CHAPTER 5

TEST, ASSESS, ADDRESS . . . DON'T GUESS!

Adjusting Treatment Priorities in Response to the Patient's Unique Terrain

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"One day, patients will say: I'm not an average patient. I am who I am. You need to understand who I am before you prescribe whatever treatment you plan to prescribe."

—EDWARD ABRAHAMS, President of Personalized Medicine Coalition

"More information is always better than less. When people know the reason things are happening, even if it's bad news, they can adjust their expectations and react accordingly. Keeping people in the dark serves only to stir negative emotions." —SIMON SINEK

Mistletoe is not a "protocol" treatment. As previous chapters have explained, there is no height and weight chart for administering mistletoe. Rather, VAE therapy begins with close observation of patient response: both visible and sensory reaction at the injection site. But even before that, as a mistletoe practitioner, I run dozens of lab tests on my patients and go through hours of patient intake inquiry. That initial data, along with real-time response and follow-up lab tests, guide the treatment progression, including mistletoe

administration. I constantly monitor my patient's metrics and adjust all treatments responsively.

In the integrative and anthroposophic worlds, we often say, "We don't treat cancer; we support the person." In this chapter, we'll look at a holistic and *terrain-based* approach to monitoring the patient's baseline starting point and their response to therapies. We'll define several aspects of the body's inner terrain, the lab tests that effectively reveal that terrain, and the levels and ranges that define true health. (It's not worthwhile to strive for the "normal ranges" of a generally unhealthy population group!) Along the way, we'll look at how lab findings influence our choices about mistletoe therapy and other integrative care, as well as how those therapies can, over time, nudge patient labs in a positive direction.

Terrain-based care: The patient as an ecosystem

When discussing my Terrain-Based Core Lab Tests™, it's helpful to first explore my underlying medical philosophy, how I regard the body as a complex ecosystem with multiple subsystems. In Western medicine, we have cardiologists, neurologists, endocrinologists, pulmonologists, gastroenterologists, urologists... and the organ-specific list goes on and on. But the body doesn't understand these silos. The body's organs are all intricately intertwined and interdependent. Learning some basics about terrain-based thinking will make it easier to follow along when we begin looking at individual blood tests and discover their ramifications for multiple body systems.

In over 25 years of caring for myself and my patients, I have learned to evaluate health through ten terrain-focused elements. This is a way of looking at health in terms of multiple whole-body layers, which affect and involve all the organs. This is a paradigm shift away from evaluating health and disease as issues affecting a single organ only.

There are certainly more than ten systemic pathways in the human body, but these are simply the most common and critical entry points that I've experienced in my practice. These Ten Terrain Components are inspired by the book I co-authored with Jess Higgins Kelley, *The*

Metabolic Approach to Cancer Care, which defines each of these concepts in robust detail and describes their associated therapies at length.[1] For our purposes here, this is only a brief summary. We'll refer to these terrain components again in chapter 9, when we look at several integrative therapies commonly used alongside mistletoe.

1. ***Epigenetics:*** The genetic blueprint that you were born with. Genetic predisposition is not destiny! Gene expression can be influenced by diet, lifestyle, trauma and stress processing, medications, nutrient deficiencies, and more. The more you know about your blueprint and its vulnerabilities and strengths, the more you can rearrange your inner home and create a terrain that's more resilient to health challenges.
2. ***Metabolic function and blood sugar balance:*** The key to keeping your motor humming along without damaging organs, weakening immune function, promoting cancer growth factors, or rendering conventional treatments less effective. Optimizing the metabolism of your healthy cells simultaneously slows the metabolism of cancer cells![2]
3. ***Toxic Burden:*** The cumulative effects of living on a toxic planet. It is not a matter of *if* you have a toxic load; it is a matter of *how much*. In integrative oncology, it's a priority to remove and avoid as many toxic assaults as possible, so the body can spend more of its energy on healing.
4. ***Microbiome and digestive function:*** The basis of many ancient medical models like Ayurveda and traditional Chinese medicine. Indeed, we can't absorb and utilize many healing nutrients without an optimal balance of microorganisms in the gut, along with a properly functioning gut lining.
5. ***Immune Function:*** Long-ignored in conventional cancer care but emerging as a new focus of immunotherapy research. Chemotherapy, radiation, and surgery do a fine job at removing the tumor. However, an intact immune system is the greatest defense against progression and recurrence.[3–7]

6. ***Inflammation:*** The driving force of progression in most of our modern diseases, including metabolic syndrome and cancer. Inflammation is stimulated by sugar, stress, and other common contemporary lifestyle factors. Chronic inflammation is a complex response to an overwhelmed terrain.

7. ***Circulation and angiogenesis:*** Refers to patterns of flow or stagnation of the blood. Includes factors such as heart rate, clotting tendencies, dehydration, exercise habits, inflammation, and stress. Circulation also looks at the altered liver function that occurs during an active cancering process, and how that impacts blood viscosity, oxygenation, and blood vessel growth.

8. ***Hormone balance:*** One of today's greatest challenges now that we live in a swimming pool of xenoestrogens and estrogen-mimicking substances pervasive in food, water, body care products, industrial chemicals, and plastic products, as well as hormone medications like steroids, birth control pills, and hormone replacement therapy. It takes work, but it is not impossible to restore balance and function for hormone receptor sites.

