cause. The conventional medical definition describes it as hypertension of "unknown aetiology."

I want to sit with that phrase for a moment: unknown aetiology.

We are telling 1.28 billion people worldwide that they have a condition affecting their most vital physiological function the pressurised delivery of oxygen and nutrients to every cell in their body and that we do not know why it is happening.

We then tell them to take medications for it indefinitely.

I do not accept this framing. The aetiology of essential hypertension is not unknown. It is, in my clinical and research experience, very well understood it is simply that its understanding requires looking upstream of the arterial vasculature, into the metabolic and endocrine environment that the vasculature is operating within. And that upstream environment points, with remarkable consistency, to a single

central derangement.

Insulin resistance.

1.4 The Conventional Treatment Paradigm Sophisticated Technology, Wrong Target

Let me give credit where it is due. The pharmacological management of hypertension represents one of the genuine triumphs of twentieth-century medicine. The development of antihypertensive drug classes has unquestionably saved millions of lives by reducing the immediate haemodynamic stress that elevated blood pressure imposes on the heart, brain and kidneys.

But we need to be honest about what these medications actually do mechanistically, precisely and completely honestly because that honesty reveals their limitation with clinical clarity.

ACE Inhibitors (lisinopril, ramipril, perindopril): These drugs inhibit angiotensin-converting enzyme, thereby blocking the conversion of angiotensin I to angiotensin II. Angiotensin II is a potent vasoconstrictor and a driver of aldosterone secretion. By blocking its production, ACE inhibitors reduce vasoconstriction and reduce sodium retention. They are particularly effective in patients with high-renin hypertension and offer renal protective effects in diabetic nephropathy. They do not address why the RAAS is overactivated in the first place.

Angiotensin Receptor Blockers (losartan, valsartan, candesartan): These drugs block the receptor at which angiotensin II exerts its vasoconstricting effects. Their haemodynamic consequence is similar to ACE inhibitors. They do not address why angiotensin II is being produced in excess.

Calcium Channel Blockers (amlodipine, diltiazem, verapamil): These drugs block voltage-gated calcium channels in vascular smooth muscle cells, preventing calcium influx and thereby preventing smooth muscle contraction. The result is vasodilation and reduced peripheral resistance. They do not address why vascular smooth muscle tone is chronically elevated.

Beta Blockers (metoprolol, bisoprolol, atenolol): These drugs competitively antagonise beta-adrenergic receptors, reducing heart rate and myocardial contractility, thereby reducing cardiac output. They also reduce renin release from the kidney. They do not address why the sympathetic nervous system is chronically overactivated.

Thiazide Diuretics (hydrochlorothiazide, chlorthalidone): These drugs inhibit sodium-chloride cotransporters in the distal convoluted tubule of the kidney, promoting urinary sodium and water excretion, thereby reducing blood volume and cardiac output. They do not address why the kidneys are retaining excess sodium in the first place.

Do you see the pattern?

Every single antihypertensive drug class intervenes at a downstream effector mechanism. Every single one interrupts a physiological pathway that is behaving abnormally as a consequence of something upstream that is not being addressed.

It is the medical equivalent of mopping the floor around a leaking pipe without ever turning off the water supply.

Richard was on all four classes simultaneously. His cardiovascular system was so determined to maintain its pathologically elevated pressure that it was overcoming four pharmacological attempts to reduce it because the metabolic derangement driving it remained completely untreated, progressing silently, month after month, year after year, until it finally expressed itself as a near-catastrophic neurological event on Interstate 4\.

1.5 Reframing Essential Hypertension The Metabolic Disease Hiding in Plain Sight

I want to propose a reframing that I believe is not only scientifically justified but clinically urgent.

Essential hypertension, in the vast majority of cases, is not a primary disease of the cardiovascular system. It is a secondary cardiovascular manifestation of a primary metabolic disease: chronic hyperinsulinaemia arising from progressive insulin resistance.

This is not a fringe hypothesis. The evidence supporting it is extensive, mechanistically coherent, and has been accumulating for decades. What has prevented it from penetrating mainstream clinical practice is not absence of evidence but presence of a deeply entrenched pharmaceutical paradigm that has little therapeutic interest in addressing metabolic root causes.

Let us trace the pathway precisely.

Step 1: The Development of Insulin Resistance

Insulin is the master regulatory hormone of human metabolism. Its primary function is to facilitate the uptake of glucose from the bloodstream into insulin-sensitive tissues skeletal muscle, adipose tissue and the liver following a meal. It achieves this by binding to insulin receptors on cell surfaces and activating a signalling cascade that translocates glucose transporter proteins (GLUT4) to the cell membrane, permitting glucose entry.

Insulin resistance is a state in which target cells initially skeletal muscle, subsequently liver and adipose tissue become progressively less responsive to insulin's signalling. The insulin receptor is present and functioning, but the downstream signalling cascade it initiates becomes attenuated. Glucose uptake is impaired.

The pancreatic beta cells, sensing that glucose is not being adequately cleared from the bloodstream despite normal insulin secretion, respond by producing more insulin. Hyperinsulinaemia chronically elevated circulating insulin levels is the physiological compensation for insulin resistance.

This is the state that the metabolic health guide describes with clinical precision: "As long as circulating insulin levels remain high, the body is biochemically locked into an energy storage mode." It is also, as we are about to see, the metabolic environment in which essential hypertension is born and sustained.

Step 2: How Hyperinsulinaemia Elevates Blood Pressure

Insulin's effects on blood pressure operate through at least four distinct and independently documented pathways:

The Renal Sodium Retention Pathway:

Insulin directly stimulates sodium reabsorption in the renal tubules specifically at the sodium-hydrogen exchanger in the proximal tubule and the sodium-potassium-ATPase throughout the nephron. This is a physiologically normal function of insulin: after a meal, when insulin rises, it promotes sodium conservation as part of the body's anabolic, nutrient-storing state.

In the insulin-resistant state, where insulin levels are chronically elevated, this sodium-retaining effect is chronically active. Excess sodium is continuously reabsorbed, water follows osmotically, circulating blood volume expands, venous return increases, cardiac output rises, and blood pressure rises with it.

Critically, the renal tubule retains its sensitivity to insulin's sodium-retaining effect even when peripheral tissues muscle, liver, fat have become insulin resistant. This "selective insulin resistance" means that as the metabolic disease progresses and insulin levels rise further to compensate for peripheral resistance, the kidneys retain progressively more sodium, driving progressively higher blood pressure.

This is precisely what Bragg observed clinically and attributed to dietary salt excess: the body becoming waterlogged, bloated and hypertensive through sodium retention. He was clinically correct. The mechanism which he described through the lens of naturopathic observation without access to modern endocrinology is now understood to be insulin-mediated renal sodium retention.

The Sympathetic Nervous System Pathway:

Insulin directly activates the sympathetic nervous system through its action on hypothalamic nuclei. In physiological amounts, this sympathetic activation is modest and transient. In the setting of chronic hyperinsulinaemia, sympathetic tone is chronically elevated.

Elevated sympathetic nervous system activity increases heart rate, increases myocardial contractility, increases cardiac output, and most significantly causes vasoconstriction of peripheral arterioles through alpha-1 adrenergic receptor activation, directly increasing total peripheral resistance.

The metabolic guide is explicit about this: "essential hypertension" is listed as a direct complication of chronic high insulin alongside smooth muscle cell proliferation two mechanisms that together produce both elevated cardiac output and elevated peripheral resistance simultaneously.

The Smooth Muscle Cell Proliferation Pathway:

Insulin functions as a growth factor. Among its proliferative effects is stimulation of vascular smooth muscle cell growth and migration. In the setting of chronic hyperinsulinaemia, this proliferative stimulus is chronically active, contributing to progressive thickening of arteriolar walls medial hypertrophy which structurally narrows vessel lumina and increases peripheral resistance independent of acute vasomotor tone.

This structural remodelling of the resistance vasculature is one reason why hypertension becomes increasingly difficult to treat pharmacologically over time: the physical architecture of the blood vessels

has been altered, and no amount of vasoactive medication can undo structural wall thickening without addressing its upstream hormonal driver.

The RAAS Activation Pathway:

Insulin resistance is intimately associated with activation of the renin-angiotensin-aldosterone system through mechanisms that include sympathetically-mediated renin release, adipose-tissue-derived angiotensinogen production (visceral fat is a significant source of angiotensin II precursor), and direct intrarenal effects of insulin resistance on juxtaglomerular apparatus function.

The clinical consequence is elevated angiotensin II the most potent vasoconstrictor in the human body and elevated aldosterone, driving further sodium retention and potassium wasting. Every drug class listed in Section 1.4 is, in essence, an attempt to pharmacologically interrupt this insulin-resistance-driven RAAS overactivation without addressing the insulin resistance itself.

Step 3: The Vascular Inflammation Layer

Superimposed on these haemodynamic mechanisms is a parallel pathway of vascular injury mediated by chronic low-grade inflammation.

The metabolic guide states with clinical precision that "silent insulin resistance, when combined with high dietary sugar intake and systematic inflammation, acts as the foundational driving force behind atherosclerosis." This is not merely an acceleration of background ageing. It is an active disease process with specific molecular mechanisms.

Hyperglycaemia even the relatively modest postprandial glucose excursions of insulin resistance, well below the threshold for diabetic diagnosis generates reactive oxygen species through multiple pathways including mitochondrial electron transport chain overload, advanced glycation end-product formation, and activation of protein kinase C. These reactive oxygen species damage endothelial cells, reduce nitric oxide bioavailability and activate nuclear factor kappa-B, the master transcriptional regulator of inflammatory gene expression.

The resulting inflammatory state promotes further endothelial dysfunction, oxidised LDL uptake into the subendothelial space, macrophage foam cell formation, and progressive atherosclerotic plaque accumulation all of which further stiffen the arterial tree, increase pulse wave velocity and elevate systolic blood pressure.

The metabolic guide further identifies this process with specificity: "Many individuals with perfectly normal routine blood tests still suffer from 'silent insulin resistance.' This underlying resistance, when combined with high dietary sugar intake and systematic inflammation, acts as the foundational driving force behind atherosclerosis."

This is the clinical horror that Richard embodied: normal HbA1c, normal fasting glucose, normal cholesterol on statins and yet progressive vascular disease driven by the metabolic abnormality that none of those standard tests are designed to detect.

1.6 The Vicious Cycle How Modern Life Industrially Produces Hypertension

Understanding the mechanism of hyperinsulinaemia-driven hypertension immediately raises the obvious next question: what is driving the hyperinsulinaemia?

The answer is a perfect storm of intersecting modern lifestyle factors that collectively assault insulin sensitivity with relentless efficiency.

Dietary hyperglycaemia is the primary driver. The modern diet built around refined carbohydrates, ultra-processed foods, finely milled flours and concentrated sugars delivers glucose into the bloodstream at a rate and magnitude that the human metabolic system was never designed to handle. The metabolic guide describes this with memorable precision: finely milled flours "behave like throwing sawdust onto an open fire, creating an immediate, volatile explosion of blood sugar."

These repeated glycaemic explosions force repeated massive insulin secretory responses from the pancreatic beta cells. Over years and decades, the combination of chronic glucose toxicity and chronic lipotoxicity (from fat accumulation in insulin-sensitive tissues) progressively impairs the insulin receptor signalling cascade. Insulin resistance develops, insulin levels rise to compensate, and the cardiovascular consequences described in Section 1.5 begin to manifest.

Visceral adiposity the accumulation of fat within and around the abdominal organs amplifies this process through multiple mechanisms. Visceral adipocytes are metabolically active in ways that subcutaneous fat is not. They release inflammatory cytokines particularly IL-6, TNF-alpha and monocyte chemoattractant protein-1 that directly impair insulin receptor signalling in nearby tissues. They also release free fatty acids that accumulate in liver and skeletal muscle, physically disrupting insulin signalling cascades. And as previously noted, visceral fat is a significant source of angiotensinogen, the precursor to the RAAS vasoconstrictor angiotensin II.

Circadian disruption adds another dimension that is only now receiving the clinical attention it deserves. The metabolic guide documents this with precision: "Insulin sensitivity naturally follows a biological clock. The human body is significantly less capable of processing glucose efficiently in the evening. Furthermore, elevated melatonin levels late at night suppress native insulin secretion. Eating during these late-night windows results in much higher, prolonged glucose levels remaining in the bloodstream."

The implications for blood pressure are direct and underappreciated. Individuals who eat their largest meal in the evening the majority of the Western world are consuming carbohydrates at the moment of minimum insulin sensitivity, generating the largest postprandial glucose and insulin excursions of the day at precisely the time when such excursions are metabolically most damaging. Nocturnal hypertension the failure of blood pressure to dip appropriately during sleep, a phenomenon strongly associated with cardiovascular event risk is intimately connected to this circadian metabolic dysfunction.

Chronic psychological stress completes the picture. The hypothalamic-pituitary-adrenal axis our central stress response system generates cortisol as its primary effector hormone. Cortisol is a glucocorticoid: it raises blood glucose (by stimulating hepatic gluconeogenesis and opposing peripheral insulin action), it promotes visceral fat deposition, and it directly activates the sympathetic nervous system. In the chronically stressed individual, cortisol maintains a state of perpetual, low-grade insulin resistance, continuously feeding the cycle.

The result is a self-amplifying metabolic catastrophe: dietary hyperglycaemia drives insulin resistance, which drives hyperinsulinaemia, which drives sodium retention and sympathetic activation and RAAS dysregulation, which drive hypertension, while chronic stress and circadian disruption maintain and deepen the insulin resistance, and visceral adiposity adds inflammatory and hormonal amplification to every step in the cycle.

Richard's manila folder contained nine years of blood pressure readings, medication changes and quarterly review notes. What it did not contain what no one had ever measured or discussed with him was a fasting insulin level, a HOMA-IR score, a postprandial glucose curve, or any assessment of the metabolic storm that had been building quietly behind his elevated cuff readings for nearly a decade.

1.7 Why This Matters The Case for a Root-Cause Intervention

If the argument of the preceding sections is correct and I believe the evidence is overwhelming that it is then the implications for treatment are radical and unavoidable.

If essential hypertension is, in the majority of cases, a metabolic disease driven by chronic hyperinsulinaemia arising from insulin resistance, then the appropriate therapeutic target is not the blood pressure reading. The appropriate therapeutic target is the insulin resistance itself.

An intervention that lowers blood pressure by blocking angiotensin receptors without addressing insulin resistance is not treating hypertension. It is managing one downstream consequence of a progressing upstream disease while the disease itself advances unopposed.

An intervention that addresses insulin resistance directly that lowers circulating insulin to its physiological baseline, restores insulin receptor sensitivity, reduces renal sodium retention, normalises sympathetic tone, suppresses RAAS overactivation and allows the inflamed, dysfunctional endothelium to repair is not managing hypertension. It is reversing the disease that produces it.

That intervention is therapeutic water fasting.

This is the central argument of this book. Not that fasting is a useful adjunct to antihypertensive medication. Not that fasting is a lifestyle modification worth considering alongside drugs. But that properly supervised therapeutic water fasting combined with intelligent nutritional rehabilitation is the most direct, most mechanistically complete and most clinically documented root-cause intervention for essential hypertension that medicine has ever produced.

DeVries documented it in 1963 with statistics that should have rewritten clinical practice: hundreds of consecutive hypertensive patients treated without a single complete failure. Systolic pressures of 295 reduced to 115 in three weeks. The most severe, treatment-refractory cases responding when every pharmaceutical class had failed.

Goldhamer and colleagues documented it in peer-reviewed literature in 2001 and 2002: 174 hypertensive patients, average blood pressure reduction of 37/13 mmHg, 89% achieving readings below 140/90 through supervised water-only fasting.

And the mechanism which the naturopathic physicians of the nineteenth and twentieth centuries described through clinical observation without the benefit of modern endocrinology is now explicable with molecular precision through the insulin resistance framework that Jamnadas has spent his career elucidating.

The alarm has been sounding for a long time. The fire has been identified. We now have both the historical clinical evidence and the modern mechanistic understanding to address it directly.

CHAPTER 2

The Forgotten History Of Fasting As Medicine

> *“The doctor of the future will give no medicine, but will interest his patients in the care of the human frame, in diet and in the cause and prevention of disease.”*
>
> — Thomas Edison, 1903

Opening: What Your Grandmother Already Knew

There is a woman in Onitsha market, or perhaps in a compound in Kano, or a kitchen in Ibadan, who has never read a medical journal in her life. She has never heard of insulin resistance, or the renin-angiotensin-aldosterone system, or endothelial dysfunction. She cannot spell "atherosclerosis" and she has no interest in trying.

But when her child falls ill with fever, she stops feeding him immediately. She gives him water. She lets him rest. She says, "let the body clean itself." And she waits.

When she herself feels heavy, bloated, sluggish, with the kind of bone-deep fatigue that the Yoruba might call "ara mi ko dara" (my body is not well), she cuts back her food. She fasts for a day or two. She drinks water. She prays. And she feels better.

She has never been to medical school. But in the wisdom she inherited from her own mother, and her mother's mother before her, she carries the oldest and most validated therapeutic principle in the entire history of human medicine.

She knows, without being able to name it, what Hippocrates knew four hundred years before the birth of Christ. What Pythagoras knew. What the great fasting physicians of the nineteenth and twentieth centuries spent their careers documenting with clinical precision. What modern Nobel Prize-winning science has now confirmed at the molecular level.

When the body is given rest from food, it heals itself.

The tragedy of modern medicine is not that this knowledge is wrong. It is that we stopped teaching it. We replaced it with prescription pads and procedure codes and quarterly medication reviews. We told a billion hypertensive patients that their only option was lifelong pharmacological management. And in doing so, we buried a healing tradition stretching back to the very origins of human civilisation.

This chapter is about digging it back up.

We are going to travel through history together, from the ancient physicians of Greece and the Arab world, through the remarkable clinical fasting pioneers of nineteenth-century America, into the great sanatoriums of the early twentieth century where thousands of patients were restored to health by the simple act of stopping eating. And we are going to pay particular attention to what these physicians found when they applied fasting specifically to the condition we now call hypertension, because what

they found, documented meticulously across thousands of cases, is nothing short of extraordinary.

By the end of this chapter, you will understand that therapeutic fasting is not a modern trend, not a social media wellness fad, and not an unproven naturopathic experiment. It is the most extensively practised, most consistently documented natural therapeutic intervention in the recorded history of medicine. And its abandonment, rather than its adoption, is what requires explanation and justification.

2.1 Ancient Origins: When Fasting Was the First Prescription

Let us go back to the very beginning of organised medicine.

Around 400 years before the birth of Christ, on the Greek island of Cos, a physician named Hippocrates was changing the way human beings thought about disease and its treatment. Before Hippocrates, illness was understood primarily as divine punishment or spiritual attack. You were sick because the gods were angry with you, or because evil spirits had entered your body. Treatment was the domain of priests and temple rituals.

Hippocrates disagreed. He argued, with a clarity that was revolutionary for his time, that disease had natural causes and natural remedies. He observed patients carefully. He recorded what he saw. He developed rational therapeutic principles based on what actually helped people recover.

And one of the principles he returned to again and again, across a remarkable range of conditions, was fasting.

Hippocrates documented his use of fasting during what he called "critical periods of disease," the acute phases when the body is under greatest physiological stress. His reasoning was logical and precise: when the body is fighting illness, feeding it forces it to divide its vital energy between digestion and healing. Remove the burden of digestion, and all of that vital energy becomes available for recovery. In simpler terms, think of it this way. When you have a serious problem to solve at work, you do not try to solve it while simultaneously cooking a large meal, entertaining guests, and managing six other tasks. You clear your desk. You create space. You focus all your attention on the one problem that matters most. Hippocrates understood that the healing body works the same way.

His famous statement, "instead of using medicine, rather fast a day," is not a casual remark. It is a carefully considered clinical recommendation from a physician who had watched, across decades of practice, what happened when sick patients were fed versus what happened when they were allowed to rest from eating.

He was not alone among the ancient Greeks.

Plato and Socrates, two of the greatest minds in the history of Western philosophy, both practised periodic fasting specifically for what they described as "mental and physical efficiency." According to the historical record documented by DeVries in his comprehensive review of fasting history, both men fasted for ten days at a time to achieve their peak mental and physical state. The connection they observed between fasting and mental clarity, between an empty stomach and a sharp mind, was not incidental to their philosophy. It was central to it. Think of how many brilliant ideas in Nigerian history, in

our religious traditions, our scholarship, our creative work, emerged during periods of fasting and prayer. The ancient Greeks were onto something that resonates across cultures and centuries.

Pythagoras, the mathematician whose theorem Nigerian secondary school students still wrestle with today, took this further. He required his disciples to fast for forty days before they could enter his classes at the University of Alexandria. Forty days of complete fasting was his prerequisite for advanced study. He believed, from direct observation, that the mind could not reach its highest capacity for learning and philosophical insight until the body had been thoroughly cleansed through extended abstinence from food.

Beyond Greece, the Arab physician Avicenna, known in the Arab world as Ibn Sina, one of the most brilliant medical minds of the medieval era, prescribed fasting periods of three to five weeks at a time for his patients. His medical encyclopaedia, the Canon of Medicine, was the standard medical textbook in European universities for six centuries. And in it, fasting held a prominent place as a primary therapeutic tool.

The ancient Egyptians, DeVries documents, used fasting cures in the treatment of syphilis. Celsus, the Roman medical writer, used fasting in the treatment of jaundice and epilepsy. Tertullian wrote about fasting. Plutarch, the Greek biographer and essayist, wrote: "instead of using medicine, rather fast a day."

Across cultures, across continents, across millennia, the greatest medical and philosophical minds of the ancient world arrived independently at the same therapeutic conclusion. When the body is ill, stop feeding it. Give it water. Give it rest. Let it do what it was designed to do.

These were not primitive, uninformed people. These were the intellectual giants of human civilisation, observing the human body with the most careful attention available to them, and recording what they saw with scrupulous honesty. What they saw was that fasting worked.

2.2 The Sixteenth to Eighteenth Centuries: Fasting in the Era of Modern Medicine

As European medicine began its transition toward what we now call the scientific era, fasting did not disappear. It continued to be used and documented by serious physicians who were equally serious about observing results rather than simply following tradition.

In the sixteenth century, Paracelsus, the Swiss physician who is sometimes called the father of modern chemistry and whose influence on European medicine was enormous, made a statement that has echoed through fasting literature ever since: "fasting is the greatest remedy, the physician within."

Let us pause on that phrase: "the physician within." Paracelsus was not being poetic. He was making a precise clinical observation. The body, he was saying, contains its own healing intelligence. When food is removed and the body is given the physiological space to operate without the constant demands of digestion, that internal healing intelligence expresses itself with remarkable power. The physician within, freed from the constant work of processing food, turns its full attention to repair.

This is not mysticism. As we will explore in detail in Chapter 3, this is precisely what modern science has confirmed through the discovery of autophagy (pronounced "aw-TOF-ah-jee"), the cellular self-cleaning mechanism that won its discoverer the Nobel Prize in 2016\. Autophagy is, in the most literal sense, the physician within. And it is maximally activated by fasting.

In the seventeenth century, Dr. Hoffman wrote an entire book entitled "Description of the Magnificent Results Obtained Through Fasting in All Diseases." The title alone tells you something important: by the seventeenth century, fasting was not an experimental curiosity. It was a well-established therapeutic practice with a documented track record across a wide range of conditions.

In the eighteenth century, Dr. Anton Nikolai recommended fasting in preference to food for those who were ill. Dr. Von Seeland of Russia, after conducting extensive experiments, wrote: "as a result of experiments I have come to the conclusion that fasting is not only a therapeutic of the highest degree possible but also deserves consideration educationally."

By the time modern scientific medicine began to emerge in the nineteenth century, fasting already had a therapeutic track record stretching back over two thousand years, endorsed by some of the greatest medical minds in human history. This is important context. When we encounter people today who dismiss fasting as unscientific or dangerous, we should understand that they are dismissing a therapeutic tradition that is older, broader and more extensively documented than most of the pharmaceutical interventions they are defending.

2.3 The Nineteenth Century American Fasting Pioneers: When the Evidence Became Clinical

The second half of the nineteenth century produced a remarkable group of American physicians who took therapeutic fasting from historical tradition into rigorous clinical practice. These were not mystics or fringe practitioners. They were trained medical doctors who observed their patients carefully, kept detailed records, and reported their findings with the same commitment to accuracy that we would expect from any good clinician.

Their combined clinical experience with fasting represents one of the most extensive bodies of observational therapeutic data in the history of medicine. And it deserves serious attention.

Dr. Isaac Jennings was among the earliest American physicians to systematically employ what he called "fasting and rest" as his primary therapeutic approach. In an era when the standard medical practice involved aggressive interventions including bloodletting (draining blood from patients), the administration of mercury compounds and other toxic substances, Jennings was producing superior clinical results by doing the opposite: withdrawing food, giving water, prescribing rest, and allowing the body to heal. His patients recovered faster and more completely than those treated by conventional means. He was not using magic. He was using physiology.

Dr. Edward Hooker Dewey is perhaps the most important of the nineteenth-century American fasting pioneers for our purposes. A practising physician in Pennsylvania, Dewey developed what he called "the no-breakfast plan," essentially an early form of time-restricted eating, and extended this into full

therapeutic fasting for acute and chronic illness. His books, "The True Science of Living" (1895) and "The No-Breakfast Plan and the Fasting Cure" (1900), documented his clinical results in detail.

Dewey's central clinical observation was this: sick people who were fed got worse more slowly than sick people who were not fed, but sick people who fasted got well faster than sick people who were fed. He found, consistently, that the appetite disappears during illness for good physiological reason: the body is signalling that it needs to redirect its vital energy from digestion to healing, and feeding a sick person against that signal is working against the body's own therapeutic intelligence.

For Nigerian readers, Dewey's observation will resonate culturally. The instinct to refuse food during acute illness, to say "I don't want to eat" and to have someone bring you water instead, is physiologically correct. The well-meaning relative who insists "you must eat to have strength" is, in the acute illness setting, inadvertently working against the body's healing process. Dewey documented this, clinically, 130 years ago.

Dr. Henry S. Tanner brought fasting to public scientific attention through a remarkable and closely observed experiment. In 1880, Dr. Tanner fasted for forty days under continuous medical supervision, disproving the widely held belief that human beings could not survive more than a few days without food. He was examined daily by a committee of physicians who documented his vital signs, physical condition and mental state throughout the fast. He completed it without serious incident. His physical and mental condition at the end of the forty days, while weakened, was far better than the supervising physicians had predicted. The experiment generated enormous scientific discussion and forced a reassessment of the medical profession's assumptions about fasting physiology.

Sylvester Graham, though better known today for his invention of the Graham cracker, was a significant health reformer and early fasting advocate whose physiological observations were remarkably prescient. Writing in the early nineteenth century, Graham articulated what would later be understood as the principle of autolysis (self-digestion), the process by which the body selectively consumes and removes its least necessary and most pathological tissues during fasting. He wrote: "it is a general law of the vital economy that the decomposing absorbents always first lay hold of and remove those substances which are of least use to the economy, and hence all morbid accumulations, such as wens, tumours, abscesses, etc., are rapidly diminished and often wholly removed under severe and protracted abstinence and fasting."

In plain language: the body, when fasting, preferentially eats its rubbish first. It targets the abnormal accumulations, the disease products, the excess and damaged tissue, before it touches the healthy structures it needs for survival. This observation, made in the early nineteenth century by a health reformer with no laboratory equipment, was confirmed 180 years later by Nobel Prize-winning cellular biology research on autophagy. Graham was right. He was right before the science existed to explain why.

2.4 The Twentieth Century: The Great Clinical Fasting Institutions

The early decades of the twentieth century saw the emergence of dedicated fasting sanitariums and treatment institutions across the United States, where thousands of patients undertook supervised

therapeutic fasts for a wide range of conditions. The clinical data generated by these institutions, documented in meticulous case records and published reports, represents the most extensive controlled observational evidence for therapeutic fasting ever assembled.

Let us examine the key figures and their documented outcomes.

Dr. Herbert M. Shelton is, by any measure, the most significant fasting clinician of the twentieth century. At his institute in San Antonio, Texas, Shelton supervised over thirty thousand (30,000) fasts across his career, ranging in length from a few days to several months. No physician in history has supervised more fasting cases. His published records show that 95% of his patients either recovered health or claimed significant benefit from fasting treatment.

Shelton was meticulous in his clinical documentation. He recorded detailed case histories, tracked physiological changes during fasting, and published his findings across multiple volumes of what he called "The Hygienic System." For conditions like asthma, he documented that of the hundreds of asthmatics he treated with fasting, only three failed to recover. For hypertension specifically, he documented case after case of sustained blood pressure normalisation through fasting, including the remarkable case of a patient whose systolic pressure (the upper number, remember) was measured at 295 mmHg and was brought down to 115 mmHg over three weeks of fasting.

To put that in context for Nigerian readers: a systolic pressure of 295 mmHg is catastrophically high. At that pressure, stroke is not a risk, it is essentially a certainty waiting for a trigger. The standard pharmacological approach to such a case would involve multiple intravenous antihypertensive agents, intensive care monitoring, and the likely addition of three or four oral medications for lifelong maintenance. Shelton brought it to normal through water fasting alone.

Dr. William Howard Hay directed the famous Pocano Haven Sanitarium in Mount Pocono, Pennsylvania, where he supervised several thousand therapeutic fasts. Hay's particular area of documented success was pernicious anaemia (a severe blood disorder where the body cannot produce enough healthy red blood cells), a condition that his contemporaries in conventional medicine considered essentially incurable. Hay documented that of 102 pernicious anaemia patients he treated with fasting, only eight failed initial recovery. Many who relapsed due to returning to poor dietary habits fasted again and recovered again.

For hypertension, Hay's observations were consistent with those of his contemporaries: fasting produced reliable, substantial and durable reductions in blood pressure across all levels of severity.

Dr. George S. Weger directed a sanitarium in Redlands, California, where he treated approximately five thousand (5,000) patients with therapeutic fasting. His published work, "The Genesis and Control of Disease" (1931), is a comprehensive clinical text documenting his outcomes across multiple disease categories. His statement on hypertension, documented by DeVries, deserves to be read by every cardiologist alive: "fasting is without doubt the most rapid and effective method of remedying high blood pressure. Indeed, hundreds of consecutive patients have been treated for this condition without a single complete failure."

Read that again carefully. Hundreds of consecutive patients. Not a single complete failure. In modern clinical trial terms, this is an extraordinary outcome. No antihypertensive drug in the history of pharmacology has ever achieved a zero failure rate across hundreds of consecutive cases. Weger was not reporting this from a position of enthusiasm or advocacy. He was a trained physician reporting his clinical results with the same precision he would apply to any other aspect of medical practice.

Dr. John M. Tilden operated a fasting institute in Denver, Colorado for decades and was one of the most prolific clinical writers in the fasting tradition. His observations on hypertension and pernicious anaemia were particularly compelling. On anaemia, he wrote that "cases of pernicious anaemia taken off their food will double their blood count in a week." On hypertension, his clinical records showed consistent normalisation of blood pressure across his patient population.

Dr. Linda Burfield Hazzard supervised nearly two thousand five hundred (2,500) fasting patients over her career. Her documented mortality rate across this entire population was seven tenths of one per cent (0.7%). To put this in perspective, the mortality rate in conventional medicine for the same conditions, treated with the available pharmacological and surgical interventions of her era, was significantly higher. The deaths that did occur in her fasting patients were, upon examination, attributable to pre-existing organic disease that had progressed beyond reversibility, not to the fasting itself.

Dr. James McEachen conducted what is perhaps the most systematically documented series of fasting treatments in the clinical literature, treating 715 cases of various diseases under carefully supervised conditions in his sanitarium near Escondido, California, between August 1952 and March 1958\. His overall improvement rate was 88.4%. His hypertension data was particularly striking: of 141 hypertensive patients treated, he recorded not a single complete failure.

The statistical data from McEachen's work deserves to be displayed clearly:

Disease

Cases

Improved or Recovered

Not Improved

High Blood Pressure

141

141

0

Colitis

88

77

11

Sinusitis

67

64

3

Anaemia

60

52

8

Arthritis

47

39

8

Asthma

29

29

0

Heart Disease

33

29

4

Kidney Disease

41

36

5

Two conditions showed zero failures: high blood pressure and asthma. Every single hypertensive patient in McEachen's series either improved significantly or recovered completely.

Dr. Robert Gross at Pawling Health Manor in Hyde Park, New York provided complementary institutional data covering the period from August 1957 to July 1963\. Across 680 total cases, he

documented a complete recovery rate of 71.2%, a partial recovery rate of 24.2%, and a failure rate of only 4.6%. He noted that a significant proportion of partial recoveries and failures occurred because patients did not remain long enough to complete the recommended fasting duration, and because the emotional state and cooperation of different patients varied considerably.

Dr. William Esser at his Florida sanitarium carefully documented 155 cases involving 31 different disease types. His complete recovery rate was 71%, partial recovery 20%, and failure 9%. His failures and partial recoveries were largely attributable to patients fasting for shorter durations than recommended due to time and financial constraints.

When you look at this body of clinical evidence together, covering tens of thousands of patients across multiple independent institutions spanning more than a century, the conclusion is overwhelming: therapeutic fasting is one of the most consistently effective interventions for hypertension, and other chronic conditions, that has ever been systematically documented.

The question is not whether it works. The historical evidence that it works is, frankly, more extensive than the evidence base for many medications currently prescribed daily in Nigerian hospitals and clinics. The question is why this evidence has been so thoroughly marginalised by mainstream medicine. We will address that question directly in Section 2.7.

2.5 The Hypertension-Specific Historical Record: What the Fasting Physicians Found

Because this book is specifically about hypertension, let us now consolidate the hypertension-specific historical evidence in one place, giving it the clinical attention it deserves.

The consistent finding across all the fasting physicians we have discussed is this: hypertension responds to therapeutic fasting more reliably and more completely than almost any other condition they treated. In DeVries' comprehensive 1963 synthesis of the fasting literature, he writes with clinical directness: "fasting is without doubt the most rapid and effective method of remedying high blood pressure. Even patients who have failed to respond to all of the customary treatment of high blood pressure do respond to fasting."

That last sentence is crucial: "even patients who have failed to respond to all of the customary treatment." These are the Richards of the world. The patients who have taken every medication their doctors prescribed, attended every quarterly review, and still cannot get their blood pressure under control. The fasting physicians documented, consistently, that even these most resistant cases responded to supervised therapeutic fasting.

Let us look at the specific mechanisms the fasting physicians observed clinically, before modern endocrinology gave us the molecular language to explain them.

The first thing they noticed was dramatic sodium excretion. Bragg, in his clinical observations, documented taking urine specimens from fasting patients each morning, labelling them and allowing them to settle, and observing large deposits of sodium crystals and other waste materials forming at the bottom of the bottles over subsequent days. He found that four days of complete water fasting was

sufficient to "de-salt" the body cells and organs in most patients, a finding that produced visible and measurable reductions in the oedema (swelling caused by fluid retention) associated with sodium excess.

In plain language: the bloating, the puffiness around the ankles and feet, the waterlogged heaviness that many hypertensive patients experience, visibly resolved within days of commencing the fast, as the kidneys began excreting the sodium that had been accumulating in the body's tissues. Modern endocrinology now tells us exactly why this happens: as circulating insulin levels fall during fasting, the insulin-mediated signal for renal sodium retention is removed, and the kidneys begin their belated work of clearing the sodium backlog.

The second thing the fasting physicians observed was a reliable and sometimes dramatic reduction in blood pressure beginning within the first few days of fasting and continuing to deepen as the fast progressed. This was not a modest, borderline reduction. Shelton's documented case of systolic 295 to 115 over three weeks is the most dramatic example, but the fasting literature is full of equally compelling individual cases alongside the aggregate statistics.

The third thing they observed, and this is perhaps the most clinically important finding, was that these reductions were durable. When patients who fasted also changed their diet and lifestyle after the fast, specifically eliminating salt, refined foods and excess carbohydrates, their blood pressure did not return to its previous levels. The cure, when accompanied by nutritional rehabilitation, was lasting.

DeVries documents this explicitly: "if the blood pressure falls below normal during the fast, it will rise to normal later, but actual hypertension does not redevelop so long as good nutritional habits are maintained after the fast."

Compare this with the pharmacological approach: when a patient stops taking their antihypertensive medication, their blood pressure returns to its previous elevated level within days to weeks, because nothing has changed in the underlying metabolic environment that was generating the elevation. The medication was suppressing the symptom; it was not addressing the cause. When fasting addresses the cause and that cause is then maintained in a healed state through appropriate nutrition, the symptom does not return.

This is the difference between management and cure.

2.6 The Scientific Foundation: Bridging Historical Observation and Modern Evidence

The great fasting physicians of the nineteenth and twentieth centuries were, in the truest sense, scientists. They observed carefully. They documented meticulously. They drew conclusions from what they actually saw, rather than from theoretical models. And their observations were consistently accurate.

What they lacked was the molecular biology to explain, at the cellular level, why fasting produced the effects they were witnessing. They knew that fasting worked for hypertension with a reliability that exceeded any other intervention available to them. They did not know, because the science did not yet

exist, about insulin receptors, RAAS signalling, autophagy pathways or inflammasome biology.

That science now exists. And it does not contradict the historical clinical observations. It explains them.

When Bragg observed that fasting "de-salts" the body, he was observing the consequence of falling insulin levels removing the renal sodium-retaining stimulus. When DeVries documented autolysis as the mechanism by which fasting dissolves pathological accumulations including arterial deposits, he was describing what we now call autophagy, the intracellular recycling system through which damaged and dysfunctional cellular components are selectively consumed and removed. When the fasting physicians observed that hypertension resolved consistently across their patient populations, they were witnessing the downstream cardiovascular consequence of insulin resistance reversal.

In 2001 and 2002, Dr. Alan Goldhamer and colleagues published the most methodologically rigorous studies of water-only fasting for hypertension in the peer-reviewed literature. Their findings, published in the Journal of Manipulative and Physiological Therapeutics and the Journal of Alternative and Complementary Medicine respectively, documented 174 hypertensive patients treated with medically supervised water-only fasting. The results were consistent with the historical clinical record: average blood pressure reductions of 37 mmHg systolic and 13 mmHg diastolic, with 89% of patients achieving readings below 140/90 mmHg by the conclusion of the fasting period.

For Nigerian patients taking antihypertensive medications, this number deserves context. The average blood pressure reduction achieved by first-line antihypertensive monotherapy (a single medication) is approximately 10 to 15 mmHg systolic. Goldhamer's fasting protocol produced an average reduction of 37 mmHg systolic. Without medication. In a supervised setting with no pharmaceutical intervention whatsoever.

Yoshinori Ohsumi's 2016 Nobel Prize in Physiology or Medicine for his discovery of the mechanisms of autophagy provided the final scientific bridge between historical naturopathic clinical observation and modern molecular biology. Ohsumi demonstrated, with rigorous laboratory precision, the exact cellular pathways through which fasting activates the body's internal cellular recycling system. He demonstrated that autophagy is selectively triggered by the nutrient-sensing pathway suppression that occurs during fasting, particularly through the inhibition of a protein complex called mTOR (mechanistic target of rapamycin, the cell's primary nutrient sensor) and the activation of AMPK (adenosine monophosphate-activated protein kinase, the cell's energy status sensor). When mTOR is suppressed and AMPK is activated, as occurs reliably during water fasting, the cell initiates a programme of selective self-digestion targeting damaged organelles, misfolded proteins, dysfunctional mitochondria and accumulated cellular waste.

Graham described this process in 1843\. Ohsumi won the Nobel Prize for characterising its molecular mechanism in 2016\. The 173-year gap between the clinical observation and the molecular explanation does not make the observation any less accurate. It simply illustrates how far ahead of formal scientific understanding careful clinical observation can sometimes be.

2.7 Why This Evidence Was Buried: The Uncomfortable Economics of Cure

At this point, a thoughtful reader, particularly a medically informed Nigerian reader who has watched family members and community members managed on lifelong antihypertensive medications, might be asking a reasonable and important question.

If the evidence for therapeutic fasting in hypertension is this extensive, stretching back over a century, documented by multiple independent physicians across thousands of patients, and now validated by modern molecular science, why does virtually no mainstream physician recommend it? Why is it not taught in Nigerian medical schools? Why is it not in the treatment guidelines of the Nigerian Cardiac Society or the World Health Organization?

The honest answer involves acknowledging some uncomfortable realities about how medical knowledge is generated, disseminated and institutionalised.

First, there is the simple issue of patentability. Therapeutic water fasting cannot be patented. No pharmaceutical company can make money from it. The economics of medical research are driven substantially by pharmaceutical investment, and pharmaceutical companies invest in researching and developing things they can patent and sell. Water cannot be patented. The absence of commercial interest in fasting has meant the absence of the large-scale, multicentre, randomised controlled trials that modern medicine requires before it will incorporate a treatment into standard guidelines.

This is not a conspiracy. It is a structural bias in how medical evidence is produced and funded. But its consequences are real: therapeutically effective interventions that cannot be commercialised are systematically under-researched relative to their clinical importance.

As Jamnadas articulates directly in his work, and as both Bragg and DeVries observed in their respective eras, modern medicine has developed a deeply entrenched tendency to reach for pharmaceutical intervention rather than lifestyle and dietary remedy, even when the evidence for the lifestyle remedy is substantial. Jamnadas frames this as a paradigm problem: the paradigm of modern cardiology is oriented around pharmaceutical and procedural intervention, and that paradigm actively resists evidence that challenges its foundational assumptions.

Second, there is the issue of the clinical complexity of supervised therapeutic fasting. It requires physician time, patient commitment, careful monitoring, and a therapeutic relationship that extends well beyond a fifteen-minute outpatient appointment. The medical system in Nigeria, as in most of the world, is structured around brief consultations and prescription writing, not extended therapeutic supervision. Even physicians who are intellectually convinced by the evidence for therapeutic fasting may find it practically very difficult to implement within the constraints of their clinical environment.

Third, as DeVries noted with some frustration in 1963, "the extraordinary value of fasting has not been recognized by the professions of healing as a whole. In spite of the careful scientific work done with fasting by physiologists, biologists and physicians, and the almost universal recommendation of the method by these people, orthodox medicine has scarcely recognized that fasting even has therapeutic properties." This was written sixty years ago, and while the emergence of intermittent fasting research and autophagy science has improved the situation considerably, the fundamental institutional conservatism he identified remains operative.

None of this changes the evidence. It simply explains why the evidence has not reached the people who need it most.

This book, among other things, is an attempt to correct that gap. Particularly for Nigerian readers and the broader African context, where hypertension prevalence is among the highest in the world and where access to sustained pharmacological management is inconsistent and expensive, the case for understanding and utilising therapeutic fasting is not merely academic. It is a matter of practical health survival.

2.8 The Cultural and Religious Dimension: What Nigerian Tradition Has Always Known

Before we close this historical chapter, there is one more dimension that deserves recognition, particularly for our Nigerian readership.

Fasting is not a foreign concept in Nigerian culture. It is not a Western health trend being imported into our communities. It is a practice as deeply embedded in Nigerian spiritual and cultural life as any other tradition we carry.

Muslim Nigerians fast for the entire month of Ramadan, abstaining from all food and water from the pre-dawn call to prayer to sunset. For thirty consecutive days, hundreds of millions of Muslims worldwide, including tens of millions in Nigeria, undertake a sustained pattern of daily intermittent fasting that modern metabolic research now confirms produces measurable improvements in insulin sensitivity, blood pressure, inflammatory markers and lipid profiles. Studies published in the Annals of Nutrition and Metabolism, the Journal of the American College of Nutrition and multiple other peer-reviewed journals have documented these Ramadan-associated metabolic improvements consistently.

Christian Nigerians fast regularly as a spiritual discipline, with many denominations practising extended fasts of three, seven, twenty-one or forty days, typically consuming only water during the fasting period. The Daniel Fast, based on the biblical account of the prophet Daniel's vegetable and water diet, is widely practised. The forty-day fast, drawing on the biblical precedents of Moses, Elijah and Jesus, is a familiar concept in Nigerian Christian practice.

Indigenous Nigerian spiritual traditions also incorporate periods of abstinence and fasting as part of ritual practice, recognising what the body seems to know instinctively: that withdrawal from food creates a different quality of physical and spiritual awareness.

What this means is that Nigerian people are, in a very real sense, culturally primed to understand and accept therapeutic fasting in a way that many Western populations are not. The concept is not alien. The practice is already present in our communities. What this book offers is the clinical science that explains why these traditions produce the health benefits that observant fasters have reported across generations.

When your Muslim neighbour comments that she always feels lighter, clearer and healthier after Ramadan, she is not imagining it. Her insulin levels have dropped. Her inflammatory markers have fallen. Her blood pressure has reduced. Her cells have undergone autophagy-mediated repair. She has

done, for spiritual reasons, something that medical science now confirms is profoundly therapeutic.

The grandmother in the Onitsha market who stops feeding her sick child is applying an instinct that Hippocrates formalised, that Shelton documented across thirty thousand cases, and that Ohsumi explained at the molecular level with a Nobel Prize.

The history of fasting as medicine is not a history that belongs to Western naturopathy or American sanitariums. It is a human history. It belongs to all of us. And for the hypertensive Nigerian reading this book, it is a history that carries a direct and urgently relevant message:

Your blood pressure can be treated at its root. The tools are older than pharmacology. They are validated by science. And they are already, in a very real sense, part of who you are.

Chapter Summary: Key Points

Therapeutic fasting as a medical intervention has a documented history stretching back more than 2,400 years, practised and recommended by some of the greatest medical and philosophical minds in human civilisation including Hippocrates, Pythagoras, Plato, Avicenna and Paracelsus.

The nineteenth century American fasting pioneers, including Dewey, Tanner, Graham and Jennings, established therapeutic fasting as a rigorous clinical practice with documented outcomes superior to the conventional medical treatments of their era.

The twentieth century fasting institutions, particularly Shelton's (over 30,000 fasts), Weger's (approximately 5,000 patients), McEachen's (715 documented cases) and Hazzard's (nearly 2,500 patients), generated the most extensive observational clinical evidence base for therapeutic fasting ever assembled.

For hypertension specifically, the historical clinical record is extraordinary: Weger documented "hundreds of consecutive patients treated without a single complete failure." McEachen's 141 hypertensive cases showed zero complete failures. Shelton documented systolic pressure reductions from 295 to 115 mmHg over three weeks of fasting.

Goldhamer's peer-reviewed studies (2001, 2002\) brought this historical evidence into the modern scientific literature with documented average reductions of 37/13 mmHg in 174 hypertensive patients, with 89% achieving readings below 140/90.

Ohsumi's 2016 Nobel Prize confirmed at the molecular level what clinical fasting practitioners had been observing for over a century, validating autolysis as autophagy and explaining the cellular repair mechanisms that fasting activates.

The marginalisation of this evidence is attributable to structural biases in pharmaceutical-driven medical research funding, not to absence of evidence. Fasting cannot be patented and therefore has not attracted the commercial research investment that other interventions have received.

Nigerian cultural and religious traditions, including Ramadan fasting, Christian fasting disciplines, and indigenous traditions of abstinence, represent a culturally embedded familiarity with fasting that aligns directly with its therapeutic applications. Nigerian people are not learning something new. They are

learning the science behind something they already know.

“The natural healing force within us is the greatest force in getting well.”

— Hippocrates

CHAPTER 3

The Physiology Of Fasting, What Actually Happens Inside Your Body

“The moment you stop eating, your body does not begin dying. It begins healing.”

— Paul C. Bragg

Opening: The Moment Everything Changes

Think about the last time you went a full day without eating. Maybe it was Ramadan. Maybe it was a church fast. Maybe it was one of those genuinely busy days where you looked up from your work at six in the evening and realised you had not eaten since the previous night.

Something happened in your body during those hours that your doctor has almost certainly never described to you.

Your cells began cleaning house. Your immune system began recalibrating. The hormones that had been keeping your blood pressure elevated began, quietly and measurably, to fall. Damaged proteins that had been accumulating inside your cells for months, perhaps years, began to be dismantled and recycled. Your brain, freed from the metabolic work of processing food, began operating with a clarity that you may have noticed but could not explain.

None of this was starvation. None of it was dangerous. All of it was purposeful, orchestrated, and encoded into your biology at a level far deeper than anything any pharmaceutical can reach.

This chapter is about what actually happens inside your body when you fast with water. Not what people assume happens. Not the frightening stories about muscle wasting and organ failure that circulate as misinformation. What actually happens, hour by hour, day by day, as traced by decades of laboratory science, clinical observation and, most recently, Nobel Prize-winning cellular biology research.

For the hypertensive reader, this chapter is particularly important, because what you are about to learn is that virtually every physiological change that fasting produces is directly, measurably antihypertensive. Not coincidentally or peripherally, but specifically, mechanistically and profoundly. By the time you finish this chapter, you will understand not just that fasting lowers blood pressure, but precisely why, at the level of hormones, kidneys, blood vessels, nervous system and individual cells.

Understanding the mechanism is not academic. It is empowering. When you know what your body is doing and why, you can work with it rather than being frightened by it. You can recognise the signs of healing for what they are, rather than misinterpreting them as danger. You can trust the process, because you understand it.

Let us begin at the beginning. The moment the last meal ends and the fast begins.

3.1 The First 12 to 24 Hours: Clearing the Runway

The first thing that happens when you stop eating is so obvious that its significance is easily overlooked. Your body stops receiving glucose from food.

Glucose is a simple sugar. It is the primary fuel your body uses for immediate energy. Every carbohydrate you eat, whether it is a bowl of rice, a piece of bread, a plate of eba or a ripe mango, is ultimately broken down into glucose in the digestive process and absorbed into the bloodstream. When glucose enters the blood, the pancreas (a gland sitting just behind the stomach) releases insulin to manage it. Insulin is the key that unlocks the door of your body's cells, allowing glucose to enter and be used for energy or stored for later.

In the first several hours after your last meal, your body is still running on the glucose and insulin from that meal. Blood glucose is gradually being taken up by cells, insulin levels are gently declining, and the digestive system is completing its work.

Somewhere between six and twelve hours after your last meal, something important happens: your blood glucose level drops to its fasting baseline and your insulin level reaches its lowest point of the day. For most people eating three meals daily, this low-insulin window occurs during the night, which is why we call the morning meal "breakfast." It literally breaks the overnight fast.

But when you extend that overnight window, when you do not eat breakfast and push through to midday or beyond, or when you begin a full water fast, something more significant happens.

Your body reaches for its emergency fuel storage.

The Glycogen System: Your Body's Short-Term Fuel Reserve

Stored in your liver and skeletal muscles is a substance called glycogen (pronounced "GLY-co-jen"). Think of glycogen as your body's version of a generator fuel tank. It is glucose that has been compacted and stored for rapid deployment when the main fuel supply is interrupted. Your liver holds approximately 100 grams of glycogen. Your muscles hold considerably more, but the muscles' glycogen is reserved for their own use and cannot be released into the bloodstream the way liver glycogen can.

When your blood glucose begins to fall after a meal and insulin drops, your liver receives a hormonal signal to begin releasing its stored glycogen, breaking it back down into glucose and releasing it into the bloodstream to maintain fuel supply. This process is called glycogenolysis (literally "glycogen breaking"), and it keeps your blood glucose reasonably stable during the hours between meals.

This is why you do not collapse between breakfast and lunch. Your liver is quietly releasing stored fuel to keep your brain and organs supplied.

The critical point for fasting physiology is this: the liver's glycogen store is finite. Under normal circumstances, with three meals a day, it is never fully depleted because it is being continuously topped up by dietary carbohydrates. But when food is withheld, the liver is drawing down its glycogen supply without topping it up. Depending on the individual's metabolic state, activity level and the size of their last meal, liver glycogen is typically fully depleted somewhere between 18 and 24 hours into the fast.

What Happens at the 18 to 24 Hour Mark

When liver glycogen is exhausted, the body faces a choice: find a different fuel source or allow blood glucose to drop to dangerous levels.

Nature, which designed this system over millions of years of evolution, did not leave this to chance. The body has a clear, well-organised backup plan.

The first part of that plan is gluconeogenesis (pronounced "gloo-co-neo-JEN-eh-sis," meaning "making new glucose"). The liver, and to a lesser extent the kidneys, can manufacture glucose from non-carbohydrate precursors, primarily glycerol (from fat breakdown) and certain amino acids (from protein). This process maintains blood glucose at a safe level even in the complete absence of dietary carbohydrates.

The second part of the plan is the initiation of fat mobilisation. With insulin levels now at their lowest point since the previous meal, and with the counter-regulatory hormones, primarily glucagon (from the pancreas) and noradrenaline (from the adrenal glands), beginning to rise, the body's fat stores begin releasing their stored fatty acids into the bloodstream.

These fatty acids travel to the liver, where they are converted into compounds called ketone bodies (specifically acetoacetate, beta-hydroxybutyrate and acetone). Ketone bodies are an alternative fuel that most tissues, including the brain, heart and skeletal muscle, can use very efficiently when glucose is not available.

This metabolic transition, from running primarily on dietary glucose to running primarily on stored fat and ketones, is the physiological pivot point around which the entire therapeutic power of fasting is organised.

Blood Pressure Effects in the First 24 Hours

Even in this first day of fasting, measurable antihypertensive effects are beginning.

As insulin falls, its direct signal to the renal tubules (the tiny filtration tubes inside the kidneys) for sodium retention is progressively removed. The kidneys, freed from insulin's sodium-conserving command, begin excreting sodium more liberally. Water follows the sodium out of the body osmotically. Circulating blood volume begins to fall modestly. Preload on the heart (the volume of blood returning to the heart for pumping) decreases. Cardiac output begins to drop.

In simpler terms: the pressure in your pipes begins to ease because there is slightly less fluid filling them.

Bragg documented this clinically, instructing his patients to collect their first morning urine samples during fasting and allowing them to settle in labelled bottles over subsequent weeks. The visible crystalline deposits that formed, composed largely of sodium and metabolic waste, were his practical illustration of the de-salting process beginning from the first days of fasting. What he was observing, though without the endocrinological framework to explain it, was insulin-mediated sodium retention being reversed as insulin levels fell.

For the hypertensive reader, this first-day effect is modest but real. If you are monitoring your blood pressure at home, you may notice a small reduction, perhaps five to eight millimetres of mercury (mmHg) in systolic pressure, by the end of the first twenty-four hours of fasting. This is not the full therapeutic effect. It is the beginning of a process that deepens considerably as the fast continues.

3.2 The 24 to 48 Hour Window: The Metabolic Crossover

The second day of a fast is physiologically the most challenging for most people, and understanding why makes it considerably easier to navigate.

By 24 to 36 hours, the body's glycogen reserves are exhausted. Gluconeogenesis is running but cannot fully replace glycogen-derived glucose. Fat mobilisation is accelerating but has not yet reached full efficiency. The brain, which is accustomed to running almost exclusively on glucose and is only beginning to adapt to using ketones, is experiencing a genuine fuel transition.

This is the window in which most people experience what is colloquially called the "keto flu," a term that, despite its informal name, describes a real and well-characterised physiological phenomenon.

Understanding the Keto Flu

The metabolic health guide describes this accurately: "A temporary feeling of being run down, lethargic, or physically exhausted. It occurs during the beginning of a fast when the body has used up its easily accessible glycogen stores, but circulating insulin levels are still too high to allow immediate access to stored body fat for fuel."

In plain language: the body is between fuel sources. The old fuel (glycogen) is running out. The new fuel (ketones from fat) is not yet fully online. The result is a temporary energy deficit that most people experience as headache, fatigue, mild nausea, irritability and difficulty concentrating.

This is deeply important to understand, because the keto flu is the most common reason people abandon therapeutic fasts prematurely, convinced that their body is telling them something is wrong. In fact, their body is telling them something is right. The discomfort is not a sign of harm. It is a sign of metabolic transition.

Think of it this way: imagine a large generator being switched from petrol power to gas power. During the switchover, there is a brief period of sputtering, reduced output and apparent dysfunction. This is not the generator failing. It is the generator transitioning. Once the transition is complete, it runs more cleanly and efficiently on the new fuel than it ever did on the old.

The keto flu typically peaks between 24 and 48 hours and begins to resolve as ketone production accelerates. Adequate hydration and electrolyte supplementation, specifically magnesium and potassium, substantially reduce the severity of these symptoms. We will address this in detail in the practical protocol chapters.

Electrolytes: A Critical Safety Point

During the 24 to 48 hour window, as the kidneys are excreting sodium at an accelerated rate (driven by falling insulin), they are also losing other electrolytes, particularly potassium and magnesium. Electrolytes are minerals that carry an electrical charge and are critical for nerve function, muscle contraction (including the heart muscle) and cellular fluid balance.

Potassium (found in foods like bananas, avocados and green leafy vegetables) is the primary intracellular electrolyte. When it falls below normal levels, a condition called hypokalaemia (pronounced "high-po-ka-LEE-me-ah," literally meaning low potassium in the blood), the consequences include muscle cramps, palpitations, weakness and, in severe cases, cardiac arrhythmia (irregular heart rhythm, that is, the heart beating in an abnormal pattern).

Magnesium is involved in over three hundred enzymatic reactions in the body and is critical for blood vessel relaxation and blood pressure regulation. Magnesium deficiency, called hypomagnesaemia (pronounced "high-po-mag-nee-SEE-me-ah"), produces muscle cramps, anxiety, insomnia, palpitations and can worsen hypertension.

For hypertensive patients fasting while on diuretic medications (water tablets), this electrolyte picture requires particular clinical attention. Diuretics already promote urinary potassium and magnesium loss as a side effect. Adding fasting-induced electrolyte excretion on top of diuretic-induced losses creates a risk of significant depletion that must be actively managed. This is one of the reasons why medical supervision is not optional for hypertensive patients undertaking extended fasting. It is essential.

The Antihypertensive Picture at 24 to 48 Hours

Beyond the keto flu and electrolyte considerations, the antihypertensive mechanisms are deepening measurably during this window.

Insulin levels are now at their genuinely lowest point. Renal sodium excretion is at its maximum for this stage. Blood volume is modestly but measurably contracted. The sympathetic nervous system (the body's "fight or flight" system, which when chronically overactivated contributes directly to elevated blood pressure) is beginning to reduce its activity as the metabolic stimulus for its overactivation, specifically chronic hyperinsulinaemia, is progressively removed.

The metabolic guide cites a landmark study (NIH, PMID 39559800\) demonstrating that food sequencing alone can reduce postprandial (after-meal) insulin by 31.7%. Fasting, by removing food entirely, achieves a far more profound insulin reduction than any dietary sequencing strategy. And as we established in Chapter 1, it is this insulin reduction that begins to unwind the sodium retention, sympathetic overactivation and RAAS dysregulation at the root of essential hypertension.

3.3 The 36-Hour Mark: Deep Ketosis and the Beginning of Healing

Somewhere around the 36-hour point, for most fasting individuals, a physiological threshold is crossed that changes the quality of the fasting experience considerably.

Jamnadas, in the metabolic health guide, identifies this milestone with precision: "The 36-Hour Mark: This milestone is critical as it allows the body to deplete its liver glycogen stores and cleanly transition

into deep ketosis, converting fat into ketones for clean, efficient energy."

Deep ketosis means that ketone production has reached a level where ketones are the primary fuel being used by the brain, heart and most other tissues. Blood levels of the primary ketone body, beta-hydroxybutyrate (pronounced "bay-ta-high-DROX-ee-BYOO-ti-rate"), are now measurably elevated, typically rising above 0.5 millimoles per litre and continuing to rise over subsequent days of fasting.

What Are Ketones and Why Do They Matter?

Ketone bodies are organic compounds produced in the liver from fatty acids when carbohydrate availability is low. They are often described as an "alternative fuel," but this undersells their significance. In many respects, ketones are a superior fuel to glucose for several tissues, particularly the heart.

The heart muscle actually prefers ketones over glucose when both are available. Studies of cardiac metabolism have demonstrated that heart muscle operating on ketones produces more ATP (adenosine triphosphate, the body's cellular energy currency) per unit of oxygen consumed than heart muscle operating on glucose. For a hypertensive patient whose heart has been working under elevated pressure load for years, this metabolic upgrade is not trivial.

But ketones do something else that is directly relevant to blood pressure management: they exert vasodilatory (blood vessel-relaxing) effects through multiple mechanisms, including activation of hydroxycarboxylic acid receptors on vascular smooth muscle cells and reduction of oxidative stress in the vascular endothelium (the inner lining of blood vessels).

In simpler terms: ketones help relax your blood vessels. Blood vessels that are more relaxed have lower resistance to blood flow. Lower resistance to blood flow means lower blood pressure.

Beta-Hydroxybutyrate as an Anti-Inflammatory Agent

Beta-hydroxybutyrate (we will abbreviate it to BHB for the remainder of this chapter) has a property that was not fully appreciated until relatively recently. It is a potent inhibitor of a protein complex called the NLRP3 inflammasome (pronounced "en-el-ar-pee-three in-FLAM-ah-some").

The NLRP3 inflammasome is a molecular structure inside immune cells that acts as an inflammatory alarm system. When it is activated, it triggers the production of inflammatory cytokines (chemical messengers that promote inflammation), particularly interleukin-1 beta and interleukin-18. In metabolically healthy individuals, the NLRP3 inflammasome is appropriately regulated, firing only when genuine immune threats (bacterial or viral pathogens) are detected. In chronically hyperinsulinaemic, metabolically deranged individuals, it is pathologically overactivated, maintaining the chronic low-grade inflammatory state that damages endothelial cells and drives vascular disease.

BHB directly suppresses NLRP3 inflammasome activity. As ketone levels rise during fasting, circulating inflammatory markers including C-reactive protein (CRP, a marker that rises when there is inflammation in the body), interleukin-6 and tumour necrosis factor-alpha (TNF-alpha) begin to fall. The vascular inflammation that has been silently injuring arterial walls begins to resolve.

This is one of the most clinically significant things happening at the 36-hour mark, and it receives almost no attention in conventional cardiology discussions of hypertension management. Chronic vascular inflammation is not just a downstream consequence of hypertension. It is an active driver of it, contributing to endothelial dysfunction, reduced nitric oxide production and progressive arterial stiffening. Suppressing it through fasting-induced ketosis is not a peripheral benefit. It is central to the antihypertensive mechanism.

The RAAS at 36 Hours

The renin-angiotensin-aldosterone system (RAAS) is the body's primary hormonal blood pressure regulation system. Renin is an enzyme released by the kidneys that converts a protein called angiotensinogen (produced by the liver) into angiotensin I, which is then converted by angiotensin-converting enzyme (ACE) into angiotensin II.

Angiotensin II is the most potent vasoconstrictor (blood vessel-narrowing agent) in the human body. It also stimulates the adrenal glands to release aldosterone, a hormone that commands the kidneys to retain sodium and excrete potassium. The combined effect of angiotensin II and aldosterone is powerful blood pressure elevation through simultaneous vasoconstriction and sodium-volume expansion.

In insulin-resistant, hyperinsulinaemic individuals, the RAAS is chronically overactivated through multiple mechanisms we detailed in Chapter 1\. As insulin levels fall progressively during fasting, this RAAS overactivation begins to unwind. By the 36-hour mark, with insulin at genuinely low physiological levels, renin release is suppressed, angiotensin II production falls, aldosterone secretion decreases, and the dual mechanisms of vasoconstriction and sodium retention that it drives begin to relax.

This is, mechanistically, precisely what ACE inhibitor and ARB medications (two of the most commonly prescribed antihypertensive drug classes) attempt to achieve pharmacologically. The difference is that fasting achieves it by addressing the upstream cause of RAAS overactivation, the insulin resistance, while pharmacological RAAS blockade simply interrupts the pathway at one point while leaving the upstream drive intact. Both reduce angiotensin II effects. Only fasting addresses why angiotensin II is elevated in the first place.

3.4 The 48 to 72 Hour Window: When the Body Begins Its Deepest Work

By 48 hours, the keto flu has typically resolved for most people. Ketone levels are rising robustly. Hunger, which peaked at 24 to 48 hours, is beginning to diminish significantly. Many fasting individuals report that by 48 hours, a notable shift has occurred: the obsessive food thoughts that characterised the first day have quietened, and an unusual sense of mental clarity and physical lightness has begun to emerge.

This is not coincidental. It is the physiological consequence of the brain completing its transition to ketone fuel and the inflammatory burden in the nervous system beginning to lift.

But what is happening at the cellular level during this window is perhaps the most therapeutically significant process of the entire fast.

Autophagy: The Physician Within

Autophagy. The word comes from the Greek words "auto" (self) and "phagein" (to eat). Literally: self-eating. It is the process by which cells identify their own damaged, dysfunctional or unnecessary components and systematically dismantle and recycle them.

To understand why this matters clinically, you need a picture of what happens inside a cell over years of metabolic stress.

Imagine a busy workshop, like a carpenter's workshop or a mechanic's workshop, that has been running for years without a proper clean-up. Tools are worn and broken. Sawdust and metal shavings have accumulated in corners. Some equipment is damaged but has not been repaired or replaced because there was never a quiet moment to stop and do maintenance. The workshop is still running, still producing, but it is doing so with increasing inefficiency, increasing risk of breakdown, and an accumulating backlog of problems that are making every job harder.

This is what happens inside cells under conditions of chronic metabolic stress. Mitochondria (the cell's energy-producing organelles, essentially the cell's "engines") become damaged by oxidative stress and begin producing less energy while generating more toxic by-products. Misfolded proteins (proteins that have been manufactured incorrectly or damaged after manufacture) accumulate and interfere with normal cellular function. Dysfunctional cellular components that should have been retired continue operating badly, consuming resources and producing inflammatory signals.

Autophagy is the cellular equivalent of a thorough workshop clean-up. It is the process by which the cell identifies everything that is damaged, misfolded, dysfunctional or no longer needed, packages it up in membrane structures called autophagosomes (pronounced "aw-TOF-ah-go-somes," basically cellular recycling bags), and delivers it to cellular recycling centres called lysosomes (pronounced "LY-so-somes") where the material is broken down into its constituent components and made available for reuse in building new, functional structures.

Yoshinori Ohsumi spent decades characterising the molecular genetics and biochemistry of this process. In 2016, the Nobel Assembly at the Karolinska Institute awarded him the Nobel Prize in Physiology or Medicine for this work. The committee's citation stated that his discoveries had "opened the path to understanding the fundamental importance of autophagy in many physiological processes, such as in the adaptation to starvation or response to infection," and had demonstrated that "autophagy can rapidly provide fuel for energy and building blocks for renewal of cellular components" and "is important for responding to starvation and other types of stress."

In plain language: when you fast, your cells clean house. And a clean cell is a healthy cell.

Autophagy and Hypertension: The Direct Connection

For the hypertensive patient, autophagy during fasting is directly relevant through several specific mechanisms.

The first is endothelial cell repair. The endothelium is the single-cell-thick lining of every blood vessel in the body. We discussed in Chapter 1 how chronic hyperglycaemia, hyperinsulinaemia and oxidative

stress damage endothelial cells, impairing their ability to produce nitric oxide and maintain appropriate vasodilation. During fasting-induced autophagy, damaged endothelial cells initiate self-repair processes, clearing oxidatively damaged proteins and dysfunctional mitochondria and restoring cellular function. Endothelial nitric oxide synthase (eNOS, the enzyme that produces the vasodilating molecule nitric oxide) function improves as the cellular environment is cleared of the oxidative debris that was impairing it.

Nitric oxide is one of the body's most important natural blood pressure regulators. It is produced by endothelial cells and diffuses directly into the underlying smooth muscle cells of the arterial wall, causing them to relax. This relaxation increases vessel diameter, reduces peripheral resistance, and lowers blood pressure. Many antihypertensive medications work, directly or indirectly, by preserving or supplementing nitric oxide signalling. Fasting restores the cellular machinery that produces nitric oxide endogenously. This is a profound difference.

The second mechanism is the autolytic (self-digesting) processing of arterial plaque components. DeVries documented this process in 1963, describing how abnormal accumulations in the body, including tumours, effusions and arterial deposits, are preferentially targeted and absorbed during fasting. He wrote: "on the fast, the body has the opportunity to redistribute its nutritive supplies, the surpluses and non-vital supplies being consumed and utilised first." Modern autophagy research has provided the molecular explanation for what DeVries was observing clinically: macrophage-mediated autophagy in atherosclerotic plaques (the fatty deposits that build up inside arterial walls) degrades oxidised LDL (the primary plaque-building material) and reduces foam cell formation, slowing plaque progression and, in some cases, contributing to plaque regression.

Bragg, writing from decades of clinical observation, stated confidently that "fasting helps keep the arteries clean, healthy, elastic and more youthful." He was right. The mechanism, which he described through the language of naturopathic observation, is now explicable through the cellular biology of autophagy.

The third mechanism is immune system recalibration. The immune system contributes to hypertension through multiple inflammatory pathways. Autoimmune activation of the RAAS, macrophage infiltration of arterial walls, and T-cell-mediated vascular inflammation are all documented contributors to elevated blood pressure in metabolically deranged individuals. Fasting-induced autophagy plays a critical role in pruning dysfunctional immune cells, reducing autoimmune activity and recalibrating the inflammatory response toward appropriate rather than chronic activation.

The Blood Pressure Picture at 48 to 72 Hours

By 48 to 72 hours, multiple antihypertensive mechanisms are now operating simultaneously:

Circulating insulin is at its physiological minimum, removing the primary stimulus for renal sodium retention, sympathetic overactivation and RAAS dysregulation. Blood volume has contracted modestly but meaningfully. Ketone-mediated vasodilation is contributing to reduced peripheral resistance. BHB-mediated NLRP3 inflammasome suppression is reducing vascular inflammatory activity. Autophagy is initiating cellular repair in endothelial cells, improving nitric oxide production capacity. Arterial smooth muscle tone is decreasing as the vasoconstricting stimuli driving it are progressively

removed.

The cumulative blood pressure reduction at this stage is typically measurable and clinically significant. Most hypertensive patients fasting under supervision will show systolic reductions of 15 to 25 mmHg by the end of the third day. Many will require medication dose reductions at this point, reinforcing why medical supervision is non-negotiable.

3.5 The 72-Hour Sweet Spot: Profound Transformation

The 72-hour mark, the completion of three full days of water fasting, represents what Jamnadas identifies as "an even more impactful threshold for profound metabolic transformation, deep cellular autophagy, and resetting immune pathways."

This is not hyperbole. The evidence for the specific importance of the 72-hour threshold comes from multiple converging lines of research.

Valter Longo and colleagues at the University of Southern California published landmark research in 2014 demonstrating that 72 hours of fasting triggers a remarkable process of immune system regeneration. The study, published in Cell Stem Cell, found that extended fasting caused old and damaged immune cells to be broken down and cleared through autophagy, and then triggered the activation of haematopoietic stem cells (blood-forming stem cells in the bone marrow) to produce new, functional immune cells. Longo described it as "a remarkable regenerative switch."

For hypertensive patients, the immune regeneration finding is directly relevant because dysfunctional immune cells, particularly activated macrophages and T lymphocytes (types of white blood cells), are significant contributors to vascular inflammation and RAAS overactivation in hypertension. Clearing dysfunctional immune populations and replacing them with newly generated, properly functioning cells is an anti-inflammatory intervention of a depth that no pharmaceutical can currently replicate.

The Gut Microbiome at 72 Hours

Jamnadas has consistently emphasised that "gut health is central to cardiovascular health." This is not a vague wellness statement. It is a specific, mechanistically supported clinical observation with direct relevance to hypertension.

The gut microbiome is the community of trillions of bacteria, viruses, fungi and other microorganisms that inhabit the large intestine. This microbial community is not merely a passive resident. It is a metabolically active organ in its own right, producing compounds that directly influence blood pressure, inflammation and insulin sensitivity.

One of the most important of these compounds is TMAO, trimethylamine N-oxide. TMAO is produced when gut bacteria metabolise certain nutrients (particularly choline and carnitine, found in red meat and eggs) and the resulting metabolite, trimethylamine, is absorbed and converted to TMAO in the liver. Elevated circulating TMAO has been consistently associated with increased cardiovascular risk, endothelial dysfunction and hypertension.

Another critical class of compounds produced by the gut microbiome is short-chain fatty acids (SCFAs), particularly butyrate, propionate and acetate. These are produced when beneficial gut bacteria ferment dietary fibre and resistant starch. The metabolic health guide describes this process: "resistant starch travels intact into the large intestine, where it acts as a premium prebiotic food source for beneficial gut bacteria. The bacteria ferment this starch, producing short-chain fatty acids, specifically butyrate. Butyrate heavily improves systemic insulin sensitivity, dampens full-body inflammation, and directly nourishes and protects the cellular lining of the colon."

Butyrate and other SCFAs also directly activate receptors in the arterial wall (specifically GPR41 and GPR43 receptors on vascular smooth muscle cells) that promote vasodilation and reduce blood pressure. Adequate SCFA production by a healthy, diverse gut microbiome is, in this sense, a continuous endogenous blood pressure-lowering mechanism.

By 72 hours of fasting, studies have shown significant shifts in gut microbiome composition. TMAO-producing bacterial species decline. SCFA-producing species, particularly Akkermansia muciniphila and Faecalibacterium prausnitzii, increase in relative abundance. The microbial community is being remodelled in a direction that is anti-inflammatory, insulin-sensitising and antihypertensive.

This is one of the most significant therapeutic effects of extended fasting that is least discussed in conventional cardiology. For patients whose hypertension is driven in part by gut dysbiosis and elevated TMAO, the microbiome remodelling that occurs during a 72-hour fast represents a meaningful and lasting therapeutic intervention.

Mental Clarity and Neural Restoration at 72 Hours

By the end of the third day of fasting, most individuals experience a quality of mental clarity that is genuinely striking. DeVries documented this across his review of the clinical fasting literature, noting that "a marked improvement in nervous and mental function occurs on the fast. The ability to reason is increased. The powers of attention and association are quickened while memory of past events is often recovered." Bragg described the development of what he called a "photographic memory" and heightened perceptiveness during extended fasting.

The modern neuroscience of this phenomenon centres on two key molecules.

BDNF (brain-derived neurotrophic factor, literally a protein that promotes the growth and maintenance of nerve cells) rises significantly during extended fasting. BDNF promotes neuronal plasticity (the brain's ability to form new connections and adapt), protects existing neurons from stress-induced damage, and improves cognitive function. The BDNF rise during fasting is driven by multiple mechanisms including ketone signalling, reduction in central inflammatory load, and activation of the AMPK pathway in brain tissue.

Serotonin regulation also improves during fasting, partially explaining the mood improvements and reduction in anxiety that many fasting individuals report. For hypertensive patients whose blood pressure is driven partly by psychological stress and anxiety-mediated sympathetic overactivation, this neurochemical recalibration is directly therapeutically relevant.

Think of it as the neural equivalent of a full system restart. Years of metabolic noise, inflammatory interference and oxidative damage have been gradually degrading the quality of neurological signalling. The extended fast clears enough of that accumulated noise for the system to begin operating closer to its original specification.

3.6 Extended Fasting Beyond 72 Hours: Deep Physiological Renovation

For patients with significant, longstanding hypertension, the most profound therapeutic effects of water fasting emerge during extended fasts beyond 72 hours, typically in the range of five to ten days or, in supervised clinical settings, up to three weeks or beyond.

This is the territory where the remarkable clinical outcomes documented by Shelton, Weger, McEachen and the other great fasting physicians were achieved. Systolic pressures of 295 normalising to 115 over three weeks. Hundreds of consecutive hypertensive cases without a single complete failure. These outcomes occurred because the physiological renovation processes initiated in the first 72 hours were given the time and metabolic space to run to their fullest expression.

De-Salting: The Week-Long Sodium Reset

Bragg observed from extensive clinical experience that four days of complete water fasting was sufficient to begin "de-salting the body cells and organs," and that the urine specimens collected daily during fasting showed progressive and visible increases in sodium and other waste material excretion. He recommended distilled water specifically for fasting, arguing that its complete freedom from inorganic minerals made it the most effective solvent for drawing these accumulated substances out of body tissues.

Modern clinical understanding validates the timeline Bragg described. The body's total exchangeable sodium pool, meaning the sodium distributed across all tissues and fluid compartments, is substantial in the chronically hypertensive, high-sodium-diet individual. It cannot be fully depleted in 24 hours. The full de-salting effect that produces lasting blood pressure normalisation requires a sustained period of very low insulin (to remove the renal sodium-retaining signal) combined with adequate water intake to facilitate urinary excretion.

The urine changes Bragg documented clinically, the darkening, the crystalline deposits that formed on settling, the progressive clearing toward the end of the fast, are observable manifestations of this sustained, deep sodium and toxin excretion that the extended fast facilitates.

Vascular Remodelling: The Arterial Rejuvenation Effect

Bragg's chapter on "Fasting Keeps Arteries Youthful" reads, in the light of modern vascular biology, as a remarkably accurate clinical description of the arterial remodelling processes that extended fasting produces.

During extended fasting, with insulin at consistently low levels, circulating BHB at therapeutic concentrations, autophagy running at high capacity, and inflammatory activity progressively suppressed, the arterial wall undergoes a genuine renovation process.

The vascular smooth muscle cells (the cells that constitute the middle layer of arterial walls and whose tone determines peripheral resistance) relax progressively as their metabolic environment improves. The insulin-driven smooth muscle cell proliferation that had been thickening the arteriolar walls begins to reverse as insulin remains absent. Collagen cross-links that had been stiffening the arterial wall are progressively modified. Flow-mediated dilation (the ability of arteries to dilate in response to increased blood flow, a measure of endothelial health) improves measurably.

The arteries, in the most literal physiological sense, become more elastic, more responsive, more youthful in their functional properties.

Baroreceptors (specialised pressure-sensing nerve endings in the aortic arch and carotid arteries that detect blood pressure and send signals to the brain to maintain it within a set range) also recalibrate during extended fasting. In chronically hypertensive individuals, baroreceptors adapt over time to elevated pressure, resetting their "normal" set point upward. Extended fasting, by maintaining genuinely lower blood pressure for an extended period, allows baroreceptor resetting toward normal, contributing to the durability of the blood pressure reduction achieved.

Rejuvenescence: The Cellular Renewal DeVries Documented

DeVries devoted significant attention to what he called rejuvenescence, the acquiring of fresh vitality and renewal of youthful characteristics in the cells and tissues of the body during fasting. His documentation of the research by Drs. Carlson and Kunde at the University of Chicago, where a 40-year-old man on a 14-day fast was found to have tissues in the physiological condition of a 17-year-old at the fast's conclusion, represents one of the most striking data points in the entire fasting literature.

The modern biology of cellular rejuvenation during fasting centres on several converging mechanisms. Autophagy clears accumulated cellular damage. Mitophagy (specifically the autophagic removal of damaged mitochondria) allows replacement by new, functional mitochondria through a parallel process called mitogenesis (mitochondria production), triggered by the same AMPK activation that drives autophagy. Stem cell activation, as documented by Longo's research, generates new functional cells to replace those cleared by autophagy. Telomere-associated proteins are reportedly preserved during periods of caloric restriction and fasting, with implications for cellular ageing rate.

Permanent increase in metabolic rate following extended fasting has also been documented experimentally. DeVries cites experiments at the Hull Biological Laboratory of the University of Chicago where fasts of 30 to 40 days produced a five to six per cent permanent increase in metabolic rate in both dogs and humans. This counterintuitive finding (conventional wisdom would predict that fasting lowers metabolic rate) reflects the metabolic renovation effect: with old, inefficient cellular machinery replaced by new functional structures, the renovated cells operate more efficiently and at higher capacity than the cells they replaced.

3.7 Signs the Fast Is Complete: What Your Body Tells You

One of the most important clinical contributions of the fasting medicine tradition is the identification of specific, observable signs that indicate when the body's primary eliminative and renovative work during a fast has been completed.

DeVries, synthesising the experience of multiple generations of fasting physicians, describes these signs with clinical precision. They are:

The Return of Genuine Hunger. Not the habitual appetite that occurs at mealtimes by conditioning, not the psychologically triggered craving that arises from seeing or smelling food, but genuine, insistent, unmistakable hunger. During the fast, hunger typically peaks at 24 to 48 hours and then disappears. By Day 3 to 5 of an extended fast, most individuals experience no desire for food and may actually feel some repugnance at the idea of eating. The return of genuine, insistent hunger after this period of food indifference signals that the body's reserve stores have been substantially utilised and the body is ready to receive and build with new nutritional material.

The Clearing of the Tongue. During fasting, the tongue typically develops a heavy white or yellowish coating. This coating is a visible indicator of active elimination, reflecting the eliminative activity of the mucous membranes throughout the digestive tract and the increased metabolic waste being processed through the body's eliminative channels. It typically appears within the first one to two days of fasting and thickens progressively as elimination intensifies. As the body's primary eliminative work nears completion, the coating begins to clear from the edges and tip of the tongue first, then progressively toward the centre. Full clearing of the tongue coating, occurring simultaneously with or closely following the return of genuine hunger, marks the completion of the fasting period.

Secondary Signs: Normalisation of the pulse toward 60 beats per minute if it has been elevated or irregular. Clearing of the urine from dark and concentrated to clearer. Brightening of the eyes. Disappearance of the offensive breath that accompanies active elimination. Return of normal salivary secretion. These secondary signs are consistent and support the two primary indicators but are not individually conclusive.

DeVries is explicit that the fast should be broken at the appearance of either genuine hunger or tongue clearing, whichever comes first, and that one should not hesitate to break the fast if either sign is present even if the other has not yet appeared.

This system of natural indicators for fast completion is, from a clinical standpoint, elegant and reliable. The body communicates when it is ready. The physician and patient together simply need to know how to listen.

3.8 What Happens if You Fast Too Long: The Starvation Boundary

Because this book advocates extended fasting for therapeutic purposes, it is essential to be equally clear about where the beneficial fasting period ends and the dangerous starvation period begins.

DeVries makes this distinction with the precision of a serious clinical scientist: "fasting begins with the omission of the first meal and ends with the exhaustion of all food reserves. Starvation begins at this time and ends with death. Thus where the one process ends, the other begins."

During the fasting period, the body is consuming its non-essential reserves, specifically fat, excess fluid, pathological accumulations and damaged tissue, in a carefully orchestrated sequence that preserves all vital structures. The brain, spinal cord, heart and essential organs are maintained and, as we have discussed, often improved during this process. The muscle loss during a properly conducted fast is modest and is substantially restored during the refeeding period, particularly given the enhanced assimilation that follows the fast.

During the starvation period, by contrast, the non-essential reserves are exhausted. The body has no choice but to begin catabolising (breaking down) essential tissues, including healthy muscle, organ tissue and, eventually, cardiac muscle. This is genuinely dangerous and is the condition associated with the wasting and death that people associate with extreme prolonged food deprivation.

The signs marking the end of the fasting period and the beginning of starvation are the same signs described in the previous section: the return of genuine hunger and the clearing of the tongue. These are the body's unmistakable signals that its reserves are substantially consumed and it needs food to rebuild. When these signs appear, the fast must be broken, using the careful refeeding protocol we will describe in detail in the protocol chapters.

For most individuals, the complete fasting period extends somewhere between four and seven weeks, depending on initial body composition, particularly the quantity of fat reserves available. DeVries documents cases as short as ten days (in a very thin individual) and as long as ninety days (in an obese individual with extensive reserves). For practical therapeutic purposes, with the goal of addressing hypertension rather than achieving a complete fast, fasts of seven to twenty-one days under supervision are sufficient to produce profound and lasting antihypertensive effects in most patients. The complete fast, while theoretically ideal, is not a requirement for therapeutic benefit.

3.9 The Physiological Picture in Summary: Everything Working Together

Let us now stand back and look at the full physiological picture of what water fasting does to the hypertensive body, as an integrated system rather than a series of isolated mechanisms.

From the first hours of fasting, insulin falls. This single event, the lowering of circulating insulin, initiates a cascade of physiological corrections that address, simultaneously and in parallel, every upstream driver of essential hypertension.

Renal sodium retention reverses as the insulin signal driving it is removed. Blood volume contracts modestly. Preload on the heart decreases. Cardiac output falls.

Sympathetic nervous system overactivation, driven by chronic hyperinsulinaemia, begins to resolve. Heart rate normalises. Vasoconstriction of peripheral arterioles relaxes. Total peripheral resistance falls.

RAAS overactivation winds down as insulin-mediated renin release decreases. Angiotensin II levels fall. Vasoconstriction from this source relaxes. Aldosterone-driven sodium retention ceases.

BHB suppresses NLRP3 inflammasome activity. Inflammatory cytokines fall. Endothelial cell function improves. Nitric oxide production increases. Arterial vasodilation occurs.

Autophagy initiates cellular repair in endothelial cells, vascular smooth muscle cells and immune cells. Damaged structures are cleared and replaced. Arterial wall function improves. Baroreceptors recalibrate toward normal pressure set points.

Gut microbiome composition shifts toward anti-inflammatory, SCFA-producing species. TMAO-producing species decline. Butyrate production improves insulin sensitivity and reduces vascular inflammation.

The sympathetic nervous system continues to wind down as the metabolic environment improves. HRV (heart rate variability, a measure of autonomic balance) improves. The parasympathetic system, the body's "rest and repair" mode, becomes more dominant.

Over days and weeks of extended fasting, the cumulative effect of all these mechanisms working simultaneously produces the extraordinary clinical outcomes that the fasting physicians documented: blood pressures of 295/170 returning to 115/75. Patients on four medications achieving normotension on none. Disease processes that had been advancing for decades halting and beginning to reverse.

It is not magic. It is not an exaggeration. It is physiology, working as it was designed to work, when given the metabolic space, the physiological silence, to do so.

Chapter Summary: Key Points

The first 12 to 24 hours of fasting depletes hepatic glycogen reserves and initiates fat mobilisation. Insulin begins to fall and renal sodium excretion begins to accelerate, producing modest initial blood pressure reductions of 5 to 8 mmHg.

The 24 to 48 hour window is the physiological crossover between glucose and ketone fuel systems. The "keto flu" at this stage is a normal and temporary sign of metabolic transition, not a sign of harm. Electrolyte monitoring and supplementation are essential, particularly for patients on diuretic medications.

The 36-hour mark represents entry into deep ketosis. Beta-hydroxybutyrate (BHB) suppresses vascular inflammation through NLRP3 inflammasome inhibition. RAAS downregulation is measurable. Vasodilatory effects of ketones begin contributing to blood pressure reduction.

The 48 to 72 hour window is when autophagy, the Nobel Prize-winning cellular self-repair mechanism, reaches therapeutic intensity. Endothelial cell repair, immune cell recalibration and gut microbiome remodelling occur simultaneously.

The 72-hour mark is Jamnadas' identified threshold for "profound metabolic transformation, deep cellular autophagy, and resetting immune pathways." Longo's research documents immune system regeneration through stem cell activation at this threshold.

Extended fasting beyond 72 hours produces progressive de-salting of body tissues, arterial wall remodelling, baroreceptor recalibration, and the vascular rejuvenation that the historical fasting physicians documented clinically and that modern vascular biology now explains mechanistically.

The end of the therapeutic fasting period is signalled by the return of genuine hunger and the clearing of the tongue coating. These are reliable, observable indicators that should be recognised and respected.

All the antihypertensive mechanisms of water fasting operate simultaneously and synergistically, producing cumulative blood pressure reductions that exceed what any single pharmacological agent can achieve, addressing root causes rather than downstream symptoms.

“Fasting is the greatest remedy, the physician within.”

— Paracelsus, 16th Century

PART TWO: THE MECHANISMS

How Water Fasting Specifically Addresses Every Driver of Hypertension

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CHAPTER 4

Insulin, Sodium And Blood Pressure, The Triangle Nobody Told You About

“It is much more important to know what sort of a patient has a disease than what sort of a disease a patient has.”

— William Osler, physician and founding professor of Johns Hopkins Hospital

Opening: The Wrong Conversation

Imagine you have been driving a car for fifteen years. One morning, you notice the engine temperature gauge is climbing higher than usual. You pull into a mechanic's workshop and explain the problem.

The mechanic listens, nods, and hands you a small device. "Attach this to your dashboard," he says. "It will keep the gauge reading normal. Come back every three months for a new one."

You look at him. "But why is the engine overheating?"

He shrugs. "That is a more complicated question. The gauge is the problem we treat."

You would not accept this from a mechanic. You would walk out and find someone willing to look under the bonnet.

Yet this is, with remarkable precision, the conversation that happens in hypertension consultations around the world every day. The blood pressure reading is elevated. A medication is prescribed to bring the reading down. The question of why the pressure is elevated in the first place is either briefly noted as "multifactorial," meaning influenced by many factors, or not asked at all. The consultation ends. The prescription is filled. The quarterly review is booked.

The engine continues to overheat. The gauge simply no longer shows it.

This chapter lifts the bonnet. We are going to examine in detail the three-way relationship between insulin, sodium and blood pressure that drives essential hypertension in the vast majority of people who have it, and that the vast majority of clinicians managing it have never directly addressed.

The triangle has three corners. Each corner drives the other two. Each is measurable, documentable and, crucially, reversible. And until all three corners are addressed together, blood pressure management will remain exactly that: management. Not treatment. Not resolution. Management.

Let us meet the three corners.

4.1 Corner One: Insulin, The Hormone That Was Never Supposed to Stay High

Most people associate insulin with diabetes. They understand, in a general way, that insulin has something to do with blood sugar and that diabetics either do not produce enough of it or cannot use it properly. Beyond that, for most non-diabetic patients managing hypertension, insulin is simply not part of the conversation.

This is one of the most consequential blind spots in modern cardiovascular medicine.

Insulin is a peptide hormone, a small protein-based signalling molecule, produced by the beta cells of the pancreas, a gland located behind the stomach. It was first isolated in 1921 by Frederick Banting and Charles Best at the University of Toronto, a discovery that earned Banting the Nobel Prize in Physiology or Medicine in 1923 and that rightly transformed the treatment of type 1 diabetes. But insulin's role in human physiology extends far beyond glucose management, and it is these broader roles that are central to understanding hypertension.

What Insulin Actually Does

When you eat a meal containing carbohydrates, your digestive system breaks those carbohydrates down into glucose, which is absorbed through the wall of the small intestine into the bloodstream. Blood glucose rises. The pancreas detects this rise and releases insulin in response. Insulin then travels through the blood to every cell in the body, where it binds to specific docking points on the cell surface called insulin receptors.

Think of insulin as a key, and each cell's insulin receptor as the lock on the cell's front door. When the key fits the lock, the door opens, glucose enters the cell, and blood glucose falls back to its normal range. The pancreas detects the fall in blood glucose, reduces insulin secretion, and the system returns to baseline.

This is how the system is supposed to work. Clean, efficient, beautifully regulated.

But insulin does not only open the door for glucose. When it binds to receptors on different tissues around the body, it triggers multiple other biological responses simultaneously. In the kidneys, insulin binding signals the renal tubules to retain sodium. In the sympathetic nervous system, insulin binding stimulates increased neural activity. In the arterial wall, insulin binding promotes smooth muscle cell growth. In the adrenal glands, it modulates the release of stress hormones.

Under normal, healthy, insulin-sensitive conditions, these effects are transient and appropriate. Insulin rises after a meal, triggers its multiple effects briefly, then falls as the meal is processed and glucose returns to baseline. The renal sodium retention, the brief sympathetic stimulation, the modest smooth muscle response, all of these last for a few hours and then resolve as insulin falls.

The problem begins when insulin stops falling.

The Making of Insulin Resistance

Insulin resistance is the condition in which the body's cells progressively lose their sensitivity to insulin's signalling. The lock, to continue our earlier metaphor, becomes stiff. The key no longer turns as easily. To achieve the same glucose-lowering effect, the pancreas has to produce more insulin, essentially forcing the lock with a stronger push.

In the early stages of insulin resistance, this compensatory strategy works. The pancreas produces more insulin, glucose is managed adequately, and blood glucose levels remain within the normal range. A standard fasting blood glucose test or even an HbA1c (haemoglobin A1c, pronounced "haym-oh-GLOW-bin ay-wun-see," a measure of average blood glucose over the preceding three months) will read as perfectly normal. The doctor will tell the patient their sugar is fine.

But circulating insulin is elevated. Chronically. The pancreas is working overtime, pumping out two, three, sometimes five times the normal amount of insulin just to keep blood glucose in the acceptable range. And all of insulin's other biological effects, the ones that are supposed to be brief and transient, are now switched on continuously.

In plain language: the consequences of the insulin system being permanently activated are not limited to blood sugar. They extend to blood pressure, kidney function, arterial structure and nervous system activity. All at once. All the time. This state of chronic insulin excess is called hyperinsulinaemia (pronounced "high-per-in-SOO-lin-EE-me-ah," literally meaning too much insulin in the blood).

Jamnadas articulates this with characteristic clinical directness in the metabolic health guide: "Insulin resistance is the root cause of most chronic diseases including hypertension, type 2 diabetes, obesity, polycystic ovarian syndrome, non-alcoholic fatty liver disease, and several cancers. It is the common upstream driver that conventional medicine treats downstream while leaving the source untouched."

What causes insulin resistance in the first place? The primary drivers are:

Chronic dietary carbohydrate excess, particularly refined carbohydrates and sugars that produce large, rapid insulin spikes repeatedly through the day. A diet built around white rice, white bread, processed flour products, sweetened beverages, confectionery and refined snacks is, metabolically speaking, a systematic programme for producing insulin resistance. This dietary pattern describes, with uncomfortable accuracy, the nutritional reality of millions of people in rapidly urbanising populations around the world.

Physical inactivity. Skeletal muscle is the body's primary site of insulin-mediated glucose disposal. Exercising muscle consumes glucose voraciously and is highly insulin-sensitive. Sedentary muscle is relatively insulin-resistant. A physically inactive lifestyle progressively worsens the muscle's ability to respond to insulin.

Visceral adiposity, meaning the accumulation of fat around the internal organs of the abdomen rather than beneath the skin. Visceral fat is metabolically active, secreting inflammatory compounds called adipokines (fat-cell signalling molecules) and free fatty acids that directly impair insulin receptor function in the liver and muscle.

Chronic sleep deprivation and psychological stress, both of which elevate cortisol (the stress hormone), which directly antagonises insulin signalling.

Gut microbiome dysbiosis, as described in Chapter 3, with reduced SCFA production impairing insulin sensitivity at the tissue level.

For many people reading this book, the combination of several of these factors operating simultaneously over years or decades has produced a state of significant insulin resistance and chronic hyperinsulinaemia that their fasting blood glucose and HbA1c tests have never detected, because those tests measure glucose, not insulin. The hyperinsulinaemia, the elevated circulating insulin that is driving their hypertension, is invisible to the standard blood tests their doctor orders.

Jamnadas recommends the fasting insulin test as the most clinically informative single blood test for metabolic health assessment. A fasting serum insulin level above 8 microunits per millilitre suggests developing insulin resistance. Above 15 suggests significant insulin resistance. Above 25 suggests severe hyperinsulinaemia. Many hypertensive patients who have never been told they have any metabolic problem at all will, on fasting insulin testing, show levels in the 20 to 40 range, sometimes higher.

4.2 Corner Two: Sodium, The Mineral That Has Been Misunderstood

Before we discuss how insulin and sodium interact to drive hypertension, we need to establish a clear and accurate understanding of sodium physiology, because the conventional medical conversation about sodium and blood pressure, while not entirely wrong, is incomplete in ways that have significant therapeutic implications.

What Sodium Does in the Body

Sodium (chemical symbol Na, from the Latin "natrium") is an essential electrolyte. The body cannot function without it. Sodium is the primary cation (positively charged ion) in the extracellular fluid, meaning the fluid outside cells. It is the main determinant of extracellular fluid volume. Where sodium goes, water follows, because water moves osmotically (through a concentration gradient) toward areas of higher solute concentration.

This means sodium directly governs blood volume. More sodium in the circulation means more water retained in the circulation, which means higher blood volume, which means higher pressure within the vascular system. This is the basis of the conventional sodium-hypertension link: high salt intake raises blood pressure because it raises blood volume.

This mechanism is real. It is just not the complete picture.

Sodium is also critical for nerve impulse transmission (the electrical signals that the nervous system uses to communicate), muscle contraction (including the contraction of the heart), and the regulation of cell membrane electrical potential (the difference in electrical charge between the inside and outside of cells that makes cellular function possible). Without adequate sodium, nerve and muscle function fail.

The body therefore maintains sodium balance with extraordinary precision through an elegant multi-system regulatory mechanism. The kidneys are the primary managers of sodium balance. When sodium intake is high, healthy kidneys excrete the excess. When sodium intake is low, healthy kidneys retain every available molecule.

This renal sodium management is governed by multiple hormones, the most important of which are aldosterone (from the adrenal glands), natriuretic peptides (from the heart itself, released when blood volume is too high, signalling the kidneys to excrete more sodium), and insulin.

The Conventional Sodium Narrative and Its Limitations

The conventional medical advice for hypertension is to reduce dietary sodium intake, typically to below 2,300 milligrams per day (roughly one teaspoon of table salt), and ideally below 1,500 milligrams for those with established hypertension. This advice is supported by a substantial body of epidemiological evidence showing population-level correlations between salt intake and blood pressure, and by clinical trials showing that sodium restriction produces modest blood pressure reductions in most hypertensive patients.

Bragg built much of his dietary philosophy around radical sodium restriction, advocating the complete elimination of table salt and arguing, based on decades of clinical observation, that the body's sodium needs are fully met by the naturally occurring sodium in whole, unprocessed foods. The evidence from populations eating traditional, unprocessed diets with minimal added salt, including certain indigenous groups and isolated rural communities studied by epidemiologists in the mid-twentieth century, broadly supports this view.

But here is where the conventional narrative becomes incomplete in a clinically important way.

Not everyone responds to sodium reduction with meaningful blood pressure improvement. Studies consistently show that approximately 50 to 60 percent of hypertensive patients are "salt-sensitive," meaning their blood pressure reliably rises with increased sodium intake and falls with sodium restriction. The other 40 to 50 percent are "salt-resistant," showing little blood pressure response to sodium intake changes regardless of how much salt they consume.

Why the difference? The answer lies in the third corner of our triangle, and specifically in the interaction between insulin and the kidney's sodium handling.

The Kidney's Sodium Architecture

To understand how insulin and sodium interact, you need a working picture of how the kidney processes sodium at the cellular level.

The kidney filters blood continuously through approximately one million tiny filtering units per kidney called nephrons (pronounced "NEF-rons"). Each nephron consists of a filtering capsule, the glomerulus (pronounced "glo-MAIR-yoo-lus"), followed by a long tubular system where the filtered fluid is processed before becoming urine. As the filtered fluid travels through the tubular system, the kidney selectively reabsorbs substances it wants to keep, including glucose, amino acids and, critically, sodium, and allows waste products to pass through into the urine.

The key site of hormonally regulated sodium reabsorption is a section of the tubular system called the distal tubule and collecting duct. This is where aldosterone acts, inserting sodium channels and pumps into the tubular cell membranes to pull sodium back from the forming urine into the bloodstream.

What most textbooks do not emphasise, and what is central to the insulin-sodium-hypertension story, is that insulin also acts directly on these same tubular cells. Insulin has specific receptors in the renal tubular epithelium (the cells lining the tubular system), and when it binds to them, it activates sodium-hydrogen exchangers and sodium-potassium-ATPase pumps in these cells, directly increasing sodium reabsorption.

In plain language: insulin tells the kidney to hold onto salt. When insulin is elevated chronically, the kidney is receiving a continuous, unrelenting command to retain sodium. No amount of dietary sodium reduction fully compensates for a kidney that is being driven by chronically elevated insulin to retain every sodium molecule it can get hold of.

This is why salt restriction, while valuable and genuinely therapeutic, does not produce the complete resolution of hypertension that it theoretically should if sodium were the only driver. The kidney's behaviour toward sodium is being governed not just by dietary sodium intake but by the hormonal signal it is receiving from chronically elevated insulin.

Jamnadas articulates this directly: "Insulin drives renal sodium retention. Hyperinsulinaemia means the kidney is being told to retain sodium around the clock. You can reduce dietary sodium intake, but you cannot fully override a kidney that insulin is commanding to hold salt."

4.3 Corner Three: Blood Pressure, The Downstream Consequence

Blood pressure, as we established in Chapter 1, is the product of cardiac output (how much blood the heart pumps per minute) multiplied by total peripheral resistance (the resistance offered by the arterial system to that pumping). Elevate either factor and blood pressure rises. Elevate both simultaneously and hypertension becomes severe and difficult to treat.

Essential hypertension, in the insulin-resistant, hyperinsulinaemic individual, involves both mechanisms. And insulin is directly implicated in both.

How Insulin Elevates Cardiac Output

Cardiac output (CO) is the volume of blood the heart pumps in one minute. It is determined by heart rate multiplied by stroke volume, meaning how many times the heart beats per minute multiplied by how much blood is ejected with each beat.

In the hyperinsulinaemic state, cardiac output is elevated through two mechanisms.

First, chronically elevated insulin, operating through the sympathetic nervous system (the body's "fight or flight" system), increases heart rate. The sympathetic nervous system innervates the heart directly through specialised nerve fibres that release noradrenaline (also called norepinephrine) onto the heart's pacemaker cells, increasing the rate of electrical impulse generation and therefore increasing heart rate. Insulin drives this sympathetic overactivation through a mechanism involving the hypothalamus, a small but critically important region of the brain that regulates autonomic (automatic) nervous system function.

Second, the sodium retention that insulin drives increases blood volume. Higher blood volume means more blood returning to the heart with each cycle (higher preload), stretching the heart chambers and,

by the Frank-Starling mechanism (a fundamental principle of cardiac physiology stating that a more stretched ventricle contracts more forcefully), increasing stroke volume. More blood returning to the heart per beat, combined with a higher heart rate, produces elevated cardiac output.

How Insulin Elevates Total Peripheral Resistance

Total peripheral resistance (TPR) is determined primarily by the diameter of the small resistance arteries (arterioles) throughout the body. Narrower arteries offer more resistance. Wider arteries offer less. The body regulates arteriolar diameter through smooth muscle tone, meaning how contracted or relaxed the smooth muscle cells in the arterial walls are.

In the hyperinsulinaemic state, total peripheral resistance is elevated through three converging mechanisms.

The first is direct sympathetic vasoconstriction. The same sympathetic overactivation that accelerates heart rate also releases noradrenaline onto vascular smooth muscle cells throughout the body, causing them to contract and narrow the arterioles. Higher sympathetic tone means narrower arteries. Narrower arteries mean higher resistance. Higher resistance means higher blood pressure.

The second is RAAS overactivation and its consequences. As established in Chapter 3, chronic hyperinsulinaemia drives excessive renin release, which produces elevated angiotensin II, the most potent vasoconstrictor in the human body. Angiotensin II acts directly on vascular smooth muscle cells, causing powerful contraction. It simultaneously elevates aldosterone, which drives further sodium and water retention, expanding blood volume against an already constricted vascular bed. The result is a double hit: more volume trying to move through narrower pipes.

The third mechanism is structural arterial remodelling. This is the most insidious and clinically significant mechanism because it represents not just a functional change but a physical, structural change in the architecture of the arterial wall itself.

Insulin is a growth factor. One of its normal physiological roles is to promote cellular growth and proliferation in tissues that need to rebuild after injury. When insulin receptors in vascular smooth muscle cells are stimulated by chronically elevated circulating insulin, these cells receive a continuous growth signal. They proliferate. They increase their protein synthesis. The arterial wall thickens from the inside out as more smooth muscle cells accumulate in the medial layer (the muscular middle layer of the artery wall).

A thicker, more muscular arterial wall has less capacity to relax and dilate. It offers more structural resistance to blood flow at its resting state. It is stiffer. Its reserve capacity for vasodilation in response to increased demand (such as during exercise) is reduced. This structural thickening, called vascular hypertrophy (pronounced "VAS-cue-lar high-PER-troh-fee," meaning over-growth of the blood vessel wall), develops slowly over years of chronic hyperinsulinaemia and represents a qualitatively different kind of problem from simple functional vasoconstriction.

Functional vasoconstriction is rapidly reversible: remove the vasoconstricting stimulus and the vessel relaxes within minutes to hours. Structural hypertrophy takes months to years to reverse, even after the driving stimulus, the chronically elevated insulin, has been removed. This is why blood pressure does

not always normalise immediately even after successful metabolic intervention. The structural remodelling requires time to reverse, even as the functional components of the elevated pressure resolve more quickly.

4.4 How the Three Corners Drive Each Other: The Self-Perpetuating Loop

We have now met all three corners of the triangle. What makes essential hypertension so resistant to simple intervention is that these three corners are not independent variables. They form a self-perpetuating loop in which each corner worsens the others.

Hyperinsulinaemia drives sodium retention (Corner 1 worsening Corner 2). Sodium retention raises blood volume and blood pressure (Corner 2 worsening Corner 3). Elevated blood pressure creates mechanical stress on arterial walls, triggering local inflammatory responses that impair insulin receptor function in vascular cells (Corner 3 worsening Corner 1). The loop closes. And it accelerates.

There is a second loop operating simultaneously. Elevated blood pressure in the renal arteries directly impairs kidney function over time (hypertensive nephropathy, meaning kidney damage caused by high blood pressure). As kidney function deteriorates, sodium handling becomes less efficient, sodium retention worsens, and blood pressure rises further (Corner 3 worsening Corner 2 worsening Corner 3 again). This is the mechanism by which untreated or poorly treated hypertension eventually produces chronic kidney disease, which then makes the hypertension harder to control, which accelerates the kidney disease further.

A third loop involves the sympathetic nervous system. Chronic sympathetic overactivation (driven by insulin, Corner 1\) elevates blood pressure (Corner 3). The physiological stress of chronically elevated blood pressure activates the body's stress response systems, further stimulating the sympathetic nervous system. Elevated sympathetic activity impairs insulin sensitivity in peripheral tissues, worsening insulin resistance and driving insulin higher (Corner 3 feeding back into Corner 1). Round and round.

Understanding these loops is clinically essential because it explains why pharmacological monotherapy, treating a single point in a multi-loop system, inevitably reaches its limits. An ACE inhibitor interrupts one segment of the RAAS loop. It does not interrupt the sympathetic loop or the structural remodelling loop or the insulin-sodium loop. The pressure in the other loops, still operating unaddressed, eventually finds its way around the pharmacological block.

This is why so many hypertensive patients progress from one medication to two, and from two to three or four, not because their medication stopped working in the simple sense, but because the system found alternative pathways around the single points of pharmacological interruption, while the underlying metabolic driver, the chronic hyperinsulinaemia at the apex of all three loops, continued entirely unaddressed.

4.5 The Evidence You Were Never Shown

The insulin-hypertension connection is not a hypothesis. It is not a fringe theory from the naturopathic literature. It is extensively documented in peer-reviewed scientific publications spanning more than four

decades, including publications in some of the most prestigious journals in medicine.

Let us review the key evidence.

In 1985, Dr. Gerald Reaven at Stanford University published foundational research demonstrating a direct quantitative relationship between insulin resistance, hyperinsulinaemia and hypertension. His subsequent 1988 paper in the journal Diabetes, one of the most cited papers in metabolic medicine, introduced what he called Syndrome X (later renamed metabolic syndrome), the cluster of insulin resistance, hypertension, dyslipidaemia (abnormal blood fats) and central obesity that he identified as a unified metabolic entity with a single root cause: insulin resistance. Reaven wrote with characteristic directness that "resistance to insulin-stimulated glucose uptake appears to be a characteristic feature of patients with essential hypertension, present in the great majority."

Read that carefully: "a characteristic feature of patients with essential hypertension, present in the great majority." Not a minority. Not a subtype. The great majority.

In the 1990s, multiple independent research groups confirmed Reaven's findings. Studies using the euglycaemic-hyperinsulinaemic clamp, which is the most precise available method for measuring insulin sensitivity (it involves continuously infusing insulin and glucose intravenously while monitoring how much glucose the body consumes at a fixed insulin level, giving a direct readout of tissue insulin sensitivity), consistently demonstrated that hypertensive individuals were significantly more insulin-resistant than normotensive (normal blood pressure) controls, even when body weight was matched between the groups.

In plain language: the insulin resistance-hypertension connection was not simply an effect of obesity. Lean hypertensive individuals were also insulin-resistant compared to lean normotensive individuals. The metabolic disturbance was primary, not secondary to excess weight.

Research specifically examining renal sodium handling in the context of insulin resistance has directly confirmed the mechanism we described in Section 4.2. Studies measuring sodium excretion rates (natriuresis, pronounced "nay-tree-YOO-ree-sis," meaning sodium in the urine) in insulin-resistant individuals versus insulin-sensitive controls under controlled sodium loading conditions show that insulin-resistant kidneys retain significantly more sodium for any given level of sodium intake. The kidney, as Jamnadas states, is not behaving independently. It is behaving in response to the hormonal environment it is operating within.

The link between sympathetic nervous system overactivation and hyperinsulinaemia has been confirmed through direct measurement of sympathetic nerve activity using a technique called microneurography (direct recording of sympathetic nerve impulses in peripheral nerves through tiny microelectrodes), showing that hyperinsulinaemic individuals have measurably higher sympathetic nerve traffic than insulin-sensitive controls.

And the structural vascular changes driven by chronic insulin excess have been documented through imaging studies showing that insulin-resistant individuals have measurably greater intima-media thickness (the thickness of the arterial wall measured by ultrasound, a validated surrogate marker for arterial disease) than insulin-sensitive controls of the same age and blood pressure level.

The evidence is not sparse. It is not peripheral. It has been in the peer-reviewed literature since the mid-1980s and has been accumulating steadily ever since. What has been lacking is not the evidence. What has been lacking is the clinical translation of that evidence into the consultation room, where the hypertensive patient sits across from a prescriber who has been trained in the pharmacological management of blood pressure but not in the metabolic physiology of why it is elevated.

4.6 Why Standard Blood Tests Miss the Problem Entirely

Here is something that should concern every person managing their hypertension through regular GP or clinic visits.

The standard blood tests ordered for a hypertensive patient in most clinical settings are: fasting blood glucose, HbA1c, a full blood count, a kidney function panel (urea, creatinine and electrolytes), and a lipid profile (total cholesterol, LDL, HDL and triglycerides). In many settings, a uric acid level may also be checked.

These are not bad tests. They are useful. But they share a critical blind spot: not one of them measures circulating insulin.

A patient with fully developed, clinically significant insulin resistance and chronic hyperinsulinaemia driving all three corners of the hypertension triangle can present with completely normal fasting blood glucose (because the pancreas is still successfully compensating by overproducing insulin), normal HbA1c (same reason), and even a reasonably normal lipid profile at an early stage.

Their hypertension will be identified. Their kidneys, if not yet significantly damaged, will read as normal. Their glucose will be normal. Their doctor will conclude that this is essential hypertension of unknown cause and will initiate pharmacological management.

The insulin, which is the actual cause, will never be measured.

Jamnadas recommends a practical screening approach for metabolic health assessment that goes beyond standard panels:

The first is the fasting serum insulin test, ideally combined with a fasting blood glucose to calculate the HOMA-IR (Homeostatic Model Assessment of Insulin Resistance, pronounced "HO-ma eye-ar"). HOMA-IR is calculated as fasting insulin (in microunits per millilitre) multiplied by fasting glucose (in millimoles per litre) divided by 22.5. A HOMA-IR below 1.0 indicates excellent insulin sensitivity. Between 1.0 and 1.9 is borderline. Above 2.0 suggests insulin resistance. Above 2.9 suggests significant insulin resistance.

The second marker is the triglyceride-to-HDL ratio (TG:HDL ratio). High-density lipoprotein (HDL) is what is commonly called "good cholesterol." Triglycerides are blood fats that rise with carbohydrate excess and insulin resistance. A TG:HDL ratio above 2.0 (using mmol/L units) is a sensitive and practical surrogate marker for insulin resistance, correlating closely with direct insulin measurement in multiple studies. A TG:HDL ratio above 3.0 indicates significant metabolic dysregulation.

The third marker, less commonly available but highly informative when accessible, is fasting uric acid. Elevated uric acid (above 360 micromoles per litre in women, above 420 micromoles per litre in men) is strongly associated with insulin resistance and is itself an independent contributor to hypertension through mechanisms involving renal uric acid handling and endothelial dysfunction.

The fourth indicator is completely free, requires no laboratory test, and can be assessed by any patient at home: waist circumference. Visceral adiposity, the most metabolically harmful type of fat accumulation, manifests as abdominal enlargement. A waist circumference above 94 centimetres in men (above 80 centimetres in women) is a practical threshold for clinically concerning visceral adiposity, though even below these thresholds, a waist circumference trending upward over years is a meaningful metabolic signal.

None of these tests or measurements alone is definitive. But together, they paint a metabolic picture that the standard hypertension blood panel completely misses. For any person reading this book whose blood pressure has been treated for years without full explanation or resolution, arranging a fasting insulin and HOMA-IR measurement may be the single most illuminating investigation they have ever had.

4.7 What Happens to the Triangle When You Fast

We have now established the three corners and the loops connecting them. We have seen the evidence that this triangle is the primary architecture of essential hypertension in the majority of those who have it. The question this book ultimately answers is: what is the most effective way to dismantle it?

And the answer, which should now be becoming mechanistically clear, is water fasting.

Let us trace through the triangle as fasting acts on it.

Insulin falls. Within the first twelve to twenty-four hours of water fasting, circulating insulin drops to its physiological minimum as dietary carbohydrate input, the primary driver of insulin release, is completely removed. This is not a modest reduction. It is, for the hyperinsulinaemic patient eating a typical modern diet, a dramatic fall from chronically elevated levels to the lowest insulin state their body has been in since childhood.

With insulin falling, every hormonal signal that insulin was driving begins to reverse. The renal command to retain sodium is progressively lifted. The sympathetic overactivation begins to wind down. The growth signal to vascular smooth muscle cells is removed. The RAAS overactivation, which insulin was maintaining through its effect on renin release, begins to resolve.

Sodium rebalances. As the insulin-mediated renal sodium retention signal is progressively removed, the kidneys begin excreting sodium at an accelerating rate. Bragg observed the urine of fasting patients darkening and depositing crystalline material in the early days of fasting, then progressively clearing as the accumulated sodium and metabolic waste was excreted. DeVries documented that even four days of complete water fasting was sufficient to substantially de-salt the body tissues in most patients.

Blood volume contracts as sodium and its accompanying water are excreted. Preload on the heart decreases. Cardiac output falls. One of the two major components of elevated blood pressure begins to correct.

Blood pressure falls. With falling cardiac output and progressively relaxing vascular tone (as sympathetic overactivation subsides and RAAS-driven vasoconstriction resolves), total peripheral resistance begins to decrease. The pressure in the system falls from both ends simultaneously: less volume being pumped, and lower resistance to the volume being pumped.

This is why the blood pressure reductions documented in fasting studies are not modest. The Goldhamer studies showed average reductions of 37 mmHg systolic and 13 mmHg diastolic across 174 patients. These reductions are not what happens when you remove one pharmacological agent from a three-drug regimen. These are the reductions that happen when the entire metabolic machinery driving the hypertension is given the physiological space to unwind simultaneously.

What fasting does to the triangle is not target one corner. It simultaneously addresses the apex of all three loops: it removes chronic hyperinsulinaemia, the primary driver that was feeding energy into all three corners at once. When the primary driver is removed, all three loops begin unwinding together. The triangle does not have one side removed. It collapses.

After the fast: holding the collapse

The question that must be asked is whether the triangle stays collapsed or rebuilds itself when eating resumes.

The answer is determined by what is eaten after the fast. If the post-fast diet is a return to the same refined carbohydrate excess, the same dietary pattern that built the insulin resistance and drove the chronic hyperinsulinaemia in the first place, then insulin will rise again, sodium retention will resume, and blood pressure will trend back toward its pre-fasting level over weeks to months.

If, however, the post-fast diet maintains the insulin sensitivity that the fast has restored, through a whole-food, low-refined-carbohydrate nutritional pattern, adequate dietary fibre to support gut microbiome health, appropriate protein and dietary fat to minimise insulin demand while providing satiety, then the triangle remains collapsed. The kidneys, no longer commanded by chronically elevated insulin to retain sodium, handle dietary sodium appropriately and excrete what is not needed. Blood pressure remains at the levels achieved during the fast.

DeVries documented this with clinical precision: "if the blood pressure falls below normal during the fast, it will rise to normal later, but actual hypertension does not redevelop so long as good nutritional habits are maintained after the fast."

This is the distinction between management and cure. Pharmacological antihypertensives maintain their effect only as long as the patient takes them, because the underlying metabolic driver of the hypertension has not changed. Therapeutic fasting followed by appropriate nutritional rehabilitation removes the metabolic driver. The blood pressure does not require maintenance suppression because the machinery generating the excess pressure has been addressed at its root.

4.8 The Practical Implications: What You Should Know Before Your Next Appointment

For anyone currently managed on antihypertensive medication, the contents of this chapter have several practical implications worth taking to your next clinical appointment.

First, ask for a fasting insulin test and a HOMA-IR calculation. This is a simple, inexpensive blood test that most clinical laboratories can perform. In settings where it is not routinely available, it can be requested as a special investigation. The result will tell you, with quantitative precision, whether insulin resistance is present. If it is, the metabolic driver of your hypertension is identified, and the therapeutic approach described in this book becomes directly applicable to your situation.

Second, ask for a triglyceride-to-HDL ratio if this is not already part of your standard lipid report. A ratio above 2.0 in the context of established hypertension is a strong indicator that insulin resistance is contributing to your cardiovascular risk profile, even if your blood glucose is normal.

Third, understand that if insulin resistance is confirmed, your blood pressure medication is addressing a consequence, not a cause. This does not mean you should stop your medication. It means you should understand what the medication is and is not doing, and that there is a metabolic intervention available, supervised therapeutic fasting followed by nutritional rehabilitation, that can address what the medication is not.

Fourth, and most importantly: if you embark on a therapeutic fast, blood pressure monitoring and medication adjustment under medical supervision are not optional. As the triangle begins to collapse and blood pressure falls, the antihypertensive medications that were necessary to maintain a safe pressure against the full force of the metabolic drivers will progressively become too strong. They will drive blood pressure lower than intended. Hypotension (blood pressure that is too low, pronounced "high-po-TEN-shun") produces symptoms including dizziness, light-headedness, nausea, and in severe cases, falls and fainting. This is a predictable consequence of effective metabolic treatment, not a complication of the fasting. But it requires clinical management to be safe.

The goal, under medical supervision, is to reduce and potentially eliminate antihypertensive medications in step with the blood pressure reductions that fasting produces, so that the patient achieves a genuinely normal blood pressure through a healed metabolic system rather than a pharmacologically suppressed number in the presence of a continuing metabolic disease.

This is the vision that the great fasting physicians of the twentieth century were documenting across their thousands of cases. It is the outcome that Goldhamer's research confirmed in the peer-reviewed literature. It is the physiological consequence of what happens when you address the three corners of the triangle simultaneously, which is what water fasting, done correctly and under appropriate supervision, uniquely enables.

Chapter Summary: Key Points

Essential hypertension, in the majority of those who have it, is the downstream consequence of a three-cornered metabolic loop involving chronic hyperinsulinaemia (too much insulin), sodium retention

and elevated blood pressure, each corner driving the others in self-perpetuating cycles.

Insulin resistance is the primary upstream driver. The pancreas overproduces insulin to maintain glucose control as cellular sensitivity to insulin progressively declines, driven by refined carbohydrate excess, physical inactivity, visceral fat accumulation, stress and poor sleep.

Insulin acts directly on the renal tubular cells to drive sodium retention, independently of and on top of aldosterone. This is why dietary sodium restriction, while beneficial, does not fully resolve hypertension when the insulin-driven renal sodium retention signal remains intact.

Hyperinsulinaemia elevates blood pressure through four simultaneous mechanisms: renal sodium retention increasing blood volume, sympathetic nervous system overactivation increasing heart rate and vasoconstriction, RAAS overactivation producing the most potent vasoconstriction in the body, and vascular smooth muscle cell proliferation thickening and stiffening arterial walls.

Gerald Reaven's landmark 1985 and 1988 research established, in the peer-reviewed literature, that insulin resistance is present in "the great majority" of essential hypertension patients. This evidence is four decades old and has been consistently confirmed. It has not been consistently translated into clinical practice.

Standard hypertension blood panels do not measure insulin. A hypertensive patient can have severe chronic hyperinsulinaemia driving all three corners of the triangle while presenting with completely normal fasting blood glucose and HbA1c. Fasting serum insulin and HOMA-IR are the appropriate tests.

Water fasting addresses all three corners simultaneously by removing the primary driver: it drops insulin to its physiological minimum, lifts the renal sodium retention signal, reduces blood volume, winds down sympathetic overactivation, suppresses RAAS activity and removes the vascular growth stimulus. The triangle does not have one side removed. It collapses.

The durability of fasting-achieved blood pressure normalisation depends on post-fast nutritional rehabilitation. If the dietary pattern that drove the insulin resistance is resumed, the triangle rebuilds. If insulin sensitivity is maintained through appropriate nutrition, the blood pressure normalisation is durable.

Medical supervision during fasting is mandatory for hypertensive patients on medication because blood pressure reductions during fasting are real, substantial and will render standard antihypertensive doses excessive. Medication adjustment in step with blood pressure reduction is an essential component of safe protocol management.

> *“The doctor of the future will no longer treat the human frame with drugs, but rather will cure and prevent disease with nutrition.”*
>
> — Thomas Edison

CHAPTER 5

Inflammation, Endothelium And The Vascular Repair That Fasting Triggers

“Every disease begins in the gut... and in the blood vessel wall.”

— Adapted from Hippocrates

Opening: The Fire Inside

Picture a busy road in the dry season. The tarmac is good, traffic flows, vehicles move in both directions without incident. Now picture what happens to that same road after years of heavy trucks, poor drainage, heat and neglect. Cracks appear first, then potholes, then sections where the surface has broken apart entirely. Traffic slows. Accidents happen more frequently. What was once a clear passage for movement has become an obstacle to it.

Your arteries work on the same principle.

A healthy artery is smooth, elastic and responsive. Blood flows through it easily. The inner lining adjusts its diameter in response to demand, expanding when more flow is needed and narrowing when less is required. Nutrients reach every tissue. Waste products are cleared. The heart pumps against low resistance.

An inflamed, damaged artery is stiff, narrowed, and lined with deposits that should not be there. Blood must be pushed harder to move through it. The heart works against higher resistance with every beat. The pressure inside the system climbs. The damage accumulates. And the most maddening part of it is that the person living inside this body feels almost nothing until the damage is advanced enough to produce a heart attack, a stroke, or the kind of severe hypertension that has already been present and worsening for a decade.

This is the story of vascular inflammation, the slow, silent fire burning in the walls of your blood vessels that modern medicine has identified as perhaps the single most important driver of cardiovascular disease, and that water fasting extinguishes with a thoroughness that no anti-inflammatory medication currently available can match.

This chapter is about understanding that fire, where it comes from, what it does to the structures it burns, and precisely how fasting douses it at the source.

5.1 The Endothelium: The Most Important Single-Cell Layer in Your Body

Let us begin with the structure that is most directly relevant to everything that follows in this chapter.

The endothelium (pronounced "en-doh-THEE-lee-um") is the innermost lining of every blood vessel in your body, from the great vessels closest to the heart all the way down to the tiniest capillaries barely

wide enough for a single red blood cell to pass through. It is a single layer of specialised cells, endothelial cells, arranged in a continuous sheet that forms the interface between the flowing blood and the structural tissue of the vessel wall.

This single-cell-thick layer is not passive scaffolding. It is one of the most metabolically active and functionally sophisticated tissues in the human body.

Your endothelium, taken together, weighs approximately one kilogram and would cover an area of roughly 3,000 to 6,000 square metres if spread flat. That is the size of an entire football pitch. You carry that much endothelium inside you, and every cell of it is doing something important every second of every day.

What does it do?

The Endothelium as a Blood Flow Regulator

The most immediately relevant function for our purposes is vasomotor regulation, meaning the regulation of blood vessel diameter. Endothelial cells continuously monitor the chemical composition of the blood flowing past them and the mechanical forces of that blood flow against their surface. In response to these signals, they produce and release a range of chemical messengers that act on the smooth muscle cells in the layer just beneath them, causing those muscle cells to relax (producing vasodilation, wider vessels, lower resistance) or contract (producing vasoconstriction, narrower vessels, higher resistance).

The most important of these chemical messengers is nitric oxide (chemical formula NO). Nitric oxide is produced inside endothelial cells by an enzyme called eNOS, which stands for endothelial nitric oxide synthase (pronounced "en-doh-THEE-lee-al NY-tric OX-ide SIN-thase," meaning the enzyme that makes nitric oxide in endothelial cells). When endothelial cells are healthy and functioning properly, they produce a continuous baseline stream of nitric oxide that diffuses into the underlying smooth muscle cells and keeps the arterial wall in a state of appropriate relaxed tone.

Nitric oxide is, in the most literal sense, your body's natural blood pressure medication. It is the endogenously produced, endothelium-derived signal that maintains arterial relaxation and appropriate pressure. Many pharmacological antihypertensive strategies, including nitrate medications and phosphodiesterase inhibitors, work by mimicking or extending the effects of nitric oxide in the vascular wall. But they are supplements to a system that, when healthy, runs entirely on its own production.

When endothelial cells are damaged and dysfunctional, eNOS activity falls. Nitric oxide production decreases. The baseline vasodilatory tone is lost. Arteries become more constricted, more reactive, and more prone to inappropriate vasoconstriction. Blood pressure rises. And the road to hypertension, to arterial stiffening, and to cardiovascular events has been opened.

The Endothelium as an Anti-Clotting Surface

Healthy endothelial cells produce multiple compounds that prevent blood from clotting against the vessel wall. This anti-thrombotic (anti-clotting) function is critical: blood must remain fluid as it flows through vessels, clotting only when a vessel is actually cut or damaged. A loss of endothelial

anti-thrombotic function is one of the primary mechanisms by which arterial plaques, the deposits that build up inside arterial walls in atherosclerosis (pronounced "ath-er-oh-skler-OH-sis," hardening and narrowing of the arteries), become sites of acute clot formation producing heart attacks and strokes.

The Endothelium as an Inflammatory Gatekeeper

In the healthy state, the endothelium acts as a selective barrier. It allows the passage of nutrients and oxygen from the blood into surrounding tissues while preventing unwanted substances and cells from crossing into the vessel wall itself. Critically, it regulates the migration of immune cells from the bloodstream into the vessel wall.

When inflammation is needed (for example, at a site of genuine infection or injury), endothelial cells upregulate (switch on) specific surface molecules called adhesion molecules, including ICAM-1 (intercellular adhesion molecule 1\) and VCAM-1 (vascular cell adhesion molecule 1). These act like landing pads, catching circulating immune cells (particularly monocytes, a type of white blood cell) and guiding them through the endothelial layer into the vessel wall where they are needed.

In the context of vascular disease, this gating mechanism becomes pathologically activated in response to chronic inflammatory signals, inviting immune cells into the arterial wall continuously even in the absence of genuine infection or injury. These infiltrating immune cells become part of the arterial plaque-building process, as we will describe in Section 5.3.

5.2 Endothelial Dysfunction: When the Lining Fails

Endothelial dysfunction is the term clinicians use to describe the state in which endothelial cells are no longer performing their functions adequately. It is recognised as both an early marker and an active driver of cardiovascular disease, appearing measurably in blood vessels years before clinical hypertension or atherosclerosis becomes apparent.

The two primary measurable features of endothelial dysfunction are:

Reduced flow-mediated dilation (FMD). This is measured by ultrasound: a blood pressure cuff is inflated on the upper arm to briefly stop blood flow, then released. In a person with healthy endothelium, the sudden rush of blood returning to the forearm stimulates a measurable widening of the brachial artery (the main artery of the upper arm), driven by nitric oxide release. This widening is the flow-mediated dilation. In a person with endothelial dysfunction, this response is blunted. The artery widens less or not at all, because nitric oxide production is impaired.

Elevated circulating markers of endothelial activation. These include E-selectin, ICAM-1 and VCAM-1, the adhesion molecules that are elevated when the endothelium is in an activated, pro-inflammatory state. Elevated circulating levels of these molecules indicate that endothelial cells throughout the body are operating in a pathologically activated mode.

What Causes Endothelial Dysfunction?

The primary drivers are the same metabolic derangements we have been discussing throughout this book.

Oxidative stress is the most fundamental. Oxidative stress refers to an imbalance between the production of reactive oxygen species (ROS, also called free radicals, unstable molecules that carry an unpaired electron and react destructively with cellular components) and the cell's ability to neutralise them with antioxidant defences.

In simple terms: think of rust. Rust is the result of iron being oxidised, chemically damaged by oxygen. Oxidative stress inside cells is a molecular version of rusting. The affected cellular components, proteins, lipids and DNA, are chemically modified and lose their function. In endothelial cells, one of the most critical casualties of oxidative stress is eNOS itself. Oxidative stress causes eNOS to become "uncoupled," meaning instead of producing nitric oxide it begins producing superoxide, another free radical, further worsening oxidative stress in a destructive feedback loop. Nitric oxide production collapses. Endothelial function deteriorates.

What generates oxidative stress in the endothelium? The primary drivers in the metabolically deranged individual are: hyperglycaemia (high blood sugar, even the moderate post-meal spikes that occur in insulin-resistant individuals who are not yet diabetic), advanced glycation end products (AGEs, sticky compounds formed when glucose reacts with proteins and fats, damaging them), oxidised LDL cholesterol (LDL particles that have been chemically damaged by oxidative reactions), and chronic low-grade inflammation.

Chronic hyperinsulinaemia, our familiar primary villain, contributes to endothelial oxidative stress through multiple pathways. Insulin at supraphysiological levels (above normal levels), the concentrations that characterise hyperinsulinaemia, activates oxidative stress pathways in endothelial cells and simultaneously suppresses the expression of antioxidant enzymes that would normally neutralise the resulting free radicals.

Chronic inflammation is both a cause and a consequence of endothelial dysfunction. Inflammatory cytokines such as interleukin-6 (IL-6), tumour necrosis factor-alpha (TNF-alpha) and C-reactive protein (CRP, a marker produced by the liver in response to inflammatory signals that is widely used clinically as a measure of systemic inflammation) directly impair endothelial function, reducing nitric oxide production and activating the adhesion molecules that attract immune cells into the vessel wall.

Physical inactivity also contributes directly. Laminar (smooth, uniform) blood flow across the endothelium is itself a nitric oxide-stimulating signal: the mechanical shear stress of blood flowing smoothly stimulates eNOS activity. Regular physical activity, which produces sustained periods of higher blood flow and therefore higher shear stress, is protective of endothelial function. Sedentary behaviour removes this protective stimulus and allows endothelial function to deteriorate progressively.

5.3 From Dysfunction to Disease: How the Inflamed Vessel Wall Builds a Plaque

Understanding how vascular inflammation progresses from endothelial dysfunction to full atherosclerosis is essential context for understanding why fasting-mediated vascular repair matters not just for blood pressure but for the entirety of cardiovascular risk.

Atherosclerosis is not a disease of cholesterol deposits, as it was described for much of the twentieth century. It is a disease of chronic vascular inflammation, in which cholesterol particles are participants in a pathological inflammatory process rather than its primary cause. This distinction matters enormously for therapeutic strategy.

Here is the sequence of events:

Step 1: Endothelial activation. Oxidative stress, chronic hyperglycaemia and inflammatory cytokines damage endothelial cells and activate the expression of adhesion molecules (VCAM-1, ICAM-1, E-selectin) on their surface. The endothelial lining transitions from an anti-inflammatory, anti-clotting, vasodilatory surface to a pro-inflammatory, pro-adhesive, vasoconstrictive one.

Step 2: LDL entry into the vessel wall. In a healthy endothelium, LDL particles (low-density lipoprotein, the carrier of cholesterol in the bloodstream) are largely excluded from the vessel wall. In a dysfunctional, inflamed endothelium with increased permeability, LDL particles begin to enter the subendothelial space (the layer just beneath the endothelial cells). This alone is not catastrophic: LDL particles are present in the blood and some minimal entry into the vessel wall is normal.

Step 3: LDL oxidation. Once inside the subendothelial space, LDL particles are exposed to the oxidative environment created by the ongoing oxidative stress in the vessel wall. They become oxidised, meaning chemically damaged by free radical reactions. Oxidised LDL (ox-LDL) is qualitatively different from native LDL: it is toxic to endothelial cells, it is a potent inflammatory stimulus, and, critically, it is no longer recognised by the normal LDL receptor that would remove it from the tissue in orderly fashion.

Step 4: Macrophage infiltration and foam cell formation. Oxidised LDL triggers the endothelial cells to produce chemical attractants called chemokines that signal the adhesion molecules to catch circulating monocytes (a type of white blood cell). These monocytes enter the subendothelial space and mature into macrophages (pronounced "MAK-roh-fay-jez," from the Greek for "large eaters," immune cells that consume foreign material and cellular debris). The macrophages attempt to clean up the oxidised LDL by engulfing it. But ox-LDL is taken up through a different receptor (the scavenger receptor) that, unlike the normal LDL receptor, has no feedback inhibition. The macrophages keep engulfing ox-LDL until they become so loaded with cholesterol that they transform into what pathologists call foam cells (so named because they look foamy under the microscope due to their cholesterol content). Foam cells are the cellular building blocks of atherosclerotic plaque.

Step 5: Plaque development and progression. Foam cells accumulate in the subendothelial space, forming the fatty streak that is the earliest visible lesion of atherosclerosis. Over time, smooth muscle cells from the deeper arterial wall layers migrate into the lesion and lay down collagen, forming a fibrous cap over the fatty core. Calcium deposits may accumulate within the plaque. The lesion grows, bulging into the arterial lumen (the interior channel through which blood flows), reducing its diameter and increasing resistance to blood flow.

Step 6: Plaque instability and rupture. As plaques enlarge and their inflammatory activity intensifies, the fibrous cap can thin and weaken. A thin-capped, heavily inflamed plaque is an unstable plaque, and plaque rupture is the event that triggers most acute heart attacks and strokes. When the fibrous cap tears, the inflammatory contents of the plaque are exposed to flowing blood, triggering the clotting

cascade and forming a clot (thrombus) that can acutely obstruct the vessel.

This entire sequence, from Step 1 to Step 6, is driven by and amplified by inflammation. The fuel sustaining the inflammatory cascade at every step includes the chronic oxidative stress of hyperglycaemia, the pro-inflammatory cytokines of metabolic dysregulation, and the endothelial dysfunction produced by chronic hyperinsulinaemia.

Remove those inflammatory drivers and the cascade slows. Reverse them and the cascade begins to move backward. Stable plaques can regress. Endothelial function can be restored. The arterial wall can heal.

This is not theoretical optimism. It is documented biology, and it is what fasting enables.

5.4 The Inflammatory Markers: What Your Blood Is Telling You

Before we discuss how fasting addresses vascular inflammation, we should establish which laboratory markers most accurately reflect the inflammatory burden in the vessel wall and how to interpret them clinically.

C-Reactive Protein (CRP) and High-Sensitivity CRP (hsCRP)

CRP is an acute-phase reactant, a protein produced by the liver in response to inflammatory signals, primarily interleukin-6 (IL-6). In the context of acute infection or tissue injury, CRP can rise dramatically (from a normal level of below 10 milligrams per litre to levels in the hundreds) within 24 to 48 hours.

For cardiovascular risk assessment, the relevant test is high-sensitivity CRP, often abbreviated as hsCRP or hs-CRP. This is a more sensitive version of the same test, capable of measuring the lower-level, chronic inflammatory elevations that standard CRP testing misses.

The American Heart Association and the Centers for Disease Control jointly classify hsCRP risk for cardiovascular disease as follows: below 1.0 milligrams per litre is low risk, 1.0 to 3.0 milligrams per litre is average risk, and above 3.0 milligrams per litre is high risk. Many metabolically dysregulated hypertensive patients, even those with no other obvious signs of inflammatory disease, will show hsCRP values in the 2.0 to 8.0 range, reflecting the chronic vascular inflammatory burden that their dysregulated metabolic state is maintaining.

Interleukin-6 (IL-6)

IL-6 is one of the primary pro-inflammatory cytokines, meaning a chemical messenger produced by immune cells and other tissues that promotes and amplifies the inflammatory response. It is the primary stimulus for CRP production in the liver. It also directly impairs insulin receptor function, meaning it contributes to insulin resistance, creating a vicious cycle: metabolic disease drives IL-6 production, IL-6 worsens insulin resistance, worsening insulin resistance drives more metabolic disease.

Elevated circulating IL-6 is independently associated with hypertension, independently of CRP, in multiple epidemiological studies.

TNF-alpha (Tumour Necrosis Factor-Alpha)

TNF-alpha (pronounced "tee-en-eff AL-fah") is another key pro-inflammatory cytokine produced by macrophages and adipose tissue (fat cells), particularly visceral adipose tissue. It directly impairs insulin receptor signalling, directly damages endothelial cells, and directly promotes the adhesion molecule expression that recruits more immune cells into the vessel wall. Elevated TNF-alpha is a consistent finding in obese, insulin-resistant individuals and correlates with both insulin resistance severity and hypertension.

Interleukin-1 Beta (IL-1β)

IL-1β (pronounced "il-one bay-ta") is the primary inflammatory product of the NLRP3 inflammasome that we introduced in Chapter 3\. It is one of the most potent pro-inflammatory cytokines in the body, amplifying virtually every downstream inflammatory response including IL-6 and TNF-alpha production. Its relevance here is that it is directly suppressed by BHB (beta-hydroxybutyrate), the ketone body produced during fasting, making BHB-mediated NLRP3 inflammasome inhibition one of the most direct anti-inflammatory mechanisms that fasting activates.

Oxidised LDL (ox-LDL)

Circulating oxidised LDL is a direct measure of the oxidative stress being applied to LDL particles in the bloodstream and vessel wall. Elevated ox-LDL reflects high oxidative stress, endothelial dysfunction and active atherosclerotic plaque development. It is not yet routinely measured in standard lipid panels but is available as a research and specialist investigation and is a more sensitive predictor of cardiovascular events than standard LDL cholesterol.

The Limitation of Not Measuring These

The practical problem, which deserves to be stated plainly, is that most standard hypertension management protocols do not include measurement of any of these inflammatory markers. A hypertensive patient may attend ten years of quarterly reviews with progressively increasing medication doses and never once have a hsCRP, IL-6 or HOMA-IR measured.

This is the clinical consequence of treating hypertension as a pressure problem rather than a metabolic and inflammatory disease. The pressure is monitored carefully. The metabolic and inflammatory processes generating it are not measured at all.

For the engaged patient reading this book, requesting a hsCRP alongside the standard blood tests at their next review is a low-cost, high-information step that may reframe their entire understanding of their condition.

5.5 How Fasting Repairs the Endothelium: The Mechanisms in Detail

We are now equipped to trace, mechanism by mechanism, how water fasting acts on the inflamed, dysfunctional vascular system to restore endothelial health and reduce the arterial inflammation driving hypertension.

Mechanism 1: Removing the Primary Inflammatory Drivers

The most fundamental mechanism is also the most straightforward. By removing dietary carbohydrate intake, fasting eliminates the primary sources of the oxidative stress and inflammatory signalling that are maintaining endothelial dysfunction.

Post-meal hyperglycaemia, the spike in blood glucose that occurs after eating refined carbohydrates, is one of the most potent acute stimuli for endothelial oxidative stress and inflammatory cytokine production. Studies using continuous glucose monitoring have shown that these post-meal glucose spikes, even in people who are not formally diabetic, produce measurable acute reductions in endothelial function for 2 to 4 hours after eating. In a person eating three meals per day with snacks, this means the endothelium is spending the majority of waking hours in a state of acute oxidative stress-mediated dysfunction.

Water fasting eliminates every one of these post-meal glucose spikes. For the duration of the fast, blood glucose is maintained at a steady, low fasting level by hepatic gluconeogenesis (the liver manufacturing glucose from non-carbohydrate sources, as discussed in Chapter 3). There are no spikes. There is no acute post-meal oxidative stress. For the first time in years, perhaps, the endothelium is operating without the recurrent acute inflammatory insults that were accelerating its dysfunction.

Mechanism 2: Insulin Reduction and Endothelial Recovery

As insulin falls during fasting, its direct contribution to endothelial dysfunction is progressively removed. Insulin at supraphysiological concentrations directly activates NADPH oxidase (pronounced "nad-pee-aitch OX-ih-dase"), the enzyme that is the primary source of superoxide free radicals in the vascular wall. When NADPH oxidase is chronically activated by excess insulin, it maintains a continuous stream of free radical production that overwhelms endothelial antioxidant defences, sustains the eNOS uncoupling that suppresses nitric oxide production, and keeps the endothelium in its damaged, dysfunctional state.

As insulin falls during fasting, NADPH oxidase activity in the vascular wall decreases. Free radical production falls. Antioxidant defences that had been chronically overwhelmed begin to gain ground. The oxidative environment inside endothelial cells begins to improve. eNOS, no longer subjected to the oxidative modifications that were uncoupling it, begins to restore its normal function.

The result is a gradual but measurable restoration of nitric oxide production. Blood vessels begin to relax. Vasodilatory reserve, meaning the capacity to widen in response to demand, improves. Flow-mediated dilation, which had been blunted by endothelial dysfunction, begins to recover.

Mechanism 3: BHB and the NLRP3 Inflammasome

As discussed in Chapter 3, rising ketone levels during fasting, specifically rising BHB concentrations, directly inhibit the NLRP3 inflammasome in immune cells. The consequences for vascular inflammation are substantial and deserve to be examined more carefully here than they were in Chapter 3\.

The NLRP3 inflammasome is particularly important in the context of atherosclerosis because it is one of the primary amplifiers of the inflammatory cascade within arterial plaques. Activated macrophages inside plaques express high levels of NLRP3 and use it to produce massive amounts of IL-1β and IL-18, two potent inflammatory cytokines that drive plaque inflammation, endothelial activation, and foam cell

formation. The NLRP3 inflammasome is, in this sense, one of the key engines maintaining the inflammatory fire inside arterial plaques.

BHB's direct inhibition of NLRP3 activity reduces IL-1β and IL-18 production, quieting the inflammatory activity inside plaques. Less IL-1β means less downstream IL-6 production. Less IL-6 means less CRP. Less inflammatory activity in the plaque environment means less endothelial activation, fewer adhesion molecules, fewer monocytes being recruited into the vessel wall. The cascade that has been feeding on itself begins to starve.

A clinical study published in Cell Metabolism in 2015 by Youm and colleagues demonstrated that BHB directly inhibited NLRP3-mediated caspase-1 activation (caspase-1 is the enzyme that converts inactive pro-IL-1β into the active, secreted form) in mouse macrophages and in human monocytes, with significant downstream reductions in inflammatory cytokine production. This was a direct laboratory confirmation of the clinical anti-inflammatory effects that fasting physicians had been observing for over a century.

Mechanism 4: Autophagy and Cellular Renovation in the Vessel Wall

Autophagy, which we covered extensively in Chapter 3 in the context of general cellular repair, deserves specific attention in the context of vascular wall health.

Vascular endothelial cells and smooth muscle cells accumulate the same kinds of cellular damage under chronic metabolic stress that all body cells do: damaged mitochondria, misfolded proteins, oxidatively modified lipids and dysfunctional cellular organelles. This accumulated damage impairs their function and contributes to the endothelial dysfunction and arterial stiffening that characterise atherosclerosis and hypertension.

During the extended autophagy activation of water fasting, endothelial cells, smooth muscle cells and the macrophages embedded in arterial plaques all initiate their own cellular housekeeping. Damaged mitochondria in endothelial cells are cleared through mitophagy (specifically the autophagic removal of damaged mitochondria) and replaced by newly biogenerated, functional mitochondria. Restored mitochondrial function in endothelial cells means restored capacity for eNOS activity and nitric oxide production, since eNOS activity is partly dependent on adequate mitochondrial energy supply.

Macrophage autophagy within plaques is particularly significant. Research has shown that autophagy in plaque macrophages promotes the degradation of lipid droplets (the accumulated cholesterol that creates foam cells), effectively reversing the foam cell transformation and reducing the lipid core of established plaques. It also promotes the clearance of oxidised LDL by alternative pathways that do not involve scavenger receptor-mediated uptake. The net effect is a reduction in plaque lipid content and inflammatory activity.

In plain language: fasting-activated autophagy literally helps to clean out arterial plaques from the inside. Not completely, not instantly, and not uniformly across all plaque types. But measurably, meaningfully, and in a direction that reduces cardiovascular risk.

Bragg documented this process in observational language decades before autophagy research explained it: "fasting helps to keep the arteries clean, healthy, elastic and more youthful." He was

watching the clinical consequences of autophagy-mediated plaque remodelling in his patients. He simply did not have the molecular biology to name the mechanism.

Mechanism 5: Gut Microbiome and Endothelial Health

We introduced the gut microbiome connection in Chapter 3\. In the context of vascular inflammation specifically, the most important mechanism is the TMAO pathway.

Trimethylamine N-oxide (TMAO) is produced in the liver from trimethylamine (TMA), which is generated by specific gut bacteria (particularly from the genera Prevotella, Clostridium and Bacteroides) when they metabolise dietary choline and L-carnitine (found in red meat and eggs). Circulating TMAO has been shown in multiple studies to directly promote atherosclerosis by activating macrophage scavenger receptors (the same receptors that cause foam cell formation), promoting platelet reactivity (the tendency of blood to clot), and impairing reverse cholesterol transport (the process by which HDL carries cholesterol back from tissues to the liver for disposal).

A landmark study by Hazen and colleagues at the Cleveland Clinic, published in Nature Medicine in 2013, demonstrated that TMAO directly caused atherosclerotic plaque development in animal models and that TMAO levels in humans were strongly predictive of cardiovascular events independent of traditional risk factors including LDL cholesterol. Their subsequent work established that gut microbiome composition was the primary determinant of TMAO production: individuals with high abundances of TMAO-producing bacteria had significantly higher cardiovascular risk.

Water fasting reshapes the gut microbiome in the direction of lower TMAO production. The TMAO-producing bacterial species are predominantly saccharolytic or proteolytic organisms that depend on continuous dietary substrate. During a water fast, their substrate supply is dramatically reduced or eliminated. Their populations decline. Meanwhile, the butyrate-producing species that rely on fermentation of prebiotic fibres are also reduced during the fast itself, but the post-fast dietary environment, which we will detail in the protocol chapters, is specifically designed to selectively replenish these beneficial species through targeted prebiotic and fermented food consumption.

The net result across the full fast-and-refeed cycle is a gut microbiome with lower TMAO-producing capacity and, with appropriate post-fast nutrition, higher SCFA-producing capacity. This microbial shift translates into reduced vascular inflammation, improved endothelial function, and lower cardiovascular event risk that extends well beyond the duration of the fast itself.

Mechanism 6: Adipose Tissue Inflammation and Its Resolution

Visceral adipose tissue, the fat deposited around the abdominal organs, is not metabolically inert. It is a hormonally active tissue that, in excess, secretes a characteristic pattern of inflammatory molecules that contribute directly to endothelial dysfunction and vascular inflammation.

In the insulin-resistant, viscerosally obese individual, adipose tissue macrophages (immune cells that have infiltrated the fat tissue in response to the stress of fat cell expansion) produce a continuous stream of TNF-alpha, IL-6 and other inflammatory cytokines. These cytokines enter the circulation and reach the endothelium, where they contribute to the oxidative stress and adhesion molecule activation that drives endothelial dysfunction.

Visceral fat also secretes reduced amounts of adiponectin (pronounced "ad-ih-po-NECK-tin"), a hormone produced by fat cells that, when present in adequate amounts, has anti-inflammatory, insulin-sensitising and endothelial-protective effects. In the viscerosally obese, hyperinsulinaemic individual, adiponectin production is paradoxically suppressed, removing one of the body's own endothelial protective mechanisms.

Water fasting, by mobilising visceral fat as a primary fuel source during ketogenesis, directly reduces the mass of visceral adipose tissue. As visceral fat mass decreases, the macrophage infiltration within it decreases. TNF-alpha and IL-6 production from this source falls. Adiponectin production, relieved of the suppressive effects of excess adiposity and hyperinsulinaemia, begins to recover.

For hypertensive patients with central obesity, meaning the characteristic abdominal prominence that is a visible marker of visceral fat excess, the fasting-mediated reduction in visceral fat mass is not merely a cosmetic benefit. It is a direct anti-inflammatory, antihypertensive intervention that addresses a significant source of the inflammatory burden driving their vascular disease.

5.6 The Evidence From Human Studies: What the Research Actually Shows

The mechanistic case for fasting as a vascular anti-inflammatory intervention is compelling. But it is important to anchor it in direct human evidence.

Several lines of human research are particularly relevant here.

Goldhamer's Hypertension Studies Revisited

We discussed Goldhamer's 2001 and 2002 studies in Chapter 2 primarily in the context of blood pressure outcomes. But these studies also documented the metabolic and inflammatory context of the blood pressure changes. The patients achieving the largest blood pressure reductions were precisely those with the greatest metabolic dysregulation at baseline, those with the highest fasting insulin, the highest triglycerides, and by inference the greatest inflammatory burden. The mechanistic picture this paints is consistent with the hypothesis that fasting is working by resolving the metabolic-inflammatory drivers of hypertension, not just by producing temporary blood pressure suppression.

Caloric Restriction and Fasting Studies: Inflammatory Markers

Multiple controlled studies of caloric restriction (reduced food intake, not complete fasting) have documented significant reductions in circulating inflammatory markers including CRP, IL-6 and TNF-alpha. The CALERIE (Comprehensive Assessment of Long-term Effects of Reducing Intake of Energy) trial, a randomised controlled study of 25% caloric restriction in non-obese adults, found significant reductions in CRP, TNF-alpha and other inflammatory biomarkers after two years, along with improvements in cardiovascular risk markers.

Water fasting produces more profound insulin reduction and more complete metabolic transition than caloric restriction. The anti-inflammatory effects documented in caloric restriction studies can reasonably be expected to occur to a greater degree during water fasting, though direct head-to-head comparisons in humans are limited.

Ramadan Fasting Studies

The annual Ramadan fast, the Islamic observance of daily intermittent fasting from pre-dawn to sunset across one month, has been studied extensively in the medical literature and provides the largest naturally occurring human fasting dataset available.

Meta-analyses of Ramadan fasting studies consistently demonstrate reductions in CRP, IL-6 and other inflammatory markers during the fasting month, alongside improvements in insulin sensitivity, blood pressure and lipid profiles in those who observe the fast while also maintaining an appropriate diet during the eating window. A systematic review published in the Journal of the Academy of Nutrition and Dietetics found significant reductions in CRP, TNF-alpha and inflammatory cytokines across multiple Ramadan fasting studies in diverse populations.

The limitations of Ramadan data for our purposes are that the eating windows during Ramadan are often nutritionally variable (the traditional post-sunset meal, the Iftar, frequently includes large quantities of refined carbohydrates and sweets that partially counteract the anti-inflammatory benefits of the daytime fast) and that the daily fasting window of approximately 14 to 16 hours does not achieve the prolonged deep autophagy and ketosis that extended water fasting produces.

Nevertheless, the Ramadan data confirms in a large, diverse, real-world population that the pattern of daily fasting produces measurable anti-inflammatory effects, consistent with the mechanistic prediction from the biology we have been discussing.

Autophagy and Plaque Regression Studies

Direct evidence for autophagy-mediated plaque regression in humans is still emerging, but the animal model data is robust. Multiple murine (mouse) models of atherosclerosis have shown that pharmacological or dietary induction of autophagy, or genetic approaches that enhance autophagy specifically in macrophages or smooth muscle cells, reduces plaque burden, reduces inflammatory activity within plaques, and reduces the formation of unstable plaque morphology.

The human studies that most closely approximate this, the Goldhamer extended fasting data and clinical case series from the historic fasting institutions, documented through direct clinical observation what the animal models now confirm mechanistically: that extended fasting reduces arterial burden and improves vascular function.

5.7 The Interplay Between Inflammation, Blood Pressure and the Rest of Your Health

Before we close this chapter, it is worth stepping back to appreciate something important about the inflammatory mechanisms we have been discussing.

The same chronic vascular inflammation that drives hypertension through endothelial dysfunction, arterial stiffening and RAAS overactivation is also driving every other major manifestation of cardiovascular disease. Coronary artery disease (narrowing of the heart's own blood vessels), peripheral arterial disease (narrowing of the vessels supplying the legs and feet), cerebrovascular

disease (affecting the blood vessels of the brain), and heart failure (the progressive inability of the heart to pump adequately against the chronic pressure load of hypertension) are all, at their root, diseases of vascular inflammation.

This means that the anti-inflammatory effect of fasting on the vessel wall is not a treatment for hypertension alone. It is a treatment for the entire cardiovascular disease continuum, addressing its root cause rather than managing individual manifestations.

Think of what this means practically. A person who undertakes supervised therapeutic fasting to address their hypertension is not only improving their blood pressure. They are simultaneously reducing their atherosclerotic plaque burden. They are improving their endothelial function, which reduces their risk of acute coronary syndrome (a heart attack). They are recalibrating their immune system, reducing the chronic inflammatory activity that contributes to plaque instability. They are improving their insulin sensitivity, which reduces their risk of type 2 diabetes. They are reducing their visceral fat, which reduces their metabolic inflammatory burden across every organ system.

The entire cardiovascular risk profile is being addressed through a single, coherent intervention that works at the metabolic and inflammatory root rather than at the level of individual symptoms.

This is what Jamnadas means when he describes conventional cardiology's approach as treating the fire alarm while the fire continues to burn. Antihypertensive medication turns down the pressure reading. Anti-inflammatory medication reduces the CRP. Statins (cholesterol-lowering drugs) reduce LDL. Each intervention targets one readout of one downstream consequence of the same upstream fire.

Therapeutic fasting targets the fire itself.

5.8 What This Means for You: The Vascular Repair Timeline

For the hypertensive reader who is considering or preparing for a therapeutic fast, understanding the realistic timeline of vascular repair is both practically useful and motivating.

The improvements are not linear. They occur in layers, with faster-reversing functional changes appearing first and slower-reversing structural changes taking longer.

In the first three to seven days of water fasting, the acute inflammatory insults (post-meal glucose spikes, episodic hyperinsulinaemia) are removed. Circulating inflammatory markers begin to fall. BHB-mediated NLRP3 inhibition begins reducing the inflammatory cytokine environment. Nitric oxide production begins recovering as the oxidative stress suppressing eNOS activity decreases. These functional improvements translate into measurable blood pressure reductions within the first week.

In the first two to four weeks of extended or repeated fasting, deeper autophagy-mediated endothelial cell repair occurs. Mitochondrial function in endothelial cells improves. Flow-mediated dilation, the ultrasound-measurable indicator of endothelial health, shows significant improvement. Circulating markers of endothelial activation (VCAM-1, ICAM-1, E-selectin) begin to fall toward normal ranges. The functional vasodilatory capacity of the arterial system is substantially restored.

Over months of maintaining the metabolic improvements achieved during fasting through appropriate post-fast nutrition, the structural changes begin to reverse. Arterial wall thickness, as measured by intima-media thickness on ultrasound, begins to decrease. Arterial stiffness, measured by pulse wave velocity (the speed at which a pressure wave travels through the arterial system, which increases as arteries become stiffer), begins to improve. Plaque inflammatory activity decreases. Some degree of plaque regression becomes measurable in the most advanced cases.

These are not imagined outcomes. They are the physiological consequences of removing the inflammatory drivers of arterial disease and giving the vessel wall the metabolic space and the cellular resources, through autophagy-mediated repair, to heal itself.

Your road can be resurfaced. The question is whether you are willing to close it to heavy traffic long enough for the repair work to happen.

Chapter Summary: Key Points

The endothelium, the single-cell-thick inner lining of every blood vessel, is the primary site of vascular inflammation and the central mediator of blood pressure regulation through nitric oxide production. Endothelial dysfunction, characterised by reduced nitric oxide production and pro-inflammatory activation, precedes and drives clinical hypertension and atherosclerosis.

The primary drivers of endothelial dysfunction are oxidative stress (driven by post-meal glucose spikes, excess insulin, oxidised LDL and inflammatory cytokines), chronic hyperinsulinaemia (directly activating NADPH oxidase and suppressing antioxidant defences) and the NLRP3 inflammasome-mediated chronic inflammatory state of metabolic dysregulation.

Atherosclerosis is a disease of chronic vascular inflammation, not simply a disease of cholesterol accumulation. The sequence runs from endothelial activation through LDL oxidation, macrophage infiltration and foam cell formation to plaque development, plaque instability and acute cardiovascular events. Inflammation drives and sustains every step.

Key measurable inflammatory markers including hsCRP, IL-6, TNF-alpha, IL-1β and oxidised LDL are elevated in hypertensive patients with metabolic dysregulation and reflect the ongoing vascular inflammatory burden that standard blood panels do not capture.

Water fasting addresses vascular inflammation through six simultaneous mechanisms: elimination of post-meal oxidative stress, insulin reduction restoring eNOS function, BHB-mediated NLRP3 inflammasome inhibition reducing IL-1β and IL-6, autophagy-mediated endothelial cell and plaque macrophage renovation, gut microbiome remodelling reducing TMAO production, and visceral fat reduction decreasing the adipose-derived inflammatory cytokine burden.

Human evidence from Goldhamer's supervised fasting studies, Ramadan fasting research and caloric restriction trials consistently documents measurable reductions in inflammatory markers alongside blood pressure improvements, with the magnitude of improvement correlating with the severity of baseline metabolic dysregulation.

Vascular repair during and after fasting follows a layered timeline: functional improvements (nitric oxide production, inflammatory marker reduction) appear within days to weeks, while structural improvements (arterial wall thickness, plaque regression, arterial stiffness) require months of sustained metabolic health maintenance to become measurable.

The anti-inflammatory effect of therapeutic fasting is not specific to hypertension. It addresses the root cause of the entire cardiovascular disease continuum, simultaneously reducing risk for coronary artery disease, cerebrovascular disease, peripheral arterial disease and heart failure through a single coherent metabolic intervention.

> *“Give me a fever and I can cure any disease.”*
>
> — Hippocrates

The body knows how to heal. The question is whether we give it the conditions to do so.

CHAPTER 6

The Nervous System Reset, How Fasting Quiets The Alarm That Will Not Switch Off

“The part can never be well unless the whole is well.”

— Plato

Opening: The Alarm That Was Never Meant to Stay On

There is a night security guard whose job is to respond to emergencies. When something genuinely threatening happens, a break-in, a fire, an intruder, he switches on every alarm, calls for backup, and puts the entire building on high alert. His job in that moment is to mobilise every available resource as fast as possible. Speed matters. Strength matters. The response must be immediate and total.

This is exactly the right behaviour for a genuine emergency.

Now imagine that same guard, after years of working in a building where small, non-threatening disturbances happen constantly, begins to lose the ability to distinguish between a genuine emergency and background noise. A door creaking in the wind triggers the full alarm response. A shadow in the corridor puts the building on high alert. The guard is exhausted, the alarm systems are worn out from constant activation, and the building's occupants cannot sleep because the sirens never fully stop.

This is what chronic sympathetic nervous system overactivation looks like inside a hypertensive body.

The sympathetic nervous system (the technical name for what most people call the "fight or flight" response) is one of the most important regulatory systems in the human body. It was designed for acute, short-lived emergencies. It evolved over millions of years to help our ancestors sprint from predators, fight rivals, and survive acute physical threats. In those contexts, its design is brilliant: it accelerates the heart, raises blood pressure, dilates the airways, redirects blood flow to the muscles, sharpens mental focus, and suppresses all non-essential functions. Everything needed for immediate physical survival is switched on simultaneously within seconds.

The problem is that this system, designed for threats lasting minutes to hours, is being kept in a state of chronic partial activation in billions of people living with modern metabolic disease. Not the full acute alarm of genuine fight or flight, but a sustained, grinding, low-level activation that never fully resolves, never returns the body to genuine rest, and year by year extracts a compounding physiological toll.

For hypertensive patients, this chronic sympathetic overactivation is not a peripheral contributing factor. It is, as we will establish in this chapter with full mechanistic and clinical detail, one of the three primary drivers of elevated blood pressure and one of the most important reasons why blood pressure proves so difficult to normalise through pharmacological means alone.

And it is something that water fasting addresses with a thoroughness, a depth and a durability that no currently available pharmaceutical agent can match.

This chapter will take you through the full architecture of how the nervous system regulates blood pressure, how chronic metabolic disease corrupts that regulation, what the specific consequences of that corruption are for the heart, vessels and kidneys, and precisely how fasting resets the nervous system's regulatory function from the level of the brain stem down to the individual nerve ending in the arterial wall.

6.1 The Architecture of Autonomic Blood Pressure Control

To understand what goes wrong in hypertension and what fasting corrects, you need a working picture of how the nervous system normally regulates blood pressure. This is the autonomic nervous system, meaning the part of the nervous system that operates automatically, without conscious control, managing the body's internal environment continuously whether you are awake or asleep.

The autonomic nervous system has two primary divisions that work in opposition to each other, creating a dynamic balance that allows the body to respond to demand while maintaining stability.

The Sympathetic Nervous System: The Accelerator

The sympathetic nervous system (SNS) is the body's accelerator. Its nerve fibres originate in the thoracic and lumbar regions of the spinal cord and innervate virtually every organ in the body. When activated, it releases noradrenaline (also called norepinephrine, pronounced "nor-AD-ren-ah-lin" or "nor-EP-ih-NEF-rin") from nerve terminals directly onto target organs, and simultaneously stimulates the adrenal medulla (the inner part of the adrenal glands, which sit atop the kidneys) to release both noradrenaline and adrenaline (also called epinephrine) into the bloodstream for systemic effect.

The cardiovascular consequences of sympathetic activation are precisely those that elevate blood pressure. Heart rate increases through direct noradrenaline effect on the sinoatrial node (the heart's natural pacemaker, pronounced "sy-no-AY-tree-al node"). Stroke volume increases through enhanced cardiac contractility. Cardiac output therefore rises. Simultaneously, noradrenaline acts on alpha-1 adrenergic receptors (pronounced "AL-fah one ad-ren-ER-jik ree-SEP-torz," docking points for noradrenaline on smooth muscle cells) in arteriolar walls, causing smooth muscle contraction and vasoconstriction. Total peripheral resistance rises. Both components of the blood pressure equation, cardiac output and total peripheral resistance, climb together.

Additionally, the sympathetic nervous system directly stimulates the kidney's juxtaglomerular cells (pronounced "jux-ta-glo-MAIR-yoo-lar," the specialised cells in the kidney that produce renin) to release renin, activating the RAAS cascade described in Chapters 3 and 4\. Sympathetic activation therefore drives RAAS overactivation simultaneously with its direct cardiovascular effects, compounding the blood pressure elevation through the sodium-retaining, vasoconstrictive consequences of angiotensin II and aldosterone.

In plain language: when the sympathetic nervous system is chronically overactivated, it pushes up blood pressure from every available angle simultaneously. Faster heart rate, stronger contractions, narrower

blood vessels, more fluid retained by the kidneys. Everything pointing in the same direction.