9. ***Stress and biorhythms:*** Refers to natural cycles of activity and rest, deep sleep, daytime light exposure, appropriate darkness at night, and our experience of seasons and moon cycles. Only in the past century have humans fully disrupted our innate circadian rhythm through electric light, blue light, night shift work, overwork, medications, and a loss of connection to natural rhythms. Recent studies now show circadian disruption to be implicated in several conditions, including cancer.[8–10]

10. ***Mental and emotional health:*** Possibly the most under-emphasized but widely influential terrain element. Our thoughts impact our response to any situation. We are what we think. The field of psychoneuroimmunology shows direct links between our psychosocial wellbeing and our ability to ward off infection and disease.[11,12]

These Ten Terrain Components are my personal take on a terrain-based treatment philosophy. However, terrain-based thinking is not an original idea. We mentioned in chapter 1 that there were several medical thought leaders in the 1800s who viewed the body and disease processes in terms of terrain or "soil." Rudolf Virchow (1821–1902) said, "Germs seek their natural habitat—diseased tissue—rather than being the cause of dead tissue."[13] This was another reference to the body's overall terrain. Many other brilliant practitioners and researchers have kept that flame of insight alive, leading up to and including Mina Bissell's past work in the 1980s and her more recent research describing the tumor microenvironment.[14,15] *Soil, terrain*, and *microenvironment* are all words for the same concept.

So how do we monitor that terrain? And what do we do when we discover some new disturbance in it? Let's first define and explore six Core Lab Tests. Then we'll return to five of the Terrain Components that are especially relevant during mistletoe therapy. We'll connect the tests to the terrain and look at possible treatment adjustments and considerations in response to test results.

The following is not a comprehensive list of all the lab tests I use in my practice. Every cancer patient has profoundly diverse underlying conditions, which call for highly personalized testing, inquiry, and observation. For now, we'll look closely at the Core Lab Tests that I use with all my patients, regardless of condition. If you wish to take a deeper dive into nuanced cancer-related lab tests, interpretation of those tests, and what we consider truly healthy ranges, please review appendix F and the resources section.

Core labs: Tests that reveal the terrain

When patients begin their integrative care journey with me, some are surprised at how deeply I monitor their inner terrain through initial and ongoing lab tests and epigenetic testing. Some don't want that much testing—they're worried about what they might discover! For those who are hesitant, I emphasize this reality: *The more we test, the clearer the picture we obtain of your current challenges. The more*

we know, the more we can effectively personalize a path back toward health. Testing empowers you. It's crucial to recognize that every test result—even discovering that you have a genetic or epigenetic challenge—can provide you only more empowering information. Becoming aware of an issue gives you options and shows you what your body needs to live at its best. Test results are not static or set in stone. Our health, even epigenetic expression, is dynamic and in a constant state of flow. The more you know, the more you can influence the direction of that flow.

You'll find you're probably already familiar with these Core Lab Tests, but we'll look at them with a more scrutinizing systems-thinking eye. With all six of the following test categories, it's crucial that you get baseline readings—*run these tests at the outset, before you begin any integrative therapy.* Rerun them monthly (or every two weeks in complex situations) for the duration of treatment and, as your terrain improves after treatment, continue running them quarterly for another two years. Then monitor them yearly thereafter.

1. CBC with differential

This is the blood test that everyone gets at an annual physical: The Complete Blood Count (CBC). Like it sounds, it lists and tallies the components of the blood. This includes the quantity of different cells (both blood cells and specific immune cells), number of platelets, and hemoglobin level. Integrative oncologists run this test too, but we home in on ratios and numbers that aren't so commonly discussed. If you want to learn even more about the ratios and all the health implications you can glean from a simple CBC, visit the Oncology Nutrition Institute (www.OncologyNutritionInstitute.com, see "Resources"). Their website offers a 90-minute web-based class solely on interpreting the CBC. For our purposes now, with our focus on mistletoe therapy, let's examine something called the Neutrophil-to-Lymphocyte Ratio (NLR) and then take a close look at eosinophil numbers.

The neutrophil-to-lymphocyte ratio (NLR)

Considering how well-researched NLR is in relation to cancer and all-cause mortality, it's amazing it isn't a standard listed ratio on the CBC. Thankfully, the math is easy. Simply look for the *absolute neutrophil count* (not the percentages) and divide it by the *absolute lymphocyte count* (again, not percentages). The resulting number should be close to 2, preferably a ratio of 2:1 to 1:1. That means an average of two neutrophils to one lymphocyte, or as low as one neutrophil to one lymphocyte. That's a slim range. It's a narrow therapeutic ratio, and if you're outside either end of it, you might have a problem developing.

This is one of the most prognostic immune tests we have for everyone, not just patients who have cancer. There are over two hundred studies looking at how NLR relates to modern diseases.[16–19] If you have too many neutrophils and too few lymphocytes, this is associated with higher all-cause mortality, meaning the risk of death from *any condition* goes up.[20] If the ratio flips, and you have fewer neutrophils and too many lymphocytes, blood cancers (leukemia, lymphoma, myelodysplastic syndromes) begin to manifest.[21] Cancer survivors who have a poor NLR have a higher recurrence and progression rate, while survivors who have an optimal NLR tend to experience robust maintenance of remission.[22–24] This simple ratio, which you can pull straight from your most recent CBC, is that significant.

NLR can be affected by cancer treatment, so it's important to monitor it frequently—twice a month or even weekly in highly complex situations. Patients are often treated for a primary cancer and, if treatment is especially aggressive, it can stress the immune system to the point of reversing their NLR. They have more lymphocytes than neutrophils. This leaves them vulnerable to blood dyscrasias, myelodysplastic conditions, idiopathic thrombocytopenia (ITP), lymphomas, and leukemias.[25] Any of those conditions can stem from that imbalanced NLR. We often see high incidents of secondary cancers, especially in women with breast cancer who may have had their cancer overtreated.[26,27] A reversed NLR is likely at play in these situations.

We can anticipate this issue. We can see who's vulnerable to imbalanced NLR by watching those numbers more closely. There are immunomodulatory remedies that can help the body bring the NLR back into balance. Not surprisingly, mistletoe is one of them. VAE therapy has a direct impact on NLR, balancing out both ends of the spectrum. It has a modulatory effect on immune cell generation, increasing or decreasing neutrophil or leukocyte numbers until that appropriate balance is reached.[28]

Eosinophils

Watching the eosinophil count is an effective way to determine if a patient is responding to mistletoe. Of course, to do that, you must run the CBC *prior* to starting mistletoe, to get a baseline reading. There's a narrow therapeutic window for this cell count. Ideally, eosinophil count should be at 2 or fewer.

Elevated baseline eosinophils – If eosinophils are elevated before starting mistletoe therapy, it's a clue that some TH-2 immune process is occurring, something allergy-related. The patient is eating or breathing something that's causing an allergic response. This is why we ask allergy-related questions on the Anamnestic Form (see appendix C). If there is an identified allergy, it's not necessarily a contraindication for mistletoe therapy. But it does mean I'll order an IL-8 cytokine test before the patient starts VAE therapy.[29] If eosinophils are elevated, but IL-8 is normal, I'm not concerned about VAE therapy. However, I do monitor patient response very closely and use greater caution with doses and timing. If both eosinophils and IL-8 are high, we wait on VAE therapy and do some detective work to determine what's causing the IL-8 spike. Ideally, we remove that obstacle (possibly an allergen the patient is exposed to constantly). Then we'll proceed with caution and a "low and slow" VAE schedule. Elevated IL-8 is associated with compromised response to conventional treatment, so determining and addressing its cause is a high priority.[30]

Elevated eosinophils after starting VAE – If eosinophils spike slightly after starting mistletoe therapy (if the number blips from 2, up

to 3 or 4) that's fine. That's expected and within a safe zone. If eosinophils weren't high to begin with, then we know that this is simply the mistletoe creating a desired effect.[31] But if the number spikes to 5 or more, we need to stop the VAE therapy and conduct some more detective work. We'll look at IL-8 levels, to determine whether this cytokine spike was triggered by mistletoe. Or we look for other possible underlying medical conditions that might involve IL-8. Even so, this won't be a complete contraindication for VAE therapy. But it does mean letting the body come back into balance as far as IL-8 and eosinophils, then returning to VAE with a very gentle titrating approach. As always, the patient's body and lab metrics should guide the rate of increase and maintenance dosage.

It's rare to see mistletoe cause an overzealous spike in eosinophils or IL-8. But it can happen, and you can catch it with simple, affordable tests. Catching it is paramount for patients to have good outcomes. In 20 years, I've had only two patients who couldn't go back on mistletoe therapy after persistent eosinophil and IL-8 spikes. With them we provided *Helleborus niger* instead (see chapter 8). This is a powerful alternative to have in your toolbox, particularly for patients with hyperallergic patterns. In some cases, changing the mistletoe host tree, dose, or brand can also alleviate a specific eosinophilic reaction.

Platelets and the M.D. Anderson Prognostic Scoring System: Mistletoe therapy and autoimmunity

When reviewing the baseline CBC, platelet count is another important marker to consider before any immunotherapy, including VAE. Similar to the NLR noted above, we may also need to consider PLR (*platelet*-to-lymphocyte ratio). When we see elevated platelets and lower lymphocytes, outcomes and prognoses are poor.[32] Elevated platelets alone are prognostic for many cancer types and indicate thick and sticky blood patterns. The latter leads to higher incidence of thrombosis, which is one of the common causes of fatality secondary to a cancer diagnosis.[33] The M.D. Anderson (MDA) Prognostic Scoring System (see appendix D) notes that "elevated

platelet count" is a possible contraindication for immunotherapy or is at least associated with poorer immunotherapy outcomes. In short, patients with elevated platelets (more than 400, according to standard of care [SOC] and over 250 by my terrain assessment) and three or more positive findings on the MDA score, should be cautious and thoughtful in implementing any immune therapies including mistletoe.[34]

2. *Comprehensive metabolic panel (CMP)*

The CMP provides a total picture of how the whole terrain is lining up in this moment, how the body is metabolizing fuel and eliminating waste products. This test provides measurements of blood sugar, electrolyte balance (sodium, potassium, chloride), calcium levels, acid-base balance, and organ function (liver, kidneys). Specifically, it shows levels of liver enzymes and waste products that are normally produced or removed by the liver and kidneys. This gives us a clear picture of how efficiently your body is able to clean up the typical waste products of metabolism. It also hints at whether you're staying hydrated well enough.

Over time, when taking a terrain-centric approach and incorporating VAE as part of the treatment, we would expect improvement in these testing parameters. Namely, we see improvement in organ function if the tumor burden is resolving in those areas, improved metabolic function if VAE is impacting the blood sugar and insulin response process, and more balanced inflammation cycles, as shown by improvement in various markers throughout the CMP and a trio of tests that we call the Trifecta Labs.

The "Trifecta Labs"

I can't take credit for naming this trio of labs; a few of my patients coined the phrase "Trifecta Labs" several years ago. I've continued insisting that every patient monitor these three metrics at least monthly, and the Trifecta moniker has stuck! The tests are not obscure. They're well-known measurements: Quantitative CRP, LDH, and ESR. But the way I evaluate them may be new to you.