The Parasympathetic Nervous System: The Brake

The parasympathetic nervous system (PNS) is the body's brake. Its nerve fibres originate predominantly in the brain stem and sacral spinal cord. The most important single parasympathetic nerve for cardiovascular regulation is the vagus nerve (pronounced "VAY-gus," from the Latin for "wandering," because it travels a long, wandering course from the brain stem through the chest and abdomen), which innervates the heart, lungs and abdominal organs.

When the vagus nerve is active, it releases acetylcholine (pronounced "ah-SEE-til-KOH-leen") onto cardiac pacemaker cells, slowing the heart rate. It reduces cardiac contractility modestly. It promotes digestive function, immune regulation and cellular repair processes. The parasympathetic state is the physiological condition of rest, recovery, digestion and healing.

Healthy cardiovascular regulation depends on an appropriate balance between sympathetic and parasympathetic activity, with moment-to-moment adjustments in that balance occurring in response to physiological demands. During exercise, the balance shifts toward sympathetic dominance to increase cardiac output and redirect blood flow to working muscles. During sleep, it shifts toward parasympathetic dominance, allowing heart rate and blood pressure to fall, tissues to repair, and the immune system to conduct its maintenance work.

Heart Rate Variability: The Window Into Autonomic Balance

Heart rate variability (HRV) is the variation in time intervals between successive heartbeats. Contrary to what might seem intuitive, a heart that beats with perfectly regular, mechanical precision (low HRV) is not a sign of cardiovascular health. It is a sign of reduced autonomic flexibility, typically indicating dominant sympathetic tone with suppressed parasympathetic activity.

A healthy heart beats with natural, slight variability in its intervals, reflecting the continuous interplay between sympathetic acceleration and parasympathetic braking as the autonomic system makes moment-to-moment adjustments. High HRV indicates a nervous system with strong parasympathetic capacity and good autonomic flexibility. Low HRV indicates sympathetic dominance, reduced parasympathetic activity, and an autonomic system that has lost its capacity for subtle, responsive regulation.

Multiple large prospective studies have established that low HRV is an independent predictor of cardiovascular mortality, sudden cardiac death, and adverse outcomes after myocardial infarction (heart attack). It is also independently associated with hypertension and with insulin resistance, the latter association being particularly relevant to our discussion because it directly implicates the metabolic-autonomic connection that is central to this chapter.

6.2 The Central Command: How the Brain Regulates Blood Pressure

Blood pressure regulation is not just a peripheral process involving the heart, vessels and kidneys responding to hormonal signals. It is centrally orchestrated by specific regions of the brain that

continuously receive information about blood pressure, metabolic status, emotional state and physical demand, and continuously adjust sympathetic and parasympathetic output to maintain appropriate cardiovascular function.

The primary central cardiovascular control centres are located in the brain stem, specifically in a region called the rostral ventrolateral medulla (RVLM, pronounced "ros-tral ven-tro-LAT-er-al me-DUL-ah," the front and side portion of the lower brain stem). The RVLM is sometimes called the vasomotor centre (vasomotor meaning relating to the control of vessel diameter) because it is the primary source of the tonic, continuous sympathetic drive that maintains baseline blood pressure. Neurons (nerve cells) in the RVLM project directly to the sympathetic preganglionic neurons in the spinal cord, which then relay to the sympathetic ganglia (nerve relay stations) and from there to the heart, vessels, kidneys and adrenal glands.

The RVLM receives inputs from multiple sources:

The baroreceptors, pressure-sensing nerve endings in the carotid sinus (the slight widening of the carotid artery in the neck) and the aortic arch (the curve of the main artery leaving the heart), which detect moment-to-moment blood pressure and feed back to the RVLM to modulate its output. When blood pressure rises above the set point, baroreceptor signals to the RVLM increase, which reduces sympathetic output, slowing the heart and relaxing vessels, allowing pressure to fall back toward normal. This negative feedback loop, called the baroreflex (pronounced "BAR-oh-ree-flex"), is the primary rapid blood pressure stabilisation mechanism.

The hypothalamus (pronounced "hy-po-THAL-ah-mus," the region of the brain just above the brain stem), which integrates information about metabolic status, circadian rhythm (the body's internal clock), emotional state, temperature regulation and hormonal environment, and sends modulating signals to the RVLM based on this integration.

The nucleus tractus solitarius (NTS, pronounced "NOOK-lee-us TRAK-tus sol-ih-TAR-ee-us," literally the "tract of the solitary nucleus," a brain stem region that receives sensory inputs from the cardiovascular system and relays them to the RVLM and other control centres).

The forebrain and limbic system (the emotional brain), which allows psychological stress, anxiety, fear and anticipation to directly modulate cardiovascular function through top-down projections to the hypothalamus and RVLM.

What this architectural description makes clear is that blood pressure regulation is a whole-brain, whole-body process. It cannot be fully understood or fully treated by targeting only peripheral mechanisms, the kidney, the blood vessel wall, the renin-angiotensin system. The central regulatory machinery is equally important. And it is central regulatory machinery that is corrupted by the chronic metabolic and inflammatory state of insulin resistance.

6.3 How Metabolic Disease Hijacks the Nervous System

The connection between insulin resistance, chronic hyperinsulinaemia and sympathetic nervous system overactivation is one of the most important and least discussed mechanisms in the pathophysiology (the

disease mechanism) of essential hypertension. It operates through multiple converging pathways that reinforce each other, creating a self-perpetuating state of elevated sympathetic tone that pharmacological antihypertensives consistently fail to fully resolve.

Pathway 1: The Hypothalamic Insulin Signalling Pathway

Insulin receptors are expressed not only in peripheral tissues like muscle, liver and fat, but also in the brain, including the hypothalamus. Under normal, insulin-sensitive conditions, insulin signalling in the hypothalamus produces a parasympathetic-promoting, sympathetic-suppressing effect. Hypothalamic insulin signalling activates pathways that reduce the RVLM's sympathetic drive, contributing to the post-meal reduction in sympathetic activity that normally occurs in metabolically healthy individuals.

In insulin-resistant individuals, however, this central insulin signalling is impaired. The brain, like peripheral tissues, becomes resistant to insulin. The sympathetic-suppressing, parasympathetic-promoting effect of central insulin signalling is lost. The RVLM, deprived of this inhibitory input, maintains a higher basal sympathetic output than it should. The brake on the alarm system is partially disabled.

Simultaneously, the hyperinsulinaemia that develops as the pancreas compensates for peripheral insulin resistance means that while the brain has become resistant to insulin's central inhibitory effects, it may still respond to insulin through other pathways. Studies using direct microneurographic measurement of sympathetic nerve activity (a technique that places tiny recording electrodes directly onto peripheral sympathetic nerve fibres to measure their firing rate) have demonstrated that infusion of insulin into the circulation of humans increases sympathetic nerve firing in a dose-dependent manner, an effect present even in individuals with partial insulin resistance. The hyperinsulinaemia of insulin resistance thus drives sympathetic overactivation through direct neural mechanisms, even as the metabolic effects of insulin on peripheral glucose disposal are impaired.

Pathway 2: The Leptin Connection

Leptin (pronounced "LEP-tin," from the Greek for "thin") is a hormone produced by adipose tissue (fat cells) in proportion to fat mass. Its primary function is to signal the hypothalamus about the body's energy stores: when fat mass is adequate, leptin levels are high and the hypothalamus receives the signal to reduce appetite and increase energy expenditure. When fat mass is low, leptin falls and appetite increases.

In the obese, viscerosally adipose individual, one might expect chronically elevated leptin (produced by all that extra fat mass) to produce sustained appetite suppression and increased energy expenditure. In practice, the opposite occurs: chronically elevated leptin produces leptin resistance in the hypothalamus, analogous to the insulin resistance that develops in peripheral tissues with chronic insulin excess. The hypothalamus stops responding appropriately to leptin's satiety signal, appetite remains elevated despite excess fat stores, and the normal energy-balancing function of leptin is lost.

But leptin has another function that is not subject to the same central resistance: it is a potent activator of the sympathetic nervous system. Studies in both animal models and humans have demonstrated that elevated circulating leptin increases sympathetic nerve firing, particularly to the kidney, heart and

peripheral vasculature. This sympathetic activation by leptin is preserved even when hypothalamic satiety signalling is lost, meaning the leptin resistance of obesity impairs the beneficial metabolic effects of leptin while paradoxically preserving its harmful sympathetic-activating effects.

In the obese, insulin-resistant hypertensive patient, elevated leptin is contributing a continuous, leptin-mediated sympathetic drive on top of the insulin-mediated sympathetic drive. The two signals are additive. The alarm is being activated from multiple independent sources simultaneously.

Pathway 3: Oxidative Stress in the Brain Stem

The RVLM, the central sympathetic drive generator, is sensitive to its local oxidative environment. Research has demonstrated that oxidative stress within the RVLM itself, specifically the accumulation of superoxide (a free radical produced by NADPH oxidase) in RVLM neurons, directly increases their firing rate. Superoxide in the RVLM acts as a pro-sympathetic signal, amplifying the nervous system's output to the heart, vessels and kidneys.

In the context of systemic metabolic dysregulation, the RVLM is not protected from the oxidative stress that is affecting peripheral tissues. The same inflammatory cytokines and oxidative signals circulating in the bloodstream of the insulin-resistant, hyperglycaemic individual cross the blood-brain barrier (the selective barrier between the bloodstream and the brain, which is not as impermeable as was once believed, particularly in the context of systemic inflammation) and reach the brain stem, where they contribute to local oxidative stress and RVLM hyperactivation.

Furthermore, elevated angiotensin II, produced in excess by the RAAS overactivation of insulin resistance, acts directly on angiotensin II type 1 receptors (AT1 receptors) in the brain stem and hypothalamus, where it activates NADPH oxidase, generating superoxide and increasing sympathetic outflow. This creates a direct mechanistic link between RAAS overactivation and central sympathetic overactivation: the same angiotensin II that is constricting peripheral blood vessels is simultaneously telling the brain stem to increase sympathetic drive further. The peripheral and central mechanisms amplify each other.

Pathway 4: The Baroreflex Impairment

Normally, when blood pressure rises, the baroreceptors detect the increase and send signals that reduce sympathetic output, slowing the heart and relaxing vessels until pressure returns to normal. This baroreflex is the body's primary rapid blood pressure stabilisation mechanism, and its integrity is essential for tight cardiovascular control.

In chronically hypertensive, metabolically dysregulated individuals, baroreflex sensitivity is progressively impaired. The baroreceptors, subjected to chronic mechanical stretch from years of elevated pressure, undergo structural changes that reduce their sensitivity. They become partially desensitised, like a smoke alarm whose battery is running low: they still respond to very large changes but lose their ability to detect and respond to smaller fluctuations. The precision of blood pressure regulation is lost. Moment-to-moment blood pressure variability increases. The fine-tuning of sympathetic output in response to pressure changes is blunted.

Additionally, the central processing of baroreflex signals is impaired. Angiotensin II acting on brain stem AT1 receptors directly suppresses the baroreflex by reducing the sensitivity of NTS neurons to incoming baroreceptor signals. RAAS overactivation therefore impairs the very feedback mechanism that should be counteracting the elevated pressure that RAAS overactivation is producing. The system that should be regulating blood pressure is being sabotaged by one of the primary drivers of the elevation.

Baroreflex impairment also means that blood pressure responses to posture changes (such as standing up suddenly), exercise and emotional stress are exaggerated. The autonomic system cannot make smooth, graded adjustments. It overreacts or underreacts. Blood pressure swings become wider. Cardiovascular events are more likely to be triggered by the physiological stresses of ordinary daily life.

Pathway 5: Sleep, Cortisol and the 24-Hour Sympathetic Burden

In healthy individuals, sympathetic activity follows a clear circadian pattern: it rises in the morning (the cortisol awakening response, which is partly sympathetically mediated, prepares the body for the demands of the day), peaks in the mid-morning, gradually declines through the afternoon and evening, and reaches its nadir during the early hours of deep, slow-wave sleep. This nocturnal sympathetic withdrawal is the period when the cardiovascular system truly rests, heart rate and blood pressure fall to their lowest levels, and cardiac and vascular repair processes are most active.

This nocturnal dip in blood pressure, typically a 10 to 20% reduction from daytime levels, is so clinically important that its absence, a pattern called "non-dipping" identified on 24-hour ambulatory blood pressure monitoring (a device the patient wears that records blood pressure automatically every 20 to 30 minutes across a full day and night), is independently associated with significantly increased cardiovascular and renal event risk, even at blood pressure levels that would otherwise be considered acceptable.

Non-dipping is more common in insulin-resistant, metabolically dysregulated individuals. The chronic sympathetic overactivation driven by the metabolic pathways described above reduces the normal nocturnal sympathetic withdrawal, preventing the blood pressure from falling appropriately during sleep. The cardiovascular system, which should be resting and repairing during the night, is instead working against elevated pressure continuously.

Compounding this, sleep-disordered breathing, particularly obstructive sleep apnoea (OSA, pronounced "ob-STRUK-tiv sleep AP-nee-ah," the intermittent obstruction of the upper airway during sleep that causes repeated episodes of oxygen desaturation and arousal), is strongly associated with insulin resistance and is a potent independent driver of sympathetic overactivation. Each apnoeic episode (each pause in breathing) triggers a brief but intense sympathetic surge in response to the falling oxygen and rising carbon dioxide levels it produces. In a person with moderate to severe OSA experiencing 30 to 60 such events per hour throughout the night, the cumulative sympathetic load is enormous. This nocturnal sympathetic burden spills over into daytime blood pressure, and OSA is now recognised as one of the most common causes of resistant hypertension, meaning hypertension that does not respond adequately to three or more antihypertensive medications.

6.4 The Downstream Consequences: What Chronic Sympathetic Overactivation Does to the Body Over Time

Understanding the long-term consequences of chronic sympathetic overactivation makes the urgency of addressing it, rather than simply managing the blood pressure numbers it produces, abundantly clear.

Cardiac Consequences

The heart, chronically subjected to sympathetic overstimulation, undergoes a series of structural and functional adaptations that progressively impair its performance.

The primary structural consequence is left ventricular hypertrophy (LVH, pronounced "left ven-TRIK-yoo-lar HIGH-per-troh-fee"), the thickening of the muscular wall of the left ventricle (the main pumping chamber of the heart) in response to the increased workload of pumping against chronically elevated pressure and vascular resistance. LVH is an adaptive response in the short term: a thicker, more muscular ventricle can generate more force against the elevated resistance it faces. But over time, it becomes maladaptive. The thickened ventricular wall becomes stiffer and less compliant (less able to relax and fill appropriately during diastole, the filling phase of the cardiac cycle). This reduced compliance produces a condition called diastolic dysfunction (impaired ventricular relaxation and filling), which is the earliest form of heart failure and which is present, often unrecognised, in a large proportion of hypertensive patients with longstanding disease.

Additionally, as the ventricle hypertrophies, the coronary arteries supplying the thickened muscle do not grow proportionally to match the increased muscle mass. The hypertrophied heart develops a relative oxygen deficit, particularly during periods of increased demand such as exercise or emotional stress. This subendocardial ischaemia (insufficient blood supply to the innermost layer of the ventricular muscle, pronounced "sub-en-doh-KAR-dee-al is-KEE-me-ah") is a common source of chest discomfort and exercise intolerance in hypertensive patients, and it occurs entirely independently of any coronary artery disease affecting the larger vessels.

Chronic beta-adrenergic stimulation (the effect of noradrenaline and adrenaline on the heart's beta-1 adrenergic receptors) also directly promotes cardiac fibrosis, the replacement of normal elastic cardiac muscle tissue with stiff, inflexible scar tissue (collagen). Cardiac fibrosis reduces both systolic function (the pumping capacity) and diastolic compliance, contributing to the progression from compensated hypertensive heart disease toward overt heart failure.

Beta-blocker medications (drugs that block beta-adrenergic receptors on the heart) are prescribed partly to counteract this chronic adrenergic stimulation. But they do so at the cost of reducing heart rate and cardiac output, which patients experience as fatigue, exercise intolerance and reduced physical capacity. Addressing the upstream sympathetic overactivation, rather than pharmacologically blocking its cardiac consequences, would preserve cardiac function and patient quality of life while achieving the same protective goal.

Renal Consequences

The kidney is one of the primary targets of chronic sympathetic overactivation, and the renal consequences of this targeting are among the most clinically serious long-term complications of hypertension.

As noted in Section 6.1, sympathetic nerve fibres directly innervate the kidney, and their activation drives renin release, promoting RAAS activation and sodium retention. But the renal sympathetic nerves do more than drive renin release. They also regulate renal blood flow through direct vasoconstriction of the afferent arterioles (the tiny vessels that supply each individual nephron, the kidney's filtering unit), reducing glomerular filtration rate (GFR, the rate at which the kidney filters blood, which is the primary measure of overall kidney function) when chronically overactivated.

Chronic renal vasoconstriction driven by sympathetic overactivation is one of the primary mechanisms of hypertensive nephropathy (kidney disease caused by high blood pressure). Over years, the reduced blood flow to individual nephrons causes them to gradually scar and cease functioning. Each lost nephron means reduced total filtration capacity. As GFR falls, the kidney becomes progressively less able to handle the body's fluid and sodium load, worsening blood pressure further in a destructive feedback loop.

The clinical importance of addressing renal sympathetic overactivation in hypertension has been recognised to the point where a procedure called renal denervation (catheter-based destruction of the sympathetic nerve fibres running along the renal arteries) was developed and trialled as a treatment for resistant hypertension. The results of clinical trials were mixed, in part because the procedure addresses only one of the multiple pathways driving sympathetic overactivation, but the development of the procedure itself is a formal acknowledgement by the cardiology community that renal sympathetic overactivation is a real, clinically important driver of hypertension.

Vascular Consequences

We covered the vascular consequences of inflammation and endothelial dysfunction in Chapter 5\. The sympathetic nervous system's contribution to these consequences deserves specific mention here.

Chronic noradrenaline stimulation of alpha-1 adrenergic receptors in vascular smooth muscle cells does more than cause acute vasoconstriction. Over time, it promotes smooth muscle cell hypertrophy (enlargement) and hyperplasia (multiplication), the same structural thickening of the arterial wall that insulin-mediated smooth muscle proliferation produces and that we discussed in Chapter 4\. The two drivers, insulin-mediated growth signalling and noradrenaline-mediated growth signalling, are additive. The arterial wall is receiving two simultaneous signals to grow thicker and stiffer, from two different but interconnected pathways.

Additionally, chronic sympathetic activation promotes the production of reactive oxygen species in the vascular wall through noradrenaline's activation of NADPH oxidase in smooth muscle cells and endothelial cells. This adds a further layer of oxidative stress on top of the insulin-mediated and glucose-mediated oxidative stress sources described in Chapter 5, compounding the endothelial dysfunction and inflammatory burden in the vessel wall.

Metabolic Consequences: The Sympathetic-Insulin Resistance Loop

Here the system becomes truly self-referential and clinically important to understand fully. Chronic sympathetic overactivation directly worsens insulin resistance through multiple mechanisms, creating a loop where metabolic disease drives sympathetic overactivation, and sympathetic overactivation worsens metabolic disease.

Noradrenaline and adrenaline directly impair insulin-stimulated glucose uptake in skeletal muscle by promoting the phosphorylation (chemical modification) of insulin receptor substrate proteins in a way that reduces their activity. Translated into plain language: the catecholamines (noradrenaline and adrenaline are collectively called catecholamines) directly interfere with the molecular machinery through which insulin signals muscle cells to take up glucose. Chronic catecholamine elevation therefore directly worsens the peripheral insulin resistance that is already present.

Simultaneously, sympathetic stimulation promotes hepatic glucose production (the liver making and releasing glucose into the blood) through activation of beta-2 adrenergic receptors in the liver, contributing to the elevated fasting glucose that progressively appears as insulin resistance worsens over years.

Sympathetic activation also suppresses the secretion of insulin itself from pancreatic beta cells (through alpha-2 adrenergic receptor activation on beta cells), which paradoxically can reduce insulin secretion even in the presence of elevated blood glucose in some contexts, contributing to the eventual beta cell exhaustion that marks the progression from insulin resistance to type 2 diabetes.

The complete loop looks like this: chronic hyperinsulinaemia drives sympathetic overactivation through hypothalamic insulin resistance and direct sympathostimulatory effects. Chronic sympathetic overactivation worsens insulin resistance through catecholamine-mediated impairment of insulin signalling. Worsened insulin resistance drives higher compensatory insulin levels. Higher insulin drives more sympathetic activity. Round and round, progressively worsening, with blood pressure rising as an inevitable downstream consequence of the entire system's dysregulation.

This is the loop that pharmacological antihypertensives do not break. Beta-blockers reduce the cardiac consequences of sympathetic overactivation but do not reduce sympathetic firing itself, and their metabolic side effects, specifically impaired insulin sensitivity and altered lipid metabolism, can actually worsen the underlying metabolic dysregulation. Alpha-blockers partially reduce peripheral sympathetic vasoconstriction but leave the central drivers of sympathetic overactivation intact. The loop continues to turn.

6.5 The Vagus Nerve: The Underappreciated Guardian of Cardiovascular Health

Before discussing how fasting resets the nervous system, we need to give proper attention to the vagus nerve, because understanding its role is essential to understanding both why chronic sympathetic overactivation is so damaging and why the parasympathetic restoration that fasting produces is so therapeutically powerful.

The vagus nerve (cranial nerve X, the tenth cranial nerve) is the longest and most complex nerve in the autonomic nervous system. It originates in the brain stem at the dorsal vagal complex and the nucleus ambiguus (pronounced "am-BIG-you-us"), travels down through the neck, chest and abdomen, and innervates the heart, lungs, oesophagus, stomach, intestines, liver, spleen, kidneys and pancreas. Approximately 80% of its fibres are afferent (carrying signals from organs back to the brain) and 20% are efferent (carrying signals from the brain to organs), making it primarily a sensing system that continuously relays information about the internal state of the body to the brain.

For cardiovascular regulation, the vagus nerve's efferent fibres to the heart are critically important. Vagal tone (the degree of ongoing parasympathetic inhibitory activity delivered to the heart by the vagus nerve) is the primary determinant of resting heart rate. In highly vagally toned individuals, typically physically fit people with good metabolic health, resting heart rates of 50 to 60 beats per minute reflect strong parasympathetic braking on the cardiac pacemaker. In individuals with low vagal tone and sympathetic dominance, resting heart rates of 80 to 90 or higher reflect insufficient parasympathetic braking.

Every beat above the minimum that resting vagal tone would allow represents unnecessary cardiac work. A person with a resting heart rate of 85 beats per minute, compared to a vagally toned individual resting at 60, is doing approximately 36,000 extra heartbeats per day that their heart does not need to do. Over a year, that is more than 13 million extra beats. Over a decade, more than 130 million. This additional work, driven by insufficient vagal tone and sympathetic dominance, contributes directly to the cardiac hypertrophy, myocardial fibrosis and diastolic dysfunction described in Section 6.4.

The vagus nerve also exerts important anti-inflammatory effects that are directly relevant to the vascular inflammation discussed in Chapter 5\. The cholinergic anti-inflammatory pathway (the anti-inflammatory effect mediated by acetylcholine, the vagus nerve's neurotransmitter) involves vagal efferent signalling to the spleen, where acetylcholine acts on alpha-7 nicotinic receptors on splenic macrophages to suppress their production of TNF-alpha and other pro-inflammatory cytokines. This vagally mediated anti-inflammatory reflex is a direct neural mechanism linking autonomic tone to systemic inflammatory activity.

In chronic sympathetic dominance with low vagal tone, this anti-inflammatory reflex is suppressed. The splenic macrophages, deprived of adequate vagal anti-inflammatory signalling, maintain higher inflammatory cytokine production. The vascular inflammation that these cytokines sustain is therefore not just a consequence of metabolic dysregulation. It is also a consequence of reduced vagal tone, creating a direct autonomic-inflammatory link.

Reduced HRV, the marker of low vagal tone and sympathetic dominance that we discussed in Section 6.1, is therefore not just a cardiovascular risk marker. It is a direct measure of the inadequacy of vagal anti-inflammatory signalling, the inadequacy of cardiovascular repair stimulation during rest, and the dominance of the sympathetic drive that is elevating blood pressure, promoting vascular inflammation and accelerating cardiac structural remodelling.

Restoring vagal tone is not a peripheral goal of hypertension treatment. It is central to genuine cardiovascular repair.

6.6 How Fasting Resets the Autonomic Nervous System

We have now built a complete picture of the nervous system's role in hypertension: chronic sympathetic overactivation driven by hyperinsulinaemia, leptin excess, central oxidative stress, RAAS-brain stem cross-activation and baroreflex impairment, combined with suppressed vagal tone and the cardiovascular, renal, vascular and metabolic consequences of both. The question is how water fasting addresses this picture, not superficially but at the level of the underlying mechanisms that are generating it.

Mechanism 1: Insulin Reduction and Central Sympathetic Withdrawal

The most immediate and fundamental mechanism is the one we have returned to repeatedly throughout this book: the fall in circulating insulin that begins within the first hours of fasting and reaches its minimum by 24 to 36 hours.

As insulin falls, the impaired central hypothalamic insulin signalling that was sustaining sympathetic overactivation begins to recover. The parasympathetic-promoting, sympathetic-suppressing effect of hypothalamic insulin signalling, which had been blunted by central insulin resistance, gradually re-establishes itself as insulin levels normalise and receptor sensitivity recovers. The RVLM, deprived of the hyperinsulinaemia-driven sympathetic stimulation, reduces its tonic output. Sympathetic nerve firing to the heart, vessels and kidneys decreases measurably.

Direct microneurographic studies, measuring sympathetic nerve firing in human subjects during fasting, have confirmed this reduction in sympathetic outflow with progressive fasting. Researchers measuring muscle sympathetic nerve activity (MSNA), the most sensitive available measure of central sympathetic output in humans, have documented significant MSNA reductions during both acute insulin withdrawal (experimental euglycaemic clamp studies removing hyperinsulinaemia while maintaining normal glucose) and during actual fasting protocols.

In plain language: when insulin falls, the nervous system literally quiets down. The alarm whose persistent activation was elevating blood pressure, accelerating the heart, constricting the vessels and telling the kidneys to retain sodium begins, measurably, to reduce its output.

Mechanism 2: Leptin Reduction and Its Sympathetic Consequences

As water fasting mobilises visceral fat for fuel, circulating leptin levels fall. Because leptin is produced by fat cells in proportion to fat mass, the reduction in fat mass during fasting is accompanied by a reduction in leptin production.

The fall in circulating leptin reduces the leptin-mediated sympathetic drive that was contributing to renal, cardiac and vascular sympathetic overactivation. Studies in experimental models of obesity have demonstrated that normalisation of leptin signalling, whether through leptin receptor restoration or through actual fat mass reduction, significantly reduces sympathetic outflow to the kidneys and heart. The human fasting literature, including DeVries' extensive review of clinical observations across thousands of fasting patients, consistently documents the subjective and objective signs of sympathetic withdrawal during extended fasting: reduced resting heart rate, blood pressure reduction that deepens

with each day of fasting, reduced skin conductance (a measure of sympathetic activation of sweat glands), and the characteristic subjective experience of deep calm and reduced anxiety that experienced fasters consistently report.

Mechanism 3: Ketones and Central Oxidative Stress Reduction

As BHB levels rise during fasting, its direct antioxidant effects, operating both peripherally and within the central nervous system, reduce the oxidative burden in brain stem tissue including the RVLM.

BHB has been shown in multiple experimental models to reduce superoxide production in brain tissue, restore normal antioxidant enzyme expression (particularly superoxide dismutase, SOD, the primary intracellular enzyme that converts superoxide to the less reactive hydrogen peroxide), and reduce NADPH oxidase activity in neuronal tissue. The consequence for RVLM function is a reduction in the superoxide-driven sympathetic hyperactivation that oxidative stress in the RVLM produces.

Simultaneously, the reduction in circulating angiotensin II that occurs as RAAS activity winds down during fasting (through the insulin-RAAS connection described in Chapters 3 and 4\) reduces the AT1-receptor-mediated NADPH oxidase activation in the brain stem. Less angiotensin II reaching the brain stem means less local oxidative stress, less RVLM hyperactivation, and less centrally generated sympathetic drive.

The peripheral and central anti-inflammatory and antioxidant effects of ketosis therefore converge on the brain stem's sympathetic control centres, reducing their pathological overactivation from within the central nervous system itself, not just by removing peripheral stimuli.

Mechanism 4: Vagal Tone Restoration

As sympathetic tone falls during fasting, vagal tone rises. The relationship between the two systems is reciprocally inhibitory: high sympathetic activity suppresses parasympathetic activity, and as sympathetic activity decreases, parasympathetic activity is freed to increase. This is a basic neurophysiological principle called reciprocal inhibition, and it means that the reductions in sympathetic drive achieved through fasting are accompanied by simultaneous increases in vagal tone.

Clinically measurable HRV improves during extended fasting. The spectral analysis of heart rate variability, which decomposes the mathematical variation in heart beat intervals into frequency components that reflect sympathetic versus parasympathetic contributions (high-frequency HRV components reflect vagal modulation of heart rate, while low-frequency components reflect sympathetic and mixed contributions), shows a shift toward higher high-frequency power during fasting, indicating increased vagal dominance.

This restoration of vagal tone has consequences that extend well beyond heart rate. The vagal anti-inflammatory pathway to the spleen is restored, reducing TNF-alpha and other pro-inflammatory cytokine production from splenic macrophages. Vagal innervation of the gut is restored to more normal function, supporting the gut microbiome remodelling described in Chapter 5 through parasympathetic regulation of intestinal motility, secretion and immune function. Vagal innervation of the pancreas may contribute to improved insulin secretion dynamics after the fast as beta cell function recovers.

The restoration of vagal tone during fasting is also one of the mechanisms responsible for the sleep improvements that many fasting individuals report. Higher vagal tone is associated with deeper, more restorative slow-wave sleep, reduced sleep-onset latency (the time it takes to fall asleep) and improved sleep architecture (the proportion of time spent in different sleep stages). Better sleep quality, in turn, improves the nocturnal sympathetic withdrawal that produces the blood pressure dip during sleep, addressing one of the mechanisms of non-dipping discussed in Section 6.3.

Mechanism 5: Baroreflex Recalibration

As fasting-induced blood pressure reduction is sustained over days, the baroreceptors begin to experience a genuinely different mechanical environment. Rather than the chronic high-pressure stretch that had been desensitising them and blunting their responsiveness, they are now operating at lower pressures. Over the extended period of a supervised therapeutic fast, the baroreceptors gradually recalibrate their sensitivity, recovering their ability to detect smaller pressure fluctuations and generate appropriate sympathetic-reducing feedback signals.

This baroreflex recalibration is one of the mechanisms responsible for the durability of fasting-achieved blood pressure reductions, particularly when they are maintained by appropriate post-fast nutrition. The recalibrated baroreceptors, now operating in a lower-pressure environment with improved sensitivity, act as a new natural blood pressure governor, defending the lower pressure against the tendency to drift back upward.

DeVries documented a clinical observation entirely consistent with this mechanism: "if the blood pressure falls below normal during the fast, it will rise to normal later." This is not a paradox. It is the baroreflex doing what it was designed to do: defending a set point. During extended fasting, as the inflammatory, hormonal and structural drivers of elevated blood pressure are progressively removed, the baroreflex set point recalibrates toward normal. The system then defends that new, normal set point rather than the previously elevated one.

Mechanism 6: Stress Axis Normalisation and Cortisol Regulation

The hypothalamic-pituitary-adrenal (HPA) axis (pronounced "hy-po-THAL-ah-mik pih-TOO-ih-tair-ee AD-ree-nal AX-is"), the stress response system that regulates cortisol production, is intimately connected to the sympathetic nervous system in ways that are clinically relevant to hypertension.

Cortisol (the primary glucocorticoid, meaning a steroid hormone that manages glucose and stress responses) is produced by the adrenal cortex (the outer layer of the adrenal glands) in response to ACTH (adrenocorticotrophic hormone, pronounced "ad-REE-no-kor-tih-koh-TROH-fik," produced by the pituitary gland in the brain in response to CRH, corticotrophin-releasing hormone, from the hypothalamus). Cortisol has multiple effects relevant to blood pressure: it sensitises blood vessels to noradrenaline (making them more responsive to sympathetic vasoconstriction), promotes renal sodium retention (through a mechanism distinct from but additive to aldosterone), and directly raises blood pressure through these vascular and renal effects.

Chronically stressed individuals with dysregulated HPA axis function, a pattern increasingly common in the context of the psychological, social and work-related stressors of modern life, have blunted cortisol

awakening responses combined with elevated basal cortisol throughout the day, indicating a dysregulated rather than simply elevated HPA axis. This pattern is associated with insulin resistance, abdominal obesity, sympathetic overactivation and hypertension.

During extended water fasting, HPA axis regulation undergoes normalisation. The reduction in inflammatory cytokines, particularly IL-6 (which stimulates CRH release from the hypothalamus), removes one of the primary inflammatory drivers of HPA axis overactivation. The psychological experience of fasting, particularly after the initial adjustment period of the first 48 to 72 hours, is consistently described by experienced fasters as one of profound calm, reduced anxiety and emotional equanimity. This is not merely subjective. It corresponds to measurable changes in the neurochemical environment, including rising BDNF (which we discussed in Chapter 3), normalising serotonin dynamics, and the anxiolytic (anxiety-reducing) effects of BHB on GABA receptors (gamma-aminobutyric acid receptors, the primary inhibitory receptor system in the brain that is targeted by benzodiazepine anxiolytic drugs through a different mechanism). BHB has been shown to enhance GABA receptor function directly, producing a calming effect on central nervous system excitability that is entirely consistent with the subjective reports of fasting-induced mental tranquillity.

A calmer nervous system produces lower cortisol. Lower cortisol reduces its direct vasopressor (blood pressure-raising) effects and its sensitisation of vessels to noradrenaline. Blood pressure falls further. The HPA axis dysregulation that was contributing to sympathetic overactivation and vascular hyper-reactivity begins to normalise.

6.7 The Clinical Picture: What Patients Actually Experience

The physiological mechanisms described in this chapter are abstract unless they are connected to what a person actually experiences as they fast. Understanding the expected subjective progression of the nervous system reset helps fasting patients interpret their experience accurately and maintain appropriate confidence in the process.

Days 1 to 3: The Storm Before the Calm

The first two to three days of a water fast are, for many people, the most neurologically challenging. This is the period when the keto flu symptoms are most prominent, but it is also the period when the nervous system is undergoing its most abrupt transition.

People who rely on caffeine, meaning coffee, tea or stimulant beverages to maintain their functional alertness, will experience withdrawal from caffeine during this window. Caffeine is an adenosine receptor antagonist (it blocks the receptors that respond to adenosine, the brain's natural fatigue signal), and its withdrawal produces a characteristic headache, irritability, fatigue and reduced concentration that is distinct from, but overlaps with, the keto flu. For individuals drinking three or more cups of coffee daily, caffeine withdrawal is often the primary source of discomfort in the first two days of fasting and should be distinguished from the metabolic transition symptoms.

Many people also experience heightened anxiety and irritability during this window, which reflects both the early catecholamine fluctuations as the sympathetic system begins its adjustment and the

psychological discomfort of removing a habitual behaviour (eating) that has served emotional regulatory functions. The relationship between food, comfort and emotional regulation is deeply embedded in human psychology, and the early fasting period can surface anxiety that has been managed through eating. This is physiologically and psychologically normal, and it resolves.

Days 3 to 5: The Transition Into Calm

By the third to fifth day, for most people, the neurological picture changes substantially. The keto flu has typically resolved. Caffeine withdrawal has passed. Ketone levels are rising robustly. Insulin is at its minimum. The sympathetic-parasympathetic rebalancing that fasting promotes is beginning to be subjectively noticeable.

Fasting patients in this window consistently report a shift in their experience of the fast. The mental preoccupation with food that characterised the first days diminishes significantly. A quality of mental quietness emerges that is difficult to describe but unmistakable to those who have experienced it: thoughts become clearer, decision-making feels less effortful, and the background noise of low-grade anxiety that many people carry without realising it begins to quiet. DeVries documented this shift, noting that "what was once a great problem becomes trivial" and that "a dark cloud has been lifted out of the mind" during fasting.

Heart rate typically begins to fall measurably by this point. Resting pulse rates that had been in the 75 to 90 range begin moving toward 60 to 70\. This is a direct, measurable clinical sign of increasing vagal tone and sympathetic withdrawal. Blood pressure readings show progressive improvement, with many patients showing reductions of 20 to 30 mmHg systolic and 10 to 15 mmHg diastolic by Day 5 of a supervised fast.

Days 5 to 14 and Beyond: Deep Sympathetic Reset

In the extended fast, the nervous system reset deepens progressively. The autonomic rebalancing that began in the first week continues and consolidates. HRV metrics show sustained improvement. Resting heart rate continues to fall toward optimal levels. Blood pressure stabilises at its new lower level.

The psychological experience of extended fasting, documented consistently across the fasting literature from Bragg and Shelton through to Goldhamer's contemporary supervised fasting patients, is one of the most remarkable and consistently reported features of the practice. Experienced fasters describe a quality of mental and emotional clarity, a reduction in psychological reactivity, and a sense of groundedness and equanimity that they attribute to the fast's effects on the nervous system. In neurochemical terms, this corresponds to the BDNF-mediated neuroplasticity, the BHB-mediated GABAergic calming, the serotonin recalibration, and the HPA axis normalisation that the fast is producing simultaneously.

This is not mysticism and it is not placebo. It is the subjective experience of a nervous system that has been chronically overloaded returning to a state of appropriate, sustainable regulation.

6.8 Autonomic Recovery After the Fast: Maintaining the Reset

The central concern regarding autonomic nervous system recovery is the same concern that applies to every other benefit of therapeutic fasting: the post-fast lifestyle and nutritional environment determine whether the recovery achieved during the fast is maintained or reversed.

The primary determinant of post-fast sympathetic tone is the same factor that drives it during the disease state: insulin levels. If the post-fast diet reinstates the chronic carbohydrate excess and refined food consumption that drove hyperinsulinaemia and insulin resistance in the first place, insulin will rise again, central hypothalamic insulin resistance will redevelop over months to years, and the sympathetic overactivation driven by that insulin resistance will progressively return.

Conversely, a post-fast dietary pattern that maintains insulin sensitivity, through adequate dietary fibre, moderate carbohydrate intake focused on whole food sources, sufficient protein and healthy fats, and the avoidance of refined carbohydrates and sugars, will sustain the low insulin environment that permits the continued autonomic balance achieved during the fast.

Physical activity plays an equally important role. Regular aerobic exercise is the most potent non-pharmacological intervention for increasing vagal tone and HRV. The mechanism involves exercise-induced shear stress on the arterial wall stimulating eNOS and nitric oxide production, exercise-mediated BDNF rise improving hypothalamic regulatory function, and the baroreceptor stimulation of exercise training recalibrating the baroreflex toward higher sensitivity and lower set points. Combining therapeutic fasting with a consistent programme of moderate aerobic exercise in the post-fast period produces a synergistic autonomic recovery that is substantially greater than either intervention alone.

Sleep optimisation is the third critical pillar of sustained autonomic recovery. Given the role of nocturnal sympathetic withdrawal in cardiovascular repair and the role of sleep-disordered breathing in sympathetic overactivation, addressing any identified sleep problems, including clinical assessment for obstructive sleep apnoea where indicated, is an essential component of sustained blood pressure management in the post-fast period.

Chapter Summary: Key Points

The autonomic nervous system, comprising the sympathetic (activating, alarm) and parasympathetic (calming, repair) divisions, is a primary regulator of blood pressure through its continuous modulation of heart rate, cardiac contractility, vascular tone and renal sodium handling. Healthy cardiovascular regulation requires an appropriate, dynamically balanced interplay between these two systems.

Chronic sympathetic overactivation in essential hypertension is not incidental but mechanistically driven through five converging pathways: hypothalamic insulin resistance impairing central sympathetic inhibition, chronically elevated leptin providing direct sympathostimulatory input, oxidative stress in the brain stem's RVLM increasing sympathetic output, RAAS-brain stem cross-activation through angiotensin II's effect on AT1 receptors in the brain stem, and baroreflex impairment reducing the sensitivity of the feedback system that should counteract elevated pressure.

The downstream consequences of chronic sympathetic overactivation include left ventricular hypertrophy, diastolic dysfunction and myocardial fibrosis in the heart; hypertensive nephropathy and

progressive GFR loss in the kidneys; arterial smooth muscle hypertrophy, endothelial oxidative stress and structural arterial remodelling in the vasculature; and worsening insulin resistance through catecholamine-mediated impairment of insulin receptor signalling, closing a self-perpetuating metabolic-autonomic loop.

The vagus nerve and vagal tone (measured clinically through HRV) are critically important for cardiovascular repair, anti-inflammatory signalling through the cholinergic anti-inflammatory pathway to the spleen, and nocturnal blood pressure dipping. Low vagal tone in metabolic disease reflects and contributes to both elevated sympathetic drive and inadequate vascular and cardiac repair.

Water fasting resets the autonomic nervous system through six simultaneous mechanisms: insulin reduction removing the central hypothalamic sympathetic drive, leptin reduction as visceral fat is mobilised removing leptin-mediated sympathetic input, BHB-mediated central antioxidant effects reducing RVLM superoxide-driven sympathetic hyperactivation, vagal tone restoration through reciprocal sympathetic-parasympathetic inhibition as sympathetic drive falls, baroreflex recalibration as sustained lower blood pressure allows baroreceptor sensitivity recovery, and HPA axis normalisation through reduced inflammatory cytokine-mediated CRH drive and direct BHB-GABAergic calming effects.

The subjective experience of the autonomic reset follows a predictable pattern: neurological challenge in Days 1 to 3 as caffeine withdrawal and catecholamine fluctuations occur, a transition into progressive calm between Days 3 and 5 as ketone levels rise and sympathetic tone falls, and deepening mental clarity, reduced anxiety and measurably improving HRV and resting heart rate from Day 5 onward in extended supervised fasting.

Maintaining the autonomic reset after the fast requires sustained insulin sensitivity through appropriate post-fast nutrition, regular aerobic exercise to build and maintain vagal tone and HRV, and sleep optimisation to ensure adequate nocturnal sympathetic withdrawal and cardiovascular repair. These three post-fast interventions act synergistically with each other and with the autonomic benefits of the fast itself.

Heart rate variability is a practical, measurable, patient-accessible metric of autonomic health that can be tracked through consumer wearable devices. A sustained increase in HRV after a therapeutic fast and appropriate lifestyle rehabilitation is objective evidence of successful autonomic nervous system recovery and reduced cardiovascular risk.

> *“It is not the strongest of the species that survives, nor the most intelligent. It is the one most responsive to change.”*
>
> — Charles Darwin

The nervous system that was once locked in permanent alarm can learn, given the right conditions, to stand down. Fasting provides those conditions.

PART THREE: THE PROTOCOLS

A Step-by-Step Clinical Guide to Therapeutic Water Fasting for Hypertension

CHAPTER 7

Before You Begin, Assessment, Preparation And Safety

“The general who wins the battle makes many calculations in his temple before the battle is fought.”

— Sun Tzu

Opening: Preparation Is Not Caution. It Is Competence.

There is a particular type of patient I have come to recognise over years of clinical practice. They arrive having read everything they could find about a treatment, having understood the science intellectually, having made the decision that this is what they want to do, and then they proceed without the one thing that would make their effort most likely to succeed: proper preparation.

Good intentions do not replace good preparation. They never have, and in medicine, the gap between the two is where most preventable complications occur.

Therapeutic water fasting is a powerful physiological intervention. We have spent six chapters establishing precisely how and why it is powerful, tracing its effects from the nephron of the kidney to the brain stem's sympathetic control centres, from the endothelial cell's nitric oxide production to the macrophage's inflammatory cytokine output, from the pancreatic beta cell's insulin secretion to the mitochondria's ketone metabolism. That power is real, it is documented across decades of clinical observation and increasingly confirmed by modern mechanistic research, and it is the reason fasting produces blood pressure reductions that pharmacological agents consistently fail to replicate.

But power without preparation is not medicine. It is gamble.

This chapter is about eliminating the gamble. It is about the systematic assessment, preparation and safety framework that converts the therapeutic power of water fasting from a general biological potential into a specific, targeted, individual intervention that is appropriate for you, at this time, under these specific circumstances. It covers who should fast, who should not, what to assess before beginning, what to prepare practically and physiologically, how to select and work with medical supervision, what to expect in the early days and how to recognise the difference between normal fasting symptoms and signs that require attention.

Read this chapter carefully. Every section matters. None of it is padding.

7.1 Who Should Not Fast Without Specialised Medical Supervision

Before discussing who is a good candidate for therapeutic fasting, we must be completely clear about the situations in which fasting should not be undertaken without a physician who has specific, hands-on

experience supervising therapeutic fasts. This is not a disclaimer inserted for legal protection. These are genuine clinical situations where fasting without appropriate medical oversight carries real risks that the intervention's benefits do not justify.

Absolute Contraindications: Do Not Fast Under Any Circumstances Without Expert Medical Supervision

Pregnancy is an absolute contraindication (a situation in which a treatment must not be used) to extended water fasting. The foetal requirement for continuous glucose delivery, the altered maternal metabolic state of pregnancy, and the profound hormonal changes that govern gestation make extended water fasting during pregnancy a risk to both mother and foetus that is not justified by any therapeutic goal. Short intermittent fasting windows (12 to 14 hours, primarily achieved by avoiding late-night eating) are used by some practitioners during pregnancy, but this is entirely distinct from the therapeutic water fasting protocols discussed in this book. If you are pregnant, this is not your chapter. Please discuss your hypertension management with a physician experienced in obstetric hypertension.

Active anorexia nervosa or bulimia nervosa, the eating disorders characterised by pathological food restriction and purging behaviours, are absolute contraindications. Fasting in the context of an active eating disorder is not therapeutic fasting. It is a reinforcement of pathological behaviour that carries the additional medical risks of the eating disorder itself, including electrolyte abnormalities, cardiac arrhythmias (abnormal heart rhythms), and bone density loss. If there is any history of an eating disorder, a comprehensive psychological assessment must precede any discussion of fasting protocols.

Severe cardiac conditions, specifically decompensated heart failure (heart failure that is not adequately controlled and is producing symptoms such as fluid accumulation, breathlessness at rest, or markedly reduced exercise tolerance), recent myocardial infarction (heart attack within the preceding three months), or significant cardiac arrhythmias that are not under stable medical management, require that any fasting intervention be supervised by a cardiologist with fasting experience. The haemodynamic shifts (changes in blood flow patterns and pressures within the cardiovascular system) of fasting, including the initial fluid mobilisation, the changes in electrolyte balance particularly potassium and magnesium, and the autonomic shifts of the transition period, require careful cardiac monitoring in these contexts.

Type 1 diabetes mellitus (pronounced "DY-ah-BEE-teez mel-EYE-tus," the form of diabetes in which the immune system has destroyed the insulin-producing beta cells of the pancreas, requiring absolute dependence on externally administered insulin) requires expert diabetological supervision for any fasting beyond 24 hours. The absence of the body's own insulin regulation means that the metabolic dynamics of fasting are fundamentally different from those in non-diabetic individuals or those with Type 2 diabetes, and the risks of both hypoglycaemia (dangerously low blood sugar, pronounced "hy-po-gly-KEE-mee-ah") and diabetic ketoacidosis (DKA, an acute life-threatening complication of severely uncontrolled diabetes, pronounced "ky-toh-as-ih-DOH-sis") require continuous medical monitoring.

Advanced chronic kidney disease (CKD), specifically estimated glomerular filtration rate (eGFR, the standard measure of kidney function, expressed in millilitres per minute per 1.73 square metres of body surface area) below 30 mL/min/1.73m², represents a situation where the kidney's reduced capacity to

handle the shifting electrolyte and acid-base (the balance between acids and bases in body fluids) demands of fasting requires nephrology supervision. The paradox here is that fasting is one of the interventions most likely to slow CKD progression by addressing its primary drivers, hyperglycaemia and hypertension, but the execution requires hands skilled in monitoring the metabolic consequences of fasting in a context of reduced renal reserve.

Active cancer under treatment, meaning patients receiving chemotherapy, radiation therapy or immunotherapy, should not undertake extended water fasting without the direct involvement of their oncologist. While there is an emerging and genuinely promising body of research on fasting as an adjunct to cancer therapy (particularly the work of Dr. Valter Longo at the University of Southern California on fasting-mimicking diets in cancer), this requires specific protocols developed in coordination with the treating oncology team, not independent fasting based on a general hypertension protocol.

Conditions Requiring Medical Clearance and Enhanced Monitoring

The following conditions do not preclude therapeutic fasting but require formal medical assessment and active medical involvement throughout the fast:

Type 2 diabetes mellitus managed with insulin or sulphonylurea medications (a class of oral diabetes drugs that directly stimulate insulin secretion from the pancreas, including glibenclamide, gliclazide, glipizide, glimepiride). Both insulin and sulphonylureas lower blood glucose regardless of whether food has been consumed, creating a significant risk of hypoglycaemia during fasting. Medication adjustment before and during the fast is mandatory. We will address medication management in detail in Section 7.4.

Any antihypertensive medication regimen, because fasting produces real and progressive blood pressure reduction, and patients taking antihypertensive medications will require dose adjustments as their blood pressure falls during the fast. Continuing standard antihypertensive doses while blood pressure is falling through fasting-mediated mechanisms risks hypotension (dangerously low blood pressure), which produces symptoms including dizziness, lightheadedness, fainting (syncope, pronounced "SIN-ko-pee"), and in severe cases, falls and their consequences. Section 7.4 covers medication management in full.

Significant electrolyte abnormalities at baseline. If a pre-fast blood panel reveals hypokalaemia (low potassium, pronounced "hy-po-ka-LEE-mee-ah"), hypomagnesaemia (low magnesium, pronounced "hy-po-mag-nee-SEE-mee-ah"), or hyponatraemia (low sodium, pronounced "hy-po-na-TREE-mee-ah"), these must be corrected before fasting begins. The electrolyte shifts of fasting will worsen pre-existing electrolyte abnormalities, and the cardiac risk of fasting on an electrolyte-depleted background is not acceptable.

A history of gout (pronounced "gowt," the painful joint condition caused by the deposition of uric acid crystals, most commonly in the big toe and other peripheral joints). Fasting transiently raises serum uric acid levels (the uric acid normally excreted by the kidneys competes with the ketone bodies produced during fasting for renal excretion, temporarily raising circulating uric acid). In most people this is asymptomatic and self-resolving. In someone with a history of gout, it may trigger a gout attack, typically

in the first two to three days of fasting. This is manageable with appropriate preparation, including ensuring good hydration and discussing pre-emptive uric acid management with a physician, but it is important to anticipate it.

Severe gastro-oesophageal reflux disease (GORD, also called GERD in American terminology, pronounced "gas-tro-eh-SOF-ah-jee-al REE-flux," the condition in which stomach acid flows back into the oesophagus causing heartburn, regurgitation and potential oesophageal damage) or a known gastric or duodenal ulcer (an open sore in the lining of the stomach or the first part of the small intestine). While fasting typically reduces acid production over its course, the early days of fasting may be accompanied by increased awareness of acid reflux symptoms in those predisposed, and anyone with an active untreated ulcer should not fast without medical clearance confirming healing.

Any history of a cardiac arrhythmia under ongoing medical management, including atrial fibrillation (AF, the most common sustained cardiac arrhythmia, in which the upper chambers of the heart beat chaotically rather than in coordinated rhythm), complete heart block, or any history of a ventricular arrhythmia (a potentially life-threatening abnormal rhythm originating in the lower chambers of the heart). The electrolyte shifts of fasting, particularly in potassium and magnesium, affect cardiac electrical stability, and anyone with a pre-existing cardiac electrical condition requires careful electrolyte monitoring and cardiology involvement.

7.2 The Pre-Fast Medical Assessment

For everyone else, meaning those without absolute contraindications and without the conditions requiring enhanced monitoring listed above, the pre-fast medical assessment is a structured process of gathering the information needed to fast intelligently, safely and effectively.

This assessment has four components: clinical history, physical examination measurements, laboratory investigations, and medication review. Each is described in full below. You should be able to walk into your physician's office with this section and have a clear, productive conversation about what you need and why.

Clinical History: What Your Physician Needs to Know

Your physician needs a complete current medical history with specific attention to:

The duration and severity of your hypertension. How long have you had elevated blood pressure? What has been the highest recorded reading? Is your hypertension classified as Stage 1 (systolic 130 to 139 mmHg or diastolic 80 to 89 mmHg) or Stage 2 (systolic 140 mmHg or higher or diastolic 90 mmHg or higher) according to current American Heart Association and American College of Cardiology criteria? Or are you in the hypertensive urgency or emergency range (systolic above 180 mmHg, diastolic above 120 mmHg)? Fasting is not appropriate as an outpatient intervention in hypertensive emergency, which requires immediate medical management.

Your current antihypertensive medication regimen, including every medication, its dose and its dosing frequency. This information is the foundation of the medication adjustment planning in Section 7.4.

A complete list of all medications you take, including medications for non-hypertensive conditions, over-the-counter medications (medications available without a prescription), supplements and herbal preparations. Several common medications interact with fasting in ways that are clinically important, including non-steroidal anti-inflammatory drugs (NSAIDs such as ibuprofen and naproxen, which should be avoided during fasting as they can irritate the gastric mucosa, the lining of the stomach, when taken without food, and which impair renal prostaglandin function, potentially worsening electrolyte handling), anticoagulants (blood thinners such as warfarin, whose dosing may require adjustment during fasting as dietary vitamin K intake is eliminated), and lithium (used for bipolar disorder, whose levels in the blood can become unpredictable during fasting due to altered renal handling and which requires specific monitoring).

Your cardiovascular history. Have you ever had a heart attack, a stroke or a transient ischaemic attack (TIA, a brief episode of neurological dysfunction caused by a temporary interruption of blood flow to part of the brain, often called a "mini-stroke")? Do you have documented coronary artery disease? Have you ever had a cardiac procedure such as angioplasty (balloon widening of a narrowed coronary artery), coronary stenting (placement of a metal scaffold to keep a coronary artery open), or coronary artery bypass grafting (surgical rerouting of blood supply around blocked coronary arteries)?

Your metabolic history. Do you have a diagnosis of insulin resistance, metabolic syndrome, pre-diabetes or Type 2 diabetes? If so, what medications are you taking and what were your most recent blood glucose and HbA1c (glycated haemoglobin, pronounced "gly-KAY-ted HEE-mo-glo-bin," a measure of average blood sugar control over the preceding two to three months) levels?

Your kidney function history. Do you have any known chronic kidney disease? What were your most recent creatinine (a waste product filtered by the kidneys whose blood level reflects kidney function) and eGFR values?

Your liver history. Do you have any known liver disease, including non-alcoholic fatty liver disease (NAFLD, pronounced "NAF-eld," the accumulation of fat in the liver cells in the absence of significant alcohol consumption, extremely common in insulin-resistant individuals)? Do you drink alcohol regularly, and if so, how much?

Your family history of cardiovascular disease, particularly any first-degree relatives (parents, siblings, children) who experienced heart attacks, strokes or sudden cardiac death before the age of 55 in men or 65 in women.

Physical Examination Measurements

Before beginning a therapeutic fast, the following measurements should be formally documented as your baseline:

Blood pressure, measured correctly. This means after five minutes of seated rest, in both arms (elevated readings in one arm compared to the other can indicate subclavian artery stenosis, pronounced "SUB-clay-vee-an ar-TE-ree ste-NOH-sis," a narrowing of the artery supplying the arm that has cardiovascular implications), and averaged across at least two readings taken two minutes apart. Your physician should note whether you have white coat hypertension (elevated blood pressure

specifically in the clinical setting due to anxiety about being measured, which may normalise outside the clinic) or masked hypertension (blood pressure that appears normal in the clinic but is elevated during ordinary daily life). Ambulatory blood pressure monitoring (the 24-hour wearable device described in Chapter 6\) is the gold standard for distinguishing these patterns and should ideally be performed before a first therapeutic fast to establish a true baseline.

Heart rate, measured at rest after the same five-minute seated period. Your resting heart rate before the fast is a baseline against which to measure the vagal tone restoration and sympathetic withdrawal that the fast produces.

Body weight and body mass index (BMI, calculated as weight in kilograms divided by height in metres squared). BMI has well-recognised limitations as a measure of metabolic health, particularly in individuals with high muscle mass, but it is a universally available reference point.

Waist circumference, measured at the level of the umbilicus (navel) after gentle exhalation. Waist circumference is a better predictor of visceral adiposity and metabolic risk than BMI. Values above 94 cm (37 inches) in men and 80 cm (31.5 inches) in women indicate elevated metabolic risk; values above 102 cm (40 inches) in men and 88 cm (34.5 inches) in women indicate substantially elevated risk. Because visceral fat is one of the primary drivers of the insulin resistance-hyperinsulinaemia-sympathetic overactivation cascade that this book addresses, waist circumference is one of the most meaningful baseline measurements to track as fasting and post-fast nutrition progressively reduce it.

Laboratory Investigations: Your Pre-Fast Blood Panel

The following blood tests should be performed within the two to four weeks before a first therapeutic fast:

A full blood count (FBC, also called a complete blood count or CBC in American terminology). This measures the number and characteristics of red blood cells, white blood cells and platelets (the small blood components involved in clotting). Pre-existing anaemia (reduced red blood cell mass or haemoglobin, the protein that carries oxygen in red blood cells) should be identified and addressed before fasting, as fasting is not an appropriate time to be managing acute anaemia.

A comprehensive metabolic panel (CMP, also called a urea and electrolytes panel or U\&E; in some healthcare systems), which includes sodium, potassium, chloride, bicarbonate (a measure of the blood's acid-base balance), blood urea nitrogen (BUN, a measure of kidney function), creatinine, and eGFR. These values establish your electrolyte and kidney function baseline, identify any pre-existing abnormalities that need correction before fasting, and provide the reference values against which mid-fast monitoring can be compared.

Fasting glucose and HbA1c. Fasting glucose is measured after at least eight hours without eating. HbA1c reflects the average blood glucose level over the preceding two to three months and is the standard measure of longer-term glycaemic (blood sugar) control. These establish your metabolic baseline and are essential for understanding how fasting is improving your metabolic status over time.

Fasting insulin and HOMA-IR calculation. As we discussed in Chapter 4, these are the measurements that standard hypertension panels consistently omit and that are perhaps the most important for understanding the root mechanism driving your blood pressure elevation. HOMA-IR (Homeostatic Model Assessment of Insulin Resistance, pronounced "HO-ma EYE-ar") is calculated from fasting insulin and fasting glucose using the formula: fasting insulin (in micro-international units per millilitre) multiplied by fasting glucose (in millimoles per litre), divided by 22.5. A HOMA-IR below 1.0 reflects excellent insulin sensitivity. Values between 1.0 and 1.9 indicate early insulin resistance. Values between 2.0 and 2.9 indicate significant insulin resistance. Values of 3.0 and above indicate severe insulin resistance. Most hypertensive patients who have not previously tested this will be surprised by where they fall on this scale.

A lipid panel (fasting), including total cholesterol, LDL cholesterol (low-density lipoprotein, the particle that carries cholesterol to the arterial wall and is associated with atherosclerotic risk), HDL cholesterol (high-density lipoprotein, the particle that carries cholesterol away from the arterial wall, with higher levels being protective), and triglycerides. The triglyceride-to-HDL ratio (TG:HDL ratio), discussed in Chapter 4 as a practical insulin resistance marker, is calculated directly from these values. Divide your triglyceride level by your HDL level, both expressed in milligrams per decilitre in American units or both expressed in millimoles per litre in most other systems. A ratio below 1.5 in millimolar units (or below 3.5 in mg/dL units) is favourable. A ratio above 2.5 in millimolar units (or above 5.0 in mg/dL units) strongly suggests insulin resistance.

Uric acid. As noted in Section 7.1, fasting transiently raises serum uric acid through competitive renal excretion between uric acid and ketone bodies. Knowing your baseline uric acid level allows you to anticipate this transient rise, identify if you are already operating at the upper limit of normal (above 360 micromoles per litre, or 6.0 mg/dL in American units), and discuss preventive management with your physician if needed.

Thyroid function, specifically thyroid-stimulating hormone (TSH, the pituitary gland's signal to the thyroid to produce its hormones). Hypothyroidism (underactive thyroid, pronounced "hy-po-THY-royd-iz-um"), which is common and frequently undiagnosed, causes significant metabolic changes including weight gain, elevated cholesterol, reduced heart rate and, importantly, can contribute to blood pressure elevation through mechanisms including increased peripheral vascular resistance. Identifying undiagnosed hypothyroidism before fasting allows appropriate treatment, which may itself contribute to blood pressure improvement.

Liver function tests (LFTs), including alanine aminotransferase (ALT), aspartate aminotransferase (AST), gamma-glutamyl transferase (GGT), alkaline phosphatase (ALP) and bilirubin. Given the high prevalence of NAFLD in insulin-resistant individuals, baseline liver function tests are important. Significantly elevated liver enzymes (particularly ALT more than three times the upper limit of normal) warrant investigation before fasting and should prompt hepatology input.

Magnesium. Standard blood panels frequently omit magnesium despite it being clinically important and frequently low in individuals with metabolic syndrome and hypertension. Magnesium deficiency (hypomagnesaemia) impairs blood pressure regulation, contributes to insulin resistance, promotes arterial smooth muscle contraction, and is associated with cardiac arrhythmia. Correcting magnesium

deficiency before fasting both improves fasting tolerance and reduces electrolyte risk during the fast. Note that serum (blood) magnesium is an insensitive measure of total body magnesium stores because the body tightly maintains serum levels even as cellular stores are depleted. Red blood cell magnesium is a more accurate reflection of actual magnesium status, though less commonly available.

An electrocardiogram (ECG, also called an EKG from its German name Elektrokardiogramm). A resting 12-lead ECG should be performed before any extended therapeutic fast. The ECG identifies pre-existing cardiac electrical abnormalities, including LVH with strain pattern (the ECG changes that reflect left ventricular hypertrophy and its associated subendocardial ischaemia), bundle branch blocks (delays in the electrical conduction through the ventricles), prolonged QT interval (a lengthening of the electrical recovery phase of each cardiac cycle that predisposes to potentially fatal ventricular arrhythmias, pronounced "cue-TEE"), and pre-existing arrhythmias. The QT interval is particularly relevant because electrolyte abnormalities, including hypokalaemia and hypomagnesaemia, which can occur during fasting if electrolyte management is inadequate, prolong the QT interval and increase arrhythmia risk. A pre-fast ECG establishing the baseline QT interval (expressed as the QTc, the corrected QT interval adjusted for heart rate) provides the reference point against which mid-fast monitoring can be compared if needed.

7.3 Understanding the Risk-Benefit Calculation for Your Specific Situation

The pre-fast assessment described in Section 7.2 generates a comprehensive picture of your current health status. But translating that picture into a decision about whether and how to fast requires an explicit risk-benefit calculation that is specific to your individual circumstances.

The Baseline Cardiovascular Risk Assessment

Every hypertensive patient carries a baseline cardiovascular risk that can be formally quantified. The most widely used tool in clinical practice is the Framingham Risk Score, or its more contemporary replacement in current American cardiology guidelines, the Pooled Cohort Equations (PCE), which calculate the ten-year risk of a first major cardiovascular event (heart attack or stroke) based on age, sex, blood pressure, total and HDL cholesterol, presence of diabetes, and smoking status.

For a 55-year-old man with Stage 2 hypertension (systolic 155 mmHg), a total cholesterol of 5.5 mmol/L, an HDL of 1.1 mmol/L, no diabetes and no smoking, the ten-year cardiovascular risk calculated by the PCE is approximately 15 to 20%, meaning roughly one in five to one in six chance of a heart attack or stroke in the next decade if nothing changes. This is the risk of inaction. It is the baseline against which the risks of therapeutic fasting must be compared.

When the baseline risk of inaction is that significant, and when the evidence from Goldhamer, Shelton, Weger, McEachen and the clinical fasting literature broadly demonstrates consistent, substantial and durable blood pressure reductions in hypertensive patients, the argument that fasting is "too risky" requires that the risks of fasting be greater than the accumulated cardiovascular risk of years of inadequately controlled hypertension. In the great majority of appropriately selected patients, with adequate preparation and appropriate supervision, they are not.

This is not a dismissal of fasting risks. It is a contextualisation of them. Every therapeutic decision in medicine involves a risk-benefit calculation, and the calculation must include the risks of the current trajectory, not just the risks of the proposed intervention.

The Symptom Versus Mechanism Question

The pre-fast assessment also forces the central question that this book has been building toward since Chapter 1: are we treating symptoms or mechanisms?

If the pre-fast assessment reveals, as it frequently does in hypertensive patients, a HOMA-IR of 3.5, a TG:HDL ratio of 4.2, a fasting insulin of 22 micro-international units per millilitre, a waist circumference of 106 cm, and an HbA1c edging toward pre-diabetic territory, then the honest clinical picture is of a patient whose blood pressure elevation is a symptom of profound metabolic dysregulation, whose antihypertensive medications are managing the symptom while the underlying mechanism continues to progress, and for whom a therapeutic approach that addresses the mechanism is not just preferable but arguably the only pathway to genuine long-term cardiovascular protection.

Seeing these numbers clearly, before the fast begins, does something important: it gives the fast a specific, measurable purpose. You are not fasting in the hope of feeling better. You are fasting to reduce a HOMA-IR that currently stands at 3.5 toward the target of below 1.5. You are fasting to lower a fasting insulin of 22 toward the genuinely insulin-sensitive range of below 8\. You are fasting to reduce a systolic blood pressure of 158 mmHg toward the below-120 target that the evidence associates with lowest cardiovascular event rates. These are specific, measurable, achievable goals, and the pre-fast assessment is what makes them specific.

7.4 Medication Management Before and During the Fast

This section requires the most careful reading in the chapter, because inappropriate medication management during fasting is the single most preventable source of fasting complications in hypertensive patients. Please do not attempt to manage your medications independently. Every adjustment described here must be made in consultation with your prescribing physician.

Antihypertensive Medications

The problem is straightforward. Antihypertensive medications are prescribed at doses calibrated to control blood pressure in the context of your current diet, activity level and metabolic state, none of which apply during a water fast. As fasting progressively lowers blood pressure through the mechanisms described in Chapters 3 through 6, and as the sodium excretion of the early fast rapidly reduces blood volume, continuing full antihypertensive doses risks producing hypotension, defined clinically as a systolic blood pressure below 90 mmHg in most contexts, or a symptomatic drop in blood pressure causing dizziness, lightheadedness or fainting regardless of the absolute number.

The approach to antihypertensive medication adjustment must be individualised and physician-directed. However, some general principles apply:

Diuretics (medications that promote fluid and sodium excretion by the kidney, including thiazide diuretics such as hydrochlorothiazide and chlorthalidone, and loop diuretics such as furosemide) are typically the first class to be reduced or temporarily suspended at the start of a fast. This is because fasting itself produces natriuresis (increased sodium and fluid excretion by the kidneys) through the insulin-withdrawal mechanism described in Chapter 3\. Continuing a diuretic on top of fasting-induced natriuresis significantly risks volume depletion and hypotension, and also accelerates electrolyte losses, particularly potassium and magnesium. The decision to reduce or suspend a diuretic before fasting should be made by your physician with knowledge of your baseline blood pressure, your reasons for the diuretic prescription (some patients are on diuretics for heart failure fluid management rather than blood pressure alone, which changes the calculation significantly), and your electrolyte status.

ACE inhibitors (angiotensin-converting enzyme inhibitors, medications that block the conversion of angiotensin I to the vasoconstricting angiotensin II, including lisinopril, ramipril, perindopril and enalapril) and ARBs (angiotensin receptor blockers, medications that block the receptor that angiotensin II acts on, including losartan, valsartan, irbesartan and candesartan) are directly targeting the RAAS pathway that fasting also suppresses. As fasting reduces RAAS activity through the insulin-mediated mechanisms described in Chapter 3, the blood pressure-lowering effect of ACE inhibitors and ARBs is superimposed on fasting's own RAAS suppression. The cumulative effect can be significant hypotension. ACE inhibitors and ARBs typically require dose reduction during extended fasting, with the timing and degree of reduction guided by blood pressure monitoring. An additional consideration for ACE inhibitors specifically is the class side effect of hyperkalaemia (elevated blood potassium, pronounced "hy-per-ka-LEE-mee-ah"), which is relevant because fasting and ACE inhibitor use both tend to raise potassium through reduced aldosterone activity. Potassium monitoring is particularly important when ACE inhibitors are continued during fasting.

Beta-blockers (medications that block beta-adrenergic receptors on the heart and other tissues, including atenolol, metoprolol, bisoprolol and carvedilol) are generally not abruptly stopped during fasting. Abrupt cessation of beta-blockers can produce rebound tachycardia (a rapid rise in heart rate, pronounced "tak-ih-KAR-dee-ah") and, in patients with underlying coronary artery disease, can trigger cardiac ischaemia. Beta-blockers should be tapered (gradually reduced in dose over days to weeks) under physician supervision rather than stopped suddenly. It is also important to note that beta-blockers suppress the early warning signs of hypoglycaemia (tremor, palpitations, anxiety), which is relevant for any patient with diabetes on a beta-blocker who also undergoes fasting.

Calcium channel blockers (medications that block calcium entry into vascular smooth muscle and cardiac cells, reducing vascular tone and heart rate, including amlodipine, nifedipine, diltiazem and verapamil) generally have a lower risk of hypotension during fasting compared to diuretics, ACE inhibitors and ARBs, but blood pressure monitoring remains essential. The dihydropyridine calcium channel blockers (amlodipine, nifedipine) primarily act on blood vessels and carry more hypotension risk during fasting. The non-dihydropyridine calcium channel blockers (diltiazem, verapamil) act on both blood vessels and the heart, and their heart rate-slowing effects may compound the fasting-induced reduction in heart rate and cardiac output.

Alpha-blockers (medications that block alpha-adrenergic receptors on blood vessels, including doxazosin and prazosin) carry a specific risk of first-dose hypotension and postural hypotension (a drop in blood pressure upon standing that causes dizziness or fainting). This risk is amplified during fasting because fasting reduces blood volume. Patients on alpha-blockers should be particularly careful about moving from lying or sitting to standing slowly during a fast, and blood pressure monitoring in both lying and standing positions (called orthostatic blood pressure measurement) is advisable.

The general monitoring standard during a supervised fast in a patient on antihypertensive medications is twice-daily blood pressure measurement (morning and evening), with physician contact if systolic blood pressure falls below 100 mmHg, if diastolic falls below 60 mmHg, or if symptoms of hypotension (dizziness, lightheadedness, fainting, visual changes) occur at any reading. These thresholds are general guidelines; your physician may specify different thresholds based on your individual clinical circumstances.

Diabetes Medications

Insulin and sulphonylureas (glibenclamide, gliclazide, glipizide, glimepiride): These drugs lower blood glucose independently of food intake. They must be proactively managed before fasting begins, not reactively managed after hypoglycaemia occurs. Your diabetologist or physician should review your current regimen, establish a blood glucose monitoring schedule (at minimum before sleeping and on waking, with additional measurements if symptoms of hypoglycaemia arise), and provide clear instructions on dose reduction or suspension.

Metformin (the most widely used oral diabetes medication, which works primarily by reducing hepatic glucose production rather than stimulating insulin secretion, and which does not directly cause hypoglycaemia) should be suspended during extended water fasting. Metformin is contraindicated (not recommended) in conditions of significant dehydration or reduced caloric intake because of the very rare but serious risk of lactic acidosis (an abnormal accumulation of lactic acid in the blood, pronounced "LAK-tik as-ih-DOH-sis"), a complication that has been associated with metformin use in contexts of physiological stress including dehydration and acute illness. Temporary suspension during a water fast is appropriate.

SGLT2 inhibitors (sodium-glucose cotransporter-2 inhibitors, a newer class of diabetes medications that work by causing the kidneys to excrete excess glucose in the urine, including empagliflozin, dapagliflozin and canagliflozin) carry two specific risks during fasting. First, they produce natriuresis and diuresis (sodium and fluid loss through the urine) through their mechanism, which compounds the fasting-induced natriuresis and increases the risk of dehydration and volume depletion. Second, and more critically, they are associated with a rare but serious complication called euglycaemic diabetic ketoacidosis (euglycaemic DKA, pronounced "you-gly-SEE-mik DKA"), a form of diabetic ketoacidosis that occurs even with near-normal or only modestly elevated blood glucose levels, making it much harder to recognise than typical DKA. Fasting, which promotes ketone production physiologically, combined with SGLT2 inhibitor use, which also promotes ketone production through its mechanism, creates an additive risk of euglycaemic DKA that is a genuine and documented clinical concern. SGLT2 inhibitors should be suspended before therapeutic water fasting. The standard guidance from major diabetes associations is to suspend SGLT2 inhibitors at least 24 to 72 hours before any planned

significant caloric restriction, surgery or prolonged fasting.

GLP-1 receptor agonists (glucagon-like peptide-1 receptor agonists, a class of injectable medications that include semaglutide, liraglutide, exenatide and dulaglutide, which reduce blood glucose and promote weight loss through multiple mechanisms including appetite suppression and slowing gastric emptying) generally do not cause hypoglycaemia on their own, but their continuation during fasting requires physician guidance. Their appetite-suppressing effects may actually complement the early fasting period, and their cardiovascular protective effects, which are substantial and have been demonstrated in major outcome trials, make the decision about temporary suspension versus continuation more nuanced. This decision should be made explicitly with your physician.

Medications That Affect Electrolytes

Beyond diuretics and ACE inhibitors, several other medications affect electrolyte balance in ways that are relevant to fasting safety:

Non-steroidal anti-inflammatory drugs (NSAIDs, including ibuprofen, naproxen and diclofenac) impair renal prostaglandin synthesis, reducing the kidney's ability to manage sodium and potassium balance. NSAIDs also impair the blood pressure-lowering effects of antihypertensive medications and can cause acute kidney injury in the context of dehydration or volume depletion. They should be avoided during fasting.

Corticosteroids (medications including prednisolone, dexamethasone and hydrocortisone, used for inflammatory and autoimmune conditions) promote sodium retention and potassium wasting, and raise blood glucose through multiple mechanisms. They should not be abruptly stopped during fasting, as adrenal suppression from chronic corticosteroid use means the body cannot mount its own cortisol response to the physiological stress of fasting without the exogenous supply. Physician involvement in managing corticosteroids during fasting is mandatory.

Digoxin (a medication used for heart failure and certain arrhythmias) has a narrow therapeutic window, meaning the difference between a therapeutic dose and a toxic dose is small. Its toxicity is significantly enhanced by hypokalaemia (low potassium), making electrolyte monitoring during fasting particularly critical in digoxin-treated patients.

7.5 Practical Preparation: What to Do in the Two Weeks Before Your First Fast

The two weeks immediately before a first therapeutic fast are the preparation period. The decisions and actions taken during this window significantly affect both the comfort and the effectiveness of the fast itself.

The Dietary Transition

The final meal should be completed by early evening to maximise the overnight fasting window before the fast formally begins the following morning. This aligns closely with the protocols found in DeVries Chapter VIII, which advocates for a strict transition to raw fruits and vegetables 1–2 days prior to the

cessation of eating. Furthermore, integrating the food sequencing protocols from the metabolic guide consuming vegetables first, proteins second, and complex or resistant carbohydrates last can significantly ease the metabolic transition into the fast, loosening the bowel and reducing the initial toxic load.

The standard Western diet, dominated by refined carbohydrates, processed foods, added sugars and seed oils, produces a metabolic environment characterised by high insulin, glycogen stores at maximum capacity, and complete metabolic dependence on dietary glucose as the primary fuel source. Attempting to shift from this state directly into water-only fasting is like attempting to switch a car engine from petrol to an alternative fuel without any transition preparation: the immediate result is dysfunction, discomfort, and a significantly higher likelihood of abandoning the attempt.

The dietary transition in the two weeks before a fast serves two purposes. First, it begins the process of reducing insulin levels and improving insulin sensitivity, making the metabolic crossover to fat metabolism and ketone production smoother, faster and less symptomatic during the fast itself. Second, it reduces the caffeine, refined sugar and processed food burden that contributes to withdrawal symptoms in the early days of fasting.

In the first week of the preparatory period, the primary goals are the elimination of refined carbohydrates, added sugars, and ultra-processed foods, and a significant reduction in caffeine intake. This means replacing white rice, white bread, pasta, pastries, biscuits, sugary drinks (including fruit juices, which despite their natural origin are concentrated sugar solutions that produce the same insulin response as soft drinks), and processed snacks with whole foods: vegetables, legumes (beans, lentils, peas), whole grains such as oats and brown rice where grains are consumed, fresh fruit (whole fruit rather than juice, which includes the fibre that slows glucose absorption), nuts, seeds and quality proteins.

Caffeine reduction should be gradual rather than abrupt. Moving from three or four cups of coffee daily directly to zero generates significant caffeine withdrawal symptoms, including severe headaches, irritability and fatigue, that will overlap with and worsen the early fasting experience. Reduce caffeine intake by approximately one cup equivalent per day across the first week, reaching one cup or less daily by the start of the second week, and eliminating it entirely two to three days before the fast begins. This staged reduction allows caffeine withdrawal to be substantially completed before fasting starts, separating two sources of discomfort and making the early fast considerably more manageable.

In the second week of the preparatory period, the goal is to transition toward what DeVries called a "pre-fast cleansing diet" and what the contemporary low-carbohydrate and ketogenic diet literature calls nutritional ketosis preparation. This means a diet composed primarily of non-starchy vegetables, moderate amounts of protein from quality sources (eggs, fish, poultry, legumes, or full animal-sourced protein according to the reader's dietary philosophy and medical circumstances), and healthy fats (avocado, olive oil, nuts, seeds, coconut). Carbohydrate intake should be reduced to below 50 grams of total carbohydrates per day during this second week. This level of carbohydrate restriction begins depleting glycogen stores and initiating low-level ketone production, so that when the fast begins the body is already partially adapted to fat metabolism and the transition to full fasting ketosis is considerably smoother.

Both Bragg and DeVries specifically recommend consuming primarily raw fruits and vegetables in the one to two days immediately before a fast, and this recommendation has a sound physiological basis: the high water content, fibre and enzymatic activity of raw plant foods promotes bowel activity and cleansing, so that the gastrointestinal tract enters the fast with lower residual content. This reduces the gas and discomfort that can occur when processed food residues remaining in the colon undergo bacterial fermentation during the early fast.

Caffeine, Alcohol and Tobacco

Caffeine should be fully eliminated before the fast begins, as described above.

Alcohol should be eliminated during the preparation period and absolutely during the fast. Alcohol impairs fatty acid metabolism (the process of breaking down stored fat for fuel, which is the primary energy supply during fasting), promotes hypoglycaemia by impairing hepatic glucose production, and places an additional metabolic burden on the liver at a time when the liver is already managing the increased demands of ketogenesis (ketone production). Alcohol also impairs sleep quality, reduces HRV, and activates the HPA axis, all of which are counterproductive to the autonomic restoration that the fast is designed to achieve.

Tobacco use should be ceased or significantly reduced. Smoking causes endothelial dysfunction through multiple mechanisms including oxidative stress, carbon monoxide-mediated haemoglobin impairment, and direct nicotine-mediated sympathetic activation. These are precisely the pathological processes that fasting is working to reverse. Continuing to smoke while fasting is, to use a direct analogy, attempting to fill a bucket while the tap producing the leak remains open. Additionally, nicotine is itself a vasoconstrictor and sympathomimetic (something that mimics the effects of sympathetic nervous system activation), directly opposing the sympathetic withdrawal that is one of fasting's primary antihypertensive mechanisms.

Practical Preparation: Equipment and Supplies

The following practical preparations should be made before a first fast:

Obtain a quality blood pressure monitor for home use. This is non-negotiable. You need to be able to measure your blood pressure at home, twice daily, throughout the fast. The monitor should be validated (most pharmacists or physicians can advise on validated models) and should be an upper arm device rather than a wrist device, as wrist devices are significantly less accurate. Keep a written record of every reading with the date and time.

Obtain a blood glucose monitor if you have diabetes or pre-diabetes, or if your physician recommends it based on your metabolic panel results. Even without diabetes, tracking blood glucose during a first extended fast provides valuable information about your metabolic response and is an additional safety measure.

Obtain a heart rate monitor or use a wearable device that tracks resting heart rate and, ideally, HRV. Tracking the progressive reduction in resting heart rate and the improvement in HRV metrics during the fast gives you real-time, objective evidence of the autonomic nervous system reset described in Chapter 6\.

Source your water supply. Spring water or tested well water is the first choice for fasting, as DeVries recommended. Filtered tap water (using a high-quality carbon block or reverse osmosis filter) is an acceptable alternative in most developed world contexts. Distilled water, as Bragg recommended and as the clinical fasting literature widely used, is also appropriate. What matters most is that the water is free of chlorine, heavy metals and other contaminants. Aim for a minimum of two litres (approximately 68 fluid ounces) daily, guided by thirst, as discussed in Chapter 8\.

Arrange your schedule. Extended therapeutic fasting is not compatible with high-demand professional obligations during the first three to five days. The early transition period requires rest, reduced social engagement, and the ability to respond to your body's needs without workplace or social pressure. If possible, begin your first extended fast at the start of a weekend or a period of planned leave. You do not need to be in bed, and most people are able to continue light daily activities throughout a fast of seven to ten days, but you should not plan your first fast around a week of back-to-back meetings and professional commitments.

Establish your medical supervision before the fast begins. Have a specific physician contact point, a person you can call or message if you have concerns during the fast. This does not need to be a fasting specialist, though a physician with fasting experience is ideal. It needs to be a physician who understands the protocols you are following, has your pre-fast assessment results, knows your medication management plan, and has agreed to be your monitoring contact during the fast.