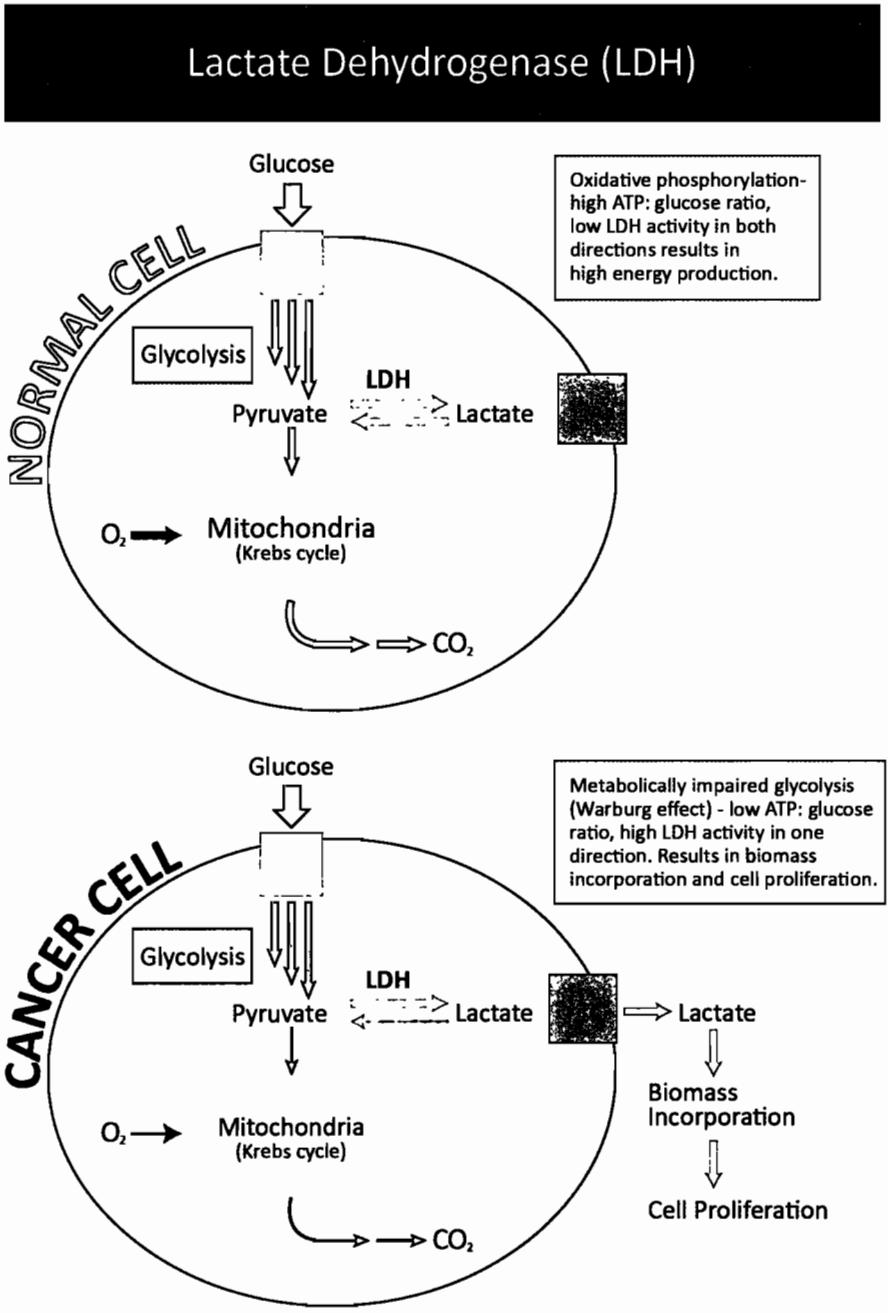
3. Quantitative CRP

C-Reactive Protein is a well-known inflammatory marker, and it's a common add-on test when running the CMP. It picks up on chronic systemic inflammation. CRP, much like NLR, is considered prognostic regarding how a patient will respond to conventional cancer treatment. If CRP is elevated, the patient is more likely to experience multiple drug resistance,[35,36] more likely to have intensified side effects of the treatment[37] (which means they may have to stop or alter treatment timing), and they'll have a poor prognosis for survival.[38] CRP is that important. Knowing a patient's CRP level, and addressing underlying inflammation head-on through diet and lifestyle, can change the outcome of SOC treatment. It's surprising that CRP is not a standard required test prior to starting conventional treatment.[39]

4. LDH

Lactate dehydrogenase (LDH) is another add-on test that is commonly regarded as a marker of tissue damage. LDH has even more value for evaluating tumor microenvironment and whether the overall body terrain is hospitable to cancer. For leukemia and lymphoma, LDH is its own tumor marker.[40] But even for all the other solid tumors, LDH is a marker of *cellular turnover;* it can roughly tell us the rate of cell division. The higher your LDH, the more rapid your rate of cell turnover.[41,42]

LDH also tells us whether the cancer cells have shifted toward something called the *Warburg Effect.* In a healthy cell, normal metabolism—the process of using oxygen to burn glucose for energy—produces a small amount of LDH as a byproduct. But cancer cells have a method for producing energy even if they're short on oxygen. This *anaerobic metabolism* is inefficient and produces far more LDH as a byproduct (image 05.01). All that excess lactate contributes to more acidification in the tumor's microenvironment and drives out oxygen even more. This begins a vicious cycle of anaerobic metabolism.[43,44] That's the Warburg Effect, and that's why we're able to look at this one blood test and see a clue about the body's entire terrain.


Lactate Dehydrogenase (LDH)
Glucose
NORMAL CELL
Glycolysis
LDH
Pyruvate
Lactate
O2
Mitochondria
(Krebs cycle)
CO2
Oxidative phosphorylation-high ATP: glucose ratio, low LDH activity in both directions results in high energy production.
Glucose
CANCER CELL
Glycolysis
LDH
Pyruvate
Lactate
Lactate
Biomass Incorporation
Cell Proliferation
O2
Mitochondria
(Krebs cycle)
CO2
Metabolically impaired glycolysis (Warburg effect) - low ATP: glucose ratio, high LDH activity in one direction. Results in biomass incorporation and cell proliferation.

Elevated LDH can indicate that the body's terrain has become cancer friendly. It tells us about the overall metabolism. Is the metabolism primarily oxygen-rich (aerobic) and therefore hostile to cancer? Or is it mostly anaerobic and therefore friendly to cancer growth, metastasis, or recurrence? Elevated LDH can also indicate that there may be damage to the heart, lungs, kidneys, or liver. If an LDH test is elevated, I immediately order the *LDH Isoenzymes* test. This can tell us precisely which organ or tissue is damaged. Sometimes, even if LDH is normal, I will check on the isoenzymes, just to elucidate other mystery symptoms in the body. LDH Isoenzymes can show which bodily tissues are aggravated or irritated. Now, if the LDH level is abnormally low, especially if the other two Trifecta Labs are elevated, this is also a reason to test the isoenzymes. Sometimes, in a state of metabolic wasting, the LDH levels may not be able to track at normal or elevated levels, but the isoenzymes still offer clues.