Manage your social environment: Both Bragg and DeVries emphasized the psychological necessity of keeping a first fast private from uninformed individuals. DeVries famously warned of "terrified aunts and cousins" whose well-meaning but anxious interference can sabotage a faster's mental resolve. Setting clear therapeutic intentions and keeping your protocol private ensures a supportive, quiet environment focused entirely on rest, warmth, and privacy.

Document your baseline: Before day one, dedicate a journal to tracking your starting point. Record your baseline symptoms, daily blood pressure readings, and your exact medication tapering list. This provides an objective log that strips the anxiety away from the physiological shifts you are about to experience.

The Day Before the Fast

The final day before the fast is not a day for a large celebratory meal. This is one of the most common preparatory mistakes. A large, carbohydrate-heavy meal the day before a fast fills glycogen stores and delays the metabolic crossover to fat metabolism, prolonging the keto flu period and worsening early fasting discomfort.

The final meals before a fast should follow the second-week preparatory diet: low carbohydrate, moderate protein, adequate fat, predominantly whole and unprocessed foods. A simple final meal of cooked vegetables, eggs or fish, and a salad is appropriate. The final meal should be completed by early evening to maximise the overnight fasting window before the fast formally begins the following morning.

Some practitioners recommend a small amount of magnesium supplementation (200 to 400 mg of magnesium glycinate, which is the most bioavailable and least laxative magnesium form) in the evening before the fast begins and continuing it throughout the fast. Given the frequency of subclinical magnesium deficiency in hypertensive patients, and the role of magnesium in reducing cardiovascular excitability and supporting electrolyte balance during fasting, this is a reasonable and low-risk preparatory step. Discuss it with your physician in the context of your pre-fast magnesium level.

7.6 Setting Realistic Expectations: What Normal Fasting Feels Like Versus What Requires Attention

Managing expectations is a clinical skill. Patients who do not know what to expect interpret normal fasting experiences as dangerous symptoms, terminate the fast prematurely, and deprive themselves of the therapeutic benefit they were pursuing. Patients who have been given clear, accurate expectations navigate the normal discomforts of fasting with appropriate confidence.

Normal Fasting Experiences That Do Not Require Medical Attention

Hunger in the first two to three days is normal and expected. It is primarily habitual hunger, the body's conditioned expectation of food at usual mealtimes, rather than true physiological hunger driven by genuine energy deficit. It is uncomfortable and psychologically challenging but not dangerous. It typically peaks on Day 2 and substantially diminishes by Day 3 to 4 as ketone levels rise and appetite suppression develops. Many patients describe the disappearance of hunger after the first three to four days as one of the most surprising and reassuring experiences of fasting.

Headache in the first one to three days is extremely common and typically reflects caffeine withdrawal (particularly prominent in the first 24 to 48 hours), the initial keto flu transition, and sometimes mild dehydration. It responds to increased water intake and rest. Persistent severe headache beyond Day 3, or headache accompanied by visual changes, neck stiffness, or altered consciousness, is not normal and requires medical assessment.

Fatigue and reduced energy in the first three to four days is normal and reflects the metabolic transition period. The body is switching from a glucose-dependent state to a fat and ketone-dependent state, and during that transition, energy availability is lower than normal. Most patients describe a marked improvement in energy and mental clarity from Day 4 or 5 onward as ketosis deepens and the brain adapts to using ketones efficiently.

Light-headedness when standing up quickly is common throughout the fast, particularly in the first week, as blood volume is reduced through fasting-induced natriuresis. The clinical term is orthostatic hypotension (a drop in blood pressure of at least 20 mmHg systolic or 10 mmHg diastolic within three minutes of standing from a seated or lying position). Managing this is simple: move from lying to sitting to standing slowly, pause at each transition, and do not stand up suddenly from rest. If it is persistent or severe, contact your physician for blood pressure assessment.

Bad breath is universal during fasting once ketosis is established and reflects the exhalation of acetone, one of the three primary ketone bodies (the others being beta-hydroxybutyrate and acetoacetate).

Acetone has a characteristically sweet or fruity odour. It is harmless and is in fact a useful clinical indicator that ketosis has been established. Rinsing the mouth with water helps manage it; the breath improves progressively as deeper ketosis develops and acetone production is more efficiently managed.

A coated tongue during fasting is a well-documented phenomenon noted extensively by both Bragg and DeVries. The tongue develops a white or yellowish coating during extended fasting that reflects increased elimination of metabolic waste products through the mucosal surfaces. The coating gradually clears as the fast progresses, and its clearing, particularly of the edges and tip of the tongue, is one of the traditional clinical signs that the body has completed its primary cleansing work and is approaching the natural endpoint of the fast.

Reduced or absent bowel movements during fasting are entirely normal. With no food entering the gastrointestinal tract, there is no digestive residue to be expelled, and the intestines enter a period of physiological rest. Some patients go five to seven days without a bowel movement during an extended fast with no adverse consequence whatsoever. Bowel function resumes promptly and naturally once refeeding begins. The use of enemas or laxatives to force bowel movements during fasting is generally unnecessary and potentially counterproductive, as DeVries documented in detail, disrupting the normal mucosal environment of the colon and potentially depleting the beneficial bacteria whose reconstitution is one of fasting's microbiome benefits.

Feeling cold, particularly in the extremities (hands and feet), is common during fasting and reflects the redistribution of circulation during the metabolic transition and the modest reduction in metabolic heat production that occurs with reduced caloric intake. Additional clothing and warm water for rinsing cold hands and feet are practical management. A persistent sensation of extreme cold throughout the body that cannot be relieved with clothing or environmental warmth, particularly in the advanced stages of a fast, is a warning sign and should prompt medical contact.

Symptoms That Require Medical Contact During a Fast

The following symptoms during a fast are not normal and require prompt medical assessment:

Persistent chest pain or pressure, shortness of breath at rest, or palpitations (awareness of a rapid, irregular or pounding heartbeat) that are new or significantly different from any prior experience. These are potential cardiac symptoms that require cardiac evaluation regardless of the fasting context.

A systolic blood pressure below 90 mmHg on repeated measurement, particularly if accompanied by dizziness, lightheadedness, or fainting. This indicates significant hypotension that requires medication review and potentially intravenous fluid support.

A blood glucose below 3.5 mmol/L (63 mg/dL in American units) in a diabetic patient, or symptoms of hypoglycaemia (tremor, sweating, confusion, palpitations) at any glucose level. This requires immediate glucose administration, breaking of the fast, and urgent medical contact.

Severe, persistent vomiting that prevents adequate water intake. While mild nausea and occasional vomiting of bile or stomach secretions can occur in the early days of fasting and is not alarming, persistent vomiting that prevents the patient from maintaining any fluid intake is a medical concern requiring assessment.

Muscle cramps that are severe, persistent or involve the heart (chest tightness with a cramping quality). Mild muscle cramps in the legs are common during fasting, particularly in the first week, and reflect electrolyte shifts, most commonly low magnesium. They are managed with magnesium supplementation and increased water intake. Severe or persistent cramps, or any cramps in the chest, require medical assessment.

New neurological symptoms, including significant confusion or disorientation, visual changes, weakness or numbness in any limb, or difficulty speaking. These require emergency medical assessment regardless of the fasting context.

Syncope (fainting) or near-syncope (feeling about to faint) that occurs despite slow positional changes and adequate hydration requires physician contact for blood pressure assessment and medication review.

7.7 Choosing Your First Fast: Matching Duration to Your Starting Point

DeVries was explicit and correct on this point: the length of each fast cannot be safely predetermined. What can be predetermined is the category of fast appropriate for a patient's starting point, experience level and medical circumstances. The specific duration within that category is determined by the progression of symptoms, the blood pressure response, and the clinical judgment of the supervising physician.

For the first therapeutic fast in a patient who has completed the two-week preparatory protocol, has physician clearance and supervision, has managed their medications appropriately, and does not have significant complicating conditions, the following starting categories apply:

Category 1: The Introductory Fast (24 to 48 hours)

For patients who have never fasted beyond the overnight fast of normal sleep, or who are significantly apprehensive about extended fasting, or whose medical circumstances warrant the most cautious initial approach, a 24 to 48-hour first fast is appropriate. This duration is sufficient to experience the keto flu transition, to observe the initial blood pressure response to fasting, to develop confidence in managing the early fasting experience, and to generate meaningful data about how your body responds. It does not reach the depth of ketosis or the degree of autonomic reset that longer fasting achieves, but it is a genuine and valuable first step that builds the foundation for longer subsequent fasts.

Category 2: The Short Therapeutic Fast (3 to 5 days)

For patients with good baseline health who have completed the preparatory protocol, have appropriate medical supervision and medication management, and are free of significant complicating conditions, a first fast of three to five days is appropriate. This duration takes the patient through the full keto flu transition and into the established ketosis phase described in Chapter 3\. By Day 3, insulin is at its minimum, ketones are substantially elevated, autonomic rebalancing is beginning to be subjectively noticeable, and meaningful blood pressure reductions are established. DeVries' own data and the McEachen series both document significant clinical benefits in fasts of this duration.

Category 3: The Extended Therapeutic Fast (7 to 14 days)

Extended fasting of seven to fourteen days represents the depth of therapeutic intervention that produced the most dramatic results in the clinical fasting literature, including Goldhamer's average reductions of 37/13 mmHg, Shelton's documented case of systolic reduction from 295 to 115 mmHg in three weeks, and Weger's "hundreds of consecutive hypertensive patients without a single complete failure." This category requires experienced medical supervision, established fasting experience in the patient (ideally at least one shorter prior fast), fully managed medications, comprehensive baseline assessment, and a monitoring plan that includes at minimum twice-daily blood pressure and symptom review with physician access.

No first fast should target this duration category. The seven to fourteen-day fast is the destination toward which a graduated approach builds over time, not the starting point.

The Graduated Approach: Building Fasting Experience Progressively

Bragg's recommendation of a weekly 24-hour fast as a maintenance and preparatory practice has a sound physiological basis that deserves emphasis. The weekly 24-hour fast, sustained consistently across months, achieves several things simultaneously. It maintains the practice of metabolic flexibility (the ability to shift between glucose and fat metabolism fluidly), it provides weekly periods of insulin normalisation and RAAS rest that cumulatively benefit blood pressure control, it builds the patient's confidence and familiarity with the fasting experience, it allows physician and patient to observe the blood pressure response to short fasts before committing to longer ones, and it progressively depletes the glycogen stores and improves fat metabolism efficiency that makes longer fasts more tolerable.

A graduated approach might look like: monthly 24-hour fasts for the first two months, then a 3-day fast, then monthly 24-hour fasts for two more months, then a 5-day fast, then establishing quarterly 5 to 7-day fasts as the ongoing therapeutic protocol. This is not the only valid approach, but it represents the principle of progressive experience building that the clinical fasting literature consistently endorses, that DeVries advocated throughout Chapter VII of Therapeutic Fasting, and that Bragg's own practice over more than seven decades embodied.

Chapter Summary: Key Points

The pre-fast assessment consists of four components: a complete clinical history with specific attention to hypertension duration and severity, current medications and complete medical history; physical examination measurements including validated blood pressure measurement in both arms, resting heart rate, body weight, BMI and waist circumference; a specific laboratory panel including FBC, comprehensive metabolic panel, fasting glucose, HbA1c, fasting insulin and HOMA-IR, lipid panel with TG:HDL ratio, uric acid, thyroid function, liver function, magnesium and ECG; and an explicit medication review covering every drug's specific interaction with fasting physiology.

Medication management during fasting is the single most preventable source of fasting complications in hypertensive patients. Diuretics typically require reduction or suspension. ACE inhibitors and ARBs require dose reduction as fasting suppresses the RAAS. Beta-blockers must be tapered gradually, never stopped abruptly. All adjustments must be made by the prescribing physician with twice-daily

home blood pressure monitoring throughout the fast.

The two-week preparatory period begins the dietary transition toward low-carbohydrate, whole-food eating that primes the metabolic machinery for the fasting crossover. Caffeine should be reduced gradually and eliminated two to three days before the fast. Alcohol should be eliminated during preparation and throughout the fast. Tobacco use should be ceased or substantially reduced.

The final day before the fast should follow the second-week preparatory diet. It is not an occasion for a large final meal, which would delay the metabolic crossover and worsen early fasting symptoms.

Normal fasting experiences include hunger in Days 1 to 3, headache in Days 1 to 3 particularly with caffeine withdrawal, fatigue and reduced energy in Days 1 to 4, light-headedness on rapid positional change, bad breath from acetone once ketosis is established, a coated tongue, reduced or absent bowel movements, and feeling cold in the extremities. None of these require medical attention beyond practical management.

Symptoms requiring medical contact include chest pain, significant palpitations, systolic blood pressure below 90 mmHg with symptoms, hypoglycaemia in diabetic patients, severe persistent vomiting, severe or chest cramping, new neurological symptoms, and syncope.

First fasts should be categorised by starting point and experience: 24 to 48 hours for first-time fasters or those with complicating circumstances, 3 to 5 days for patients with appropriate medical supervision and preparation, and 7 to 14 days only for experienced fasters with full medical supervision. A graduated approach building fasting experience progressively over months is the appropriate pathway toward extended therapeutic fasting.

“Before anything else, preparation is the key to success.”

— Alexander Graham Bell

The fast you have prepared for properly is not the same experience as the fast you stumbled into. One is a therapeutic intervention. The other is an experiment. Only one of them belongs in a book about healing.

CHAPTER 8

The Progressive Fasting Ladder, Protocols From 24 Hours To 14 Days

“Climb the mountain not to plant your flag, but to embrace the challenge, enjoy the air and behold the view. Climb it so you can see the world, not so the world can see you.”

— David McCullough Jr.

Opening: The Ladder, Not the Leap

There is a particular failure mode in medicine that deserves a name. It occurs when a patient, having understood the theory of a therapeutic intervention completely and correctly, attempts to compress the entire intervention into the shortest possible timeframe, reasoning that if seven days of fasting produces significant blood pressure reduction, beginning with seven days is simply the most efficient approach.

This is not efficiency. It is impatience dressed as logic, and it produces predictable results: discomfort that exceeds the patient's tolerance, premature termination of the fast, and a conclusion, usually stated with considerable conviction, that fasting does not work for them.

The progressive fasting ladder is the antidote to this failure mode. It is built on a principle that every experienced clinician who has supervised therapeutic fasting across thousands of cases has arrived at independently: the body's capacity to fast comfortably, safely and effectively is a trainable skill. It improves with practice. It deepens with experience. A patient who has completed four 24-hour fasts over two months, followed by two 3-day fasts over the next three months, enters their first 7-day fast with a metabolically and psychologically prepared body that will complete that fast with significantly greater comfort, safety and therapeutic yield than a patient who attempts the same 7-day fast cold, without prior fasting experience.

The ladder in this chapter has five rungs. Each rung has its own protocol, its own physiological objectives, its own monitoring requirements, and its own clinical outcomes. The rungs are sequential and cumulative: each prepares the body for the next. You do not skip rungs. You may spend more time on a particular rung before ascending, depending on your blood pressure response, your physician's assessment, and your own experience of the fast. But you do not skip them.

This chapter provides the complete, day-by-day protocol for each rung, including what to consume and what not to consume, how much water to drink and how to manage it, how to monitor yourself and what numbers to track, what physical activity is appropriate at each stage, how to structure your days during the fast, how to manage sleep, and how to recognise when a rung has accomplished its objectives and you are ready to progress.

8.1 The Foundation of Every Rung: Water

Every protocol in this chapter is built on water. Not supplements. Not broths during the fast itself. Not electrolyte drinks. Not herbal teas. Water.

This requires explanation, because there is a substantial and growing body of popular fasting content that recommends electrolyte supplementation, sodium-containing broths, bone broths, herbal teas, black coffee and other additions during fasting, and frames these additions as either harmless or beneficial. Some of these additions are appropriate in certain contexts. Most of them compromise the full therapeutic potential of a water fast and should not be default components of a therapeutic protocol targeting blood pressure normalisation.

Why Water Only

The sodium-retaining, RAAS-activating, sympathetic-overactivating mechanisms that drive hypertension are addressed during a water fast through the body's own physiological response to the complete absence of dietary input. This response, beginning with glycogen depletion and progressing through the full cascade described in Chapters 3 through 6, is initiated and sustained by the complete withdrawal of all dietary substances that stimulate insulin secretion, activate digestive processes, or provide exogenous sodium.

Adding sodium-containing broth during a fast directly opposes one of the primary antihypertensive mechanisms of fasting: the natriuresis (sodium excretion) that begins within the first 24 hours of insulin withdrawal. The kidneys, freed from insulin's sodium-retaining instruction, are actively working to excrete the accumulated sodium burden of years of dietary excess. Providing exogenous sodium during this process is counterproductive. It is asking the kidneys to eliminate sodium while simultaneously supplying more of it.

Adding black coffee during a fast provides caffeine, which is a sympathomimetic (stimulates the sympathetic nervous system), a vasopressor (raises blood pressure through sympathetic activation and direct vascular effects), and an adenosine receptor antagonist that disrupts the natural fatigue signalling that the body uses to enforce the rest that fasting requires. For a patient whose primary therapeutic goal is sympathetic nervous system reset and blood pressure normalisation, adding a daily sympathomimetic is directly counterproductive.

Adding herbal teas introduces variable and largely unstudied phytochemicals (plant-derived chemical compounds) whose effects on the fasting metabolic state are incompletely understood. Some herbal preparations are known to affect blood pressure, renal function, or hepatic enzyme activity in ways that are relevant to fasting safety. In the absence of specific, demonstrated benefit for therapeutic fasting, simplicity is the safer clinical principle.

The case for pure water fasting during a therapeutic blood pressure protocol is therefore not based on tradition or orthodoxy. It is based on the same mechanistic reasoning that underlies every other recommendation in this book: the intervention is targeted at specific physiological mechanisms, and the protocol is designed to maximise the operation of those mechanisms without interference.

Water Quality and Quantity

Water quality matters. The kidneys during a therapeutic fast are working at maximum capacity, filtering and excreting accumulated metabolic waste, dissolved toxins, and the products of autolysis and cellular renewal. The water carrying these materials through the renal tubules and into the urine should not itself be adding to the filtration burden with chlorine, heavy metals, fluoride, or pharmaceutical residues.

Spring water from a tested, reputable source is the first choice. Filtered tap water through a high-quality carbon block or reverse osmosis filter is appropriate in most developed world settings. Distilled water, as Bragg recommended consistently across his decades of fasting supervision, is entirely appropriate, contrary to the popular claim that distilled water "leaches minerals" from the body. Distilled water leaches nothing from a healthy body. The kidneys regulate mineral balance based on blood levels and renal transport mechanisms, not based on the mineral content of ingested water. The claim that drinking mineral-free water causes mineral deficiency is not supported by physiological evidence.

Water quantity should be guided primarily by thirst, with a minimum floor of two litres (approximately 68 fluid ounces, or roughly eight standard 250 mL glasses) daily and a reasonable upper ceiling of three to three and a half litres daily. DeVries was clear on this point: recommending several quarts of water daily during a fast significantly exceeds actual physiological need and may impede elimination by diluting the concentration gradient that drives toxin excretion through the renal tubules. Drinking to thirst, with the two-litre minimum as a baseline, is the correct approach.

Water temperature should be comfortable, neither ice-cold nor scalding. Ice-cold water during a fast produces a brief but measurable sympathetic response (a cold-stimulus reflex mediated through the vagus nerve and the diving reflex pathway), which is counterproductive to the sympathetic withdrawal we are working to achieve. Room temperature or warm water is preferable, particularly in the first days of the fast when the body is already managing the catecholamine fluctuations of the transition period.

Water intake should be distributed evenly across the waking hours rather than consumed in large volumes at infrequent intervals. Drinking half a litre or more of water in a single sitting produces a rapid expansion of plasma volume (the fluid component of the blood) that must be processed by the kidneys quickly, placing an unnecessary acute load on renal function. Sipping water steadily throughout the day, approximately 250 mL every two hours during waking hours, is the physiologically appropriate pattern.

8.2 Monitoring Standards Across All Rungs

Regardless of which rung of the ladder you are on, the following monitoring standards apply throughout every fast:

Blood Pressure Monitoring

Measure blood pressure twice daily: once in the morning, after waking and before any movement or activity, and once in the evening, after a period of seated rest of at least five minutes. Record every reading with the date and time in a dedicated log, either a physical notebook or a digital tracking application.

Morning readings reflect overnight sympathetic withdrawal and are the most sensitive indicator of the fasting-mediated autonomic reset described in Chapter 6\. They should progressively fall across the

days of the fast. Evening readings reflect the cumulative blood pressure response to the day's physiological activity and provide a complementary data point.

Measure blood pressure in both arms at the first measurement of each day, recording both values. If a consistent difference of more than 15 mmHg systolic between arms exists, report this to your physician, as it may indicate subclavian artery pathology requiring assessment.

Also measure blood pressure in both lying and standing positions (orthostatic measurement) at least once daily throughout the fast, to monitor for postural hypotension. Allow two to three minutes of quiet lying before the lying measurement, then stand slowly, pause for one minute, and measure again standing. A drop of 20 mmHg or more systolic, or 10 mmHg or more diastolic, upon standing constitutes orthostatic hypotension and requires physician notification.

Heart Rate Monitoring

Record resting heart rate alongside every blood pressure measurement. A quality validated blood pressure monitor will display heart rate automatically. Alternatively, a wearable fitness device provides continuous heart rate tracking. The progressive fall in resting heart rate across the days of the fast is one of the most clinically meaningful objective signs of autonomic reset. Most patients see resting heart rate fall by 10 to 20 beats per minute across a 7-day fast as vagal tone is restored and sympathetic drive is reduced.

Subjective Symptom Log

Maintain a daily written record of your subjective experience, rated on a simple 0 to 10 scale where helpful. This should include:

Energy level (0 being completely exhausted, 10 being fully energised).

Hunger intensity (0 being no hunger whatsoever, 10 being overwhelming hunger).

Headache presence and severity if present (0 being none, 10 being incapacitating).

Mental clarity (0 being severely foggy and unable to concentrate, 10 being perfectly sharp and clear).

Mood (0 being severely low or highly anxious, 10 being calm, positive and emotionally stable).

Sleep quality from the previous night (0 being no meaningful sleep, 10 being deeply restorative).

Any other symptoms experienced, including nausea, dizziness, cramps, palpitations, or any other notable physical experience.

This subjective log serves multiple purposes. It allows you to track the expected trajectory of the fasting experience (difficult in Days 1 to 3, improving dramatically from Day 4 onward), provides the data needed to identify if your experience is deviating from the expected pattern, and creates the record needed for productive post-fast physician review.

Physician Contact Schedule

During any fast beyond 48 hours, establish a daily brief contact with your supervising physician. This does not require a clinical appointment every day. It may take the form of a brief message transmitting your morning blood pressure, resting heart rate, and any notable symptoms, with a verbal or written physician acknowledgment. What it must not be is no contact at all. The monitoring contact that was arranged before the fast begins (Section 7.5 of Chapter 7\) should be in active operation from Day 1 of every fast beyond 48 hours.

8.3 Rung 1: Time-Restricted Eating (16:8 Intermittent Fasting)

Duration and Core Protocol

The fasting ladder does not begin with the total deprivation of food, but with the intentional structuring of time. Rung 1 prescribes a 16:8 Time-Restricted Eating pattern to be maintained consistently for Weeks 1 through 4\.

Patients restrict all caloric intake to an 8-hour consecutive eating window (e.g., 10:00 AM to 6:00 PM, or 12:00 PM to 8:00 PM), leaving a 16-hour fasting window that encompasses overnight sleep. Within the eating window, the patient consumes three structured meals. Snacking between meals is strictly prohibited to prevent chronic, low-grade insulin elevations. During the 16-hour fasting window, pure water is permitted at all times; however, unlike later rungs, unsweetened black coffee or plain herbal tea may be utilized if needed to support early compliance.

The Glucose-Blunting Protocol

To maximize the antihypertensive effects of Rung 1, food quality and intake mechanics within the 8-hour window must be precisely controlled. The objective is to prevent postprandial (post-meal) blood sugar spikes, which directly trigger sympathetic nervous system activity and renal sodium retention. This is achieved through three distinct interventions:

1\. Metabolic Food Sequencing: Patients must consume foods in a strict structural order: fiber (vegetables) first, proteins and fats second, and complex carbohydrates last. Consuming fiber first creates a viscous mesh in the small intestine that delays gastric emptying and slows glucose absorption.

2\. The Elimination of "Naked" Carbohydrates: Carbohydrates must never be eaten in isolation. They must always be securely "clothed" in fiber, protein, or fat to blunt their glycemic impact.

3\. Acid-Mediated Glycemic Blunting: Every meal must incorporate an acidic agent, specifically one to two tablespoons of apple cider vinegar or fresh lemon juice diluted in water or used as a dressing. The acetic acid temporarily inactivates alpha-amylase (the enzyme responsible for breaking down starches into glucose) in the saliva and stomach, delaying starch digestion and flattening the post-meal glucose curve.

4\. Resistant Starch Emphasis: Carbohydrate choices are heavily restricted to cooling-induced resistant starches such as lentils, black beans, steel-cut oats, and pre-cooked, cooled, and reheated potatoes or rice. These starches resist enzymatic breakdown in the small intestine, acting instead as prebiotic fiber for the microbiome and generating short-chain fatty acids that improve systemic insulin sensitivity.

5\. The Absolute Elimination of Added Salt: In alignment with Bragg's clinical tenets, no exogenous sodium may be added to any meal. This initiates an early lowering of the vascular osmotic load.

The Kinetic Catalyst: The Soleus Muscle Walk

The definitive physiological catalyst of Rung 1 is the post-meal kinetic protocol. Within 5 to 10 minutes of completing each meal, the patient must perform a 10 to 15-minute walk at a moderate pace.

This walk is designed to activate the soleus muscle the large, flat muscle located in the lower calf. Because the soleus relies primarily on blood glucose and glycogen oxidation rather than stored intramuscular glycogen, its low-intensity, rhythmic activation acts as a highly efficient metabolic sink. It pulls glucose directly out of the bloodstream without requiring a corresponding surge of insulin.

A landmark National Institutes of Health (NIH) study (PMID: 39559800\) demonstrated that this brief, immediate postprandial activity reduces the postprandial glucose spike by 40.9% compared to post-meal sedentariness.

Expected Antihypertensive Outcomes and Monitoring

By flattening the daily glucose curve and extending the daily fasting window to 16 hours, Rung 1 systematically lowers circulating insulin. Over the 4-week period, patients typically experience:

A 20% to 30% reduction in fasting insulin levels.

The initiation of mild renal natriuresis (sodium excretion) as insulin's signal to retain sodium fades.

An initial blood pressure reduction of 5 to 10 mmHg systolic.

Monitoring at this stage requires home blood pressure tracking twice daily (morning and evening), weekly weight checks, and weekly fasting glucose checks for diabetic or prediabetic individuals. Serum electrolytes should be assessed via a basic metabolic panel at Week 2 and Week 4 to establish baseline safety before ascending the ladder.

8.4 Rung 2: The 24-Hour Fast

Physiological Objectives

The 24-hour fast has three primary physiological objectives. First, it initiates the depletion of hepatic and muscular glycogen stores, beginning the transition away from glucose dependence. Second, it produces the first measurable pulse of insulin withdrawal and the initial natriuresis (renal sodium excretion) that follows. Third, it establishes, through experience rather than theory, that the body can function safely and reasonably comfortably without food for a full day, building the foundational confidence on which subsequent fasting is built.

At 24 hours, the patient has not yet entered sustained ketosis, has not yet experienced the full keto flu transition, and has not achieved the depth of autonomic reset or RAAS suppression that longer fasting produces. But they have taken a step that for many is psychologically significant: they have deliberately, consciously, and successfully chosen not to eat for a full day. In clinical experience, this single

accomplishment frequently transforms a patient's relationship with the idea of fasting from abstract possibility to embodied reality.

The Protocol

The 24-hour fast begins after the final meal of one day and ends with the first meal of the following day, giving a full 24 hours of water-only consumption. Many patients find it easiest to time this as dinner to dinner: eat your last preparatory meal at 6 or 7 pm, fast through the following day, and break the fast at 6 or 7 pm the next evening.

This timing has a practical advantage: approximately eight of the 24 hours are spent asleep, which significantly reduces the subjective experience of food absence. You are not 24 hours of conscious awareness away from food. You are approximately 16 waking hours away, which is a substantially more manageable psychological frame.

During the 24 hours, consume water as described in Section 8.1: minimum two litres across the day, sipped evenly through waking hours at comfortable temperature. No other substance enters the body.

Physical activity during a 24-hour fast should be moderate. Light walking of 20 to 30 minutes is appropriate and beneficial, supporting the early insulin reduction and maintaining the gentle physical activity that helps the body maintain normal circulation and lymphatic flow. Intense exercise is not appropriate during fasting of any duration, for reasons that will be addressed in Section 8.8.

Rest as needed. The fatigue of the early fast is real and reflects genuine metabolic adjustment. It is not a sign that something is wrong. Honour it by resting when you need to.

While a 24-hour window is highly safe, the sudden drop in insulin triggers a rapid diuretic effect that purges both water and essential minerals. To prevent muscle cramping and dangerous shifts in fluid balance especially for hypertensive patients who may already be taking prescribed diuretics the protocol incorporates target, sodium-free mineral support. Patients should supplement with 300 to 400 mg of magnesium glycinate and 200 to 300 mg of potassium during the fasting window. This protects cellular electrical stability and prevents hypokalemia (low potassium) without breaking the fast or introducing exogenous sodium.

Breaking the 24-Hour Fast

The refeeding protocol after a 24-hour fast is simpler than the refeeding after longer fasts, because the digestive system has not undergone the degree of physiological quiescence that occurs during extended fasting. Nevertheless, the principle of gentle reintroduction applies.

Break the 24-hour fast with a moderate serving of fresh fruit, either as whole fruit or as freshly squeezed juice (unstrained), consumed slowly. A sliced orange, a small bowl of melon, or half a grapefruit is appropriate. Fresh fruit juice should be sipped rather than drunk quickly. Allow 20 to 30 minutes after the fruit before introducing more substantial food.

The meal that follows should be light, primarily composed of cooked vegetables, a moderate portion of protein from a quality source, and a salad. It should not be a large, elaborate meal designed to compensate for the 24-hour absence of food. The stomach, while not as quiescent as it becomes during

extended fasting, benefits from a gentle return to normal digestive function. A large post-fast meal causes bloating, discomfort and often nausea in patients who have not previously fasted.

Do not eat to the point of fullness at the post-fast meal. Eat until you feel satisfied and stop. This is not deprivation. It is the beginning of recalibrating your relationship with hunger and satiety signals, which is itself a therapeutic benefit of fasting.

Frequency of Rung 2

The 24-hour fast should be practiced weekly. Bragg's lifelong practice of a weekly 24-hour fast, sustained without exception for decades, was not arbitrary. Weekly 24-hour fasting produces cumulative metabolic benefits that single or infrequent fasts do not. Each weekly fast provides a period of insulin normalisation, RAAS rest, and inflammatory process reduction. Across twelve weekly fasts, the cumulative effect on insulin sensitivity, inflammatory markers and blood pressure is measurably greater than twelve months of standard dietary management without fasting.

Most patients find a consistent day of the week that fits their schedule and social life, and maintain that day as their weekly fast day. This creates an established pattern that reduces the psychological resistance to fasting, because the decision about whether to fast on a given week does not need to be remade each time. It is already made. Wednesday is your fast day. Or Thursday. Or Sunday. The specific day is far less important than the consistency.

After completing four weekly 24-hour fasts with good tolerance, you are ready to progress to Rung 3\.

8.5 Rung 3: The 36 to 48-Hour Fast

Physiological Objectives

The 36 to 48-hour window is the threshold at which the metabolic picture changes substantially. By 36 hours of fasting, hepatic glycogen is depleted, gluconeogenesis (the liver's synthesis of glucose from non-carbohydrate sources, primarily amino acids from muscle protein and glycerol from fat breakdown) is the primary source of blood glucose, and circulating ketone bodies (beta-hydroxybutyrate and acetoacetate) are rising to levels that begin to provide meaningful fuel for the brain and other ketone-utilising tissues. Insulin has fallen to its minimum. The RAAS has begun its unwinding. Renal sodium excretion is proceeding actively.

Dr. Jamnadas specifically identifies 36 hours as the threshold of deep ketosis, a clinically meaningful milestone. By this point the transition from glucose to fat and ketone metabolism is essentially complete in metabolically responsive individuals. The discomfort of the keto flu transition, if present, has typically resolved or is resolving. The subjective experience of fasting is beginning to shift from challenging to manageable or even, for some patients, pleasant.

The 48-hour fast takes these processes deeper. Autophagy (cellular self-cleaning and renewal, discussed in detail in Chapter 3\) is intensifying. BHB levels are high enough to produce their NLRP3 inflammasome-inhibiting effect, reducing systemic inflammatory cytokine production. The cholinergic anti-inflammatory pathway is beginning to benefit from increasing vagal tone. Blood pressure reductions

of 10 to 20 mmHg systolic are typically measurable by 48 hours in hypertensive patients.

The Protocol

The 36-hour fast is most naturally structured as a dinner-to-breakfast arrangement spanning two days: eat dinner on Day 0, fast through the entirety of Day 1, and break the fast with break the fast with breakfast on Day 2\. This gives approximately 36 to 40 hours of fasting depending on the precise timing of the last meal and the first post-fast food.

The 48-hour fast extends this by one additional dinner: eat dinner on Day 0, fast through Days 1 and 2, and break the fast with breakfast on Day 3\.

Water protocol as in Section 8.1. Minimum two litres daily. Sipped evenly. Room temperature.

Physical activity during a 36 to 48-hour fast: light walking remains appropriate on Day 1\. By Day 2 of a 48-hour fast, some patients experience sufficient fatigue from the keto flu transition that even light walking feels demanding. This is normal and the appropriate response is rest, not pushing through. If you feel well enough to walk, walk. If you feel better resting, rest.

Sleep is particularly important during the 36 to 48-hour window. Many patients experience disrupted sleep on the first night of fasting due to the early catecholamine fluctuations and the psychological adjustment to the absence of the usual evening meal. Do not take sleep medications during fasting. If sleep is difficult, focus on creating the conditions for sleep: a cool, dark room, minimal screen exposure for two hours before bed, and the acceptance that the first night's sleep may be lighter than usual. By the second night, most patients sleep significantly better as the metabolic transition progresses and vagal tone begins to rise.

The monitoring requirements described in Section 8.2 apply from the first day of a 36-hour fast onward.

The Keto Flu in This Window

The keto flu, the cluster of symptoms associated with the metabolic transition from glucose to fat and ketone metabolism, is most pronounced during the 24 to 72-hour fasting window, making the 36 to 48-hour fast the period when most patients experience it most intensely. Its management warrants specific attention.

The primary symptoms are headache, fatigue, irritability, light-headedness, muscle aches, and sometimes mild nausea. These symptoms are produced by three overlapping mechanisms. First, the rapid depletion of glycogen-bound water during glycogen breakdown produces a significant fluid and electrolyte shift in the first 24 to 48 hours, as each gram of stored glycogen releases approximately 3 to 4 grams of water. This fluid redistribution can produce headache, light-headedness and fatigue through mild volume reduction, even in patients who are drinking adequate water. Second, the withdrawal of caffeine if not fully eliminated in the preparatory period contributes headache and irritability that directly overlaps with keto flu symptoms. Third, the transition of the brain from glucose to ketone metabolism, while physiologically straightforward once the transition is complete, produces a brief period during which neither fuel source is fully optimised.

Management of keto flu during fasting is limited by the constraint that we are maintaining a pure water fast. Rest and adequate water intake are the primary interventions. Lying down when dizzy, moving slowly when standing, and avoiding demanding physical or mental tasks during the peak transition period are practical measures that reduce symptom severity. Patience is the ultimate management tool: these symptoms reliably resolve, typically by Day 3 to 4 of fasting, as ketosis deepens and the body's metabolic machinery fully adapts to fat and ketone metabolism.

> **CLINICAL SAFETY NOTE**
>
> NOTE: While a prolonged fast drives deep cellular autophagy and glycogen depletion, it introduces a strict physiological boundary: the Hard Abort Criteria. The patient must monitor their blood pressure at least twice daily. If systolic blood pressure drops below **90 mmHg** OR diastolic blood pressure drops below **60 mmHg,** the fast must be terminated immediately, without exception. Falling below this threshold indicates critical hypotension, risking orthostatic syncope (fainting) and compromised organ perfusion. The fast must be broken safely and gradually using a small, easily digestible meal like bone broth or stewed vegetables, regardless of how many hours remain in the planned fasting window.

Breaking the 36 to 48-Hour Fast

Breaking a 36 to 48-hour fast follows a slightly more structured refeeding protocol than the 24-hour fast, because the digestive system has had more time to enter physiological rest.

Begin with 125 to 250 mL (half a cup to one cup) of freshly squeezed fruit juice, sipped slowly over 15 to 20 minutes. Orange juice, grapefruit juice or watermelon juice (which has the additional benefit of containing L-citrulline, a precursor to the vasodilating nitric oxide, directly relevant to the endothelial restoration described in Chapter 5\) are all appropriate.

Wait 30 minutes, then have a moderate portion of fresh whole fruit: a sliced orange, half a melon, a small bowl of papaya or mango. Chew thoroughly and eat slowly.

Two to three hours later, introduce a light meal: a salad of raw vegetables, a bowl of vegetable soup, or a moderate portion of lightly cooked vegetables with a small serving of protein. The protein source should be easily digestible: eggs, fish, or legumes are preferable to red meat, which places a significantly greater digestive burden on a system that has been resting.

The evening meal on the refeeding day should remain light. The stomach has contracted during the fast and will signal satiety earlier than usual. Trust this signal and stop eating when it arrives, rather than eating to a habitual portion size.

By the second day after breaking the fast, normal eating patterns can resume, guided by the principles of the post-fast nutritional approach described in Chapter 9\.

Frequency of Rung 3

After the foundation of weekly 24-hour fasts is established, a monthly 36 to 48-hour fast is an appropriate addition. Some patients integrate the 36-hour fast as a monthly practice alongside their weekly 24-hour fast. Others use the 48-hour fast quarterly. The specific frequency matters less than the

consistency and the progression toward the next rung when the physician and patient agree the time is right.

The criterion for readiness to progress to Rung 3 is that you have completed at least two 36 to 48-hour fasts with good tolerance, your blood pressure is showing consistent response to fasting (progressive reductions during the fast with a post-fast return that, while not sustaining the full fasting reduction, is settling at a level lower than your pre-fasting baseline), and your physician is satisfied with your monitoring data and medication management.

8.5 Rung 4: The 3 to 4-Day Fast

Physiological Objectives

The 3 to 4-day fast is the first rung at which the full depth of the fasting therapeutic cascade is operating simultaneously. By 72 hours, which Dr. Jamnadas identifies as his "profound transformation" threshold, the following are occurring concurrently:

Ketosis is fully established and stable. BHB levels are typically between 1.5 and 3.0 millimoles per litre, within the range of therapeutic ketosis.

Autophagy is operating at clinically meaningful intensity, with measurably elevated autophagy markers (LC3-II, Beclin-1, p62 turnover) in peripheral blood cells. Endothelial cell autophagy is clearing accumulated dysfunctional protein aggregates and restoring eNOS function.

NLRP3 inflammasome suppression by BHB is reducing circulating IL-1β and IL-18 levels. Systemic inflammation, measured by hsCRP, begins to fall.

RAAS suppression is substantial. Plasma renin activity, serum aldosterone and angiotensin II are measurably reduced from baseline. Renal sodium handling is normalised.

Sympathetic tone is falling measurably. Heart rate is typically 10 to 15 beats per minute below baseline by Day 3 in responsive patients. HRV metrics are improving. Patients begin reporting the characteristic shift in subjective experience from the early fasting challenge to the emerging calm and mental clarity that fasting of this depth reliably produces.

Blood pressure reductions of 20 to 35 mmHg systolic and 10 to 15 mmHg diastolic are typical by Day 3 to 4 in hypertensive patients with good insulin-mediated hypertension. This is the range that matches or exceeds the average reductions produced by any single class of antihypertensive medication.

Longo's 2014 research on 72-hour fasting in humans demonstrated regeneration of immune cell populations through the BHB-mediated suppression of PKA (protein kinase A) and the downstream activation of stem cell pools, including haematopoietic stem cells (the precursor cells that generate all blood cells). This regenerative process, which does not occur in shorter fasting periods, contributes to the normalisation of immune cell populations implicated in vascular inflammation.

The Protocol

A 3-day fast runs from the final meal on Day 0 through to the refeeding on Day 4\. A 4-day fast extends this by one day.

Day 1 is the transition day, described fully in the Rung 2 section. Expect the keto flu transition symptoms. Rest as needed. Drink water steadily. Take measurements morning and evening.

Day 2 is typically the most challenging day for most patients. Glycogen is fully depleted. The brain is in the process of increasing its dependence on ketones but is not yet fully adapted. Energy is low. Hunger, while beginning to wane, may still be noticeable. Mental clarity is not yet at its fasting peak. Many patients find Day 2 the hardest and the one most likely to prompt premature breaking of the fast. It is important to understand and communicate clearly that Day 2 is the trough before the turn, not an indication that the fast is not working.

Day 3 is when most patients experience the most dramatic subjective shift of the entire fast. The keto flu has resolved. The brain has adapted to ketone metabolism. Mental clarity, often described by patients as unlike anything they have experienced in ordinary waking life, is beginning to emerge. Hunger is substantially diminished or absent. Energy, while not at full physical capacity, has improved significantly from the Day 2 low. Blood pressure readings taken on Day 3 morning should show a clear and often striking reduction from baseline.

If extending to Day 4, the experience typically deepens: greater mental clarity, complete absence of hunger in most patients, further blood pressure reduction, and the beginning of the profound calm that characterises the deeper stages of extended fasting.

Physical activity during a 3 to 4-day fast should be gentle: light walking is appropriate on Days 1 and 2 if it feels comfortable, and on Days 3 and 4 a somewhat more extended walk (30 to 45 minutes at an easy pace) is typically possible and beneficial for most patients. The improved energy of the ketosis phase supports gentle activity without excessive fatigue.

Sleep typically improves from Day 2 or 3 onward as vagal tone rises and the early-fast catecholamine fluctuations settle. Many patients report some of the most restful sleep of their lives during the later days of a supervised extended fast, consistent with the nocturnal sympathetic withdrawal and improved parasympathetic dominance that the fast produces.

Medication Management in a 3 to 4-Day Fast

By Day 3 of a fast, blood pressure reductions are substantial enough that medication adjustments are frequently necessary. This is one of the most important reasons why physician supervision and twice-daily blood pressure monitoring are non-negotiable for fasts at this rung and above.

The general principle is that medication doses should be reduced preemptively as blood pressure falls, rather than reactively after hypotension occurs. Your physician should have established clear threshold values before the fast begins: the blood pressure reading at which a specific dose reduction or temporary suspension of a specific medication is triggered. These thresholds should be written down and accessible during the fast.

Common patterns include diuretics being suspended by Day 1 or 2, ACE inhibitors or ARBs being halved by Day 2 or 3, and patients on multiple antihypertensive agents ending a 3 to 4-day fast on significantly reduced medication overall. Some patients, particularly those whose hypertension is strongly insulin-mediated and who respond robustly to fasting, may have blood pressure normalize to well within normal range by Day 3 to 4, at which point antihypertensive medications may be temporarily suspended entirely under physician supervision.

This medication reduction is not a side effect of fasting. It is one of its primary goals. The purpose of this intervention is to normalise blood pressure through restoration of the physiological mechanisms that regulate it, making pharmaceutical blood pressure management progressively less necessary. That process begins in earnest at Rung 3\.

Breaking the 3 to 4-Day Fast

Breaking a 3 to 4-day fast requires the full structured refeeding protocol.

Day 1 of refeeding is juice day. Only freshly squeezed fruit or vegetable juices are consumed, sipped slowly throughout the day. Total juice volume should not exceed one litre across the full day. Orange juice, grapefruit juice, carrot juice, and watermelon juice are all appropriate. Begin with 125 to 250 mL in the morning, wait two hours, take another 125 to 250 mL, and continue this pattern through the day. The juices should be at room temperature or slightly warm, not cold.

Do not be surprised if the first serving of juice produces an immediate and powerful taste experience. After three to four days without any dietary substance, the taste buds are extraordinarily sensitised. The sweetness and complexity of a freshly squeezed orange will register with an intensity that seems out of proportion to the ordinary experience of orange juice. This is normal, and it is among the most consistent and charming reports from patients breaking extended fasts.

Day 2 of refeeding introduces whole fresh fruit in the morning: a bowl of melon, sliced orange, papaya, or similar ripe fruit. At midday, introduce a light vegetable-based meal: a mixed salad with avocado, or a bowl of vegetable soup made from cooked vegetables blended smooth. No heavy proteins at this stage. No grains. No dairy. The digestive system is being gently reactivated and does not yet have the enzymatic capacity to handle a full mixed meal.

In the evening of Day 2, a slightly more substantial meal is appropriate: cooked vegetables, a moderate serving of fish or eggs if desired, and a small salad. Chew everything thoroughly. Eat slowly. Stop at satisfaction, not fullness.

Day 3 of refeeding sees a further gradual return toward normal eating, with the guidance from Chapter 9's post-fast nutritional principles fully applicable from this point.

The importance of the refeeding protocol cannot be overstated. DeVries' Chapter IX of Therapeutic Fasting documents multiple cases of fasts broken incorrectly on solid food, leading to outcomes ranging from severe gastric distress to death in the most extreme cases of fasts broken on large, indigestible solid meals. The stomach after even three to four days of fasting has contracted, the digestive glands have significantly reduced their secretory activity, and the peristaltic musculature of the intestine (the wave-like contractions that move food through the gut) has been at rest. Reintroducing food gently

through liquids first, then soft foods, then progressively more complex foods, is the physiologically appropriate sequence. It is not optional.

Frequency of Rung 4

Quarterly 3 to 4-day fasts, combined with weekly 24-hour fasts as maintenance, represent a sustainable and clinically meaningful long-term protocol for hypertension management. Many of the patients in the clinical fasting literature who achieved the most durable and impressive blood pressure outcomes were on protocols of this general character: regular short fasts for maintenance and periodic extended fasts for deeper therapeutic renewal.

After completing at least two 3 to 4-day fasts with good tolerance, consistent blood pressure response, and physician satisfaction with monitoring data, you are ready to consider Rung 4\.

8.6 Rung 5: The 5 to 7-Day Fast

Physiological Objectives

The 5 to 7-day fast represents the threshold at which the clinical fasting literature's most dramatic blood pressure outcomes were achieved. Goldhamer's landmark 2001 and 2002 studies used fasts in this range and beyond, producing average reductions of 37/13 mmHg with 89% of subjects normalising to below 140/90 mmHg. Weger's "hundreds of consecutive hypertensive patients without a single complete failure" were fasted for durations that frequently included fasts of this length. McEachen's 141 hypertensive patients, not a single one failing to show improvement, were fasted across a range that included significant numbers at 5 to 7 days and beyond.

By Day 5, the following mechanisms are operating at their deepest level within the typical supervised fasting window:

RAAS suppression is at or near its maximum. Plasma aldosterone is substantially reduced, the kidneys have excreted a significant proportion of the accumulated sodium burden of years of hyperinsulinaemia, and the structural changes in the kidney's juxtaglomerular apparatus that chronically elevated RAAS activity produces are beginning, slowly, to normalise.

Endothelial repair is well underway. Autophagy has cleared dysfunctional eNOS enzyme complexes and the accumulated protein aggregates in endothelial cells that impaired their function. Fresh eNOS enzyme is being synthesised and expressed. Nitric oxide production, the body's natural vasodilatory and anti-thrombotic mechanism, is recovering.

Arterial plaque autolysis, as documented by Shelton, DeVries, and consistent with the mechanistic evidence on cholesterol plaque macrophage autophagy, is progressing. The autolysomal (self-digesting cellular compartment) processing of oxidised LDL-laden foam cells within plaques, the process that reduces plaque volume and stabilises plaque architecture, requires the sustained, deep autophagy of extended fasting to achieve meaningful scale.

Visceral fat mobilisation is substantial by Day 5 to 7\. Leptin levels have fallen significantly as visceral fat stores are metabolised. The leptin-mediated sympathetic drive discussed in Chapter 6 is reduced

proportionally. The adipokine (fat-cell-derived hormone) balance is shifting: adiponectin (the anti-inflammatory, insulin-sensitising adipokine that is deficient in obese insulin-resistant individuals) is rising as visceral fat shrinks.

The autonomic reset described in Chapter 6 is at its deepest measurable level. HRV metrics in patients who have reached Day 5 to 7 of a supervised fast typically show their most significant improvement from baseline. Resting heart rate is at its fast-period minimum. The subjective experience of mental clarity, emotional equanimity and reduced anxiety that fasting produces is at its most pronounced.

The Protocol

The 5 to 7-day fast follows the same daily structure as the 3 to 4-day fast, extended by two to three additional days. What changes is not the daily protocol but the depth and completeness of the physiological processes operating.

Days 1 through 3 follow the trajectory described in Rung 3: transition, trough, and turn.

Days 4 and 5 represent the deepening. Mental clarity is typically at its maximum. Physical energy, while not at normal capacity (some degree of physical weakness is normal in extended fasting as muscle protein makes a small but measurable contribution to gluconeogenesis), is sufficient for light activity and normal cognitive function. Many patients report being surprised by how productive intellectually they are in the later days of an extended fast: the clarity of thought that the clean ketone-fuelled brain produces is one of the most consistently reported and most compelling aspects of therapeutic fasting.

Days 6 and 7 are characterised by stability. The metabolic state is established and sustained. Blood pressure is at its fast-period minimum. The physiological renovation processes are operating at full depth. Most patients in supervised facilities who have reached this stage describe the experience in terms that share a common quality: a sense of having arrived somewhere, a feeling of unusual clarity and groundedness that is qualitatively different from ordinary waking consciousness.

Physical activity in Days 4 through 7 should remain gentle: 30 to 45-minute easy walks are appropriate for most patients. Some patients feel well enough for slightly more extended walking. The test is simple: if the activity feels comfortable and sustainable, continue. If it produces significant fatigue or dizziness, stop and rest.

Medication Management in a 5 to 7-Day Fast

By Day 5 to 7, it is common for patients who entered the fast on multiple antihypertensive medications to be on substantially reduced or completely suspended antihypertensive drug regimens. Blood pressure readings of 110/70 or lower are not uncommon in patients who entered the fast with readings of 160/100 or higher. At these blood pressure levels, continued antihypertensive dosing is contraindicated.

The medication reduction at this stage must be managed carefully and proactively. Your physician should be reviewing your blood pressure data at minimum once daily at this rung and should be making medication adjustments in real time based on the readings you are transmitting. Do not wait until hypotensive symptoms occur to report low blood pressure readings. The principle is anticipatory reduction, not reactive suspension.

It is also at this stage that the question of which medications to reintroduce and at what doses after the fast becomes clinically important. This question is addressed in Chapter 9\. For now, the principle to establish clearly is that the blood pressure achieved at Day 5 to 7 of a supervised fast on minimal or no antihypertensive medication represents the body's own regulated blood pressure in the absence of the metabolic drivers of elevation. It is the target. Post-fast nutrition and lifestyle management should be designed to maintain proximity to this level.

Monitoring Enhancements at Rung 5

At Rung 5, in addition to the standard monitoring described in Section 8.2, the following additional monitoring is recommended:

A mid-fast blood panel at Day 3 or 4, including electrolytes (sodium, potassium, chloride, bicarbonate), creatinine and eGFR, and blood glucose. This provides reassurance that electrolyte balance is maintained, kidney function is stable, and blood glucose is within a safe range. Most patients on water-only fasting with no diabetes maintain blood glucose in the 3.5 to 4.5 mmol/L range (63 to 81 mg/dL) during extended fasting through gluconeogenesis and the brain's progressive shift to ketone utilisation, but confirmation through measurement is appropriate at this depth of fasting.

Uric acid measurement at the mid-fast panel if the patient has a history of gout or had an elevated baseline uric acid level.

ECG if any palpitations, unusual cardiac awareness, or irregular pulse is noted at any point during the fast.

Breaking the 5 to 7-Day Fast

The refeeding protocol for a 5 to 7-day fast is the most critical of all the rungs, because the degree of digestive quiescence is at its maximum and the consequences of breaking the fast incorrectly are most severe.

The duration of the juice-only phase correlates with the length of the fast. Using DeVries' ratio guidance: a fast of 5 to 7 days warrants approximately 2 full days of juice-only refeeding before introducing soft whole foods.

Day 1 of refeeding: Juice only. Begin with 125 mL of freshly squeezed orange juice in the morning, sipping slowly over 20 minutes. Wait 2 hours. Take another 125 mL. Continue this pattern through the day, not exceeding one litre of total juice volume. The juice should be at room temperature. The first swallow will produce an extraordinary taste experience. Savour it and eat slowly. If nausea occurs, wait longer between servings and reduce the volume to 100 mL per serving.

Day 2 of refeeding: Continue juice in the morning (same approach as Day 1). At midday, introduce a small portion of fresh ripe fruit: half an orange, a small bowl of melon or papaya. Chew thoroughly. In the afternoon, juice again. In the early evening, a small bowl of blended vegetable soup (tomatoes, courgette, and leafy greens blended smooth with no added salt, cream or stock) is appropriate. This is the first solid food the digestive system has encountered in 5 to 7 days. It should be consumed slowly and in a small volume, no more than 200 to 300 mL.

Day 3 of refeeding: A small serving of whole fresh fruit in the morning. A light vegetable salad at midday with half a ripe avocado for healthy fat and gentle caloric density. A small portion of steamed fish or two soft-boiled eggs in the evening with cooked vegetables.

Day 4 onward: Continue the gradual reintroduction described in Day 3, increasing variety and volume slowly. Follow the post-fast nutritional principles in Chapter 9\.

The guiding principle throughout refeeding is this: the digestive system is reawakening from a physiological rest, not recovering from starvation. It does not need to compensate for lost volume by eating large meals quickly. It needs to be gently, progressively reactivated, with each new food introduced after the previous one has been successfully processed. Patients who understand and embrace this principle complete refeeding comfortably and maximise the therapeutic benefit of the fast. Patients who are impatient with it risk the discomfort and, in extreme cases, the acute gastrointestinal complications documented in the historical fasting literature.

Frequency of Rung 5

For hypertensive patients whose primary therapeutic goal is blood pressure normalisation and whose metabolic assessment reveals significant insulin resistance, two 5 to 7-day fasts per year, separated by approximately six months, represent an aggressive and clinically ambitious protocol that is consistent with the evidence from supervised fasting clinics. Combined with weekly 24-hour fasts as maintenance, this schedule provides quarterly significant fasting interventions that cumulatively and progressively address the root mechanisms of hypertension.

After completing one 5 to 7-day fast with good tolerance and physician satisfaction, progression to Rung 5 can be considered for appropriate patients. Rung 5 is not appropriate for all patients. It requires careful individual assessment.

8.7 Rung 6: The 10 to 14-Day Fast

Physiological Objectives

The 10 to 14-day fast represents the upper boundary of what this book's protocol recommends for unsupervised or minimally supervised outpatient therapeutic fasting. Fasts beyond 14 days exist and have been conducted safely by experienced fasting clinicians, but they require a level of intensive clinical supervision, monitoring infrastructure and physician expertise that places them outside the scope of a protocol book aimed at hypertensive patients and their physicians. Fasts of 14 days and beyond require a dedicated fasting clinic or inpatient environment with daily physician assessment, regular laboratory monitoring and immediate access to medical intervention.

Within the 10 to 14-day window, however, the physiological objectives are substantial and the clinical evidence compelling.

By Day 10, the arterial remodelling that sustained fasting initiates is operating at its deepest measurable level. The structural thickening of the arterial wall that chronic hyperinsulinaemia and sympathetic noradrenaline stimulation produced, the smooth muscle hypertrophy and hyperplasia described in

Chapters 4 and 6, is being reversed as the proliferative signals that drove it (insulin, noradrenaline, angiotensin II) are removed and sustained autolysis processes the accumulated structural excess.

The rejuvenescence documented by Carlson and Kunde at the Hull Biological Laboratory of the University of Chicago, in which a 40-year-old man's tissues measured physiologically equivalent to those of a 17-year-old after 14 days of fasting, reflects the cumulative effect of autophagy, cellular renewal, improved assimilation, and the replacement of senescent (aged and poorly functioning) cellular populations with newly generated healthy cells. The Longo immune regeneration data documenting stem cell activation and immune cell renewal at 72 hours is even more pronounced by Day 10 to 14\.

Baroreflex recalibration, which begins in shorter fasts but deepens with sustained exposure to lower blood pressure, is at its most advanced. The baroreceptors, having operated in a lower-pressure environment for 10 to 14 days, have substantially recalibrated their sensitivity. The autonomic system is defending a new, lower set point.

Blood pressure outcomes in this range in the clinical literature include Shelton's documented case of systolic reduction from 295 to 115 mmHg over three weeks, Weger's consistent reports of complete blood pressure normalisation in hundreds of hypertensive patients, and Goldhamer's data showing the most dramatic reductions occurring in the patients with the highest baseline pressures who were able to sustain fasting to this depth.

Who Is Appropriate for Rung 6

Rung 5 is appropriate only for patients who have:

Completed at least one Rung 5 fast (5 to 7 days) with good tolerance and documented therapeutic response.

Pre-fast assessment confirming no absolute contraindications and no significant complicating conditions that would require more intensive monitoring than twice-daily readings and daily physician contact can provide.

A physician supervisor who has reviewed the prior fasting records, the pre-fast assessment, the current medication status, and has formally agreed to provide daily monitoring contact throughout the fast.

Adequate personal circumstances to rest as needed, reduce professional and social obligations during the fast, and respond to physician guidance without delay if clinical concerns arise.

The primary additional requirement beyond Rung 5 is the enhanced monitoring protocol described below.

The Protocol

Days 1 through 7 follow the Rung 5 protocol precisely. The days of transition, trough, turn and deepening have been described in full.

Days 8 through 10 represent a further consolidation and deepening of the established ketotic, autophagic, and autonomically rebalanced state. Many patients at this stage describe what DeVries called "a feeling of lightness, buoyancy, and good health" that is qualitatively distinct from any prior

experience. The absence of hunger is complete. Mental clarity is extraordinary. Physical energy, while modest by normal standards, is sustainable for light activity.

Days 11 through 14, for those who extend to this depth, are characterised by stability and depth. The physiological renovation processes are continuing. The tongue, which typically coats heavily in the early days of fasting and gradually clears as elimination progresses, should be showing substantial clearing by this point. Its clearing is one of the traditional clinical indicators that the body has completed the primary phase of its autolytic housecleaning.

Physical activity in Days 8 through 14 should remain gentle. Easy walking of 30 to 45 minutes daily is appropriate for most patients. Some patients in the later days of extended fasting report feeling more energetic than in the middle days, consistent with the improved ketone metabolism and the completion of the keto-transition period. Light walking is an appropriate expression of this energy. Intense or prolonged exercise is not.

Enhanced Monitoring for Rung 6

In addition to the standard monitoring described in Section 8.2, Rung 6 requires:

A comprehensive laboratory panel at Day 5 to 7 of the fast, including full electrolytes, renal function, liver function, blood glucose, and a full blood count. This mid-fast panel is a safety checkpoint that confirms the body is managing the extended fast without electrolyte dysregulation, renal strain, or haematological (blood cell) abnormalities.

A second laboratory panel at Day 10 to 12, repeating the same tests. By this point, any tendency toward electrolyte abnormality that was not apparent at the earlier panel will be detectable and manageable before it reaches clinical significance.

Daily physician contact throughout, rather than the minimum of daily brief messaging described for shorter fasts. At Rung 5, the physician should actively review the transmitted data each day and make specific comments or recommendations based on it. This is not a passive monitoring relationship; it is an active clinical supervision.

ECG if any cardiac symptoms arise, without exception.

Breaking the 10 to 14-Day Fast

The refeeding protocol for a 10 to 14-day fast follows DeVries' ratio guidance: a fast of this length warrants approximately 3 full days of juice-only refeeding before introducing soft whole foods, and a further 3 days of soft whole foods before introducing a wider dietary range.

Days 1 to 3 of refeeding: Juice only. Begin with 100 mL of freshly squeezed orange juice in the morning of Day 1, sipping over 20 to 30 minutes. The volume and frequency of servings are increased incrementally across the three days, from 100 mL every 3 hours on Day 1 to 150 mL every 2 hours on Day 2 to 200 mL every 2 hours on Day 3\. Total juice volume should not exceed 800 mL on Day 1, 1,000 mL on Day 2, or 1,200 mL on Day 3\.

Days 4 to 6 of refeeding: Introduce fresh whole fruit in the morning. At midday, introduce blended vegetable soup or a very small, finely chopped salad with avocado. In the evening, a small serving of steamed fish or two soft-boiled eggs with cooked vegetables. Portions remain small. The digestive system is reawakening slowly and should not be rushed.

Days 7 onward: Continue gradual expansion of food variety and volume, following the post-fast nutritional principles in Chapter 9\.

A Clinical Observation on Refeeding Psychology

One of the most consistent and clinically important observations across the fasting literature, and one that is entirely consistent with the autonomic and appetite-regulatory mechanisms described in earlier chapters, is that patients who have completed extended fasts typically emerge with a dramatically altered relationship with food.

The hunger that was chronic, habitual and emotionally laden before the fast has been reset. The desire for processed foods, refined carbohydrates and sugar, which drove the dietary patterns that produced the insulin resistance and hypertension in the first place, is substantially reduced or absent in many patients in the immediate post-fast period. Foods that previously held powerful hedonic (pleasure-associated) pull have lost much of their appeal. Simple, whole foods taste extraordinary in a way that was not accessible before the fast recalibrated the sensory apparatus.

This is not a guarantee of permanent dietary change. Appetite is shaped by habit, and habits reassert themselves over time if not actively supported by new patterns. But the post-fast window is a period of unusual openness to dietary restructuring, and it is the window in which the nutritional foundations of the post-fast lifestyle described in Chapter 9 should be established with as much intention and commitment as the fast itself received.

8.8 Physical Activity During Fasting: A Complete Guide

Physical activity during fasting requires its own dedicated section because the question is asked consistently and the guidance in popular fasting content is frequently incorrect in ways that are clinically relevant.

The Physiological Basis of Activity Guidelines During Fasting

During a water fast, the body's energy supply is derived entirely from stored fat (primarily) and the modest contribution of gluconeogenesis from amino acids and glycerol. The total energy available from fat stores is very large: a person with 15 kilograms of body fat carries approximately 135,000 kilocalories of stored energy, sufficient to fuel weeks of fasting at basal metabolic rates. Physical activity does not run the risk of depleting this supply in any meaningful sense during a 14-day fast.

However, physical activity during fasting does impose demands on the body that must be weighed against the body's current capacity. Three considerations are relevant:

First, intense exercise requires the mobilisation of carbohydrate for fuel at high intensities. Since glycogen is depleted during fasting and gluconeogenesis cannot match the glucose demand of

high-intensity exercise, intense exercise during fasting forces the body into a degree of protein catabolism (breakdown of muscle protein for gluconeogenesis) that exceeds what fasting alone produces. This is counterproductive: one of the remarkable features of properly conducted water fasting is the preferential mobilisation of fat and abnormal tissue while healthy muscle and vital organs are well preserved. Intense exercise during fasting compromises this preferential sparing of healthy muscle.

Second, the electrolyte shifts and blood pressure reductions of fasting increase the risk of exercise-associated hypotension. The orthostatic hypotension that can occur upon standing during fasting is amplified during and immediately after physical exertion, when blood is redistributed to working muscles and cardiac output demands are elevated. The combination of volume depletion from fasting-induced natriuresis and exercise-induced cardiovascular demands can produce syncope (fainting) in susceptible individuals.

Third, DeVries noted explicitly that resting patients during fasting consume their nutritive reserves more slowly than active patients, allowing longer fasting periods and emergence from the fast in better physical condition. This is simply the physiology of basal metabolic rate: a resting body burns less energy per unit time than an active one, meaning stored reserves last longer and the fasting therapeutic window can extend further.

Practical Activity Guidelines by Rung

Rung 1 (24-hour fast): Light walking of 20 to 30 minutes at a comfortable pace. Normal daily activities. No structured exercise sessions.

Rung 2 (36 to 48-hour fast): Light walking on Day 1\. Rest as needed on Day 2\. Normal daily activities at a reduced pace. No structured exercise.

Rung 3 (3 to 4-day fast): Light walking of 20 to 30 minutes daily if it feels comfortable. Rest on any day when fatigue is prominent. No exercise beyond easy walking.

Rung 4 (5 to 7-day fast): Easy walking of 30 to 45 minutes daily in Days 4 through 7 when energy permits. Rest on Days 1 through 3\. Slow, gentle yoga or stretching is appropriate from Day 4 onward if desired. No aerobic exercise, resistance training or any exercise that elevates heart rate significantly above resting.

Rung 5 (10 to 14-day fast): Easy walking of 30 to 45 minutes daily in Days 5 through 14\. Gentle stretching. Rest whenever fatigue calls for it. The same prohibitions on structured exercise apply.

The consistent principle across all rungs is that the fast is doing the work. Your job during the fast is to rest, hydrate, monitor, and allow the body's extraordinary physiological intelligence to operate without interference. Physical activity is supportive and gentle. It is not the mechanism of therapeutic effect. The mechanism is the fasting itself.

8.9 Sleep During Fasting

Sleep during fasting deserves specific attention because it is simultaneously one of the most commonly reported difficulties in the early fast and one of the most dramatic areas of improvement in the later fast.

The first one to two nights of a fast are frequently associated with disrupted sleep. The mechanisms are the early catecholamine fluctuations of the transition period (elevated noradrenaline in the early fast can reduce sleep quality), the withdrawal of the habitual evening meal that for many people served as a relaxation and sleep-onset cue, caffeine withdrawal if not fully completed before the fast began, and the simple psychological activation of beginning a new and demanding undertaking.

Practical sleep management in the early fast:

Create optimal sleep conditions: a dark, cool room, minimal electronic screen exposure for two hours before bed, and avoidance of stimulating activity in the evening.

If sleep does not come immediately, do not lie in bed becoming increasingly frustrated with wakefulness. Frustration with sleeplessness is itself a sympathetic activator that makes sleep less likely. Read a physical book (not a screen), listen to quiet music, or simply rest in a comfortable position without the pressure of needing to sleep.

Do not take sleep medications during fasting. Benzodiazepines, non-benzodiazepine hypnotics (such as zolpidem), and antihistamine-based sleep aids all interact with the fasting metabolic state in ways that are unpredictable and potentially problematic. The fasting body's enhanced drug sensitivity, documented by DeVries citing multiple experimental animal studies and consistent with the known pharmacokinetic changes of fasting states, means that medications taken during fasting may produce stronger effects than expected.

From Day 3 or 4 onward, sleep typically improves substantially. The rising vagal tone, the settling of catecholamine fluctuations, the BHB-mediated GABAergic calming, and the HPA axis normalisation all contribute to sleep quality improvement that most patients find striking. Many describe some of the deepest and most restorative sleep of their lives in the later days of a supervised extended fast.

Chapter Summary: Key Points

The progressive fasting ladder has five rungs, each building on the previous: Rung 1 (24-hour weekly fast), Rung 2 (36 to 48-hour monthly fast), Rung 3 (3 to 4-day quarterly fast), Rung 4 (5 to 7-day biannual fast), and Rung 5 (10 to 14-day annual or biannual fast for appropriate patients with full medical supervision). No rung should be skipped.

Every protocol is built on pure water, minimum two litres daily, sipped evenly at room temperature. No broths, herbal teas, coffee or electrolyte drinks during the fast itself. The rationale is mechanistic: each addition interferes with one or more of the specific physiological processes the fast is designed to maximise.

Monitoring standards apply across all rungs: twice-daily blood pressure measurement in both arms, resting heart rate with every reading, daily subjective symptom log, and physician contact from the first day of any fast beyond 48 hours. Enhanced monitoring including mid-fast laboratory panels applies from Rung 4 onward.

Medication management is the single most important safety consideration for hypertensive patients and must be proactively managed by the prescribing physician before and throughout every fast at every

rung. Medication reduction as blood pressure falls during fasting is not a complication to be avoided but a therapeutic goal to be anticipated and managed.

Refeeding is as clinically important as the fast itself. Every rung has a specific refeeding protocol scaled to the length of the fast, beginning with juice only, progressing through soft whole foods, and advancing to normal eating over days whose number correlates with the duration of the fast. Breaking any extended fast on solid food without a juice-first transitional period risks serious gastrointestinal consequences.

Physical activity during fasting is gentle: light walking appropriate from Rung 1, extending to 30 to 45-minute easy walks in the later days of Rungs 4 and 5\. Intense exercise is not appropriate at any rung during a water fast.

Sleep improves progressively across the days of extended fasting as vagal tone rises, catecholamine fluctuations settle, and BHB-mediated central calming deepens. No sleep medications should be taken during fasting.

The post-fast window is a period of unusual metabolic and psychological openness to dietary restructuring. Chapter 9 provides the complete framework for converting this opening into durable, sustained therapeutic benefit.

“Do not go where the path may lead. Go instead where there is no path and leave a trail.”

— Ralph Waldo Emerson

The trail through the fasting ladder has been walked by tens of thousands of patients before you. Each rung has been documented, studied and refined. Your job is not to blaze new territory but to follow the map carefully, trust the science, and give your body what it has been designed to do when given the right conditions.

CHAPTER 9

Maintenance, The Annual Fasting Calendar And Post-Fast Nutrition

“It is not enough to take steps which may someday lead to a goal; each step must be itself a goal and a step likewise.”

— Johann Wolfgang von Goethe

Opening: The Fast Is the Reset. The Life After Is the Result.

There is a clinical pattern I have observed repeatedly across years of working with hypertensive patients on fasting protocols, and it is important enough to name directly at the opening of this chapter.

A patient completes a 7-day supervised fast. Their blood pressure, which entered the fast at 162/98 mmHg on three antihypertensive medications, finishes the fast at 118/74 on one medication at half its original dose. Their fasting insulin has fallen from 24 micro-international units per millilitre to 7\. Their HOMA-IR has dropped from 4.1 to 1.2. Their resting heart rate is 58 beats per minute. They feel, as patients consistently describe it, like a different person. Clearer. Lighter. Calmer.

They leave the fast genuinely transformed.

Six months later, they return for follow-up. Blood pressure is 148/92. They are back on two full-dose antihypertensive medications. Fasting insulin is 19\. HOMA-IR is 3.4. Resting heart rate is 76\.

What happened?

In almost every case, the answer is the same: the fast was treated as an event rather than as the beginning of a new physiological standard. The dietary patterns that built the hyperinsulinaemia, insulin resistance and sympathetic overactivation that drove the hypertension were resumed within weeks of the fast ending. The metabolic terrain that fasting had cleared was re-occupied by the same forces that had disrupted it. The body, following its adaptive logic faithfully, rebuilt the insulin resistance, reinstated the RAAS overactivation, restored the sympathetic tone, and returned the blood pressure to the level that reflected the metabolic environment it was once again living in.

This is not a failure of fasting. It is a failure of the post-fast framework.

Fasting is the most powerful single intervention available for resetting the physiological mechanisms that drive hypertension. But it is a reset, not a permanent reprogramming. The reset creates a window of metabolic sensitivity and physiological openness that is unlike any other period in the patient's experience. Within that window, the dietary, lifestyle and behavioural choices made in the first weeks and months after the fast determine whether the therapeutic gains of fasting are sustained, built upon, and converted into permanent cardiovascular protection, or progressively eroded and eventually lost.

This chapter provides the complete architecture of post-fast maintenance: the nutritional principles that sustain the insulin sensitivity the fast restored, the annual fasting calendar that provides regular therapeutic renewal, the laboratory monitoring schedule that tracks the maintenance of metabolic health over time, the lifestyle factors whose consistent presence is synergistic with fasting's benefits, and the approach to medication management as blood pressure is progressively and permanently normalised.

9.1 The Post-Fast Metabolic Window: Why the First Four Weeks Matter Most

When a patient breaks an extended fast and begins refeeding, the body is in a state that has no equivalent in normal dietary life. Its metabolic machinery has been recalibrated. Insulin sensitivity is at its maximum, because insulin levels have been at their minimum for days to weeks and insulin receptor expression and downstream signalling pathways have been upregulated (increased in number and sensitivity) in response to the prolonged absence of insulin stimulation.

In practical terms, this means that the body in the immediate post-fast period is unusually efficient at using insulin. Small amounts of insulin, produced in response to modest dietary carbohydrate, produce a large metabolic effect. Glucose is cleared from the bloodstream rapidly and efficiently. Fat cells, responding to the suddenly insulin-sensitive signalling environment, are highly responsive to insulin's fat-storage instructions.

This cuts both ways.

If the post-fast diet is composed of whole, unrefined foods with moderate carbohydrate content from natural sources, the body uses its enhanced insulin sensitivity productively. Nutrients are absorbed efficiently, cellular renewal proceeds rapidly, and the metabolic improvements achieved during the fast are consolidated and extended. Each post-fast meal in this context is operating in a highly favourable metabolic environment.

If the post-fast diet immediately returns to refined carbohydrates, added sugars and ultra-processed foods, the high-insulin-sensitivity state means that the pancreas produces a large insulin response to a relatively modest glucose load, and that insulin then acts powerfully on fat cells to restore fat storage and on the liver to suppress ketone production and restore glycogen. The rapid reinstatement of chronic hyperinsulinaemia in a highly insulin-sensitive environment can, paradoxically, drive a faster re-accumulation of visceral fat and a more rapid re-establishment of insulin resistance than would occur if the same dietary mistakes were made in a less insulin-sensitive metabolic state.

The post-fast window is therefore simultaneously the period of greatest opportunity and the period of greatest vulnerability. The choices made during the first four weeks after an extended fast have a disproportionate influence on the long-term trajectory of metabolic health. This is why the refeeding protocol of Chapter 8 extends seamlessly into the nutritional framework of this chapter without a sharp boundary: the transition from refeeding to maintenance nutrition is gradual, deliberate and architecturally continuous.

9.2 The Nutritional Principles of Post-Fast Maintenance

The post-fast nutritional framework is not a diet in the prescriptive sense of a list of permitted and forbidden foods with specific portion sizes and calorie counts. It is a set of physiological principles whose consistent application across a wide variety of individual food preferences, cultural traditions and practical circumstances produces the metabolic outcomes we are targeting: maintained insulin sensitivity, sustained low-normal insulin levels, adequate dietary fibre for gut microbiome health, sufficient protein for tissue maintenance and cellular renewal, and the elimination of the specific dietary drivers of hyperinsulinaemia and vascular inflammation.

Principle 1: Eliminate the Primary Drivers of Hyperinsulinaemia

Chapter 4 identified the five primary drivers of insulin resistance and chronic hyperinsulinaemia: refined carbohydrate excess, physical inactivity, visceral adiposity, sleep deprivation and psychological stress, and gut dysbiosis. The first of these, refined carbohydrate excess, is entirely within dietary control and is the most important nutritional target of post-fast maintenance.

Refined carbohydrates are carbohydrates that have been processed to remove their fibre, micronutrient content and structural complexity, leaving primarily rapidly digestible starch and sugar. They include white rice (the polishing process removes the bran and germ, leaving only the starchy endosperm), white bread and white flour products (the milling process removes bran and germ), refined breakfast cereals (most commercial breakfast cereals are heavily processed and contain significant added sugar regardless of their marketing claims), sugary beverages of all kinds including commercial fruit juices, which despite their natural origin are concentrated sugar solutions that produce rapid and large insulin responses, confectionery, pastries, biscuits, and the enormous category of ultra-processed foods that line the central aisles of every modern supermarket.

These foods must be eliminated from the post-fast diet, not reduced, not limited to weekends, not managed with portion control. Eliminated. The reason is mechanistic and has been established in detail across Chapters 3 and 4: these foods produce rapid, large insulin spikes that, consumed multiple times daily as they are in the typical modern diet, drive the chronic hyperinsulinaemia that is the primary metabolic driver of the hypertension we are treating. There is no safe frequency of consumption of these foods for a patient whose primary diagnosis is hyperinsulinaemia-mediated hypertension. Each exposure is a step backward from the therapeutic goal.

This is not a popular message in a world that is accustomed to nutrition advice framed in terms of moderation. But moderation is appropriate for foods whose harm operates through accumulation or excess. It is not appropriate for foods that produce a pathological physiological response at every consumption, regardless of quantity. Smoking advice does not recommend moderate smoking. The nutritional advice for hyperinsulinaemia-mediated hypertension should not recommend moderate refined carbohydrate consumption.

Added sugars specifically deserve emphasis. The liver processes fructose (the sugar found in table sugar sucrose alongside glucose, and present in high concentrations in high-fructose corn syrup) through a pathway that is almost entirely hepatic (liver-based) and that does not require insulin for its initial processing. This has led to the mistaken popular conclusion that fructose is "safe" for people managing insulin levels. The reality is that hepatic fructose metabolism directly promotes de novo

lipogenesis (DNL, the synthesis of fat from carbohydrate in the liver), increasing visceral fat accumulation, promoting hepatic insulin resistance (the liver-specific insulin resistance that drives excess hepatic glucose output), and raising triglyceride levels. Fructose from whole fruit, consumed with the fibre and micronutrients that accompany it in the intact fruit, is absorbed slowly and does not produce these adverse effects at the quantities present in whole fruit. Fructose from added sugars, sugary drinks and refined foods is concentrated, rapidly absorbed and highly lipogenic. It must be eliminated entirely from the post-fast diet.

Principle 2: Build the Diet Around Foods That Sustain Insulin Sensitivity

Eliminating the drivers of hyperinsulinaemia is necessary but not sufficient. The post-fast diet must also actively provide the nutritional substrates that support insulin sensitivity, vascular health, gut microbiome diversity and the cellular renewal processes that fasting initiated.

Non-starchy vegetables form the nutritional foundation of the post-fast diet. Leafy greens (spinach, kale, Swiss chard, collard greens, rocket, watercress), cruciferous vegetables (broccoli, cauliflower, Brussels sprouts, cabbage, bok choy), and a wide variety of other vegetables (courgette, aubergine, bell peppers, tomatoes, cucumber, celery, asparagus) should constitute the largest portion of every main meal by volume. They provide dietary fibre for gut microbiome health and SCFA (short-chain fatty acid) production, magnesium and potassium for blood pressure regulation and cardiac function, polyphenols (plant-derived compounds with antioxidant and anti-inflammatory properties) that directly support endothelial function, folate and B vitamins for homocysteine regulation (homocysteine, pronounced "ho-mo-SIS-teen," is an amino acid whose elevated blood levels are an independent cardiovascular risk factor managed in part through dietary B vitamin adequacy), and virtually no insulin-stimulating potential.

Legumes (beans, lentils, chickpeas, peas, soybeans) deserve specific mention as one of the most undervalued food groups in cardiovascular nutrition. Their combination of soluble fibre, moderate protein, and complex carbohydrate with a low glycaemic index (a measure of how rapidly a food raises blood glucose, with lower values indicating slower, more gradual glucose release) produces a modest, sustained insulin response rather than the rapid spike of refined carbohydrates. Multiple large epidemiological studies have associated regular legume consumption with lower blood pressure, improved insulin sensitivity and reduced cardiovascular event risk. In populations that have historically eaten legumes as a dietary staple, including many communities across West Africa, the Middle East, the Mediterranean basin and South Asia, the metabolic health advantages are measurable and consistent. For the patient transitioning from the post-fast refeeding protocol to long-term maintenance nutrition, legumes are one of the most practical and versatile dietary foundations available.

Whole grains, meaning grains consumed with their bran and germ intact (whole oats, brown rice, quinoa, barley, millet, whole wheat where grains are consumed at all), produce a significantly lower insulin response than their refined counterparts because the intact fibre and structural complexity slow glucose release. They also provide magnesium, B vitamins and additional fibre. The distinction between whole and refined grains is not trivial: the difference in glycaemic response between brown rice and white rice, or between whole oat porridge and processed breakfast cereal, is substantial and clinically meaningful for insulin management.

Healthy fats from whole food sources do not stimulate insulin secretion and provide essential fatty acids, fat-soluble vitamins and the structural lipids needed for cellular membrane integrity and hormone synthesis. Avocado provides monounsaturated fat alongside potassium and fibre. Extra virgin olive oil provides oleocanthal and oleacein, polyphenols with documented anti-inflammatory properties. Nuts and seeds provide mixed polyunsaturated and monounsaturated fats alongside fibre, magnesium and plant sterols (compounds that competitively reduce cholesterol absorption in the gut). Fatty fish (salmon, mackerel, sardines, herring, anchovies) provide the long-chain omega-3 fatty acids EPA (eicosapentaenoic acid, pronounced "EYE-koh-sah-pen-tah-ee-NO-ik") and DHA (docosahexaenoic acid, pronounced "DOK-oh-sah-hek-sah-ee-NO-ik"), which reduce triglycerides, decrease platelet aggregation (the clumping together of platelets that initiates blood clot formation), modestly reduce blood pressure, and have direct anti-inflammatory effects on the vascular endothelium. The evidence base for omega-3 fatty acids in cardiovascular risk reduction is among the most robust in nutritional science.

Quality protein sources provide the amino acids needed for cellular renewal, particularly for the post-fast period when the body is actively rebuilding the protoplasm (cellular substance) generated by the fasting period's autolytic processes. The preferential protein sources in the post-fast context are those that provide protein with the lowest concomitant inflammatory, oxidative or insulin-stimulating burden: fish (particularly the fatty fish listed above), eggs (a complete protein source providing all essential amino acids alongside choline, an essential nutrient for liver function, and lutein, an antioxidant with cardiovascular benefits), legumes (which uniquely combine protein with the fibre and slow carbohydrate that supports insulin sensitivity), and where animal proteins are consumed, poultry and game over processed meats and red meat, which carry higher inflammatory and oxidative burdens from their saturated fat, haem iron (a form of dietary iron that promotes oxidative stress at high intakes) and, in the case of processed meats, added sodium and nitrate preservatives.

Principle 3: Protect and Nourish the Gut Microbiome

Chapter 5 described the role of gut dysbiosis and elevated TMAO in cardiovascular risk. The fasting period produces a significant beneficial shift in the gut microbiome, reducing TMAO-producing species and increasing SCFA-producing bacteria including Akkermansia muciniphila. The post-fast diet determines whether this shift is sustained and built upon or reversed.

The dietary pattern that most consistently supports a cardiovascular-protective gut microbiome is characterised by high dietary fibre diversity. The research on gut microbiome diversity is clear: the number of distinct plant species consumed per week is one of the strongest predictors of microbiome diversity, and microbiome diversity is associated with reduced cardiovascular risk, improved insulin sensitivity, and lower levels of inflammatory markers. A target of 30 or more distinct plant species per week, counting every different vegetable, fruit, legume, whole grain, nut, seed and herb as a separate species, is a practical and well-researched goal.

This does not require exotic or expensive foods. A week's diet that includes five different vegetables, three different fruits, two different legumes, two different whole grains, four different nuts or seeds, and a variety of herbs has already reached 16 plant species. Adding variety across the week, rotating the specific vegetables and fruits purchased rather than defaulting to the same small repertoire, is the

practical implementation.

Fermented foods provide both dietary fibre and live bacterial cultures that directly seed the gut microbiome with beneficial species. Natural yogurt (full-fat, unsweetened, without additives), kefir (a fermented milk beverage with a broader bacterial profile than yogurt), kimchi (a Korean fermented vegetable preparation, typically cabbage), sauerkraut (fermented cabbage), and other traditionally fermented foods are valuable additions to the post-fast diet. Their inclusion in daily meals provides a continuous input of beneficial bacteria that supports the microbiome shift initiated by fasting.

Principle 4: Manage Sodium Without Eliminating It

The sodium-insulin-blood pressure triangle described in Chapter 4 makes sodium management an important component of post-fast dietary maintenance. However, the approach to sodium in the post-fast framework differs from the blanket salt restriction that standard hypertension guidelines typically recommend.

The primary sodium management target is not the elimination of all dietary sodium but the elimination of added sodium in ultra-processed and industrially prepared foods, which account for approximately 75 to 80% of dietary sodium intake in populations eating a Western-pattern diet. Processed meats (bacon, ham, sausages, salami, deli meats), canned foods with added salt, commercial sauces and condiments, packaged snack foods, and most restaurant meals are the dominant sources of this sodium burden. Eliminating these foods for the other nutritional reasons already described simultaneously and substantially reduces dietary sodium without any need for deliberate salt restriction in the preparation of home-cooked whole foods.

The use of small amounts of unrefined salt (sea salt or Himalayan pink salt, which contain trace minerals alongside sodium chloride), as a permissive fallback in home cooking of whole foods is not a significant cardiovascular concern when the overall dietary pattern is whole-food based and sodium from processed foods has been eliminated. The obsessive avoidance of salt in cooking that standard dietary advice sometimes promotes is not necessary in the context of a diet that has already eliminated the major sodium-contributing food categories.

In alignment with the strict elimination of added sodium, the post-fast maintenance framework replaces commercial table salt with natural, mineral-rich enhancers. Patients utilize pure kelp granules, garlic powder, and a wide array of aromatic herbs to season foods. Kelp provides a naturally savory, salty flavor profile while supplying essential trace minerals and iodine, supporting thyroid function without triggering the fluid retention associated with sodium chloride. When these strict alternatives are entirely inaccessible, the protocol permits a highly controlled fallback: the minimal use of unrefined, hand-harvested sea salt or Himalayan pink salt. While these contain trace elements, they are treated strictly as a secondary alternative to prevent the disruption of vascular pressure dynamics.

Potassium is the dietary counterpart to sodium in blood pressure regulation. Diets high in dietary potassium consistently produce lower blood pressure independent of sodium intake, and the potassium-to-sodium ratio in the diet is as important as absolute sodium intake in determining blood pressure outcomes. The whole-food, plant-forward diet described in this chapter is inherently high in dietary potassium through its emphasis on vegetables, legumes, whole grains and fruit, all of which are

potassium-rich. A diet built around these foods naturally provides a favourable potassium-to-sodium ratio without requiring specific potassium supplementation in most cases.

Magnesium, whose importance for blood pressure regulation, cardiac function and insulin sensitivity was established in Chapter 7, should be consciously ensured through dietary sources. Magnesium-rich foods include leafy green vegetables (magnesium is at the centre of the chlorophyll molecule, so the greener the vegetable the higher its magnesium content), legumes, whole grains, nuts (particularly almonds, cashews and Brazil nuts), seeds (particularly pumpkin seeds, which are among the highest-magnesium foods available), and dark chocolate with a high cocoa content (70% or above), which contains both magnesium and polyphenols with cardiovascular benefit. For patients with identified magnesium insufficiency on baseline assessment, supplemental magnesium glycinate at 200 to 400 mg daily is a reasonable adjunct to dietary sources.

To optimize the highly sensitive post-fast metabolic terrain, the protocol introduces an organic acid catalyst: Paul Bragg’s classic Apple Cider Vinegar (ACV) cocktail. Taken strictly during the post-fast maintenance phase, and never during an active water fast, this tonic leverages acetic acid to support gastrointestinal and vascular recovery. Mechanistically, acetic acid delays gastric emptying, which slows the breakdown of dietary starches and flattens postprandial (after-meal) blood glucose spikes. Furthermore, it activates AMP-activated protein kinase (AMPK) in the liver and skeletal muscle, upregulating fatty acid oxidation and enhancing insulin receptor sensitivity. For the hypertensive patient, this translates to a dampened insulin response, directly protecting the vascular endothelium from the inflammatory surges that drive arterial stiffness.

Recipe and Daily Timing:

The cocktail is built around a specific dilution ratio to maximize gastric comfort while providing a therapeutic dose of acetic acid.

The Formulation: Mix 1 to 2 teaspoons of raw apple cider vinegar into 8 ounces of filtered, room-temperature water.

The Schedule: The protocol mandates taking this mixture three times daily, exactly 15 to 20 minutes before each primary meal.

This precise timing ensures that the acetic acid enters the stomach ahead of the bolus (chewed food), giving the acid time to signal the gastric mucosa to begin enzyme production and slow down gastric emptying.

Sourcing and Quality Metrics:

The therapeutic success of this protocol depends entirely on the chemical composition of the vinegar used. Standard, clear commercial vinegars will not produce the intended metabolic effects because the pasteurization and filtration processes strip out the active biological components.

Raw and Unfiltered: The vinegar must be completely raw and unrefined to preserve the organic acids.

The Mother: The bottle must clearly contain the mother, which is the cloudy sediment of beneficial bacteria, proteins, and enzymes that settles at the bottom. The bottle should be shaken gently before

each use to distribute these active elements.

Principle 5: Manage Eating Patterns, Not Just Food Choices

The timing and pattern of eating interacts with insulin regulation in ways that are clinically important and that extend beyond the question of which specific foods are consumed.

Time-restricted eating (TRE, sometimes called intermittent fasting in popular usage, though it is distinct from the therapeutic water fasting that is the primary subject of this book) involves confining all food consumption to a specific daily window, typically 8 to 10 hours, and fasting for the remaining 14 to 16 hours. During the fasting portion of TRE, insulin levels fall to their minimum as described in earlier chapters, RAAS activity reduces, and the autophagy, fat mobilisation and sympathetic withdrawal processes of fasting operate at a modest but measurable level.

The evidence base for TRE in blood pressure management is growing. A landmark randomised controlled trial published in Cell Metabolism in 2019 (Sutton et al.) demonstrated that early TRE (confining eating to a 6-hour window in the morning and early afternoon) produced significant reductions in systolic blood pressure, insulin levels, oxidative stress markers, and morning cortisol compared to a control group eating the same foods over a typical 12-hour window, without any caloric restriction. These results were produced by the timing of eating alone, confirming that when we eat is a meaningful determinant of the metabolic environment, not just what we eat.

The practical implementation of TRE in the post-fast context is straightforward and does not require the psychological demands of a full fast. The most accessible TRE pattern is a 16:8 protocol: 16 hours of fasting (including overnight sleep) and an 8-hour eating window. If the first meal of the day is at noon and the final meal is at 8 pm, a 16:8 TRE pattern is established without any change in what is eaten, only when.

For hypertensive patients, the evidence from Sutton et al. and from subsequent TRE research suggests that earlier eating windows (morning and afternoon rather than afternoon and evening) produce greater blood pressure benefits than later eating windows, consistent with the circadian biology of insulin secretion, cortisol rhythms, and the autonomic nervous system's diurnal variation. An 8:00 am to 4:00 pm or 9:00 am to 5:00 pm eating window is the most metabolically favourable, though a noon to 8:00 pm window is the most practically achievable for most people with conventional work and social schedules.

Meal frequency within the eating window is less important than meal composition and the maintenance of the eating window itself. Two or three meals within the 8-hour window, without snacking between meals (each snack, no matter how small or how "healthy," produces an insulin response that prevents insulin from falling between meals), maintains a more favourable insulin profile across the day than the same foods eaten as five or six smaller meals and snacks spread across a 12-hour window.

9.3 The Annual Fasting Calendar

The annual fasting calendar is the structural framework that converts the one-time therapeutic reset of a first extended fast into a sustained, progressively deepening programme of metabolic renewal. It answers the practical question: after the first extended fast, how should fasting be integrated into the

year?

The calendar has three tiers, operating simultaneously: the weekly maintenance fast, the monthly intermediate fast, and the quarterly or biannual deep therapeutic fast. Each tier serves a distinct purpose, and the three operate synergistically.

Tier 1: The Weekly 24-Hour Maintenance Fast

The weekly 24-hour fast is the foundation of the annual calendar. It is the discipline that Bragg maintained without exception for more than seven decades and that the clinical fasting literature consistently endorses as the minimum ongoing fasting practice for metabolic health maintenance.

Its purpose is not dramatic therapeutic transformation. It is maintenance. Each weekly 24-hour fast provides one full day of insulin normalisation, one full day of RAAS rest, one full day of reduced sympathetic tone, one full day of autophagic activity, and one full day of gut microbiome rebalancing. These are modest effects in isolation, but accumulated across 52 weeks, their impact is compounding and clinically significant.

The weekly 24-hour fast also serves as a metabolic recalibration mechanism that counteracts the minor dietary drifts that inevitably occur over the course of a normal week of eating. No one maintains perfect dietary adherence across seven days of ordinary life every week of the year. Social events, travel, work pressures, family occasions and simple appetite variation will produce weekly dietary fluctuations that include foods outside the ideal post-fast nutritional framework. The weekly 24-hour fast is the reset that prevents these fluctuations from accumulating into a progressive erosion of the metabolic gains achieved through extended fasting.

Establish a consistent weekly fast day and protect it. The most common barriers to weekly fasting are social (a habitual fast day that conflicts with recurring social eating occasions), professional (work events or travel that disrupts the schedule) and motivational (the fast day feeling increasingly demanding as memory of the extended fast's benefits fades). Anticipating these barriers and having strategies for managing them, including alternative fast days when the primary day is genuinely unavoidable, maintaining a written record of blood pressure across fast days to preserve objective evidence of benefit, and periodically reviewing the pre-fast assessment data to remind oneself of the metabolic baseline from which the fasting programme began, preserves consistency across the year.

Tier 2: The Monthly 36 to 48-Hour Intermediate Fast

Once the weekly 24-hour fast is established as a stable practice, a monthly 36 to 48-hour fast adds a deeper monthly renewal cycle to the calendar. The 36 to 48-hour fast takes the patient through the full keto-transition threshold, into the initial stage of established ketosis, and provides a meaningful monthly pulse of the deeper therapeutic mechanisms: NLRP3 inflammasome suppression, autophagic activity at therapeutic intensity, and measurable HRV improvement.

The monthly 36 to 48-hour fast is most easily positioned around the weekly fast day: beginning the fast on the Tuesday evening before a Wednesday fast day and extending through to the Thursday morning creates a 36 to 40-hour fast that incorporates the established weekly fast day pattern with a modest extension.

Some patients prefer to do the monthly extended fast as a separate practice: beginning on a Saturday evening and ending on a Monday morning, for example, using the weekend structure to accommodate the greater rest needs of the longer fast. The specific timing matters less than the consistency: one 36 to 48-hour fast per month, every month, throughout the year.

Tier 3: The Quarterly or Biannual Deep Therapeutic Fast

The deep therapeutic fast of 5 to 14 days (Rungs 4 and 5 of the Chapter 8 ladder) is the annual calendar's highest-intensity intervention. Its frequency depends on the patient's clinical objectives, physician assessment and fasting experience level.

For patients in the first year of their fasting programme, two 5 to 7-day fasts spaced approximately six months apart (one in spring and one in autumn, for example) represent an ambitious but achievable protocol that is consistent with the evidence from supervised fasting clinics. These two extended fasts, combined with 52 weekly 24-hour fasts and 12 monthly 36 to 48-hour fasts, constitute a comprehensive annual programme that provides approximately 80 to 90 total days of therapeutic fasting across the year.

For patients whose initial metabolic assessment revealed severe insulin resistance (HOMA-IR above 4.0), significantly elevated TMAO or inflammatory markers, or blood pressure above 160 mmHg systolic at baseline, an initial period of more intensive fasting (three 5 to 7-day fasts in the first year, separated by a minimum of eight weeks between each) accelerates the metabolic restoration and may be appropriate under close physician supervision.

For patients who have maintained the annual calendar for two or more years and whose metabolic markers have normalised (HOMA-IR below 1.5, fasting insulin below 8, blood pressure consistently below 120/80 without antihypertensive medication), the extended fasting frequency may reasonably be reduced to one 5 to 7-day fast per year as a maintenance and renewal practice, with the weekly and monthly shorter fasts continuing as the primary ongoing programme.

A Sample Annual Calendar

The following represents one practical implementation of the three-tier annual calendar for a patient in their first year of the fasting programme, beginning after completing their first extended fast:

January: Weekly 24-hour fasts (4 times). Monthly 36 to 48-hour fast (1 time). Begin the year with a 5-day fast in the third week, under physician supervision, as the first deep therapeutic fast of the year.

February through May: Weekly 24-hour fasts (4 per month). Monthly 36 to 48-hour fast (1 per month). No extended fast in these months: this period consolidates the metabolic gains from the January fast through consistent maintenance fasting and the post-fast nutritional framework.

June: Weekly 24-hour fasts (4 times). Monthly 36 to 48-hour fast (1 time). Second deep therapeutic fast of the year in the third week, targeting 7 days under physician supervision, building on the experience and fasting adaptation from January.

July through November: Weekly 24-hour fasts (4 per month). Monthly 36 to 48-hour fast (1 per month). Same consolidation period as February through May.

December: Weekly 24-hour fasts (4 times). Monthly 36 to 48-hour fast (1 time). End-of-year review with physician, comparing current metabolic markers with baseline. Adjust the following year's calendar based on outcomes.

This calendar is a template, not a prescription. Individual circumstances, physician judgment, personal schedule and clinical response all inform the specific implementation. What it illustrates is the structural principle: the deep therapeutic fasts are spaced to allow adequate metabolic recovery and rebuilding between them, the weekly and monthly maintenance fasts are uninterrupted throughout the year, and the programme is reviewed and adjusted based on objective metabolic outcomes rather than maintained inflexibly regardless of results.

9.4 Laboratory Monitoring on the Annual Calendar

The pre-fast assessment described in Chapter 7 establishes the baseline. Annual and periodic monitoring tracks the trajectory of metabolic health over time, confirms that the fasting programme is producing its intended effects, identifies any emerging concerns early enough to address them, and provides the objective data that sustains both the physician's clinical confidence in the programme and the patient's motivation to maintain it.

Recommended Monitoring Schedule

Every six months, or around each deep therapeutic fast, the following panel should be repeated:

Fasting glucose and fasting insulin, for HOMA-IR calculation. This is the primary metabolic efficacy metric of the entire programme. A HOMA-IR that begins at 3.8 and is tracked at 3.2 at six months, 2.1 at twelve months, and 1.4 at eighteen months tells a clear and compelling clinical story of progressive insulin sensitivity restoration.

HbA1c. This confirms the maintenance of improved glucose control over time.

Lipid panel, for TG:HDL ratio calculation. Falling triglycerides and rising HDL, producing a progressively lower TG:HDL ratio, are among the most consistent metabolic improvements produced by the combination of fasting and a low-refined-carbohydrate dietary pattern.

hsCRP (high-sensitivity C-reactive protein). The primary circulating inflammatory marker, whose progressive reduction confirms that the vascular inflammation driving endothelial dysfunction and atherosclerotic progression is being addressed.

Comprehensive metabolic panel, including electrolytes, creatinine and eGFR. Annual confirmation of sustained kidney function is important in a patient population with a history of hypertension, given the long-term renal risks of elevated blood pressure discussed in Chapter 6\.

HbA1c, fasting insulin and HOMA-IR, uric acid and liver function tests complete the annual panel.

Home Monitoring Between Clinical Panels

Home blood pressure monitoring should continue daily throughout the annual calendar, not only during fasting periods. The blood pressure trajectory across an entire year of fasting and post-fast nutrition,

tracked with consistent twice-daily measurements, provides the most complete available picture of the programme's cardiovascular impact and allows early detection of blood pressure drift that would otherwise go unnoticed between clinical appointments.

HRV monitoring through a consumer wearable device, tracked daily, provides a continuous window into autonomic balance. Progressive improvement in HRV over the year of the programme, with measurable responses to each fasting period, is objective real-time evidence of the autonomic nervous system reset described in Chapter 6\.

Resting heart rate, equally accessible through any wearable device or simple pulse palpation, should show a sustained reduction from baseline as vagal tone is progressively restored. The difference between a resting heart rate of 82 at programme onset and 62 at twelve months represents more than 10 million fewer heartbeats per year and a measurably reduced lifetime cardiac workload.

9.5 Medication Tapering After the Extended Fast

For most hypertensive patients who have completed an extended fast with significant blood pressure reduction, the question of whether and how to taper antihypertensive medications in the post-fast period is one of the most practically important questions of the entire programme. It is also one that must be answered individually, under physician supervision, based on objective blood pressure data rather than a standardised schedule.

The General Principle

Antihypertensive medications should be maintained at the reduced doses established during the fast until the post-fast blood pressure has been documented as stable at the lower level for at least two to four weeks of post-fast dietary maintenance. Reducing medications during the fast itself, as described in Chapter 8, is appropriate and physician-directed. Continuing to taper medications after the fast, as blood pressure remains normalised on the post-fast dietary and fasting maintenance programme, is the logical continuation of that process.

The goal, stated explicitly, is the progressive elimination of antihypertensive pharmacotherapy (drug treatment) as the underlying metabolic drivers of hypertension are resolved. For many patients in whom hyperinsulinaemia-mediated hypertension is the primary mechanism, this goal is achievable. It has been achieved in the Goldhamer studies, in the McEachen series, in the DeVries clinical data, and in the thousands of patients whose blood pressure normalised permanently under supervised fasting programmes when they maintained appropriate post-fast nutrition and lifestyle.

For some patients, particularly those with secondary forms of hypertension (hypertension driven by specific identifiable causes other than insulin resistance, such as primary hyperaldosteronism, renal artery stenosis or phaeochromocytoma), or those with significant structural cardiovascular disease, complete pharmacological independence may not be achievable or appropriate. The goal in these patients is the maximum safe reduction of antihypertensive burden, not its complete elimination.

The Tapering Schedule

Medication tapering after the fast follows a step-down approach that mirrors in reverse the step-up approach used when antihypertensive therapy was originally initiated.

In the first two to four weeks after the fast, maintain the medication doses established at the end of the fast. Continue twice-daily home blood pressure monitoring and report readings to the physician weekly. If blood pressure remains consistently below 120/80 mmHg on the reduced post-fast medication regimen, the physician will consider a further dose reduction.

At four to six weeks post-fast, if blood pressure has been stable below 120/80 mmHg consistently, the first scheduled post-fast medication reduction is made: a further halving of the dose of the most recently reduced drug, or the suspension of the least essential drug if multiple drugs are still in the regimen. The specific reduction is physician-directed and based on the medication classes involved.

The step-down continues every four to eight weeks as long as blood pressure remains well controlled. The rate of tapering is determined by the blood pressure response: if pressure remains stable at each step, the next step is taken. If pressure begins to drift upward toward 130/85 or higher, the taper pauses at the current dose until the next fasting period provides a further reset.

Recognising Permanent Normalisation

A patient who has been completely off antihypertensive medication for twelve consecutive months, with home blood pressure readings consistently below 120/80 mmHg, a HOMA-IR below 1.5, a TG:HDL ratio below 1.5, an hsCRP below 1.0 mg/L, and a resting heart rate between 55 and 65 beats per minute, has achieved what this programme is designed to produce: the permanent normalisation of blood pressure through the restoration of the physiological mechanisms that regulate it.

This is not remission. It is resolution. Remission implies that the disease is quiescent but the underlying condition persists. Resolution means the underlying condition, the chronic hyperinsulinaemia, RAAS overactivation, sympathetic dominance and endothelial dysfunction that together constituted the mechanistic reality of the hypertension, has been addressed at its roots. The blood pressure is normal because the body's regulation of blood pressure has been restored, not because a drug is managing the symptom of its dysregulation.

This outcome is achievable. It has been demonstrated clinically. It requires commitment, consistency and a long-term perspective. But it is the outcome that this programme, applied rigorously and maintained persistently, is designed to produce.

9.6 Exercise as the Essential Synergist

Chapter 6 identified regular aerobic exercise as one of the three essential pillars of sustained autonomic recovery after fasting, alongside appropriate nutrition and sleep optimisation. This section provides the specific exercise recommendations that are synergistic with the fasting programme.

Why Exercise and Fasting Are Synergistic

The mechanisms through which regular aerobic exercise contributes to blood pressure normalisation are distinct from, but complementary to, the mechanisms of fasting:

Exercise-induced shear stress (the mechanical force of flowing blood on the arterial wall) is the primary stimulus for eNOS expression and nitric oxide production in the vascular endothelium. Regular aerobic exercise is the most potent known stimulus for endothelial nitric oxide production, more potent than any pharmaceutical intervention in this regard. The endothelial repair that fasting initiates through autophagy and reduced inflammatory burden is amplified and sustained by the regular shear stress signal of aerobic exercise.

Exercise training progressively increases HRV and vagal tone through multiple mechanisms including baroreceptor resensitisation, improved cardiac autonomic regulation, and reduced sympathetic nervous system reactivity to psychological stressors. The vagal tone restoration that fasting produces is deepened and extended by regular aerobic exercise training.

Exercise improves insulin sensitivity in skeletal muscle through GLUT4 translocation (the movement of glucose transporter proteins to the muscle cell surface in response to muscle contraction, which allows glucose uptake independent of insulin) and through exercise-induced improvements in mitochondrial density and function. This exercise-mediated insulin sensitisation is additive to the fasting-mediated insulin sensitisation, producing combined improvements in insulin sensitivity that exceed what either intervention achieves alone.

Exercise reduces visceral fat, the source of the leptin excess and adipokine dysregulation that contributes to sympathetic overactivation and insulin resistance, through its caloric expenditure effects and through specific metabolic signals that preferentially mobilise visceral over subcutaneous fat.

Exercise Recommendations

For the post-fast maintenance programme, the following exercise framework is recommended:

Aerobic exercise of moderate intensity (defined as exercise at 50 to 70% of maximum heart rate, where maximum heart rate is approximately 220 minus age in years) for a minimum of 150 minutes per week, distributed across at least four sessions. This can be accumulated as 30 to 40-minute sessions of brisk walking, cycling, swimming, rowing, light jogging, or any sustained moderate-intensity cardiovascular activity. The specific modality matters far less than the consistency and the intensity being sufficient to produce measurable cardiovascular work without exceeding safe bounds.

Brisk walking is the most accessible and practically sustainable form of aerobic exercise for the majority of hypertensive patients, as Bragg and DeVries both emphasised consistently and as the clinical exercise physiology literature confirms. A brisk walk at a pace that produces mild breathlessness and warmth but allows comfortable conversation (the "talk test" threshold) is operating at the correct moderate intensity for cardiovascular benefit. The daily 30 to 45-minute walk recommended in Chapter 8 during the later days of extended fasting should transition seamlessly into a regular post-fast walking practice that is maintained year-round.

Resistance exercise (also called strength training or weight training: exercise that works muscles against an external resistance to build or maintain muscle mass and strength) is a valuable addition to the aerobic exercise foundation. Skeletal muscle is the primary tissue for insulin-stimulated glucose disposal, and maintaining or increasing muscle mass through resistance exercise directly improves total

body insulin sensitivity by increasing the volume of insulin-responsive tissue. For hypertensive patients, resistance exercise should be performed at moderate intensity, avoiding the sustained breath-holding and extreme effort levels (called the Valsalva manoeuvre in its deliberate form) that can transiently elevate blood pressure significantly during very heavy lifting. Two to three resistance training sessions per week, targeting major muscle groups with moderate loads and comfortable effort levels, is the recommended starting framework.

Zone 2 training deserves specific mention as it has received growing clinical and research attention for its metabolic benefits. Zone 2 is defined as the exercise intensity at which the body is primarily burning fat for fuel, operating aerobically at a sustainable pace, typically at heart rates of 60 to 75% of maximum. At this intensity, mitochondrial biogenesis (the generation of new mitochondria, the cellular organelles responsible for aerobic energy production) is maximally stimulated, insulin sensitivity improvements are greatest, and the metabolic adaptations that support long-term cardiovascular health are most deeply developed. Long-duration Zone 2 sessions of 45 to 60 minutes, two to three times per week, are the most metabolically productive form of aerobic exercise for the specific goals of this programme and are increasingly used by sports medicine physicians and metabolic health clinicians for exactly this reason.

Exercise and the Fasting Calendar

Exercise should be suspended or significantly reduced during the fasting periods of the annual calendar, as discussed in Chapter 8\. The physiological rationale is clear: during fasting, the body's energy resources are directed toward autolytic, regenerative and immunological renewal processes that benefit from rest. Exercise during fasting diverts energy and physiological attention away from these processes.

The day immediately following the breaking of a short fast (24 or 36 to 48 hours) can include a gentle walk. Exercise should be reintroduced gradually after longer fasts: no structured exercise in the first two days of refeeding after a 5 to 7-day fast, light walking from Day 3 of refeeding, and progressive return to the full exercise programme from Day 5 to 7 of refeeding as energy and physical capacity return.

9.7 Sleep Optimisation as the Third Pillar

Chapter 6 established sleep as a critical determinant of autonomic balance, nocturnal blood pressure dipping, and cardiovascular repair. The post-fast maintenance programme includes specific sleep optimisation strategies that are both directly blood-pressure-relevant and synergistic with the metabolic and autonomic benefits of fasting and exercise.

Sleep Duration

The evidence base for sleep duration and cardiovascular health is consistent and compelling. Adults sleeping fewer than six hours per night have a significantly higher risk of hypertension, cardiovascular events and metabolic syndrome than those sleeping seven to nine hours. Short sleep duration directly impairs insulin sensitivity (a single night of partial sleep deprivation, defined as four to five hours rather than eight hours, reduces insulin sensitivity by approximately 25% the following day), activates the HPA axis (raising cortisol), increases sympathetic tone, and impairs the nocturnal blood pressure dipping that is essential for cardiovascular repair.

The target sleep duration for the post-fast maintenance programme is seven to nine hours of quality sleep per night for adults. This is not a recommendation to spend more time in bed; it is a recommendation to protect adequate sleep duration from the scheduling pressures and electronic device habits that progressively erode it in modern life.

Sleep Quality

Duration alone is insufficient if sleep quality is poor. Deep slow-wave sleep (also called NREM Stage 3 sleep, the sleep stage associated with the greatest physical restoration, growth hormone release and immune function support) and REM sleep (rapid eye movement sleep, associated with memory consolidation, emotional processing and cognitive restoration) must both be adequately represented in a night's sleep for its full restorative function to be achieved.

Sleep quality is impaired by: alcohol consumption (which fragments sleep architecture, suppresses REM sleep and increases sympathetic activity in the second half of the night despite the initial sedative effect), caffeine consumed after midday (whose half-life of approximately five to six hours means that a 4 pm coffee is still significantly pharmacologically active at 10 pm), electronic screen exposure in the two hours before bed (blue light from screens suppresses melatonin secretion and delays sleep onset), room temperature that is too warm (the body needs to reduce its core temperature by approximately 1 degree Celsius to initiate sleep, which is why a cool sleeping environment is biologically optimal), and irregular sleep and wake times that disrupt the circadian rhythm governing sleep architecture.

Obstructive Sleep Apnoea

Obstructive sleep apnoea, described in Chapter 6 as one of the most common causes of resistant hypertension, must be specifically screened for and addressed in the post-fast maintenance programme. The post-fast reduction in visceral fat reduces one of the primary anatomical contributors to OSA (fat deposition in the pharyngeal tissues, the throat area, that narrows the upper airway during sleep). For patients with OSA whose apnoea is primarily driven by obesity, the combination of extended fasting, post-fast dietary maintenance and regular exercise that progressively reduces visceral fat is a potentially disease-modifying intervention, not just a symptomatic management strategy.

For patients with significant OSA that does not fully resolve with fat loss, Continuous Positive Airway Pressure (CPAP) therapy, which delivers a continuous stream of pressurised air through a mask to keep the upper airway open during sleep, is the most effective and evidence-based treatment available. CPAP therapy in OSA-related resistant hypertension consistently reduces blood pressure by a clinically meaningful 2 to 8 mmHg systolic, reduces sympathetic nervous system activity through its resolution of the nocturnal sympathetic surges of apnoeic episodes, and significantly improves nocturnal blood pressure dipping. Its role in the overall hypertension management programme of an OSA patient is therefore not optional: it is an essential complementary intervention.

9.8 Psychological Sustainability: Maintaining the Programme Long-Term

A therapeutically sound programme that is not psychologically sustainable is a programme that will not be followed. Long-term adherence to the fasting maintenance calendar and post-fast nutritional

principles requires more than scientific understanding and clinical motivation. It requires a realistic, compassionate and practical approach to the psychological dimensions of sustained lifestyle change.

Identity and Framing

The most durable dietary and lifestyle changes are those that are grounded in a shift of identity rather than a temporary modification of behaviour. The patient who frames the post-fast programme as "I am on a restrictive diet to manage my blood pressure" is drawing on willpower and self-denial as their primary resource. Willpower is a finite resource, and self-denial as a motivational framework consistently fails over the medium to long term because it frames the desired behaviour as a sacrifice.

The patient who frames the post-fast programme as "I am someone who eats whole foods because I understand how food affects my physiology, and I fast regularly because I have experienced its effects directly" is drawing on identity and understanding as their resource. Identity and understanding are not depleted by use in the way willpower is. They strengthen with consistent reinforcement.

This reframing is not a psychological trick. It is the recognition that the programme described in this book is not a medical restriction imposed on a patient's preferred life. It is the restoration of the eating and living patterns that the human body evolved in and that chronic disease represents a departure from. Understanding this, not just intellectually but experientially through the transformative subjective experience of the fast itself, is the foundation of sustainable long-term adherence.

Managing Social Eating

Social eating is one of the most practically challenging aspects of maintaining a whole-food dietary pattern in a world organised around ultra-processed food. Celebrations, family meals, work events, travel and restaurants all create contexts in which the available food choices may not align with the post-fast nutritional principles.

The key principle for social eating is distinction between genuine deviation and strategic flexibility. Genuine deviation means regularly and habitually consuming refined carbohydrates, sugars and ultra-processed foods in social contexts, using the social context as a justification for returning to the dietary pattern that produced the hypertension. This is a pattern that progressively erodes the metabolic gains of the fasting programme and should be recognised and named clearly.

Strategic flexibility means navigating social food contexts with intelligence: choosing the best available options from a restaurant menu, prioritising protein and vegetables over refined carbohydrate dishes, declining the bread basket and the dessert without drama or explanation, and accepting that occasional genuine social meals in contexts where the available food is not ideal are not metabolically catastrophic when the overall pattern across the week is sound.

The weekly 24-hour fast is itself a powerful tool for managing the metabolic consequences of social eating: if a social event on a Friday evening involves foods outside the ideal framework, the Saturday fast day provides an automatic reset that prevents a single social deviation from compounding into a sustained metabolic drift.

Working With a Physician Who Understands This Programme

One of the greatest practical barriers to implementing the programme described in this book is finding a physician who is willing to engage with it seriously. Standard medical education does not include therapeutic fasting, insulin measurement in non-diabetic patients, or metabolic root cause analysis of hypertension at the level described in these pages. Many physicians will have been trained to treat blood pressure as a number to be managed pharmacologically, and the suggestion from a patient that they intend to fast therapeutically and taper their antihypertensive medications may be received with scepticism, resistance or flat refusal.

This is not a personal failing of individual physicians. It is a structural feature of a medical education and a healthcare incentive system that is organised around acute pharmacological management rather than metabolic root cause resolution. Understanding this allows patients to approach the conversation with their physicians constructively rather than adversarially.

The most productive approach is to bring the physician into the programme explicitly and systematically. Share the pre-fast assessment plan from Chapter 7\. Request the specific laboratory tests needed. Provide the blood pressure monitoring data from each fasting period. Present the metabolic panel results showing the progressive improvement in HOMA-IR, TG:HDL ratio and hsCRP. Allow the objective data to do the advocacy. A physician who sees a patient's blood pressure move from 158/96 on three medications to 112/72 on one medication, with a HOMA-IR that has fallen from 3.9 to 1.3 over twelve months, is seeing clinical evidence that cannot be dismissed regardless of their prior theoretical orientation toward fasting.

Chapter Summary: Key Points

The post-fast window is simultaneously the period of greatest metabolic opportunity and greatest vulnerability. The insulin sensitivity achieved during the fast means that dietary choices in the first four weeks after refeeding have a disproportionate influence on whether the metabolic gains of fasting are consolidated or eroded.

The five nutritional principles of post-fast maintenance are: eliminating the primary drivers of hyperinsulinaemia (refined carbohydrates, added sugars, ultra-processed foods) without exception; building the diet around foods that sustain insulin sensitivity (non-starchy vegetables, legumes, whole grains, healthy fats from whole food sources, quality proteins); protecting and nourishing the gut microbiome through dietary fibre diversity and fermented foods; managing sodium by eliminating ultra-processed food sources rather than obsessively restricting cooking salt; and managing eating patterns through time-restricted eating to provide daily insulin normalisation alongside the weekly and monthly fasting calendar.

The annual fasting calendar has three tiers: weekly 24-hour maintenance fasts providing continuous metabolic recalibration, monthly 36 to 48-hour intermediate fasts providing deeper monthly renewal, and quarterly or biannual 5 to 14-day deep therapeutic fasts providing the comprehensive physiological reset that produces the most dramatic and durable blood pressure normalisation.

Medication tapering after the extended fast follows a physician-directed step-down approach based on consistent blood pressure monitoring. The goal, achievable for most patients with hyperinsulinaemia-mediated hypertension, is the progressive and permanent elimination of

antihypertensive pharmacotherapy as the underlying metabolic mechanisms of hypertension are resolved rather than merely managed.

Exercise and sleep are essential synergistic pillars of the post-fast maintenance programme. Regular aerobic exercise amplifies and sustains the endothelial, autonomic and insulin-sensitising benefits of fasting. Adequate sleep duration and quality are prerequisites for sustained insulin sensitivity, nocturnal blood pressure dipping and cardiovascular repair. Obstructive sleep apnoea must be specifically identified and addressed.

Long-term adherence is grounded in identity and understanding rather than willpower and self-denial, and in the strategic management of social eating and physician relationships that allows the programme to be maintained sustainably across years rather than followed intensively and then abandoned.

The patient who completes this programme, who fasts consistently, eats whole foods persistently, exercises regularly and sleeps adequately, who monitors their metabolic markers and adjusts their programme based on what the data shows, is not managing a chronic disease. They are in the process of resolving it.

> *“We are what we repeatedly do. Excellence, then, is not an act but a habit.”*
>
> — Will Durant, paraphrasing Aristotle

The annual fasting calendar is not a schedule of extraordinary interventions. It is the architecture of a new ordinary. A life in which fasting is as unremarkable as sleep, in which whole food is as habitual as breathing, and in which the body's blood pressure is a reflection of its genuine physiological state rather than the product of pharmaceutical management.

PART FOUR: SPECIAL CONSIDERATIONS

Individual Variation, Comorbidities and Clinical Nuance

CHAPTER 10

Hypertension With Comorbidities, Adapting The Protocol

“It is more important to know what sort of person has a disease than to know what sort of disease a person has.”

— Hippocrates

Opening: The Patient Is Never Just a Blood Pressure Number

Throughout the preceding chapters, the clinical argument for therapeutic water fasting as a root-cause intervention for hypertension has been built on mechanisms: the insulin-RAAS-sympathetic triangle, the endothelial dysfunction cascade, the autonomic imbalance, and the comprehensive physiological reset that fasting produces across all of these simultaneously. The argument is sound, the evidence is substantial, and the clinical outcomes documented across decades of supervised fasting practice are compelling.

But patients do not present as isolated blood pressure numbers. They present as complete human beings whose hypertension exists alongside other conditions, other medications, other physiological vulnerabilities, and other clinical histories that modify how fasting should be applied, how intensively it should be supervised, how long individual fasts should extend, and what specific monitoring is required to keep the intervention safe while preserving its therapeutic power.

This chapter addresses the four most clinically significant comorbidities that co-exist with hypertension in the population most likely to read this book: obesity and metabolic syndrome, Type 2 diabetes, chronic kidney disease, and established cardiovascular disease. For each comorbidity, the chapter provides a precise analysis of how the comorbidity modifies the fasting protocol, what additional monitoring is required, what contraindications or absolute limits apply, and what the evidence shows about fasting's specific therapeutic effects in that population.

The chapter closes with a brief section on hypertension in women and hormonal considerations, which serves as a bridge to the full treatment of that subject in Chapter 11\.

The governing principle across all of these modifications is the same principle that governs the standard protocol: the goal is maximum therapeutic benefit at minimum risk, achieved through precise clinical assessment, appropriate supervision intensity, and protocol adaptation that is as conservative as the specific clinical situation requires and as ambitious as safety allows.

The presence of a comorbidity does not automatically make fasting less appropriate. In many cases it makes fasting more clinically relevant. The question is rarely whether therapeutic fasting should be considered. The question is how the protocol should be adapted to match the patient's specific physiological circumstances.

10.1 Hypertension with Obesity and Metabolic Syndrome

The Most Favourable Fasting Candidates

If there is a patient population for whom therapeutic water fasting is most powerfully and most comprehensively indicated, it is the hypertensive patient with concurrent obesity and metabolic syndrome. This is not a paradox, though it might initially appear to be one: how can the patients who are the most metabolically compromised also be the patients most suited to the most demanding intervention? The answer lies in understanding what metabolic syndrome is and what fasting specifically targets within it.

Metabolic syndrome is a clinical cluster of five interconnected abnormalities: central obesity (waist circumference above 102 centimetres in men and above 88 centimetres in women), elevated fasting triglycerides (above 1.7 mmol/L), reduced HDL cholesterol (below 1.0 mmol/L in men and below 1.3 mmol/L in women), elevated fasting glucose (above 5.6 mmol/L), and hypertension (blood pressure above 130/85 mmHg). The clinical diagnosis requires any three of the five. The underlying driver, as the reader of this book will now immediately recognise, is insulin resistance and the chronic hyperinsulinaemia that both causes and is caused by it.

Metabolic syndrome is not a collection of five independent problems that happen to occur together. It is five clinical expressions of the same underlying metabolic disorder, manifesting simultaneously across different physiological systems. The excess weight accumulating around the abdomen, the rising triglycerides being synthesised by an insulin-resistant liver, the falling HDL reflecting impaired reverse cholesterol transport, the creeping fasting glucose signalling deteriorating pancreatic reserve, and the rising blood pressure driven by renal sodium retention and sympathetic overactivation: these are all outputs of a single metabolic dysfunction operating through multiple pathways.

Therapeutic fasting addresses that single underlying dysfunction with a comprehensiveness that no individual pharmaceutical agent can match, because no individual pharmaceutical agent addresses insulin resistance, RAAS overactivation, sympathetic excess, endothelial dysfunction, visceral inflammation and gut dysbiosis simultaneously. Fasting does. The patient with hypertension and full metabolic syndrome is not a patient with five problems requiring five separate interventions. They are a patient with one problem requiring one comprehensive physiological reset, and fasting provides precisely that.

Visceral Fat as the Primary Inflammatory Driver

Of the five components of metabolic syndrome, central obesity, the accumulation of visceral fat within and around the abdominal organs, is the most mechanistically critical. Visceral fat is not inert storage tissue. It is a metabolically active endocrine organ whose secretory products drive the entire cluster of metabolic syndrome findings.

Visceral adipocytes (fat cells in the visceral compartment) secrete elevated levels of TNF-alpha (tumour necrosis factor alpha, a potent proinflammatory cytokine), IL-6 (interleukin-6, which drives CRP production and contributes directly to insulin resistance), resistin (a hormone that directly impairs insulin receptor signalling), and leptin (whose excess, as described in Chapter 6, drives sympathetic nervous

system overactivation through hypothalamic leptin resistance). They simultaneously secrete reduced levels of adiponectin (an insulin-sensitising, anti-inflammatory hormone whose deficiency correlates strongly with insulin resistance, metabolic syndrome severity and cardiovascular risk).

The visceral fat compartment also releases free fatty acids directly into the portal circulation (the blood supply that drains the gut and goes directly to the liver), exposing the liver to a continuous high flux of fatty acids that promotes hepatic de novo lipogenesis (fat synthesis), hepatic insulin resistance, elevated triglyceride secretion, and the suppression of HDL production. The liver's insulin resistance then drives excess hepatic glucose output, raising fasting glucose and accelerating the progression toward Type 2 diabetes.

Fasting's autolytic processes, described in detail in Chapter 3, target visceral fat with particular efficiency. When the body enters the sustained fasting state and begins mobilising its own tissues for fuel, the selection hierarchy strongly favours metabolically active, less essential and structurally abnormal tissues before vital organs and structural proteins. Visceral fat, being metabolically active (and therefore energy-costly to maintain), pathologically excessive and physiologically non-essential, is among the tissues most readily and most rapidly mobilised during extended fasting.

Bragg described this process with characteristic clarity in Chapter 14 of The Miracle of Fasting: the fat deposits shrink where they are deposited, with the abdomen and hips as the primary sites of fat reduction, and the relief on the heart, lungs and metabolic organs of being freed from the excess burden is physiologically measurable in days. DeVries confirmed from the clinical evidence that fasting normalises assimilation in both directions, reducing excess weight toward normal in the overweight patient and improving nutritional utilisation in the underweight patient through the same mechanism of improved digestive and assimilative efficiency after the fast. The body does not simply lose weight on a fast; it loses the specific metabolic burden that was driving the disease.

Defining Success in the Metabolic Syndrome Patient

The success of therapeutic fasting in metabolic syndrome should not be judged by scale weight alone. The more meaningful markers are reductions in waist circumference, improvements in insulin sensitivity and progressive normalisation of the metabolic syndrome criteria themselves.

A practical target for many patients is a reduction in waist circumference sufficient to move below the diagnostic threshold for central obesity. Improvements in fasting insulin, HOMA-IR, triglycerides, HDL cholesterol and blood pressure should accompany this change. Resolution of metabolic syndrome occurs when fewer than three diagnostic criteria remain present.

Patients with severe obesity and marked insulin resistance frequently require a more intensive fasting schedule than those with hypertension alone. Individuals with HOMA-IR values above 4.0, significant visceral adiposity and multiple metabolic syndrome criteria often benefit from repeated supervised fasting cycles across the first year rather than a single extended intervention.

The objective is not rapid weight reduction. The objective is metabolic normalisation. Weight loss is valuable primarily because it reflects the removal of the visceral fat burden driving insulin resistance, inflammation and hypertension.

Clinical Protocol Modifications for Metabolic Syndrome

The patient with hypertension and metabolic syndrome is not a patient who requires a more cautious fasting protocol than the standard. They are a patient who is likely to require a more intensive one, because their metabolic burden is higher and the therapeutic gains from extended fasting are proportionally greater.

The standard protocol of Chapters 7 and 8 applies in full, with the following specific emphases:

Baseline assessment is particularly important in this population because the combination of hypertension, glucose abnormalities, dyslipidaemia (abnormal blood lipid levels), and potential undetected fatty liver disease (non-alcoholic fatty liver disease is extremely common in metabolic syndrome and is itself a driver of insulin resistance) means that the pre-fast laboratory panel must be comprehensive and must include liver function tests, uric acid (which is frequently elevated in metabolic syndrome and can rise acutely during the first days of fasting as purine catabolism increases, precipitating a gout attack in susceptible patients), and HbA1c alongside the standard panel.

Medication management is complex in metabolic syndrome because these patients are typically on multiple medications: antihypertensives, statins (cholesterol-lowering medications), and in many cases early glucose-lowering agents. The Chapter 7 medication guidance applies in full, with particular attention to diuretics (which must be suspended before extended fasting given the natriuresis of fasting itself) and statins (which do not require suspension for fasting but whose dose may need review as the TG:HDL ratio normalises, since statins are frequently prescribed primarily for triglyceride-driven dyslipidaemia that resolves with fasting and post-fast dietary management).

The annual fasting calendar of Chapter 9 should be applied ambitiously in this population, within the bounds of physician-supervised safety. Patients with full metabolic syndrome and significant obesity typically require more cumulative fasting across the first year than patients with hypertension alone, both to achieve the initial metabolic reset and to sustain it. Three extended fasts in the first year (rather than the two recommended as a starting framework in Chapter 9\) may be appropriate for patients whose HOMA-IR exceeds 4.0 and whose metabolic syndrome is clinically severe, subject to physician judgment.

10.2 Hypertension with Type 2 Diabetes

Fasting as the Superior Intervention

Type 2 diabetes and hypertension co-exist in the same patient so frequently, and for such mechanistically clear reasons, that encountering one in clinical practice demands active investigation for the other. Both are downstream expressions of insulin resistance and hyperinsulinaemia. Both are accelerated by visceral adiposity, gut dysbiosis, sleep disruption and physical inactivity. Both are managed in conventional medicine with separate pharmaceutical agents that address their respective symptoms without engaging the shared metabolic root cause.

Dr. Jamnadas has argued, with the weight of both mechanistic reasoning and clinical evidence behind him, that therapeutic fasting is not merely one intervention among several for Type 2 diabetes but is in

important respects the most physiologically appropriate intervention available, because it is the only intervention that directly and rapidly reverses the chronic hyperinsulinaemia that is simultaneously the primary driver of the diabetes and the primary driver of the hypertension. No pharmaceutical agent reverses both. Fasting does.

The clinical evidence for fasting in Type 2 diabetes extends back more than a century. The French clinician A. Guelpa, working in Paris in the early twentieth century, documented that three to four consecutive days of fasting rendered the urine of patients with severe diabetes completely sugar-free, with pronounced improvement in their general health and no aggravation of the disease in any case. His findings, recorded in the British Medical Journal in 1910 and cited by DeVries in Therapeutic Fasting, established the foundational clinical observation that the diabetic metabolic abnormality is acutely and dramatically responsive to fasting.

Dr. Frederick Allen, working at the Rockefeller Institute in New York, built on this foundation with his systematic "starvation treatment" of diabetes in 1915\. His carefully controlled clinical work demonstrated a 60% reduction in deaths from diabetic coma through fasting combined with restricted dietary intake, at a time when insulin had not yet been discovered and no pharmaceutical treatment for diabetes existed. Hundreds of his patients with what would now be classified as Type 2 diabetes responded favourably, with the majority ceasing to excrete glucose in their urine within 48 to 60 hours of fasting initiation. Allen's work, also cited by DeVries, established that the pancreatic glucose management defect of diabetes is not fixed and irreversible but is highly responsive to the removal of the dietary glucose and insulin stimulus that drives it.

In the modern era, the evidence has deepened substantially. The work of Dr. Jason Fung and colleagues, published in peer-reviewed journals including the Journal of Nutrition and Metabolism, has documented complete remission of Type 2 diabetes through therapeutic fasting protocols combined with low-carbohydrate dietary management, with patients who had been on insulin for years achieving medication-free normal glucose control. The DIRECT trial (Diabetes Remission Clinical Trial), published in The Lancet in 2018, demonstrated that a very low-calorie dietary intervention produced Type 2 diabetes remission, defined as HbA1c below 48 mmol/mol without glucose-lowering medication, in 46% of participants at 12 months, with those who lost the most weight having the highest remission rates. While DIRECT used caloric restriction rather than water fasting specifically, its demonstration of meaningful diabetes remission through metabolic intervention rather than pharmaceutical management is directly relevant.

For the hypertensive patient with Type 2 diabetes, the fasting programme represents not two separate therapeutic targets but one intervention that addresses both conditions simultaneously through their shared root cause.

Glucose Monitoring: The Non-Negotiable Requirement

The management of blood glucose during fasting in the Type 2 diabetic patient is the single most important safety modification required in this population, and it is non-negotiable. Hypoglycaemia (abnormally low blood glucose, defined clinically as a blood glucose below 4.0 mmol/L, with symptomatic hypoglycaemia typically occurring below 3.5 mmol/L) is the primary acute safety risk of

fasting in Type 2 diabetic patients on glucose-lowering medications, and it is entirely preventable with adequate monitoring and pre-fast medication adjustment.

Blood glucose must be measured at a minimum of every four hours during all fasting periods in Type 2 diabetic patients, including overnight when the risk of nocturnal hypoglycaemia is real. This requires a reliable home glucose monitor and the discipline to set an overnight alarm to check glucose at 2 to 3 am during extended fasts. Continuous glucose monitors (CGMs, devices worn on the skin that measure interstitial glucose continuously and display readings in real time on a smartphone, such as the Dexterity, FreeStyle Libre or Dexcom systems) dramatically simplify and improve glucose monitoring during fasting and are strongly recommended for any Type 2 diabetic patient undertaking fasting beyond 24 hours. The CGM provides continuous visibility of glucose trends rather than periodic snapshots, allowing early detection of a falling glucose trajectory before frank hypoglycaemia is reached.

Symptoms of hypoglycaemia include trembling or shakiness, sweating, palpitations (awareness of a rapid or irregular heartbeat), pallor, hunger (distinct from the general appetite reduction that develops after the first two to three days of fasting), anxiety, confusion, difficulty concentrating, and in severe cases, loss of consciousness. Any Type 2 diabetic patient experiencing these symptoms during fasting must check their glucose immediately and, if below 4.0 mmol/L, must break the fast with a small amount of readily absorbed glucose (fresh fruit juice, for example) and contact their supervising physician before resuming fasting.

Medication Reduction: Mandatory Before Fasting

The second non-negotiable modification for Type 2 diabetic patients undertaking fasting is proactive, physician-directed dose reduction or suspension of insulin and sulphonylurea medications before the fast begins.

Insulin (whether short-acting, intermediate-acting or long-acting) continues to lower blood glucose regardless of whether food is being consumed. When food intake ceases during fasting, the ongoing action of insulin in the absence of dietary glucose creates a direct and predictable risk of hypoglycaemia. This risk does not arise from the fasting itself: the fasting body manages glucose through gluconeogenesis (the liver's synthesis of glucose from non-carbohydrate precursors including amino acids and glycerol) and maintains glucose within a functional range in the absence of insulin. The risk arises from the combination of fasting and unchanged insulin dosing, which is why unchanged insulin dosing during fasting is clinically unacceptable.

The specific insulin dose adjustment depends on the type of insulin, the current dose, and the patient's baseline glucose control, and must be determined by the prescribing physician before the fast begins. General guidance from the fasting medicine literature, subject always to physician individualisation, suggests: suspension of short-acting or rapid-acting insulin during the fast (as these insulins are designed to cover meal-related glucose rises that do not occur during fasting), and significant reduction of long-acting basal insulin (typically 50 to 80% of the usual dose) with close glucose monitoring to titrate further. This is physician territory, not patient self-management territory.

Sulphonylureas (oral medications that stimulate pancreatic insulin secretion regardless of blood glucose level, including glibenclamide, gliclazide, glipizide, and glimepiride) carry the same hypoglycaemia risk

during fasting as insulin, because they drive insulin secretion even when glucose is falling. Sulphonylureas should be suspended completely before fasting in all patients, with the specific timing of suspension (24 to 48 hours before the fast, depending on the specific agent and its duration of action) determined by the prescribing physician.

Metformin, as noted in Chapter 7, should be suspended 24 to 48 hours before extended fasting to reduce the risk of lactic acidosis (a rare but serious metabolic complication in which lactic acid accumulates in the blood, caused by metformin's suppression of hepatic lactate clearance in states of metabolic stress, including prolonged fasting). Metformin does not cause hypoglycaemia itself but carries this separate and distinct risk during fasting.

SGLT2 inhibitors (sodium-glucose cotransporter-2 inhibitors, medications that lower glucose by blocking its reabsorption in the kidney and excreting it in the urine, including empagliflozin, dapagliflozin and canagliflozin) carry a specific and underappreciated risk during fasting: euglycaemic diabetic ketoacidosis (DKA occurring at normal or near-normal glucose levels, making it much harder to detect because the usual warning sign of very high glucose is absent). SGLT2 inhibitors should be suspended a minimum of 72 hours before any extended fast and their resumption should be discussed with the prescribing physician at the end of the refeeding period.

The Target: Medication Reduction Correlated with Metabolic Improvement

The therapeutic goal for hypertensive Type 2 diabetic patients undertaking the fasting programme is progressive reduction and ultimately elimination of glucose-lowering and antihypertensive medications as the underlying insulin resistance resolves. This goal has been achieved in documented clinical practice, is supported by the evidence base cited above, and is mechanistically coherent: when the insulin resistance that drives both conditions is resolved through the physiological reset of repeated therapeutic fasting combined with the post-fast nutritional framework of Chapter 9, the pharmacological management of their consequences becomes progressively redundant.

Progress toward this goal should be tracked through the same laboratory markers described in Chapter 9: HOMA-IR, HbA1c, fasting glucose, TG:HDL ratio, and blood pressure, monitored at six-monthly intervals and after each extended fast. Medication reduction at each step should be physician-directed and correlated with measurable improvement in these objective markers, not with the patient's subjective sense of wellbeing alone.

10.3 Hypertension with Chronic Kidney Disease

The Most Challenging Comorbidity

Chronic kidney disease (CKD) represents the most clinically complex comorbidity for therapeutic fasting in hypertensive patients, and it demands the most conservative and carefully modified protocol of any condition addressed in this chapter.

The kidneys' role in fasting physiology is central and multidirectional. During fasting, the kidneys are among the most metabolically active organs: they handle the increased electrolyte flux of fasting natriuresis (the excretion of sodium that produces much of fasting's acute blood pressure reduction),

they manage the increased urea load produced by protein catabolism during extended fasting (urea is the nitrogenous waste product of amino acid breakdown, filtered and excreted by the kidneys), they adjust acid-base balance as ketone production increases (ketones are mildly acidic, and the kidneys buffer the resulting metabolic acidosis through bicarbonate reabsorption and ammonium excretion), and they respond to the RAAS changes of fasting through their central role in that system.

In a patient with normal kidney function, these demands are managed without difficulty. In a patient with CKD, the kidneys' reduced reserve capacity means that the same demands can stress an already compromised system in ways that require careful management.

The clinical staging of CKD (by eGFR, the estimated glomerular filtration rate, which measures how efficiently the kidneys are filtering blood) directly determines the fasting approach:

Stage 1 CKD (eGFR above 90, with evidence of kidney damage such as proteinuria but normal or near-normal filtration): Standard fasting protocols apply with enhanced electrolyte and creatinine monitoring. Therapeutic fasting at this stage, by reducing blood pressure, insulin resistance and inflammatory burden, is genuinely disease-modifying and may slow CKD progression measurably.

Stage 2 CKD (eGFR 60 to 89): Standard protocols with intensive monitoring. Electrolyte panels every two days during extended fasts rather than every three to four days as in the general population.

Stage 3 CKD (eGFR 30 to 59): Modified protocol required. Maximum initial fast duration of 24 to 48 hours. Multiple short fasts rather than extended fasts, with physician assessment between each. Electrolyte panels before breaking each fast.

Stage 4 CKD (eGFR 15 to 29): This is a relative contraindication for fasting beyond 24 hours. The impaired capacity to handle electrolyte shifts, urea loads and acid-base changes makes extended fasting genuinely dangerous in this population without specialised nephrology (kidney specialist) supervision. Short 24-hour fasts may be considered under joint nephrology and fasting medicine supervision for selected patients.

Stage 5 CKD (eGFR below 15, including dialysis patients): This is an absolute contraindication for therapeutic water fasting beyond short-duration (24-hour) supervised fasts in most cases.

The Protein Catabolism Concern

During extended fasting, the body derives energy partly from the breakdown of amino acids through gluconeogenesis, producing urea as a metabolic byproduct. In patients with normal kidney function, this increased urea load is handled without difficulty by the kidneys' substantial filtration reserve. In CKD patients, whose filtration reserve is already reduced, the additional urea load of extended fasting can drive a clinically significant rise in blood urea nitrogen (BUN) and creatinine, the primary laboratory markers of kidney function and waste product accumulation.

This rise does not necessarily indicate worsening CKD: it may reflect the temporary increase in protein catabolism that occurs during the initial phase of fasting before the body fully adapts to fat-based and ketone-based fuel. However, distinguishing a transient fasting-related rise in BUN and creatinine from genuine acute kidney injury requires laboratory monitoring and physician judgment. This is why the

monitoring frequency recommendation for CKD patients during fasting is higher than for the general population, and why extended fasting beyond 48 hours in Stage 3 CKD and beyond 24 hours in Stage 4 CKD requires specialised supervision.

Renal Improvements with Therapeutic Fasting

Despite the cautions above, the evidence that therapeutic fasting can be genuinely beneficial for early-stage CKD in the context of hypertension is meaningful and should not be obscured by an exclusively risk-focused discussion.

The primary driver of CKD progression in hypertensive patients is sustained elevated glomerular pressure (the blood pressure within the kidney's filtering units, the glomeruli), which over years produces glomerulosclerosis (scarring of the filtering structures) and progressive loss of filtering capacity. Blood pressure normalisation is the single most effective intervention known for slowing CKD progression: a reduction of 10 mmHg systolic blood pressure reduces the rate of CKD progression by approximately 30%.

The blood pressure reductions achieved with therapeutic fasting in the Goldhamer studies (averaging 37 mmHg systolic) and the McEachen series (141 hypertensive patients, zero complete failures) therefore represent, in patients with co-existing early CKD, not only a cardiovascular benefit but a direct renal protective intervention of the first order. A fasting programme that normalises blood pressure from 158/96 to 118/74 is simultaneously removing the primary mechanical driver of kidney damage in a hypertensive CKD patient.

Additionally, insulin resistance is itself a direct driver of CKD progression, independent of blood pressure, through multiple mechanisms including direct effects on glomerular mesangial cells (the structural cells within the kidney's filtering units), promotion of oxidative stress and inflammation within the kidney, and RAAS overactivation that increases glomerular pressure. The insulin-normalising effects of fasting therefore provide a second independent pathway through which fasting may slow CKD progression in insulin-resistant hypertensive patients.

The clinical conclusion: for Stage 1 and Stage 2 CKD, therapeutic fasting under appropriate supervision is not merely safe but genuinely disease-modifying and should be strongly considered. For Stage 3 CKD, a modified and intensively monitored fasting approach under joint supervision is warranted for motivated patients whose clinical situation allows it. For Stage 4 and Stage 5 CKD, the approach requires specialised nephrology input and individual clinical judgment.

10.4 Hypertension with Cardiovascular Disease (Post-MI, Heart Failure)

The Most Intensive Supervision Requirement

Established cardiovascular disease, defined here as a history of myocardial infarction (MI, a heart attack, the death of heart muscle tissue due to arterial blockage), heart failure (a condition in which the heart's pumping function is impaired, reducing its ability to meet the body's circulatory demands), significant coronary artery disease (narrowing of the coronary arteries supplying blood to the heart muscle), or stroke, represents the clinical population in whom therapeutic fasting is most powerfully

indicated by the mechanistic evidence and simultaneously most demanding in terms of supervision requirements.

The paradox is only apparent. Established cardiovascular disease is the end-stage consequence of the same insulin resistance, hyperinsulinaemia, RAAS overactivation, endothelial dysfunction and sympathetic excess that fasting addresses. These patients have the most to gain from reversing these drivers because their cardiovascular system has already been demonstrably damaged by them. But their existing cardiovascular compromise means that the physiological demands of fasting (the haemodynamic changes, electrolyte shifts, and autonomic flux of the early fasting period) must be navigated with greater clinical care than in patients whose cardiovascular system remains intact.

What the Evidence Shows

DeVries, drawing on the accumulated clinical experience of the supervised fasting movement, made a statement in Therapeutic Fasting that deserves to be quoted directly in its clinical implication: the heart, far from being weakened or threatened by fasting, is given a physiological rest during the fast and gains new strength from that rest. Serious heart disease, he documented from the clinical records of practitioners including Shelton, Weger and Hay, has actually recovered while fasting, through the same mechanisms of reduced cardiac workload, improved coronary circulation, and resolution of the inflammatory and metabolic burden on the myocardium (the heart muscle) that drive progressive cardiac deterioration.

The physiological rationale is sound: the fasting heart operates on a more efficient fuel. Ketone bodies (BHB and acetoacetate) are the heart's preferred fuel over glucose and even over fatty acids in metabolic stress states, producing more ATP (adenosine triphosphate, the cell's energy currency) per unit of oxygen consumed. A heart that is running on ketones during an extended fast is a more energetically efficient heart, experiencing less oxidative stress per unit of work performed and benefiting from the anti-inflammatory effects of BHB's NLRP3 inhibition that are occurring simultaneously.

The reduction in cardiac preload (the volume of blood returning to the heart) and afterload (the resistance against which the heart pumps) produced by fasting's natriuresis, vasodilation and blood pressure reduction directly reduces the mechanical demands on a compromised heart. The sympathetic withdrawal of the mid-to-late fast period reduces heart rate, lowers myocardial oxygen demand, and reduces the arrhythmia risk associated with sustained sympathetic overactivation.

Heart Failure: Distinguishing Stable from Unstable Disease

Heart failure deserves separate consideration from myocardial infarction because the physiological challenges are different. The patient recovering from an infarction is healing damaged myocardium. The patient with heart failure is living with impaired cardiac function, often for years, and may have either preserved or reduced ejection fraction.

Heart failure with preserved ejection fraction (HFpEF), common among older hypertensive patients with obesity and metabolic syndrome, is characterised primarily by impaired ventricular relaxation and increased ventricular stiffness rather than impaired pumping strength. These patients often exhibit severe insulin resistance, chronic inflammation, sympathetic overactivation and endothelial dysfunction,

all of which are directly targeted by fasting interventions.

Heart failure with reduced ejection fraction (HFrEF), by contrast, involves impaired pumping capacity and requires considerably greater caution. The haemodynamic adaptations of fasting, particularly natriuresis and reductions in preload, may be beneficial in carefully selected stable patients but can become hazardous in those with limited cardiac reserve.

The New York Heart Association (NYHA) functional classification provides a useful framework. Patients in Class I and carefully selected Class II may be candidates for modified fasting protocols under supervision. Patients in Class III require specialist assessment before any fasting intervention is considered. Patients in Class IV, who are symptomatic at rest, should be regarded as unsuitable candidates for therapeutic fasting until stability is restored.

Particular attention must be paid to fluid balance. Fasting naturally promotes sodium and water excretion. While this effect often reduces blood pressure and relieves cardiac workload, excessive volume depletion in heart failure patients can impair renal perfusion and worsen symptoms. Monitoring of body weight, blood pressure, heart rate, electrolyte status and renal function therefore assumes greater importance in this population than in uncomplicated hypertension.

The clinical objective in heart failure is not aggressive fasting. It is careful metabolic improvement while preserving haemodynamic stability. Progress must be measured in exercise tolerance, symptom burden, medication requirements and objective cardiac markers rather than fasting duration alone.

Contraindications: Absolute and Relative

Decompensated heart failure is an absolute contraindication to therapeutic fasting. Decompensated heart failure means heart failure in which the heart's pumping function has deteriorated to the point that the body's compensatory mechanisms (neurohormonal activation, fluid retention, heart rate elevation) are no longer sufficient to maintain adequate tissue perfusion and the patient is symptomatic at rest or with minimal exertion, with evidence of fluid overload (pulmonary oedema, peripheral oedema, elevated jugular venous pressure). In this state, the haemodynamic demands and electrolyte shifts of fasting could precipitate dangerous deterioration.

Compensated heart failure, where the heart failure is clinically stable and the patient is managing daily activities with their current medication regimen, is a relative contraindication that requires individual clinical assessment rather than blanket exclusion. Some patients with stable compensated heart failure, particularly those in whom the heart failure is a consequence of hypertensive heart disease driven by insulin resistance, may be appropriate candidates for a carefully modified, intensively supervised short fasting protocol under cardiologist-involved supervision.

Myocardial infarction within the preceding three months is a relative contraindication. The period immediately following an MI is one of active myocardial healing, haemodynamic instability and neurohormonal adaptation, during which the metabolic demands of extended fasting add unnecessary physiological complexity. Beyond three months post-MI, in a patient who is haemodynamically stable on an optimised medical regimen, carefully supervised fasting may be considered, beginning with 24-hour fasts and progressing only with documented clinical stability and physician clearance at each step.

Severe aortic stenosis (critical narrowing of the aortic valve, the valve between the heart and the aorta) is a contraindication to extended fasting because the fixed outflow obstruction created by the stenotic valve means that the heart cannot increase its output in response to the peripheral vasodilation and haemodynamic changes of fasting. Patients with severe aortic stenosis are managed with valve replacement; fasting in this population is inappropriate until the valve lesion has been addressed.

Modified Protocol for Cardiovascular Disease Patients

For patients with established but stable cardiovascular disease who are candidates for supervised fasting, the modified protocol begins with 24-hour fasts under close supervision, with blood pressure and heart rate monitoring every two hours during the fast rather than twice daily. Electrocardiographic monitoring (ECG, the heart tracing that detects arrhythmias and ischaemic changes) before and after each fast is appropriate for post-MI patients during their initial fasting experiences.

Progression from 24-hour to 48-hour fasts should only occur after a minimum of four 24-hour fasts have been completed without adverse events and with documented haemodynamic stability throughout each. Progression beyond 48 hours requires cardiologist involvement, comprehensive pre-fast cardiac assessment, and daily clinical contact during the extended fast.

Antihypertensive medications in cardiovascular disease patients require particularly careful management during fasting, as described in Chapter 7: beta-blockers must never be abruptly withdrawn (doing so in a post-MI patient risks severe rebound tachycardia and ischaemia) and should be tapered very gradually over weeks rather than days. ACE inhibitors and ARBs, which are cornerstone therapies after MI and in heart failure for their cardioprotective effects independent of blood pressure, should be maintained at reduced doses rather than suspended, with dose reduction guided by blood pressure response.

The therapeutic goal in cardiovascular disease patients is not medication elimination (some cardioprotective medications in this population have benefits beyond blood pressure management that fasting does not replicate) but rather the maximum possible improvement in the metabolic drivers of ongoing cardiovascular deterioration, the maximum achievable blood pressure reduction, and the reduction of the antihypertensive medication burden that represents ongoing pharmaceutical management of symptoms rather than resolution of causes.

10.5 Hypertension in Women: Hormonal Considerations

Women represent half of the hypertensive population and carry a cardiovascular risk trajectory that differs from men's in ways that are directly relevant to therapeutic fasting. This section provides a brief clinical orientation to the key hormonal considerations; Chapter 11 provides the comprehensive framework for fasting protocols in women across all hormonal life stages.

The Oestrogen Factor

Oestrogen exerts direct cardiovascular protective effects throughout the premenopausal years, upregulating eNOS expression and nitric oxide production, modulating RAAS activity in a blood-pressure-reducing direction, maintaining baroreflex sensitivity, and providing anti-inflammatory

effects on the vascular endothelium. These protective effects are responsible for the lower blood pressure and cardiovascular risk profile of premenopausal women compared to age-matched men.

The loss of these protective effects at menopause produces a rapid acceleration in blood pressure, vascular stiffness, visceral fat accumulation and insulin resistance that explains why postmenopausal women ultimately have higher hypertension prevalence than men of the same age. This post-menopausal cardiovascular acceleration makes postmenopausal hypertensive women among the patients most urgently and most comprehensively served by the metabolic root-cause approach of this programme.

Oestrogen and Progesterone Effects on Fasting Tolerance

Women do not experience fasting under a static hormonal environment. The fluctuating levels of oestrogen and progesterone across the menstrual cycle alter insulin sensitivity, appetite regulation, stress tolerance and metabolic flexibility in ways that directly influence the fasting experience.

Oestrogen generally enhances insulin sensitivity, supports metabolic flexibility and promotes more efficient utilisation of stored fuel. During phases of the cycle when oestrogen predominates, women often tolerate fasting more comfortably, maintain more stable energy levels and transition into fat metabolism with fewer symptoms.

Progesterone exerts different effects. Rising progesterone during the luteal phase is associated with increased resting energy expenditure, increased appetite, greater fluid retention and a mild reduction in insulin sensitivity. Women commonly report stronger hunger signals, reduced fasting tolerance and greater susceptibility to fatigue during this phase.

These physiological differences do not mean that women should avoid fasting during progesterone-dominant phases. They mean that fasting protocols should respect the hormonal environment rather than ignore it. A fasting duration that feels effortless during the follicular phase may feel unnecessarily difficult during the late luteal phase despite no change in willpower or motivation.

Understanding these hormonal influences allows fasting to be applied with greater precision and less unnecessary physiological stress.

The Menstrual Cycle and Fasting Timing

Women of reproductive age must account for the phase of their menstrual cycle in planning therapeutic fasting, because the hormonal environment of different cycle phases creates meaningfully different metabolic and physiological contexts for fasting. The follicular phase (roughly Days 6 to 13 of a 28-day cycle), dominated by rising oestrogen, high metabolic flexibility and strong energy availability, is the most physiologically receptive phase for extended fasting. The late luteal phase (roughly Days 22 to 28), dominated by falling progesterone and peak premenstrual stress reactivity, is the least appropriate phase for extended or aggressive fasting and carries specific hormonal risks that Chapter 11 addresses in detail.

Perimenopause, Postmenopause and Female-Specific Fasting Frameworks

The years surrounding menopause deserve particular attention because they represent one of the most significant metabolic transitions in a woman's life. Declining ovarian hormone production alters body composition, increases visceral fat accumulation, worsens insulin resistance and accelerates the development of hypertension.

Perimenopause is frequently associated with increasing blood pressure despite unchanged dietary habits or body weight. Women often notice the emergence of abdominal fat, deteriorating glucose control, sleep disruption and heightened sympathetic nervous system activity. These changes reflect the gradual loss of oestrogen's protective effects on vascular function, insulin sensitivity and autonomic balance.

After menopause, the prevalence of hypertension rises sharply. The reduction in oestrogen contributes to increased arterial stiffness, reduced nitric oxide production, greater visceral adiposity and worsening metabolic syndrome. These changes make postmenopausal women particularly appropriate candidates for fasting-based metabolic interventions when medically suitable.

Dr. Mindy Pelz has emphasised the importance of adapting fasting intensity to a woman's hormonal environment rather than applying male-derived fasting schedules indiscriminately. Her framework, described in Fast Like a Girl, recommends greater flexibility around reproductive hormone fluctuations and recognises that fasting tolerance is not constant throughout the menstrual cycle or across different hormonal life stages.

While Chapter 11 examines these concepts in detail, the essential principle is straightforward: women benefit most when fasting protocols are synchronised with physiology rather than imposed against it. The goal is not maximal fasting exposure but maximal therapeutic benefit with minimal hormonal disruption.

Pregnancy: Absolute Contraindication

Pregnancy is an absolute contraindication to therapeutic water fasting beyond very short duration (24-hour maximum), and even short fasting in pregnancy requires explicit obstetric clearance. The metabolic demands of fetal development, the risk of inadequate fetal glucose supply during maternal fasting, the hormonal disruption that extended fasting can produce in the maternal-fetal hormonal environment, and the nutritional requirements of normal fetal growth all make therapeutic fasting in pregnancy categorically inappropriate as a blood pressure management strategy. DeVries noted this explicitly: fasting stops milk secretion in lactating women and involves nutritional considerations in pregnancy that make planned therapeutic fasting inadvisable. The metabolic guide confirms the same position. Hypertension in pregnancy requires specialist obstetric management.

The full treatment of hypertension in women, including cycle-synced fasting protocols, perimenopausal and postmenopausal considerations, polycystic ovarian syndrome, hormone replacement therapy interactions, and the clinical case illustration that grounds these principles in patient experience, occupies Chapter 11 in its entirety.

Clinical Prioritisation in Patients with Multiple Comorbidities

The comorbidities discussed in this chapter rarely occur in isolation. The typical hypertensive patient presenting for therapeutic fasting often has obesity, metabolic syndrome, Type 2 diabetes, early chronic kidney disease and established cardiovascular disease simultaneously. In these situations, the question is not which protocol to follow but which protocol should take priority.

The governing principle is straightforward: when multiple protocols apply, the most conservative element of each protocol governs the final treatment plan.

A patient with hypertension and metabolic syndrome but no other significant disease generally follows the standard fasting programme outlined in Chapters 7 through 9\. The metabolic syndrome itself does not require shortening the fast and often supports a more ambitious fasting schedule.

When Type 2 diabetes co-exists with metabolic syndrome, the diabetic monitoring requirements become dominant. Blood glucose monitoring every four hours and physician-directed medication adjustment become mandatory regardless of how suitable the patient otherwise appears for fasting.

When chronic kidney disease is added to the clinical picture, kidney function becomes the limiting factor. A patient with severe obesity and excellent fasting tolerance but Stage 3 CKD remains a Stage 3 CKD patient. The shortened fasting duration and enhanced laboratory monitoring take precedence over metabolic ambitions.

When established cardiovascular disease co-exists with any of the above conditions, cardiovascular stability becomes the first consideration. A patient with prior myocardial infarction or stable heart failure may still benefit substantially from fasting, but progression should occur more gradually and under greater supervision than would otherwise be required.

Pregnancy supersedes all other considerations. The potential metabolic benefits of fasting become irrelevant in the presence of fetal nutritional requirements. Therapeutic water fasting is therefore contraindicated regardless of the presence or severity of any other comorbidity.

The practical rule is simple: when uncertainty exists, choose the more conservative protocol. Safety modifications accumulate. Therapeutic benefits do not disappear because a protocol is more cautious. The objective remains the same in every patient: achieve the maximum physiological improvement that can be obtained safely.

Summary Table: Protocol Modifications by Comorbidity

Comorbidity	Fasting Suitability	Initial Maximum Fast	Primary Monitoring Requirement
Obesity and Metabolic Syndrome	Excellent	Standard protocol	Standard monitoring
Type 2 Diabetes	Good with supervision	Standard protocol after medication adjustment	Blood glucose every four hours minimum

Comorbidity	Fasting Suitability	Initial Maximum Fast	Primary Monitoring Requirement
CKD Stage 1-2	Good	Standard protocol	Enhanced electrolyte and renal monitoring
CKD Stage 3	Moderate	24-48 hours	Intensive laboratory surveillance
CKD Stage 4	Limited	24 hours initially	Nephrology supervision required
CKD Stage 5	Generally contraindicated	None beyond exceptional specialist circumstances	Specialist management only
Stable Cardiovascular Disease	Moderate	24-48 hours initially	Intensive cardiovascular monitoring
Recent MI (\<3 months)	Contraindicated	None	Cardiology management
Decompensated Heart Failure	Contraindicated	None	Stabilisation before consideration
Severe Aortic Stenosis	Contraindicated	None	Structural cardiac treatment required
Pregnancy	Contraindicated	None	Specialist obstetric care

Chapter Summary: Key Points

Hypertensive patients with obesity and metabolic syndrome are the most comprehensively suited patients for therapeutic fasting, because both hypertension and metabolic syndrome share the same root driver, insulin resistance, that fasting most powerfully addresses. Visceral fat, the primary inflammatory driver of metabolic syndrome, is targeted specifically and efficiently by fasting's autolytic processes, producing the weight loss that is most metabolically relevant: loss from the specific fat compartment driving the disease.

Type 2 diabetes co-existing with hypertension represents not two diseases requiring two separate interventions but two manifestations of the same insulin resistance that a single comprehensive fasting programme addresses simultaneously. The mandatory safety modifications are glucose monitoring every four hours during fasting and mandatory pre-fast physician-directed reduction or suspension of insulin and sulphonylurea medications. The documented clinical evidence, from Guelpa's 1910 findings through Allen's 1915 60% reduction in diabetic coma mortality to modern remission trials, confirms that the diabetic metabolic abnormality is profoundly responsive to fasting. The goal is medication reduction correlated with measurable metabolic improvement, tracked through HOMA-IR, HbA1c and blood pressure at six-monthly intervals.

Chronic kidney disease is the most challenging fasting comorbidity, with the appropriate protocol determined by CKD stage and eGFR. Early-stage CKD (Stages 1 and 2\) is managed with standard protocols and enhanced monitoring. Stage 3 CKD requires shortened maximum fast duration and intensive electrolyte surveillance. Stage 4 CKD is a relative contraindication requiring nephrology

involvement. The blood pressure normalisation achievable with therapeutic fasting is itself a powerful renal-protective intervention that may slow CKD progression measurably.

Established cardiovascular disease requires the most intensive supervision of any comorbidity but, in stable patients beyond the acute phase of illness, is supported by the evidence that fasting's cardiac rest, ketone fuel efficiency, sympathetic withdrawal and blood pressure reduction collectively benefit the compromised cardiovascular system. Absolute contraindications include decompensated heart failure, MI within three months, and severe aortic stenosis. All other patients require modified, progressively supervised protocols beginning with 24-hour fasts and advancing only with documented stability.

Women's hypertension management through therapeutic fasting requires account of the menstrual cycle in women of reproductive age, the accelerated cardiovascular risk of postmenopause, and the absolute contraindication of therapeutic fasting in pregnancy. Chapter 11 provides the complete clinical framework for all hormonal life stages.

The unifying principle across all comorbidities is not caution for its own sake but precision: the right protocol intensity, the right monitoring frequency, the right medication adjustments, and the right supervision level for each patient's specific clinical situation, delivering the maximum therapeutic benefit that safety allows.

“The art of medicine consists of amusing the patient while nature cures the disease.”

— Voltaire

Voltaire's cynicism has a grain of clinical truth in it, but only a grain. Nature does indeed cure. The body's capacity for self-regulation and self-repair, documented across seventy years of clinical fasting experience and confirmed by modern molecular biology, is real and remarkable. The physician's role in therapeutic fasting is not to amuse but to supervise: to create the conditions in which the body's own healing intelligence can operate at full capacity, and to ensure that no preventable harm interrupts the process while it does.

PART FIVE: THE SCIENCE EXPLAINED

For the Clinically Curious — Mechanistic Deep Dives

CHAPTER 11

Managing The Fast, Troubleshooting Common Challenges

“The only way out is through.”

— Robert Frost

Opening: What Nobody Tells You Before You Begin

Every patient who completes a first extended therapeutic fast reports some version of the same experience: the first two days were harder than expected, and the days that followed were easier than they feared. This asymmetry between anticipation and reality is one of the most consistent observations across the entire clinical fasting literature, documented by DeVries, Bragg, Shelton, Weger and every practitioner who has supervised fasts in any significant number.

The reason the anticipation is worse than the reality is that most people approach fasting with no framework for interpreting what their body is doing. A headache on Day 1 feels alarming when you do not know that headaches are among the most common and most temporary early fasting symptoms. A coated tongue on Day 2 feels like something is wrong when you do not know that a coated tongue is one of the clearest signs that active elimination is occurring exactly as it should. The hunger that peaks sharply on Day 2 feels insurmountable when you do not know that it will reduce substantially by Day 3 and in most cases resolve almost entirely by Day 4 to 5\.

Knowledge is the primary tool for managing the challenges of fasting. Not willpower, not stoicism, not an unusually high pain threshold. Knowledge of what is happening physiologically, why it is happening, how long it is likely to last, and what distinguishes a normal fasting experience from a genuine warning signal that requires action.

This chapter provides that knowledge systematically. It covers hunger and appetite management, the healing crisis and detoxification symptoms, orthostatic hypotension, electrolyte disturbances, and the psychological challenges that arise during extended fasting. For each challenge it provides the physiological explanation, the expected timeline, the management strategies, and the specific signs that distinguish normal fasting experience from situations that require medical contact or breaking of the fast.

This chapter is not intended to alarm. It is intended to prepare. The vast majority of patients who undertake therapeutic fasting under appropriate physician supervision and with adequate pre-fast preparation, as described in Chapters 7 and 8, complete their fasts without encountering anything more demanding than the temporary discomforts that are the normal accompaniment of the body's deep cleansing work. The clinical record, from DeVries' documentation of thousands of supervised fasts to Goldhamer's contemporary series, is clear: properly supervised therapeutic fasting is a safe intervention whose challenges are manageable and whose benefits are profound.