5. ESR

Erythrocyte Sedimentation Rate (ESR) is also commonly added onto the CBC when a practitioner is looking for signs of inflammation. ESR refers to how quickly the erythrocytes fall out of solution, how quickly they settle out of the blood. This indicates how freely flowing or how "sticky" the blood is. Sticky blood is one of many indicators of systemic inflammation. If sedimentation takes a long time, if that number is elevated above 10, it means there is a thick, sticky blood matrix. This can indicate a toxic, sludgy, less fluid blood flow. Elevated ESR can also hint at an autoimmune process. That's because autoimmune reactions make the blood agglutinate.

As you can see, each of these Trifecta Labs is powerful on its own. There are hundreds of studies looking at each of these metrics on their own in relation to cancer. But taken together, the three tests give me an even more complete picture of the patient's inflammatory status and level of oxidative damage.

CRP by itself can tell us a lot. LDH can tell us a lot. Sedimentation rate can tell us a lot. But if all three are high, I know with certainty

that *cancer is in the driver's seat.* We need to take focused and directed action immediately. If all three are within my functional ranges, then I feel confident that *the patient is in the driver's seat.* In my experience, the Trifecta Labs have consistently been more prognostic than scan results and tumor markers. I am *far more* concerned about patients who have clear scans and normal cancer markers, but all three of their Trifecta Labs are elevated. I am *far less* concerned about the patient whose scans still show tumors present, and their tumor markers are still elevated, but their Trifecta Labs are perfect. In that moment, their body is actually managing the cancer. The patient is in the driver's seat; the cancer is not.

VAE can definitely impact the dance and expression of the Trifecta Labs. If these labs are not stabilizing and trending downward, we may want to take a closer look at how the patient is responding to VAE therapy (and any other therapies). I'll ask deeper questions about their cytokine reactions and quality of life (QOL) symptoms. Despite all our best efforts, stubborn, elevated Trifecta Labs might just indicate that our goals of restoring cellular communication and overcoming the massive oxidative stress are simply out of reach. If those lab findings also coincide with loss of QOL and ability to function normally, it may be time to discuss palliative and end of life care (see chapter 11). This does not mean we have given up! It simply means we need to be realistic and continue supporting the wishes of the patient, while we determine if there are other options available to us. I find, in these moments, that more oxidative and cytotoxic therapies actually hasten death. Too often, that's all that is offered. In contrast, those who take a much-needed break from aggressive SOC or integrative care can sometimes right the ship, allowing us to reevaluate and move forward in treatment again.

Sometimes a patient will tell me that their conventional practitioner said that CRP, LDH, and ESR are normally elevated during treatment. That may be common, but it isn't healthy. My patients who proactively work on these inflammatory markers through diet, lifestyle changes, and other natural therapies are able to maintain healthy Trifecta Labs

even during conventional treatment. They're able to do that because they're keeping their terrain as healthy as possible. As a result, they wind up responding better to treatment, too.

I've seen patients celebrate that they're done with chemotherapy and radiation, and their scans look good. But their Trifecta Labs are clearly off. Too often there is a recurrence or progression of cancer within months of these findings. This effect is an increasing subject of study. We know that if a cancer survivor has a high CRP, the cancer is more likely to have a fatal recurrence.[46] Conversely, I have many patients who still have a tumor present, but they're *managing it well.* The relationship between systemic inflammation, anaerobic metabolism, and cancer is that tightly interwoven.

All that said, I must clarify that every lab result needs to be regarded within the greater context of the patient's lifestyle and general condition. For instance, if the Trifecta Labs have been consistently good, and suddenly only the CRP is high, that might be purely because the patient had a recent injury. If only the ESR is high, it could be due to a mild autoimmune reaction, perhaps a recent exposure to gluten. Or maybe LDH is high because the patient just completed a major workout or took a long hike. It's possible for transient events to throw off a person's chemistry. Lab results are clues that must be examined within their greater context.

We never treat a lab; we never treat a target. We support the entire person and treat the entire terrain. Any time we get myopic about one lab looking a little off, it's wise to take a step back and look at that bigger picture. How's this one lab result playing against the entire terrain?

6. D3 levels (25-OH and 1,25-OH)

Vitamin D_3 is a powerful nutrient that interacts with almost every terrain component: immune function, mental health, metabolism, inflammation, and circadian rhythm. Vitamin D is so well-researched, so well-known for its diverse health effects that it has its own institute in the NIH: The Vitamin D Council. It's stunning that we know so

much about it, even in conventional medicine, and yet tend to downplay it and rarely monitor D levels with any regularity.

The first vitamin D revelation that I share with my patients is the fact that your D levels are NOT fine at 30—that's the cutoff for low-normal, per conventional medicine. Those levels may be normal for the general population, but the general population is not healthy. *I want to see levels above 50 in healthy individuals and 80 to 100 in those who are actively cancering*—as long as their serum calcium levels stay within range (9.5 or lower).[46] The next vitamin D revelation is regarding how to address deficiency. When D levels are low, the best, most effective source is sun exposure (get outside!). The next best source is food. My last resort is supplementation. When supplementing vitamin D, it's crucial to monitor serum calcium levels (through the CMP), and always provide K2 along with D to ensure appropriate balance and absorption.[47,48]

D levels are highly influential on both conventional and integrative treatment success. That includes mistletoe therapy. In my practice, I've noticed that patients with low D3 levels do not have as strong a response on mistletoe as those with normal or optimal levels. Both in practice and in published studies, I've also noticed that patients who are vegan or vegetarian, those who are morbidly obese, and those who take antacids, steroids, or cholesterol lowering medications are all chronically low in D3.[49–52] Given that up to 70 percent of the population is D-depleted (based on true healthy levels, not unhealthy "norms"),[53,54] this is a conversation we need to have before starting VAE therapy or any other treatment. Address vitamin D deficiencies and insufficiencies first! Of course, vitamin D can act like a hormone, so once balanced levels are achieved, switch to maintenance dosing based on test results.