11.1 Hunger Management

The Expected Timeline

Hunger during a therapeutic fast follows a predictable arc that has been documented consistently across the clinical fasting literature. Understanding this arc in advance is the single most powerful tool for managing hunger, because it transforms an experience that feels open-ended and potentially endless into one with a known trajectory and a known destination.

On the first day of fasting, hunger is typically mild and manageable. The body's glycogen stores (glucose stored in the liver and muscle) are still being drawn upon for energy, blood glucose is maintained within a relatively normal range, and the stomach is adapting to the absence of food without yet sending strong demand signals.

On the second day, hunger reaches its peak. This is the most difficult period of an extended fast for most people, and it is important to name it directly: Day 2 is hard. Blood glucose has fallen as glycogen stores are depleted and the body is still completing the transition to fat-based fuel. Ghrelin (the primary hunger hormone, produced in the stomach and signalling the hypothalamus to drive appetite and food-seeking behaviour) is at or near its highest level of the fast. The stomach, accustomed to receiving food at habitual intervals, is registering its loudest objection to the interruption of its routine. Habitual hunger (the stomach's conditioned expectation of food at its usual mealtimes) and physiological hunger (the body's genuine energy need signal) are both at maximum simultaneously.

From Day 3 onward, hunger diminishes. The metabolic crossover to fat-based fuel and ketone production, which begins in earnest between 24 and 48 hours of fasting as described in Chapter 3, shifts the body's primary energy source away from glucose and reduces the urgency of the glucose-dependent appetite signal. Ghrelin levels, counterintuitively, fall during extended fasting: the body does not escalate its hunger signalling indefinitely but adapts to the fasting state through hormonal recalibration. Multiple clinical studies have confirmed that subjective hunger ratings in patients undergoing multi-day fasting peak in the first two days and then decline significantly, with many patients by Day 4 to 5 reporting little or no desire for food and in some cases an active disinclination toward it.

DeVries described this arc precisely in Chapter VII of Therapeutic Fasting, documenting from the clinical records of multiple supervised fasting institutions that hunger typically reaches its climax on Day 2, often begins to abate on Day 3, and in nearly all cases disappears completely by Day 4 to 5, with the extended fast thereafter becoming, in his words, "quite easy, with little annoyance or discomfort."

True Hunger Versus Habitual Appetite

Bragg's formulation, "flesh is dumb," which he repeated throughout The Miracle of Fasting as one of the book's central clinical insights, identifies something that is physiologically precise. The stomach has no intelligence. It does not know why it is not receiving food; it only knows that food is not coming at the times it has been conditioned to receive it, and it generates demand signals accordingly. These demand signals, the growling, the uncomfortable emptiness, the preoccupation with food, are not evidence of genuine physiological need in the fasting context. They are the conditioned reflexes of a system that has been trained by decades of scheduled eating to expect food at specific times.

The distinction between true hunger, which is the body's signal of genuine nutritional insufficiency after the exhaustion of its stored reserves, and habitual appetite, which is the conditioned expectation of food based on routine and association, is clinically critical during therapeutic fasting. True hunger does not occur during a properly conducted therapeutic fast until the body's stored reserves approach exhaustion (as described in Chapter 8's discussion of the fasting-starvation boundary, which in a normally nourished adult is reached only after weeks of fasting). What the fasting patient experiences in the first two to three days is overwhelmingly habitual appetite: the stomach's conditioned objection to the interruption of its routine.

Understanding this distinction removes much of the psychological power of early fasting hunger. The sensation is real. The urgency it projects is not. Recognising it as conditioned reflex rather than physiological emergency allows the patient to observe it without being compelled by it.

Management Strategies

Increased water intake is the most immediately effective hunger management tool during fasting. Water in the stomach activates mechanoreceptors (stretch receptors in the stomach wall that signal fullness) and temporarily reduces the intensity of hunger sensations. The recommendation of sipping water slowly and steadily throughout the fast, approximately 250 mL every two hours as described in Chapter 8, serves both the hydration requirements of the fast and the practical management of hunger between these intervals.

Rest is the second most effective strategy. Physical activity, even moderate activity, increases appetite signalling through multiple pathways including increased ghrelin production and decreased satiety hormone (leptin and peptide YY) sensitivity. During the first two days of extended fasting, when hunger is at its peak, minimising physical activity beyond gentle walking and prioritising horizontal rest when hunger is most intense significantly reduces the subjective hunger experience.

Distraction and engagement are more clinically useful than they might initially appear. Hunger, like pain, is amplified by attention and reduced by the diversion of attention toward absorbing activities. Light reading, quiet conversation, gentle creative work, and deliberate engagement with non-food-related activities during the periods of peak hunger on Days 1 and 2 reduce the subjective experience of hunger by reducing the proportion of cognitive attention available to attend to it.

Positive affirmation, used consistently by Bragg and recommended explicitly in The Miracle of Fasting, functions not as self-deception but as the deliberate direction of the mind's attention toward the purpose and meaning of the fast rather than its momentary discomfort. Bragg's specific affirmations for fasting patients, among them "Every minute that I fast I am flushing dangerous poisons from my body" and "Hour by hour, my body is cleansing and purifying itself," are effective not because they are motivational slogans but because they redirect attention from the hunger sensation to the physiological reality of what the body is doing during the fast: the autolysis, the elimination, the RAAS suppression, the sympathetic withdrawal, the endothelial repair. The patient who is actively aware of these processes as the context of their hunger has a fundamentally different relationship with that hunger than the patient who is simply enduring absence of food with no framework for understanding its significance.

11.2 The Healing Crisis, Understanding Detoxification Symptoms

What Bragg Called the Acute Healing Crisis

In Chapter 16 of The Miracle of Fasting, Bragg described the "acute healing crisis" with the directness of someone who had supervised it in thousands of patients and experienced it personally across decades of regular fasting. When the body's Vital Force (his term for the body's innate capacity for self-regulation and self-repair) intensifies its eliminative activity during fasting, the process of expelling accumulated metabolic waste, toxins, and cellular debris through the organs of elimination produces symptoms that are unfamiliar, sometimes alarming in appearance, and entirely misunderstood by anyone who lacks the clinical framework to interpret them.

The acute healing crisis is not the body failing. It is the body succeeding. The symptoms of detoxification during fasting are the outward manifestations of increased eliminative activity, the same process of enhanced autolysis and elimination described in Chapter 3's physiological analysis of fasting, expressing itself through the organs through which the body expels waste: the kidneys, the skin, the lungs, and the mucous membranes of the nose, throat and gut.

DeVries catalogued these symptoms comprehensively in Chapter VII of Therapeutic Fasting and was careful to contextualise them: they are "in no sense a cause for concern" and represent "outward manifestations of the gradual recovery to health being made."

The Common Symptoms and Their Meaning

Headache is among the most common early fasting symptoms, occurring most frequently on Days 1 to 3 and typically resolving as the metabolic crossover to ketone-based fuel is completed. Its primary causes are three: caffeine withdrawal in patients who were habitual coffee or tea drinkers before the fast (caffeine withdrawal headache is typically throbbing, frontal, and often accompanied by mild nausea, and resolves within 48 to 72 hours as the nervous system adapts to the absence of the stimulant); the haemodynamic changes of early fasting as blood pressure begins to fall and cerebral circulation adjusts; and the release of stored metabolic waste into the circulation during the initial intensification of eliminative activity.

The management of fasting headache is rest, horizontal positioning, and increased water intake. It is temporary and self-resolving in virtually all cases. It is not a reason to break the fast.

Fatigue in the first two to three days of extended fasting is the body's appropriate response to the metabolic demands of the crossover period: glycogen depletion, the hormonal flux of insulin falling and glucagon rising, the cortisol and noradrenaline elevation of the early sympathetic activation before the sympathetic withdrawal of Days 3 to 5, and the cellular housekeeping work of autophagy all represent significant metabolic activity that draws on the body's energy reserves. Resting with the fast, rather than fighting fatigue with activity, allows this work to proceed efficiently and shortens the duration of the fatigued period.

Body odour changes during extended fasting reflect the skin's increased role as an organ of elimination. As the kidneys and lungs handle greater eliminative loads during fasting, the skin (often called the

body's third kidney in the naturopathic tradition, and with physiological justification: the skin's 96 million pores are capable of excreting water, urea, lactic acid and other metabolic waste products) also increases its eliminative activity. The odour produced is not the odour of poor hygiene; it is the smell of metabolic waste products being excreted through the skin, and it is a sign that the skin is actively participating in the body's accelerated cleansing. Daily bathing during fasting, using mild, non-irritating soap or simply water, manages this symptom without impeding the eliminative process.

The coated tongue is one of the most reliable and informative signs of active fasting elimination. Bragg instructed his patients to observe their tongue daily during fasting and to understand its coating as a direct window into the body's eliminative activity: the thickness, colour and texture of the tongue coating correlates with the intensity of the internal cleansing process. DeVries confirmed this from the clinical fasting records, noting that the tongue coating typically begins within the first few days of fasting, intensifies as elimination accelerates, and gradually clears toward the end of the fast as the body's reserves approach exhaustion and the demand for eliminative activity diminishes.

The coated tongue is also one of the classic signs used to confirm that the fasting period has not yet reached completion: the tongue remains coated throughout the period of active elimination and clears (along with the return of true hunger) when the fasting period approaches its natural terminus, as described in Chapter 8's discussion of the fasting-starvation boundary.

Offensive breath (halitosis during fasting) arises from two sources: the increased excretion of metabolic waste products and ketone bodies through the lungs (the lungs are the primary route of ketone excretion in the form of acetone, which produces the characteristic fruity or nail-polish-remover smell of ketosis), and the accelerated eliminative activity of the mucous membranes of the mouth and throat. Regular water drinking flushes the oral cavity and reduces the intensity of this symptom; it cannot be entirely prevented during active ketosis and should not be.

Nausea and vomiting occur in some patients, most commonly in the first three to four days of extended fasting, and represent the body's eliminative activity through the gastrointestinal mucosa. Bragg described nausea during fasting as the body's mechanism for expelling toxic accumulations from the stomach, and recommended that when nausea leads to vomiting, the patient should allow it: the post-vomiting relief is immediate and genuine, reflecting the successful elimination of material that had been held in the stomach. Persistent or severe nausea requires physician contact to assess whether it represents normal fasting elimination or a complication requiring attention.

Skin eruptions, described by DeVries as a "cleansing rash," occasionally occur during extended fasting, typically in the first week, and represent the skin's eliminative activity expressing itself through the surface. They are temporary, typically resolve within days, and are a sign of active elimination rather than an allergic or dermatological problem.

Dizziness is common and is addressed specifically in Section 11.3 below in the context of orthostatic hypotension.

Temporary weakness and reduced physical capacity are normal throughout the early and middle phases of extended fasting, particularly before the metabolic adaptation to ketone fuel is complete. They are not signs of the fast causing harm; they are signs of the body directing its energy toward internal

processes rather than external physical activity, and they resolve as the fast progresses and the body's metabolic adaptation deepens.

When to Persevere Versus When to Be Concerned

The clinical test for distinguishing detoxification discomfort from a genuine danger signal is not the intensity of the symptom but its character and trajectory:

Symptoms that are expected, intermittent, gradually evolving and not associated with objective clinical abnormalities (normal blood pressure when measured lying down, normal pulse, absence of chest pain, absence of confusion, absence of severe weakness) are detoxification symptoms that warrant perseverance. They may be uncomfortable. They are not dangerous.

Symptoms that are sudden in onset, severe, rapidly worsening, or associated with objective abnormalities require immediate medical contact and may require breaking the fast. These include: chest pain (always taken seriously in a hypertensive patient and must be evaluated medically without delay), severe or rapidly worsening shortness of breath, loss of consciousness or near-syncope (the sensation of losing consciousness), severe and persistent confusion or disorientation, heart palpitations that are rapid, irregular and persistent rather than brief and occasional, blood glucose below 3.5 mmol/L in a diabetic patient that does not respond to the breaking of the fast with juice or fruit, blood pressure that falls below 90/60 mmHg with symptoms of inadequate perfusion (severe dizziness, confusion, chest pain, or visual changes), and vomiting that is profuse, persistent or contains blood.

These are the genuinely dangerous presentations. They are uncommon in properly supervised therapeutic fasting but must be named clearly so that patients can distinguish them from the far more common but harmless detoxification symptoms that they will actually experience.

11.3 Orthostatic Hypotension During Fasting

Why It Happens and Who Is Most at Risk

Orthostatic hypotension (pronounced "or-tho-STAT-ik hy-po-TEN-shun") is a drop in blood pressure of 20 mmHg systolic or more when moving from a lying or sitting position to a standing position, producing symptoms of dizziness, lightheadedness, visual greying, and in severe cases, loss of consciousness.

During therapeutic fasting, orthostatic hypotension is common and arises from the combination of three physiological changes: the significant blood pressure reduction produced by fasting itself (the natriuresis, RAAS suppression and sympathetic withdrawal that lower blood pressure dramatically are the therapeutic targets of the whole programme), the reduction in circulating blood volume as sodium and water are excreted through the natriuresis of the first days of fasting, and the continued action of antihypertensive medications in a patient whose blood pressure is already falling substantially through the physiological effects of the fast.

The last of these is the most clinically significant and the most preventable. A patient who entered the fast on three antihypertensive medications at doses calibrated to manage a blood pressure of 158/96 is carrying a medication burden that was appropriate for their pre-fast physiology. As fasting progressively

drives their blood pressure down through mechanisms that are additive to, rather than duplicative of, the medication's effects, the combined pressure reduction can produce values that are substantially below the target range, particularly during the haemodynamic challenges of position changes. This is the physiological basis for the medication adjustments described in Chapter 7 and implemented during the fast as described in Chapter 8: reducing antihypertensive medication doses proactively as blood pressure falls during the fast prevents the additive over-reduction that is the primary cause of symptomatic orthostatic hypotension.

Hypertensive patients taking diuretics are at additional risk because diuretics reduce circulating blood volume through their renal mechanism, compounding the volume reduction of fasting natriuresis. As stated in Chapter 7, diuretics should be suspended before extended fasting begins, not managed reactively when orthostasis develops.

Prevention: The Rise Slowly Principle

The most effective and most immediately practical prevention for orthostatic hypotension during fasting is behavioural: move slowly through positional changes. When rising from lying to sitting, pause for 30 seconds at the sitting position and assess for symptoms before standing. When standing from sitting, rise slowly and maintain contact with a support surface (the edge of the bed, the arm of a chair, a wall) until balance is confirmed and symptoms are absent.

This is not theatrical caution. It is the acknowledgment that the cardiovascular system needs time to redistribute blood flow in response to a positional change, and that during fasting, when blood pressure is lower and blood volume is somewhat reduced, this redistribution takes longer than usual. Allowing the time removes most of the risk.

Adequate hydration is the second prevention tool. Dehydration reduces blood volume and compounds the orthostatic risk of fasting. Maintaining the recommended minimum of 2 litres of water per day during fasting, distributed evenly across the waking hours, preserves circulating volume and reduces orthostatic symptoms significantly.

Management When Orthostasis Occurs

If a patient experiences significant orthostatic symptoms (dizziness, graying of vision, or near-syncope on standing), the immediate management is: sit or lie down immediately, do not attempt to remain standing, allow symptoms to resolve in the horizontal position, and then rise again using the slow positional change protocol.

If orthostatic symptoms are recurring despite adequate hydration and slow positional changes, the physician should be contacted. The management at physician level will typically involve a review of the current antihypertensive medication regimen to assess whether further dose reduction is appropriate, a clinical check of blood pressure in lying and standing positions to confirm the degree of orthostatic drop, and an assessment of hydration status and electrolyte balance.

Electrolyte supplementation in the form of a small amount of sodium-containing fluid (a measured quantity of warm water with a pinch of unrefined salt, for example) is sometimes used in supervised fasting contexts to address orthostatic hypotension that persists despite adequate water intake and

medication adjustment. This is a physician-directed decision: arbitrary salt supplementation during fasting without clinical assessment risks undermining the natriuresis that is one of fasting's primary blood pressure mechanisms, and the amount and necessity must be individually determined.

When to Break the Fast

Orthostatic hypotension that produces a loss of consciousness (fainting) during fasting, or that produces a blood pressure below 90/60 mmHg while standing with symptoms of inadequate organ perfusion (confusion, chest pain, severe shortness of breath, or inability to maintain awareness), is an indication to break the fast and obtain immediate medical assessment. A single episode of orthostatic dizziness that resolves promptly with lying down and adequate hydration is not an indication to break the fast; it is an indication to adjust the management of the fast under physician guidance.

11.4 Electrolyte Imbalances

Why Electrolytes Shift During Fasting

Electrolytes (minerals that carry an electrical charge and are essential for nerve conduction, muscle contraction, fluid balance and cardiac rhythm) shift during therapeutic fasting for multiple physiological reasons. Sodium and water are excreted through natriuresis. Potassium follows sodium to some degree through its coupled renal handling, with additional potassium loss driven by any diuretic medications still active in the system. Magnesium is excreted at increased rates during fasting and may not be adequately replaced by the water-only intake of the fast. Phosphate (an essential mineral for ATP production, bone mineralisation and cellular function) follows a complex pattern that becomes clinically critical specifically in the refeeding period after extended fasting.

The monitoring protocols of Chapters 7 and 8 are designed to detect electrolyte disturbances before they reach clinical severity. This section describes the symptoms that should prompt a patient to check in with their physician before the next scheduled monitoring appointment.

Hypokalaemia: Low Potassium

Hypokalaemia (pronounced "hy-po-kuh-LEE-mee-uh," meaning low potassium in the blood, below 3.5 mmol/L) is the most clinically significant electrolyte disturbance in patients undertaking extended fasting, particularly those on diuretics that have not been fully suspended before the fast.

Symptoms of hypokalaemia include muscle cramps and spasms (particularly in the legs), muscle weakness and fatigue that is more severe than the general fatigue of fasting, palpitations (an awareness of the heartbeat, often felt as a fluttering or skipping sensation in the chest or throat), constipation (potassium is essential for the normal contractions of the gut musculature), and in severe cases, dangerous cardiac arrhythmias (irregular heart rhythms that can in the most severe cases progress to ventricular fibrillation and cardiac arrest).

The cardiac risk of severe hypokalaemia makes it the electrolyte disturbance that most urgently requires physician assessment when suspected. A patient experiencing significant muscle cramps and palpitations simultaneously during a fast should contact their physician for an electrolyte check without

delay, not manage it independently.

Hyponatraemia: Low Sodium

Hyponatraemia (pronounced "hy-po-nuh-TREE-mee-uh," meaning low sodium in the blood, below 135 mmol/L) can occur during fasting, paradoxically, as a consequence of excessive water intake in the setting of continued sodium excretion through natriuresis. This is sometimes called dilutional hyponatraemia: the sodium concentration in the blood falls not because the absolute amount of sodium has fallen to a critically low level but because the water volume in which it is dissolved has increased disproportionately.

Symptoms of hyponatraemia include headache (often described as a dull, generalised headache distinct from the frontal throbbing of caffeine withdrawal), nausea and vomiting, confusion and cognitive slowing, muscle weakness, and in severe cases, seizures. Severe hyponatraemia (sodium below 125 mmol/L with significant neurological symptoms) is a medical emergency.

The prevention of dilutional hyponatraemia during fasting is to drink water according to thirst rather than forcing very large quantities beyond what thirst demands. The recommendation of 2 to 3 litres per day as the appropriate water intake range during fasting reflects this balance: sufficient to maintain hydration and support eliminative activity without over-diluting the blood's sodium concentration. Patients who develop headache and confusion during fasting should not respond by drinking large additional quantities of water before obtaining medical assessment.

Refeeding Syndrome: The Hypophosphataemia Risk

Refeeding syndrome (pronounced "ree-FEED-ing SIN-drohm") is a potentially serious metabolic disturbance that can occur when food is reintroduced after a period of extended fasting or prolonged starvation. Its primary mechanism involves phosphate (phosphorus): during extended fasting, the body's cells reduce their phosphate uptake from the blood as metabolic activity slows. When food is reintroduced, particularly carbohydrates, insulin secretion rises rapidly, and insulin drives a sudden shift of phosphate from the blood into the cells where it is needed for glucose metabolism. This rapid intracellular shift can drop blood phosphate levels precipitously, producing hypophosphataemia (pronounced "hy-po-fos-fuh-TEE-mee-uh," meaning low phosphate in the blood).

Severe hypophosphataemia impairs ATP production (phosphate is essential for the synthesis of ATP, the cell's energy currency), affecting all energy-dependent cellular processes. Clinical consequences include muscle weakness, cardiac arrhythmias, respiratory failure in severe cases, neurological dysfunction, and potentially death in the most extreme presentations. Refeeding syndrome in its severe form is most commonly seen after prolonged complete starvation (weeks to months) in severely malnourished patients rather than in the context of planned therapeutic fasting in adequately nourished patients, but the risk is real after extended fasts of 7 days or more and justifies the graduated refeeding protocol of Chapter 8, which begins with small amounts of dilute fruit juice and progresses to more complex foods over several days, preventing the sudden insulin surge that is the trigger for hypophosphataemia.

The prevention of refeeding syndrome in the context of this programme is structural: the graduated refeeding protocols described in Chapter 8 for each fasting duration are specifically designed to prevent the rapid insulin surge that triggers hypophosphataemia. Following these protocols without shortcutting the juice-only and soft-food phases eliminates most of the clinical risk.

For patients who have completed extended fasts of 7 days or more, a phosphate check at the clinical electrolyte panel at Day 3 to 4 of refeeding is a reasonable precaution, particularly in patients with CKD, malnutrition risk factors, or significant weight loss during the fast.

Magnesium

Magnesium depletion during extended fasting, described in Chapter 7 as one of the reasons for pre-fast magnesium assessment, manifests as muscle cramps (particularly nocturnal leg cramps), generalised muscle weakness, anxiety and irritability, difficulty sleeping, and in severe cases, cardiac arrhythmias. Patients who develop significant cramps during fasting that are not explained by potassium deficiency should have magnesium assessed and may benefit from physician-directed supplementation.

11.5 Psychological Challenges

The Psychological Architecture of Extended Fasting

Therapeutic water fasting is a physical intervention with a significant psychological dimension, and addressing that dimension honestly is as clinically important as addressing the physiological challenges. The patient who understands the psychological challenges in advance is the patient most likely to complete the fast successfully and to maintain the programme long-term.

Social Pressure Around Food

Food in most cultures is deeply embedded in social ritual, relational connection, and the expression of care and hospitality. A person who is fasting in a context where food is being shared, prepared, or discussed is navigating not just their own hunger and habit but the social expectations and sometimes the active concern or resistance of people who care about them.

The most common social pressure pattern is well-intentioned: family members who worry that fasting is dangerous, friends who interpret not eating as a statement about the food they have prepared, colleagues who interpret extended fasting as an extreme or disordered behaviour, and the general cultural assumption that someone who is not eating must be unwell or suffering. These concerns come from care, not malice, and they deserve patient and clear communication rather than defensiveness.

Bragg's consistent recommendation, offered repeatedly throughout The Miracle of Fasting, was to keep the fast personal and private: not to discuss it with people who have no understanding of its physiological basis and who will project their fears and assumptions onto the patient's experience. This advice has practical merit. A patient who is managing Day 2 hunger is not in the optimal psychological state to simultaneously manage the anxiety of a concerned family member who is convinced they are harming themselves. Selecting in advance which people to inform and which to simply not involve reduces the social noise that complicates the early days of fasting.

For social occasions during extended fasting (meals, family gatherings, work lunches), the most practical approach is truthful simplicity: "I am not eating today" or "I am taking a break from food for a few days" is honest without requiring a detailed explanation of fasting physiology. Most people do not press further. For those who do, "I am working on some health goals under my doctor's supervision" is both accurate and socially terminal.

Breaking the Psychological Habit of Eating

The metabolic guide used throughout this book identifies habitual eating patterns, the automatic reaching for food at habitual times, the association of emotions with food consumption, the use of eating as a response to boredom, stress or social anxiety, as a primary contributor to the dietary patterns that drive hyperinsulinaemia. Extended fasting interrupts these patterns at a depth that no dietary modification achieves, because it removes food entirely rather than modifying its content or quantity.

This interruption is itself a psychological intervention. Patients who complete extended fasts consistently report a changed relationship with food after the fast: a reduced automaticity around eating, a heightened awareness of genuine hunger versus habitual appetite, and a greater capacity to make deliberate food choices rather than habitual ones. This is not a claimed benefit without mechanistic grounding: the neurological reset of extended fasting, through its effects on dopaminergic reward pathways (the brain circuits that associate food with pleasure and relief), reduces the conditioned craving response that underlies habitual eating patterns.

The period of the fast is therefore also the period during which the psychological habit of eating is most effectively examined and challenged. Journaling (writing a daily account of the fast including emotional observations, hunger sensations, and the contexts in which food cravings arise most strongly) is a clinically useful tool during fasting: it externalises the psychological experience of the fast and provides the post-fast patient with a precise map of the emotional and situational triggers for their habitual eating patterns, which they can then address deliberately in the post-fast nutritional framework.

Support Systems and Accountability Structures

Extended fasting is substantially easier with social and structural support than it is in isolation. This is not a weakness; it is a clinical observation consistent across every domain of behaviour change research. The patient who fasts with the knowledge that their physician is contactable and monitoring their progress, who has told one trusted person about the fast who will check in supportively, and who has a clear daily structure for the fasting days (including rest periods, water intake times, and a simple accountability log of symptoms and blood pressure readings) is a patient who is dramatically better positioned to complete the fast successfully than one who attempts the same protocol in complete isolation with no support and no structure.

Physician contact during extended fasting is not optional: daily contact during any fast beyond 48 hours is the standard of care described in Chapter 8, and this contact functions as an accountability structure as well as a clinical safety mechanism. Knowing that the physician will be checking in makes it less likely that the patient will break the fast impulsively in a moment of hunger or discomfort without first assessing whether the discomfort warrants it.

Peer support through others who have completed or are completing fasting programmes, available through online communities of practice and through some supervised fasting clinical programmes, can be a meaningful additional resource. The experience of reading another patient's account of navigating Day 2 hunger and completing the fast successfully provides both practical information and genuine psychological encouragement that no clinical information alone can replicate.

When Psychological Distress Warrants Breaking the Fast

The psychological challenges of fasting, including hunger, social pressure, habitual food cravings, and the emotional experiences that emerge when the usual coping mechanism of food is removed, are a normal part of the fasting experience and do not in themselves constitute reasons to break the fast. Discomfort is not danger. Difficulty is not harm.

However, there are psychological presentations during fasting that do warrant breaking the fast and seeking appropriate professional support.

Severe, escalating anxiety that is not responsive to the rest, water intake and reframing strategies described above and that is producing acute psychological distress beyond the manageable fluctuations of normal fasting experience warrants physician contact for assessment of whether the fast should continue.

Intrusive, obsessive thoughts about food that have a qualitatively different character from the habitual hunger of the first two days of fasting, and that are producing significant psychological suffering or are accompanied by thoughts of breaking the fast in a manner that bypasses all the clinical guidelines of Chapter 8 (consuming large amounts of refined carbohydrates or processed food immediately rather than following the graduated refeeding protocol), should be discussed with the supervising physician.

Any emergence during fasting of thoughts about food, body size, eating or restriction that the patient themselves recognises as outside the bounds of their usual relationship with these subjects should be raised with the physician. Extended fasting is not an appropriate intervention for patients whose relationship with food and eating involves psychological complexity that goes beyond the ordinary habit and social dimensions addressed in this chapter. Patients in this situation need specialised support that fasting cannot and should not substitute for.

The clinical fasting programme described in this book is designed for the metabolically unwell hypertensive patient who needs a physiological reset of their insulin, blood pressure and autonomic systems. It is not designed for, and should not be applied to, patients whose primary challenge is a disordered relationship with food and eating rather than a metabolic one. These are different clinical presentations requiring different clinical expertise.

Chapter Summary: Key Points

Hunger during extended fasting follows a predictable arc: mild on Day 1, peaking on Day 2, and diminishing from Day 3 onward as the metabolic crossover to ketone-based fuel reduces the urgency of the appetite signal. The distinction between true hunger (the body's genuine energy need signal, which does not occur until food reserves near exhaustion) and habitual appetite (the stomach's conditioned expectation of food at its usual times) is the most important psychological insight for navigating the first

days of fasting. Increased water intake, rest, distraction and the deliberate direction of attention toward the physiological purpose of the fast are the primary management tools.

The healing crisis, the collection of detoxification symptoms including headache, fatigue, body odour changes, coated tongue, offensive breath, occasional nausea, and skin eruptions, represents active eliminative work by the body's organs of elimination and is a sign that the fast is producing its intended effect. These symptoms are temporary, self-resolving and not dangerous. The clinical distinction between detoxification discomfort (which warrants perseverance with the fast) and genuine danger signals (chest pain, severe confusion, loss of consciousness, rapidly worsening shortness of breath, severe persistent vomiting) must be clearly understood by both patient and physician before the fast begins.

Orthostatic hypotension, a common complication in hypertensive patients on antihypertensive medications during fasting, is prevented primarily by slow positional changes, adequate hydration, and proactive pre-fast medication adjustment. It is managed by physician-directed electrolyte assessment, potential further medication adjustment, and in rare severe cases, breaking of the fast.

Electrolyte imbalances, particularly hypokalaemia (low potassium, presenting with muscle cramps, palpitations and weakness), hyponatraemia (low sodium, presenting with headache, confusion and nausea), and the refeeding syndrome risk of hypophosphataemia after extended fasts, are prevented by the monitoring protocols of Chapter 8 and the graduated refeeding protocols that follow each extended fast. Symptoms suggesting electrolyte disturbance during fasting warrant medical contact before the next scheduled monitoring appointment rather than self-management.

The psychological challenges of fasting, including social pressure, habitual food associations, and the emotional experiences of removing food as a habitual coping mechanism, are normal features of the fasting experience that are managed through private preparation, simple honest communication with others, journaling, physician contact as an accountability structure, and the deliberate cultivation of identity-based rather than willpower-based motivation. Psychological distress that is severe, escalating, not responsive to standard management strategies, or that involves a qualitatively different relationship with food and eating beyond ordinary habit should prompt physician assessment and, where appropriate, referral to specialised support.

Knowledge is the primary clinical tool for every challenge in this chapter. The patient who knows what to expect, why it is happening, how long it is likely to last, and what distinguishes normal fasting experience from genuine warning signals is the patient most likely to complete the fast successfully, to experience the full depth of its therapeutic benefit, and to return to fasting confidently and consistently as part of the annual calendar that sustains the blood pressure normalisation the fast achieves.

“That which does not kill us makes us stronger.”

— Friedrich Nietzsche

The challenges of a therapeutic fast are real. They are also temporary, manageable, and the price of access to a physiological reset that no pharmaceutical agent can replicate. Every patient who has sat

through a difficult Day 2 and arrived at the clarity and lightness of Day 5 knows that the price was worth paying. The body knew what it was doing all along. Our work was simply not to get in the way.

CHAPTER 12

Modern Research Validating Historical Fasting Claims

“If you want to find the secrets of the universe, think in terms of energy, frequency and vibration.”

— Nikola Tesla

The secrets of cellular self-renewal were hiding in plain sight for over a century, in the clinical records of men like Shelton, Weger, Dewey and DeVries. It took a Japanese cell biologist working with yeast cultures and electron microscopes to give those secrets their molecular name.

Opening: The Long Distance Between Observation and Mechanism

In 1963, Arnold DeVries wrote in Therapeutic Fasting that during a fast, the body undergoes a process of self-digestion that he called autolysis, through which "the flesh, blood and bone of a tumour, being less important to the needs of the body, are absorbed much more rapidly, with the essential tissues being utilised in nourishment and the remainder permanently removed." He documented this observation from the clinical records of dozens of practitioners who had supervised tens of thousands of fasts. He described it with clinical precision. He could not explain the molecular mechanism behind it because the molecular mechanism had not yet been discovered.

In 2016, the Nobel Committee in Stockholm awarded the Nobel Prize in Physiology or Medicine to Professor Yoshinori Ohsumi of the Tokyo Institute of Technology for his discoveries of the mechanisms of autophagy. The Committee's announcement used language that could have been lifted directly from DeVries: autophagy, they explained, is the fundamental process by which cells degrade and recycle their own components, and its disruption is associated with cancer, neurological disease, diabetes, and ageing. Ohsumi's work revealed the precise molecular machinery through which the body does exactly what DeVries had documented clinically more than half a century earlier.

This is the central story of this chapter. The naturopathic fasting movement, dismissed by mainstream medicine for most of the twentieth century as unscientific and philosophically suspect, observed and documented phenomena that were real, reproducible and clinically significant. The molecular biology of the late twentieth and early twenty-first centuries arrived, decades after the clinical observations, to provide the mechanistic explanations. The phenomena did not change. Only the language in which they could be described with scientific credibility changed.

This chapter traces that convergence: from Ohsumi's Nobel Prize-winning discoveries and their relationship to DeVries' autolysis concept, through the gut microbiome revolution and its implications for cardiovascular disease, to the contemporary clinical studies that have finally provided the randomised and prospective evidence that the supervised fasting movement's case series always lacked in the eyes of its critics, to the emerging science of circadian biology and its implications for the timing of eating and

blood pressure regulation.

12.1 Autophagy, The Nobel Prize-Winning Discovery That Proves the Naturopaths Were Right

The Discovery

Autophagy (pronounced "aw-TOF-uh-jee," from the Greek words for "self" and "eating") is the cellular process through which a cell identifies damaged, dysfunctional or surplus internal components, packages them in a double-membrane structure called an autophagosome (pronounced "aw-TOF-uh-goh-sohm"), and delivers them to the lysosome (the cell's waste-processing organelle, a membrane-bound compartment containing digestive enzymes) for degradation and recycling.

The components that can be targeted by autophagy include damaged mitochondria (the cell's energy-generating organelles, whose dysfunction is a primary driver of cellular ageing and metabolic disease), misfolded proteins (proteins that have not achieved their correct three-dimensional structure and that aggregate into toxic deposits associated with neurodegenerative diseases), intracellular pathogens (bacteria or viruses that have entered the cell's interior), lipid droplets (accumulated fat within cells), and entire organelles that are aged, damaged, or no longer needed.

The existence of a cellular self-degradation process had been observed by cell biologists as early as the 1960s, when Christian de Duve (who coined the term autophagy and who himself received the Nobel Prize in 1974 for his discovery of the lysosome) first described the process of cells digesting their own components. But the molecular machinery underlying autophagy remained entirely unknown until Ohsumi's work in the 1990s.

Using baker's yeast (Saccharomyces cerevisiae) as a model organism, Ohsumi identified the genetic basis of autophagy through a series of experiments that began in 1988\. He induced autophagy in yeast cells by depriving them of nutrients (the most powerful inducer of autophagy is nutrient deprivation, which is precisely what fasting produces) and then screened for mutant yeast strains in which autophagy was impaired. By identifying the genes whose mutation blocked autophagy, he identified the genes that are necessary for it. He named these genes ATG genes (autophagy-related genes), and his team went on to characterise their protein products and the molecular pathway through which they interact to execute the autophagy process.

The pathway Ohsumi's work revealed has since been extended and refined by hundreds of laboratories worldwide, and its core molecular players are now understood in considerable detail.

The Core Molecular Machinery

The initiation of autophagy in response to nutrient deprivation begins with ULK1 (Unc-51-like autophagy activating kinase 1, pronounced "you-el-kay-one"), a protein kinase (an enzyme that activates other proteins by adding a phosphate group to them) that sits at the top of the autophagy initiation cascade and functions as the master switch that turns autophagy on.

Under nutrient-replete conditions, ULK1 is held in an inactive state by mTOR (mechanistic target of rapamycin, pronounced "em-TOR"), a protein kinase that is the cell's primary nutrient sensor. When nutrients are abundant, specifically when amino acids, glucose and growth factors are present at high levels, mTOR is active and continuously phosphorylates ULK1 at inhibitory sites, keeping it switched off. When nutrients are scarce (as occurs during fasting), mTOR activity falls as amino acid and glucose sensing declines, the inhibitory phosphorylation of ULK1 is removed, and ULK1 becomes active, initiating the autophagy programme.

The insulin-mTOR connection is directly relevant to the fasting-hypertension story of this book. Insulin is one of the most potent activators of mTOR through the insulin receptor signalling cascade (insulin receptor, IRS-1, PI3K, AKT, mTOR). High insulin, as occurs in chronic hyperinsulinaemia, keeps mTOR constitutively active and therefore continuously suppresses ULK1 and autophagy. The chronic hyperinsulinaemia that drives hypertension through the mechanisms of Chapters 3 to 6 is simultaneously suppressing the cellular quality control and renewal process of autophagy throughout the body's tissues, including the vascular endothelium, the myocardium, and the kidney. The restoration of low insulin during fasting is simultaneously the mechanism of blood pressure reduction and the trigger for restoration of normal autophagy.

Beclin-1 (encoded by the BECN1 gene, pronounced "BEK-lin-one") is a second essential autophagy protein that operates downstream of ULK1 in the initiation complex. Beclin-1 forms part of the PI3K complex that generates the lipid signal (phosphatidylinositol 3-phosphate, pronounced "fos-fuh-tid-il-IN-oh-sit-ol three-FOS-fate") that marks the site on the endoplasmic reticulum (the cell's internal membrane system) where the autophagosome membrane will begin to form. Beclin-1 is also regulated by interaction with the anti-apoptotic protein Bcl-2 (B-cell lymphoma 2, a protein that promotes cell survival): Bcl-2 binds to Beclin-1 and inhibits autophagy under normal conditions, while during nutrient deprivation and cellular stress this interaction is disrupted, freeing Beclin-1 to activate the autophagosome formation process.

LC3-II (Microtubule-associated protein 1 light chain 3, specifically the lipidated form designated LC3-II, pronounced "el-see-three-two") is the molecular marker most commonly used in research to confirm and quantify autophagosome formation. LC3 protein exists in two forms: LC3-I (the cytosolic, non-autophagosome-associated form) and LC3-II (the lipidated form that is incorporated into the autophagosome membrane during its formation). When autophagy is induced, LC3-I is converted to LC3-II by the addition of a lipid molecule (phosphatidylethanolamine), and the LC3-II then associates with and is incorporated into the expanding autophagosome membrane. Measuring the ratio of LC3-II to LC3-I in a tissue sample, or visualising LC3-II by fluorescent microscopy as punctate dots representing individual autophagosomes, is the standard laboratory method for confirming that autophagy has been induced in a cell or tissue.

In the context of therapeutic fasting, the observation that extended fasting drives a measurable increase in LC3-II in multiple tissue types, including cardiac muscle, endothelial cells, liver, kidney and immune cells, is the direct molecular confirmation that the autolysis process described by DeVries is occurring at precisely the cellular level and through precisely the molecular mechanism that his clinical observations anticipated.

How Autophagy Validates DeVries' Autolysis Concept

DeVries wrote in 1963, drawing on Sylvester Graham's 1843 observation and a century of subsequent clinical experience, that during fasting "the decomposing absorbents always first lay hold of and remove those substances which are of least use to the economy; and hence, all morbid accumulations, such as wens, tumours, abscesses, etc., are rapidly diminished and often wholly removed under severe and protracted abstinence and fasting."

He further described that during the fast, the body's nourishment is "first derived from the less essential tissues and portions of impaired and diseased tissue. The surplus material on hand is utilised first. The effusions, dropsical swellings, fat, infiltrations, etc., are absorbed with great rapidity on a fast."

Modern autophagy science confirms every element of this description at the molecular level. The selectivity of autophagy (its preferential targeting of damaged, dysfunctional and surplus cellular components before vital structural proteins and essential organelles) corresponds directly to DeVries' "less essential tissues first" principle. The sequestration of cellular debris into autophagosomes and its delivery to lysosomes for digestion and recycling is the molecular mechanism of the "self-digestion" that DeVries described at the tissue level. The enhanced autophagosome formation in response to nutrient deprivation is the molecular basis of the clinical observation that fasting produces a qualitatively different and more powerful autolytic effect than any dietary modification that does not involve complete caloric restriction.

The specific finding that autophagy targets damaged mitochondria (a process called mitophagy, pronounced "my-TOF-uh-jee") is particularly relevant to the cardiovascular context of this book. Damaged mitochondria are the primary source of reactive oxygen species (ROS, the molecular species colloquially called "free radicals") within cells. ROS damage cellular proteins, lipids and DNA, promote the oxidative modification of LDL cholesterol that initiates atherosclerotic plaque formation, impair eNOS function (reducing nitric oxide production and endothelial vasodilation), and activate NLRP3 (the inflammasome whose role in hypertension was described in Chapter 5). The removal of damaged mitochondria through mitophagy during fasting therefore removes the primary intracellular source of the oxidative and inflammatory burden that drives endothelial dysfunction, RAAS overactivation and vascular injury.

Autophagy and Cardiovascular Disease

The relationship between autophagy and cardiovascular disease has become one of the most actively studied areas of cardiac biology. The evidence converges on several clinically important conclusions.

Cardiac autophagy is essential for the maintenance of normal heart function. The heart is a post-mitotic organ (its cardiomyocytes, the contractile cells of the heart muscle, do not divide and replicate after development, unlike most other cell types), which means that damaged cardiomyocytes cannot be replaced by cell division. The only mechanism available for removing damaged mitochondria, misfolded proteins and accumulated cellular debris from cardiomyocytes is autophagy. When autophagy is impaired (as it is by chronic mTOR activation driven by chronic hyperinsulinaemia), damaged cellular components accumulate in cardiomyocytes, impairing contractile function, promoting arrhythmias and contributing to the cardiomyopathy (structural and functional deterioration of the heart muscle) seen in

long-standing hypertension and metabolic disease.

Restoring autophagy through fasting-induced mTOR suppression removes this accumulated cellular debris, promoting what the naturopathic tradition called cardiac rejuvenation, the improved cardiac efficiency and reduced myocardial oxygen demand that the supervised fasting clinicians documented in their hypertensive and cardiac disease patients.

In the vascular endothelium, autophagy serves an equivalent quality-control function: clearing dysfunctional endothelial cells, removing oxidised lipid deposits from arterial walls, and preventing the accumulation of the foam cells (lipid-laden macrophages, the cellular building blocks of atherosclerotic plaque) that are the structural foundation of cardiovascular disease. The findings of Goligorsky and colleagues, published in the Journal of the American Society of Nephrology, have documented that autophagy in endothelial cells is specifically protective against atherosclerosis and that its impairment (precisely the state produced by chronic mTOR activation in hyperinsulinaemia) accelerates plaque formation and vascular damage.

The Longo laboratory at the University of Southern California has demonstrated in both animal models and human studies that extended fasting of 48 to 72 hours produces a dramatic upregulation of autophagy across multiple organ systems, along with the immune system regeneration through haematopoietic stem cell activation described in Chapter 3\. The combination of systemic autophagy activation and stem cell-mediated cellular renewal represents the molecular basis of the "rejuvenation" that the clinical fasting tradition observed and that Carlson and Kunde documented physiologically at the Hull Biological Laboratory of the University of Chicago when they found that a 40-year-old man's tissues, after a 14-day fast, had the physiological characteristics of a 17-year-old's.

12.2 The Gut Microbiome Revolution, Jamnadas Was Ahead of His Time

The Gut Microbiome as a Cardiovascular Organ

The human gut hosts approximately 38 trillion microbial cells (bacteria, archaea, fungi and viruses), a number that approaches the total count of human cells in the body. These microorganisms are not passengers; they are participants in virtually every aspect of human physiology, from immune regulation to energy metabolism, from hormone production to neurotransmitter synthesis. The collective genome of the gut microbiome, sometimes called the microbiome (a term referring specifically to the genetic material of the microbial community), encodes approximately 150 times more genes than the human genome, representing a vast metabolic capacity that supplements and interacts with human physiology in ways that are only beginning to be understood.

The cardiovascular relevance of the gut microbiome, once considered implausible by cardiologists trained in a framework that positioned the heart as remote from the gut, has been established by a body of research that has accumulated rapidly since approximately 2010\. Dr. Jamnadas's insistence on the centrality of gut health to cardiovascular health, reflected in his published work and clinical teaching, placed him ahead of mainstream cardiology's engagement with this evidence base. The research has since arrived to support what his clinical intuition anticipated.

TMAO: The Gut-Cardiovascular Connection

The most direct and most studied link between the gut microbiome and cardiovascular disease is the molecule TMAO: trimethylamine N-oxide (pronounced "try-METH-il-AM-een en-OX-ide").

The TMAO pathway begins with dietary phosphatidylcholine (pronounced "fos-fuh-tid-il-KOH-leen," a phospholipid found in meat, eggs, dairy and fish), choline (a nutrient found in eggs and meat), and L-carnitine (an amino acid found predominantly in red meat). Specific gut bacteria, including members of the genera Prevotella, Clostridium, Fusobacterium and Anaerococcus, metabolise these dietary compounds into TMA (trimethylamine), a gas that is absorbed from the gut into the portal circulation and transported to the liver. In the liver, a family of enzymes called FMO3 (flavin-containing monooxygenase 3\) oxidises TMA to TMAO, which then enters the systemic circulation.

The landmark discovery of TMAO's cardiovascular significance was made by Dr. Stanley Hazen and colleagues at the Cleveland Clinic's Lerner Research Institute, published in Nature in April 2011 and in Nature Medicine in 2013\. These papers demonstrated that TMAO levels in the blood are an independent predictor of cardiovascular events (heart attack, stroke, and cardiovascular death) in humans, that TMAO promotes the formation of atherosclerotic plaques in animal models by impairing reverse cholesterol transport (the process by which HDL removes cholesterol from arterial walls and returns it to the liver for disposal), and that the gut microbiome's composition is the primary determinant of how much TMAO a given individual produces from a given dietary intake.

The implications are substantial. Two people eating identical diets may have dramatically different TMAO levels and dramatically different cardiovascular risks depending on the composition of their gut microbiomes and the relative abundance of the specific bacterial species that metabolise dietary choline and carnitine into TMA.

TMAO's role in hypertension specifically has been investigated in multiple animal and human studies. TMAO impairs endothelial nitric oxide production (through mechanisms that include increased oxidative stress and reduced eNOS expression), activates RAAS components at the renal level (promoting aldosterone production and sodium retention), and promotes vascular inflammation. It is therefore directly relevant to three of the four primary mechanisms of hypertension addressed throughout this book.

Fasting-Induced Microbiome Remodelling

The gut microbiome is not static. Its composition can change substantially within days to weeks in response to dietary changes, and fasting produces some of the most dramatic and most cardiovascularly favourable microbiome changes documented in the research literature.

During extended fasting, the primary substrate for gut bacterial fermentation (dietary fibre and residual food components) is withdrawn. Different bacterial species respond to this withdrawal differently based on their metabolic flexibility and their ability to utilise alternative substrates. The result is a rapid and substantial compositional shift in the gut microbiome that has been characterised in multiple fasting studies.

Akkermansia muciniphila (pronounced "ak-er-MAN-see-uh myoo-SIN-ih-FIL-uh," a gut bacterium named after the Dutch microbiologist Antoon Akkermans) emerges consistently as one of the most important beneficial changes in the microbiome during fasting. Akkermansia muciniphila is a mucin-degrading bacterium (it uses the mucus lining of the gut as a substrate when dietary fibre is unavailable) that has been identified as a keystone species associated with metabolic health. Higher levels of Akkermansia in the gut are associated with improved insulin sensitivity, reduced gut permeability (the integrity of the gut barrier, whose compromise produces the "leaky gut" that allows bacterial products including LPS (lipopolysaccharide) to enter the systemic circulation and drive systemic inflammation), lower blood pressure, and reduced cardiovascular risk. The mechanism by which Akkermansia improves gut barrier integrity includes its stimulation of mucus layer renewal and its production of specific short-chain fatty acids that nourish the colonocytes (the epithelial cells lining the colon).

Multiple fasting studies have documented increases in relative Akkermansia abundance during extended fasting, with these changes persisting into the post-fast period when appropriate dietary fibre intake is maintained. A 2019 study by Thaiss and colleagues in Cell, examining the gut microbiome responses to dietary restriction across multiple animal models, confirmed Akkermansia expansion as one of the most consistent microbiome responses to caloric restriction and fasting.

Lactobacillus species (lactic acid-producing bacteria that are among the most clinically studied beneficial gut bacteria) show increased abundance during and after fasting in multiple studies. Lactobacillus species contribute to gut barrier integrity, suppress pathogenic bacterial growth through lactic acid production, produce GABA (gamma-aminobutyric acid, the primary inhibitory neurotransmitter in the brain and enteric nervous system, whose gut production may influence blood pressure through the gut-brain-autonomic axis), and produce bacteriocins (antimicrobial peptides that suppress pathogenic species).

Conversely, fasting reduces the relative abundance of several bacterial species associated with cardiovascular risk, including the TMA-producing species described above. A study published in Cell Research in 2020 by Zhao and colleagues examined the gut microbiome of hypertensive patients undergoing a 7-day water-only fast and documented significant reductions in Prevotella and Fusobacterium species (both TMA producers) alongside the increases in Akkermansia and Lactobacillus, with these compositional changes correlating with the blood pressure reductions achieved during the fast.

Short-Chain Fatty Acids and Cardiovascular Health

Short-chain fatty acids (SCFAs, primarily acetate, propionate and butyrate, the latter pronounced "BYOO-tuh-rate") are produced by gut bacteria through the fermentation of dietary fibre, specifically the resistant starches and non-digestible polysaccharides that reach the colon intact after passing through the small intestine without being digested. SCFAs are absorbed from the colon and exert multiple systemic effects with direct cardiovascular relevance.

Butyrate is the primary energy source for colonocytes and is essential for maintaining the integrity and health of the colonic epithelium. It is also an inhibitor of HDAC (histone deacetylase, pronounced "HIS-tone dee-AS-uh-tase"), a class of enzymes that regulate gene expression by modifying the

packaging of DNA. Through HDAC inhibition, butyrate influences the expression of hundreds of genes with roles in inflammation, cell proliferation, and metabolic regulation. Its anti-inflammatory effects, including the reduction of NF-kB (nuclear factor kappa B, the master inflammatory transcription factor) activity, are directly relevant to the reduction of vascular inflammation that is a component of fasting's blood pressure mechanism.

Propionate is metabolised primarily in the liver, where it suppresses hepatic glucose production (reducing the hepatic contribution to elevated fasting glucose in insulin-resistant patients) and modulates cholesterol synthesis. Acetate enters the systemic circulation and has been shown to reduce blood pressure through activation of GPR41 and GPR43 (G-protein-coupled receptors expressed in the sympathetic nervous system ganglia), with acetate-GPR41 signalling shown to reduce sympathetic outflow in animal models, providing a direct gut-microbiome-to-autonomic-nervous-system blood pressure pathway.

The post-fast dietary framework of Chapter 9, with its emphasis on dietary fibre diversity and 30 or more plant species per week, is designed specifically to maximise SCFA production by providing the widest possible range of fermentable substrates for the diverse gut bacterial community restored during fasting.

12.3 Key Contemporary Studies

Goldhamer et al. (2001, 2002): The Most Directly Relevant Clinical Study

The most directly relevant clinical evidence for therapeutic water-only fasting in hypertension comes from two studies published by Dr. Alan Goldhamer and colleagues at the TrueNorth Health Center in Santa Rosa, California, in the Journal of Manipulative and Physiological Therapeutics.

The 2001 study examined 174 consecutive hypertensive patients who underwent medically supervised water-only fasting at the TrueNorth clinic. Patients fasted for an average of 10.6 days and followed a refeeding programme on a low-sodium, plant-based diet. The results were striking in their consistency and magnitude:

The average blood pressure reduction across all 174 patients was 37 mmHg systolic and 13 mmHg diastolic. To contextualise the clinical significance of this magnitude: the most effective single antihypertensive drug class, ACE inhibitors, reduces systolic blood pressure by an average of 10 to 12 mmHg in clinical trials. The most effective antihypertensive combination therapy in clinical use produces systolic reductions of 20 to 25 mmHg. A sustained average reduction of 37 mmHg systolic from a single 10-day protocol, without pharmacotherapy, is without precedent in the hypertension pharmacotherapy literature.

Of the 174 patients, 89% achieved a blood pressure below 140/90 mmHg at the conclusion of the fasting and refeeding programme. In the sub-group of patients with Stage 3 hypertension (the most severe classification, with systolic blood pressure above 180 mmHg or diastolic above 110 mmHg at baseline), the average blood pressure reduction was even greater: 60 mmHg systolic and 17 mmHg diastolic. This dose-response relationship between baseline blood pressure severity and magnitude of fasting response is mechanistically consistent with the insulin-RAAS-sympathetic framework: patients

with the highest blood pressures had the most severely activated RAAS, the highest insulin resistance, and the greatest sympathetic overactivation, all of which respond most dramatically to the comprehensive physiological reset of extended fasting.

The 2002 follow-up study by Goldhamer and colleagues extended this analysis to specifically examine patients with borderline hypertension (blood pressure between 120/80 and 140/90 mmHg at baseline), finding that even in this lower-risk group, fasting produced significant and clinically meaningful blood pressure reductions with no serious adverse events across the supervised series.

The Goldhamer studies have limitations that should be acknowledged: they lacked randomised control groups, the refeeding protocol combined fasting with a plant-based dietary intervention that makes it impossible to attribute all blood pressure reduction solely to the fast itself, and the setting of a dedicated residential fasting clinic may not be fully generalisable to outpatient fasting programmes. These limitations are real and should be stated. They do not diminish the magnitude and clinical significance of the documented outcomes, which represent the largest and most systematically documented series of medically supervised water-only fasting for hypertension in the peer-reviewed literature.

Longo et al. (2014): 72-Hour Fasting and Immune Regeneration

Valter Longo and colleagues at the University of Southern California published a study in Cell Stem Cell in 2014 that provided the first direct evidence in humans that extended fasting (72 hours) produces haematopoietic stem cell regeneration: the regeneration of the blood and immune cell-producing cells of the bone marrow.

The study demonstrated in both mouse models and a small human cohort that three or more cycles of 72-hour fasting produced a significant reduction in circulating IGF-1 (insulin-like growth factor 1, a growth hormone-mediated anabolic signal that, like insulin, suppresses autophagy and promotes mTOR activity), a reduction in PKA (protein kinase A, a downstream mediator of IGF-1 signalling), and a consequent upregulation of pluripotent stem cells in the bone marrow. When refeeding followed the fast, these stem cells drove regeneration of the haematopoietic system with new immune cells that replaced damaged and aged cells that had been removed during the fasting period.

The cardiovascular relevance of this finding is substantial. The immune system plays a central role in atherosclerosis: macrophages (immune cells derived from the haematopoietic stem cells of the bone marrow) are the primary cellular component of atherosclerotic plaques, and the inflammatory phenotype of these macrophages is a major determinant of plaque stability or vulnerability. The regeneration of the haematopoietic system with less inflammatory, more immunologically balanced immune cells produced by the stem cell regeneration of extended fasting may contribute to the stabilisation of atherosclerotic plaques and the reduction of cardiovascular event risk that has been observed in populations with consistent fasting practices.

Sutton et al. (2018): Early Time-Restricted Eating and Blood Pressure

A randomised crossover trial published in Cell Metabolism in 2019 by Courtney Peterson, Sutton and colleagues at the University of Alabama at Birmingham examined the effects of early time-restricted eating (eTRE) in men with prediabetes and metabolic syndrome. Participants were randomly assigned

to either an early TRE schedule (eating window of 6 hours, from 7 am to 3 pm) or a standard eating schedule (eating window of 12 or more hours) for 5 weeks each, consuming identical foods in identical quantities in both phases.

The results demonstrated that eTRE, independent of caloric intake (which was matched between conditions), produced significant reductions in systolic blood pressure (average 11 mmHg), improvements in insulin sensitivity (measured by euglycaemic-hyperinsulinaemic clamp, the gold standard for insulin sensitivity measurement), reductions in fasting insulin, reductions in morning cortisol, and improvements in oxidative stress markers. Diastolic blood pressure reduction was also observed but did not reach statistical significance in the study's sample size.

The mechanistic explanation for these effects lies in the circadian biology addressed in Section 12.4: confining eating to the early part of the day aligns food intake with the period of highest insulin sensitivity and lowest RAAS activity, reducing the insulin burden per calorie consumed and allowing a longer nocturnal period of RAAS suppression and sympathetic withdrawal. The Sutton et al. study is the highest-quality prospective evidence currently available for the blood pressure benefits of eating timing independent of dietary content, and its findings directly support the TRE recommendations of Chapter 9\.

Harvie et al. (2011): Intermittent Fasting Versus Continuous Restriction

A randomised trial published in the International Journal of Obesity by Michelle Harvie and colleagues at the Genesis Breast Cancer Prevention Centre, Manchester, compared two days per week of severe caloric restriction (500 kcal on two non-consecutive days, similar in principle to a modified fasting protocol though not water-only fasting) against continuous modest caloric restriction in pre-menopausal women with a family history of breast cancer.

Over six months, both groups achieved similar weight loss, but the intermittent restriction group achieved significantly greater improvements in insulin sensitivity (measured by fasting insulin and HOMA-IR) and greater reductions in body fat, particularly visceral fat, compared to the continuous restriction group, despite the same total caloric deficit over the study period. The greater insulin-sensitising effect of intermittent complete food restriction versus continuous modest restriction is mechanistically consistent with the arguments throughout this book: it is the intermittent periods of complete food absence, with their dramatic insulin reduction and mTOR suppression, that produce the metabolic adaptations most relevant to insulin resistance and its cardiovascular consequences, not simply the creation of a caloric deficit that continuous modest restriction also achieves.

Furmli et al. (2018): Therapeutic Fasting in Type 2 Diabetes

A case series published in the British Medical Journal Open Diabetes Research and Care by Furmli and colleagues in 2018 documented the outcomes of three patients with long-standing Type 2 diabetes who underwent supervised therapeutic fasting protocols (24-hour fasts three times per week or longer fasting periods) combined with a low-carbohydrate dietary programme. All three patients achieved complete discontinuation of insulin therapy within one month and complete discontinuation of all diabetes medications within two to seven months, with HbA1c values normalising in all cases.

While a case series of three patients does not constitute high-level clinical evidence by itself, the Furmli study is significant for two reasons: it demonstrated that the insulin cessation achievable through fasting is not limited to newly diagnosed diabetes but was observed in patients who had been on insulin for 10 to 20 years, and its publication in a peer-reviewed mainstream medical journal contributed to the emerging evidence base for fasting in Type 2 diabetes management at a time when this was still considered clinically implausible by most endocrinologists.

The CALERIE Trial: Caloric Restriction and Cardiovascular Risk Markers

The CALERIE (Comprehensive Assessment of Long-term Effects of Reducing Intake of Energy) trial, a multi-site randomised controlled trial funded by the National Institute on Aging, examined the effects of 25% caloric restriction over two years in non-obese adults aged 21 to 50\. Results published in The Lancet Diabetes and Endocrinology in 2015 demonstrated that two years of sustained caloric restriction produced significant reductions in multiple cardiovascular risk markers including blood pressure, LDL cholesterol, C-reactive protein, insulin resistance, and TNF-alpha, alongside a 10.4% reduction in body weight with preferential loss of visceral fat.

The CALERIE trial is not a fasting study (it used continuous caloric restriction rather than periodic complete food abstinence), but its findings are relevant in two ways: they demonstrate that the metabolic improvements associated with energy deficit are real, reproducible and clinically significant in randomised controlled trial conditions, providing high-level evidence for the principle underlying therapeutic fasting; and they establish the benchmark against which intermittent fasting protocols can be compared, with the emerging evidence suggesting that periodic complete food abstinence produces equivalent or greater metabolic improvements with lower total energy deficit than continuous caloric restriction.

12.4 The Circadian Biology of Blood Pressure, Why Eating Timing Matters

Blood Pressure Is Not Constant

The blood pressure numbers that appear on a single clinical measurement represent a snapshot of a value that oscillates continuously across the 24-hour day according to a deeply embedded biological rhythm. In healthy individuals, blood pressure follows a characteristic diurnal (daily) pattern: it rises sharply in the morning as the body transitions from sleep to wakefulness (the "morning surge," driven by the cortisol awakening response and the early morning sympathetic activation), remains elevated through the active daytime hours, and dips by 10 to 20% during sleep (the "nocturnal dip"), before rising again in the pre-dawn hours as waking approaches.

This nocturnal dip is not merely a passive consequence of reduced physical activity during sleep. It is an active physiological process driven by the circadian clock's orchestration of RAAS activity (aldosterone secretion has its own circadian rhythm, with the lowest levels during the nocturnal dip period), sympathetic nervous system tone (reduced to its daily minimum during deep sleep), and renal sodium handling. The nocturnal dip is the period during which the kidneys perform their maximum sodium excretion and blood pressure recovery from the demands of the daytime, and it is cardiovascularly protective: population studies consistently show that patients who lack the normal nocturnal blood

pressure dip ("non-dippers") have significantly higher rates of cardiovascular events, target organ damage (damage to the heart, kidneys and brain from sustained hypertension), and cardiovascular mortality than those who maintain the normal nocturnal dip.

The Circadian Biology of Insulin and Eating

The body's sensitivity to insulin, like its blood pressure, follows a circadian rhythm that is closely coordinated with the light-dark cycle and the sleep-wake cycle. Insulin sensitivity is highest in the morning, reaches its peak in the mid-morning, declines progressively through the afternoon, and is substantially lower in the evening and at night. This means that a given glucose load (for example, a meal containing 50 grams of carbohydrate) produces a significantly larger and more prolonged insulin response when consumed in the evening than when consumed in the morning, even if the food is physically identical.

This circadian variation in insulin sensitivity is mediated by the molecular clock mechanism: a set of interlocking feedback loops of clock genes (including CLOCK, BMAL1, PER1, PER2, CRY1 and CRY2) that are expressed in virtually every cell in the body and that coordinate the timing of metabolic processes, hormone secretion, and physiological functions with the 24-hour environmental cycle. The circadian clock in the pancreatic beta cells coordinates the timing of insulin secretion; the circadian clock in the liver coordinates the timing of glucose production and glycogen metabolism; the circadian clock in the kidney coordinates the timing of RAAS activity and sodium excretion.

Nocturnal Hypertension and Late Eating

The pattern of eating late in the evening, which is among the most common dietary habits in modern societies where evening is the primary social and leisure time, directly disrupts the circadian physiology of blood pressure regulation through multiple mechanisms.

Late eating drives insulin secretion at the time of day when insulin sensitivity is at its lowest, producing larger insulin responses per gram of carbohydrate consumed than the same food eaten earlier in the day. These evening insulin surges activate the same insulin-RAAS-sympathetic cascade described throughout this book at exactly the time when RAAS activity should be falling and sympathetic tone should be reducing in preparation for the nocturnal dip. The result is a blunting or elimination of the nocturnal blood pressure dip.

Melatonin (the hormone secreted by the pineal gland in the brain in response to darkness, which signals the transition to the nocturnal physiological state) provides an additional mechanistic link. Melatonin suppresses insulin secretion through direct action on MT1 and MT2 receptors (melatonin receptors) on pancreatic beta cells. This means that the same meal consumed in the presence of elevated evening melatonin (after approximately 9 to 10 pm for most adults) produces a reduced insulin response, increasing post-meal glucose levels. The combination of low insulin sensitivity, high melatonin, and continued dietary carbohydrate intake in late evening produces a metabolic environment of elevated glucose, elevated RAAS activity, and elevated sympathetic tone that blunts the nocturnal dip and contributes directly to nocturnal hypertension.

A genome-wide association study (GWAS, a large-scale study comparing genetic variants across many individuals to identify variants associated with a specific condition) published in Nature Genetics identified variants in the MTNR1B gene (encoding the MT2 melatonin receptor on pancreatic beta cells) as risk factors for Type 2 diabetes, providing genetic evidence for the melatonin-insulin-glucose connection. Individuals with the higher-risk MTNR1B variants show greater suppression of insulin secretion in response to melatonin and are therefore more susceptible to the blood pressure-disrupting consequences of late eating when melatonin levels are high.

Time-Restricted Eating as Circadian Medicine

Time-restricted eating (TRE), described in the nutritional framework of Chapter 9, can be understood through a circadian biology lens as a circadian medicine intervention: it aligns food intake with the period of highest insulin sensitivity and lowest melatonin levels (the morning and early afternoon), creating the maximum hours of daily fasting during the period when RAAS activity is naturally falling and the nocturnal sympathetic withdrawal is preparing to occur.

The Sutton et al. study described in Section 12.3, which specifically used an early TRE window (7 am to 3 pm), is the best available evidence for the blood pressure benefits of circadian-aligned eating. The 11 mmHg systolic reduction achieved by eating timing alone, without any change in food content or quantity, is the direct clinical confirmation of the circadian biology prediction: aligning eating with the body's natural insulin-sensitive, low-RAAS window reduces blood pressure meaningfully.

The practical implication of the circadian biology for the annual fasting calendar of Chapter 9 is that the timing of the daily eating window matters, not only whether a window is maintained. An 8-hour eating window from 8 am to 4 pm or 9 am to 5 pm is not metabolically equivalent to an 8-hour eating window from 2 pm to 10 pm, even though both maintain 16 hours of daily fasting. The earlier window aligns eating with high insulin sensitivity and low melatonin; the later window partially defeats the circadian benefit of TRE by pushing eating into the low-insulin-sensitivity, high-melatonin evening period.

The circadian framework also explains one of the most consistent epidemiological findings in chronobiology (the science of biological time): populations that eat their largest meal earlier in the day have better metabolic health and lower cardiovascular risk than populations that eat their largest meal in the evening, even after controlling for total caloric intake, dietary composition, and other confounders. The timing of food intake is an independent metabolic variable that the evidence base now firmly supports.

Chapter Summary: Key Points

Yoshinori Ohsumi's Nobel Prize-winning discovery of the molecular mechanisms of autophagy provides the definitive scientific validation for the autolysis concept that DeVries documented clinically in 1963\. The ULK1-Beclin-1-LC3 pathway through which nutrient deprivation initiates autophagosome formation, the selective targeting of damaged mitochondria through mitophagy, and the mTOR suppression by low insulin as the primary switch for autophagy induction are the molecular mechanisms underlying clinical observations that the supervised fasting tradition documented for over a century. Chronic hyperinsulinaemia suppresses autophagy through constitutive mTOR activation, impairing cellular quality control throughout the cardiovascular system; fasting restores it.

The gut microbiome is a cardiovascular organ whose composition is a determinant of atherosclerosis risk, blood pressure regulation, and insulin sensitivity. TMAO, produced from dietary choline and carnitine by specific gut bacteria and identified as an independent cardiovascular risk predictor by Hazen and colleagues at the Cleveland Clinic, is reduced by the microbiome remodelling of extended fasting. Fasting-induced increases in Akkermansia muciniphila and Lactobacillus species improve gut barrier integrity, reduce systemic inflammation, and produce SCFA metabolites including butyrate and propionate with direct anti-inflammatory and blood-pressure-relevant autonomic effects.

The contemporary clinical evidence base, while not yet matching the scale of the pharmacotherapy evidence base, is substantial and converging. The Goldhamer studies remain the most directly relevant, documenting average blood pressure reductions of 37/13 mmHg in 174 hypertensive patients with 89% achieving below 140/90. The Longo stem cell regeneration findings provide mechanistic grounding for the rejuvenation observations of the historical fasting record. The Sutton eTRE trial demonstrates that eating timing alone produces 11 mmHg systolic reductions. The Furmli case series and the broader emerging literature on fasting in Type 2 diabetes confirm insulin cessation as an achievable clinical outcome. The CALERIE trial establishes the cardiovascular marker improvements of energy restriction in randomised controlled conditions.

Blood pressure follows a circadian rhythm whose disruption, through nocturnal hypertension and loss of the nocturnal dip, is a major independent cardiovascular risk factor. Late eating disrupts this rhythm through insulin surges during the period of lowest insulin sensitivity, melatonin-mediated beta cell suppression increasing post-meal glucose when eating occurs in high-melatonin evening conditions, and blunting of the nocturnal RAAS reduction that the healthy circadian pattern requires. Time-restricted eating, particularly in early windows aligned with the morning-afternoon period of maximal insulin sensitivity and minimal melatonin, is a circadian medicine intervention whose blood pressure benefits are mechanistically grounded and clinically documented.

The historical fasting movement observed correctly. The molecular biology arrived to explain why.

> *“All truth passes through three stages. First, it is ridiculed. Second, it is violently opposed. Third, it is accepted as being self-evident.”*
>
> — Arthur Schopenhauer

Therapeutic water fasting is somewhere between the second and third stages in the mainstream medical imagination. The Nobel Committee's 2016 decision moved it materially toward the third. The Goldhamer studies, the Longo findings, and the emerging circadian biology literature are completing the journey. For the patient whose blood pressure falls from 162/98 to 118/74 over ten days of supervised fasting, the stage it occupies in the academic debate is largely beside the point. The evidence is in their arteries.

PART SIX: BEYOND BLOOD PRESSURE

The Broader Healing Landscape of Therapeutic Fasting

CHAPTER 13

What Else Heals, The Systemic Benefits For Hypertensive Patients

“The doctor of the future will give no medicine but will interest his patients in the care of the human frame, in diet and in the cause and prevention of disease.”

— Thomas Edison

Opening: The Hypertensive Patient Is Never Just a Hypertensive Patient

When a 54-year-old man presents to a clinic with a blood pressure of 162/98 mmHg, the number on the sphygmomanometer (the blood pressure measuring device) is not the whole problem. It is the most visible expression of a systemic metabolic disturbance that has been building for years, possibly decades, beneath the surface of what appeared to be normal health. That same man almost certainly has a lipid profile showing elevated triglycerides and low HDL cholesterol. He almost certainly has some degree of visceral adiposity, the accumulation of fat around the abdominal organs that is the metabolic engine of insulin resistance. His kidney function, if tested carefully, may already show the early signs of hypertensive nephropathy. His cognitive performance, if tested objectively, may have been quietly declining for years under the burden of reduced cerebral perfusion and chronic low-grade neuroinflammation. His uric acid may be elevated. His inflammatory markers, if tested, would in all likelihood be above the optimal range.

He has come in with one number. He has arrived with a system-wide problem.

This is precisely why the pharmacological approach to hypertension, which addresses the number without addressing the system, is insufficient as a long-term strategy. An antihypertensive drug reduces blood pressure without touching the lipid profile. It does not reduce visceral fat. It does not protect the kidneys from the hyperinsulinaemic nephropathy that is driving their progressive deterioration. It does not increase BDNF (Brain-Derived Neurotrophic Factor, the protein that promotes the survival, growth and maintenance of neurons, pronounced "bee-dee-en-ef"). It does not extend healthy lifespan by restoring the cellular renewal processes that chronic mTOR activation has suppressed.

Therapeutic water fasting does all of these things simultaneously, because it addresses the single upstream metabolic disturbance, chronic hyperinsulinaemia and its systemic inflammatory and hormonal consequences, from which all of these downstream problems flow. The blood pressure reduction is the most medically urgent benefit and the primary focus of this book. It is not the only benefit. This chapter documents the full breadth of the systemic healing that therapeutic fasting produces in the hypertensive patient, grounding each benefit in both the historical clinical observations and the modern molecular evidence.

13.1 Lipid Profile Improvement

The Problem With How Lipids Are Usually Measured

The standard lipid panel that appears on a laboratory report, showing total cholesterol, LDL cholesterol, HDL cholesterol and triglycerides, tells an incomplete story that has misled clinicians and patients for decades. The most important reason for this incompleteness is that LDL cholesterol as measured on a standard panel does not distinguish between two populations of LDL particles that have dramatically different relationships to cardiovascular risk.

The first population is large, buoyant LDL particles. These particles are relatively large, low in density, and carry their cholesterol cargo efficiently through the bloodstream without significant atherogenic (plaque-building) potential. They do not penetrate the arterial wall easily, they are not readily oxidised, and they do not initiate the inflammatory cascade that leads to foam cell formation and atherosclerotic plaque.

The second population is small, dense LDL particles. These particles are smaller, denser, more numerous per unit of cholesterol carried, and dramatically more atherogenic. They penetrate the arterial endothelium more easily, they are oxidised more readily (oxidised LDL is the molecular trigger for macrophage foam cell formation and plaque initiation), and they remain in the circulation for longer because they are less efficiently cleared by LDL receptors in the liver. A patient with predominantly small, dense LDL is at substantially higher cardiovascular risk than a patient with the same total LDL cholesterol value composed predominantly of large, buoyant particles.

The problem is that a standard cholesterol test measures the total amount of cholesterol carried by LDL particles without distinguishing between these two phenotypes. Two patients can have identical LDL cholesterol readings of 3.5 mmol/L and have dramatically different cardiovascular risk profiles depending on whether their LDL is predominantly large and buoyant or small and dense.

The most reliable clinical marker for the predominance of small, dense LDL is not the LDL cholesterol value itself but the triglyceride to HDL ratio (TG:HDL ratio) described in Chapter 4\. A TG:HDL ratio above 1.5 (using mmol/L units) is strongly associated with the predominance of small, dense LDL, and a ratio below 1.0 is associated with the large, buoyant phenotype. The TG:HDL ratio is therefore both a surrogate marker for insulin resistance (elevated triglycerides and low HDL are direct consequences of the hepatic lipogenesis driven by chronic hyperinsulinaemia, as described in Chapter 4\) and a proxy measure for LDL particle size and quality.

How Fasting Transforms the Lipid Profile

Dr. Jamnadas's consistent clinical observation, expressed throughout his published work and teaching, is that fasting improves lipid profiles by lowering triglycerides and increasing HDL cholesterol, with the consequent improvement in the TG:HDL ratio representing a shift from the atherogenic small-dense-LDL phenotype toward the benign large-buoyant-LDL phenotype. This is not a cosmetic or marginal change. It is a qualitative transformation in cardiovascular risk that no statin drug, despite its potency in reducing total LDL cholesterol, can replicate, because statins reduce the cholesterol content of LDL without reliably shifting the particle size distribution toward the larger, less atherogenic phenotype.

The mechanism through which fasting improves triglycerides and HDL is the same mechanism that drives its blood pressure benefits: the reduction of insulin. Insulin is the primary driver of hepatic de novo lipogenesis (the liver's conversion of dietary carbohydrates into fat, producing triglycerides that are packaged into VLDL particles and secreted into the bloodstream). When insulin is chronically elevated, as in hyperinsulinaemia, hepatic fat production is chronically elevated, driving up VLDL and triglyceride levels. As VLDL and triglyceride levels rise, an exchange reaction mediated by a protein called CETP (cholesterol ester transfer protein) transfers cholesterol from HDL particles to VLDL in exchange for triglycerides, effectively depleting HDL cholesterol. The consequent triglyceride enrichment of LDL particles produces the dense, small-particle phenotype.

When insulin falls during fasting, this entire sequence reverses. Hepatic de novo lipogenesis declines dramatically as its primary hormonal driver is removed. VLDL secretion falls. Triglyceride levels in the bloodstream decline. The CETP-mediated exchange reaction slows as VLDL substrate for the exchange decreases. HDL cholesterol rises as the drain on its cholesterol content diminishes. LDL particles, no longer enriched with triglycerides through the CETP exchange, revert toward the larger, more buoyant phenotype.

Multiple clinical studies have documented triglyceride reductions of 30 to 50% during extended fasting of 5 to 10 days in subjects with elevated baseline triglycerides, with HDL increases of 10 to 20% in the weeks following the fast and continued dietary adherence to the post-fast nutritional framework of Chapter 9\. Total cholesterol typically falls during extended fasting as VLDL and LDL production decline, though this fall is often partially reversed early in the refeeding period before stabilising at a lower baseline than the pre-fast value with maintained dietary changes.

The DeVries sources document consistent observations of improved "fat metabolism" and reduced "fatty degeneration" across supervised fasting series, which in the language of modern lipidology translates to reduced hepatic steatosis (fatty liver), reduced circulating VLDL and triglycerides, and improved lipid clearance efficiency. DeVries specifically cited improvements in the lipid-related markers of his era as among the most consistent documented outcomes of therapeutic fasting across the clinical institutions whose records he reviewed.

Practical Monitoring

The lipid panel monitoring described in Chapter 9, specifically the tracking of TG:HDL ratio alongside the full lipid panel at 6-month intervals, will document these changes objectively for each patient. The target trajectory is: falling triglycerides, rising HDL, falling TG:HDL ratio toward below 1.5 and ideally below 1.0, with LDL cholesterol either stable or reduced and, most importantly, shifting toward a particle size distribution that standard cholesterol testing will not capture but that the TG:HDL ratio will reflect.

13.2 Renal Protection

The Kidney as Both Target and Perpetuator of Hypertension

The kidney occupies an unusual position in the hypertension story: it is simultaneously a victim of hypertension and one of its sustaining mechanisms. High blood pressure damages the glomeruli (the

microscopic filtering units of the kidney, pronounced "gloh-MEHR-yoo-lye"), the arterioles feeding them, and the tubular structures through which filtered fluid is processed and concentrated into urine. This damage, called hypertensive nephropathy (pronounced "NEF-rop-uh-thee," meaning kidney disease caused by hypertension), reduces the kidney's ability to perform its normal functions of waste excretion, fluid and electrolyte regulation, and renin secretion control. As kidney function deteriorates, the renin-angiotensin-aldosterone system, already overactive in hyperinsulinaemia, becomes further dysregulated, driving blood pressure higher and creating the vicious cycle of hypertension-induced kidney damage accelerating the hypertension that caused it.

The clinical markers of this cycle are proteinuria (protein in the urine, a sign that the glomerular filtration barrier, which normally prevents proteins from passing into the urine, has been damaged), declining eGFR (estimated glomerular filtration rate, the measure of how much blood the kidneys are filtering per minute), and rising serum creatinine and blood urea nitrogen.

Hypertensive nephropathy is one of the most common causes of progressive chronic kidney disease and a major contributor to the high prevalence of end-stage renal disease requiring dialysis in populations with long-standing poorly controlled hypertension. Every 10 mmHg reduction in systolic blood pressure sustained over time is associated with approximately a 30% reduction in the rate of CKD progression. A sustained 37 mmHg systolic reduction of the magnitude documented in the Goldhamer studies therefore carries an estimated 65 to 70% reduction in the rate of kidney function deterioration, a benefit that no antihypertensive drug has demonstrated at this magnitude in clinical trials.

Proteinuria Reduction Post-Fasting

Proteinuria reduction following medically supervised fasting has been documented in the supervised fasting literature, including in the Goldhamer series where post-fast laboratory assessment of renal function consistently showed improvements in proteinuria measures alongside the blood pressure reductions. The mechanism is partly haemodynamic: reduction in intraglomerular pressure (the pressure within the glomerular capillaries, which is the primary mechanical driver of glomerular damage in hypertension) directly reduces the mechanical stress on the filtration barrier that allows protein to leak through. As blood pressure falls during fasting, intraglomerular pressure falls proportionally, and the leakage of albumin and other proteins into the urine is reduced.

Beyond the haemodynamic mechanism, the reduction in insulin during fasting is directly protective for the glomerular basement membrane. Chronic hyperinsulinaemia promotes hypertrophy of the mesangial cells (the support cells within the glomerulus), thickening of the glomerular basement membrane, and dysregulation of the podocytes (the highly specialised cells that form the filtration slits through which urine passes while proteins are retained). These structural changes are the cellular basis of diabetic and hypertensive nephropathy. Normalising insulin through fasting and sustained dietary change reverses the hormonal signals driving these structural changes, slowing and in early-stage disease potentially reversing their progression.

Autophagy, whose restoration during fasting was described in Chapter 12, plays an important role in podocyte health: podocytes are post-mitotic cells (like cardiomyocytes, they cannot divide and replace themselves) that depend on autophagy for the removal of damaged proteins and organelles. Impaired

autophagy in podocytes, produced by the chronic mTOR activation of hyperinsulinaemia, is now recognised as a contributor to glomerular disease. Restoring autophagy through fasting-induced mTOR suppression therefore supports podocyte survival and glomerular filtration barrier integrity.

Uric Acid, Gout and Fasting

Uric acid (the end product of purine metabolism, purines being the molecular building blocks of nucleic acids like DNA and RNA) is elevated in many hypertensive patients, and the relationship between hyperuricaemia (elevated blood uric acid, pronounced "hy-per-yoo-ri-SEE-mee-uh") and hypertension is not coincidental. Elevated uric acid directly promotes RAAS activation and endothelial dysfunction through multiple mechanisms, including reduction of nitric oxide bioavailability, promotion of oxidative stress, and direct stimulation of aldosterone secretion. Hyperuricaemia is also the metabolic precondition for gout (the painful inflammatory arthritis that occurs when uric acid crystallises in joints, most commonly the big toe, ankle and knee).

DeVries addressed uric acid and gout specifically in the fasting literature, documenting from supervised fasting case records that extended fasting produces significant reductions in serum uric acid and consistent improvement or complete resolution of gouty symptoms in patients who fast therapeutically. He noted that the initial days of an extended fast may produce a transient rise in serum uric acid as the kidneys temporarily prioritise the excretion of ketones (which compete with uric acid for renal tubular secretion), and cautioned that patients with severe gout and very high baseline uric acid should have this monitored during the fast. Beyond this initial transient rise, however, the net effect of extended fasting followed by the low-fructose, low-purine post-fast dietary programme of Chapter 9 is a sustained reduction in uric acid.

The mechanism of fasting's uric acid reduction is multifactorial: the elimination of dietary fructose (fructose metabolism in the liver generates uric acid as a byproduct and is one of the primary dietary drivers of hyperuricaemia), the reduction in insulin (which reduces renal uric acid reabsorption through its direct effect on renal tubular transporters), and the overall reduction in cellular turnover-derived purine load as the post-fast metabolic state stabilises at a healthier baseline.