Terrain-labs integration: Looking at labs from multiple terrain perspectives

As mentioned earlier, I constantly evaluate my patients through the lens of multiple terrain-based body systems. While we don't have room here to evaluate all ten of those terrain components, let's look at how

mistletoe particularly interacts with five of them. We'll notice how terrain-based testing can evaluate the patient's baseline and monitor the shifts we want to see through the course of treatment.

Stress and biorhythms

In the integrative oncology world, when we think of mistletoe therapy, we often think of its effects on the immune system, its direct effects on the tumor, and perhaps the secondary effects on mental and emotional health. But I first learned about VAE therapy through an anthroposophic lecture on how mistletoe's primary effect was to *restore rhythm* in the body. In the anthroposophic medicine (AM) world, cancer is regarded first as a *loss of rhythm,* both within the body and between the body and its surrounding environment. That concept challenged me and stuck with me. Rudolf Steiner, the co-founder of AM, once said, "One can ascend to a higher development only by bringing rhythm and repetition into one's life. Rhythm holds sway in all nature." This is a beautiful holistic theory, and it has scientific support. We know now, through multiple studies, that night shift workers with dysregulated circadian rhythm, experience higher incidence of metabolic diseases and cancer.[55–59] In 2017, the Nobel Prize in Physiology/Medicine went to researchers studying circadian rhythm biology and its implications in human health.[60] In recent years, we have also learned that every individual cell maintains a particular rhythm,[61,62] and that the microbiome and our response to *any* therapy is circadian rhythm dependent![63,64] *Rhythm holds sway.*

When evaluating a patient's relationship with natural rhythms and how they process stress, I begin with plenty of biographical inquiry and lifestyle questions. Observational data and a comprehensive patient history are given equal weight with lab work and other quantitative testing. I want to know the patient's career history and relational patterns, along with bedtime routines and average amount of sleep, bowel and appetite patterns, average time spent outdoors, experience of seasonal weather, and typical stress levels and how they process it. I hope to see cycles, *healthy rhythmic patterns.* But if someone is coming to me

because of an active cancering process, more often I see areas of zero rhythm: night shift work, chronic sleep deprivation, constant insatiable hunger, artificial light exposure from dawn to bedtime, no time spent outdoors, constant stress, no periods of rest or release.

Once I have a detailed picture of the lifestyle vulnerabilities and the changes that could rebuild natural rhythms for the patient, I begin choosing the lab tests that would shine even more light on their situation. As always, every patient completes a CMP. To me, the metabolic panel reveals both metabolic function and the *inherent rhythms* of those metabolic organs. Metabolic systems are rhythmic systems, constantly rotating through the tasks of producing energy and cleaning up waste byproducts. The CMP can show me where that rhythm has stalled.

I also look at a patient's D_3 level for clues about their natural rhythms. Of course, D levels hint at whether they're spending enough time outside without sunscreen. Vitamin D also impacts hundreds of epigenetic factors involved in metabolic function, hormone regulation, and immune response. It influences the very rhythm of our biology and can affect personal biography, too, as low D levels are associated with depression. Specifically, vitamin D appears to be involved in serotonin and dopamine pathways. If a patient's D levels are low, it is a reason for me to ask about all these other QOL and rhythm-oriented factors.[65,66]

After looking at the CMP and D_3 levels, we look at a couple of specialty labs directly related to circadian rhythm: The Adrenal Stress Index (ASI) and melatonin levels. The ASI looks at cortisol output at multiple points during a 24-hour period. Cortisol output is not static; it has a rhythm. Many patients today show fairly healthy output during the day, but very low cortisol in the morning and then an uptick in the late evening. That's the opposite of how a cortisol graph should look. Cortisol should be secreted about an hour before we wake up, creating a spike that raises body temperature and blood sugar, making us want to jump out of bed ready for the day. Instead, in chronically stressed patients, cortisol levels are sluggish in the morning and may get even lower during the day. Then at night, the body overcompensates, trying to increase cortisol in preparation for the next morning. All night long

the cortisol level is slightly elevated, and the patient never gets deep restful sleep.[67,68] This can be measured with an ASI test. Similarly, we can measure melatonin levels and will often see a complementary dysregulation. Where cortisol is chronically elevated at night, melatonin is often chronically too low.

Healthy sleep–wake rhythms are crucial to healing in any disease state, but especially during cancer treatment. Addressing these issues early in the treatment cycle will affect the efficacy of all other treatments.[69] Thankfully, treating disrupted sleep-wake cycles begins with simple lifestyle choices—from daytime sunlight exposure and melatonin supplementation to removing all electronic devices from the bedroom. We'll discuss some of these integrative treatments and lifestyle choices in chapter 9.

For now, let it suffice to say that all integrative therapies work better when the patient cultivates healthy natural rhythms in daily life. Mistletoe therapy has a unique circular relationship with body rhythms. Its effects are stronger when the patient intentionally reestablishes a healthy circadian rhythm, and mistletoe itself helps enhance biological rhythms. It both fosters rhythmic balance and is enhanced by strengthening circadian rhythm.