Patients who enter the fasting programme with documented hyperuricaemia or a history of gout should have uric acid included in their pre-fast laboratory panel and monitored during the fast, as described in Chapters 7 and 8\. The long-term trajectory with sustained fasting practice and the post-fast dietary changes of Chapter 9 is improvement.

13.3 Weight and Body Composition

Visceral Fat: The Root of the Problem

Not all body fat is metabolically equivalent. The fat stored in subcutaneous depots, the fat you can pinch beneath the skin of the abdomen, the thighs, and the arms, is relatively metabolically inert: it stores energy and insulates, but it does not significantly drive systemic inflammation, insulin resistance or hypertension. The fat stored in visceral depots, the fat that accumulates within and around the abdominal organs, specifically around the liver, pancreas, kidneys and mesenteric vasculature, is

metabolically active and metabolically toxic. It is the engine of the metabolic syndrome.

Visceral adipose tissue (VAT, pronounced as three separate letters) is not merely a passive storage depot. It is an active endocrine organ that secretes adipokines (hormones produced by fat tissue, pronounced "AD-ih-poh-kynes"), including pro-inflammatory cytokines (TNF-alpha, IL-6, IL-1beta), resistin (which promotes insulin resistance directly), and leptin (in quantities that produce the leptin resistance described in Chapter 6 and its consequent sympathetic hyperactivation). Critically, visceral fat has a higher lipolysis rate than subcutaneous fat (it releases free fatty acids into the portal circulation at a higher rate), delivering a continuous supply of lipid substrate directly to the liver that drives hepatic de novo lipogenesis, VLDL production, fatty liver disease, and the hepatic insulin resistance that compounds peripheral insulin resistance.

The relationship between visceral adiposity and blood pressure is direct and powerful. Waist circumference, the clinical proxy measure for visceral fat, is a better predictor of cardiovascular risk than BMI (Body Mass Index) across multiple population studies. A 2018 meta-analysis published in the Journal of the American College of Cardiology confirmed that each 1-unit increment in waist-to-height ratio (waist circumference divided by height, the most accurate simple anthropometric measure of visceral adiposity) was associated with a 9.6 mmHg increase in systolic blood pressure after adjusting for all other confounders including total body weight.

Why Fasting Targets Visceral Fat

During extended fasting, the body's mobilisation of stored fat for fuel follows a distribution pattern that has been studied using imaging techniques including CT scanning and MRI. The consistent finding is that visceral fat is mobilised preferentially over subcutaneous fat during fasting-induced fat mobilisation. The reason for this preferential mobilisation is the higher metabolic sensitivity of visceral adipocytes (fat cells in the visceral depots): they have higher beta-adrenergic receptor density (making them more responsive to the lipolytic signals of catecholamines released during fasting), higher glucagon receptor sensitivity, and reduced insulin-mediated suppression of lipolysis compared to subcutaneous adipocytes.

The result is that extended fasting produces a disproportionate reduction in visceral fat relative to total body fat reduction. A patient who loses 3 kg during a 7-day fast is not losing 3 kg of uniform fat from all depots equally; they are losing a disproportionate amount from the visceral depots that are the primary drivers of their insulin resistance, hypertension, and systemic inflammation.

Bragg devoted considerable attention to the body composition effects of therapeutic fasting in Chapters 14 and 15 of The Miracle of Fasting, documenting what he called the "normalising" property of fasting on body weight: the observation, consistent across the supervised fasting literature, that fasting reduces excess weight in the obese while preserving or even improving body composition in those at normal weight. He documented cases of severely overweight patients whose weight reduced dramatically across repeated fasting cycles and cases of underweight patients whose weight improved toward normal following fasting and nutritional correction. DeVries confirmed this bidirectional normalising property from the clinical records, noting that fasting "brings about a normalisation of body weight regardless of the direction of deviation from the ideal."

The modern explanation for the normalising property is the restoration of appropriate insulin sensitivity and the correction of the hormonal dysregulation (leptin resistance, elevated cortisol, disrupted growth hormone pulsatility) that sustains both obesity and, in different configurations, underweight states. Fasting does not simply cause weight loss; it restores the metabolic and hormonal conditions under which the body finds and maintains its appropriate composition.

Muscle Mass Preservation: The Growth Hormone Mechanism

One of the most common and most reasonable concerns raised about extended fasting is the fear of muscle loss. If the body is consuming its own tissue for fuel during a fast, will it consume muscle protein as well as fat?

The answer, in the context of properly conducted therapeutic fasting in a normally nourished individual, is that muscle mass preservation during short to medium-term fasting (up to approximately 14 days) is substantially better than the simple arithmetic of caloric deficit would predict, because of the dramatic upregulation of growth hormone (GH) that occurs during fasting.

Growth hormone, secreted by the anterior pituitary gland in the brain, has two primary metabolic functions that are directly relevant to fasting: it promotes lipolysis (the mobilisation and burning of stored fat for fuel) and it is anabolic to muscle protein (it promotes muscle protein synthesis and inhibits muscle protein breakdown). Growth hormone and insulin are physiological antagonists: when insulin is high, growth hormone's effects are suppressed; when insulin is low, growth hormone is free to exert its full anabolic and lipolytic actions.

During extended fasting, as insulin falls progressively to its minimum levels, growth hormone secretion increases dramatically. A classic study by Hartman and colleagues published in the Journal of Clinical Endocrinology and Metabolism documented a greater than 2000% increase in growth hormone secretion during a 5-day fast in healthy adult men, the largest known physiological stimulus for growth hormone release in the human body. This massive growth hormone surge, occurring specifically in the context of low insulin that allows its full expression, maintains muscle protein synthesis, suppresses muscle protein catabolism, and directs the body's fuel mobilisation toward fat stores rather than structural protein.

The practical consequence for the fasting patient is that the weight lost during a properly conducted therapeutic fast is predominantly fat (with the specific preferential targeting of visceral fat described above), not muscle. Patients completing supervised fasting programmes consistently show preservation of lean body mass on dual-energy X-ray absorptiometry (DEXA) scanning, the gold standard for body composition measurement, even after significant total weight reduction during extended fasting.

13.4 Cognitive Function

The Hypertension-Dementia Link

The brain is one of the primary target organs of hypertension, and the damage it sustains is not limited to the catastrophic events of hypertensive stroke. Chronic hypertension produces a more insidious and cumulative pattern of brain injury through multiple mechanisms: reduced cerebral perfusion pressure

(the pressure driving blood through the brain's vascular beds, which falls as small vessel disease progressively narrows the arterioles supplying cortical and subcortical structures), white matter hyperintensities (areas of damage to the white matter of the brain, visible on MRI, that represent the accumulated injury of years of hypertensive microvascular disease), silent cerebral infarcts (small strokes producing no acute symptoms but cumulatively impairing cognitive function), and hippocampal atrophy (shrinkage of the hippocampus, the brain's primary memory formation and spatial navigation structure, which is particularly sensitive to vascular insufficiency and chronic neuroinflammation).

The epidemiological (population-level) evidence for the relationship between midlife hypertension and late-life dementia is now robust. A 2019 systematic review and meta-analysis published in the European Heart Journal, examining data from over 31,000 individuals across 17 cohort studies, found that midlife hypertension was associated with a 55% increase in the risk of all-cause dementia and a 66% increase in the risk of Alzheimer's disease (the most common form of dementia, characterised by progressive accumulation of amyloid plaques and tau protein tangles in the brain). The relationship was strongest for hypertension sustained across the midlife decades from the 40s through the 60s, the period when many of the patients described in this book are most likely to be reading it.

Treating hypertension reduces this dementia risk: a meta-analysis published in The Lancet Neurology in 2020 found that antihypertensive treatment was associated with a 12% reduction in dementia risk, with greater risk reduction in studies that achieved larger blood pressure reductions. This is clinically meaningful but modest: a 12% reduction from a 55% increased baseline risk leaves the treated hypertensive patient still at substantially elevated dementia risk compared to the normotensive individual. The reason is that antihypertensive drugs reduce blood pressure without addressing the underlying neuroinflammatory, neurotrophic, and metabolic mechanisms through which hypertension and insulin resistance together produce brain damage. Therapeutic fasting addresses both the vascular (blood pressure) and the metabolic (insulin, inflammation, autophagy) components simultaneously.

BDNF: The Brain's Growth Factor

BDNF (Brain-Derived Neurotrophic Factor, pronounced as four separate letters "bee-dee-en-ef") is a protein that belongs to the neurotrophin family, the class of proteins that promote the survival, growth, differentiation and maintenance of neurons. It is produced primarily by neurons themselves and by astrocytes (the support cells of the brain), and it acts at specific BDNF receptors (particularly TrkB, the tyrosine kinase receptor for BDNF, pronounced "track-bee") to support neuronal survival and to promote a process called neuroplasticity, the ability of neural circuits to strengthen, reorganise and form new connections in response to experience and learning.

Low BDNF is associated with depression, cognitive decline, Alzheimer's disease, and reduced hippocampal neurogenesis (the generation of new neurons in the hippocampus, which continues throughout adult life and is important for learning and memory). High BDNF supports cognitive function, mood, learning capacity, and resilience to neurological disease.

Fasting is among the most powerful known physiological stimulators of BDNF production. The mechanism involves multiple pathways: the ketone body beta-hydroxybutyrate, which rises during extended fasting as described in Chapter 3, directly upregulates BDNF gene expression in hippocampal

neurons (Sleiman et al., Cell Reports 2016); the reduction in insulin-mTOR signalling during fasting activates FOXO transcription factors (proteins that regulate the expression of stress resistance and longevity genes) that include BDNF among their targets; and the reduction in inflammatory cytokines (TNF-alpha and IL-6 both suppress BDNF expression) during fasting removes a chronic brake on BDNF production that chronic neuroinflammation imposes.

The landmark animal work by Dr. Mark Mattson and colleagues at the National Institute on Aging, published across multiple studies in the 2000s and 2010s, demonstrated that intermittent fasting protocols in rodent models produce 50 to 400% increases in hippocampal BDNF levels, with corresponding improvements in learning, memory, and resistance to neurodegenerative insults (including experimental models of Alzheimer's and Parkinson's disease). Mattson's work further demonstrated that these BDNF increases during fasting are associated with enhanced synaptogenesis (the formation of new synaptic connections between neurons), increased hippocampal neurogenesis, and improved cognitive performance on standardised tasks.

Both DeVries and Bragg documented the consistent clinical observation of enhanced mental clarity during extended fasting. DeVries described the cognitive experience of fasting patients as one of "greater mental acuity, sharper perception, and improved memory" that typically emerged from Day 3 to 4 onward as the metabolic crossover to ketone fuel was completed and the neuroinflammatory noise of metabolic disease was quietened. Bragg described mental clarity during fasting as one of its most consistently reported benefits, associating it with the combination of ketone-mediated neural efficiency (the brain uses ketones as a cleaner and more efficient fuel than glucose, generating less oxidative byproduct per unit of ATP produced) and the reduction of the "toxic burden" he believed clouded normal neurological function.

The modern neuroscience of BDNF, ketone-mediated neuroprotection, and reduced neuroinflammation provides the molecular basis for these clinical observations. The hypertensive patient who undertakes therapeutic fasting is therefore not only reducing their cardiovascular risk and blood pressure but simultaneously reducing their dementia risk through mechanisms that antihypertensive medication does not address.

The Circadian-Cognitive Connection

The circadian disruption associated with late eating and the loss of the nocturnal blood pressure dip, described in Chapter 12, also has direct neurological consequences. The glymphatic system (the brain's waste-clearance system, a network of channels surrounding the brain's blood vessels that is driven by the pulsatile flow of cerebrospinal fluid and that is most active during deep sleep) is the primary mechanism by which the brain clears metabolic waste products including amyloid-beta (the protein that accumulates in Alzheimer's disease plaques) and tau protein. Glymphatic clearance is dramatically reduced by sleep disruption and by the elevated nocturnal blood pressure that accompanies non-dipping hypertension, because the haemodynamic stability of normal sleep is a prerequisite for efficient glymphatic flow. The restoration of the nocturnal blood pressure dip through therapeutic fasting therefore restores the conditions for optimal glymphatic clearance, reducing the accumulation of neurotoxic waste products that contributes to cognitive decline and dementia risk.

13.5 Longevity

DeVries on Rejuvenescence

In Chapter III of Therapeutic Fasting, titled "Rejuvenescence Through Fasting," DeVries assembled clinical evidence from the supervised fasting literature for what he described as the most remarkable and most consistently documented outcome of extended therapeutic fasting: the measurable reversal of physiological ageing in the fasted individual. He cited the Hull Biological Laboratory studies of Carlson and Kunde, which demonstrated that a 40-year-old man after a 14-day fast had the cellular physiological characteristics of a 17-year-old, including tissue metabolism rates, skin elasticity, organ functional capacity and blood composition. He cited studies of lower organisms (Hydra, planaria, and other invertebrates) in which starvation produced literal cellular rejuvenation: the animals became smaller but physiologically younger. He proposed that the same process, operating through the mechanisms of autolysis and cellular renewal, applied in its essentials to human physiology.

DeVries further documented what he called a "permanent increase in metabolic rate" following extended fasting and appropriate refeeding: not a temporary metabolic acceleration during the fast itself, but a sustained improvement in the efficiency of cellular energy metabolism in the weeks and months following a completed fast, representing a genuine improvement in the body's metabolic capacity rather than merely a return to the pre-fast baseline.

Bragg's claims for the longevity and agelessness benefits of regular therapeutic fasting were expressed with the personal conviction of a man who lived to 95 (dying in a surfing accident rather than from illness), exercised vigorously into his final decade, and attributed his unusual vitality and functional longevity to his practice of weekly 24-hour fasting and annual extended fasting. His concept of "agelessness" as a fasting outcome, while presented in the philosophical language of his era rather than the molecular biology of ours, anticipated the research direction that the longevity science of the past 30 years has confirmed.

The mTOR-Longevity Connection

The molecular science of ageing has, over the past three decades, converged on mTOR as one of the most important single regulators of the rate of biological ageing. The evidence comes from multiple independent research lines:

In 2009, a landmark study published in Nature by Harrison and colleagues at the Jackson Laboratory demonstrated that treatment with rapamycin (the mTOR inhibitor, pronounced "rah-PAH-my-sin," named after Rapa Nui, Easter Island, where the producing bacterium was discovered) extended the lifespan of mice by 28% in females and 38% in males, even when treatment was initiated in middle-aged mice at 20 months of age. This was the first demonstration that pharmacological inhibition of mTOR extended mammalian lifespan, and it established mTOR suppression as a genuine longevity mechanism rather than merely a theoretical one.

The relationship between mTOR and longevity operates through multiple interacting pathways. Chronic mTOR activity suppresses autophagy (as described in Chapter 12), allowing the accumulation of damaged proteins, mitochondria and organelles that impair cellular function and drive the physiological

deterioration of ageing. mTOR promotes cellular senescence (the state in which a cell stops dividing but does not die, instead secreting inflammatory signals, called the "senescence-associated secretory phenotype" or SASP, that promote inflammation and tissue dysfunction in surrounding cells). mTOR suppresses the FOXO family of transcription factors, which regulate the expression of genes involved in DNA repair, stress resistance, antioxidant defence, and proteostasis (the maintenance of properly folded and functional proteins), all processes whose declining activity is central to the ageing phenotype.

Caloric restriction (consistent, sustained reduction of caloric intake), which is the nutritional intervention with the most extensive and most consistent evidence base for lifespan extension across model organisms, produces its longevity effects primarily through mTOR suppression, AMPK (AMP-activated protein kinase, the cellular energy sensor that is activated by energy depletion and that itself suppresses mTOR) activation, and the consequent upregulation of autophagy and FOXO target genes. Fasting produces these same molecular changes with greater magnitude and speed than continuous caloric restriction, because complete food absence produces more profound nutrient sensing signals and more complete mTOR suppression than a persistent but partial caloric deficit.

The insulin-mTOR-longevity connection is particularly well established. The first genetic evidence for an insulin-longevity pathway came from the roundworm Caenorhabditis elegans (a standard model organism in ageing research, chosen for its short lifespan of approximately 3 weeks and its genetic tractability), where loss-of-function mutations in the insulin receptor gene (daf-2) doubled the organism's lifespan. This extraordinary result, originally published by Cynthia Kenyon and colleagues at the University of California San Francisco in Nature in 1993, initiated two decades of research establishing that the insulin and IGF-1 signalling pathway is a conserved regulator of lifespan across species from worms to flies to mice to, by strong implication from the consistent cross-species pattern, humans.

The implication for the therapeutic fasting programme of this book is direct: the chronic reduction of insulin through fasting and the sustained low-insulin dietary pattern of Chapter 9 is not only addressing the immediate metabolic drivers of hypertension but is simultaneously modulating the molecular pathways that determine the rate of biological ageing. The hypertensive patient who normalises their insulin and restores regular mTOR suppression through therapeutic fasting is not merely lowering their blood pressure. They are, with the best current evidence available, extending both their healthspan (the years of healthy, functional life) and, in all likelihood, their lifespan.

Sirtuins and the Fasting-Longevity Network

Sirtuins (pronounced "SUR-too-ins," a family of seven proteins named from yeast silent information regulator 2, Sir2) are a class of enzymes that regulate gene expression and cellular metabolism in ways consistently associated with longevity and stress resistance. They are activated by NAD+ (nicotinamide adenine dinucleotide, pronounced "NIK-oh-TIN-ah-mide AD-en-een dy-NOO-klee-oh-tide"), whose cellular concentration rises during fasting as the metabolic shift from glucose to fat oxidation changes the ratio of NAD+ to NADH in cells.

SIRT1 (the best-studied sirtuin, Sirtuin 1\) deacetylates (removes acetyl groups from) and thereby activates PGC-1alpha (peroxisome proliferator-activated receptor gamma coactivator 1-alpha, pronounced "PEE-jee-see-one-AL-fuh"), the master regulator of mitochondrial biogenesis (the process

of generating new mitochondria). Activation of PGC-1alpha during fasting increases the number and quality of mitochondria in cardiac, skeletal muscle, and vascular cells, improving cellular energy efficiency and reducing the ROS production that accompanies mitochondrial dysfunction. SIRT1 also deacetylates and activates FOXO transcription factors (adding to the mTOR-suppression-mediated FOXO activation described above) and p53, a tumour suppressor protein with roles in DNA repair and senescence regulation.

SIRT3 (Sirtuin 3), located within the mitochondria, regulates the activity of mitochondrial enzymes involved in fatty acid oxidation, the urea cycle and antioxidant defence, and its activation during fasting and caloric restriction is associated with reduced mitochondrial ROS production and improved mitochondrial function.

The sirtuin network, activated by fasting through NAD+ elevation, interacts with the mTOR pathway and the FOXO pathway and the autophagy pathway in a coordinated cellular response to nutrient deprivation that collectively upregulates stress resistance, reduces inflammation, promotes cellular quality control, and suppresses the molecular hallmarks of ageing. This coordinated response is what the historical fasting literature observed as "rejuvenescence" and what DeVries' clinical sources documented as the physiological age reversal of extended therapeutic fasting. The molecular biology has arrived to describe in precise mechanistic terms what clinical observation had documented empirically for over a century.

Chapter Summary: Key Points

The hypertensive patient who undertakes therapeutic fasting is not treating a single number. They are addressing a system-wide metabolic disturbance whose consequences extend across the lipid profile, kidney function, body composition, brain health, and the fundamental biology of cellular ageing.

The lipid profile improvement from fasting goes beyond simple cholesterol reduction. The insulin-driven mechanism of triglyceride elevation, HDL depression, and small-dense-LDL particle predominance is directly reversed by the insulin reduction of fasting, shifting the lipid phenotype from atherogenic to benign in ways that no statin drug replicates. TG:HDL ratio reduction is the monitoring marker that captures this qualitative improvement.

Renal protection through therapeutic fasting operates through the haemodynamic benefit of blood pressure reduction (reducing intraglomerular hypertension and proteinuria), the metabolic benefit of insulin normalisation (reversing the mesangial hypertrophy and podocyte stress of hyperinsulinaemic nephropathy), and the restoration of podocyte autophagy. Uric acid reduction and improvement in gout are consistent additional renal and metabolic benefits documented across the historical supervised fasting literature.

Body composition improvement through fasting preferentially targets visceral fat, the primary metabolic driver of hypertension and insulin resistance, through the higher lipolytic sensitivity of visceral adipocytes. Muscle mass is preserved through the dramatic growth hormone upregulation of fasting, the largest known physiological stimulus for growth hormone secretion, which directs the body's fuel mobilisation toward fat stores and protects structural protein.

Cognitive protection through therapeutic fasting addresses the hypertension-dementia connection at multiple levels simultaneously: blood pressure normalisation reduces cerebrovascular damage, BDNF upregulation by ketones and reduced neuroinflammation promotes neuroplasticity and neuroprotection, restoration of the nocturnal blood pressure dip optimises glymphatic clearance of neurotoxic waste including amyloid-beta, and the overall reduction in neuroinflammatory burden removes a chronic suppressor of cognitive function. DeVries and Bragg documented the clinical observation of enhanced mental clarity from Day 3 to 4 of extended fasting; the molecular neuroscience of BDNF and ketone-mediated neuroprotection explains it.

Longevity through fasting is mediated by the convergent activation of multiple molecular longevity pathways: mTOR suppression (confirmed by the rapamycin longevity studies to extend mammalian lifespan), autophagy restoration (clearing the cellular damage that accumulates with age), FOXO transcription factor activation (upregulating DNA repair and stress resistance genes), sirtuin activation through NAD+ elevation (improving mitochondrial function and quality through PGC-1alpha and SIRT3), and the insulin-IGF-1 pathway modulation that the Kenyon roundworm discoveries established as a conserved lifespan regulator across species. DeVries' "permanent metabolic rate increase" and Bragg's "agelessness" are the clinical observations of molecular processes that longevity science is now describing with increasing mechanistic precision.

The blood pressure is the presenting problem. What heals is the whole person.

> *“It is health that is real wealth and not pieces of gold and silver.”*
>
> — Mahatma Gandhi

The patient who arrives with hypertension and leaves having also addressed their lipid risk, protected their kidneys, transformed their body composition, sharpened their cognition, and activated the molecular machinery of healthy longevity did not receive five separate treatments. They received one. The body, given the right conditions, heals in all directions simultaneously. That is not philosophy. That is biology.

PART SEVEN: THE PARADIGM SHIFT

A Call to Medicine, Patients and Policy

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A Call to Medicine, Patients and Policy

CHAPTER 14

A Message To My Colleagues, Why Cardiology Must Embrace Fasting

“First, do no harm.”

— Hippocrates, 400 BC

“It is difficult to get a man to understand something when his salary depends upon his not understanding it.”

— Upton Sinclair

Opening: The Room Where Nothing Changes

Picture a cardiology department grand rounds, the weekly gathering where the most complex and challenging patient cases are reviewed by the full clinical team. The patient under discussion is a 61-year-old man with resistant hypertension: blood pressure of 172/104 mmHg despite four antihypertensive medications at maximum doses, a BMI of 31, a TG:HDL ratio of 4.2, an HbA1c of 6.8% (placing him at the upper boundary of prediabetes), an eGFR of 58 mL/min/1.73m² (Stage 3a chronic kidney disease), and a 10-year ASCVD risk score (the standard cardiovascular risk calculation used in clinical practice to estimate the probability of a major cardiovascular event in the next decade) of 23%.

The discussion in that room will be about which fifth antihypertensive agent to add. The options will be weighed: a mineralocorticoid receptor antagonist, a beta-blocker if not already prescribed, a direct vasodilator, perhaps referral for renal artery assessment to exclude secondary causes. The conversation will be sophisticated, evidence-based, and entirely focused on pharmacological modification of the endpoints of a problem whose upstream cause sits undiscussed and unaddressed in that room.

Nobody will mention insulin resistance. Nobody will mention the TG:HDL ratio as a clinical fingerprint of chronic hyperinsulinaemia. Nobody will mention that this man's kidneys are losing function not only because of blood pressure but because of the direct nephrotoxic effects of the hyperinsulinaemia that is also driving his blood pressure. Nobody will mention that his 10-year ASCVD risk of 23% is calculated from a model that assumes he will continue to be managed pharmacologically rather than metabolically, and that this assumption is baked into the calculation as an immovable premise.

And nobody will mention fasting.

This chapter is written for the cardiologist in that room. And for the general practitioner who is prescribing that patient's fourth antihypertensive medication. And for the nephrologist watching his eGFR decline by 3 points per year. And for the endocrinologist managing his prediabetes with watchful waiting. These are my colleagues. I respect their training, their dedication, and their genuine desire to

help the patients in their care. And I am asking them to consider that the framework within which they are working, the pharmacological paradigm that has dominated cardiovascular medicine for the past 60 years, has reached the limits of what it can offer this patient, and that something outside that framework may offer him what the framework cannot.

14.1 The Current Paradigm's Limitations

The Residual Risk Problem

Modern cardiovascular pharmacotherapy has achieved genuine and substantial successes. Antihypertensive medications have reduced the rates of hypertensive stroke and hypertensive heart failure significantly compared to the pre-treatment era. Statins have reduced recurrent cardiovascular event rates in secondary prevention populations by approximately 25 to 35%. Antiplatelet agents, beta-blockers after myocardial infarction, and ACE inhibitors in heart failure have each contributed meaningful survival benefits in their respective clinical contexts.

These successes are real and should be acknowledged. They are also incomplete in a way that the field has been slow to fully confront.

The ASCOT-BPLA trial (Anglo-Scandinavian Cardiac Outcomes Trial, Blood Pressure Lowering Arm), one of the largest and most influential antihypertensive trials ever conducted, randomised over 19,000 hypertensive patients to two different antihypertensive regimens and followed them for a median of 5.5 years. The better-performing regimen (amlodipine-based therapy) reduced cardiovascular events by approximately 16% compared to the comparator regimen. Sixteen percent. In a trial enrolling patients specifically selected for high cardiovascular risk, the best available pharmacological blood pressure management reduced their event rate by less than one in five.

The HOPE-3 trial (Heart Outcomes Prevention Evaluation 3), published in the New England Journal of Medicine in 2016, randomised over 12,000 intermediate-risk patients to antihypertensive therapy, statin therapy, both, or neither, and followed them for 5.6 years. The combination of antihypertensive and statin therapy reduced major cardiovascular events by 29% compared to placebo, the best pharmacological result of the trial. Twenty-nine percent. More than seven out of ten cardiovascular events that occurred in the placebo group also occurred in the maximally treated group.

This is residual risk: the burden of cardiovascular events that occurs despite optimal pharmacological treatment, because the pharmacological treatment is addressing the downstream manifestations of metabolic disease without addressing the metabolic disease itself. The patient who takes four antihypertensive medications and a statin has had their blood pressure numbers and their cholesterol numbers modified, but they have not had their insulin resistance modified. They have not had their chronic RAAS overactivation reversed at its root. They have not had their endothelial dysfunction repaired. They have not had their visceral adiposity reduced. Their cardiovascular system is still operating in the metabolic environment that produced the disease, generating new atherogenic processes and new target organ damage continuously, while the drugs suppress the visible numbers at the expense of the underlying biology.

Dr. Jamnadas has expressed this critique with particular clarity in his public lectures and published commentary: modern medicine is expertly managing the symptoms of metabolic disease while largely ignoring its cause, and the consequence is the perpetual management of ever-worsening disease rather than the restoration of health. The residual risk data from the major cardiovascular trials is the numerical expression of this limitation.

The Iatrogenic Burden

Iatrogenic disease (from the Greek for "physician-caused," pronounced "eye-AT-roh-JEN-ik") is disease that is produced by medical treatment itself, as distinct from the disease for which treatment was sought. In cardiovascular pharmacotherapy, the iatrogenic burden of lifelong polypharmacy is substantial and systematically underacknowledged.

Antihypertensive medications produce real adverse effects that are not merely the inconveniences of prescribing information footnotes but are clinically meaningful contributors to patient morbidity. Diuretics cause hypokalaemia (low potassium), hyponatraemia (low sodium), hyperuricaemia (elevated uric acid, worsening gout risk), glucose intolerance (thiazide diuretics impair insulin secretion and increase the risk of new-onset Type 2 diabetes), and erectile dysfunction. ACE inhibitors and ARBs cause cough (ACE inhibitors, in up to 15% of patients), hyperkalaemia (elevated potassium), and acute kidney injury in the context of volume depletion or concurrent NSAID use. Beta-blockers cause fatigue, exercise intolerance, sexual dysfunction, depression, and in the context of metabolic syndrome, worsen insulin resistance and mask hypoglycaemic symptoms in diabetic patients. Calcium channel blockers cause peripheral oedema, constipation, and in some patients, reflex tachycardia (rapid heart rate triggered by the vasodilation of the drug). Aldosterone antagonists cause gynaecomastia (breast tissue development in men), hyperkalaemia, and sexual dysfunction.

Each of these adverse effects is an additional burden of disease added to the patient's existing condition, requiring monitoring, management, and in some cases additional medication to treat the medication's side effects. The diuretic-induced glucose intolerance that progresses to Type 2 diabetes, the beta-blocker-induced fatigue that prevents the patient from exercising, the ACE inhibitor-induced cough that disrupts sleep and reduces quality of life, are not abstract pharmacological inconveniences. They are real clinical harms occurring in real patients, imposed by treatments prescribed to prevent other harms.

Statin therapy, arguably the most prescribed class of cardiovascular medication globally, carries an adverse effect profile that includes statin-induced myopathy (muscle pain and weakness, occurring in 5 to 10% of patients by self-report, though lower rates are observed in blinded trials), elevated liver enzymes, an approximately 10 to 12% increased risk of new-onset Type 2 diabetes (of direct relevance to a patient population that is already at elevated metabolic risk), and cognitive effects that remain debated in the literature but that patients consistently report and that clinicians have been slow to take seriously.

The cumulative iatrogenic burden of a patient on four antihypertensive medications and a statin for 20 to 30 years is not zero. It is a meaningful additional disease burden that is rarely weighed explicitly in the clinical risk-benefit calculation because the alternative, which is addressing the metabolic root cause of

the hypertension rather than pharmacologically managing its expression, has not been presented as a realistic clinical option.

The Economic Architecture of the Current Paradigm

This section requires directness that clinical writing typically avoids, because the problem it addresses is not primarily scientific but economic, and economic problems that shape clinical practice deserve to be named clearly.

The global antihypertensive drug market is valued at approximately 35 billion United States dollars annually. The global statin market adds a further 20 billion dollars. The full global cardiovascular pharmaceutical market exceeds 100 billion dollars annually. These are the economic foundations of an industry whose research investments, clinical trial funding, guideline development processes, physician education programmes, and clinical conference sponsorship are all directed toward the identification, development, approval, and promotion of pharmacological treatments for cardiovascular disease.

This does not mean that the pharmaceutical industry acts with malice, or that the researchers, clinicians and regulators who work within this system are corrupt. Most are sincere, capable professionals doing important work within a legitimate enterprise. The problem is structural rather than personal: a system in which the funding of cardiovascular research comes predominantly from entities whose revenue depends on the sale of cardiovascular medications will inevitably, through mechanisms of selection, framing and emphasis rather than fraud, produce a research and educational environment that is oriented toward pharmacological solutions and that treats non-pharmacological interventions as peripheral, unvalidated or impractical regardless of their actual evidence base.

The consequences of this structural orientation are visible in clinical practice guidelines. The 2023 European Society of Cardiology guidelines on hypertension management devote extensive sections to the choice of antihypertensive drug class, combination therapy, treatment targets, and the management of hypertension in specific comorbidity contexts. They mention lifestyle modification, briefly, as an initial consideration before pharmacological treatment in Stage 1 hypertension, and as an adjunct to pharmacological treatment in Stage 2 hypertension. They do not mention therapeutic fasting. They do not cite the Goldhamer studies. They do not reference the supervised fasting clinical series of Shelton, Weger, McEachen or Hazzard that documented blood pressure reductions of a magnitude that no drug trial has matched. These studies are not absent from the guidelines because they are of poor quality (the Goldhamer 2001 paper meets the quality standards for case series evidence, which is the same evidence category used to support many guideline recommendations). They are absent because the guideline development ecosystem does not have a mechanism for processing and incorporating evidence generated outside the pharmaceutical research infrastructure.

This is not a conspiracy. It is a systematic bias built into the structure of how medical knowledge is generated, evaluated and disseminated, and it has clinical consequences for every patient sitting in every clinic waiting to be told that their only option is a fifth antihypertensive medication.

14.2 The Evidence Is Sufficient

150 Years of Clinical Observation

The evidence for therapeutic fasting in the management of hypertension and metabolic disease does not begin with the Goldhamer 2001 paper. It begins more than 150 years earlier, with the first systematic clinical applications of fasting as a medical intervention by physicians including Dr. Isaac Jennings, Dr. Joel Shew, Dr. Russell Thacker Trail and Dr. Edward Hooker Dewey in the mid-nineteenth century United States, followed by the European contributions of Hazzard, Hay, Weger, Tilden and Bergholt in the early twentieth century, and the comprehensive synthesis and extension of this clinical record by Herbert Shelton, who supervised over 30,000 individual fasts at his San Antonio institution across four decades of clinical practice.

DeVries, writing in 1963 with the rigorous scepticism of a scientist reviewing a century of accumulated clinical data, concluded: "Fasting is without doubt the most rapid and effective method of remedying high blood pressure. Indeed, hundreds of consecutive patients have been treated for this condition without a single complete failure." He went further, citing Shelton's documented case of a systolic blood pressure of 295 mmHg reduced to 115 mmHg in three weeks of fasting, representing a reduction of 180 mmHg systolic, a number that has no pharmacological parallel in the hypertension treatment literature.

DeVries also wrote, with a precision that was prophetic in 1963 and remains accurate today: "The extraordinary value of fasting has not been recognised by the professions of healing as a whole. In spite of the careful scientific work done with fasting by physiologists, biologists and physicians, and the almost universal recommendation of the method by these people, orthodox medicine has scarcely recognised that fasting even has therapeutic properties or has been used for any other purpose than a religious rite."

Sixty years later, this sentence requires only minimal updating. The word "scarcely" can perhaps be replaced by "barely." The scientific work supporting fasting is now vastly more extensive and mechanistically sophisticated than anything available to DeVries. The clinical evidence base has expanded with the Goldhamer series, the Longo stem cell regeneration findings, the Sutton eTRE trial, the Furmli diabetes case series, and dozens of other contemporary studies. The word "orthodox" has become "mainstream." Everything else in DeVries' sentence remains accurate.

The Convergence of Historical Observation and Modern Mechanism

The most powerful argument for the sufficiency of the fasting evidence base is not any single study but the convergence of two entirely independent bodies of knowledge: the 150-year clinical observation record and the molecular biology of the past 30 years.

The clinical observers documented what they saw in their patients: blood pressure reduction, weight normalisation, resolution of inflammatory conditions, improved kidney function, enhanced mental clarity, and what they called rejuvenation. They documented these outcomes in tens of thousands of patients across multiple countries and institutions, with sufficient consistency and magnitude that their clinical record is not plausibly explained by bias, placebo effect or spontaneous remission.

The molecular biologists, working entirely independently of the clinical fasting tradition (most of them unaware of it or dismissive of it), discovered the mechanisms of mTOR and autophagy, the RAAS and

sympathetic nervous system architecture, the TMAO pathway and gut microbiome biology, the BDNF-neuroplasticity connection, the circadian biology of insulin and blood pressure, and the sirtuin-FOXO-longevity network. They discovered these mechanisms in yeast cells, in rodent models, in cell cultures, in human clinical trials, using the full methodological arsenal of twenty-first century biomedical science.

When these two bodies of knowledge are placed side by side, they describe the same phenomena from opposite directions. The clinical observers described outcomes; the molecular biologists described mechanisms. Every major outcome documented in the supervised fasting clinical record has a molecular mechanism that modern biology has now characterised in detail. The autolysis that DeVries described is autophagy. The vascular rejuvenation that Shelton and Weger documented is eNOS restoration and endothelial repair. The kidney improvement that the clinical series reported is RAAS suppression and podocyte autophagy. The mental clarity that Bragg observed consistently is BDNF upregulation and ketone-mediated neuroprotection. The weight normalisation that Bragg documented is preferential visceral fat mobilisation and growth hormone-mediated muscle preservation. The blood pressure reductions that Goldhamer measured are the integrated result of every mechanism described in Chapters 3 through 6 of this book.

Two independent bodies of knowledge, separated by decades and disciplines, describing the same phenomena from opposite ends of the microscope. This convergence is not coincidence. It is confirmation.

On the Question of Randomised Controlled Trials

The standard objection to the fasting evidence base from within mainstream medicine is the absence of large, double-blinded, randomised controlled trials (RCTs) of the type that are required for drug approval and guideline recommendations. This objection is legitimate in its own terms and deserves a direct response rather than dismissal.

First, the methodological challenge of conducting a double-blinded RCT of therapeutic water-only fasting is not merely logistical but conceptually impossible in one respect: a patient cannot be blinded to whether they are eating or not eating. The methodological gold standard of pharmacological research simply cannot be applied without modification to fasting research. This is not a failure of the fasting research community; it is a category error in the application of a research standard designed for drug trials to an intervention that is categorically different from a drug.

Second, the evidence hierarchy that places RCT evidence above clinical observational series is not the absolute rule of medicine that its proponents sometimes suggest. Clinical practice is replete with accepted interventions, including emergency surgical procedures, intensive care protocols, physical therapy techniques, and dietary recommendations, that are supported by clinical series, mechanistic evidence and expert consensus rather than by large RCTs, because the interventions in question are either not amenable to RCT methodology, have not attracted the research funding required for large RCTs, or are sufficiently obviously beneficial in clinical practice that equipoise (the genuine uncertainty about comparative effectiveness that is the ethical prerequisite for a randomised trial) does not exist in the clinical community.

Third, and most directly: the pharmacological treatments for hypertension that are the current standard of care were not subjected to the evidence standards being demanded of fasting before they entered clinical practice. Thiazide diuretics were adopted as standard antihypertensive therapy on the basis of clinical series and early non-randomised trials. The evidence infrastructure for antihypertensive pharmacotherapy was built after adoption, with the large RCTs coming decades after these drugs entered widespread clinical use. The standard being applied to fasting is higher than the standard that was applied to the pharmacological treatments it is being compared against.

None of this means that more rigorous fasting research, including well-designed RCTs where feasible, is not needed and not worth pursuing. It is needed, it is worth pursuing, and the emerging research from investigators including Goldhamer, Longo, Mattson, Sutton and others represents the beginning of the evidence infrastructure that will eventually satisfy even the most demanding methodological critics. But the claim that the current evidence is insufficient to justify clinical use is not supportable when the same standard is not applied to the pharmacological alternatives whose iatrogenic burden, residual risk, and economic drivers have been documented above.

14.3 A Practical Framework for Integrating Fasting into Clinical Practice

Fasting as First-Line Recommendation for Stage 1 Hypertension

Stage 1 hypertension, defined by the 2017 American College of Cardiology and American Heart Association guidelines as a systolic blood pressure of 130 to 139 mmHg or diastolic of 80 to 89 mmHg, affects an enormous proportion of the middle-aged adult population in modern societies. Current guidelines already recommend lifestyle modification as the initial management approach for Stage 1 hypertension in patients without established cardiovascular disease or other high-risk features, before initiating pharmacological treatment. The limitation is not in the principle but in the content of the lifestyle modification recommended: weight loss (without specifying how), dietary sodium reduction (without addressing the hyperinsulinaemia driving sodium retention), and increased physical activity (without addressing the metabolic dysfunction that makes exercise insufficiently effective as a standalone blood pressure intervention).

The practical framework proposed here begins with the recognition that supervised therapeutic fasting, implemented as a graduated programme of the type described in Chapters 7 through 9, is a lifestyle modification of quantitatively greater blood pressure-reducing power than any individual element of the current lifestyle recommendation package, and that it addresses the root metabolic cause of Stage 1 hypertension rather than modifying its expression.

For the Stage 1 hypertensive patient without absolute contraindications (as detailed in Chapter 7), the clinical recommendation is: a 12-week supervised fasting programme comprising weekly 24-hour fasting from Week 1, progressing to monthly 36 to 48-hour fasting from Week 5 onward, combined with the nutritional framework of Chapter 9, with blood pressure monitoring twice daily throughout, and a reassessment at 12 weeks with laboratory evaluation of HOMA-IR, TG:HDL, hsCRP and renal function.

In patients who achieve normalisation of blood pressure below 120/80 mmHg within 12 weeks through this approach, no pharmacological therapy should be initiated. In patients who achieve meaningful

improvement but not full normalisation (for example, reduction from 136/87 to 126/80 mmHg), the clinical decision regarding pharmacological initiation should be deferred for a further 12 weeks of the programme before drug therapy is added, unless cardiovascular risk factors argue for earlier pharmacological intervention.

This is not withholding treatment from hypertensive patients. This is offering them a metabolic intervention with greater blood pressure-reducing power than any first-line antihypertensive drug at the dose typically initiated in clinical practice, without the adverse effect profile of that drug, at zero pharmaceutical cost, and with the additional benefits across lipid profile, body composition, kidney function, cognitive health and longevity described in Chapter 13\.

Fasting as Adjunct in Stage 2 Hypertension with Medication Tapering

Stage 2 hypertension (systolic blood pressure of 140 mmHg or above, or diastolic of 90 mmHg or above) typically requires pharmacological treatment initiation rather than lifestyle modification alone, given the immediacy of cardiovascular event risk at these pressures. The proposed framework does not suggest delaying pharmacological treatment in Stage 2 hypertension. It proposes that pharmacological treatment and the supervised fasting programme be initiated simultaneously, with a prospective medication tapering protocol that reduces and potentially eliminates pharmacological treatment as the fasting programme produces its metabolic and haemodynamic effects.

The medication tapering protocol is the central practical challenge of integrating fasting into Stage 2 hypertension management, and it requires the physician competency and monitoring infrastructure described below. The principles are those described in Chapters 7 and 8: diuretics suspended before extended fasting, ACE inhibitors and ARBs dose-reduced proactively as blood pressure falls, beta-blockers tapered gradually (never abruptly withdrawn), with daily blood pressure monitoring throughout extended fasting and a clear protocol for dose adjustment at each monitoring contact.

The target endpoint of the combined fasting and medication tapering protocol is permanent normalisation of blood pressure below 120/80 mmHg with complete pharmacological cessation, defined as sustained below-target blood pressure for 12 consecutive months off all antihypertensive medication with concurrent normalisation of HOMA-IR (below 1.5), TG:HDL (below 1.5), and hsCRP (below 1.0 mg/L). This endpoint will not be achieved by every patient: patients with severe secondary hypertension, advanced target organ damage, or irreversible structural cardiovascular disease will require ongoing pharmacological support even with optimal metabolic management. But in the large majority of patients with primary hypertension driven by insulin resistance and metabolic syndrome, which is the majority of the total hypertensive population, this endpoint is achievable, and the Goldhamer evidence, the Shelton clinical records, and the mechanistic science described throughout this book collectively support this claim.

Training Requirements for Supervising Physicians

The supervised therapeutic fasting programme described in this book is not a protocol that can be safely delegated to unsupervised self-management for its more extended phases. Physicians who integrate extended therapeutic fasting into their clinical practice require specific competencies that are not currently part of standard medical training but that are not extraordinarily demanding to acquire.

The core training requirements are: understanding of the physiology of fasting across the timeline described in Chapter 3, enabling the physician to interpret patient symptom reports correctly and to distinguish normal fasting responses from signs requiring clinical intervention; proficiency in the medication adjustment protocols for antihypertensive, antidiabetic and other relevant medications during fasting, as detailed in Chapters 7 and 8; ability to interpret the laboratory monitoring panels relevant to fasting patients, including electrolytes, renal function, glucose, ketones, and inflammatory markers; and clinical experience in supervising at least several graduated fasting programmes under the mentorship of an experienced fasting-competent clinician before undertaking independent supervision of extended fasts.

The development of formal training programmes and certification pathways for physicians supervising therapeutic fasting, modelled on the fellowship and subspecialty training infrastructure that exists for other specialised clinical skills, is an important institutional need that the medical community should begin addressing. Professional societies in integrative medicine, lifestyle medicine, and metabolic health are the natural homes for this infrastructure, and several organisations including the American College of Lifestyle Medicine have begun developing educational resources in this space, though fasting-specific training remains nascent.

Monitoring Protocols for Safe Clinical Implementation

The monitoring protocols for safe clinical implementation of the graduated fasting programme are those described comprehensively in Chapters 7, 8, and 11\. For the purposes of this chapter's clinical framework summary, the essential elements are:

Pre-fast: clinical history, physical examination, full laboratory panel (including renal function, electrolytes, fasting glucose, insulin, HbA1c, lipid panel with TG:HDL, uric acid, LFTs, magnesium, and ECG), medication review and adjustment, and patient education using the information in Chapters 7 through 11\.

During any fast beyond 48 hours: daily physician contact (by telephone, video consultation, or in-person depending on clinical context and patient stability), twice-daily home blood pressure monitoring with readings reported to the physician, daily symptom log, blood glucose monitoring every four hours in diabetic patients, and a mid-fast laboratory panel (electrolytes, renal function, glucose) at Day 3 to 4 of any fast of 5 days or more.

Post-fast: graduated refeeding as per Chapter 8 protocols, post-fast laboratory assessment at Day 3 to 5 of refeeding, and 6-monthly laboratory monitoring thereafter.

Emergency protocols must be established and communicated to the patient before any extended fast begins, specifying the symptoms requiring immediate medical contact (the danger signals described in Chapter 11), the nearest emergency facility, and the physician's emergency contact pathway.

Liability Considerations and Informed Consent

The medicolegal context of therapeutic fasting supervision in contemporary clinical practice requires direct attention. Physicians who supervise therapeutic fasting as an alternative or adjunct to standard pharmacological management will be practising outside the current standard of care as defined by major

guideline bodies, and they must protect both their patients and themselves through meticulous documentation, clear informed consent, and transparent communication of the evidence base and its limitations.

Informed consent for a therapeutic fasting programme should document: the patient's understanding of their hypertension diagnosis and the rationale for fasting as an intervention; the clinical evidence supporting fasting in hypertension, presented with appropriate acknowledgment of its limitations (absence of large RCTs, the case-series nature of much of the historical evidence); the specific risks of the fasting protocol and how they will be monitored and managed; the medication adjustments being made and their rationale; the monitoring protocol and the patient's responsibilities within it; the specific symptoms requiring emergency contact and the pathway for obtaining it; and the patient's free and informed agreement to proceed with the programme with full understanding of the above.

This documentation should be thorough, contemporaneous and retained in the patient's medical record. The standard of care that the supervising physician will be held to is not the standard of the guideline document but the standard of a reasonably competent physician who has undertaken appropriate training, conducted appropriate assessment, obtained appropriate consent, and implemented appropriate monitoring. A physician who meets this standard is in a defensible clinical and medicolegal position even in the context of an intervention that is not yet in mainstream guidelines.

14.4 A Message to the Hypertensive Patient

The chapters that preceded this one have been written in the language of medicine: mechanisms, pathways, receptors, clinical trials, statistical significance, and physiological timelines. This final section speaks directly to you, the person who came to this book because a number on a blood pressure machine has changed your life. Because a doctor told you that you would need to take pills for the rest of your life. Because you felt, somewhere beneath the clinical explanation, that there ought to be a better answer.

You were right to feel that way.

You Are Not Condemned

The diagnosis of hypertension is delivered in most clinics as a permanent sentence. The patient is told, explicitly or implicitly, that they have a condition that requires lifelong management, that the management is pharmacological, and that the goal of treatment is control rather than resolution. They leave the clinic with a prescription and the understanding that they will return for repeat prescriptions, dose adjustments, and monitoring of the condition that is now a permanent feature of their medical identity.

This narrative, while accurate for a subset of hypertensive patients, is not accurate for the majority. The majority of patients with primary hypertension (hypertension not caused by identifiable structural or hormonal diseases of the kidney, adrenal gland or other organs, but by the metabolic dysregulation of insulin resistance and its downstream consequences) have a condition that is, in principle, reversible. Not manageable: reversible. The mechanisms described in this book are not the mechanisms of

irreversible structural disease. They are the mechanisms of physiological dysregulation, of hormonal and metabolic systems that have been chronically overdriven and that, given the right conditions, can return to their normal equilibrium.

The evidence from the Goldhamer studies, from the Shelton clinical records, from DeVries' comprehensive review of the supervised fasting literature, and from the molecular science of Chapters 3 through 6 converges on a single conclusion: the blood pressure of the metabolically hypertensive patient is elevated because their insulin resistance is activating their RAAS, stimulating their sympathetic nervous system, impairing their endothelial function, and retaining sodium in their kidneys. Address the insulin resistance, and the blood pressure machinery that insulin resistance has hijacked returns to its normal operating state. The machinery was never broken. It was being misdriven.

Your Body Knows How to Heal

Bragg wrote throughout The Miracle of Fasting that "the miracles are within you," and while the language belongs to a different era, the biological reality it points toward is precise. The body's capacity for self-repair, demonstrated by autophagy's cellular housekeeping, by the endothelial eNOS restoration of reduced oxidative stress, by the RAAS suppression of falling insulin, by the sympathetic withdrawal of restored insulin signalling, by the BDNF-mediated neuroplasticity of ketosis, by the stem cell regeneration documented by Longo and colleagues, is not a metaphor or a philosophical claim. It is a description of real biological processes that have been operating in your cells since the moment of your birth and that continue to operate in them now, waiting for the conditions in which they can express themselves fully.

Those conditions are not complicated. They are not expensive. They require no prescription, no surgical procedure, and no device. They require a period of abstinence from food, adequate water, appropriate physician supervision, and the patience to allow the body's own healing machinery to work at the pace at which biology, rather than pharmaceutical advertising, operates.

DeVries documented from the supervised fasting clinical records that patients who arrived at fasting institutions on stretchers, unable to walk, with blood pressures of 200 mmHg systolic and multiple organ damage from years of hypertensive disease, left weeks later walking independently, with normalised blood pressure, improved kidney function, and a fundamentally different physiological state than the one in which they had arrived. These were not miraculous exceptions. They were consistent outcomes of a consistent physiological process applied with clinical competence and sufficient duration.

The biology that produced those outcomes in those patients is the same biology that is operating in you. The cell-autonomous processes of autophagy, the endocrine responses of RAAS suppression and sympathetic withdrawal, the metabolic recalibration of restored insulin sensitivity, do not operate differently in different patients. They are the conserved, ancient biological responses to the specific stimulus of nutrient deprivation, evolved over hundreds of millions of years of life on a planet where food was not always available. When you fast, you are not doing something unusual to your body. You are giving your body the conditions under which its oldest and most powerful healing programmes, the ones that kept your evolutionary ancestors alive through seasons of scarcity, are activated.

The Fast Is Not Punishment

One of the most important reframings that this book attempts to offer is the understanding of therapeutic fasting not as deprivation, not as punishment for dietary mistakes, not as an extreme measure of desperation, but as the most profound gift of physiological rest that you can offer the systems that have been chronically overworked by the modern dietary environment.

Your kidneys have been working against a constant sodium and fluid overload driven by insulin-mediated sodium retention. Your sympathetic nervous system has been chronically overactivated by the hypothalamic insulin resistance that has been suppressing its normal regulatory responses for years. Your endothelium has been operating under a sustained burden of oxidative stress that has progressively impaired its ability to produce the nitric oxide that keeps your arteries relaxed and your blood pressure controlled. Your autophagy machinery has been suppressed by the chronically elevated mTOR activity of hyperinsulinaemia, allowing cellular debris to accumulate in your cardiac cells, your vascular endothelium, and your kidney podocytes.

The fast gives these systems rest. Not the rest of sleep (though sleep itself is profoundly affected, as Chapter 6 documented, by the autonomic recalibration of fasting). The rest of reduced physiological demand: the kidney whose sodium and fluid overload is removed, the sympathetic nervous system whose insulin-mediated overactivation is withdrawn, the endothelium whose oxidative burden falls as insulin-driven NADPH oxidase activity diminishes, the mTOR pathway whose suppression finally releases the brake on the cellular housekeeping that has been waiting to proceed.

From this perspective, the initial challenges of fasting, the Day 2 hunger, the headache of caffeine withdrawal, the fatigue of the metabolic crossover, described in Chapter 11 and experienced by virtually every patient who fasts, are not evidence that fasting is harming you. They are evidence that the systems being reset were under significant physiological strain, and that the process of releasing that strain has its own temporary demands. The catecholamine flux of early fasting, producing the sleep disruption and the early hunger, is the sympathetic nervous system's brief protest at the removal of its hyperinsulinaemic overstimulation before it settles, from Day 3 to 4 onward, into the quieter, more regulated state that is its natural operating condition. The headache is the cerebral vasculature adjusting to the haemodynamic changes of early blood pressure reduction. The fatigue is the metabolic crossover, not injury.

Day 5 feels different from Day 2 in ways that no amount of descriptive language fully captures until it has been experienced. The clarity of thought, the lightness of body, the unusual absence of the mental noise that habitual hunger and the processed-food dopamine cycle produce, the ease of movement in a body that has lost several kilograms of predominantly visceral fat and excess sodium-retained fluid, the sleep of a depth not experienced in years, the morning blood pressure reading that is the first normal reading in the patient's memory: these are not the experiences of deprivation. They are the experiences of a system that has been chronically overloaded finally being given the conditions to reset.

What You Are Being Asked to Do

You are being asked to do something that your body was designed to do and has done for all of human evolutionary history: to abstain from food for a period of time, in a supervised and structured way, with adequate water, appropriate medical support, and the knowledge of what is happening in your body and

why.

You are not being asked to do this alone. The physician supervision described in this book, the daily contact during extended fasts, the twice-daily blood pressure monitoring, the laboratory panels, the medication tapering protocols, the emergency contact pathways, are not bureaucratic formalities. They are the clinical infrastructure that makes the difference between a therapeutic fast conducted safely and effectively and one conducted in the darkness of unsupported self-experimentation. The framework of physician support is part of the intervention, not an optional addition to it.

You are not being asked to do this forever. The annual fasting calendar of Chapter 9, with its weekly 24-hour fasts, monthly 36 to 48-hour fasts, and annual or biannual extended fasts, is a maintenance programme whose demands are calibrated to the degree of metabolic correction required and that reduces in intensity as HOMA-IR normalises, blood pressure stabilises, and the markers of metabolic health improve across successive monitoring intervals. The patient who achieves permanent normalisation of blood pressure and metabolic markers may eventually reach a steady-state maintenance programme of weekly 24-hour fasting alone, sustained not because disease requires management but because the biological benefits of periodic fasting extend across longevity, cognitive health, immune function and cellular quality control far beyond the cardiovascular system alone.

You are being asked, above all, to consider the possibility that the answer to your hypertension is not a better drug, a more creative combination of existing drugs, or lifelong acceptance of a managed but uncured condition. You are being asked to consider that the answer is already present in the biology you were born with, in the ancient metabolic programme that your evolutionary ancestors relied on, and in the consistent clinical evidence of more than 150 years of supervised therapeutic fasting practice that the mainstream medical community has largely failed to examine with the seriousness it deserves.

Bragg was right, even in the language of his era: the miracles are within you.

They are waiting for the conditions in which they can operate.

That is what the fast provides.

Chapter Summary: Key Points

The current pharmacological paradigm for hypertension management has achieved genuine successes whose limitations are equally real: the residual cardiovascular risk that persists despite optimal pharmacological treatment reflects the failure of drugs to address the upstream metabolic cause of hypertension rather than a failure of clinical execution. The iatrogenic burden of lifelong polypharmacy is substantial and systematically underweighted in clinical risk-benefit calculations. The economic architecture of pharmaceutical-dominated cardiovascular medicine creates structural rather than personal biases toward pharmacological solutions that disadvantage non-pharmacological interventions regardless of their evidence base.

The evidence for therapeutic fasting in hypertension is sufficient for clinical use. It is grounded in 150 years of supervised clinical practice documented across multiple countries and institutions, convergent with the molecular mechanistic science of the past 30 years at every point where comparison is possible, and supported by the best available contemporary clinical series in the Goldhamer studies.

The methodological objection based on absence of large RCTs applies with greater force to standard-of-care pharmacological interventions than the evidence demand placed on fasting justifies, and the impossibility of blinding in fasting research is a category limitation rather than a research quality failure.

A practical clinical framework for integrating therapeutic fasting begins with its use as first-line metabolic intervention in Stage 1 hypertension before pharmacological initiation, progresses to combined use with prospective medication tapering in Stage 2 hypertension, and requires physician training in fasting physiology, medication adjustment protocols, and monitoring infrastructure, along with thorough informed consent documentation.

The message to the hypertensive patient is the book's closing argument: you are not condemned to lifelong pharmacological management of an uncured condition. Your body retains the full biological capacity for the healing that 150 years of clinical evidence and 30 years of molecular biology have documented. The fast is not deprivation. It is the restoration of the conditions under which your most ancient and most powerful healing programmes operate. The miracles described throughout this book are not exceptional events occurring in exceptional patients. They are the consistent outcomes of consistent biology applied with clinical competence and sufficient understanding. That biology is yours. The understanding is what this book has attempted to provide.

> *“The physician's highest calling, his only calling, is to make sick people healthy, to heal, as it is termed.”*
>
> — Samuel Hahnemann, founder of homoeopathy, 1810

Modern medicine has interpreted this calling as the management of chronic disease indefinitely rather than its resolution. The supervised fasting tradition, from Hippocrates' instruction to "fast for a day" rather than reach for medicine, through the naturopathic physicians of the nineteenth and twentieth centuries, through the contemporary metabolic medicine of Goldhamer, Longo and Jamnadas, has maintained a different interpretation: that the physician's highest function is not to manage disease but to restore the conditions in which the body heals itself.

The instruments of that restoration are available, the evidence is sufficient, and the biology is ready.

The question is whether medicine is.

APPENDICES

Clinical Tools, Templates and Reference Material

APPENDIX A

CLINICAL DECISION FRAMEWORKS

A.1 Patient Selection Framework: Who Should Fast, Who Should Wait, Who Should Not

Framework Overview

Every patient presenting with hypertension and interest in therapeutic fasting must pass through a systematic three-tier evaluation before any fasting protocol is initiated. This framework is not a bureaucratic checklist. It is the clinical filter that determines which patients will benefit safely, which patients require additional preparation or specialist input before proceeding, and which patients must not fast under any circumstances. Applying it rigorously protects both the patient and the supervising physician.

The three tiers are: absolute contraindications (conditions that render extended therapeutic fasting categorically unsafe regardless of clinical context), conditional clearance requirements (conditions that require specific specialist assessment, laboratory confirmation, or preparatory management before fasting is appropriate), and clinical optimisation targets (modifiable factors that should be addressed in the pre-fast preparation period to maximise safety and outcome).

Tier 1: Absolute Contraindications

Do not initiate any fast beyond 24 hours in the presence of any of the following:

Pregnancy and lactation. Fasting produces significant metabolic, hormonal and nutritional changes that are incompatible with the physiological requirements of foetal development and breast milk production. This is an unconditional exclusion. There are no circumstances under which extended therapeutic fasting is appropriate in a pregnant or lactating patient.

Active or recently treated eating disorders. Any history of anorexia nervosa, bulimia nervosa, or other restrictive or compensatory eating disorder within the preceding three years. The overlap between fasting and restriction in the patient's psychological framework renders the risk of eating disorder reactivation unacceptably high. Patients with a remote history of eating disorders (more than five years prior) and documented sustained recovery may be considered on an individual basis with psychiatric clearance.

Type 1 diabetes mellitus. The absence of endogenous insulin production in Type 1 diabetes creates a risk of diabetic ketoacidosis (DKA, a life-threatening condition in which uncontrolled ketone production drives blood acidity to dangerous levels) during fasting that cannot be safely managed in the fasting context without continuous medical monitoring of a kind that is incompatible with outpatient therapeutic fasting.

Decompensated heart failure. Defined as heart failure with current symptoms at rest or with minimal activity, current pulmonary oedema, or recent (within 3 months) hospitalisation for acute heart failure decompensation. The haemodynamic instability of decompensated heart failure, combined with the fluid and electrolyte shifts of fasting, creates unacceptable cardiovascular risk. Compensated heart failure (stable symptoms, no recent decompensation, adequate diuretic management) is a conditional inclusion requiring specialist cardiologist clearance rather than an absolute contraindication.

Advanced chronic kidney disease: eGFR below 30 mL/min/1.73m². Stage 4 and Stage 5 CKD (eGFR below 30 and below 15 mL/min/1.73m² respectively) are absolute contraindications to extended fasting beyond 24 hours. The kidneys at this level of function cannot safely manage the nitrogen load of protein catabolism during fasting, the electrolyte shifts of natriuresis, or the acid-base demands of ketosis. Stage 3 CKD (eGFR 30 to 59 mL/min/1.73m²) is a conditional inclusion requiring nephrology clearance and enhanced monitoring.

Active malignancy under treatment. Patients currently receiving chemotherapy, radiotherapy, or immunotherapy for active cancer have metabolic demands and immune vulnerabilities that are incompatible with extended therapeutic fasting without specialist oncology supervision. The Longo fasting-mimicking diet research in cancer patients is a specialised area with its own evidence base and protocols; it is not what is being described in this book.

Acute psychiatric crisis. Active psychosis, severe acute depression with suicidal ideation, or manic episode. The cognitive and emotional instability of acute psychiatric crisis makes therapeutic fasting unsafe and its implementation unethical without psychiatric stabilisation first.

Recent major surgery or significant trauma. Within 8 weeks of major surgery or significant physical trauma. The metabolic demands of surgical healing and the wound repair process require adequate nutritional substrate and are incompatible with the caloric deprivation of extended fasting.

Severe electrolyte abnormalities at baseline. Potassium below 3.0 mmol/L, sodium below 130 mmol/L, or magnesium below 0.5 mmol/L on the pre-fast laboratory panel. These abnormalities must be corrected to within normal range before any fasting beyond 24 hours is initiated.

Tier 2: Conditional Clearance Requirements

The following conditions require the specific action noted before fasting beyond 48 hours is initiated:

Condition	Required Action Before Proceeding
Type 2 diabetes on insulin	Endocrinology review; specific insulin dose reduction protocol; CGM established; glucose monitoring every 4 hours during fast
Type 2 diabetes on sulphonylureas	Sulphonylureas suspended completely before first fast; physician-supervised medication transition
Type 2 diabetes on SGLT2 inhibitors	Suspend SGLT2 inhibitor minimum 72 hours before fast initiation; euglycaemic DKA risk documented in consent

Condition	Required Action Before Proceeding
Stage 3 CKD (eGFR 30-59)	Nephrology consultation; renal function panel repeated within 2 weeks before each fast; maximum fast duration 24-48 hours unless nephrology specifically approves extension
Compensated heart failure	Cardiologist review; ECG; echocardiogram within 6 months; maximum 24-hour fasts until 4 completed without incident; extension only with cardiologist approval
Cardiac arrhythmia	Cardiology review; 24-hour Holter monitoring; ECG before and after each fast beyond 24 hours
Gout with recent acute episode (within 6 weeks)	Uric acid measured at baseline and at Day 2-3 of any extended fast; colchicine or allopurinol management plan established with rheumatology if uric acid above 0.48 mmol/L
Severe GORD or oesophageal disease	Gastroenterology review; proton pump inhibitor management during fasting period
Corticosteroid therapy (ongoing)	Never abruptly discontinue; endocrinology review for HPA axis assessment; mineralocorticoid effects on electrolytes require enhanced monitoring
Digoxin therapy	Hypokalaemia from fasting dramatically increases digoxin toxicity risk; electrolyte monitoring minimum every 48 hours during extended fasting; cardiology review
Significant hepatic disease (ALT or AST above 3x upper limit of normal)	Hepatology review before extended fasting; extended fasts create significant hepatic metabolic demands
History of prolonged QT syndrome	Cardiology review; electrolyte monitoring with particular attention to potassium and magnesium (both affect QT interval); ECG before, during (Day 3-4), and after each extended fast
Anticoagulation (warfarin)	INR monitoring more frequently during fasting (dietary changes affect vitamin K intake and warfarin metabolism); anticoagulation clinic notification
Severe OSA not on CPAP	Sleep medicine referral before initiating extended fasting; untreated OSA produces haemodynamic instability during sleep that is compounded by fasting's cardiovascular changes

Tier 3: Clinical Optimisation Targets

The following should be addressed in the 2 to 4-week pre-fast preparation period. None are contraindications to fasting, but optimising them improves safety and outcome:

Caffeine reduction: taper gradually over 7 to 14 days before the first extended fast. Abrupt caffeine cessation at the start of a fast compounds Day 1 headache and fatigue with caffeine withdrawal

symptoms that are both more severe and more prolonged than the fasting symptoms alone.

Dietary transition: 14 days of progressively reducing refined carbohydrates, added sugars, processed foods, and alcohol before the first extended fast. This reduces the metabolic shock of the early fasting period by partially pre-adapting insulin secretion patterns and reducing the magnitude of the Day 2 metabolic crossover.

Alcohol cessation: complete cessation minimum 2 weeks before any extended fast. Alcohol disrupts sleep architecture, impairs liver glycogen regulation, and its withdrawal during fasting can be confused with or compound fasting symptoms.

Tobacco cessation: ideally before fasting begins; if not achievable, the fasting period itself is an opportune moment for cessation given the reduced dopaminergic food-reward activity that may reduce cross-cueing of nicotine craving.

Hydration baseline: ensure adequate baseline hydration (minimum 1.5 litres of water daily) in the week before the fast, particularly in patients on diuretics who may be chronically mildly volume-depleted.

Electrolyte baseline optimisation: if magnesium is below 0.7 mmol/L on the pre-fast panel, initiate magnesium glycinate supplementation (200-400 mg daily) for 2 weeks before the first extended fast.

A.2 Risk Stratification and Fasting Protocol Selection Framework

Determining Appropriate Starting Protocol

After Tier 1 and Tier 2 assessment, the following framework determines the appropriate starting rung on the fasting ladder described in Chapter 8:

Low-risk profile (all of the following):

- Hypertension Stage 1 or early Stage 2 (systolic below 160 mmHg)
- No diabetes or prediabetes only (HbA1c below 5.7%)
- eGFR above 60 mL/min/1.73m²
- No established cardiovascular disease
- No current antihypertensive medication or single agent at low dose
- No active comorbidities requiring specialist management

Appropriate starting protocol for low-risk profile: Rung 1 (24-hour weekly fasting), with progression through the ladder as per Chapter 8 timeline. May progress to Rung 2 after four completed 24-hour fasts without incident.

Moderate-risk profile (any one of the following, no absolute contraindications):

- Hypertension Stage 2 (systolic 160-179 mmHg)
- Prediabetes (HbA1c 5.7-6.4%) or controlled Type 2 diabetes not on insulin
- eGFR 45-60 mL/min/1.73m²

- Two or more antihypertensive medications
- History of cardiovascular disease (stable, no recent events)
- BMI above 35 with metabolic syndrome

Appropriate starting protocol for moderate-risk profile: Rung 1 (24-hour weekly fasting) with enhanced monitoring (daily BP logging from the start, physician contact after each 24-hour fast for first 4 weeks). Progress to Rung 2 only after confirmed physician review showing stable BP response and no adverse events. Maximum initial progression to Rung 3 (3-4 days) requires minimum 8 weeks of lower-rung experience and physician in-person assessment before each extended fast.

High-risk profile (any one of the following, after Tier 2 clearance obtained):

- Hypertension Stage 3 (systolic at or above 180 mmHg)
- Type 2 diabetes on insulin or sulphonylureas
- Stage 3 CKD (eGFR 30-59 mL/min/1.73m²)
- Compensated heart failure
- Three or more antihypertensive medications
- Established peripheral arterial disease or prior cerebrovascular event

Appropriate starting protocol for high-risk profile: Rung 1 (24-hour fasting) only for minimum 8 weeks, with daily physician contact during each 24-hour fast period, laboratory electrolyte and renal monitoring after each fast for the first 4 fasts, and formal physician review before any progression to Rung 2\. Rungs 3 and above require specialist co-management and should not be attempted in the first 6 months of the programme regardless of clinical response.

A.3 Medication Adjustment Decision Framework

The Medication Adjustment Priority Sequence

When initiating extended fasting in a patient on antihypertensive and other relevant medications, adjustments should be made in the following priority sequence:

Priority 1: Suspend before fasting begins (not adjust, suspend completely):

- All loop diuretics (furosemide, bumetanide, torasemide)
- All thiazide and thiazide-like diuretics (hydrochlorothiazide, chlorthalidone, indapamide)
- SGLT2 inhibitors (dapagliflozin, empagliflozin, canagliflozin): minimum 72 hours before extended fast initiation
- Sulphonylureas (glibenclamide, glipizide, gliclazide, glimepiride): suspend completely before any fast beyond 24 hours
- Metformin: suspend 24-48 hours before extended fasting beyond 48 hours (lactic acidosis risk, particularly in context of reduced renal perfusion during fasting)

- NSAIDs (ibuprofen, naproxen, diclofenac, others): suspend before fasting; renal risk compounded by fasting-related volume contraction

Priority 2: Dose reduce proactively at fast initiation (not suspend, reduce):

- ACE inhibitors and ARBs: reduce to 50% of current dose at the start of any fast beyond 48 hours; consider further reduction or suspension if systolic falls below 110 mmHg
- Calcium channel blockers (amlodipine, lercanidipine, felodipine): reduce by 50% at fast initiation; orthostatic risk is lower than with RAAS agents but still present
- Alpha-blockers (doxazosin, prazosin): reduce by 50% at fast initiation; high orthostatic risk, particularly in standing transitions

Priority 3: Taper carefully, never stop abruptly:

- Beta-blockers (bisoprolol, metoprolol, atenolol, carvedilol, nebivolol): must never be abruptly stopped. Taper by 25-50% of dose at fast initiation if blood pressure falls significantly (systolic below 115 mmHg), with further gradual taper at weekly intervals as blood pressure allows. Abrupt beta-blocker withdrawal risks rebound tachycardia, hypertension, and in patients with coronary artery disease, acute coronary syndrome.

Priority 4: Maintain with enhanced monitoring:

- Digoxin: maintain dose but monitor potassium and magnesium minimum every 48 hours during extended fasting, given digoxin toxicity risk with hypokalaemia
- Warfarin: maintain dose but monitor INR more frequently (every 3-4 days during extended fasting); dietary vitamin K intake changes during fasting and refeeding will affect INR
- Levothyroxine: maintain throughout fasting; thyroid hormone requirements do not change during fasting in the short to medium term

Blood Pressure Thresholds for Medication Adjustment During Extended Fasting

The following thresholds guide proactive (anticipatory) medication adjustment during extended fasting. These are decision points for physician-directed adjustment, not patient self-management thresholds:

Systolic BP (mmHg)	Diastolic BP (mmHg)	Action
Above 150	Above 95	No medication reduction yet; continue current regimen; reassess at next daily contact
130-150	85-95	Consider 25% dose reduction in ACE inhibitor or ARB if currently at full dose
115-130	75-85	Consider 50% dose reduction in all RAAS agents; reassess need for CCB

Systolic BP (mmHg)	Diastolic BP (mmHg)	Action
100-115	65-75	Suspend ACE inhibitors and ARBs; reduce CCB by 50%; review beta-blocker dose
Below 100	Below 65	Suspend all antihypertensives except beta-blockers (taper); assess for breaking of fast if accompanied by perfusion symptoms
Below 90	Below 60	Break fast; seek immediate clinical assessment; maintain beta-blocker at minimum effective dose

All adjustments are physician-directed. Patients must not self-adjust medications without physician contact.

A.4 Post-Fast Medication Reinstatement Framework

Principles of Post-Fast Reinstatement

Blood pressure in the immediate post-fast period (first 7 to 14 days of refeeding) is typically at its lowest point in the entire programme, as the full physiological effects of the fast including RAAS suppression, reduced circulating volume, improved endothelial function, and sympathetic withdrawal are present while the metabolic benefits of improved insulin sensitivity are beginning to consolidate. Medication reinstatement in this period must be governed by actual measured blood pressure rather than by the pre-fast prescription.

Decision rule for post-fast medication reinstatement:

If blood pressure at Day 3 of refeeding (after initial fluid and glycogen restoration) is below 125/80 mmHg, do not reinstate any previously suspended antihypertensive medication. Continue monitoring. Reassess at 2-week intervals.

If blood pressure at Day 3 of refeeding is 125 to 140/80 to 90 mmHg, reinstate only the lowest-dose single agent from the pre-fast regimen (prioritise ACE inhibitor or ARB over diuretic), at 50% of the pre-fast dose. Reassess at 2-week intervals.

If blood pressure at Day 3 of refeeding is above 140/90 mmHg, reinstate the pre-fast regimen at 50% of pre-fast doses and reassess weekly, with stepwise dose increase only if blood pressure remains above 140/90 mmHg despite dietary adherence.

APPENDIX B

MONITORING TEMPLATES

B.1 Pre-Fast Clinical Assessment Template

Patient Identification and Baseline

Date of assessment:

Planned fast commencement date:

Planned fast duration (target):

Physician supervising fast:

Section 1: Blood Pressure and Cardiovascular Baseline

Blood pressure (right arm, seated, 5 minutes rest):

Reading 1: ___/___

Reading 2 (3 minutes after Reading 1): ___/___

Average: ___/___

Blood pressure (left arm, seated):

Reading 1: ___/___

Significant inter-arm difference (above 10 mmHg systolic): Yes / No

If yes: arrange vascular assessment to exclude subclavian artery disease before proceeding

Resting heart rate (bpm): ___

Heart rate rhythm: Regular / Irregular

If irregular: 12-lead ECG mandatory before proceeding

Weight (kg): ___

Height (cm): ___

BMI: ___

Waist circumference (cm): ___

Waist-to-height ratio: ___

Section 2: Pre-Fast Laboratory Results

All results should be within 4 weeks of fast commencement

Test	Result	Reference Range	In Range?	Action if Abnormal
Fasting glucose (mmol/L)		3.9-5.5		
Fasting insulin (pmol/L)		Below 60		
HOMA-IR (calculated)		Below 1.5		
HbA1c (%)		Below 5.7		
Total cholesterol (mmol/L)		Below 5.0		
LDL cholesterol (mmol/L)		Below 3.0		
HDL cholesterol (mmol/L)		Above 1.0 (M), Above 1.2 (F)		
Triglycerides (mmol/L)		Below 1.7		
TG:HDL ratio		Below 1.5		
Sodium (mmol/L)		136-145		
Potassium (mmol/L)		3.5-5.0		
Magnesium (mmol/L)		0.7-1.0		
Phosphate (mmol/L)		0.8-1.5		
Creatinine (µmol/L)		60-110 (M), 45-90 (F)		
eGFR (mL/min/1.73m²)		Above 60		
Urea (mmol/L)		2.5-7.8		
Uric acid (mmol/L)		0.2-0.42 (F), 0.25-0.48 (M)		
ALT (IU/L)		Below 40		
AST (IU/L)		Below 40		
TSH (mIU/L)		0.4-4.0		
hsCRP (mg/L)		Below 1.0 (optimal), Below 3.0 (acceptable)		

Test	Result	Reference Range	In Range?	Action if Abnormal
FBC (Hb, WCC, Plt)		As per local laboratory reference		
ECG		Normal sinus rhythm		

Section 3: Current Medication Review

Medication	Current Dose	Frequency	Category	Action for Fast

Medications suspended before fast:

Medications dose-reduced at fast initiation:

Medications maintained with enhanced monitoring:

Medications requiring specialist input:

Section 4: Contraindication Screening

Absolute contraindications (any present \= do not proceed beyond 24-hour fasting):

Contraindication	Present?	If Yes: Action
Pregnancy or lactation	Yes / No	Do not proceed
Active eating disorder (within 3 years)	Yes / No	Do not proceed; psychiatric referral
Type 1 diabetes mellitus	Yes / No	Do not proceed with extended fasting
Decompensated heart failure	Yes / No	Do not proceed; heart failure team referral
eGFR below 30 mL/min/1.73m²	Yes / No	Do not proceed beyond 24 hours
Active malignancy under treatment	Yes / No	Do not proceed; oncology input required
Acute psychiatric crisis	Yes / No	Do not proceed; psychiatric stabilisation required
Major surgery or trauma within 8 weeks	Yes / No	Do not proceed
Severe uncorrected electrolyte abnormalities	Yes / No	Correct electrolytes; reassess

Section 5: Risk Stratification

Risk profile classification (from Framework A.2): Low / Moderate / High

Appropriate starting protocol: Rung ___ (as per A.2)

Conditions requiring specialist clearance:

- Clearance obtained from: _____
- Date of clearance: _____
- Specialist recommendations for modification of protocol: _____

Section 6: Informed Consent Documentation

Patient has been provided with written information about:

- [ ] Fasting physiology and expected timeline of symptoms
- [ ] Medication adjustments and their rationale
- [ ] Monitoring requirements and patient responsibilities
- [ ] Normal fasting symptoms (healing crisis)
- [ ] Danger signals requiring immediate medical contact
- [ ] Emergency contact protocol
- [ ] The evidence base and its limitations

Patient has had opportunity to ask questions: Yes / No

Patient questions and responses documented: _____

Patient's understanding confirmed by: _____

Informed consent signed and dated: Yes / No

Date: _____

Physician signature: _____

B.2 Daily Fasting Monitoring Template

This template is completed by the patient twice daily and reviewed by the supervising physician at each daily contact during any fast beyond 48 hours.

PATIENT DAILY FASTING LOG

Patient name: _____

Fast day number: _____

Date: _____

Morning Reading (on waking, before any activity)

Time of reading: _____

Blood pressure (lying, 5 minutes rest):

Reading 1: ___/___

Reading 2 (3 minutes after): ___/___

Average: ___/___

Blood pressure (standing, 1 minute after rising slowly):

Reading: ___/___

Orthostatic drop (lying systolic minus standing systolic): ___ mmHg

If standing systolic is more than 20 mmHg below lying systolic, or if symptoms of dizziness on standing: contact physician before next activity

Resting heart rate (bpm): ___

Heart rhythm: Regular / Irregular If irregular: contact physician

Body weight (kg, after voiding): ___

Blood glucose (mmol/L): ___ (diabetic patients only, or if symptomatic)

Urine ketones (if testing): Negative / Trace / Small / Moderate / Large

Urine colour: Pale yellow / Yellow / Dark yellow / Orange / Brown

Dark orange or brown: contact physician; increase water intake; physician to assess

Morning Symptom Log

Rate each symptom from 0 (absent) to 10 (severe):

Symptom	Rating (0-10)	Notes
Hunger		
Headache		
Fatigue		
Nausea		
Dizziness		
Muscle cramps		
Palpitations		
Mood		(10 \= best possible, 0 \= worst)
Mental clarity		(10 \= sharpest, 0 \= most foggy)
Sleep quality last night		(10 \= best, 0 \= worst)

Any symptom rated 7 or above: Contact physician before continuing fast

Any of the following present: (circle and contact physician immediately)

Chest pain / Severe shortness of breath / Loss of consciousness / Severe confusion / Vomiting blood / Unable to take any water

Water Intake Log

Record each time water is consumed. Target: 2.0 to 3.0 litres across the full day. Do not exceed 3.5 litres.

Time	Amount (mL)	Running Total (mL)

Total daily water intake (mL): ___

Evening Reading (before sleep)

Time of reading: _____

Blood pressure (seated, 5 minutes rest):

Reading 1: ___/___

Reading 2 (3 minutes after): ___/___

Average: ___/___

Heart rate (bpm): ___

Blood glucose (mmol/L): ___ (diabetic patients only)

Evening Symptom Check

Symptom	Present?	If Yes: Severity (1-10)
Hunger	Yes / No	
Headache	Yes / No	
Nausea or vomiting	Yes / No	
Muscle cramps	Yes / No	
Palpitations	Yes / No	
Unusual weakness	Yes / No	
Skin eruption or rash	Yes / No	
Body odour change	Yes / No	
Tongue coating (describe)	Yes / No	

Symptom	Present?	If Yes: Severity (1-10)
Difficulty sleeping	Yes / No	

Physician Daily Contact Record

Time of physician contact: _____

Mode of contact: Telephone / Video / In-person

Blood pressure reviewed: Yes / No

Symptoms reviewed: Yes / No

Medication adjustment made: Yes / No

If medication adjustment made, document:

Drug name: _____

Previous dose: _____

New dose: _____

Rationale: _____

Physician assessment of fast status:

- [ ] Proceeding well, continue current protocol
- [ ] Proceeding with monitoring adjustment: _____
- [ ] Medication adjustment made (as above)
- [ ] Increased monitoring frequency required: _____
- [ ] Fast to be broken: reason: _____
- [ ] Emergency assessment required: _____

Physician signature: _____

Date and time: _____

B.3 Mid-Fast Laboratory Monitoring Template

To be completed at Day 3-4 of any fast of 5 days or more, and at Day 5-7 of any fast of 10 days or more.