Immune function

Similar to evaluating a patient's rhythmic patterns, evaluating immune system function begins with thorough inquiry into the patient's history. I want to know if they get sick often, if they experience fevers frequently, or if they *never* get fevers. All extremes are of interest to me. I'm certainly interested if I hear that someone gets sick all the time. But more often than not, patients come to me saying, "I'm the one who never got sick. Until I got cancer!" This pattern of never getting sick is a red flag in the opposite direction. Healthy immune function involves getting sick occasionally: burning through an infection, experiencing and then resolving a good healthy fever.

Once I've got that broad immune history down, I look at quantitative labs. D3 levels show up here. Vitamin D's association with immune

function is well established. Remember, I want to see levels of 80 to 100 for someone who is actively cancering. I also look at the patient's CBC, noting their NLR and combing through all their white blood cell counts. I look for levels that are out of range for an optimally healthy person (not just levels based on population norms). Again, look at appendix F to get those true healthy ranges. There are immune function clues here that you might not see if you were evaluating the CBC using the conventional normal ranges.

Beyond D3 and general CBC white blood cell counts, it's possible to request additional tests to determine specific counts for NK cells (CD56+ cells) and activated T cells (both helper and killer cells). There's a single test by Labcorp (see Resources) that can provide both of those. It's good to acquire the baseline and then monitor these levels during VAE therapy. Labcorp provides reference ranges, but I also keep in mind that VAE therapy affects these cell counts. I expect all of them to be "mid- to high-end normal" during treatment. If they're low, it's a flag that there's a serious underlying health condition that needs to be addressed.

I also evaluate zinc levels, because of that nutrient's key role in supporting immune function. It's important to request a Red Blood Cell (RBC) zinc test, instead of a standard serum zinc level. Serum zinc can occasionally look healthy simply because you hit it at a good moment. RBC zinc essentially provides a three-month average of the mineral status. That's much more accurate. (In fact, any time I measure any mineral status, I ask for the RBC version.) In general, when zinc levels are low, macrophage and NK cell function are compromised.[70] Clinically, I've noticed that if zinc levels are poor, the response to VAE therapy may not be as robust. This is likely due to effects on immune cell quantities and function. Ideally, zinc insufficiency would be corrected before starting immune-modulating therapies.

Inflammation

Chronic systemic inflammation is the driver of cancer metastasis, and it fuels many other metabolic diseases too. This terrain layer is

intertwined with blood sugar balance, dysregulated biorhythms, and associated chronic stress. As mentioned earlier, inflammation cycles get "stuck" and refuse to resolve when the terrain is overwhelmed by dietary and lifestyle factors. When it comes to monitoring and determining multiple root causes of chronic inflammation, the Trifecta Labs are key. Those three labs are how we assess whether a patient is maintaining homeostasis in those inflammatory pathways, or whether the inflammatory fires have gotten out of control.

Outside of the Trifecta, other labs that give insight into inflammation include: *fibrinogen activity*, *uric acid* and, believe it or not, *ferritin*. Fibrinogen activity levels are well known as an indicator of thick sticky blood patterns causing hypercoagulation and chronic systemic inflammation. If CRP is high, fibrinogen activity is likely high, too. It's another test that can shine light on the whole inflammatory picture. Meanwhile, uric acid can show us issues with methylation, poor immune function, oxidative stress from inflammatory processes, acidosis, and mineral imbalances.[71] It can also be an indication that we should ask if the patient is getting enough hydration and enough dietary magnesium, or explore whether they're consuming too many dietary oxalates. Ferritin levels are also informative. There are many types of anemia, and only one is true iron deficient anemia. Practitioners are too often seduced into prescribing iron when they note low RBC, hemoglobin, or hematocrit levels. For patients who have cancer, this can wind up feeding the inflammatory metastatic fire.[72,73] You must make sure ferritin levels are within their sweet zone (see appendix F). If true iron deficiency anemia is diagnosed, consider rebuilding the blood through naturopathic dietary and herbal approaches, instead of iron supplementation.

Mistletoe therapy has a unique relationship to this terrain factor. As mentioned in chapter 2, it is distinctly immunomodulatory in its interaction with inflammatory states. It initially prompts an acute, and highly beneficial, inflammatory response. That acute inflammation and transient cytokine release is helpful for activating the immune system. This "good inflammation" will spike, then resolve in a healthy

wave. Meanwhile, other components in VAE can decrease many markers of unhealthy chronic inflammation including: IL-6, CRP, COX-2, NFkB, and VEGF.[74,75]

Mental and emotional health

Similar to evaluating a person's circadian health, evaluating mental and emotional health requires extensive lifestyle and biographical inquiry. Unfortunately, if I began every new patient intake with this terrain focus, I'm pretty sure all my patients would run away! We all have a strong preference for discussing the tangibles. *Let me change my diet, let me take this supplement, I'll even learn Tai Chi, but if you ask me about my childhood, I'm out of here!* And yet this terrain factor is critically important, especially when treating cancer. When I have totally compliant patients who are doing everything right with their diet and lifestyle and treatments, and they're still seeing no treatment response, I know with certainty that this terrain factor is the primary obstacle. This is real. We know now that mental and emotional challenges can affect immune cell counts and activity.[76–80]

If I hit blocks during verbal inquiry, I will often order a few quantitative tests and use that hard data to introduce the topic more obliquely. Yes, there are quantitative tests that can shed light on a patient's mental and emotional health. On a very basic level, blood sugar has a significant impact on emotional wellbeing. Anxiety, depression, and bipolar conditions are very sensitive to the ups and downs of blood sugar.[81,82] Vitamin D_3 shows up as an influencer for this terrain factor, as well, with compromised levels manifesting as depression or seasonal affective disorder (SAD).[83] Sometimes these simple lab tests can be conversation starters. I might say, "You know, these ranges are associated with pretty extreme energy swings," or "a level this low typically triggers noticeable depression." Then I can simply ask how that issue has manifested for them. This opens the conversation a little more gently than hitting it head-on during our first encounter.