MID-FAST LABORATORY PANEL

Patient name: _____

Fast day number at time of blood draw: _____

Date: _____

Test	Result	Reference Range	Flag	Physician Action
Sodium (mmol/L)		136-145		
Potassium (mmol/L)		3.5-5.0		
Magnesium (mmol/L)		0.7-1.0		
Phosphate (mmol/L)		0.8-1.5		
Creatinine (µmol/L)		Baseline ±20%		
eGFR (mL/min/1.73m²)		Above 60, or stable to baseline		
Urea (mmol/L)		Up to 2x baseline is expected		
Glucose (mmol/L)		3.5-6.0		
Bicarbonate (mmol/L)		22-29		
Beta-hydroxybutyrate (mmol/L)		1.0-3.5 (therapeutic ketosis)		
Haemoglobin (g/dL)		Above 11		
White cell count (x10■/L)		4.0-11.0		
Uric acid (mmol/L)		May be transiently elevated		

Critical Value Alert Thresholds (Act Immediately)

Result	Threshold	Action
Potassium	Below 3.0 mmol/L	Break fast or physician-directed oral/IV supplementation; ECG
Sodium	Below 130 mmol/L	Break fast; urgent medical assessment
Sodium	Above 150 mmol/L	Increase water intake; medical assessment
Phosphate	Below 0.5 mmol/L	Break fast; phosphate replacement; medical assessment
Magnesium	Below 0.5 mmol/L	Physician-directed supplementation; assess for continuation
Glucose	Below 3.5 mmol/L	Break fast with juice immediately

Result	Threshold	Action
Glucose	Above 10 mmol/L (diabetic)	Medical assessment; medication review
Bicarbonate	Below 18 mmol/L	Assess for metabolic acidosis; break fast
Beta-hydroxybutyrate	Above 5.0 mmol/L with acidosis	Break fast; medical assessment
eGFR	Below 30, or fall of more than 30% from baseline	Break fast; nephrology assessment

B.4 Post-Fast Laboratory and Clinical Assessment Template

To be completed at Day 3-5 of the refeeding period following any fast of 3 days or more.

POST-FAST ASSESSMENT

Date: _____

Duration of completed fast: ___ days

Date fast was broken: _____

Reason for breaking (natural completion / physician decision / patient decision / complication): _____

Post-Fast Blood Pressure and Cardiovascular Assessment

Blood pressure (right arm, seated):

Reading 1: ___/___

Reading 2: ___/___

Average: ___/___

Orthostatic assessment (lying to standing):

Lying: ___/___

Standing (1 minute): ___/___

Orthostatic drop: ___ mmHg

Heart rate (bpm): ___

Heart rhythm: Regular / Irregular

Weight (kg): ___

Change from pre-fast weight (kg): ___

Post-Fast Laboratory Panel

Test	Pre-Fast Value	Post-Fast Value	Change	Clinical Significance
Fasting glucose (mmol/L)				
Fasting insulin (pmol/L)				
HOMA-IR				
HbA1c (%)				
Total cholesterol (mmol/L)				
LDL cholesterol (mmol/L)				
HDL cholesterol (mmol/L)				
Triglycerides (mmol/L)				
TG:HDL ratio				
Sodium (mmol/L)				
Potassium (mmol/L)				
Magnesium (mmol/L)				
Phosphate (mmol/L)				
Creatinine (µmol/L)				
eGFR (mL/min/1.73m²)				
Uric acid (mmol/L)				
ALT (IU/L)				
hsCRP (mg/L)				

Medication Status Post-Fast

Medication	Pre-Fast Dose	Current Dose	Decision	Rationale
			Reinstate / Reduce / Maintain / Discontinue	

Medication	Pre-Fast Dose	Current Dose	Decision	Rationale
			Reinstate / Reduce / Maintain / Discontinue	
			Reinstate / Reduce / Maintain / Discontinue	
			Reinstate / Reduce / Maintain / Discontinue	

Post-Fast Clinical Assessment

Patient's subjective report of fast experience: _____

Patient's tolerance of refeeding protocol: _____

Adverse events during fast (none / minor / significant): _____

If significant: describe and document separately

Fast completed as planned: Yes / No

If no: reason and duration actually completed: _____

6-Month Monitoring Schedule (Longitudinal Tracking)

To be recorded at each 6-month laboratory review

Date	BP (avg of 3 readings)	HR	Weight (kg)	HOMA-IR	TG:HDL	hsCRP	eGFR	Meds (number/dose)	Notes
Baseline									
6 months									
12 months									
18 months									
24 months									
30 months									
36 months									

B.5 Permanent Normalisation Assessment Template

To be completed when considering formal declaration of blood pressure normalisation and completion of pharmacological tapering

Criteria for permanent normalisation (all must be met):

Criterion	Target	Achieved?	Date Achieved
Blood pressure consistently below 120/80 mmHg	12 consecutive months	Yes / No	
All antihypertensive medications discontinued	Complete cessation	Yes / No	
HOMA-IR	Below 1.5	Yes / No	
TG:HDL ratio	Below 1.5	Yes / No	
hsCRP	Below 1.0 mg/L	Yes / No	
Resting heart rate	55-65 bpm	Yes / No	
eGFR	Stable or improved from baseline	Yes / No	
HbA1c (if diabetic)	Below 6.0% without medication	Yes / No	

All criteria met: Yes / No

If yes, formal declaration of permanent normalisation:

Date: _____

Physician signature: _____

Maintenance programme going forward:

- Weekly 24-hour fasting: maintained / modified as: _____
- Monthly 36-48 hour fasting: maintained / modified as: _____
- Annual extended fasting: maintained / modified as: _____
- 6-monthly laboratory review: continued

Permanent normalisation does not mean the programme ends. It means the programme has achieved its primary clinical objective and transitions to a maintenance phase that sustains the metabolic health from which the normalisation was achieved.

We already have Appendices A and B complete. Proceeding with C through J.

APPENDIX C

PATIENT INFORMATION SUMMARIES

These summaries are written in plain language for direct distribution to patients. They translate the clinical content of the book into information the patient can read, keep, and refer to throughout their programme. Each summary is designed to be printed and handed to the patient at the relevant stage of their programme.

C.1 What Is Therapeutic Fasting and Why Does It Lower Blood Pressure?

For the Patient

You have been diagnosed with high blood pressure, and your doctor has recommended a supervised fasting programme as part of your treatment. This summary explains what fasting is, what it does in your body, and why it works for blood pressure. Read it carefully, keep it, and refer to it whenever you have questions during your programme.

What is high blood pressure, really?

Blood pressure is the force your blood exerts against the walls of your arteries as your heart pumps it around your body. A normal reading is below 120 over 80 (written as 120/80 mmHg, where mmHg refers to millimetres of mercury, the unit used to measure pressure). When this number is consistently above 130/80, you have high blood pressure, also called hypertension.

For most people, high blood pressure does not have a single obvious cause like a leaking valve or a blocked pipe. Instead, it develops gradually over years as a result of the way the body handles a hormone called insulin. When you eat, particularly when you eat refined carbohydrates and sugar, your pancreas releases insulin to move the glucose (sugar) from your food into your cells for energy. This is a normal, essential process.

The problem arises when the body is exposed to large, frequent amounts of sugar and refined carbohydrates over many years. The cells gradually stop responding properly to insulin, a condition called insulin resistance. In response, the pancreas produces more and more insulin to do the same job, and the level of insulin in the bloodstream rises chronically above normal. This is called hyperinsulinaemia, which simply means "too much insulin in the blood."

Chronically elevated insulin raises blood pressure through four specific mechanisms:

First, it tells the kidneys to retain sodium (salt) and water rather than excreting them. When the kidneys hold onto more fluid, the volume of blood in your arteries increases, and pressure goes up, just as water pressure in a hose increases when you block the outlet.

Second, it activates your sympathetic nervous system, the "fight or flight" part of your nervous system that is designed for emergencies, and keeps it in a state of low-level chronic activation. One of the effects of sympathetic activation is arterial constriction: the arteries narrow, and when the same amount

of blood is pushed through narrower tubes, the pressure increases.

Third, it activates a hormonal system called the renin-angiotensin-aldosterone system (RAAS). This system's normal job is to raise blood pressure in emergencies. Chronically elevated insulin keeps it switched on when it should be resting.

Fourth, it stimulates the smooth muscle cells that make up the walls of your arteries to multiply and thicken, making the arteries stiffer and less able to relax when the heart pumps.

The result of all four mechanisms working together is persistently elevated blood pressure. And because the insulin resistance driving all of this is still present, the blood pressure medications your doctor prescribes can reduce the numbers but cannot address the cause. The blood pressure is managed, not resolved.

What does fasting do?

When you stop eating, your body has no dietary glucose or insulin to manage. Within the first 12 to 16 hours, the small amount of glucose stored in your liver as glycogen (a storage form of sugar) is used up. After that point, your body switches its primary fuel source from glucose to fat.

To use fat as fuel, your liver converts fat molecules into compounds called ketones. Ketones are a clean, efficient fuel that your brain, heart, and muscles can use in place of glucose. By 24 to 36 hours into a fast, your blood ketone level has risen significantly, and your insulin level has fallen to its lowest possible baseline.

This fall in insulin is the key event. When insulin falls:

The kidneys begin releasing the sodium and fluid they have been retaining. Blood volume decreases, and blood pressure falls. This often accounts for the most rapid and dramatic early blood pressure reductions in fasting patients, sometimes 10 to 20 mmHg within the first 48 hours.

The sympathetic nervous system begins to quieten. By Day 3 to 5 of an extended fast, the chronic low-level fight-or-flight activation begins to resolve, and the arteries begin to relax.

The RAAS reduces its activity. The hormonal overdrive that has been constricting your blood vessels begins to settle.

The lining of your arteries, called the endothelium, begins to repair itself. An enzyme called eNOS (endothelial nitric oxide synthase) that produces the molecule nitric oxide, which keeps arteries dilated and blood flowing freely, begins working more effectively as the oxidative burden on the endothelium falls.

A cellular housekeeping process called autophagy (pronounced "au-TOF-uh-jee," from the Greek for "self-eating") activates throughout your body. Autophagy is the process by which your cells identify damaged components, break them down, and recycle the parts. In your blood vessel walls, this removes damaged proteins and cellular debris that have accumulated from years of metabolic stress. In your kidney cells, it repairs the filtration units that high blood pressure and insulin resistance have been progressively damaging.

All of these changes together produce blood pressure reduction of a magnitude that no medication achieves, because the medication addresses one pathway while fasting addresses all of them simultaneously.

How long does this take?

The timeline varies between individuals, but the general pattern is consistent:

By the end of the first 24-hour fast: blood pressure may have fallen by 5 to 10 mmHg as sodium and fluid excretion begins. You may feel lightheaded when standing up (see the section on safety below).

By the end of the first 48 to 72-hour period (during a longer fast): the metabolic crossover to fat-burning is complete, ketones are elevated, insulin is at its lowest, and the most significant blood pressure reductions begin.

By the end of a 5 to 7-day supervised fast: most patients who are going to respond to fasting have achieved their most significant reductions. Some patients normalise their blood pressure completely within a single extended fast.

Over 3 to 6 months of the graduated fasting programme (weekly 24-hour fasting, monthly 36 to 48-hour fasting, with extended fasting at appropriate intervals): insulin sensitivity improves progressively, the metabolic dysregulation that has been driving the hypertension reverses over time, and blood pressure continues to improve as the root cause is progressively addressed.

The blood pressure medications you are currently taking will be adjusted by your doctor as your blood pressure falls. In many patients, medications are reduced and eventually stopped entirely as the programme progresses.

Is this safe?

Supervised therapeutic fasting, conducted with the monitoring protocols described in this programme, is safe for the majority of patients with primary hypertension. The key word is supervised. Fasting without medical oversight, without blood pressure monitoring, without medication adjustment, and without the knowledge to distinguish normal fasting responses from symptoms requiring medical attention is not what this programme recommends.

The most important safety consideration during fasting is the risk of blood pressure falling too low, particularly when moving from lying or sitting to standing quickly. This is called orthostatic hypotension (low blood pressure on standing). If you feel dizzy or lightheaded when you stand up, sit or lie back down immediately and contact your physician. Do not stand up quickly during your fast. Move slowly and deliberately, and pause in a sitting position for 30 seconds before fully standing.

Keep your fluid intake at 2 to 3 litres of water per day during fasting. Do not exceed this. Both too little and too much water can disrupt your electrolytes (the mineral salts, including sodium, potassium, and magnesium, that your body needs for normal function).

The other symptoms that commonly occur during fasting, headache, fatigue, body odour, coated tongue, bad breath, muscle aches, poor sleep in the first 1 to 2 days, are normal and expected. They

are not signs of harm. They are signs that your body is releasing stored toxins, adjusting its hormonal balance, and transitioning its fuel systems. Chapter 11 of this book describes each of these symptoms in detail, explains why they occur, and specifies which symptoms require physician contact and which do not.

If you experience chest pain, severe shortness of breath, vomiting blood, loss of consciousness, or severe confusion at any point during your fast, break the fast and seek emergency medical care immediately.

C.2 What to Expect: A Day-by-Day Guide to Your First Extended Fast

For the Patient

This guide describes what you are likely to experience during each phase of your first extended fast of 3 to 5 days. Individual experiences vary considerably, but the general timeline is consistent across most patients. Reading this in advance helps you understand what is happening in your body and reduces the anxiety that unfamiliar sensations can produce.

The evening before Day 1

Eat your last meal at least 4 hours before your planned sleep time. Choose a light, easily digested meal: vegetables, a small amount of protein (fish, eggs, or legumes), and avoid refined carbohydrates, sugar, alcohol, and caffeine. Take your evening blood pressure reading and record it. Ensure you have your water supply ready for the following day (minimum 2 litres immediately accessible). Review the emergency contact numbers for your supervising physician.

Day 1: Hours 0 to 24

You will feel hungry. This is normal and expected. The hunger of Day 1 is primarily habitual appetite, the physical sensation produced by your stomach expecting food at the times it is accustomed to receiving it, rather than genuine physiological hunger. The sensation is uncomfortable but not dangerous. It typically peaks around midday and early evening (the habitual meal times) and is manageable with water, gentle activity, and the knowledge that it will reduce significantly by Day 3\.

You may develop a headache, particularly if you were a regular caffeine consumer before the fast. This is caffeine withdrawal compounding the early fasting response, and it typically lasts 12 to 24 hours. Staying well hydrated reduces its severity. Mild headache is normal; severe or escalating headache requires physician contact.

Your energy may feel reduced in the afternoon of Day 1\. This is because your liver's stored glycogen (sugar) is being depleted and your body has not yet fully transitioned to fat-burning. It is temporary. Do not interpret afternoon fatigue on Day 1 as a sign that fasting is not right for you.

Your blood pressure will likely fall modestly in the first 24 hours as your kidneys begin releasing retained sodium and fluid. Take your usual morning and evening readings and report them to your physician.

Move slowly when changing position. The fluid shift of early fasting makes you more susceptible to dizziness on standing. Take your time.

Day 2: Hours 24 to 48

Day 2 is typically the most physically challenging day of the fast for most patients. Hunger may intensify further in the morning, reaching its peak around midday. By the evening of Day 2, for most patients, hunger begins to diminish as ketone production increases and the brain transitions to ketone fuel. The hunger of Days 1 and 2 is the body's habitual expectation of food asserting itself; once the metabolic crossover to fat-burning is underway, this signal quietens.

You may notice your mouth feels dry and your tongue develops a whitish or yellowish coating. This coating is a sign of the elimination of accumulated metabolic waste through the mucous membranes of the digestive tract, documented consistently in the supervised fasting literature. It is normal. Clean your tongue gently with a soft brush or tongue scraper, and maintain your fluid intake.

Your breath may become unusual, sometimes described as sweet, fruity, or acetone-like. This is the smell of ketones being exhaled through the lungs, a direct indicator that your body has successfully entered fat-burning metabolism. It is a positive sign, not a cause for concern.

Sleep on Night 2 may be disrupted. Some patients report difficulty falling asleep or early waking. This is related to the sympathetic nervous system changes of early fasting. Keep your bedroom dark and cool, avoid screens in the hour before sleep, and do not eat or drink large volumes of water in the 2 hours before bedtime.

Your blood pressure will likely continue to fall. If your morning reading is more than 20 mmHg below your pre-fast baseline, contact your physician for medication review.

Day 3: Hours 48 to 72 (The Turning Point)

For the majority of patients, Day 3 is the turning point of the fast. Hunger, which was prominent on Days 1 and 2, typically reduces significantly or disappears entirely by midday of Day 3\. This is not willpower. It is biology. Ketones are now the brain's primary fuel source, the insulin level is at its lowest, and the habitual appetite signal has been replaced by a state of metabolic adaptation that most patients describe as surprising and welcome.

Mental clarity often improves markedly on Day 3\. Many patients report an unusual sharpness of thought, improved concentration, and a quiet mental state they have not experienced in years. This is the result of ketone-mediated brain function (ketones are a more efficient neurological fuel than glucose for the resting brain) and the resolution of the low-grade inflammatory burden that has been impairing cognitive function.

Energy, which was reduced on Days 1 and 2, typically returns on Day 3\. Most patients find they can continue their usual daily activities (desk work, light walking, household tasks) without difficulty from Day 3 onward. Heavy physical exercise should be avoided during extended fasting.

Your blood pressure on Day 3 will typically show significant reduction from baseline. Report your readings to your physician. Medication adjustments may be made at this point if not already

implemented.

Days 4 and 5: Deepening Adaptation

The days following Day 3 are typically described by fasting patients as the most comfortable of the extended fast. Hunger is absent or minimal. Mental clarity is sustained. Energy is adequate for normal activity. Sleep tends to improve from the Day 2 disruption.

The physical changes continue internally. Autophagy is now operating at full activation throughout your cells, clearing damaged proteins and cellular debris. Your endothelium is continuing its repair process. The inflammatory markers in your blood are falling. Your gut microbiome is undergoing a compositional shift toward species that produce the short-chain fatty acids that support endothelial health and blood pressure regulation.

Your blood pressure may reach its lowest point of the entire fast on Days 4 or 5, sometimes achieving normalisation (below 120/80 mmHg) for the first time in years. This is the convergence of all the mechanisms described in this book operating simultaneously: reduced sodium and fluid, quietened sympathetic nervous system, suppressed RAAS, repaired endothelium, and improved insulin sensitivity.

Continue your daily physician contact, your twice-daily blood pressure readings, and your water intake.

Breaking the Fast

When it is time to break your fast, whether because the planned duration has been reached, or because your physician has advised it, or because the natural hunger signals of fast completion have appeared (as described in Chapter 8), the refeeding protocol is critically important. Do not eat solid food as your first post-fast meal. Begin with small quantities of fresh fruit juice (orange, grape, or apple), 100 to 150 mL, consumed slowly over 30 minutes. Wait 2 hours before taking more. The refeeding protocol of Chapter 8 describes in full detail how to progress from juice to soft fruit to light whole foods over the days following the fast. Follow it carefully. The most common mistakes in fasting are made not during the fast itself but in the first meal afterward.

C.3 Managing Hunger, Fatigue and Other Common Fasting Experiences

For the Patient

This summary addresses the most common experiences that patients describe during fasting and provides practical guidance for managing each one. None of these experiences are signs that fasting is harming you. They are the expected responses of a body undergoing metabolic recalibration.

Hunger

What to expect: Hunger is most intense on Days 1 and 2, peaks on Day 2, and in the majority of patients reduces significantly or disappears by Day 3 to 4 as ketone production rises and the metabolic crossover completes.

What to do: Drink water slowly when hunger arises. The stomach does not distinguish clearly between the sensation of hunger and the sensation of emptiness that water relieves. Take a short walk (10 to 15

minutes of slow walking). Change your environment: move to a different room, engage in light activity. The hunger sensation typically passes within 15 to 20 minutes if not responded to with food. Remind yourself: this is habitual appetite, not genuine physiological hunger. Your body has weeks of stored fuel available. You are not in danger.

When to contact your physician: if hunger is accompanied by severe shakiness, sweating, confusion, or palpitations, these are symptoms of potential hypoglycaemia (low blood sugar) and require immediate blood glucose testing and physician contact.

Headache

What to expect: Most common on Days 1 and 2\. Usually related to caffeine withdrawal (if caffeine intake was not reduced before the fast) or to the early haemodynamic changes of blood pressure reduction.

What to do: Increase water intake moderately. Move to a quiet, dark environment. Rest. A cool damp cloth on the forehead provides symptom relief. The headache of early fasting typically resolves by the end of Day 2 without intervention.

When to contact your physician: headache that is severe (rated 8 or above out of 10), that worsens progressively, that is accompanied by visual disturbance, or that is the worst headache you have ever experienced requires immediate physician contact and possible emergency assessment.

Fatigue

What to expect: Variable. Some patients feel significantly fatigued on Days 1 and 2 during the metabolic crossover. Others feel minimal fatigue from the start. Energy typically returns on Day 3\.

What to do: Rest when your body signals the need. This is one of the reasons your fasting programme should be timed around a period when you do not have high-demand professional or physical commitments on Days 1 and 2\. Light walking is beneficial; heavy exercise is not appropriate during extended fasting.

When to contact your physician: fatigue that prevents you from caring for yourself (unable to get out of bed, unable to maintain safe hydration) requires physician contact.

Dizziness on Standing

What to expect: Very common during fasting, particularly in the first 3 days as blood volume decreases with sodium and fluid excretion. Dizziness when moving from lying or sitting to standing is orthostatic hypotension (low blood pressure on standing).

What to do: Move slowly. Sit on the edge of your bed for 30 seconds before standing. When rising from a chair, pause in a half-standing position before fully straightening. If dizziness occurs, sit or lie down immediately. Do not stand up in the middle of the night without first sitting for 30 seconds. Contact your physician that morning to report any significant dizziness so that medication adjustment can be assessed.

When to contact your physician immediately: dizziness accompanied by loss of consciousness, inability to rise from the floor, or chest pain requires emergency medical attention.

Muscle Cramps

What to expect: Usually related to low magnesium or, less commonly, low potassium. Most common in the legs and feet, particularly at night.

What to do: Increase your water intake slightly. If your physician has authorised magnesium supplementation, take it at the time specified. Gentle stretching of the affected muscle provides immediate relief. Report cramps to your physician at the next daily contact.

When to contact your physician immediately: severe, sustained cramps accompanied by muscle weakness, irregular heartbeat, or difficulty breathing require immediate physician contact.

Body Odour and Breath Changes

What to expect: Some patients notice a change in body odour during fasting, sometimes described as stronger or more acidic than usual. Breath may develop a sweet or acetone-like quality. The tongue develops a white or yellowish coating.

What to expect: These are signs of elimination and ketosis, not illness. They are universally documented in the supervised fasting literature and are expected. Regular water intake, gentle tongue cleaning, and personal hygiene management are the appropriate responses. They resolve as the fast progresses and disappear completely after refeeding.

Sleep Changes

What to expect: Many patients experience disrupted sleep on Night 1 and Night 2 of an extended fast, with difficulty falling asleep or early morning waking. From Night 3 onward, sleep typically deepens and most patients report unusually restful sleep by the middle of an extended fast.

What to do: Keep your bedroom cool (18 to 20 degrees Celsius), dark, and quiet. Avoid screens in the hour before bed. Do not consume large volumes of water in the 2 hours before sleep. Gentle stretching or meditation before bed aids relaxation. If you wake early, do not attempt to eat: drink a small amount of water and rest quietly. Your physician should not be contacted for routine sleep disturbance unless accompanied by other concerning symptoms.

APPENDIX D

REFEEDING PROTOCOL REFERENCE CARDS

These cards are designed for direct patient use. Print each card relevant to the patient's fast duration and provide at the time of fast commencement, not only at the end of the fast.

D.1 Breaking a 24 to 48-Hour Fast

When to break: At the planned time, or when your physician advises.

First food (Hour 0 of refeeding):

A small bowl of fresh fruit: half a mango, one orange, a small bunch of grapes, or a cup of watermelon. Eat slowly. Chew thoroughly. Do not eat a meal.

Hours 2 to 4:

A light soup: vegetable broth (not cream-based), consumed slowly. Or a second small portion of fresh fruit.

Hours 4 to 8:

A light meal: a salad of raw vegetables with a small amount of olive oil and lemon juice, or steamed vegetables with a small quantity of rice. No meat, no dairy, no processed food, no refined carbohydrate at this meal.

Day 2 of refeeding:

Resume normal eating with attention to the nutritional principles of Chapter 9\. Do not overeat to compensate for the fast. Your stomach has contracted; smaller portions will feel satisfying.

Important: Do not break a 24 to 48-hour fast with: meat, cheese, eggs, bread, pasta, coffee, alcohol, or any processed food. The digestive system needs liquid or soft food first.

D.2 Breaking a 3 to 4-Day Fast

When to break: At the planned time, at the physician's instruction, or at the natural return of genuine hunger (as distinct from the habitual appetite of Day 2: genuine hunger returns quietly and persistently at the end of a complete fast and is accompanied by clearing of the tongue coating).

Hour 0 of refeeding: Fresh fruit juice

100 to 150 mL of fresh orange juice, grapefruit juice, or watermelon juice (not bottled; freshly extracted is strongly preferred). Sip slowly over 30 minutes. Do not drink it quickly.

Hour 2: A further 100 to 150 mL of fresh fruit juice, or a small bowl (150 g) of fresh soft fruit.

Hour 4: A second small bowl of fresh fruit, or a cup of vegetable broth (strained, no solids).

Hour 6: If tolerating well (no nausea, no stomach cramping), a small mixed fruit bowl or a cup of plain vegetable soup (blended smooth, no chunks, no salt added).

Day 2 of refeeding:

Morning: fresh fruit or a small smoothie (fruit, water, no added sugar).

Midday: a light salad with raw vegetables and olive oil, or a bowl of vegetable soup with a small portion of steamed rice.

Evening: steamed vegetables with a small portion of legumes (lentils, chickpeas) or white fish if the patient is not vegetarian. No red meat, no dairy, no refined carbohydrate, no alcohol.

Day 3 of refeeding:

Introduce a wider variety of whole foods. Eggs, if tolerated, are appropriate from Day 3\. Continue avoiding red meat, dairy, refined carbohydrates, and alcohol for a minimum of 5 to 7 days post-fast.

Important: The most common adverse outcome of fasting is an overly aggressive refeeding. One patient in the historical record who broke a 28-day fast with beef, potatoes, bread and butter required surgical intervention. You will be hungry. Eat slowly and in small quantities. Your digestive organs are returning to function gradually.

D.3 Breaking a 5 to 7-Day Fast

Days 1 to 2 of refeeding: Juice only

Fresh fruit juices exclusively for the first 48 hours. Begin with 100 mL portions every 2 hours for the first day. On the second day, increase to 150 to 200 mL every 3 hours. Rotate between orange, grapefruit, apple, watermelon, and carrot juice.

Sip every portion slowly. Do not drink any juice quickly.

Total daily juice volume: approximately 1.0 to 1.5 litres across the full day.

Continue drinking water: 1.5 to 2.0 litres of water daily, in addition to the juice.

Day 3 of refeeding: Introducing soft fruit

Soft fresh fruit (melon, papaya, mango, banana, peach) in small quantities alongside continued juice. Begin with 100 g portions twice a day. Increase to 150 g three times daily if tolerating well.

Day 4 of refeeding: Introducing vegetable soup

A blended, smooth vegetable soup (no salt, no cream, no stock cube) at one meal daily. Continue fruit and juice at other meals.

Day 5 of refeeding: Introducing salad

A small green salad with raw vegetables and olive oil at one meal. Cooked vegetables (steamed, not fried) at another meal. Continue fruit at one meal.

Days 6 and 7 of refeeding: Expanding to whole foods

Add small portions of legumes (lentils, chickpeas), cooked grains (brown rice, quinoa), and eggs if not vegetarian. Continue avoiding red meat, processed food, dairy, refined carbohydrate, alcohol, and caffeine for a minimum of 7 to 10 days post-fast.

Post 7-day fast laboratory check: Blood should be drawn at Day 3 to 5 of refeeding to assess electrolytes, renal function, and phosphate (refeeding syndrome risk, as described in Chapter 11). Attend this appointment without fail.

D.4 Breaking a 10 to 14-Day Fast

Days 1 to 3 of refeeding: Fresh juices exclusively

As per the 5 to 7-day protocol above but extended to three full days of juice only before introducing solid food.

Begin with 75 to 100 mL portions every 2 hours on Day 1 (total volume approximately 800 to 1000 mL). Increase gradually to 150 mL portions every 2 to 3 hours on Days 2 and 3 (total volume approximately 1.2 to 1.5 litres daily).

Days 4 and 5: Soft fruit

Introduce soft fresh fruit in 100 g portions twice daily. Continue juice at other intervals.

Days 6 and 7: Vegetable broth and soup

Strained vegetable broth (Day 6), then blended vegetable soup (Day 7).

Days 8 and 9: Raw salad and cooked vegetables

Small green salad at one meal. Steamed vegetables at one meal. Fruit at one meal. Juice at remaining intervals.

Days 10 and 11: Introducing protein

Small portions of legumes (100 g cooked) or two eggs. Continue vegetable base for all other meals.

Day 12 onward: Progressive normalisation

Gradually expand to a full whole-food diet as per Chapter 9 nutritional principles. Avoid red meat, dairy, refined carbohydrates, alcohol, and caffeine for a minimum of 14 days post-fast.

Mid-refeeding laboratory check: Mandatory at Day 3 and Day 7 of refeeding. Refeeding syndrome (a dangerous fall in phosphate, potassium, and magnesium as cells resume normal metabolism and take up these minerals rapidly) is a real risk after extended fasting, most significant in the first 72 hours of refeeding. Your physician will monitor for this. Do not miss these appointments.

APPENDIX E

ANNUAL FASTING CALENDAR TEMPLATES

E.1 Annual Fasting Programme Overview

The annual fasting calendar operationalises the three-tier maintenance programme of Chapter 9\. It is presented here in two formats: a strategic overview for programme planning, and a monthly template for day-to-day scheduling.

The Three-Tier Annual Structure

Tier 1: Weekly 24-Hour Fasting (52 times per year)

The foundation of the maintenance programme. One 24-hour fasting period every week, ideally on the same day each week for routine establishment. From dinner one evening to dinner the following evening is the most common and practical approach. This tier maintains ongoing insulin sensitivity, provides weekly autophagy activation, sustains the gut microbiome compositional changes established during extended fasting, and prevents the gradual metabolic drift that follows any single extended fast without ongoing dietary maintenance.

Tier 2: Monthly 36 to 48-Hour Fasting (12 times per year)

Once per month, extend the weekly 24-hour fast to 36 to 48 hours. This provides a deeper metabolic reset than the weekly fast, with more complete glycogen depletion, higher ketone production, and a more significant RAAS and sympathetic suppression cycle. In months when a Tier 3 extended fast is planned, the Tier 2 monthly fast is replaced by the Tier 3 event.

Tier 3: Extended Fasting, 3 to 14 Days (2 to 4 times per year depending on protocol assignment)

The extended fasts provide the deepest metabolic, inflammatory, and cardiovascular reset. Their frequency and duration are determined by the patient's clinical response, risk profile, and programme stage:

Patients in the active correction phase (first 12 months of the programme, or until blood pressure normalisation is achieved) should target two to four extended fasts per year, with durations progressing through the Rung 3 to 5 ladder of Chapter 8 as clinical response allows.

Patients in the maintenance phase (blood pressure normalised, HOMA-IR below 1.5, medications stopped or at minimum dose) may reduce to one or two extended fasts per year, typically aligned with the major seasonal transitions of the year.

E.2 Monthly Planning Template

Complete this template for each month of the programme. Review with your physician at each monthly contact.

MONTHLY FASTING CALENDAR

Month and Year: _____

Programme month number (1, 2, 3...): _____

Current programme phase: Active correction / Maintenance

Current blood pressure average (last 2 weeks): ___/___

Current medications: _____

Weekly 24-Hour Fasts Planned:

Week	Fast Day (day of week)	Fast Period (from/to)	Completed?	Notes
Week 1		Dinner ___ to Dinner ___	Yes / No	
Week 2		Dinner ___ to Dinner ___	Yes / No	
Week 3		Dinner ___ to Dinner ___	Yes / No	
Week 4		Dinner ___ to Dinner ___	Yes / No	

Monthly 36 to 48-Hour Fast (if not a Tier 3 month):

Planned dates: ___ to ___

Duration target: 36 hours / 48 hours

Completed: Yes / No

Duration actually completed: ___

Notes: _____

Extended Fast (Tier 3, if applicable this month):

Planned start date: _____

Planned end date: _____

Target duration: ___ days

Pre-fast physician assessment completed: Yes / No

Pre-fast laboratory panel completed: Yes / No

Physician contact established: Yes / No

Refeeding protocol card provided: Yes / No

Post-fast:

Actual duration completed: ___ days

Reason for any difference from planned: _____

Post-fast laboratory: Completed ___ / Results reviewed ___

Medication adjustment post-fast: _____

Monthly Blood Pressure Summary:

Date	Morning BP	Evening BP	Notes

Monthly average BP: ___/___

Lowest reading this month: ___/___

Highest reading this month: ___/___

E.3 Suggested Annual Calendar by Programme Phase

Phase 1: Active Correction (Months 1 to 6\)

Month	Weekly Fasts	Monthly Fast	Extended Fast
1	x4 (24-hour each)	One 36-hour fast	None (build foundations first)
2	x4 (24-hour each)	One 48-hour fast	None
3	x4 (24-hour each)	One 48-hour fast	One 3-day fast (Rung 3\)
4	x4 (24-hour each)	None (extended fast month)	One 4-day fast (Rung 3\)
5	x4 (24-hour each)	One 48-hour fast	None
6	x4 (24-hour each)	None (extended fast month)	One 5-day fast (Rung 4\)

Phase 2: Active Correction (Months 7 to 12\)

Month	Weekly Fasts	Monthly Fast	Extended Fast
7	x4 (24-hour each)	One 48-hour fast	None
8	x4 (24-hour each)	None (extended fast month)	One 5-day fast (Rung 4\)

Month	Weekly Fasts	Monthly Fast	Extended Fast
9	x4 (24-hour each)	One 48-hour fast	None
10	x4 (24-hour each)	None (extended fast month)	One 7-day fast (Rung 5\)
11	x4 (24-hour each)	One 48-hour fast	None
12	x4 (24-hour each)	None (extended fast month)	One 7-day fast (Rung 5, annual review)

Phase 3: Maintenance (Year 2 and Beyond, Blood Pressure Normalised)

Quarter	Weekly Fasts	Monthly Fasts	Extended Fasts
Q1	x12 (24-hour)	Two 48-hour fasts	Optional: One 3-5 day fast
Q2	x13 (24-hour)	Two 48-hour fasts	None
Q3	x13 (24-hour)	Two 48-hour fasts	Optional: One 3-5 day fast
Q4	x14 (24-hour)	Two 48-hour fasts	None

Maintenance extended fasts may be reduced in frequency or eliminated if blood pressure, HOMA-IR, and metabolic markers remain consistently within target ranges on weekly and monthly fasting alone. This assessment is made jointly with the supervising physician at each 6-monthly review.

APPENDIX F

LABORATORY REFERENCE RANGES AND INTERPRETATION GUIDE

F.1 Core Laboratory Panel: Reference Ranges and Clinical Interpretation

This appendix provides the supervising physician with the reference ranges used throughout the book, the clinical interpretation framework for each test in the context of the fasting hypertension programme, and guidance on when abnormal results require action versus observation.

Glucose and Insulin Metabolism

Fasting glucose (mmol/L)

Optimal: 3.9 to 5.0

Acceptable: 5.0 to 5.5

Prediabetes range: 5.6 to 6.9

Diabetes: 7.0 and above

In the fasting programme context: A fall in fasting glucose from prediabetes range to optimal range over the course of 6 to 12 months of the programme is one of the primary markers of metabolic correction. A fall in fasting glucose during an extended fast to below 3.9 mmol/L requires physician assessment; below 3.5 mmol/L requires breaking the fast.

Fasting insulin (pmol/L)

Optimal: below 43 pmol/L (approximately 6 µU/mL)

Acceptable: 43 to 60 pmol/L

Elevated (indicating insulin resistance): above 60 pmol/L

Significantly elevated: above 90 pmol/L

In the fasting programme context: Fasting insulin reduction is the primary mechanistic target of the programme. A fall from elevated baseline (commonly 90 to 180 pmol/L in the metabolically hypertensive patient) to optimal range confirms that the root driver of hypertension is being corrected. Measure at baseline and at each 6-monthly review.

HOMA-IR (Homeostatic Model Assessment of Insulin Resistance)

Calculated as: fasting glucose (mmol/L) x fasting insulin (µU/mL) divided by 22.5

Optimal: below 1.5

Acceptable: 1.5 to 2.5

Insulin resistance: above 2.5

Significant insulin resistance: above 4.0

In the fasting programme context: HOMA-IR is the single most informative metabolic marker for tracking the programme's primary objective. A reduction to below 1.5 confirms that the physiological root cause of primary hypertension is resolved. Permanent normalisation requires sustained HOMA-IR below 1.5 for 12 consecutive months.

HbA1c (%)

Optimal: below 5.4%

Acceptable (non-diabetic): 5.4 to 5.6%

Prediabetes: 5.7 to 6.4%

Diabetes: 6.5% and above

In the fasting programme context: HbA1c reflects average glucose control over the preceding 3 months. It changes more slowly than fasting glucose or HOMA-IR and is most informative at 6-monthly intervals.

Lipid Panel and TG:HDL Ratio

Triglycerides (mmol/L)

Optimal: below 1.1

Acceptable: 1.1 to 1.7

Borderline elevated: 1.7 to 5.6

Severely elevated (hypertriglyceridaemia): above 5.6

In the fasting programme context: Triglycerides are the lipid fraction most directly driven by insulin and dietary carbohydrate. They are among the first markers to improve with fasting, often falling 30 to 50% within the first extended fast. A baseline triglyceride above 1.7 mmol/L in a non-diabetic patient is strong evidence of underlying hyperinsulinaemia.

HDL cholesterol (mmol/L)

Optimal (male): above 1.3

Acceptable (male): 1.0 to 1.3

Low (male): below 1.0

Optimal (female): above 1.5

Acceptable (female): 1.2 to 1.5

Low (female): below 1.2

In the fasting programme context: HDL cholesterol typically rises gradually over 3 to 6 months of the programme as insulin resistance resolves and triglycerides fall. It is a slower-moving marker than triglycerides.

TG:HDL ratio

Optimal: below 1.0

Acceptable: 1.0 to 1.5

Elevated (suggests small dense LDL predominance and insulin resistance): above 1.5

High (strong surrogate marker of insulin resistance): above 2.5

In the fasting programme context: The TG:HDL ratio is the single most clinically useful lipid-based surrogate marker for insulin resistance. It is more informative than total LDL cholesterol in the metabolically hypertensive patient. Normalisation of the TG:HDL ratio to below 1.5 is a programme milestone that confirms meaningful metabolic improvement.

LDL cholesterol (mmol/L)

Optimal (primary prevention, low cardiovascular risk): below 3.0

Optimal (primary prevention, high cardiovascular risk): below 2.6

Optimal (secondary prevention, established cardiovascular disease): below 1.8

In the fasting programme context: LDL cholesterol may paradoxically rise transiently in the first 1 to 3 months of a fasting programme due to mobilisation of stored fats and improvement in LDL particle size distribution (the shift from small dense to large buoyant LDL particles, which is a favourable change but may transiently increase measured LDL). This transient rise should not be treated without further assessment of LDL particle size. By 6 months, LDL typically stabilises or falls in most patients.

Renal Function

Creatinine (µmol/L)

Male reference range: 60 to 110 µmol/L

Female reference range: 45 to 90 µmol/L

In the fasting programme context: Creatinine rises transiently during extended fasting due to mild dehydration and increased protein catabolism. A rise of up to 20% above baseline during an extended fast is expected and does not require breaking the fast. A rise above 30% from baseline, particularly if accompanied by oliguria (reduced urine output) or a fall in eGFR below 30 mL/min/1.73m², requires immediate physician assessment.

eGFR (mL/min/1.73m²)

Normal: above 60

Stage 3a CKD: 45 to 59

Stage 3b CKD: 30 to 44

Stage 4 CKD: 15 to 29

Stage 5 CKD: below 15

In the fasting programme context: Improvement in eGFR over 12 to 24 months of the programme is one of the most clinically significant long-term outcomes, reflecting reduced intraglomerular hypertension as insulin and RAAS activity normalise. A sustained improvement of 5 or more mL/min/1.73m² from baseline at 12 months constitutes clinically meaningful renal protection.

Urea (mmol/L)

Reference range: 2.5 to 7.8 mmol/L

In the fasting programme context: Urea rises during extended fasting due to increased protein catabolism (the body breaking down protein for gluconeogenesis, the production of glucose from non-glucose sources). A rise to twice the baseline value during extended fasting is expected and normal. Values above three times baseline require assessment of renal function.

Uric acid (mmol/L)

Male reference range: 0.25 to 0.48 mmol/L

Female reference range: 0.15 to 0.35 mmol/L (pre-menopausal), 0.20 to 0.42 mmol/L (post-menopausal)

In the fasting programme context: Uric acid rises transiently in the first 2 to 4 days of extended fasting due to reduced renal excretion of urate as the kidneys prioritise ketone excretion. In patients with a history of gout, this transient rise can precipitate an acute gout attack. Patients with a history of gout should have uric acid measured at baseline and at Day 2 to 3 of any extended fast, with a prophylactic colchicine or allopurinol protocol in place for those with baseline uric acid above 0.42 mmol/L.

Electrolytes

Sodium (mmol/L)

Reference range: 136 to 145 mmol/L

Critical low: below 125 mmol/L

Critical high: above 155 mmol/L

In the fasting programme context: Sodium typically falls modestly in the first 2 to 3 days of extended fasting as the kidneys excrete the sodium that insulin was retaining. A fall to 132 to 135 mmol/L is common and does not require treatment. A fall below 130 mmol/L requires physician assessment. A fall below 125 mmol/L requires breaking the fast and urgent medical management. Hyponatraemia below 120 mmol/L is a medical emergency.

Potassium (mmol/L)

Reference range: 3.5 to 5.0 mmol/L

Critical low: below 3.0 mmol/L

Critical high: above 6.0 mmol/L

In the fasting programme context: Potassium is the electrolyte of greatest concern during extended fasting, particularly in patients on diuretics (which reduce potassium), ACE inhibitors or ARBs (which can raise potassium), or digoxin (where hypokalaemia dramatically increases toxicity risk). Monitor at baseline, at Day 3 to 4 of any extended fast, and immediately if muscle cramps, palpitations, or weakness develop. A value below 3.0 mmol/L requires immediate physician assessment and directed supplementation before continuation of the fast. A value below 2.5 mmol/L requires breaking the fast and urgent electrolyte replacement.

Magnesium (mmol/L)

Reference range: 0.7 to 1.0 mmol/L

Deficient: below 0.7 mmol/L

Critical low: below 0.5 mmol/L

In the fasting programme context: Magnesium is consistently underappreciated in clinical practice despite its role in over 300 enzymatic reactions, including those governing smooth muscle tone, cardiac conduction, and insulin signalling. Deficiency is common at baseline in hypertensive patients (magnesium excretion is increased by insulin resistance, stress, diuretic use, and a processed-food diet low in green vegetables and nuts). Baseline deficiency should be corrected before extended fasting. During fasting, magnesium may fall modestly; values below 0.6 mmol/L during an extended fast warrant physician-directed supplementation with magnesium glycinate or magnesium citrate (forms with better bioavailability than magnesium oxide).

Phosphate (mmol/L)

Reference range: 0.8 to 1.5 mmol/L

Critical low: below 0.5 mmol/L (refeeding syndrome threshold)

In the fasting programme context: Phosphate is the refeeding syndrome marker of primary concern after extended fasting. During fasting, phosphate remains relatively stable in the bloodstream (as the breakdown of body tissues releases intracellular phosphate into circulation). With refeeding, insulin rises, cells take up glucose rapidly, and phosphate is driven back into cells along with glucose. If the refeeding is too aggressive (too much carbohydrate too quickly), serum phosphate can fall precipitously to dangerous levels within 24 to 72 hours of refeeding, producing muscle weakness, cardiac arrhythmia, respiratory failure, and haemolytic anaemia. This is refeeding syndrome. The graduated refeeding protocol of Appendix D is specifically designed to prevent it. Phosphate must be measured at Day 3 to 5 of refeeding after any fast of 5 days or more.

Inflammatory Markers

hsCRP (high-sensitivity C-reactive protein, mg/L)

Optimal cardiovascular risk: below 1.0

Average cardiovascular risk: 1.0 to 3.0

High cardiovascular risk: above 3.0

Acute inflammation (not useful for cardiovascular risk assessment): above 10

In the fasting programme context: hsCRP is the most accessible and clinically validated circulating marker of vascular and systemic inflammation. Baseline elevation above 3.0 mg/L in the absence of acute illness reflects the chronic inflammatory state driven by hyperinsulinaemia, visceral adiposity, and gut dysbiosis. Reduction to below 1.0 mg/L over the course of the programme confirms resolution of the inflammatory burden driving endothelial dysfunction and accelerated atherosclerosis.

Liver Function

ALT (Alanine aminotransferase, IU/L)

Reference range: below 40 IU/L (male), below 35 IU/L (female)

AST (Aspartate aminotransferase, IU/L)

Reference range: below 40 IU/L

In the fasting programme context: ALT and AST may rise transiently in the first week of extended fasting due to mobilisation of hepatic fat (fatty liver disease is common in the metabolically hypertensive patient, and fat mobilisation from the liver during ketosis temporarily elevates liver enzymes). A rise to two times the upper limit of normal during an extended fast is acceptable and does not require breaking the fast. A rise above three times the upper limit of normal requires physician assessment. Values should return to baseline or below by 4 to 6 weeks post-fast.

APPENDIX G

MEDICATION QUICK REFERENCE

G.1 Antihypertensive Medications: Fast-Reference Guide for Supervising Physicians

This reference provides a summary of the key clinical considerations for each major antihypertensive drug class during the fasting programme. It is a quick-access tool, not a substitute for the detailed guidance of Appendix A and Chapters 7 and 8\.

ACE Inhibitors (Ramipril, Lisinopril, Perindopril, Enalapril)

Mechanism: Block conversion of angiotensin I to angiotensin II, reducing RAAS-mediated vasoconstriction and aldosterone-driven sodium retention.

During fasting: Dose reduce by 50% at initiation of any fast beyond 48 hours. As fasting independently suppresses the RAAS, the combined effect of ACE inhibition and fasting-mediated RAAS suppression can produce excessive blood pressure reduction. Monitor blood pressure daily. If systolic falls below 110 mmHg, suspend. If systolic falls below 100 mmHg, break fast and seek urgent assessment.

Key risks during fasting: Hypotension, particularly orthostatic. Hyperkalaemia (potassium rise) if combined with potassium-sparing agents or significant dehydration. Acute kidney injury risk if volume-depleted (ensure adequate water intake throughout fast).

Post-fast: Do not automatically reinstate at pre-fast dose. Reassess blood pressure at Day 3 of refeeding and titrate dose to maintain systolic 110 to 130 mmHg.

Angiotensin II Receptor Blockers (Losartan, Valsartan, Irbesartan, Candesartan, Olmesartan, Telmisartan)

Mechanism: Block the angiotensin II receptor, producing the same downstream effect as ACE inhibitors without the ACE inhibitor cough.

During fasting: Same protocol as ACE inhibitors: 50% dose reduction at fast initiation beyond 48 hours, with monitoring and suspension thresholds as above.

Key risks during fasting: As per ACE inhibitors. Telmisartan has the longest half-life of the ARB class (approximately 24 hours); its effects persist longer after dose reduction or suspension.

Post-fast: As per ACE inhibitors.

Calcium Channel Blockers (Amlodipine, Lercanidipine, Felodipine, Nifedipine)

Mechanism: Block calcium entry into vascular smooth muscle cells and cardiac cells, producing vasodilation and, in some agents, reduced heart rate.

During fasting: Reduce by 50% at fast initiation. Orthostatic risk is lower than with RAAS agents but present. Amlodipine has a very long half-life (30 to 50 hours), meaning that dose reduction produces a gradual rather than rapid effect; this should be factored into timing.

Key risks during fasting: Peripheral oedema (pre-existing oedema from amlodipine will resolve with fasting-mediated diuresis; this is beneficial rather than concerning). Reflex tachycardia in some patients; monitor heart rate.

Post-fast: Reassess. Many patients on CCBs for blood pressure control will find blood pressure adequately maintained post-fast without reinstatement.

Beta-Blockers (Bisoprolol, Metoprolol, Atenolol, Carvedilol, Nebivolol)

Mechanism: Block adrenergic receptors, reducing heart rate, cardiac output, and (for non-selective agents) some peripheral vasoconstriction. Also suppress renin release from the kidney.

During fasting: NEVER abruptly discontinue. Reduce by 25% at fast initiation if blood pressure falls significantly (systolic below 115 mmHg). Further gradual taper only if blood pressure continues to fall and remains below 115 mmHg. Abrupt beta-blocker withdrawal produces rebound tachycardia, hypertension, and in patients with coronary artery disease, the risk of acute coronary syndrome is real and must not be dismissed.

Key risks during fasting: Masking of hypoglycaemic tachycardia in diabetic patients (beta-blockers block the compensatory heart rate rise that normally accompanies hypoglycaemia, reducing the patient's ability to detect low blood sugar). More frequent glucose monitoring in diabetic patients on beta-blockers during fasting. Exercise intolerance (patients on beta-blockers will have reduced capacity for physical activity during fasting; this is expected and should not prompt attempting to compensate with greater activity).

Post-fast: Maintain during refeeding until blood pressure is assessed at Day 3 to 5\. Taper further if blood pressure remains well-controlled without other agents.

Diuretics (Furosemide, Bumetanide, Hydrochlorothiazide, Chlorthalidone, Indapamide, Spironolactone)

Mechanism: Various mechanisms of sodium and water excretion by the kidney. Loop diuretics (furosemide, bumetanide) are the most potent. Thiazides and thiazide-like agents provide more moderate diuresis. Spironolactone is a mineralocorticoid receptor antagonist that reduces aldosterone-mediated sodium retention.

During fasting: Loop and thiazide diuretics must be suspended before extended fasting begins. The fasting-mediated natriuresis (sodium and water excretion) is substantial and, combined with pharmacological diuresis, produces a volume depletion that risks acute kidney injury, electrolyte disturbance, and haemodynamic collapse.

Spironolactone: may be continued at reduced dose in some patients under close electrolyte monitoring (it reduces aldosterone-driven sodium retention but also reduces potassium excretion, which may help offset the potassium losses of other fasting mechanisms). Discuss individually with physician.

Key risks during fasting (if not suspended): Severe hypokalaemia, hyponatraemia, hypovolaemia (low blood volume), acute kidney injury.

Post-fast: Do not automatically reinstate diuretics post-fast. The fasting programme has achieved its diuretic effect through metabolic means; pharmacological diuresis may no longer be required. Reassess sodium, potassium, and blood pressure at Day 3 of refeeding before any reinstatement decision.

Metformin

Mechanism: Reduces hepatic glucose production and improves insulin sensitivity.

During fasting: Suspend 24 to 48 hours before any fast beyond 48 hours, and resume only when normal eating has been established for 48 hours. The mechanism of metformin-associated lactic acidosis (a rare but serious complication) is potentiated by fasting-related reduction in renal perfusion and hepatic lactate clearance. The risk is low in patients with normal renal function but is not zero, and the precaution is simple to implement.

Post-fast: Resume when full normal eating has been re-established. Consider whether metformin is still required: the programme's improvement in insulin sensitivity may render metformin redundant in some patients.

SGLT2 Inhibitors (Dapagliflozin, Empagliflozin, Canagliflozin)

Mechanism: Block renal glucose reabsorption, causing glucose excretion in the urine, reducing blood glucose, and producing a mild diuretic and natriuretic effect.

During fasting: Suspend minimum 72 hours before any extended fast. The risk of euglycaemic diabetic ketoacidosis (a form of DKA that occurs at normal or near-normal blood glucose levels, making it easy to miss) is significantly elevated in patients on SGLT2 inhibitors who are fasting. Fasting stimulates ketone production; SGLT2 inhibitors simultaneously reduce the renal threshold for DKA development. The combination has produced DKA fatalities in the literature and the 72-hour pre-fast suspension is mandatory.

Post-fast: Resume only after full normal eating is re-established and blood glucose and ketone levels have been confirmed within normal range.

APPENDIX H

NUTRITIONAL FRAMEWORK REFERENCE

H.1 Nutritional Principles for the Post-Fast and Inter-Fast Period

The nutritional framework of the post-fast period is not a diet in the conventional sense. It is not a list of forbidden foods and permitted foods, a calorie target, or a macronutrient formula. It is a set of principles that, when applied consistently, maintain the metabolic improvements achieved through fasting and prevent the progressive return of the insulin resistance that drove the hypertension in the first place.

Principle 1: Insulin Management is the Primary Nutritional Goal

Every food choice in the inter-fast period should be evaluated primarily by its insulin response, not its calorie content or its conventional nutritional label. The foods that chronically elevate insulin are refined carbohydrates (white bread, white rice, pasta, biscuits, cakes, pastries), added sugars (in all forms including fruit juice, honey, maple syrup, and the dozens of sugar synonyms in processed food ingredient lists), and ultra-processed foods (any food produced industrially with more than 5 ingredients, most of which are unfamiliar to a domestic kitchen).

These foods are not restricted because of their calorie content but because of their insulin-stimulating effect. A food that produces a large, rapid insulin spike followed by a rapid glucose fall recreates the chronic hyperinsulinaemic state that the fasting programme is designed to resolve.

The foods that do not chronically elevate insulin are those that have always formed the human dietary foundation before industrialisation: whole vegetables, whole fruits (consumed whole, not juiced), legumes, whole grains consumed as intact grains rather than flour, nuts, seeds, fish, eggs, and unprocessed animal foods in moderate quantities.

Principle 2: Time-Restricted Eating as a Daily Fasting Practice

The compression of all daily eating into a window of 6 to 10 hours, with no caloric consumption outside that window, is the daily application of the circadian biology and metabolic principles that extended fasting demonstrates in concentrated form. The Sutton 2019 eTRE (early time-restricted eating) trial demonstrated an 11 mmHg systolic reduction on a 6-hour eating window aligned to the morning (approximately 7am to 1pm or 8am to 2pm) without any change in calorie intake. Earlier eating windows (breakfast and lunch as the day's two or three meals, with no evening meal) produce the most significant circadian and metabolic benefits.

A practical target for most patients in the inter-fast period is a 16:8 structure: 16 hours of fasting (including sleep) and 8 hours of eating, with the eating window aligned to the earlier part of the day wherever practical. This means the last meal of the day is taken no later than 7 to 8pm, and breakfast is not taken before 11am to 12pm, or alternatively breakfast is the day's first meal and the last meal is consumed by 3 to 4pm.

Principle 3: Fibre and the Gut Microbiome

The gut microbiome improvements achieved during extended fasting, particularly the increases in Akkermansia muciniphila and Lactobacillus species, and the increases in short-chain fatty acid production, are maintained in the inter-fast period by a diet high in diverse plant fibres. Different species of gut bacteria preferentially ferment different types of fibre; dietary diversity supports microbiome diversity, which in turn supports the endothelial health and blood pressure-regulating functions of the SCFA-producing microbial community.

Target: a minimum of 30 different plant species per week (this includes vegetables, fruits, whole grains, legumes, nuts, seeds, and herbs and spices). This number, derived from the American Gut Project and the work of Professor Tim Spector, has been associated with significantly greater gut microbiome diversity in population studies.

Principle 4: Protein Adequacy for Muscle Preservation

Fasting-mediated growth hormone elevation and the autophagy-driven recycling of damaged muscle proteins preserve lean mass during extended fasting better than conventional caloric restriction. In the inter-fast period, adequate protein intake ensures that muscle protein synthesis can proceed normally.

Target: 1.2 to 1.6 g of protein per kilogram of body weight per day, from predominantly whole-food sources (fish, eggs, legumes, nuts, seeds, and moderate quantities of unprocessed animal protein if consumed). This target is particularly important in patients over 60 years, in whom sarcopenia (age-related muscle loss) is a concurrent clinical concern alongside blood pressure management.

Principle 5: Sodium Reduction as a Permanent Dietary Feature

The fasting programme achieves a profound de-salination of the body's tissues during extended fasting, as documented by Bragg's urine specimens and by the clinical observations of every major supervised fasting practitioner. This benefit is maintained by a permanently reduced dietary sodium intake in the inter-fast period.

Target: dietary sodium below 1500 mg (1.5 g) per day, achieved not through laborious counting but through the practical elimination of the primary sources of dietary sodium in the modern diet: processed foods, restaurant meals, cured and smoked meats, canned soups and vegetables with added salt, commercial sauces and condiments, and the salt shaker at the table.

When this sodium target is combined with adequate potassium intake from a vegetable-rich whole-food diet, the potassium-to-sodium ratio in the diet shifts toward the physiologically favourable range that was the human dietary norm before industrialisation, and that is independently associated with lower blood pressure and reduced cardiovascular risk.

H.2 Quick Reference: Foods to Emphasise and Limit

Emphasise

Vegetables: All non-starchy vegetables in unlimited quantities. Dark leafy greens (spinach, kale, chard, rocket) provide folate, magnesium, and nitrates (dietary nitrates are converted by oral bacteria to nitric oxide, the endothelial vasodilator whose impaired production is central to hypertensive vascular disease). Cruciferous vegetables (broccoli, cauliflower, Brussels sprouts, cabbage) provide sulforaphane and fibre supporting microbiome diversity. Alliums (garlic, onion, leeks, chives) provide organosulphur compounds with independently documented blood pressure-reducing effects.

Whole fruits: One to two portions daily (not juiced). Berries (blueberries, strawberries, raspberries) have the most favourable insulin response and the highest polyphenol density. Citrus fruits provide flavonoids and vitamin C supporting endothelial health.

Legumes: Lentils, chickpeas, black beans, kidney beans, and all other legumes. Among the most beneficial foods for blood pressure and metabolic health: low glycaemic index, high fibre, high potassium, high magnesium.

Whole grains: Oats, brown rice, quinoa, barley, and buckwheat consumed as intact whole grains (not as flour-based products). The fibre matrix of intact grains significantly slows glucose absorption and insulin response compared to the same grain consumed as flour.

Fish: Fatty fish (salmon, sardines, mackerel, herring, anchovies) twice or more weekly. The long-chain omega-3 fatty acids EPA and DHA reduce triglycerides, have anti-inflammatory effects, and reduce cardiovascular mortality in population studies.

Nuts and seeds: A small handful (30 g) daily. Walnuts provide ALA (a plant omega-3 precursor) and polyphenols. Flaxseeds and chia seeds provide the highest plant-based ALA content. Almonds and cashews provide magnesium and arginine, a precursor to nitric oxide. Brazil nuts provide selenium. Pumpkin seeds provide zinc and magnesium.

Olive oil: Extra-virgin, cold-pressed olive oil as the primary cooking fat. The polyphenol content of high-quality extra-virgin olive oil (absent from refined olive oil and most seed oils) provides anti-inflammatory and endothelial-protective effects independent of its fatty acid profile.

Herbs and spices: Garlic (raw or lightly cooked), ginger, turmeric, cinnamon, and chilli (cayenne) all have documented or plausible blood pressure-relevant effects through anti-inflammatory, vasodilatory, or insulin-sensitising mechanisms.

Limit

Refined carbohydrates: White bread, white rice, pasta, pastry, biscuits, cakes, crackers, breakfast cereals, and any grain product made from refined (white) flour. These foods produce the most rapid and large insulin responses of any food category.

Added sugar and sweetened beverages: Sugar in all forms added to food or beverages, including fruit juice (which delivers the sugar of fruit without its fibre, producing a rapid insulin response similar to refined carbohydrate), commercially sweetened yoghurts, sauces, condiments, and all soft drinks including those labelled "natural" or "pressed."

Ultra-processed foods: If the food was manufactured industrially, contains more than five ingredients, includes ingredients a domestic cook would not have at home (stabilisers, emulsifiers, artificial flavours, preservatives, colour additives, modified starches), or is designed to override normal satiety signals (highly palatable combinations of refined carbohydrate, fat, and salt are specifically engineered to promote overconsumption), it should be limited or avoided.

Processed meat: Bacon, sausage, ham, salami, hot dogs, deli meats. The salt content, nitrate preservatives, and saturated fat profile of processed meat make it the food category most consistently associated with cardiovascular risk in large population studies.

Alcohol: Reduces blood pressure medication efficacy, disrupts sleep architecture, impairs liver glycogen regulation, stimulates insulin secretion, and is a source of empty calories. Moderate reduction is helpful; cessation is ideal, particularly in the active correction phase of the programme.

APPENDIX I

RECOMMENDED READING AND RESEARCH

I.1 Primary Clinical and Scientific References

For the clinician who wishes to go deeper into the evidence base underlying each chapter of this book.

On the Physiology and History of Therapeutic Fasting:

DeVries, A. (1963). Therapeutic Fasting. Chandler Book Company, Los Angeles. The most systematic and scientifically rigorous early synthesis of the supervised fasting clinical literature. Its chapter on the safety and physiological reactions to fasting remains clinically relevant.

Bragg, P.C. and Bragg, P. The Miracle of Fasting. Bragg Health Crusades, Santa Barbara. The popular presentation of the supervised fasting tradition. Read alongside DeVries for the complementary relationship between popular and clinical accounts of the same practice.

Shelton, H.M. The Hygienic System, Volume III: Fasting. Dr Shelton's Health School, San Antonio, 1934\. The most comprehensive clinical fasting manual ever written, based on Shelton's supervision of over 30,000 individual fasts.

On the Clinical Evidence for Fasting in Hypertension:

Goldhamer, A., Lisle, D., Parpia, B., Anderson, S.V., and Campbell, T.C. (2001). Medically supervised water-only fasting in the treatment of hypertension. Journal of Manipulative and Physiological Therapeutics, 24(5), 335-339.

Goldhamer, A.C., Lisle, D.J., Sultana, P., Anderson, S.V., Parpia, B., Hughes, B., and Campbell, T.C. (2002). Medically supervised water-only fasting in the treatment of borderline hypertension. Journal of Alternative and Complementary Medicine, 8(5), 643-650.

On Autophagy:

Ohsumi, Y. Nobel Lecture, December 7, 2016\. Autophagy: An intracellular recycling system. The Nobel Committee for Physiology or Medicine, Karolinska Institute, Stockholm. Available at nobelprize.org.

Levine, B. and Kroemer, G. (2008). Autophagy in the pathogenesis of disease. Cell, 132(1), 27-42.

On Insulin Resistance and Hypertension:

Reaven, G.M. (1988). Role of insulin resistance in human disease. Diabetes, 37(12), 1595-1607. The original description of Syndrome X (metabolic syndrome) and the first systematic articulation of the relationship between insulin resistance and cardiovascular disease.

DeFronzo, R.A. and Ferrannini, E. (1991). Insulin resistance: a multifaceted syndrome responsible for NIDDM, obesity, hypertension, dyslipidemia, and atherosclerotic cardiovascular disease. Diabetes Care, 14(3), 173-194.

On the RAAS and Fasting:

Atlas, S.A. (2007). The renin-angiotensin aldosterone system: pathophysiological role and pharmacologic inhibition. Journal of Managed Care and Specialty Pharmacy, 13(8), S9-S20.

On Inflammation, Endothelium and BHB:

Youm, Y.H. et al. (2015). The ketone metabolite β-hydroxybutyrate blocks NLRP3 inflammasome-mediated inflammatory disease. Nature Medicine, 21(3), 263-269.

Zhu, X.H. et al. (2015). Beta-hydroxybutyrate-associated enhanced endothelial nitric oxide synthase signalling. Journal of Cardiovascular Pharmacology, 65(6), 568-574.

On TMAO and Cardiovascular Risk:

Wang, Z. et al. (2011). Gut flora metabolism of phosphatidylcholine promotes cardiovascular disease. Nature, 472(7341), 57-63.

Tang, W.H.W. et al. (2013). Intestinal microbial metabolism of phosphatidylcholine and cardiovascular risk. New England Journal of Medicine, 368(17), 1575-1584.

On Time-Restricted Eating and Blood Pressure:

Sutton, E.F. et al. (2019). Early time-restricted feeding improves insulin sensitivity, blood pressure, and oxidative stress even without weight loss in men with prediabetes. Cell Metabolism, 27(6), 1212-1221.

On Fasting and Stem Cell Regeneration:

Cheng, C.W. et al. (2014). Prolonged fasting reduces IGF-1/PKA to promote hematopoietic stem cell-based regeneration and reverse immunosuppression. Cell Stem Cell, 14(6), 810-823.

On BDNF and Fasting:

Sleiman, S.F. et al. (2016). Exercise promotes the expression of brain derived neurotrophic factor (BDNF) through the action of the ketone body β-hydroxybutyrate. eLife (subsequently published in Cell Reports, 2016).

On Caloric Restriction, mTOR and Longevity:

Harrison, D.E. et al. (2009). Rapamycin fed late in life extends lifespan in genetically heterogeneous mice. Nature, 460(7253), 392-395.

Kenyon, C. et al. (1993). A C. elegans mutant that lives twice as long as wild type. Nature, 366(6454), 461-464.

On Growth Hormone During Fasting:

Hartman, M.L. et al. (1992). Augmented growth hormone (GH) secretory burst frequency and amplitude mediate enhanced GH secretion during a two-day fast in normal men. Journal of Clinical Endocrinology and Metabolism, 74(4), 757-765.

I.2 For the Patient: Accessible Further Reading

Jamnadas, P. (various dates). The Fasting Cure and related lectures. Available at pranavjamnadas.com and via YouTube. Dr. Jamnadas's own patient-facing explanations of the metabolic mechanisms of fasting, delivered in his characteristic accessible style.

Pelz, M. (2022). Fast Like a Girl. Hay House. A practical and accessible guide to fasting for women, with particular attention to hormonal considerations. Recommended supplementary reading for female patients in the programme.

Fung, J. (2016). The Obesity Code. Greystone Books. The most accessible physician-authored explanation of the role of insulin in obesity and metabolic disease. Highly recommended for patients who want to understand the metabolic science behind the programme.

Fung, J. (2016). The Complete Guide to Fasting. Victory Belt Publishing. A practical guide to fasting types, protocols, and troubleshooting. Recommended for patients who want greater practical detail than this book's protocol chapters provide.

Attia, P. (2023). Outlive: The Science and Art of Longevity. Harmony Books. An evidence-based guide to longevity medicine from a physician who has written extensively and accessibly about insulin resistance, metabolic health, and cardiovascular risk.

APPENDIX J

GLOSSARY OF CLINICAL AND SCIENTIFIC TERMS

Every technical term used in this book is defined here in plain language. If a term is unfamiliar when encountered in the text, look it up here first.

ACE inhibitor (Angiotensin-Converting Enzyme inhibitor): a class of blood pressure medication that blocks an enzyme called ACE, preventing the production of a hormone called angiotensin II that constricts blood vessels and promotes sodium retention. Examples include ramipril, lisinopril, and perindopril.

Aldosterone: a hormone produced by the adrenal glands (small glands that sit on top of the kidneys) that instructs the kidneys to retain sodium and water and excrete potassium. Elevated aldosterone is one of the mechanisms by which insulin resistance raises blood pressure.

Angiotensin II: a potent vasoconstrictor (blood vessel constricting hormone) that is the primary active hormone of the renin-angiotensin-aldosterone system (RAAS). It raises blood pressure by narrowing blood vessels and stimulating aldosterone release. Blocked by ACE inhibitors and ARBs.

ARB (Angiotensin II Receptor Blocker): a class of blood pressure medication that blocks the receptor through which angiotensin II acts. Different mechanism from ACE inhibitors, same downstream effect. Examples include losartan, valsartan, and candesartan.

ASCVD risk score (Atherosclerotic Cardiovascular Disease risk score): a calculation that estimates a patient's percentage risk of suffering a major cardiovascular event (heart attack or stroke) in the next 10 years, based on age, sex, blood pressure, cholesterol levels, diabetes status, and smoking history.

Atherosclerosis: the progressive accumulation of cholesterol, immune cells, fibrous tissue, and calcium within the walls of arteries, producing plaques that narrow the artery and can rupture to cause heart attacks and strokes. Sometimes called "hardening of the arteries."

Autophagy (pronounced au-TOF-uh-jee): from the Greek for "self-eating." The cellular process by which cells identify damaged or unnecessary components, enclose them in a membrane structure called an autophagosome, and break them down for recycling. Activated during fasting and suppressed by insulin. The subject of the 2016 Nobel Prize in Physiology or Medicine awarded to Yoshinori Ohsumi.

BDNF (Brain-Derived Neurotrophic Factor): a protein that promotes the growth, survival, and maintenance of neurons (brain cells). Elevated during fasting (particularly by beta-hydroxybutyrate, the primary ketone body) and by exercise. Important for cognitive function, memory, and protection against neurodegenerative disease.

Beta-blocker: a class of medication that blocks the effects of adrenaline and other stress hormones on the heart and blood vessels, reducing heart rate and blood pressure. Examples include bisoprolol, metoprolol, and carvedilol. Must never be abruptly stopped.

Beta-hydroxybutyrate (BHB): the primary ketone body produced by the liver from fatty acids during fasting or very low carbohydrate intake. Used as fuel by the brain, heart, and muscles in the absence of glucose. Also functions as a signalling molecule with anti-inflammatory effects, including inhibition of the NLRP3 inflammasome.

Calcium channel blocker: a class of blood pressure medication that prevents calcium from entering the muscle cells of blood vessel walls, causing them to relax and the vessels to widen. Examples include amlodipine, lercanidipine, and nifedipine.

Cardiac output: the volume of blood the heart pumps per minute. Blood pressure equals cardiac output multiplied by total peripheral resistance (the resistance of the blood vessels to blood flow).

Catecholamines: a group of stress hormones including adrenaline (epinephrine) and noradrenaline (norepinephrine), released by the adrenal glands and sympathetic nerve endings. They increase heart rate, constrict blood vessels, and raise blood pressure. Chronically elevated in hyperinsulinaemia due to sympathetic nervous system overactivation.

CGM (Continuous Glucose Monitor): a small device worn on the skin that measures blood glucose levels every few minutes through a sensor inserted just below the skin surface, transmitting readings to a smartphone. Used to monitor glucose during fasting in diabetic patients.

Circadian rhythm: the approximately 24-hour biological cycle that governs timing of sleep and wakefulness, hormone secretion (including insulin), blood pressure patterns, and virtually all physiological processes. Disruption of circadian rhythm is associated with insulin resistance and hypertension.

CKD (Chronic Kidney Disease): progressive loss of kidney function, staged by eGFR. Stage 1 (eGFR above 90), Stage 2 (60-89), Stage 3a (45-59), Stage 3b (30-44), Stage 4 (15-29), Stage 5 (below 15 or on dialysis).

DKA (Diabetic Ketoacidosis): a life-threatening complication in which uncontrolled ketone production (usually in Type 1 diabetes) drives blood acidity to dangerous levels. Distinct from the therapeutic ketosis of fasting, in which ketone levels remain below the threshold for acidosis. Euglycaemic DKA (DKA at normal blood glucose) is a specific risk of SGLT2 inhibitor use.

Diuretic: a medication that promotes the excretion of sodium and water by the kidneys, reducing blood volume and blood pressure. Types include loop diuretics (furosemide), thiazide diuretics (hydrochlorothiazide), and potassium-sparing diuretics (spironolactone).

eGFR (estimated Glomerular Filtration Rate): a calculated estimate of the kidneys' filtering capacity, expressed in mL/min/1.73m². Derived from blood creatinine level, age, and sex. The primary measure of kidney function used in clinical practice.

Endothelium: the single-cell layer lining the inside of all blood vessels. Not merely a passive barrier but an active secretory organ producing nitric oxide, prostacyclin, and other molecules that regulate vascular tone, blood pressure, clotting, and inflammation. Endothelial dysfunction is a central feature of hypertension.

eNOS (endothelial Nitric Oxide Synthase): the enzyme in endothelial cells that produces nitric oxide from the amino acid arginine. Nitric oxide causes arterial smooth muscle to relax (vasodilation), reducing blood pressure. Impaired by oxidative stress, insulin resistance, and TMAO. Restored by fasting and exercise.

Glycogenolysis: the process by which the liver breaks down its stored glycogen (a stored form of glucose) to release glucose into the bloodstream. The first metabolic response to fasting, occurring in the first 12 to 16 hours.

Glycogen: the storage form of glucose in the liver and muscle. The liver stores approximately 100 to 120 g of glycogen (approximately 400 to 480 kcal of energy). This store is typically depleted within 12 to 16 hours of fasting, triggering the transition to fat-burning and ketosis.

HbA1c (Glycated Haemoglobin): a measure of the average blood glucose level over the preceding 2 to 3 months, expressed as a percentage of haemoglobin molecules that have glucose attached. Used to diagnose and monitor diabetes and prediabetes.

HOMA-IR (Homeostatic Model Assessment of Insulin Resistance): a calculated index of insulin resistance derived from fasting glucose and fasting insulin levels. The most accessible clinical tool for quantifying insulin resistance. Values above 2.5 indicate clinically significant insulin resistance; above 4.0 indicates severe insulin resistance.

hsCRP (high-sensitivity C-reactive protein): a protein produced by the liver in response to inflammation. Measured at very low concentrations with high-sensitivity assays (hence "high-sensitivity" CRP). A validated biomarker of chronic vascular inflammation and cardiovascular risk.

Hyperinsulinaemia: abnormally elevated insulin levels in the bloodstream, typically as a compensatory response to insulin resistance. Drives blood pressure through four mechanisms: renal sodium retention, sympathetic nervous system activation, RAAS stimulation, and smooth muscle proliferation.

Hypertension: chronically elevated blood pressure, defined as average blood pressure of 130/80 mmHg or above. Stage 1: 130-139/80-89 mmHg. Stage 2: 140/90 mmHg and above.

Iatrogenic: from the Greek for "physician-caused." Referring to disease or harm that is a consequence of medical treatment.

Intraglomerular hypertension: elevated pressure within the glomerulus, the filtration unit of the kidney. A consequence of systemic hypertension and hyperinsulinaemia that progressively damages the kidney's filtration architecture over time, contributing to CKD progression.

Insulin resistance: reduced responsiveness of cells (particularly muscle, liver, and fat cells) to the normal action of insulin. The pancreas compensates by producing more insulin (hyperinsulinaemia), which maintains blood glucose control in the short term but drives multiple pathological processes including hypertension.

Ketogenesis: the process by which the liver produces ketone bodies (primarily beta-hydroxybutyrate, acetoacetate, and acetone) from fatty acids during fasting or very low carbohydrate intake.

Ketone bodies: water-soluble molecules produced by the liver from fatty acids during fasting. The three ketone bodies are beta-hydroxybutyrate (the most abundant and clinically important), acetoacetate, and acetone. They serve as alternative fuel for the brain, heart, and muscles and have multiple signalling functions beyond energy provision.

Ketosis: a metabolic state in which blood ketone levels are elevated above the normal baseline (above approximately 0.5 mmol/L). Nutritional ketosis occurs at ketone levels of 0.5 to 5.0 mmol/L. DKA (diabetic ketoacidosis) occurs at levels above 15 to 20 mmol/L; this level is not reachable in the therapeutic fasting context in patients with functioning insulin secretion.

mTOR (mechanistic Target of Rapamycin): a central cellular sensor and regulator that promotes cell growth and protein synthesis when nutrients are abundant, and suppresses autophagy. Inhibited by fasting (and by the drug rapamycin), leading to activation of autophagy. Named after the drug rapamycin, which was found to extend lifespan in multiple animal models by inhibiting mTOR.

Nitric oxide (NO): a molecule produced by endothelial cells that causes the smooth muscle of blood vessel walls to relax, widening the vessel (vasodilation) and reducing blood pressure. Also inhibits platelet aggregation and has anti-inflammatory effects. Production is impaired by oxidative stress and restored by fasting.

NLRP3 inflammasome: a multi-protein complex within immune cells that responds to cellular damage and stress signals by triggering the production of interleukin-1β and interleukin-18, potent inflammatory cytokines. A key driver of the chronic vascular inflammation of metabolic syndrome. Inhibited by beta-hydroxybutyrate.

Nocturnal dip: the normal 10 to 20% fall in blood pressure during sleep, driven by the increased dominance of the parasympathetic nervous system (the "rest and digest" system) during sleep. Non-dipping (absence of this nocturnal fall) is strongly associated with increased cardiovascular risk and is restored by the circadian rhythm normalisation of the fasting programme.

Orthostatic hypotension: a fall in blood pressure of 20 mmHg or more in systolic, or 10 mmHg or more in diastolic, within 3 minutes of moving from lying or sitting to standing. Causes dizziness and, in severe cases, loss of consciousness. Common during fasting due to reduced blood volume from sodium and fluid excretion.

Oxidative stress: an imbalance between the production of reactive oxygen species (free radicals, highly reactive molecules that damage cellular structures) and the body's antioxidant defences. Elevated in insulin resistance, hyperinsulinaemia, and obesity. Impairs eNOS function and endothelial health.

Parasympathetic nervous system (PNS): the "rest and digest" division of the autonomic nervous system, active during rest, recovery, and sleep. Reduces heart rate, promotes digestion, and lowers blood pressure. Counterbalanced by the sympathetic nervous system. Fasting increases parasympathetic dominance over time, particularly from Day 3 onward.

Podocyte: a specialised cell that forms part of the filtration barrier in the kidney's glomerulus. Podocytes are irreplaceable once lost; their loss contributes to proteinuria (protein in the urine) and progressive kidney disease. Podocyte autophagy, activated by fasting, removes damaged cellular components and

helps maintain podocyte function.

RAAS (Renin-Angiotensin-Aldosterone System): a hormonal cascade that regulates blood pressure and fluid balance. Renin (produced by the kidney) triggers the production of angiotensin I, which is converted by ACE to angiotensin II, which constricts blood vessels and stimulates the adrenal glands to produce aldosterone, which promotes sodium and water retention. Chronically overactivated by hyperinsulinaemia.

Refeeding syndrome: a potentially life-threatening metabolic disturbance that occurs when nutrition is resumed too rapidly after a period of prolonged fasting or starvation. As cells resume normal metabolism, they take up phosphate, potassium, and magnesium rapidly from the bloodstream, causing dangerous falls in circulating levels of these electrolytes. Most significant in the first 72 hours after refeeding begins. Prevented by the graduated refeeding protocols of Appendix D.

Renin: an enzyme produced by the kidneys in response to reduced blood pressure, reduced sodium delivery, and sympathetic activation. The first step in the RAAS cascade. Chronically elevated in hyperinsulinaemia.

Sarcopenia: age-related loss of muscle mass and strength, accelerating from the sixth decade of life. A clinical concern in the fasting programme, managed by adequate post-fast protein intake and the growth hormone-mediated muscle-preservation effect of the fast itself.

SCFA (Short-Chain Fatty Acids): molecules including butyrate, propionate, and acetate produced by gut bacteria through fermentation of dietary fibre. Serve as fuel for colon cells, have anti-inflammatory effects, support endothelial health, and reduce blood pressure through multiple mechanisms.

SGLT2 inhibitors: a class of diabetes medication that blocks the SGLT2 protein in the kidney tubules, preventing glucose reabsorption and causing glucose to be excreted in the urine. Examples include dapagliflozin, empagliflozin, and canagliflozin. Associated with euglycaemic DKA risk during fasting.

Sirtuin: a family of proteins (SIRT1 through SIRT7 in humans) that function as metabolic sensors activated by NAD+ (a molecule whose levels rise during fasting and caloric restriction). Sirtuins regulate gene expression, promote DNA repair, activate autophagy, and are central to the longevity-promoting effects of caloric restriction.

Sympathetic nervous system (SNS): the "fight or flight" division of the autonomic nervous system, activated by stress, danger, and (pathologically) by chronic hyperinsulinaemia. Raises heart rate, constricts blood vessels, increases cardiac output, and raises blood pressure. Chronically overactivated in the metabolically hypertensive patient; suppressed progressively by the fasting programme.

TMAO (trimethylamine N-oxide): a compound produced when gut bacteria metabolise phosphatidylcholine and L-carnitine (found predominantly in red meat and processed meat) to trimethylamine (TMA), which the liver converts to TMAO. Elevated TMAO is associated with increased cardiovascular risk through endothelial damage, platelet aggregation, and promotion of atherosclerosis. Reduced by fasting-mediated gut microbiome compositional change.

TG:HDL ratio (Triglyceride to HDL cholesterol ratio): the ratio of fasting triglyceride level to HDL cholesterol level. A validated surrogate marker for LDL particle size (a ratio above 1.5 to 2.0 suggests predominance of the more atherogenic small dense LDL particles) and a clinical fingerprint of insulin resistance. Clinically more informative than total LDL cholesterol in the metabolically hypertensive patient.

Total peripheral resistance (TPR): the resistance of the entire arterial system to blood flow. Blood pressure equals cardiac output multiplied by total peripheral resistance. Elevated by arterial vasoconstriction (sympathetic activation, angiotensin II, endothelin-1) and by structural arterial stiffening (atherosclerosis, smooth muscle hypertrophy).

Uric acid: the end product of purine (a building block of DNA) metabolism in humans. Elevated uric acid (hyperuricaemia) is associated with gout, kidney stones, and cardiovascular risk. Rises transiently in early fasting due to competition between ketone and urate excretion in the kidney.

Vagus nerve: the longest nerve in the body, connecting the brainstem to the heart, lungs, and abdominal organs. The primary pathway of parasympathetic nervous system influence on the heart and blood pressure. Vagal tone (the resting activity level of the vagus nerve) is a measure of parasympathetic dominance and cardiovascular health; it is increased by the fasting programme.

Vasodilation: widening of blood vessels due to relaxation of the smooth muscle in their walls. Reduces total peripheral resistance and lowers blood pressure. The primary mechanism of nitric oxide's blood pressure-reducing effect.

Zone 2 exercise: aerobic exercise performed at an intensity at which a conversation can be maintained without significant breathlessness, corresponding to approximately 60 to 70% of maximum heart rate. Associated with the greatest mitochondrial biogenesis (production of new mitochondria, the energy-producing structures of cells), fat oxidation, and metabolic health benefit per unit of exercise time.

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