If I have a patient's epigenetic profile, I can also look for certain genetic SNPs (single-nucleotide polymorphisms) associated with

mental health challenges. This includes: MAO, BDNF, COMT, VDR and/or CYP2R1, ADRB2, and MTHFR. Some of these are associated with serious anxiety or rage. Others are associated with personalities that can easily get stuck in life.[84–87] Such conditions respond exceptionally well to low-dose psychotropics, intermittent fasting, meditation, and prayer. When I approach the patient with both a test result and a solution based in solid brain science, it suddenly lets them get curious about mental and emotional health from the entry points of epigenetics and brain health.

Similar to the relationship between VAE therapy and rhythm restoration, there is a circular relationship between VAE and mental health. If a patient has a major challenge in this terrain factor, it can result in lackluster treatment effects across the board. But as soon as the patient takes a small step toward addressing mental and emotional self-care, all other treatments can begin to take root, including mistletoe. Continuing a positive cycle, VAE therapy can further enhance mental health through its ability to enhance beta-endorphin levels.[88] This lesser-known effect of mistletoe may be the reason for a frequently reported side benefit: an enhanced sense of purpose and spiritual clarity.

Metabolic function and blood sugar balance

Choosing and embracing a diet that supports metabolic flexibility is a major key to cancer treatment success. We'll look at a few cancer-fighting dietary choices in chapter 9, but for now it's important to know that the body achieves metabolic flexibility when it no longer needs a steady flow of sugar to feel sane. In short, that means a low- or no-carb diet and eating at strategic times. This approach nourishes healthy cells while causing severe stress for cancer cells—making them more vulnerable to both conventional and integrative treatments.[89]

That said, testing begins with simple inquiry about a patient's dietary habits, then we progress to keeping a dietary journal or using a health and diet and macronutrient monitoring app like Cronometer or MyFitnessPal. These apps provide immediate feedback and help

patients discover, on their own, how much sugar they're actually consuming each day.

In terms of quantitative testing, we need to go beyond the patient's fasting blood glucose level. It's possible to simply hit that test on a good day. The HbA1C is much more accurate, as it provides a three-month average. Even then, a patient may be maintaining good blood sugar levels, but cranking out abnormal amounts of insulin to do so. Thus, it's important to check fasting insulin levels, too. It is possible to see a normal fasting blood glucose and a normal HbA1C, along with insulin in the teens, twenties, or higher. That insulin is a driver of cell growth, including cancer cells. It attaches as a ligand to IGF receptors and stimulates cellular replication.[90] If you see high insulin levels, it's wise to test IGF-1 as well.

In addition to blood sugar-oriented testing, the standard CMP and the Trifecta Labs are also key for evaluating metabolic function. The CMP gives me a picture of all those activities associated with metabolism and detoxing the byproducts of normal metabolism. The Trifecta Labs show me what kind of fuel the body is burning in its mitochondrial factories. It shows me whether the metabolic fires are burning cleanly or inefficiently.

Ultimately, metabolic challenges and blood sugar issues can render certain conventional treatments ineffective. This includes radiation, chemotherapy, PARP inhibitors, and other aromatase inhibitors. People who are metabolically flexible (consistently eating lower-carb) see more robust response from all their treatments, both conventional and integrative.[91] Lab tests focused on metabolism and blood sugar can be the motivation that helps patients embrace a cancer-fighting diet.

In my own practice, I've witnessed the power of establishing a foundation of metabolic flexibility and then combining that with VAE therapy. Lower carb intake creates great stress for cancer cells. That leaves the cancer more vulnerable to all treatments, including integrative therapies like mistletoe. In yet another circular relationship, we've also seen mistletoe help mitigate blood sugar and insulin production challenges in animal studies.[92,93] We're still learning which constituents

in mistletoe might be responsible for these effects, but it's yet another possible side benefit of VAE therapy.

Final Thoughts on Specialty Tests and Tumor Markers

There are literally hundreds of other lab tests that we can conduct for any patient. We list some of the more common ones in appendix F, and recommended laboratories are noted in the Resources Section. Physicians who want to explore more nuanced testing and learn how to respond effectively to lab findings, especially related to epigenetics, tumor markers, and cytotoxicity screening, should consider further education through the Physicians' Association for Anthroposophic Medicine (PAAM) or the *Metabolic Approach to Cancer, Mastermind Course* through DrNasha, Inc. (see Resources). Ultimately, it's the patient's condition and goals that guide the breadth and depth of testing strategies. When exploring more refined testing options, three good rules of thumb come to mind:

- Not every lab result is cause for concern. It's the practitioner's responsibility to shine light on whether a certain lab finding necessitates treatment action.
- Don't treat an epigenetic SNP unless it's expressing. For example, if a patient has a SNP indicating that they could run chronically low on a certain nutrient, always run an evaluation for that nutrient to confirm they are indeed deficient.
- Tumor markers are useful metrics. But they're not the be-all, end-all evaluation of the cancering process. The Trifecta Labs are often more prognostic than elevated tumor markers. Review all metrics within their larger context.

Ultimately, labs are incredibly impactful when they become tools to motivate empowering change, especially changes related to diet and lifestyle. Discussing significant lab results can be a positive tipping point moment in a patient's journey. It can be a gateway to much deeper personal discoveries. Always remember, we're not here to treat cancer. We're here to support the person and nurture their entire terrain.

PART 3:

HUMAN-CENTERED MEDICINE

"Still, as ambitious cancer researchers study soil as well as seed, one sees the beginnings of a new approach. It would return us to the true meaning of 'holistic': to take the body, the organism, its anatomy, its physiology—this infuriatingly intricate web—as a whole. Such an approach would help us understand the phenomenon in all its vexing diversity; it would help us understand when you have cancer and when cancer has you. It would encourage doctors to ask not just what you have but what you are."

—SIDDHARTHA MUKKHERJEE
("Cancer's Invasion Equation,"
The New Yorker, Sept. 11, 2017)